WELCOME TO

AHNS 2024 ANNUAL MEETING AT

MAY 15-16, 2024

COSM 2024

CHICAGO

FINAL PROGRAM

Held During the Combined Otolaryngology Spring Meetings

AHNS President: Robert Ferris, MD, PhD
Program Chair: Patrick Ha, MD
Program Co-Chairs: Sidharth Puram, MD, PhD, FACS and Nicole Schmitt, MD, FACS

THE RESEARCH AND EDUCATION FOUNDATION OF THE AMERICAN HEAD AND NECK SOCIETY

Dear AHNS members and attendees,

You make a difference in the lives of your patients every day. Each person you examine, diagnosis, treat and follow through their path as a patient receives the benefits of your education, experience and wisdom. Many whom you may never meet experience the impact of your research as you strive to harness scientific knowledge to human advantage. As you stand on the shoulders of those who preceded you, you mentor and teach the next generation of surgeon scientists.

The Research and Education Foundation of the AHNS is proud to play a role in the efforts of our members through funding research grants, career development awards and opportunities for underrepresented medical students to build our ranks. But there is more to be done, much more.

In 2018 the AHNS underwent a reorganization to better empower you – AHNS members. Known as AHNS 2.0, the intent is to foster the creative thinking of Section and Service Members to realize transformative initiatives that embody the mission of the society. It is the aim of the Foundation to support this important work – and we need your help to do so.

Our goal is to grow the corpus of the Foundation by 20%, to reach $6 million by 2027. We welcome donations of any amount and ask you to consider one of the following options:

CENTURION CLUB – Centurion Club members pledge $1,000 of support annually.
FIVE IN FIVE - 5 in 5 members pledge $5,000 of support annually for five years.
Gifts of any size can be made monthly, annually or as a one- time donation.

Please, make your gift today.
Together we make a difference.

TABLE OF CONTENTS

The AHNS gratefully acknowledges the following companies for educational grant support of the 2024 Annual Meeting:

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SAVE THE DATE!

AHNS Future Meeting Schedule

AHNS 2025 Annual Meeting at COSM
May 14-18, 2025 • New Orleans, Louisiana
Hyatt Regency New Orleans

AHNS 12th International Conference on Head and Neck Cancer
July 18-22, 2026 • Boston, Massachusetts

The American Head & Neck Society (AHNS)
11300 W. Olympic Blvd., Suite 600
Los Angeles, CA 90064
Phone: (310) 437-0559
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www.ahns.info

The American Head & Neck Society is managed by
BSC Management, Inc.
Phone: (310) 437-0555
Fax: (310) 437-0585
E-Mail: info@bscmanage.com
www.bscmanage.com

Official Language

The official language of the conference is English. Simultaneous translation will not be offered.

GENERAL INFORMATION

The American Head and Neck Society's 2024 Annual Meeting
May 15-16, 2024 • Hyatt Regency Chicago • 151 East Wacker Drive, Chicago, Illinois 60601

WiFi Access
Network: COSM2024   **|**   Password: COSM2024

COSM Registration Hours

Location: Riverside Exhibit Hall

Registration Onsite Dates and Times:

Tuesday, May 14	12:00 PM - 5:00 PM
Wednesday, May 15	6:30 AM - 5:00 PM
Thursday, May 16	6:30 AM - 4:00 PM
Friday, May 17	6:30 AM - 4:00 PM
Saturday, May 18	6:30 AM - 4:00 PM
Sunday, May 19	7:00 AM - 10:00 AM

COSM Exhibit Hall

Location: Riverside Exhibit Hall

Exhibit Dates and Times:

Thursday, May 16	9:00 AM - 4:00 PM
Friday, May 17	9:00 AM - 4:00 PM
Saturday, May 18	9:00 AM - 4:00 PM

Tabletop Exhibits

Location: Grand Ballroom Foyer

Tabletop Exhibits Dates and Times:

Wednesday, May 15	9:00 AM - 4:00 PM
Sunday, May 19	9:00 AM - 12:00 PM

Coffee breaks and lunch will be served in the Exhibit Hall (Wednesday and Sunday excluded)

Dates and Times:

Wednesday, May 15	9:45 AM – 10:15 AM
	2:45 PM – 3:15 PM
Thursday, May 16	9:45 AM – 10:15 AM
	2:45 PM – 3:15 PM
Friday, May 17	9:45 AM – 10:15 AM
	2:45 PM – 3:15 PM
Saturday, May 18	9:45 AM – 10:15 AM
	2:45 PM – 3:15 PM
Sunday, May 19	9:45 AM – 10:15 AM

Questions? Comments?
Join the conversation behind the scenes …
X: AHNS2024   **Follow us** @AHNSinfo

Speaker Ready Room

Location: Grand Group Office

Dates and Times:

Tuesday, May 14	2:00 PM - 8:00 PM
Wednesday, May 15	6:30 AM - 6:00 PM
Thursday, May 16	6:30 AM - 6:00 PM
Friday, May 17	6:30 AM - 6:00 PM
Saturday, May 18	6:30 AM - 6:00 PM
Sunday, May 19	6:30 AM - 10:00 AM

AHNS Centurion Club Lounge

Location: Skyway 260

Dates and Times:

Wednesday, May 15	7:00 AM - 5:00 PM
Thursday, May 16	7:00 AM - 5:00 PM

Poster Hall

All posters are displayed in Riverside Exhibit Hall
View/search all posters via the App or COSM's
Poster Archive via www.cosm.md.

1st Combined Poster Session: AAFPRS, AHNS, ARS

Dates and Times:

Wednesday, May 15	1:00 PM - 7:00 PM
Thursday, May 16	9:00 AM - 7:00 PM

2nd Combined Poster Session: ABEA, ALA, ANS, AOS, ASPO, TRIO

Dates and Times:

Friday, May 17	9:00 AM - 7:00 PM
Saturday, May 18	9:00 AM - 6:00 PM

AHNS 2024 Annual Meeting Educational Objectives

1. Assess and apply therapeutic options for the head and neck, salivary gland, and thyroid cancer patient in a multidisciplinary environment, including:
   a. Role of palliative surgery in head and neck cancer
   b. De-escalation of patients with low risk HPV+ oropharynx squamous cell carcinoma
   c. Consideration related to reconstruction in specialized populations including children, older adults, and in patients with a vessel-depleted neck
   d. Molecular markers, conservative management, and targeted therapy for thyroid cancer
   e. New technologies in head and neck cancer including augmented reality, intraoperative margin assessment, advancement in robotics, artificial intelligence, and parathyroid imaging
   f. Understanding state-of-the-art management for rare tumors including adenoid cystic carcinoma, Merkel cell carcinoma, nasopharyngeal cancer, and esthesioneuroblastoma
   g. Management of salivary gland tumors and surgical decision-making nuances
   h. Surgical approaches to mandibular reconstruction using 3D printing, skull base reconstruction advances, and transoral thyroidectomy
   i. Progress and opportunities in the management of pre-malignant lesions
   j. Management of complex skull base tumors and surgical decision-making
2. Assess emerging research that lead to better understanding of the pathogenesis of head and neck cancer and its treatment, including:
   a. New breakthroughs for disease detection, pre-treatment staging, and assessment of treatment response.
   b. New forms of targeted therapy for head and neck cancer – current and emerging agents
   c. The importance of neoadjuvant and adjuvant immunotherapy trials and their evolving role in head and neck oncology and its management
   d. The genomic landscape of head and neck cancer including what is known and future directions
   e. Key clinical trials in head and neck cancer that are ongoing as well as new trials likely to emerge
   f. Evolving role of ctDNA in the management of HPV+ oropharyngeal cancer
3. Assess and apply the process, outcomes, and quality of delivering care to head and neck cancer patients, including:
   a. Rational use of computer-aided, virtual surgical planning for mandibular reconstruction
   b. Opportunities for improving disparities in head and neck cancer including clinical trial participation, patient access, and utilizing informatics to advance equity
   c. Understanding the focus practice designation for complex thyroid and parathyroid surgery
   d. Incorporation of survivorship into the management of head and neck cancer patients by assessing critical evidence related to data drive surveillance, quality of life challenges, integrative therapy (acupuncture, cannabis), and timing and involvement of speech and language pathologist
   e. How cost-effectiveness is important to consider in considering novel treatments
4. Recognize the vital role of nurses, speech language pathologists, audiologists, nutritionists, social workers, pain specialists, mental health practitioners, physical therapists, dental oncologists in achieving maximal functional outcomes and increase interdisciplinary cooperation.
   a. Use of complementary services to improve physical and emotional well-being
   b. Use of NP/PA led survivorship clinics that allow more time for patient counseling

GENERAL INFORMATION

AHNS 2024 CME Credit Claim Process

After the meeting, an email will be sent to attendees with a link to the on-line survey and claim form.

For any questions, please contact rebecca@ahns.info.

American Head & Neck Society Statement of Professionalism and Ethics

The American Head and Neck Society is committed to promulgating and promoting professionalism and ethical behavior in its membership. As members, we value the trust placed in us by our patients, colleagues and society, and therefore willingly pledge to uphold the ethical and professional principles and virtues of medicine as outlined below.

We have a fundamental and sacred duty to our patients. Therefore, we will:
- Recognize that the welfare of our patients is the paramount priority.
- Serve as advisors to our patients to help them navigate complex medical decisions.
- Discuss the risks, benefits and alternatives of appropriate therapeutic options.
- Be respectful of our patients' viewpoints and beliefs.
- Support our patients physically, emotionally and spiritually.
- Care for and support our patients at the end of life.
- Offer support and care to our patients' families.
- Strive to enhance and maximize our clinical, surgical and interpersonal competence.
- Maintain a caring and respectful demeanor.
- Offer care without regard to gender, age, religion, sexual orientation, socioeconomic status or ethnicity.

We have a responsibility to our colleagues and teachers. Therefore, we will:
- Willingly acknowledge our skills and expertise to those wishing to learn.
- Honor our teachers for devoting their time and energy on our behalf.
- Assist our colleagues, technically, intellectually, emotionally and spiritually.
- Respect our colleagues from other disciplines and practice multidisciplinary care.
- Provide legal opinions based only on evidenced-based practice and standards of care.

We also have an obligation to the faith entrusted in us by society. Therefore, we will:
- Perform self regulation by developing and adhering to professional, ethical and evidence-based practice standards.
- Disclose and limit conflict of interest.
- Practice medicine honestly, compassionately and confidentially.
- Educate the public within the bounds of our expertise.

ABOUT THE AMERICAN HEAD AND NECK SOCIETY

History of the Society

On May 13, 1998, The American Head and Neck Society (AHNS) became the single largest organization in North America for the advancement of research and education in head and neck oncology. The merger of two societies, the American Society for Head and Neck Surgery and the Society of Head and Neck Surgeons, formed the American Head and Neck Society.

The contributions made by the two societies forming the AHNS are significant in the history of surgery in the United States. Dr. Hayes Martin conceived the Society of Head and Neck Surgeons in 1954, a surgeon considered by many to be the "father of modern head and neck tumor surgery." The purpose of the society was to exchange and advance the scientific knowledge relevant to the surgery of head and neck tumors (exclusive of brain surgery) with an emphasis on cancer of the head and neck. Two years later, The American Society for Head and Neck Surgery was organized with the goal to "facilitate and advance knowledge relevant to surgical treatment of diseases of the head and neck, including reconstruction and rehabilitation; promote advancement of the highest professional and ethical standards as they pertain to the practice of major head and neck surgery; and to honor those who have made major contributions in the field of head and neck surgery, or have aided in its advancement".

The new Society remains dedicated to the common goals of its parental organizations.

OUR MISSION

The mission of AHNS is to advance education, research, quality of care, and equity for the head and neck oncology patient and care team.

THE VALUES THAT WE HAVE UNANIMITY ARE:

- » Excellence
- » Innovation
- » Inclusion
- » Community

THE GOALS OF THIS SOCIETY ARE TO PROMOTE OPTIMAL CARE FOR PATIENTS WITH HEAD AND NECK NEOPLASMS BY:

- » Being the premier educational resource for head and neck surgery and oncology
- » Being the leader in the promotion of head and neck cancer research
- » Supporting a diverse and equitable population of engaged members
- » Having a sufficient organizational capacity to achieve the Mission.

WHY JOIN AHNS?

The American Head and Neck Society is the single largest organization in North America for the advancement of research and education in head and neck oncology - www.ahns.info.

BENEFITS OF AHNS MEMBERSHIP

- » Annual online subscription to JAMA Otolaryngology-Head and Neck Surgery
- » Discounts on Annual Meeting registration fees
- » Ability to create a Public Profile in the "Find-a-Physician Directory" accessible by patients and referring physicians
- » Opportunities to partake in educational offerings, including those planned by the society and those co-sponsored by the society
- » Access to the AHNS subspecialty Section online forums at no additional cost
- » Ability to apply for research grant awards offered yearly
- » Opportunity to post regional meetings and courses on the AHNS Related Meetings webpage
- » Ability to view the AHNS Job Board
- » Cutting-edge education and professional development programs

AHNS PRESIDENT

ROBERT L. FERRIS, MD, PHD

Robert L. Ferris, MD, PhD is Hillman Professor of Oncology and Director of the UPMC Hillman Cancer Center, Senior Vice President for Oncology Programs, Associate Senior Vice Chancellor for Cancer Research, and Professor of Otolaryngology, of Immunology, and of Radiation Oncology at the University of Pittsburgh.

As a head and neck surgical oncologist and translational tumor immunologist, his lab performs neoadjuvant "window" trials developing novel immune-oncology agents, combinations and biomarkers. Dr. Ferris's NIH-funded laboratory is focused on reversal of immune escape and immunotherapy using monoclonal antibodies and vaccines, leading to the first randomized phase II-III trials of head and cancer immunotherapy in the world. He was founding director of the Hillman Tumor Microenvironment Center, launched in 2012. He is a Principal Investigator of the University of Pittsburgh Specialized Program of Research Excellence (SPORE) grant for translational head and neck research and three R01 grants focused on T cell receptor dynamics and immune phenotypes regulating response to immunotherapy.

Dr. Ferris has published >400 peer-reviewed scientific and clinical publications that have been cited >52,000 times. He was lead investigator of several practice-changing, prospective randomized trials, including Checkmate-141 published in NEJM which led to the FDA approval of Nivolumab for head and neck cancer, ECOG 3311, testing radiation dose-deintensification after transoral robotic surgery (TORS) for HPV+ oropharynx cancer, which was incorporated into the latest NCCN guidelines. He currently leads ECOG-ACRIN 3132, using p53 mutational testing in HPV-negative cancer, to predict response to radiation versus chemoradiation.

Dr. Ferris has served on the Editorial Boards of JNCI, JCO, Journal of Immunotherapy of Cancer, Clinical Cancer Research, Cancer, and Cancer Immunology Research. He is Editor in Chief of Oral Oncology. He recently completed a 6-year term co-chairing the NCI Steering Committee for Head and Neck Cancer, serves as a standing member of NCI Committee A reviewing Cancer Centers and previously chaired the NIH Tumor Microenvironment study section. He has co-founded two early phase immuno-oncology companies, in therapeutics discovery and development and in cellular therapeutic strategies for solid and liquid tumors.

He is married to Laura Ferris, MD, PhD, and is proud of their 3 children, Rachel (22), Anna (20) and Adam (17).

2024 PROGRAM CHAIR

PATRICK HA, MD

Patrick Ha, MD is a Professor and the Chief of Head and Neck Oncologic Surgery in the Department of Otolaryngology – Head and Neck Surgery (OHNS) at the University of California, San Francisco. He also holds the Irwin Mark Jacobs and Joan Klein Jacobs Distinguished Professorship in Head and Neck Surgery. In addition to his clinical and research work, he serves as the Medical Director for the UCSF Mission Bay Adult Services. His current area of research is focused on the molecular changes occurring in salivary gland adenoid cystic carcinoma, and he has held multiple NIH and foundation grants towards this aim. In addition, he serves as Editor in Chief of the journal Head and Neck. He has won many teaching awards and enjoys mentoring students and residents.

2024 PROGRAM CO-CHAIRS

DR. SID PURAM, MD, PHD, FACS

Dr. Sid Puram is Chief of Head and Neck Surgery at Washington University in St. Louis, Director of the Head and Neck Tumor Center at Siteman, and Associate Professor of Otolaryngology and Genetics. Dr. Puram graduated from MIT, followed by an MD-PhD at Harvard Medical School. He went on to residency at Harvard/Massachusetts Eye and Ear with an in-folded postdoctoral fellowship with Drs. Bradley Bernstein and Aviv Regev at the MIT Broad Institute/Massachusetts General. Thereafter, he completed a surgical oncology/microvascular free flap fellowship at the James Cancer Center/Ohio State University. Currently, Dr. Puram maintains a clinical practice focused on head and neck oncologic surgery, including transoral robotic surgery, open skull base approaches, and microvascular reconstruction. His multiple R01-funded group has been a leader in genetic, transcriptional, and epigenetic heterogeneity in head and neck cancer and its relationship to cancer phenotypes including metastasis and treatment response, with pioneering work in single cell sequencing. He has published over 160 peer-reviewed articles, including studies in Nature, Cell, and Nature Genetics, and delivered over 40 invited national and international lectures. He is Co-Chair of the NCI Clinical Proteomic Tumor Analysis Consortium Thyroid Working Group, Co-Chair of the NRG Oncology Head and Neck Translational Committee, Chair of the Microvascular Committee for the American Academy of Otolaryngology-Head and Neck Surgery, and an active member of the NCI Recurrent/Metastatic Task Force and NRG Head and Neck Core Committee.

NICOLE SCHMITT, MD, FACS

Dr. Schmitt is an Associate Professor of Otolaryngology – Head and Neck Surgery at Emory University. She obtained her medical degree at Washington University, then completed residency in Otolaryngology with a research fellowship at the University of Washington. Dr. Schmitt then completed an ablative and research fellowship in head and neck surgery at the University of Pittsburgh. After five years with joint appointments at Johns Hopkins University and the National Institutes of Health, Dr. Schmitt was then recruited to Emory to serve as Co-Director for Translational Research in the Head and Neck Program at Winship Cancer Institute. Dr. Schmitt cares for head and neck cancer patients across the state of Georgia and beyond, with a focus on salivary tumors. Her funded research spans from basic science to clinical trials, focusing on ototoxic hearing loss, drug repurposing, cancer chemoprevention, geriatric head and neck oncology, and novel therapeutic combinations to enhance the anti-tumor immune response. She currently serves as Principal Investigator on several clinical trials for head and neck cancer, including a first-in-human trial of the IAP antagonist tolinapant combined with radiation in cisplatin-ineligible patients. Dr. Schmitt is also passionate about inspiring the next generation of otolaryngologists, serving as the Director of Medical Student Research in the Department of Otolaryngology at Emory. Dr. Schmitt serves on the head and neck committees of NRG Oncology and ECOG-ACRIN. She is also an Associate Editor for Head and Neck.

HAYES MARTIN BIOGRAPHY

HAYES MARTIN, MD

Hayes Martin was born in Dayton, a small town in north central Iowa. He attended the University of Iowa at Iowa Falls before being accepted to the medical school in 1913 on the same campus, finishing 4 years later in a class of 20.

World War I began in April 1917 while Hayes was in his final year of medical school. Many of his classmates at the medical school were in the Army ROTC units; however, Dr. Martin opted for the Navy, which he joined on the day America entered the war. He traveled to Europe on the USS Arkansas and was assigned to his permanent duty station at the U.S. Navy Air Station, La Trinite Sur Mer, France – a small seaside village on the southern coast of Brittany. The purpose of this base was antisubmarine warfare using blimps and kite balloons. Dr. Martin was made commanding officer of the air station for a brief period of time when the line officer in charge had become ill; it was a unique position for a medical officer in the Navy to take command during wartime.

After the war, Dr. Martin returned to the U.S and sought out an internship at the old Poly Clinic Hospital in New York City, which was temporarily made into a Veteran's Administration hospital. Part of his internship was spent at Bellevue in the fourth surgical division, where he felt he would have the best possible training in general surgery. The chief of the second division was John A. Hartwell, MD, the distinguished surgeon memorialized by the Fellow's Room in the library of the New York Academy of Medicine. Dr. Hartwell suggested that Dr. Martin go to Memorial Hospital to learn about cancer.

Dr. Martin received an internship at Memorial in the summer of 1922 and stayed on as a resident until 1923. He then had two years at the second surgical service at Bellevue, where he operated to his heart's content and got the surgical education he so strongly desired. Once he finished his residency, Dr. Martin returned to Memorial where he joined as clinical assistant surgeon on the staff.

Dr. Martin made the use of aspiration biopsy on all solid tumors popular throughout Memorial. Now, this procedure is done throughout the world. Dr. Martin co-authored the first report on the subject published in the Annals of Surgery. Numerous other articles followed, including Dr. Martin's two most famous publications, "Cancer of the Head and Neck," published in two issues of the Journal of the American Medical Association in 1948, and "Neck Dissection," appearing in Cancer in 1951. These two papers were so extensively requested that the American Cancer Society made reprints by the thousands available to those who requested them as many as 20 years after publication. Dr. Martin's bibliography encompasses more than 160 articles.

In 1934, Dr. Martin was appointed Chief of the Head and Neck Service at Memorial Hospital. It wasn't until 1940 that surgery began to take over as the treatment of choice for the majority of cancers of the head and neck. In that year, the beginnings of improved anesthesia permitted advances in surgery. Later, during World War II, antibiotics became available and surgery began to dominate much of head and neck cancer management. Dr. Martin wrote extensively on many subjects, most within the realm of head and neck surgery. His ideal was to be the complete head and neck surgeon and he treated a wide variety of head and neck abnormalities. His book, Surgery of the Head and Neck Tumors, was published in 1957.

Dr. Martin retired from active practice in 1957 at the age of 65. He performed his last operation at Memorial Hospital, assisted by Dr. Elliot Strong, in October 1959, but continued to see patients in his office until he passed away in 1977.

Past Hayes Martin Lecturers

Ted Teknos, MD (2023)
Gregory Weinstein, MD (2022)
James Netterville, MD (2021)
Admiral William H. McRaven (2019)
Adalsteinn D. Brown, PhD (2018)
Mark K. Wax, MD (2017)
Ashok R. Shaha, MD (2016)
John A. Ridge, MD, PhD (2015)
Patrick J. Gullane, MD (2014)
Jonas T. Johnson, MD (2013)
Gregory T. Wolf, MD (2012)
Randal S. Weber, MD (2011)
Adel El-Naggar, MD (2010)
Charles W. Cummings, MD (2009)
Waun Ki Hong, MD (2008)
Jesus E. Medina, MD (2007)
Keith S. Heller, MD (2006)

Richard K. Reznick, MD, MEd (2005)
Christopher J. O'Brien, MD (2004)
Michael Johns, MD (2003)
Eugene Myers, MD (2002)
William Wei, MS (2001)
Robert M. Byers, MD (2000)
Jean-Louis H. LeFebvre, MD (1999)
Jatin P. Shah, MD (1998)
Blake Cady, MD (1997)
Joseph N. Attie, MD (1996)
Helmuth Goepfert, MD (1995)
John G. Batsakis, MD (1994)
Ronald H. Spiro, MD (1993)
John M. Lore, MD (1992)
Ian Thomas Jackson, MD (1991)
Alando J. Ballantyne, MD (1990)
George A. Sisson, MD (1989)

M.J. Jurkiewicz, MD (1988)
Elliot W. Strong, MD (1987)
Donald P. Shedd, MD (1986)
Alfred S. Ketcham, MD (1985)
William A. Maddox, MD (1984)
John J. Conley, MD (1983)
Milton Edgerton, MD (1982)
Richard H. Jesse, MD 1981)
Condict Moore, MD (1980)
Edward F. Scanlon, MD (1979)
Harvey W. Baker, MD (1978)
Harry W. Southwick, MD (1977)
Edgar L. Frazell, MD (1976)
Charles C. Harrold, MD (1975)
Arthur G. James, MD (1974)
Oliver H. Beahrs, MD (1973)
William S. MacComb, MD (1972)

HAYES MARTIN LECTURER

Thursday, May 16, 2024 8:00 AM – 9:00 AM | Grand Ballroom EF

DOUGLAS R. LOWY, M.D

Douglas R. Lowy, M.D., is Chief of the Laboratory of Cellular Oncology and, since 2010, has also served as Principal Deputy Director of the National Cancer Institute (NCI). Dr. Lowy received his medical degree from New York University School of Medicine in 1968, and trained in internal medicine at Stanford University and dermatology at Yale University. He has directed a research laboratory at NCI since 1975, after receiving training as a Research Associate in the National Institute of Allergy and Infectious Diseases. Dr. Lowy is a member of the National Academy of Sciences (NAS) and of the Institute of Medicine of the NAS. For his research with John Schiller on technology that enabled the preventive HPV vaccines, they have jointly received numerous honors, including the 2007 Federal Employee of the Year Service to America Medal from the Partnership for Public Service, the 2011 Albert B. Sabin Gold Medal Award, the 2012 National Medal of Technology & Innovation (awarded in 2014), the 2018 Szent-Györgyi prize and the 2017 Lasker-DeBakey Clinical Medical Research Award, the country's most prestigious honor for biomedical research. Dr. Lowy has also received the National Medal of Honor for Basic Research from the American Cancer Society and is a fellow of the AACR Academy.

JOHN J. CONLEY BIOGRAPHY

Although he looked and sounded like an English nobleman, Dr. John Conley was born in Carnegie, Pennsylvania, a small steel mill town just outside of Pittsburgh. He graduated from the University of Pittsburgh and later its school of medicine. He interned at Mercy Hospital in Pittsburgh. During that year, the nuns who ran the hospital suggested that Dr. Conley take a residency in cardiology and come back to Mercy as their cardiologist.

He went to Kings County Hospital in Brooklyn, a very busy city hospital with a huge patient population. Shortly after he began his training, he had an arrhythmia diagnosed as paroxysmal atrial tachycardia. Little was known about this benign condition at that time. Dr. Conley was told that cardiology was too stressful and that he should go into an easier, less-stressful field with better working hours, like ENT. He did an otolaryngology residency at Kings County Hospital. This was followed by four years of military service during World War II, which included experience in otolaryngology and plastic and reconstructive and maxillofacial surgery in the U.S. Army Medical Corps, both in this country and in the South Pacific theater. Exposure to the construction of war wounds would prove invaluable to him later on in applying these principles to reconstruction following ablative head and neck surgery.

Dr. Conley returned to New York City after the war. He became an assistant and then an associate of Dr. George T. Pack, a technically superb general oncologic surgeon at Memorial Hospital who taught Dr. Conley major ablative surgery of the head and neck. They worked day and night catching up with the backlog of surgery that was neglected during the war years. The combination of his training in otolaryngology, the exposure to ablative surgery, and the World War II experience in reconstructive surgery set the stage for Dr. Conley to evolve his unique approach to head and neck surgery.

Ironically, despite the admonition of the cardiologists about hard work, Dr. Conley did a prodigious amount of major head and neck reconstructive surgery. This proved to be more than ample to provide training to many fellows. His commitment to education is further attested to by the position he held for many years as Clinical Professor of Otolaryngology at the College of Physicians and Surgeons at Columbia University. He loved his appointment at Columbia and particularly his involvement in teaching the residents.

Dr. Conley's vast surgical experience, together with active research interests, led to the authorship of almost 300 contributions to the scientific literature, and eight books. As a result of his productivity and rhetorical eloquence, he was very much in demand as a speaker in this country and abroad. He gave many prestigious eponymous lectures in our field and received many awards for his work, including the Philip H. Hench Award as the Distinguished Alumnus of the University of Pittsburgh School of Medicine, and the DeRoaldes and Newcomb Awards of the American Laryngological Association.

Dr. Conley's contributions to the scientific literature, many technical innovations and surgical experience placed him in the position to receive many honors and important leadership positions, such as President of the American Academy of Otolaryngology and Ophthalmology, member of the Board of Governors of the American College of Surgeons, founding member of the Society of Head and Neck Surgeons, and founding member and first President of the American Society for Head and Neck Surgery. During those years, Dr. Conley used, to the great benefit of us all, his wisdom and diplomacy in carrying out such high-level responsibilities.

Past John J. Conley Lecturers

Tim Chan, MD, PhD (2023)
Robert L. Ferris, MD, PhD (2022)
Rebekah Gee, MD (2021)
Michael Porter, MBA, PhD (2019)
Brian O'Sullivan, MD, FRCPC, FRCPI, FASTRO (2018)
Johannes Fagan, MBChB, MMed, FCORL (2017)
Robert S. Bell, CM, MSc, MD, FRCSC (2016)
Jonathan Irish, MD, MSc, FRCSC (2015)
Antonio Fojo, MD, PhD (2014)
Patrick J. Gullane, MB, FRCSC, FRACS (2013)
Julie A. Freischlag, MD (2012)

Benjamin S. Carson, Sr., MD (2011)
Robert L. Comis, MD (2010)
James D. Smith, MD (2009)
Carolyn Dresler, MD (2008)
Kenneth I. Shine, MD (2007)
John Stone, MD, MACP (2006)
James F. Battey Jr., MD (2005)
David C. Leach, MD (2004)
Jonathan D. Moreno, MD (2003)
Rabbi David Saperstein (2002)
Edward Hughes, MD (2001)

JOHN J. CONLEY LECTURE

Wednesday, May 15, 2024 10:15 AM – 11:15 AM | Grand Ballroom EF

MARTY MAKARY, MD, MPH, FACS

Dr. Marty Makary is professor of surgery and chief of Islet Transplant Surgery at Johns Hopkins.

His research focuses on the appropriateness of care, administrative waste in health care, and the affordability of health insurance for vulnerable populations.

Dr. Makary is a leading voice for physicians, writing in the Wall Street Journal, the New York Times, and the Washington Post, and was the first editor-in-chief of MedPage Today. He has published over 250 peer-reviewed scientific articles on topics ranging from public health to surgical technique. He served in leadership at the World Health Organization and is the recipient of the Nobility in Science Award from the National Pancreas Foundation.

His 1st New York Times bestseller, called Unaccountable, was turned into the TV series, The Resident.

His 2nd New York Times bestselling book, *The Price We Pay*, is the recipient of the 2020 Business Book of the Year Award and sold nearly a quarter-million copies. For his work on this topic, Dr. Makary was invited to be one of the architects of the recent federal hospital price transparency rule, which requires every U.S. hospital to post cash prices for common shoppable services and requires insurance companies to disclose their secret discounts.

His newest book, called BLIND SPOTS, comes out in 3 months and is already a bestseller based on pre-orders. His talk today will cover some of the research in his new book about the blind spots of modern medicine.

Dr. Makary has been a visiting professor at over 25 medical schools and is a member of the National Academy of Medicine. He is a graduate of Jefferson Medical College and the Harvard School of Public Health. He completed a surgical residency at Georgetown and fellowship training in surgical oncology at Johns Hopkins.

JATIN P. SHAH BIOGRAPHY

Professor Jatin P. Shah graduated from the Medical College of Maharaja Sayajirao University in Baroda, India, where he received his basic training in General Surgery. He completed a Fellowship in Surgical Oncology and Head and Neck Surgery at Memorial Sloan Kettering Cancer Center, (MSKCC) and joined its full-time faculty in 1975.He was Chief of the Head and Neck Service and Leader of the Head and Neck Disease Management Team at MSKCC for 23 years. He is Professor of Surgery at the Weil Medical College of Cornell University and holds The Elliott W. Strong Chair in Head and Neck Oncology at Memorial Sloan-Kettering Cancer Center in New York City.

Dr Shah is a national and international leader in the field of Head and Neck Surgery, having served as President of The New York Cancer Society, The New York Head and Neck Society, The Society of Head and Neck Surgeons, The North American Skull Base Society and the International Academy of Oral Oncology. He is Founder of The International Federation of Head and Neck Oncologic Societies, (IFHNOS) and serves as it's Chief Executive Officer (CEO) . He was Chairman of the AJCC task force on Head and Neck for 20 years, and serves on the Head and Neck and Thyroid committees of the NCCN. He has served in varying capacities for The American Board of Surgery and The American College of Surgeons.

Professor Shah has been the recipient of numerous awards from various parts of the world, including Honorary Fellowships and Doctorates from the UK, Scotland, Ireland, Belgium, Greece, Australia and India. He is the recipient of the Blokhin Gold medal, and Pirogov Medal from Russia, the Gunnar Holmgren medal from Sweden, and the "Ellis Island Medal of Honor" from the United States. He was named the Most Distinguished Physician in the USA by the American Association of Physicians from India in 2011, and received the Life Time Achievement award from the Global Association of Physicians of Indian Origin. He has been listed in the "Best Doctors in America" directories 60 times for the past two decades. Dr. Shah is also an honorary member of several head and neck societies in Europe, Asia, Australia, Africa and South America.

He serves on the Editorial and Review Boards of 18 scientific journals and has published over 650 peer-reviewed articles, which have been cited over 60,000 times according to Google scholar. His h index is 142. In addition he has published, 73 book chapters and 14 books. His textbook of Head and Neck Surgery and Oncology, now in its 5th Edition, has won numerous prizes for the best published book in Otolaryngology-Head and Neck Surgery. He developed and lead the "IFHNOS World Tour Program", a global CME program in Head and Neck Surgery and Oncology, offered in 26 countries over the last six years. He has established the Global On Line Fellowship (GOLF) program in Head and Neck Surgery and oncology in collaboration with IFHNOS and MSKCC, and has also initiated an International fellowship program in Clinical surgery at various head and neck centers around the world.

As a physician, scientist and educator , Dr. Shah is a much sought after speaker who has delivered over 1,800 scientific presentations including, 80 eponymous lectures and keynote addresses, and visiting professorships in the United States, Canada, United Kingdom, Scotland, Sweden, Belgium, Netherlands, Germany, Italy, Spain, Poland, Czech Republic, Estonia, Russia, Ukraine, Belarus, Armenia, Croatia, Albania, Romania, Greece, Turkey, Egypt, UAE, Saudi Arabia, South Africa, India, Pakistan, China, South Korea, Japan, Hong Kong, Taiwan, Singapore, Malaysia, Thailand, Indonesia, Philippines, Australia, New Zealand, Argentina, Brazil, Chile, Peru, Ecuador, Colombia, Venezuela, Panama, and Mexico.

In recognition of his outstanding contributions and international leadership in Head and Neck Surgery, Memorial Sloan Kettering Cancer Center, has established The "Jatin Shah Chair in Head and Neck Surgery and Oncology" and the "Jatin Shah Annual Lectureship". The International Federation of Head and Neck Oncologic Societies has established "The Jatin Shah Lecture" at its world congresses, and the American Head and Neck Society has established the "Jatin Shah Symposium" at its annual meeting.

JATIN P. SHAH SYMPOSIUM: GENOMIC LANDSCAPE OF HNSCC: WHERE WE ARE AND WHERE WE ARE GOING

Thursday, May 16, 2024 | 10:15 AM – 12:00 PM | Grand Hall IJ

Moderator: Richard Wong, MD, FACS

A series of presentations will describe the genomic, transcriptomic, proteomic, immune and microbial landscapes and heterogeneity of head and neck squamous cell carcinoma. Recent discoveries in these topics and the clinical implications of new findings will be emphasized, with presentation of an original abstract as well.

At the conclusion of this session participants will be able to:

- Demonstrate an understanding of the genomic, transcriptomic, proteomic, immunologic, and microbial landscapes as well as tumor heterogeneity in head and neck squamous cell carcinoma.
- Recognize the impact of these various landscapes on the development of novel biomarkers for head and neck squamous cell carcinoma.
- Develop an understanding of how multi-omics can be deconvoluted to impact clinical decision making and generate novel therapies for head and neck cancer.

1. Introduction – *Richard Wong, MD, FACS*
2. Mutational Landscape and Dynamic Tumor DNA Biomarkers in Head and Neck Squamous Cell Carcinoma – *Nishant Agrawal, MD, FACS*
3. Going Down the Rabbit Hole: Tumor Heterogeneity in Head and Neck Cancer – *Sidharth Puram, MD, PhD, FACS*
4. Proteomics in Head and Neck Cancer: Lessons Learned and Current Directions – *Ben Major, PhD*
5. Immune Landscape of Head and Neck Cancer – *Nicole Schmitt, MD*
6. Association of Novel Tumor-Immune Microenvironment Measurements with Recurrence Outcomes in Head and Neck Cancer Patients Receiving Definitive Organ Preservation Therapy – *William J. Benjamin, MPH*
7. New Directions in Microbiome Research Across Oncology - *Susan Bullman, PhD*
8. Transcriptomic Landscape of Head and Neck Cancer – *Neil Hayes, MD, MPH, MS*
9. Q&A

PRESIDENTIAL CITATIONS

BARBARA BURTNESS, MD

Yale Cancer Center
New Haven, CT

Dr. Barbara Burtness is a medical oncologist whose research and practice focus on cancers of the head and neck. Dr. Burtness is a graduate of Bryn Mawr College and the SUNY Stony Brook School of Medicine. She trained in internal medicine at Yale-New Haven Hospital and in Medical Oncology at Memorial-Sloan Kettering Cancer Center. She is currently Anthony N. Brady Professor of Medicine at the Yale University School of Medicine and Chief Translational Research Officer, Associate Director of Translational Research, Co-Leader of the Developmental Therapeutics Program and Division Chief, Head and Neck/Sarcoma Oncology at Yale Cancer Center. She is Director of the Yale Specialized Program of Research Excellence in Overcoming Treatment Resistance in Head and Neck Cancer. As chair of the ECOG-ACRIN Head and Neck Cancer Therapeutics Committee, she has led a program of cooperative group trials that pioneered incorporation of targeted therapy, treatment deintensification for HPV-associated cancers, molecular selection and novel treatment paradigms to improve the survival and functional outcomes of patients with head and neck cancer. She co-chaired the National Cancer Institute Clinical Trials Planning Meeting on TP53-mutated head and neck cancer, is a member of the NCI Head and Neck Steering Committee, is a standing member of NCI the Institutional Training and Education Study Section (Subcommittee F), and co-chair of the Society for Immunotherapy of Cancer Head and Neck Guidelines Committee. She chairs the ECOG-ACRIN Task Force for Advancement of Women and previously served as Yale Cancer Center Interim Associate Director for Diversity, Equity and Inclusion. Dr. Burtness edits the text *Molecular Determinants of Head and Neck Cancer* and has authored or co-authored over 250 publications. She has conducted numerous phase I–III investigator-initiated trials, and led the phase III trial that established PD-1 inhibition as first-line standard of care for recurrent or metastatic head and neck cancer. Dr. Burtness' laboratory studies aurora kinase signaling in head and neck cancer, leveraging mechanistic insights to develop synergistic combinations, funded by NIDCR, the DOD, and Stand Up to Cancer.

PRESIDENTIAL CITATIONS

DR. DAVID W. EISELE, MD

Dr. David W. Eisele is the Andelot Professor and Director of the Department of Otolaryngology – Head and Neck Surgery at Johns Hopkins University School of Medicine in Baltimore, Maryland.

Dr. Eisele attended Dartmouth College, where he was a member of the Sigma Alpha Epsilon fraternity. He graduated from Cornell University Medical College and completed residency training in otolaryngology – head and neck surgery at the University of Washington. Following his residency training in 1988, Dr. Eisele joined the faculty at Johns Hopkins University School of Medicine where he eventually became Professor of Otolaryngology, Professor of Oncology, and Professor of Anesthesiology and Critical Care Medicine. He was the founding Director of the Johns Hopkins Head and Neck Cancer Center and served as Chief of the Division of Head and Neck Surgery.

In 2001, Dr. Eisele joined the faculty at the University of California, San Francisco as Professor and Chairman of the Department of Otolaryngology - Head and Neck Surgery. At UCSF he was the Irwin Mark Jacobs and Joan Klein Jacobs Endowed Chair in Head and Neck Cancer and directed the Head and Neck Oncology Program at the UCSF Comprehensive Cancer Center. He also served as President of the UCSF Medical Staff. In 2102, he returned to Johns Hopkins in his present role.

Dr. Eisele is a past President of the American Board of Otolaryngology- Head and Neck Surgery and a former member of the NCCN Head and Neck Cancer Panel. He has served as a member of the Residency Review Committee for Otolaryngology, Chair of the Advisory Council for Otolaryngology - Head and Neck Surgery for the American College of Surgeons, President of the American Head and Neck Society, and as Vice-President of the Triological Society. He served as President of the Maryland Society of Otolaryngology and is a former Governor of the American College of Surgeons.

Dr. Eisele's clinical interests include benign and malignant tumors of the head and neck, with special interest in salivary gland and oral cavity neoplasms. His research interests have included functional stimulation of the upper airway for obstructive sleep apnea, electrophysiological nerve monitoring during head and neck surgery, dysphagia, head and neck cancer treatment outcomes, and minimally invasive salivary gland surgery.

LAURA FERRIS, MD, PHD

Laura Korb Ferris, MD, PhD received her PhD in immunology from The Johns Hopkins School of Medicine and her MD from The University of Maryland and she completed her residency in dermatology and fellowship in cutaneous oncology at the University of Pittsburgh. Currently, she is Professor of Dermatology, Clinical Vice Chair, and Director of Clinical Trials at the University of Pittsburgh Department of Dermatology where she directs both the psoriasis and pigmented skin lesions clinics. She is also Chief of Dermatology for UPMC Community and Ambulatory Medicine and is part of the University of Pittsburgh Hillman Cancer Center melanoma program. Her research interests include strategies to improve melanoma early detection both through screening and the use of novel technologies. She has been a principal investigator on over 120 dermatology clinical trials for therapies for psoriasis, atopic dermatitis, hidradentitis suppurativa, and other skin diseases. She has also been involved in clinical trials of several melanoma detection tools as well as a multi-cancer early detection blood test. She is a past president of the Pennsylvania Academy of Dermatology and is on the Board of Directors of the Melanoma Research Foundation.

PRESIDENTIAL CITATIONS

RACHELLE GISH-JOHNSON MSN, CRNP, FNP-BC

Rachelle Gish-Johnson is an Advanced Practice Provider at The University of Pittsburgh Medical Center (UPMC) Hillman Cancer Center. She graduated from the University of Pittsburgh located in Pittsburgh, Pennsylvania with her Bachelor of Nursing Science in 2010 and Master of Science in Nursing in 2014. She achieved American Nurses Credentialing Center (ANCC) Family Nurse Practitioner Board Certification in 2015. She accepted an appointment by UPMC Department of Otolaryngology in Head and Neck Surgical Oncology in 2015 where she has practiced for the past nine years. Mrs. Gish-Johnson's professional interests include clinical research, quality improvement, and patient education. When not practicing medicine, Rachelle is an avid Orange Theory Fitness member and dedicated mother of two, Arlo and June, who she raises with her husband, Andy.

JENNIFER R. GRANDIS, MD

Dr. Jennifer R. Grandis is an ENT physician scientist who is interested in the impact of gender on career development in medicine and science. Her cancer research is focused on elucidating and targeting key signaling pathways and genomic alterations in head and neck cancer with the goal of enabling precision medicine studies. She has leveraged her access to head and neck cancer patients and their biospecimens to optimize translational research studies that include developing novel therapies in the laboratory for clinical application as well as generating and interrogating relevant preclinical models to determine the underlying mechanism of clinical findings. In her institutional roles at the University of Pittsburgh and since 2015, at UCSF, she has facilitated collaborations between clinicians and investigators with an emphasis on developing a robust research infrastructure to support clinical and translational cancer studies. She has published over 400 papers in the peer-reviewed literature and been continuously funded by the NIH since joining the faculty in 1993. Dr. Grandis is an elected member of the American Society for Clinical Investigation the Association of American Physicians and the National Academy of Medicine. She is an American Cancer Society Clinical Research Professor.

EHAB HANNA, MD

Ehab Hanna, M.D., FACS, is an internationally recognized head and neck surgeon and expert in the treatment of patients with skull base tumors and head and neck cancer. After earning his medical degree, Dr. Hanna completed a surgery internship at Vanderbilt University Medical Center, and residency in Otolaryngology-Head and Neck Surgery at The Cleveland Clinic Foundation. He then pursued advanced fellowship training in skull base surgery and head and neck surgical oncology at the University of Pittsburgh Medical Center. In 1994 he was appointed as faculty in the department of Otolaryngology Head and Neck Surgery at the University of Arkansas for Medical Sciences where he quickly rose to the rank of full Professor. He was then recruited to MD Anderson in 2004 to lead their Skull Base Tumor program and the Multidisciplinary Head and Neck Center. Dr. Hanna is currently a Professor and Vice Chair of the Department of Head and Neck Surgery with a joint appointment in the Department of Neurosurgery, MD Anderson Cancer Center. He also serves as an Adjunct Professor of Otolaryngology and Head and Neck Surgery at Baylor College of Medicine. He served as the medical director of the Multidisciplinary Head and Neck Center for 20 years (2004-2023) and is currently the director of the Skull Base Tumor program. For the last 15 years, Dr. Hanna has consistently been named one of America's Best Doctors and Top Doctors in Cancer. In addition to patient care, Dr. Hanna is actively engaged in clinical and translational research with emphasis on skull base tumors. He authored over 350 publications, invited articles, book chapters, and editorials. He co-edited several major textbooks on Cancer of the Head and Neck, Cancer of the Larynx, and Comprehensive Management of Skull Base Tumors. He served as the Editor-in-Chief of the journal of Head & Neck for 15 years from 2007 to 2022. Dr. Hanna served as the President of the North American Skull Base Society (2013-2014) and the President of the American Head and Neck Society (2018-2019). He is currently the Secretary General of the International Federation of Head & Neck Oncologic Societies, the largest organization in the world for Head and Neck Oncology.

PRESIDENTIAL CITATIONS

QUYNH-THU LE, MD

Quynh-Thu Le, MD is the Katharine Dexter McCormick & Stanley McCormick Memorial Professor and Chair of the Department of Radiation Oncology at Stanford University. She co-directs the Radiation Biology Program of the Stanford Cancer Institute. Her clinical focus is on radiation management of head and neck cancer (HNC). She has led multicenter phase II and III clinical trials, testing the addition of novel drugs as well as radiosensitizer or radioprotector with chemoradiotherapy in HNC. Her lab works on approaches to regenerate salivary glands after radiation damage, identification of biomarkers of prognosis and treatment resistance in HNC, and development of novel treatment strategies for HNC with a focus on the tumor microenvironment and Galectin-1.

She currently co-chairs the NRG Oncology Group of the NCI-sponsored National Clinical Trial Network (NCTN), which conducts practice-changing phase II-III trials in many cancers. Before that, she chaired the HNC Committee of NRG Oncology for ten years. She has received grant support from ASCO, ASTRO as well as P01, R01 and R21 grants from the NIH. She has served as a reviewer for several journals and NIH study sections. She has been actively involved in many national and international organizations such as ASTRO, ASCO and AARC and ARS. She was inducted into the Fellowship of the American College of Radiology (FACR), the American Society of Therapeutic Radiology and Oncology (FASTRO) and the Institute of Medicine / National Academy of Medicine (IOM/NAM). She was also honored with the Caltech Distinguished Alumni Award.

JOHN ANDREW "DREW" RIDGE, MD, PHD

John Andrew "Drew" Ridge was born in 1950. He doesn't answer to "John." After attending the University of Chicago he received the Ph.D. in Biochemistry from Stanford University in 1978 and the M.D. in 1981. He undertook training in General Surgery at the University of Colorado and Surgical Research and Surgical Oncology fellowships at Memorial Sloan-Kettering Cancer Center.

He worked at UCSF before moving to the Fox Chase Cancer Center to limit his practice to head and neck oncology. He was the first incumbent to the Louis Della Penna Family Chair in Head & Neck Oncology and is an Emeritus Professor of Surgical Oncology and of Otolaryngology – Head & Neck Surgery. While retired, he still loves to teach and continues to do so. A surgical oncology fellowship position has been endowed in his name.

Dr. Ridge devoted his academic career to multidisciplinary management of head and neck cancer, with a strong commitment to clinical research. While an unapologetic advocate for surgical treatment, he was influential in the design and execution of several clinical trials evaluating non-surgical regimens. A former ECOG Head & Neck Committee Co-Chair and member of the RTOG Head & Neck Steering Committee, he was Co-Chair of the Surgical Oncology Committee of the NRG Cooperative Group. An NRG travel grant for young head & neck surgeons has been named in his honor.

He co-chaired two of the first Cancer Therapy Evaluation Program (CTEP) Clinical Trials Planning Meetings: one for HPV-Related Head & Neck Cancer and one for Transoral Resection of Oropharynx Cancer. Both gave rise to cooperative group trials and reflected his tenure as Co-Chair of the CTEP Head & Neck Steering Committee.

Dr. Ridge was a member of the NCCN Head and Neck and Thyroid panels from their inception and has been a writing member of both committees as well as the AJCC 8th Edition Cancer Staging Committee for head & neck and thyroid cancers. He served as a Governor of the American College of Surgeons.

After they met at Sloan-Kettering, he married Elin Sigurdson in 1989. A prominent academic surgical oncologist interested primarily in colorectal and breast cancer, she too worked at the Fox Chase Cancer Center. Their son, Lukas, and twin daughters, Kelsey and Hannah, have careers in the dramatic and visual arts and in the study of politics. A fencer, Drew competed internationally representing the United States. With respectable results on the FIE World Cup circuit, he was also a member of eleven US Fencing Association Veteran World Championship Teams (and FIE medalist). He enjoys the Rockies but has found that his knees and core no longer tolerate heli-skiing.

Having been active in many professional organizations, he is a past-president of the American Head and Neck Society.

EUGENE N. MYERS, MD, FACS, FRCS EDIN (HON)

Eugene N. Myers MD, FACS, FRCS Edin (Hon) comes from a long line of physicians including his Grandfather Samuel Nicholas, his father David and three Uncles. HIs father was the Chairman of the Department of Otorhinology in the Temple University School of Medicine. His son, Jeffrey, is the Alando Ballantyne Professor and Chairman of the department of Head and Neck Surgery at the MD Anderson Cancer Center and the University of Texas. His grandson, Keith, is a physician who recently graduated with an MD from Temple University School of Medicine.

Dr. Myers graduated with a B.S in Economics from the Wharton School of the University of Pennsylvania and his M.D. degree from Temple University School of Medicine. He did his internship at Mt. Sinai School of Medicine in New York City followed by a residency in Otolaryngology at the Massachusetts Eye and Ear Infirmary/Harvard Medical School. During his residency, he benefited greatly from the mentorship of William W. Montgomery who was a Professor at the prestigious Massachusetts Eye and Ear Infirmary/ Harvard Medical School and inspired Dr. Myers to pursue a career in academic Otolaryngology. Military service followed as a Captain in the U.S. Army stationed as an otolaryngologist in the 97th General Hospital in Frankfurt, Germany. He then served as a Special Fellow in Head and Neck Surgery with Dr. John Conley in New York City.

Dr. Myers was appointed Chairman of the Department of Otolaryngology in the University of Pittsburgh School of Medicine in 1972 and under his leadership transformed it into a world-renowned Department. He estimates that he did 9,000 operations during the 33 years as Chairman. He has made many contributions including the development and implementation of the treatment of patients who have extracapsular spread of cancer in their cervical lymph nodes and also introduced the technique of skull base surgery.

Dr. Myers academic achievements include the publication of more than 300 peer reviewed articles, 20 textbooks, including the popular Cancer of the Head and Neck and Operative Otolaryngology-Head and Neck Surgery, and 150 book chapters. He has delivered more than 750 lectures, including 48 eponymous lectures, and has participated in numerous panels and round tables. There are more than 80 full Professors of Otolaryngology Worldwide who did all or a part of their training in the department during Dr. Myers Chairmanship. Thirty-five of these Professors are now Chairman of their own departments in Universities around the World.

Dr. Myers has held numerous leadership positions including President of the American Board of Otolaryngology, the American Academy of Otolaryngology-Head and Neck Surgery, the American Society of Head and Neck Surgery, the American Laryngological Association, and the Pan American Association of Otolaryngology-Head and Neck Surgery.

In 2021, Dr. Myers was elected to the inaugural class of the Hall of Distinction of the American Academy of Otolaryngology-Head and Neck Surgery. He is also featured in Who's Who: A Lifetime of Achievement. He has received numerous awards and medals from: The Comenius University of Slovakia, The International Federation of Otolaryngological Societies, The Confederation of European Otolaryngological Societies, the deRoaldes Medal of the American Otolaryngological Association and the—Eugene N. Myers Medal of the International Sialoendoscopy Society.

Dr. Myers was the founder of the International Department of the American Academy of Otolaryngology-Head and Neck Surgery and organized a Worldwide network of National Societies. He is an Honorary Member of the National Society of 20 countries and is a member of the Editorial Board of the journal of many national societies. He remains deeply involved in international affairs including membership in the International Steering Committee of the American Academy of Otolaryngology - Head and Neck Surgery. He is also frequently invited to lecture and preside in round table and panel discussions in meetings overseas.

He is a member of the Board of Directors of the Eye and Ear Foundation of Pittsburgh and the Support for Persons with Oral and Head and Neck Cancer (SPOHNC) He is also a member of the Pittsburgh Golf Club and the Chaine des Rotisseurs.

Dr. Myers and his wife Barbara (deceased) were married for 65 years. Their son Jeffrey Myers is the Alando Ballantyne Professor and Chairman of the Department of Head and Neck Surgery at the MD Anderson Cancer Center- University of Texas. Their daughter Marjorie Fulbright is an Executive Recruiter in San Francisco. He has 5 overachieving Grandsons all of whom he loves very much.

CHARLES W. CUMMINGS, MD

Dr. Charles Cummings was born in Boston, Massachusetts, in November of 1935. He graduated from Deerfield Academy in 1953, Dartmouth College in 1957, and the University of Virginia Medical School in 1961. He was an intern at Dartmouth and completed a year of general surgery residency at the University of Virginia. Dr. Cummings entered the Air Force in 1963, was discharged in July 1965, and entered residency training in Otolaryngology-Head and Neck Surgery at the Harvard Medical School, Massachusetts Eye and Ear Infirmary, finishing the program in 1968.

Dr. Cummings worked in private practice in Boston and on the clinical staff at the Massachusetts Eye and Ear Infirmary until the end of 1975 when he moved to Syracuse, New York and became an Associate Professor in the Department of Otolaryngology – Head and Neck Surgery at the State University of New York Upstate Medical University. Two years later, he assumed chairmanship of the Department of Otolaryngology – Head and Neck Surgery at the University of Washington where he remained until the end of 1990 when he became Director of the Department of Otolaryngology – Head and Neck Surgery at Johns Hopkins. He was Chief of Staff of The Johns Hopkins Hospital from 1997 through 1999. In 2003, Dr. Cummings stepped down as Director. Dr. Cummings was also the Executive Medical Director for Johns Hopkins International from 2003 until 2011. In addition, he has served as interim chair of the Department of Dermatology (2007 - 2009) and the Department of Orthopaedics from (9/2011 - 9/2013) He returned to the Department of OTO/HNS at that time as Distinguished Service Professor of Oncology and Emeritus Andelot Professor of Otolaryngology/Head and Neck Surgery. He retired from Johns Hopkins in June 2022.

He has written 144 scientific papers and was the founder and Senior Editor of the text, *Cummings Otolaryngology – Head and Neck Surgery*, which is now in its seventh edition, edited by Dr Paul Flint He has also co-authored two surgical atlases, one on laryngeal surgery and another on surgical access and reconstruction in the field of laryngology and head and neck surgery. Dr. Cummings served as a Director of the American Board of Otolaryngology, as Chairman of the Residency Review Committee and Chairman of the Advisory Council for Otolaryngology to the American College of Surgeons. He is a Past President of the American Association for Academic Departments of Otolaryngology, American Broncho-Esophagological Association, the American Academy of Otolaryngology – Head and Neck Surgery and the American Society for Head and Neck Surgery. Dr. Cummings has received numerous honors for his work, including the Chevalier Jackson Award (American Broncho-Esophagological Association), the Newcomb Award (American Laryngological Association), the Ogura lecturer for the Triological Society, The Hayes Martin lecturer for the American Head and Neck Society, The Daniel Baker Lecturer for the Triological Society, and others. He was presented with the 2009 Johns Hopkins Heritage Award, and the Johns Hopkins Distinguished Alumnus award in 2013. He was the recipient of the Walter Reed Distinguished Alumni Award from the University of Virginia in 2017. He was honored with The Johns Hopkins Dean's Mentorship Award in June 2022.

He has been honored by many International Head and neck Societies as an honorary member.

Many of his former residents and faculty are currently in meaningful Academic positions or Chairing Departments of Otolaryngology- Head and Neck Surgery at leading Academic Institutions, a source of great personal pride.

DISTINGUISHED SERVICE AWARD

JONAS T. JOHNSON, MD

Jonas T. Johnson, MD is Emeritus Chairman and Distinguished Service Professor in the Department of Otolaryngology at the University of Pittsburgh School of Medicine. His lifelong clinical commitment has been to people with head and neck cancer, providing care in an environment of education and research.

Dr. Johnson has contributed over 600 manuscripts to the peer reviewed literature. He has written over 120 chapters in scientific books and served as editor or contributing editor in of over 20 textbooks.

Dr. Johnson served as editor in chief of the Laryngoscope (2003- 2011) He was coordinator of education for the American Academy of Otolaryngology - Head and Neck Surgery and president of that organization (2003). He served as Secretary of The American Society for Head and Neck Surgery and was on the leadership team which undertook the merger of the two head and neck organizations into the American Head and Neck Society (1998). Dr. Johnson served as President of the AHNS (2004) and subsequently president of the Triologic Society (2014).

Jonas Johnson withdrew from surgical practice in 2016. At that time, he re-engineered his clinical practice with the collaboration of Dr. Marci L Nilsen PhD to originate a Survivorship Clinic for Head and Neck Cancer Survivors at the University of Pittsburgh Medical Center. In the ensuing years, this clinic has served over 2,500 patients in over 5,000 visits. This clinical effort had offered opportunity to better know and understand the burden of toxic side effects suffered by this patient cohort while offering opportunity to provide multidisciplinary rehabilitative care in an environment of clinical research.

Past Distinguished Service Award Recipients

Donald T. Weed, MD 2023	Ernest A. Weymuller, Jr., MD 2007
Paul Friedlander, MD 2022	John A. Ridge, MD, PhD 2006
Terry Day, MD 2021	Wayne Koch, MD 2005
William Lydiatt, MD 2019	Marc D. Coltrera, MD 2004
Brian P. Burkey, MD, MEd 2018	Helmuth Goepfert, MD 2003
Dennis H. Kraus, MD 2017	Jonas T. Johnson, MD 2001
Ehab Hanna, MD 2016	Harold J. Wanebo, MD 1999
Carol R. Bradford, MD 2015	David L. Larson, MD 1999
Jesus E. Medina, MD 2014	John J. Coleman, III MD 1999
Dennis H. Kraus, MD 2013	Elliot W. Strong, MD 1995
Ashok R. Shaha, MD 2012	Ashok R. Shaha, MD 1991
Randal S. Weber 2011	Stephan Ariyan, MD 1990
Mark K. Wax, MD 2010	Jatin P. Shah, MD 1989
Keith S. Heller, MD 2009	
Helmuth Goepfert, MD 2008	

Past Special Recognition Award Recipients

Paul B. Chretien, MD 1984	Edgar L. Fazell, MD 1988
John M. Lore, Jr., MD 1985	Harvey W. Baker, MD 1989
William S. MacComb, MD 1986	Vahram Y. Bakamjian, MD 1991
Calvin T. Klopp, MD 1987	Jean-Louis Lefevbre, MD 1995

MARGARET F. BUTLER OUTSTANDING MENTOR OF WOMEN IN HEAD AND NECK SURGERY AWARD

Dr. Margaret Butler was the first female Otolaryngology chair in the United States. In 1906, she was appointed Chair of Ear, Nose and Throat at Women's Medical College of Pennsylvania. As a respected otolaryngologist and an ambassador of the specialty, Dr. Butler provided a blueprint for future generations of female otolaryngologists.

The purpose of the Margaret F. Butler, MD Champion of Women in Head and Neck Surgery Award is to recognize individuals who have demonstrated leadership in promoting gender diversity in the field of Head and Neck Surgery and its related endeavors, have consistently supported and promoted women in head and neck surgery, served as mentors leading to mentee career advancement, successful research and publications.

2024 Awardee:

CAROL R. BRADFORD, MD, MS, FACS

An internationally recognized head and neck cancer surgeon scientist and leader in academic medicine, Carol R. Bradford, MD, MS, FACS, is the dean of The Ohio State University College of Medicine and vice president for Health Sciences of The Ohio State University Wexner Medical Center. She also holds the Leslie H. and Abigail S. Wexner Dean's Chair in Medicine and is a professor of Otolaryngology – Head and Neck Surgery.

Dean Bradford specializes in head and neck cancer surgery, focusing her research on identifying and evaluating biomarkers that can predict outcomes. She also pioneered the use of sentinel lymph node biopsy as a safe and reliable tool to stage patients with melanoma of the head and neck. She has published more than 330 peer-reviewed articles and authored more than 20 book chapters.

Throughout her career, Dean Bradford has received many awards recognizing her dedication to education, research and patient care. She is regularly recognized on Castle Connolly's lists of Top Doctors and Exceptional Women in Medicine.

She was elected the first woman president of the American Head and Neck Society in 2012 and has since received both a Distinguished Service Award and a Presidential Citation from the society. In 2024, she received the Margaret F. Butler Outstanding Mentor of Women in Head and Neck Surgery Award.

In 2020, she served a one-year term as president of the American Academy of Otolaryngology-Head and Neck Surgery, and was inducted into the academy's Hall of Distinction in 2023. In 2019, she received the Helen F. Krause Memorial Trailblazer Award from the Women in Otolaryngology section.

Dean Bradford is a fellow of the American College of Surgeons, American Head and Neck Society, Triological Society and American Laryngological Association. She is also a member of the prestigious National Academy of Medicine, the Gold Humanism Honor Society and the Courage to Teach initiative, which is an integral component of the Humanism & the Arts in Medicine program at Ohio State.

CONGRATULATIONS TO THE AHNS 2024 MANUSCRIPT AWARD WINNERS!

Robert Maxwell Byers Award: Camaren M. Cuenca, BS[2] and David J. Fei-Zhang[1], BA, Entitled work: *Assessment of Social Vulnerability in Laryngeal Cancer Prognosis and Treatment in the United States,* [2]Northwestern University Feinberg School of Medicine, and [1]Baylor College of Medicine.

Randal Weber, MD Award for Quality, Safety and Value in Head and Neck Oncology: Elif Baran, HBsc, Department of Otolaryngology-Head & Neck Surgery, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada, Entitled work: *Using Artificial Intelligence to automate the extraction of staging criteria from the electronic health records of oropharyngeal cancer patients.*

Best Resident Basic Science Research Paper: Robert Saddawi-Konefka, MD, PhD , Entitled work: *Characterization of the Primary Tumor-Sentinel Node ImmunoMigratome Demonstrates a Key Role for Dendritic Cell Trafficking in the Successful Response to Immunoradiotherapy.*

Best Resident Clinical Paper Best Prevention and Early Detection Papers: Kelly L. Schmidt, MD, University of Missouri Department of Otolaryngology Head and Neck Surgery, Entitled work: *Social Determinants of Health in Donor Site Morbidity in Head and Neck Cancer Reconstructive Limbs: Anterolateral Thigh and Fibula Free Tissue Transfers.*

Best Prevention and Early Detection Paper: Tyler J. Gallagher, BS, Keck School of Medicine of the University of Southern California, Entitled work: *Prevalence and Predictive Factors for HPV Vaccination Among Older Adults in the United States*

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The American Head & Neck Society is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The American Head & Neck Society designates this live activity for a maximum of **13.25 *AMA PRA Category 1 Credit(s)™***. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ABOHNS Continuous Certification

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn their required annual part II self-assessment credit in the American Board of Otolaryngology – Head and Neck Surgery's Continuing Certification program (formerly known as MOC). It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of recognizing participation.
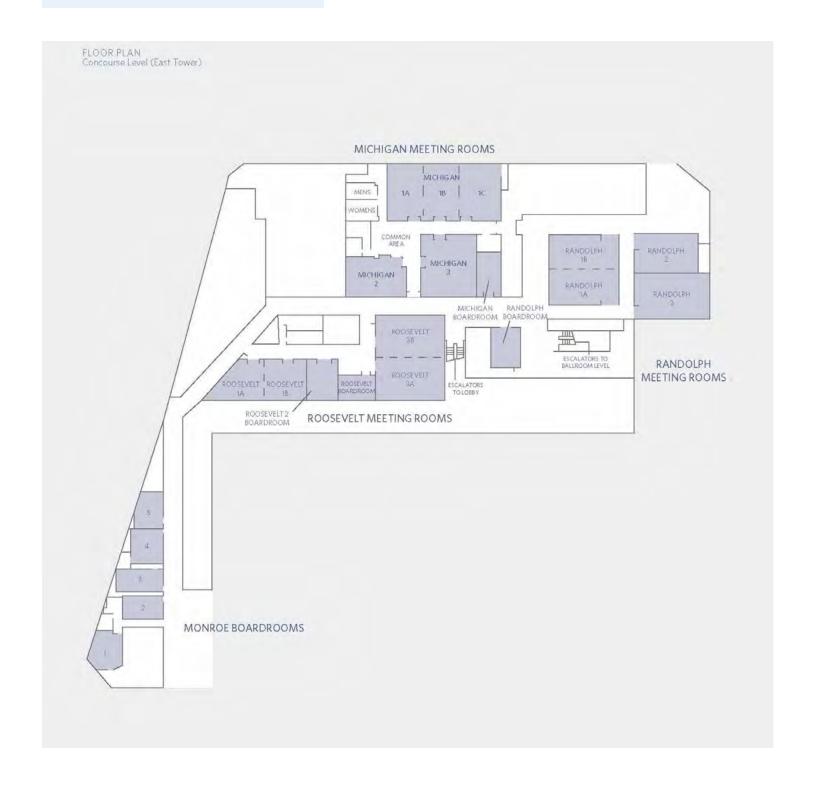
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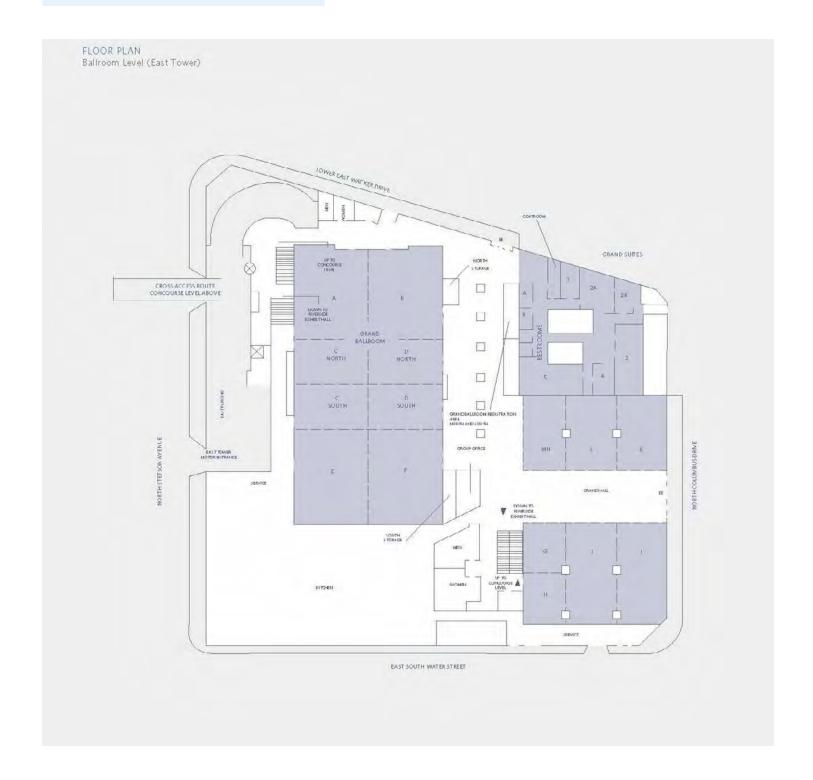
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You can find the Disclosures for the Faculty, Presenters, and Planning Committee by following the link in the QR Code here.

HOTEL FLOOR PLANS

FLOOR PLAN
Concourse Level (East Tower)

MICHIGAN MEETING ROOMS

MICHIGAN
1A | 1B | 1C

MENS

WOMENS

COMMON
AREA

MICHIGAN
3

MICHIGAN
2

RANDOLPH
1B

RANDOLPH
2

RANDOLPH
1A

RANDOLPH
3

MICHIGAN
BOARDROOM

RANDOLPH
BOARDROOM

ROOSEVELT
3B

ESCALATORS TO
BALLROOM LEVEL

RANDOLPH
MEETING ROOMS

ROOSEVELT
1A

ROOSEVELT
1B

ROOSEVELT
BOARDROOM

ROOSEVELT
3A

ESCALATORS
TO LOBBY

ROOSEVELT 2
BOARDROOM

ROOSEVELT MEETING ROOMS

5

4

3

2

1

MONROE BOARDROOMS

HOTEL FLOOR PLANS

FLOOR PLAN
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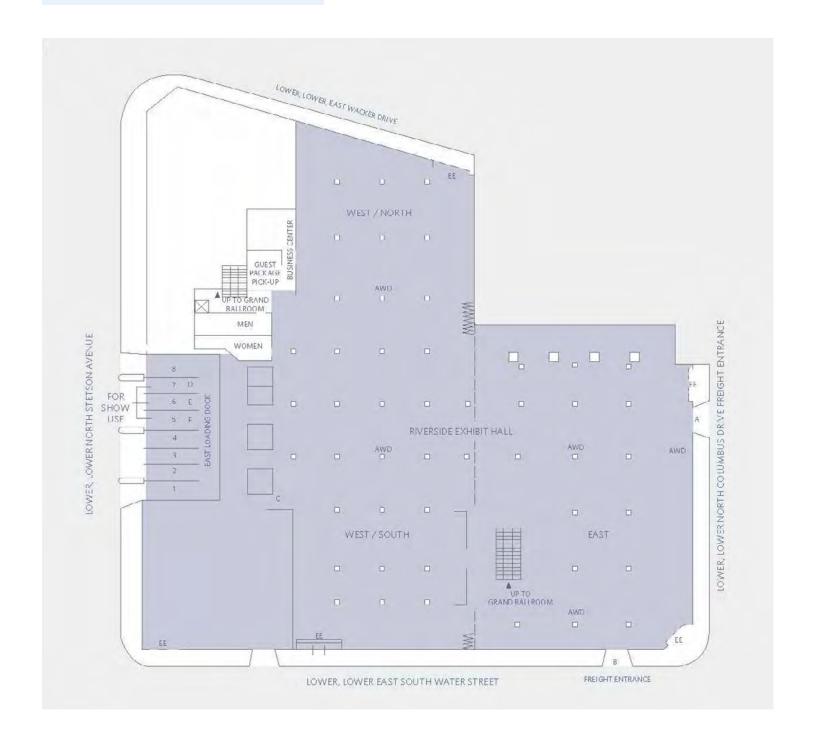
HOTEL FLOOR PLANS

Tuesday, May 14, 2024 (Pre-Meeting Courses)

8:30 am – 5:05 pm   **Grand Hall K**

2024 AHNS Innovation and Entrepreneurship Symposium (non-CME)

Course Director: Jose P. Zevallos, MD, MPH Course Co-Director: Baran Sumer, MD

This symposium will be an introductory, all-day course designed for surgeons and academic physicians. It offers insights into entrepreneurship, covering key aspects such as intellectual property protection, capital raising, balancing clinical responsibilities, navigating technology transfer offices, patenting, commercialization, manufacturing, regulatory compliance, and conflict of interest management.

Welcome and Introduction – *Jose P. Zevallos, MD, MPH*

The Creative Process for Surgeons – *Carl Snyderman, MD*

Now That I have a Good Idea, How Do I Develop It? Therapeutics and Medical Devices – *Peter Santa Maria, MD, PhD*

Protecting Your Idea: The Disclosure and Intellectual Property Process – *Tom Meyers*

Leveraging University Resources Panel
Moderator: Nishant Agrawal, MD, FACS
Panelists: Melissa Byrn, Barbara Flynn, MD, David Johnson, PhD, Jennifer Ponting, JD, Robert Rosa, MD

Surgeons as Entrepreneurs Panel: Conceptualization of Your Idea and Launching Your Start-Up
Moderator: Jose P. Zevallos, MD, MPH
Panelists: Nishant Agrawal, MD, FACS, Alex Langerman, MD, SM, FAC, Peter Santa Maria, MD, PhD, Carl Snyderman, MD

Networking Lunch

Keynote Lecture in Entrepreneurship and Innovation, "Commercializing Your Discoveries: An Entrepreneur's Perspective" – *Stan Lapidus*

The inaugural AHNS Lecturer in Entrepreneurship and Innovation will be Stan Lapidus. Stan is a serial inventor and entrepreneur. He is the founder of two multibillion-dollar diagnostics companies, Cytyc and Exact Sciences. Stan is the inventor of Cytyc's Thin-Prep pap test used worldwide for cervical cancer screening. He is the co-inventor of Exact's Cologuard test for early detection of colorectal cancer. Stan serves as a director of seven companies and is chair of three of them. Stan has held faculty appointments at MIT and Tufts Medical School. He holds 37 US patents and is an elected fellow of the American Institute of Medical and Biological Engineering. He is also a co-founder of Droplet Biosciences.

Creating Your Pitch Deck – *Theresa Tribble, MBA*

How to Raise Capital, from Seed to Series A and Beyond – *Jennifer Fried, MBA, Alex Langerman, MD, SM, FACS*

Venture Capital Panel: Working with Surgeon Founders
Moderator: Baran Sumer, MD
Panelists: Clay Heighten, MD, Tony Natale, MD

"Entrepreneurship While Keeping Your Day Job" Panel
Moderator: Alex Langerman, MD, SM, FACS
Panelists: Chris Holsinger, MD, Baran Sumer, MD, Jose P. Zevallos, MD, MPH

Closing Remarks - *Jose P. Zevallos, MD, MPH*

8:00 am – 12:50 pm   **Grand Hall L**

Thyroid, Parathyroid, and Neck Ultrasound Course Didactic Session

12:00 pm – 12:15 pm   **Grand Hall L**

Lunch

SCIENTIFIC PROGRAM

1:00 pm – 5:00 pm   Grand Hall MN

Thyroid, Parathyroid, and Neck Ultrasound Course Hands On Session

The objective of this course is to introduce the practicing surgeon to office-based ultrasound examination of the thyroid and parathyroid glands and related pathology. The distinction of normal from malignant lymphadenopathy is emphasized with a demonstration of the comprehensive examination of lymph node basins in cervical zones I-VI. The process of ultrasound guided FNA of thyroid nodules and enlarged lymph nodes is demonstrated in didactic lecture format. In addition skill sessions allow the surgeon to learn varied techniques of FNA of lesions in phantom models.

The use of patient volunteers with thyroid and parathyroid pathology and lymphadenopathy will allow supervised hands-on experience with transverse and longitudinal ultrasound methods. Participants will be instructed in the practical details and hurdles in developing office-based ultrasound.

1:00 pm – 5:00 pm   Grand Hall L

Head & Neck Microvascular Reconstructive Workshop for Residents/Fellows (non-CME)

Course Director: Jamie Ku, MD, BS and Course Co-Director: Steven Chinn, MD, MPH, BS

This workshop will highlight key harvest techniques of both common and uncommon reconstructive procedures utilizing multimedia presentations, including videos and images. In the second part of the workshop, a group of experts will provide insights and pearls of wisdom as they work through defect-oriented cases of to provide solutions to some of the most challenging head and neck reconstructive defects.

At the conclusion of this session participants will be able to:

» Identify key harvest techniques of both common and uncommon head and neck reconstructive procedures.

» Understand the various reconstructive options to some of the most challenging head and neck cancer defects.

The AHNS gratefully acknowledges support of this workshop from KLS Martin

Part I: Flap Harvest Videos

1. Pedicled Flaps
   a. Submental Flap – *Alice Lin, MD*
   b. Supraclavicular Flap – *Andrew Holcomb, MD*
   c. Pectoralis Flap – *Andrew Holcomb, MD*

2. Arm-based Flaps
   a. Lateral Arm Flap – *Stephen Kang, MD*
   b. Ulnar Artery Flap – *Steven Chinn, MD, MPH, BS*
   c. Radial Forearm Flap – *Sarah Rohde, MD, MMHC*
   d. Osteocutaneous Radial Forearm Flap – *Sarah Rohde, MD, MMHC*

3. Abdominal-based Flap
   a. Deep Inferior Epigastric Perforator Flap – *Matthew Hanasono, MD, FACS*

4. Thigh-based Flaps

   a. Anterolateral Thigh Flap – *Michael Fritz, MD*
   b. ALTO – *Avinash Mantravadi, MD, FACS*
   c. Profunda Artery Perforator Flap – *Jamie Ku, MD, BS*

5. Scapular-based Flaps
   a. Scapular Flap – *Matthew Spector, MD*
   b. Scapular Tip Flap – *Matthew Spector, MD*
   c. Serratus Rib/Muscle Flap – *Michael Fritz, MD*
   d. Thoracodorsal Perforator Flap – *Matthew Spector, MD*
   e. Latissimus Dorsi Flap – *Michael Fritz, MD*
   f. Mega Flap – *Matthew Spector, MD*

6. Lower Extremity Flaps
   a. Medial Sural Artery Perforator Flap – *Allen Feng, MD*
   b. Fibula Flap – *Sidharth Puram, MD, PhD, FACS*
   c. Iliac Crest Flap – *Matthew Hanasono, MD, FACS*

Part II: How I Do It: Case-based Solutions

1. Total Maxillectomy Reconstruction – *Matthew Spector, MD, Michael Fritz, MD, Stephen Kang, MD*

2. Facial Reanimation – *Brandon Prendes, MD, Phillip Daniel Knott, MD, FACS*

3. Subtotal/Total Glossectomy – *Steven Chinn, MD, MPH, BS, Allen Feng, MD, Jamie Ku, MD, BS*

4. Pharyngectomy Reconstruction – *Andrew Huang, MD, Scott Roof, MD, BA, Kevin Contrera, MD, MPH*

5. Oropharyngeal Reconstruction – *Kendall Tasche, MD, BA, Douglas Chepeha, MD, MScPH, FACS, FRCS(C)*

6. Hostile Neck
   a. IMA Exposure – *Matthew Hanasono, MD, FACS*
   b. Angular Vessel Exposure – *Michael Fritz, MD*
   c. Transverse Cervical Exposure – *Steven Chinn, MD, MPH, BS*
   d. Dorsal Scapula – *Steven Chinn, MD, MPH, BS*

6:00 pm – 7:30 pm   Michigan 3

Women of H&N Service Reception

The AHNS gratefully acknowledges support of this event from Intuitive Surgical

2024 Margaret Butler Award for Outstanding Mentor of Women in Head and Neck Surgery, Dr. Carol Bradford.

SCIENTIFIC PROGRAM

Wednesday, May 15, 2024

7:00 am – 5:00 pm	Skyway 260

Centurion Lounge

7:00 am – 8:00 am	Grand Ballroom EF

New Member Induction Ceremony

8:00 am – 8:05 am	Grand Ballroom EF

Introduction

Robert Ferris, MD, PhD, Patrick Ha, MD, FACS, Nicole Schmitt, MD, FACS and Sidharth Puram, MD, PhD, FACS

8:05 am – 8:40 am	Grand Ballroom EF

Distinguished Keynote Lecturer: Clinical Trials and the Retreat from Radical Operations

Introduction: Patrick Ha, MD, FACS
Norman Wolmark, MD, FACS, FRCSC

8:40 am – 8:45 am	Grand Ballroom EF

Introduction

Bill Lydiatt, MD

8:45 am – 9:45 am	Grand Ballroom EF

Presidential Address

Robert Ferris, MD, PhD

9:45 am – 10:15 am	Break with Exhibitors	Riverside Exhibit Hall

10:15 am – 11:15 am	Grand Ballroom EF

John Conley Lecture – Blind Spots: The Business of Medicine, The Appropriateness of Care, and Unexplored Areas of Research

Introduction: Sidharth Puram, MD, PhD, FACS
Keynote Speaker: Marty Makary, MD

11:15 am – 12:00 pm	Grand Ballroom EF

Scientific Session 1: Reconstruction/ QOL

Moderators: Catherine Haring, MD and Mary Jue Xu, MD

1. Impact of baseline emotional distress on long-term quality of life in head and neck cancer patients – *Kimberly Oslin, MD*
2. Trajectories of Neck Disability and Dysphagia Symptoms in Survivors of Head and Neck Cancer – *Marci L. Nilsen, PhD, RN, CHPN, FAAN*
3. The 5 item modified frailty index predicts postoperative morbidity, not survival following laryngectomy – *Eoin F. Cleere, MB, BCh, MCh*
4. Impact of Frailty on Treatment Selection in Locally Advanced Laryngeal Squamous Cell Carcinoma – *James R. Xu, BS*
5. Hardware Exposure Following Mandibular Reconstruction Using Osteocutaneous versus Soft Tissue Microvascular Free Tissue Transfer – *Hasan Abdulbaki, BA*
6. Tranexamic Acid in Head and Neck Microvascular Free Flap Reconstruction – *Micah K. Harris, MD*

SCIENTIFIC PROGRAM

11:15 am – 12:00 pm   Grand Hall IJ

Neoadjuvant Immunotherapy: Standard of Care and Ongoing Trials

Moderator: Kelly Malloy, MD

This session will provide a review of the current science of neoadjuvant immunotherapy in head and neck oncology, from its use in melanoma and cutaneous squamous cell carcinoma to newer investigations for mucosal malignancies. We will also have an opportunity to consider fresh science in this arena via the presentation of a relevant abstract during the session.

At the conclusion of this session participants will be able to:

» Apply standard of care neoadjuvant immunotherapy options in appropriate melanoma patients.

» Use appropriate neoadjuvant immunotherapy for cutaneous SCC of the head and neck.

» Identify clinical trial opportunities for neoadjuvant immunotherapy in mucosal head and neck cancer patients.

1. Response-Adapted Oncologic Surgery for Cutaneous Squamous Cell Carcinoma: Personalized Approach in the Immunotherapy Era – *Shorook Naara, MD, PhD*
2. Standard of Care and New Horizons in Neoadjuvant Immunotherapy for Melanoma – *Jeffrey Sosman, MD*
3. Emerging Role of Neoadjuvant Immunotherapy for Cutaneous Squamous Cell Carcinoma – *Neil Gross, MD, FACS*
4. Advances in Neoadjuvant Immunotherapy for HNSCC – *Ravindra Uppaluri, MD, PhD*

12:00 pm – 1:00 pm   Lunch with Exhibitors   Riverside Exhibit Hall

1:00 pm – 2:00 pm   Grand Ballroom EF

Patient Care Debates Part I: TORS vs XRT for Stage I-II HPV+ Oropharynx Cancer

Moderator: Chris Holsinger, MD

Despite prospective studies to de-escalate treatment for HPV+ oropharynx cancer, RTOG1016 and HN005, for now, definitive treatment for most patients appears to be 70Gy XRT + cisplatin. However, frontline surgery with 50Gy post-operative RT has been shown as a feasible treatment approach for selected patients. However, there is considerable variation in practice across the US. In this session, two leaders in TORS and de-escalation approaches using XRT present their recommendation for which patients are ideally suited for treatment de-escalation.

At the conclusion of this session participants will be able to:

» Integrate recent prospective clinical trials data with expert opinion to optimize treatment selection for patients with HPV+ OPC.

» Identify which patients are ideally suited for frontline surgery using TORS + neck to optimize function outcome and reduce the extent of adjuvant therapy.

» Identify which patients are eligible for XRT treatment de-escalation using tumor hypoxia fMISO PET.

1. The Controversy, Conundrum, and a Poll – *Chris Holsinger, MD*
2. TORS is the Only Evidence-Based Approach for De-escalation – *Greg Weinstein, MD*
3. Using Hypooxia to De-escalate Radiation – *Nancy Lee, MD*
4. Rebuttal and Reply – *Greg Weinstein, MD*
5. Rebuttal and Reply – *Nancy Lee, MD*
6. Summary – *Chris Holsinger, MD*

Patient Care Debates Part II: Are the Days of Targeted Therapy Over or are the Brightest Days Ahead?

Moderator: Sidharth Puram, MD, PhD, FACS

This debate will explore the emergence of biologic-based therapies for head and neck cancer, specifically focusing on the advantages, challenges, and prospects related to targeted therapy. Our debaters will consider true patient-specific, targeted molecular agents vs broad scale, `off the shelf,` patient agnostic approaches such as immunotherapy.

At the conclusion of this session participants will be able to:

» Describe the emerging biologic therapies in head and neck cancer.

» Compare the advantages and disadvantages of various targeted agents compared to other emerging therapies (e.g. immunotherapy).

» Appraise the current trial data in this area and integrate these data into ongoing discussions of future therapies.

1. Introduction and Audience Poll – *Sidharth Puram, MD, PhD, FACS*

2. Pro-targeted Genomics/Molecular Therapy Position – *Luc Morris, MD, MSc*
3. Pro-Immunotherapy Position – *Clint Allen, MD, BS*
4. Pro- targeted Genomics/Molecular Therapy Rebuttal – *Luc Morris, MD, MSc*
5. Pro- Immunotherapy Rebuttal – *Clint Allen, MD, BS*
6. Conclusion and Audience Poll – *Sidharth Puram, MD, PhD, FACS*

1:00 pm – 2:00 pm   Grand Hall IJ

Disparities in Head and Neck Cancer Care: Are We Making Progress? What Are The Opportunities?

Moderator: Caitlin McMullen, MD, BS

During this session, our speakers will review the current state of disparities in head and neck cancer care. Novel strategies to increase access to high quality care and clinical trials will be presented.

At the conclusion of this session participants will be able to:

» Articulate the current state of disparities in head and neck cancer care and the importance of addressing barriers to high quality care.

» Implement strategies during clinical trial design to encourage the enrollment of underrepresented patient populations.

» Apply new technology to identify disparities and develop strategies that can address critical obstacles.

1. The Role of AI in Disparities and Solutions – *Vasu Divi, MD*
2. Promoting Diversity in Clinical Trial Participation – Access and Telehealth - *Leila Mady, MD, PhD, MPH*
3. Engagement and Care of Patients with Poor Access – *Gina Jefferson, MD*
4. Assessment of Social Vulnerability in Laryngeal Cancer Prognosis and Treatment in the United States – *Camaren M Cuenca, BS*
5. Social Determinants of Health in Donor Site Morbidity in Head and Neck Cancer Reconstructive Limbs: Anterolateral Thigh and Fibula Free Tissue Transfers – *Emma Elbert, BS*

2:00 pm – 2:45 pm   Grand Ballroom EF

Survivorship 2024

Moderator: Barry Wenig, MD

With improvement in care, there are ever growing numbers of Head and Neck cancer survivors. This session will detail the complexities of cancer survivorship, changing symptoms over time, and explore challenges in optimizing best care for this population.

At the conclusion of this session participants will be able to:

» Recognize various Quality of Life (QoL) management challenges such as lymphedema, xerostomia, and osteoradionecrosis (ORN).

» Identify the timing and profile of late effects of radiation on swallowing and function.

» Integrate complementary and support services to address psychological needs of survivors.

1. Introduction – *Barry Wenig, MD*
2. Managing QoL Challenges Part 1 – *Jeffrey Liu, MD*
3. Managing QoL Challenges Part 2 – *Theresa Guo, MD*
4. Late Effects of Radiation Therapy – *Rosemary Martino, PhD*
5. QoL Psychological Effects - *Trevor Hackman, MD*

2:00 pm – 2:45 pm   Grand Hall IJ

Challenges in Salivary Tumors: A Case-Based Discussion

Moderator: Jessie Maxwell, MD, MPH
Panelists: Kiran Kakarala, MD, William Ryan, MD, Shaum Sridharan, MD, Mirabelle Sajisevi, MD

We will use a case-based format to discuss challenges in the management of salivary gland neoplasms. Topics and controversies to be presented include management of the facial nerve, the role of neck dissection, indications for adjuvant radiation, and soft tissue reconstruction for low- and high-grade salivary gland malignancies.

At the conclusion of this session participants will be able to:

» Articulate the indications for facial nerve sacrifice and various methods for facial nerve reconstruction or facial re-animation.

» Develop a treatment paradigm for soft tissue reconstruction of parotid gland defects.

» Convey the role of adjuvant radiation for close or positive margins in low- and intermediate-grade salivary gland carcinoma.

1. Parotid Acinic Cell Carcinoma
2. Carcinoma Ex Pleomorphic Adenoma
3. Salivary Gland Neoplasm of Uncertain Malignant Potential (SUMP)

SCIENTIFIC PROGRAM

2:45 pm – 3:15 pm	Break with Exhibitors	Riverside Exhibit Hall

3:15 pm – 4:00 pm	Grand Ballroom EF

Scientific Session 2: Cancer Biology/TME

Moderators: Katherine Wai, MD and Richard Harbison, MD, MS, BS

1. Circulating Tumor DNA Kinetics Following Induction Chemotherapy Predicts Response in HPV+ Oropharyngeal Squamous Cell Carcinoma – *Zachary M. Huttinger, MD, PhD*
2. Cancer stem cells resist targeting by tumor infiltrating lymphocytes in a three-dimensional in vitro model – *Colleen Hochfelder, MD*
3. Prognostic utility of a gene expression profile that quantifies anti-tumor immunity in HPV+ OPSCC – *Dominick Rich, BS*
4. Characterization of the Primary Tumor-Sentinel Node ImmunoMigratome Demonstrates a Key Role for Dendritic Cell Trafficking in the Successful Response to Immunoradiotherapy – *Robert Saddawi-Konefka, MD, PhD*
5. Durable Antitumor Immunity After Successful Primary Tumor Responses to IO Therapy is Conferred by CD8 Tex-stem Cells Residing Within Regional Lymphatics – *Robert Saddawi-Konefka, MD, PhD*
6. Decreased T-cell repertoire and lower density of antigen-presenting cells in the tumor microenvironment of immunosuppressed patients with non-melanoma skin cancer suggest impaired innate immunity is a key driver of immunosuppression – *Jennifer L. Anderson, MD, PhD*

3:15 pm – 4:00 pm	Grand Hall IJ

Translational Advances in Thyroid Cancer

Moderator: Alessa Colaianni, MD

We will use a case-based presentation to discuss translational advances in thyroid cancer, including the use of molecular markers, guidance in patient selection for surgery or conservative surveillance, and use of targeted therapy in advanced disease.

At the conclusion of this session participants will be able to:

» Describe molecular markers and biological correlatives relating to the management of thyroid cancer.

» Describe current trends in the rationale for surgical selection versus conservative surveillance in the management of thyroid cancer.

» Describe recent advances in targeted therapy for advanced thyroid cancer and demonstrate how these therapies interplay with surgery in the multidisciplinary management of advanced thyroid cancer.

1. Introduction and Case Presentation – *Alessa Colaianni, MD*
2. Molecular Markers and Biological Correlatives in Thyroid Cancer – *Elizabeth Cottrill, MD*
3. Surgical Selection vs Conservative Surveillance of Thyroid Cancer – *Merry Sebelik, MD*
4. Integration of Targeted Therapy and Surgery in Advanced Thyroid Cancer Clinical Trials – *Mark Zafereo, MD*
5. Surgical and Oncologic Outcomes of Conversion Surgery vs Immediate Surgery for Patients with Low-Risk Papillary Thyroid Carcinoma – *Helena Levyn, MD*
6. Q&A

4:00 pm – 5:00 pm	Grand Ballroom EF

Women in Head and Neck Surgery Panel - How to Build Impactful Programs

Moderators: Shirley Su, MBBS and Karen Choi, MD

Building a coherent and innovative body of work that fulfills a critical need is key to having a lasting impact in Head and Neck Surgery. This can be a clinical service, innovative research, an educational program or perusing an unique interest. We have selected three women who are leaders in their respective fields, to share their personal experience in building outstanding programs. #AHNSWomen

At the conclusion of this session participants will be able to:

» Understand the steps in building a unique program, including key collaborations and strategizes to advocate for your ideas and efforts in a highly competitive field.

» Identify strategies to increase the impact of and be known for your work.

» Recognize potential pit falls and how to overcome them.

1. Introduction and Overview – *Shirley Su, MBBS*
2. Building a Cutting Edge Research Program – *Carole Fakhry, MD MPH*
3. Building an Innovative Clinical Program – *Jan Lewin, PhD*
4. Following Your Own Path and Building Unique Programs – *Susan McCammon, MD*
5. Q&A – *Karen Choi, MD*

SCIENTIFIC PROGRAM

4:00 pm – 5:00 pm   Grand Hall IJ

Rare Tumors: Update on Translational Biology and Clinical Management

Moderator: Thomas J. Ow, MD

As head and neck oncology specialists, we are commonly presented with rare malignancies that pose unique clinical challenges, as well as barriers to progress in regards to clinical and translational research. This hour will examine four `rare` but common malignancies that we face: namely Esthesioneuroblastoma, Adenoid Cystic Carcinoma, Merkel Cell Carcinoma, and Nasopharyngeal Carcinoma. Experts in their respective fields will provide a brief update for each of these topics, including recent advances in translational research and clinical approaches for these entities. An accepted abstract discussing PRMT5 inhibition in Adenoid Cystic Carcinoma will also be featured.

At the conclusion of this session participants will be able to:

- » Discuss recent advances in the diagnosis and treatment of Esthesioneuroblastoma, Adenoid Cystic Carcinoma, Merkel Cell Carcinoma, and Nasopharyngeal Carcinoma.
- » Appraise recent clinical trials and translational research discoveries for Esthesioneuroblastoma, Adenoid Cystic Carcinoma, Merkel Cell Carcinoma, and Nasopharyngeal Carcinoma.
- » Formulate new hypotheses for future clinical and translational research studies of Esthesioneuroblastoma, Adenoid Cystic Carcinoma, Merkel Cell Carcinoma, and Nasopharyngeal Carcinoma.

1. Introduction – *Thomas J. Ow, MD*
2. Olfactory Neuroblastoma: Clinical and Translational Advances – *Nyall London, MD, PhD*
3. Adenoid Cystic Carcinoma: Clinical and Translational Advances – *Anuraag Parikh, MD*
4. PRMT5 Inhibition Has a Potent Anti-Tumor Activity Against Adenoid Cystic Carcinoma of Salivary Glands – *Evgeny Izumchenko, PhD*
5. Merkel Cell Carcinoma – *Jason Rich, MD*
6. Nasopharyngeal Carcinoma – *Hyunseok Kang, MD*
7. Q&A

5:00 pm – 6:00 pm   Grand Ballroom EF

AHNS Business Meeting

6:00 pm – 7:00 pm   Grand Ballroom EF

Fellowship Information Session

The AHNS Advanced Training Council's Fellowship Information Session presents information about the many Head & Neck and Endocrine fellowship opportunities offered through the Society. Fellowship directors from AHNS-accredited programs will be on hand to introduce themselves and talk with potential fellowship applicants. Information about the fellowship application and match process will also be available.

6:00 pm – 7:30 pm   Grand Hall IJ

NRG-HN006 Clinical Trial Update: Randomized Phase II/III Trial of Sentinel Lymph Node Biopsy Versus Elective Neck Dissection for Early-Stage Oral Cavity Cancer

Presenter: Stephen Lai, MD, PhD

SCIENTIFIC PROGRAM

Thursday, May 16, 2024

7:00 am – 5:00 pm   Skyway 260

Centurion Lounge

7:00 am – 8:00 am   Grand Ballroom EF

Research Award Ceremony

Moderator: Miriam Lango, MD
The University of Texas MD Anderson Cancer Center, AHNS Publication & Awards Service Chair

8:00 am – 9:00 am   Grand Ballroom EF

Hayes Martin Lecture: The Preventive HPV Vaccine: Reducing the Risk of Orophayrnx and other HPV associated Cancers

Introduction: Nicole Schmitt, MD, FACS
Keynote Speaker: Douglas Lowy, MD

9:00 am – 9:45 am   Grand Ballroom EF

Difficult/Scary Cases

Moderator: Steve Chinn, MD, MPH, BS
Panelists: Danny Enepekides, MD, FRCS, Ian Ganly, MD, PhD, Miriam Lango, MD, Kyle Mannion, MD

This session offers a comprehensive discussion of challenging cases, including resection and reconstruction of advanced oral cavity, anaplastic thyroid cancer, salvage surgery, and advanced skin cancer. The panel will present four cases to experts to facilitate insightful discussions on the complex surgical and reconstructive decision-making in complex head and neck cancer care.

At the conclusion of this session participants will be able to:

- » Navigate the challenges of complex oncologic surgery, adaptive surgical approaches, and decision-making under complex scenarios.
- » Recognize the challenges associated with response adjusted surgery for advanced cancers.
- » Understand innovative techniques in reconstruction in complex cases.

1. Case Presentation and Discussion #1: Oral Cavity
2. Case Presentation and Discussion #2: ATC
3. Case Presentation and Discussion #3: Salvage Surgery
4. Case Presentation and Discussion #4: Advanced Skin
5. Q&A

9:00 am – 9:45 am   Grand Hall IJ

Scientific Session 3: Mucosal

Moderators: Kathryn Van Abel, MD and Daniel Clayburgh, MD, PhD, FACS

1. Investigation of the early neoplastic transformation of oral squamous cell carcinoma using genetically engineered mouse organoids – *Casey A. Collet, BS*
2. DNA Damage Precedes Viral Integration in HPV-Transformed Tonsillar Keratinocytes – *Kimberly Chan, MD*
3. Is Pathological complete response (PCR) a surrogate endpoint of overall survival in patients with technically unresectable oral cavity cancers? A real world data of 900 plus patients – *Shatabdi Chakraborty*
4. Rates of Recurrence in Patients with Early-Stage Oral Tongue Cancer Managed with Surgery Without Postoperative Radiation – *Mae Wimbiscus, BA*
5. Survival Outcomes in Recurrent Oral Cavity and Oropharyngeal Squamous Cell Carcinoma – *Isaac Solomon, BA*
6. Characterization of the Oral Cavity Microbiome in Patients with OCSCC and Leukoplakia – *Ann Powers, MD*

9:45 am – 10:15 am   Break with Exhibitors   Riverside Exhibit Hall

SCIENTIFIC PROGRAM

Video Session: Advancements in Surgical Innovation - Head and Neck Surgery and Reconstruction

Moderator: Katelyn Stepan, MD, BA

We will use case management format to discuss advancements in head and neck surgery including integrating institutional 3D printing for craniofacial reconstruction, remote-access thyroidectomy, and lateral arm reconstruction for parotid defects.

At the conclusion of this session participants will be able to:

» Describe benefits of 3D printing applications in craniofacial reconstruction.

» Compare and contrast the most common remote-access thyroid and parathyroid techniques currently used.

» Identify reconstructive advantages of the lateral arm for parotid reconstruction.

1. Introduction – *Katelyn Stepan, MD, BA*
2. Craniofacial Reconstruction with Institutional 3D Printing – *Kyle VanKoevering, MD*
3. *Q&A*
4. Remote-Access Thyroidectomy – *Jeremy Richmon, MD, FACS*
5. Q&A
6. Lateral Arm Reconstruction for Parotid Defects – *Stephen Kang, MD*

Skull Base Tumor Board

Moderator: Ian Witterick, MD, MSc, FRCSC
Panelists: Ivan El-Sayed, MD, Marc Cohen, MD, PhD, Ari Rosenberg, MD, Larissa Sweeny, MD

We will use a case management format to discuss tumor subtypes, orbital preservation, induction chemotherapy, long-term complications and provide an update on sinonasal tumor management.

At the conclusion of this session participants will be able to:

» Choose treatment modalities for management of different types of sinonasal malignancies.

» Develop a management strategy for preservation or sacrifice of the orbit.

» Recognize long-term complications associated with treatment of sinonasal malignancies.

1. Case and Panel Discussion

Jatin Shah Symposium: Genomic Landscape of HNSCC: Where We Are and Where We Are Going

Moderator: Richard Wong, MD, FACS

A series of presentations will describe the genomic, transcriptomic, proteomic, immune and microbial landscapes and heterogeneity of head and neck squamous cell carcinoma. Recent discoveries in these topics and the clinical implications of new findings will be emphasized, with presentation of an original abstract as well.

At the conclusion of this session participants will be able to:

» Demonstrate an understanding of the genomic, transcriptomic, proteomic, immunologic, and microbial landscapes as well as tumor heterogeneity in head and neck squamous cell carcinoma.

» Recognize the impact of these various landscapes on the development of novel biomarkers for head and neck squamous cell carcinoma.

» Develop an understanding of how multi-omics can be deconvoluted to impact clinical decision making and generate novel therapies for head and neck cancer.

1. Introduction – *Richard Wong, MD, FACS*
2. Mutational Landscape and Dynamic Tumor DNA Biomarkers in Head and Neck Squamous Cell Carcinoma – *Nishant Agrawal, MD, FACS*
3. Going Down the Rabbit Hole: Tumor Heterogeneity in Head and Neck Cancer – *Sidharth Puram, MD, PhD, FACS*
4. Proteomics in Head and Neck Cancer: Lessons Learned and Current Directions – *Ben Major, PhD*
5. Immune Landscape of Head and Neck Cancer – *Nicole Schmitt, MD*
6. Association of Novel Tumor-Immune Microenvironment Measurements with Recurrence Outcomes in Head and Neck Cancer Patients Receiving Definitive Organ Preservation Therapy – *William J. Benjamin, MPH*
7. New Directions in Microbiome Research Across Oncology – *Susan Bullman, PhD*
8. Transcriptomic Landscape of Head and Neck Cancer – *Neil Hayes, MD, MPH, MS*
9. Q&A

SCIENTIFIC PROGRAM

12:00 pm – 1:00 pm	Lunch with Exhibitors	Riverside Exhibit Hall

1:00 pm – 1:45 pm — Grand Ballroom EF

Reconstructive Challenges in Special Populations

Moderator: Shaum Sridharan, MD

This session will use case examples to highlight the unique challenges encountered when considering reconstruction in specific populations, including children, the elderly, and the previously treated patient.

At the conclusion of this session participants will be able to:

» Understand the unique considerations behind pediatric free flap surgery including differences between pediatric and adult patients, development of a reconstruction paradigm in pediatric patients, and understanding how free tissue reconstruction in pediatrics allows for wider applications of oncologic principles.

» Identify effective strategies for reconstruction in compromised necks, including alternative donor and recipient vessels, vein grafting, and locoregional salvage options.

» Become familiar with practical considerations around free tissue reconstruction in the elderly, perioperative management of comorbid conditions, and outcomes.

1. Special Considerations for Pediatric Free Tissue Transfer – *Mark El-Deiry, MD FACS*
2. The Vessel-Depleted Neck – *Sarah Rhode, MD, MMHC*
3. Reconstruction in Older Adults: Risks and Benefits of Different Options – *Patrik Pipkorn, MD, MSCI*
4. Finite-element Analysis of Optimal Mandibular Osteotomy Angles to Optimize Reconstructive Plate Stress for Patients Undergoing Simulated Mandibular Body Reconstruction – *Hugh A. Kim, MD*

1:45 pm – 2:45 pm — Grand Ballroom EF

Evolution of Immunotherapy in Head and Neck Cancer

Moderator: Sufi Thomas, PhD

This session will highlight key developments and future directions in immunotherapy for head and neck cancer. Leaders in the field will discuss treatment paradigms in the R/M and PULA settings and current criteria for patient selection based on biomarker profiles.

At the conclusion of this session participants will be able to:

» Articulate the current immunotherapy paradigms in the R/M and PULA settings.

» Select patients for immunotherapy based on biomarker profiles.

» Identify priority areas for future studies.

1. Combination Therapy for the Recurrent/Metastatic Setting – *Marcelo Bonomi, MD*
2. Immunotherapy in the PULA Setting (Not Neo-Adjuvant Surgical Setting) – *Quynh-Thu Le, MD*
3. Biomarkers and Patient Selection – *Adam Luginbuhl, MD*
4. Immunogenicity and Efficacy of an E6/E7-Targeted Prophylactic MRNA Lipid Nanoparticle Vaccine for Oropharynx Cancer – *Natalie Silver, MD, MS, FACS*
5. Neoadjuvant Cytokine (IRX-2) Immunotherapy for Resectable Oral Cavity Carcinoma: Final Results of the INSPIRE Trial – *Gregory T. Wolf, MD*
6. Panel Discussion

1:00 pm – 1:30 pm — Grand Hall IJ

Premalignant Lesions: Progress and Opportunities

Moderator: Kerstin Stenson, MD, FACS

Oral premalignant lesions will be discussed in relation to their pathogenesis and diagnosis. Specific focus on types of surgical treatment and up-to-date, novel clinical trials will be presented.

At the conclusion of this session participants will be able to:

» Explain the mechanisms by which oral premalignant lesions develop into invasive cancer.

» Understand methods to diagnose oral premalignant lesions and recognize when surgery should be offered.

» Recommend various treatment strategies including chemoprevention, surgery and current clinical trials.

1. Introduction – *Kerstin Stenson, MD, FACS*

2. Premalignant Lesions: When and How to Operate – *Alexandra Kejner, MD*
3. Clinical Trials for Premalignant Lesions – *Jennifer Gross, MD*
4. Q&A

1:30 pm – 2:45 pm   Grand Hall IJ

New Technologies in Head and Neck Cancer

Moderator: Urjeet Patel, MD, FACS

We will use a lecture format to briefly cover a variety of emerging practices in head and neck surgery which all demonstrate use of new technology to advance the field. We will ensure adequate time for questions from the audience for all speakers.

At the conclusion of this session participants will be able to:

» Integrate emerging techniques that employ new technology.

» Evaluate technologic innovation and compare outcomes to standard practices.

» Recognize bona fide advances and implement change in clinical practice where warranted.

1. Unlocking Predictive Biomarkers in Oral Cancer through Integrated Bioinformatics and Spatial Profiling – *Michael M. Allevato, PhD*
2. Swallow Watch: An Automated Dysphagia Alert Program for Patients with Head and Neck Cancer Treated with Radiotherapy – *Yue Ma, MD*
3. Advances in Robotics in Head and Neck Cancer – *Ryan Jackson, MD*
4. Parathyroid Imaging – *Marika Russell, MD, FACS*
5. Intra-Operative Margin Imaging – *Andrew Birkeland, MD*
6. Augmented Reality – *Michael Topf, MD*
7. Artificial Intelligence in Head and Neck Surgery – *Robert Brody, MD, BA*
8. Q&A

2:45 pm – 3:15 pm   **Break with Exhibitors**   **Riverside Exhibit Hall**

3:15 pm – 4:00 pm   Grand Ballroom EF

Dealer's Choice: Latest and Greatest Clinical Trials

Moderator: Jamie Ku, MD, BS

Key clinical trials experts will present one clinical trial, recently completed or ongoing, of their choice that they feel has the potential to or has already had a significant impact in the field of head and neck oncology. We will discuss why the trial was chosen, how it has changed the field or its practice-changing implications, how the trials are incorporated in multi-disciplinary discussions, and any future directions.

At the conclusion of this session participants will be able to:

» Identify four practice-changing clinical trials that are ongoing or recently completed in the field of head and neck oncology.

» Explain why these clinical trials are practice-changing or have the potential to significantly impact the way we treat our head and neck cancer patient population.

» Practically apply the completed clinical trials into the multi-disciplinary management of head and neck cancer patients or understand how these trials will impact patient care in the near future.

1. Introduction – *Jamie Ku, MD, BS*
2. Clinical Trials for Lymph Node Sparing Radiation Treatment – *John de Almeida, MD, MSc*
3. Incorporating Immunotherapy in the Definitive Therapy Setting: A Closer Look at EA3161 – *Julie Bauman, MD*
4. Hiding in Plain Sight - The Cisplatin Ineligible Population: NRG HN004 & HN012 – *Vanita Takiar, MD*
5. Xevinapant in Head and Neck Cancer: Putting the Pop in Apoptosis – *Julie Bauman, MD*

3:15 pm – 4:00 pm   Grand Hall IJ

Scientific Session 4: Potpourri

Moderators: Catherine Haring, MD and Tammara Watts, MD, PhD

1. Using Artificial Intelligence to automate the extraction of staging criteria from the electronic health records of oropharyngeal cancer patients – *Elif Baran*
2. Does Central Neck Dissection Negatively Influence Hypoparathyroidism After Angiography-Guided Thyroidectomy? – *Pablo Moreno Llorente, PhD, MD, FEBS*
3. A Novel Technique for In-Office Secondary Tracheoesophageal Prosthesis Placement with Immediate Voicing in Post-Laryngectomy Patients – *Abdullah Adil, MD*
4. Impact of Second Touch Visits Before Surgical Intervention on Postoperative Radiation Therapy (PORT) Delays – *Antonio Bon Nieves, BS*
5. Impact of Timely Postoperative Radiation Therapy (PORT) on Survival Outcomes in Head and Neck Cancer Patients – *Niketna Vivek*

4:00 pm – 5:00 pm   Grand Ballroom EF

HPV+Oropharyngeal Squamous Cell Carcinoma

Moderator: Vikas Mehta, MD

The goal of this session will be to discuss the latest evidence and future directions regarding the diagnosis and management of HPV-positive oropharyngeal cancer. The topics that will be covered include: 1) The use of circulating tumor DNA for diagnosis, prognosis, therapeutic decision-making and surveillance, 2) Consideration of contralateral and retropharyngeal nodal metastases 3) Current and future de-escalation trials/strategies.

At the conclusion of this session participants will be able to:

» Identify the use of circulating tumor DNA for diagnosis, prognosis, therapeutic decision-making and surveillance.

» Recognize the risk factors for contralateral and retropharyngeal nodal metastases and how to incorporate these factors into the therapeutic approach.

» Demonstrate an understanding of current and future de-escalation trials/strategies.

1. Current State of HPV + OPSCC – *Vikas Mehta, MD*
2. Circulating Tumor HPV DNA in the Clinic: From Diagnosis to Surveillance – *Eleni Rettig, MD*
3. Management of the Neck in HPV+ Oropharyngeal Squamous Cell Carcinoma: Controversies in the Era of De-escalation – *Apostolos Christopoulos, MD, MSc*
4. Personalizing Treatment Deintensification for HPV-associated Oropharynx Cancer – *Barbara Burtness, MD*
5. Survival Outcomes for Subjects Enrolled in a Single Arm, Open Label Trial of Therapy De-escalation in Patients With Stage I-III HPV + Oropharyngeal SCC – *Herschel Patel, MD*
6. Impact of Induction Chemotherapy on Circulating Tumor DNA in HPV-Associated Oropharyngeal Cancer – *Christopher J. Hughes, MBBS*
7. Saliva Compared to Blood-based Cell-free Tumor DNA in HPV-negative Head and Neck Squamous Cell Carcinoma – *Liyona Kampel, MD, PhD*

4:00 pm – 5:00 pm   Grand Hall IJ

Reconstruction Debates Part I: Virtual Surgical Planning vs Free Hand Reconstruction of Oromandibular Defects

Moderator: Neal Futran, MD, DMD

We will use a case management format to illustrate the oromandibular defect and determine parameters for reconstruction. Panelists will take a position for virtual surgical planning or free hand reconstruction of the defect.

At the conclusion of this session participants will be able to:

» Distinguish the different options for reconstruction of the oromandibular defect.

» Differentiate the differences between virtual surgical planning and free hand reconstruction of the defect.

» Select the appropriate reconstructive technique for reconstructing oromandibular defects.

1. Introduction and Case Presentation – Neal Futran, MD, DMD
2. Pro-free Hand Position – Matthew Spector, MD
3. Pro-VSP Position – Matthew Old, MD
4. Pro-free Hand Response – Matthew Spector, MD
5. Pro-VSP Response – Matthew Old, MD
6. Wrap up and Audience Poll – Neal Futran, MD, DMD

Reconstruction Debates Part II: Palliative Surgery

Moderator: Susan McCammon, MD

We will use a case-based discussion to examine treatment options using palliative surgery vs. non-surgical approaches for symptom management and preventive measures to improve the quality of life. We will also discuss how to discuss uncertainties of relatively new non-surgical approaches and prognosis with limited data.

At the conclusion of this session participants will be able to:

» Distinguish palliative and curative intent in surgical and nonsurgical treatments and recognize the impact of risk tolerance and toxicity profile in patient decision making.

» Recommend treatment options using palliative surgery vs. non-surgical approaches to improve the quality of life, differentiating current- versus future-state suffering.

» Integrate patient-specific factors into treatment recommendations with prognostic uncertainty in relatively new non-surgical approaches.

1. Introduction – *Susan McCammon, MD*
2. Surgical Treatment with Palliative Intent – *Greg Farwell, MD, FACS*
3. Nonsurgical Treatment with Palliative Intent – *Christine Chung, MD*

4:13 pm – 5:00 pm   Grand Ballroom AB

Combined ARS and AHNS Panel: ICSNT: How It Can Help Your Practice

Moderator: Edward Kuan, MD, FARS
Panelists: Daniel Beswick, MD, FARS; Nyall London, MD, FARS; James Palmer, MD, FARS; Timothy Smith, MD, FARS; Shirley Su, MD; Eric Wang, MD, FARS; Marilen Wang, MD, FARS

5:00 pm – 5:30 pm   Grand Ballroom EF

Panel Discussion: Update on Focused Practice Designation for Complex Thyroid/Parathyroid Surgery

Moderator: Michael Singer, MD
Panelists: Elizabeth Cottrill, MD, Brian Nussenbaum, MD, MHCM, Gregory Randolph, MD, David Steward, MD

A new focused practice designation (FPD) for adult complex thyroid and parathyroid surgery, co-administered by the American Board of Otolaryngology–Head and Neck Surgery (ABOHNS) and the American Board of Surgery (ABS), will offer head and neck surgeons the opportunity to demonstrate their particular expertise in this area. The background for this designation, the process for application and its potential impact on the field will be discussed.

At the conclusion of this session participants will be able to:

» Differentiate between subspeciality certification and focused practice designation.

» Articulate the pathways and process by which the FPD for adult complex thyroid and parathyroid surgery will be able to be obtained.

» Assess the potential value for their practice of applying for the FPD for adult complex thyroid and parathyroid surgery.

1. Introduction – *Michael Singer, MD*
2. Introduction to Process & Timing of FPD – *Brian Nussenbaum, MD, MHCM*
3. Panel Discussion: Background of FPD, Impact on Head and Neck Practices, Impact on Residencies and Training/Fellowships

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5:30 pm – 7:00 pm   Riverside Exhibit Hall

Poster Session and "Meet the Authors" Poster Tours

7:00 pm – 8:00 pm   Grand Hall LMN

President's Reception

Please join AHNS President, Dr. Robert Ferris, for complimentary drinks and appetizers. This is open to all AHNS attendees.

ORAL PAPERS

Panel Discussion: Neoadjuvant Immunotherapy: Standard of Care and Ongoing Trials

(Wednesday, May 15, 2024 | 11:15 AM - 12:00 PM)
Room: Grand Ballroomo GHIJ

AHNS01: RESPONSE-ADAPTED ONCOLOGIC SURGERY FOR CUTANEOUS SQUAMOUS CELL CARCINOMA: PERSONALIZED APPROACH IN THE IMMUNOTHERAPY ERA - Shorook Naara, MD, PhD[1]; Dan Yaniv[1]; Jobran Mansour[1]; Priyadharsini Nagarajan[2]; Michael R Migden[3]; Jeffrey N Myers[1]; Ehab Y Hanna[1]; Neil D Gross[1]; Moran Amit[1]; [1]Department of Head and Neck Surgery, MD Anderson Cancer Center, Houston, Texas; [2]Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, Texas; [3]Department of Dermatology, The University of Texas MD Anderson Cancer Center, Houston, Texas

Background: Non-melanoma skin cancer, specifically cutaneous squamous cell carcinoma (cSCC), exhibits remarkable responsiveness to immunotherapy.In a phase 2 trial, 75% of patients with stage III/IV resectable cutaneous squamous cell carcinoma of the head and neck treated with neoadjuvant cemiplimab exhibited complete or major pathologic responses and median recurrence free survival of 42.3 months.In select cases, post-neoadjuvant treatment, surgical resection may encompass the new residual tumor area, rather than the initial tumor, influenced by the assessment of treatment response and the surgeon's discretion. Response-adapted oncologic surgery refers to a smaller extent resection based on the post-immunotherapy tumor size rather than the original tumor size. Given the promising response rate to neoadjuvant treatment and the morbidity associated with cSCC excision in the head and neck region, we sought to retrospectively analyze the surgical resection extent.

Aim: This study aimed to assess whether "response-adapted oncologic surgery" (RAOS), surgical resection based on the post immunotherapy tumor extent, is non-inferior to "standard resection" (SR),surgical resection in patients treated with neoadjuvant immunotherapy for head and neck cutaneous SCC,in terms of final margins and survival outcomes.

Methods: A retrospective analysis was conducted at a tertiary cancer center, encompassing patients who underwent neoadjuvant treatment followed by surgical resection for head and neck cutaneous SCC between 2018-2021. The extent of oncologic surgical resection was determined by the discretion of head and neck surgeons.We performed a clinical correlation assessment between clinical and imaging evaluation of tumor size. Primary outcome measures included pathological margin status, with secondary outcomes focusing on progression-free survival(PFS) and disease-specific survival(DSS).

Results: Forty-two patients were included in the study, with a mean age of 72 years. Of these,35 were males, and 22 were in stage III-IV.Tumor size assessment, via imaging or clinical evaluation, demonstrated a correlation of 84%, suggesting a relatively strong agreement between the tumor size determined through physical examination and imaging methods. Nineteen patients underwent RAOS, while the remaining had SR. In the RAOS group, resection extent was 46% in the length and width dimensions from what would have been the resection extent if SR was employed. Analysis of final surgical margins revealed that 84.2% of the RAOS group had negative margins, 10.5% had close margins, and 5.2% had positive margins, compared to 91.3%, 0%, and 8.7% in the SR group, respectively (p=0.18). Survival analysis indicated comparable rates of local and regional recurrence between both groups (p=ns). The 2-year PFS was 84% in SR versus 80% in the RAOS group (p=0.44), while the 2-year DSS was 75% in SR and 90% in RAOS (p=0.32).

Conclusion: Our data suggest that in the era of neoadjuvant immunotherapy for cSCC, response-adapted oncologic surgery is non-inferior to standard resection (SR). This study underscores the importance of personalized approaches, incorporating pretreated tumor size and stage considerations, in the paradigm shift towards optimizing outcomes for cutaneous squamous cell carcinoma patients. The findings advocate for including prospective response-adapted oncologic surgery as an outcome measure in phase 3 trials to assess the safety of RAOS in the context of immunotherapy aiming for organ preservation and minimizing surgical morbidity.

Scientific Session 1: Recon/QOL

(Wednesday, May 15, 2024 | 11:15 AM - 12:00 PM)
Room: Grand Ballroom EF

AHNS02: IMPACT OF BASELINE EMOTIONAL DISTRESS ON LONG-TERM QUALITY OF LIFE IN HEAD AND NECK CANCER PATIENTS - Kimberly Oslin, MD[1]; Eric Adjei Boakye, PhD, MA[2]; Samantha Tam, MD[1]; Courtney Rose[3]; Kyle Leonard, MD[1]; Veronica Bernacchi, PhD, RN[4]; Steven S Chang, MD[1]; Suhael Momin, MD[1]; Farzan Siddiqui, MD, PhD[5]; Vivian F Wu, MD, MPH[1]; Amy Williams, PhD, LP[6]; [1]Department of Otolaryngology - Head & Neck Surgery, Henry Ford Health System; [2]Department of Public Health Sciences, Henry Ford Health System; [3]Department of Research Design and Analysis, Henry Ford Health System; [4]College of Nursing, Michigan State University; [5]Department of Radiation Oncology, Henry Ford Health System; [6]Office of Professionalism and Physician Wellness, Beaumont Health

Introduction: Psychosocial symptoms (e.g., emotional distress, anxiety, and depression) are under-recognized and under-treated in patients diagnosed with cancer. Head and neck cancer (HNC) patients are particularly vulnerable to poor psychosocial health due to the often disfiguring and permanently life-altering nature of HNC treatment. Prior research suggests that psychosocial symptoms contribute to poor quality of life in HNC patients. However, the association between pre-cancer treatment anxiety and depression on quality of life after HNC treatment is unknown. This study examined the associations between pre-treatment anxiety and depression and long-term quality of life among patients with HNC.

Methods: This is a retrospective study of patients diagnosed with HNC (between 2015 and 2022) who engaged in psychosocial evaluation with psych-oncology at a tertiary care center in the Midwest prior to treatment. Data was collected through two surveys, the Hospital Anxiety and Depression Scale (HADS) and the Functional Assessment of Cancer Therapy – Head & Neck (FACT-HN). HADS is a self-reported screening questionnaire for emotional distress, and FACT-HN is a patient-reported instrument that assesses physical, social/family, emotional, and functional well-being as well as HNC-specific symptoms.

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The exposure variables were the two HADS 7-item subscales that measure depressive (HADS-D) and anxious (HADS-A) symptoms in the prior week, which were collected during the pretreatment evaluation. We classified the scores as normal (0–7) vs. mild/moderate/severe (8–21). The outcome variables were the FACT-HN subscales (i.e., social/familial, emotional, functional, and physical well-being) collected during follow-up (i.e., 2-3 years after cancer diagnosis). Mann-Whitney U tests were used to examine the association between HADS-D and HADS-A and each of the four FACT-HN subscales.

Results: This study included 47 patients who presented for their two- or three-year follow-up with a median age of 65.5 years. Of the 47 patients, 12.8% reported mild to severe depressive symptoms and 23.4% mild to severe anxious symptoms prior to treatment. The median social/familial well-being score was 24.5 (IQR=21.0-26.0), emotional well-being was 19.0 (IQR=14.0-20.0), functional well-being was 21.0 (IQR=13.0-26.0) and physical well-being was 26.0 (IQR=20.0-28.0). In bivariate analyses, there were statistically significant associations between HADS-A and physical (P<0.0001), emotional (P=0.0003), and functional (P=0.0098) well-being. Patients with mild to severe anxiety reported worse physical (median=18.0 vs. 27.0), emotional (12.0 vs. 19.6), and functional (13.0 vs. 22.5) well-being than those that reported no anxiety. HADS-D was significantly associated with physical (P=0.0067) and functional (P=0.0558) well-being. Patients who experienced mild to severe depression reported worse physical (19.0 vs. 27.0) and functional (10.0 vs. 22.0) well-being than those that reported no depression.

Conclusions: Patients with higher anxiety and depression prior to HNC treatment were found to have worse self-reported physical and functional well-being even two or three years from the end of their treatment. Additionally, higher pretreatment anxiety was associated with poorer posttreatment emotional well-being. These results highlight the urgent need for psychosocial assessment and care to optimize HNC outcomes, such as quality of life, especially in patients identified to be at risk prior to treatment.

AHNS03: TRAJECTORIES OF NECK DISABILITY AND DYSPHAGIA SYMPTOMS IN SURVIVORS OF HEAD AND NECK CANCER - Marci L Nilsen, PhD, RN, CHPN, FAAN[1]; Jinhong Li, MS[2]; Jonas T Johnson, MD[3]; Fendi Obuekwe, BS[3]; Sara Piva, PhD, PT[4]; James L Coyle, PhD, CCCSLP[4]; Health Skinner, MD, PhD[3]; Dan P Zandberg, MD[3]; Mario G Solari, MD[3]; Susan Sereika, PhD[1]; [1]University of Pittsburgh, School of Nursing; [2]University of Pittsburgh, School of Public Health; [3]University of Pittsburgh, School of Medicine; [4]University of Pittsburgh, School of Health and Rehabilitation Sciences

Objective: Emerging evidence suggests that neck disability and impairment often coincide with other negative treatment outcomes, particularly dysphagia, in individuals who receive radiation for head and neck cancer (HNC). In cross-sectional studies, increased neck disability and impairment were associated with worsening patient-reported dysphagia symptoms and higher rates of penetration/aspiration. However, few studies have described the evolution of neck disability and dysphagia over time in this population. This analysis aimed to describe the trajectories of neck disability and dysphagia following diagnosis and treatment of HNC and to determine predictors of trajectory group membership.

Methods: Survivors diagnosed with head and neck squamous cell carcinoma of the oral cavity, oropharynx, and laryngopharynx and treated with radiation were included in the analysis. Survivors diagnosed with recurrence, second primary, or distant metastasis were excluded. All survivors were seen at a multidisciplinary HNC survivorship clinic between 2017 to 2022 and completed validated patient-reported outcome measures (PROMs) during their visit. Neck disability and symptoms of dysphagia were measured using the Neck Disability Index (NDI) and Eating Assessment Tool-10 (EAT-10), respectively. Higher scores on the PROMs indicate worsening symptoms burden. PROMs were measured at pre-treatment through 16 months post-radiation, with all survivors having at least three visits. Group-based trajectory modeling was employed to reveal distinct trajectories and identify predictors of trajectory group membership for neck disability and dysphagia following diagnosis through treatment. Dual trajectory analysis was used to explore the association between NDI and EAT-10.

Results: The majority of the survivors were white (91.3%), male (83.9%), and married (67.4%), with an average age of 66.7 years (range: 41-88, SD=8.7). The primary cancer site was the oropharynx (48.4%), followed by oral cavity (33.3%) and laryngopharynx (18.3%). Most survivors with an oropharyngeal primary were HPV+ (84.6%). At the time of diagnosis, most survivors presented with advanced-stage disease (III/IV, 65.6%) and underwent surgery plus adjuvant treatment (58.9%). Of the survivors who underwent surgery, 92.5% underwent a neck dissection. For NDI (n=93), the following three trajectories were identified: 1) stable-mild, 2) curvilinear-decreasing from moderate to mild, then increasing to moderate, and 3) stable-moderate/severe. Surgery plus adjuvant treatment (OR=4.03, p=.032) and neck dissection (OR=4.50, p=.025) were associated with increased odds of being in group 2 (i.e., curvilinear-decreasing from moderate to mid then increasing to moderate) compared to membership in group 1 (stable-mild). Two trajectories were also identified for EAT-10 (n=100): 1) stable-significant symptoms (i.e., risk of residual/aspiration), and 2) linearly decreasing symptoms, but swallow remains impaired. No significant predictors of dysphagia trajectory group membership were identified. Dual trajectory analysis revealed a strong relationship between the developmental trajectories for neck disability and dysphagia based on either conditional or joint probabilities.

Conclusion: While some trajectories suggest improvement of symptoms over time, HNC survivors who undergo multimodal therapy or a neck dissection are at risk for increasing neck disability over time. Moreover, our analysis highlighted that some HNC survivors experience persistent and significant symptoms of dysphagia and neck disability. A more robust, longitudinal study, including objective measures of symptoms, is needed to confirm these findings.

AHNS04: THE 5 ITEM MODIFIED FRAILTY INDEX PREDICTS POSTOPERATIVE MORBIDITY, NOT SURVIVAL FOLLOWING LARYNGECTOMY - Eoin F Cleere, MB, BCh, MCh; Justin Hintze; David Brinkman; James Griffin; Conrad Timon; John Kinsella; Paul Lennon; Conall Fitzgerald; St James' Hospital, Dublin, Ireland

Introduction: Surgical decision making in advanced laryngeal and hypopharyngeal tumours is complex. Given the reported rates of major complications, clinicians must consider patients suitability to undergo resection of these tumours. Frailty (a state of reduced physiologic reserves and functional decline) is a potential marker of patients at risk of increased postoperative

morbidity. We sought to analyse if frailty (measured using the 5-item modified frailty index (5mFI)) predicted increased complications following laryngectomy surgery. Secondarily, we aimed to assess if patients with laryngeal or hypopharyngeal cancers identified as frail using the 5mFI had a reduced overall survival (OS) following these procedures.

Methods: We performed a STROBE-compliant retrospective study of patients over a 10-year period (2013 – 2022) at our institution. Patients who underwent a laryngectomy, pharyngo-laryngectomy or a pharyngo-laryngo-oesophagectomy were considered for inclusion. Partial laryngectomy surgeries and surgical cases that were abandoned due to unresectable tumours were excluded. For the purposes of analysis, patients were classified as non-frail (5mFI 0-1) or frail (5mFI 2-5) based on their 5mFI scores. Confounding variables were controlled when analysing postoperative morbidity by multivariable regression and case matching was performed for analysis of 3-year OS.

Results: A total of 233 laryngectomy surgeries were performed during the 10-year period with 82 (35.2%) being classified as frail and 151 (64.8%) as non-frail using the 5mFI. Total laryngectomy was performed in 157 patients (67.4%), followed by pharyngo-laryngo-oesophagectomy in 47 patients (20.2%), and pharyngo-laryngectomy in 29 patients (12.4%). Eighty-nine patients underwent salvage surgery (38.4%). The most frequent closure method was unsupported primary closure (104 patients, 44.6%) followed by primary closure with an onlay pectoralis major flap (58 patients, 24.9%), free flap closure (27 patients, 11.6%) and gastric pull-up (44 patients, 18.9%). There were no significant differences between frail and non-frail cohorts in terms of sex, smoking status, surgery performed, closure method, previous treatment or disease staging. Frail patients had a significantly greater mean age (66.3 years vs. 62.2 years, p=0.006). On multivariable regression, frail patients were significantly more likely to develop postoperative pharyngocutaneous fistula (OR 2.62, 95% CI 1.33 – 5.18, p=0.006), postoperative delirium (OR 4.71, 95% CI 2.45 – 9.02, p<0.001), require return to theatre (OR 3.46, 95% CI 1.77 – 6.76, p<0.001), increased hospital length of stay (LOS) (b 25.53 days, 95% CI 14.64 – 36.41, p<0.001) and be discharged to a non-home location (OR 5.31, 95% CI 2.49 – 11.35, p<0.001) with no difference in 90-day postoperative mortality. In case-matched patients, 3-year OS was similar in frail (47.1%, 95% CI 29.8% - 62.5%) and non-frail patients (50.0%, 95% CI 32.4% - 65.3%) (p=0.715).

Conclusions: Increased risk of postoperative morbidity and prolonged LOS is seen in patients classified as frail using the 5mFI following laryngectomy procedures. However, at 3 years, patients deemed as frail using the 5mFI do not have inferior OS, supporting the oncologic benefit of resecting advanced laryngeal or hypopharyngeal tumours in this cohort. Use of the 5mFI pre-operatively may allow identification of frail patients requiring increased supports in the peri-operative period to optimise their peri-operative risk.

AHNS05: IMPACT OF FRAILTY ON TREATMENT SELECTION IN LOCALLY ADVANCED LARYNGEAL SQUAMOUS CELL CARCINOMA - James R Xu, BS[1]; Danielle Bottalico, MD[2]; Chandana A Reddy, MS[3]; Robin Davis, MS[3]; Kathleen Dennert[3]; Eric D Lamarre, MD[2]; Neil M Woody, MD[3]; [1]Case Western Reserve University School of Medicine, Cleveland, OH; [2]Department of Otolaryngology, Head and Neck Institute, Cleveland Clinic, Cleveland, OH; [3]Department of Radiation Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH

Purpose/Objective(s): Frailty is a multidimensional syndrome of decreased endurance, strength, and physiologic reserve with increased vulnerability to stressors. Studies have examined the impact of frailty on surgical outcomes of head and neck cancers, but limited studies have explored the role of frailty in treatment decisions. Furthermore, few have controlled for cancer type and stage, which impact treatment paradigms, prognoses, and outcomes. Locally advanced (stage III/IV) laryngeal squamous cell carcinoma where laryngectomy remains an important curative tool is an area where selection of treatment for frail patients may be especially crucial. The primary objective of this study was to explore the role of frailty in treatment decisions in this group. As frailty may also have social and financial support implications, a secondary objective was to explore the potential role of socioeconomic determinants on treatment selection.

Materials/Methods: From an IRB-approved institutional registry, we identified patients with stage III/IV laryngeal squamous cell carcinoma treated between 2020 and 2022. For each patient, the 11-factor modified frailty index (mFI-11) was calculated. Functional health status was determined using Karnofsky Performance Scale (KPS), with a KPS less than 50 defined as impaired status. Frailty was defined as 3+ on mFI-11.

Treatment modality, tumor characteristics, demographics, recurrence, and survival outcomes were collected for each patient. Furthermore, socioeconomic support factors including history of mental illness, financial status, and presence of family or friend social support were evaluated. All statistical analyses were performed using SAS v9.4 with statistical significance set at p < 0.05.

Results: A total of 82 patients were identified, of whom 23.2% (19) were frail and 76.8% (63) were not frail. In the frail group, 57.9% were stage III compared to 36.5% in the non-frail group. In the frail group, 52.6% received chemoradiation, 36.8% received radiation only, and 10.5% received surgery. In the non-frail group, 63.5% received chemoradiation, 6.3% received radiation only, and 30.2% received surgery, revealing significantly greater rates of surgery in the non-frail group (p = 0.0032).

26 (31.7%) patients had limited financial support, 28 (34.1%) had a history of mental illness, and 5 (6.1%) had no social support. No statistically significant differences in the treatment modalities were noted when patients were stratified by these social variables.

Overall median survival time for all patients was 38 months, 61.4 months for non-frail patients, and 29 months for frail patients (p = 0.023). There was no statistically significant difference in the survival when stratified by the social variables.

Conclusion: Frailty is associated with treatment selection, and shared decision making is likely crucial specifically for frail patients. The sequelae of treatment, whether surgical, non-surgical or both, may be more harmful in frail patients if functional status is unacceptable even when cure is achieved or survival is increased. Further exploration of the appropriate selection of treatment strategy for frail laryngeal cancer patients is needed to better understand how to maximize cure and quality of life.

AHNS06: HARDWARE EXPOSURE FOLLOWING MANDIBULAR RECONSTRUCTION USING OSTEOCUTANEOUS VERSUS SOFT TISSUE MICROVASCULAR FREE TISSUE TRANSFER - Hasan Abdulbaki, BA[1]; Angeline A Truong, BS[1]; Chase M

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Heaton, MD[2]; Philip D Knott, MD[2]; Andrea M Park, MD[2]; Mary J Xu, MD[2]; Katherine C Wai, MD[2]; [1]University of California-San Francisco, School of Medicine; [2]Department of Otolaryngology-Head & Neck Surgery, University of California-San Francisco
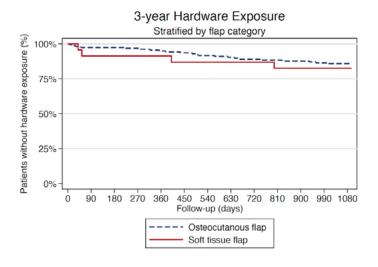
BACKGROUND: Hardware exposure following microvascular free tissue transfer (MFTT) can be a cause of significant morbidity. Osteocutaneous MFTTs are the preferred choice for mandibular defect reconstruction, yet occasionally, patient anatomy or medical comorbidities may not make them suitable candidates for bony reconstruction. In such cases, a soft tissue MFTT may be required. To date, however, data on the risk of hardware exposure in osteocutaneous MFTT compared to soft tissue MFTT remains limited.

OBJECTIVE: To compare the rate of and time to hardware exposure among patients undergoing osteocutaneous MFTT compared to soft tissue MFTT.

METHODS: Retrospective analysis of patients receiving MFTT at a tertiary care center between 11/2011-6/2023. Patients were excluded if they had a non-mandibular primary defect or their age was less than 18. The primary outcome was time to hardware exposure and the secondary outcome was rate of exposure stratified by follow-up period. Chi-squared tests and logistic regression were used for univariate analysis, where appropriate. Cox proportional hazard models were employed to analyze the relationship between time to hardware exposure in osteocutaneous versus soft tissue MFTT. *A priori*, we adjusted for adjuvant radiation and/or chemoradiation, diabetes or active immunosuppression, and indication for surgery (cancer versus non-cancer).

RESULTS: Overall, 178 patients were included. Of those, 155 (87.1%) received an osteocutaneous free flap surgery, and 23 (12.9%) received a soft tissue free flap surgery. Indication for surgery included tumor in 125 (70.2%) patients, osteoradionecrosis in 36 (20.2%) patients, trauma in 6 (3.4%) patients, and other causes in 10 (5.6%) patients. On univariate analysis, 25 (16.1%) osteocutaneous patients developed hardware exposure, compared to 4 (17.4%) soft tissue patients (p=0.878). Adjuvant radiation and/or chemoradiation was independently associated with a higher rate of hardware exposure (p=0.034). At 1 year, 8 (5.2%) of osteocutaneous patients and 2 (8.7%) of soft tissue patients developed hardware exposure. At 3 years, 22 (14.2%) osteocutaneous patients and 4 (17.4%) soft tissue patients developed hardware exposure. After adjustment, time to hardware exposure did not differ significantly between osteocutaneous patients and soft tissue patients at 1 year [HR 1.33 (95% CI 0.27-6.60), p=0.728] or 3 years [HR 1.01 (95% CI 0.33-3.04), p=0.988]. Hazard of hardware exposure was however increased with adjuvant radiation and/or chemoradiation at 1 year [HR 13.96 (95% CI 1.54-126.92), p=0.019] and at 3 years [HR 4.23 (95% CI 1.57-11.41), p=0.004].

CONCLUSIONS: Time to hardware exposure did not differ significantly between osteocutaneous and soft tissue free flap reconstruction, however adjuvant radiation and/or chemoradiation was associated with increased hazard of hardware exposure. Exposure rate increased by almost 10% from 1 year to 3 years postoperatively for both approaches. These data may help counsel patients on longer-term risk of MFTT for mandibular reconstruction.

3-year Hardware Exposure
Stratified by flap category

AHNS07: TRANEXAMIC ACID IN HEAD AND NECK MICROVASCULAR FREE FLAP RECONSTRUCTION -

Micah K Harris, MD[1]; Fuat B Bengur, MD[1]; Olivier Bourguillon, MD[1]; Lucien Khalil, MD[1]; Matthew Bottegal[1]; Joshua D Smith, MD[2]; Matthew E Spector, MD[1]; Kevin J Contrera, MD[1]; Mark Kubik, MD[1]; Mario G Solari, MD[1]; Shaum Sridharan, MD[1]; [1]University of Pittsburgh Medical Center; [2]University of Michigan

Introduction: Tranexamic acid (TXA) is commonly used in surgical settings to reduce blood loss. Due to its antifibrinolytic properties, TXA may increase the risk of thrombosis. In this study, we sought to evaluate the safety and efficacy of intraoperative TXA administration for head and neck free flap reconstruction.

Methods: A prospective cohort of patients from February 2021 to October 2023 were enrolled. Patients received three grams of intravenous TXA intraoperatively, in addition to topical TXA to the donor, recipient, and neck dissection sites. Patients were compared to a retrospective cohort from August 2019 to January 2021 who did not receive TXA. All patients, including those in the retrospective cohort, met criteria for TXA. Exclusion criteria included allergy to TXA, elevated creatinine, anticoagulation except aspirin, and history of intracranial bleeding, seizure disorder, or thromboembolic disease. Sociodemographic and comorbid variables were collected along with previous treatment history and perioperative details. Outcomes included postoperative hematoma formation, microvascular thrombosis, estimated blood loss (EBL), and transfusion rate. Multivariate linear and logistic regression were utilized to identify associations between predictors and outcomes.

Results: A total of 369 patients underwent free flap reconstruction (49.9% thigh, 25.5% fibula, 14.6% forearm, 10% other), of which 197 received TXA (33.3% female, 60.6 ±12.7 years old) and 172 did not (29.1% female, 61.1 ±13.2 years old). Average EBL was lower in the TXA group (193 ±100.6 mL *versus* 263.5 ±189.7 mL, p<0.001), as was the rate of postoperative transfusion (13.2% *versus* 31.4%, p<0.05). On multivariate linear regression, TXA administration was associated with decreased EBL when controlling for age, diabetes, operative duration, and ischemia duration (p<0.001). Moreover, TXA administration was associated with decreased postoperative transfusion rate on multivariate logistic regression when controlling for age and gender (OR 2.94, 95% CI 1.19-

7.25, *p*<0.05). In patients who received TXA *versus* those who did not, rates of postoperative hematoma formation (5.1% [2 donor and 8 recipient] *versus* 7.6% [6 donor and 8 recipient], *p*>0.05) and flap vascular compromise requiring operating room takeback (6.1% *versus* 8.1%, *p*>0.05) were similar.

Conclusion: The use of TXA in major head and neck microvascular reconstruction may be a safe adjunct to decrease blood loss and need for transfusion, with no increase in the rate of flap vascular compromise.

Panel Discussions: Disparities in Head and Neck Cancer Care: Are We Making Progress? What Are The Opportunities?

(Wednesday, May 15, 2024 | 1:00 PM - 2:00 PM)
Room: Grand Ballroom GHIJ

AHNS08: ASSESSMENT OF SOCIAL VULNERABILITY IN LARYNGEAL CANCER PROGNOSIS AND TREATMENT IN THE UNITED STATES - David J Fei-Zhang, BA[1]; Camaren M Cuenca, BS[2]; Angela D Haskins, MD[2]; Amy L Dimachkieh, MD[3]; Jill N D'Souza, MD[4]; Anthony M Sheyn, MD[5]; Jeffrey C Rastatter, MD, MS[6]; Daniel C Chelius, MD[3]; [1]Northwestern University - Feinberg School of Medicine; [2]Baylor College of Medicine; [3]Texas Children's Hospital; [4]Louisiana State University Health Sciences Center - School of Medicine; [5]St Jude Children's Research Hospital; [6]Ann & Robert H Lurie Children's Hospital of Chicago

Background: Studies investigating the impacts of social determinants of health (SDoH) on laryngeal cancer have focused on the impact of individual factors on patient outcomes, namely those of socioeconomic status, insurance status, and tobacco usage. This has often limited inquiry into the inter-relational influence of a broad range of SDoH and masked findings that may be generalizable to real-world contexts. Using the Center for Disease Control and Prevention's Social Vulnerability Index (SVI) and a national patient cohort from the SEER database, this study examines a wide scope of SDoH-factors and their interactions, specifically those of socioeconomic status, minority-language status, household composition, and housing and transportation, to quantify their differential associations as well as combined influence on laryngeal cancer prognosis, treatment, and follow-up.

Methods: This retrospective cohort study analyzed patients from 1975-2017 with laryngeal squamous cell neoplasms in the NCI-Surveillance, Epidemiology, and End Results Program (NCI-SEER) database. Overall social vulnerability and its contributions from 15 SDoH variables, grouped by socioeconomic status (SES), minority and language status (ML), household composition (HC), and housing and transportation (HT) were ranked and scored across all US counties, yielding a social vulnerability index (SVI). SVI scores were matched to each patient's county of residence as recorded by the NCI-SEER database and univariate linear regressions were performed on length of care (months of follow-up/surveyed) and prognosis (months survival) while univariate logistic regressions were performed on advanced staging at presentation and treatment modalities across SVI quintiles.

Results: Across 74,495 laryngeal cancer patients, 65-84 years (n = 34,651, 46.5%), male (n = 60,114, 80.7%), non-Hispanic white race/ethnicity (n = 56,606, 76.0%) were the most represented characteristics. Glottic (n = 39,779, 53.4%), supraglottic (n = 25,672, 34.5%), and subglottic (n = 1129, 1.5%) primary sites were well-represented. With increasing overall social vulnerability, there was a significant 34.37% (72.83 to 47.80 months) decrease in survival time and 28.09% (80.99 to 58.24 months) decrease in time under surveillance between the lowest and highest overall-social vulnerability groups. SES was the greatest contributor to these overall vulnerability trends for both survival and surveillance time, followed by HC and HT by magnitude. Advanced staging at presentation was associated with increasing overall social vulnerability (OR 1.15; 95%CI 1.13-1.16; p<0.001), with the highest contributors by magnitude to this overall vulnerability trend being SES, HC, and then HT. Higher overall social vulnerability was also associated with increased odds of receiving chemotherapy (OR 1.13; 95%CI 1.11-1.14; p<0.001) and decreased odds of surgical resection (OR 0.91; 95%CI 0.90-0.92; p<0.001) or radiation therapy (OR 0.97; 95%CI 0.96-0.99; p<0.001). All treatment receipt trends with increasing overall vulnerability saw similar per-magnitude contributions by SES, HC, and HT as prior.

Conclusions: In this SDoH-study of adults with laryngeal cancers, substantial decreases in care and prognosis were observed with increasing overall social vulnerability while delineating specific associations of several SDoH-themes. By adjusting for complex SDoH-interactions, our nuanced analysis elucidates the most pertinent social vulnerabilities of laryngeal cancer disparities to guide future research and initiatives.

AHNS09: SOCIAL DETERMINANTS OF HEALTH IN DONOR SITE MORBIDITY IN HEAD AND NECK CANCER RECONSTRUCTIVE LIMBS: ANTEROLATERAL THIGH AND FIBULA FREE TISSUE TRANSFERS - Emma Elbert, BS[1]; Kelly L Schmidt, MD[2]; Elena Doctor, MS, CSCS, CSPS[3]; Patrick Tassone, MD, MS[2]; Tabitha Galloway, MD, FACS[2]; [1]University of Missouri School of Medicine; [2]University of Missouri Department of Otolaryngology Head and Neck Surgery; [3]University of Missouri Therapy Services

Introduction: Free tissue transfer is a frequently utilized technique for complex head and neck cancer reconstruction. Despite the widespread use of free flaps, donor site morbidity and functional change remain understudied, especially in relation to the comorbid social issues common among head and neck cancer patients. The objective of this study is to identify morbidity and functional changes associated with lower extremity donor sites and to elucidate the role of the social determinants of health (SDoH) on postoperative outcomes among patients undergoing free flaps for head and neck oncologic reconstruction.

Methods: Information about demographics, insurance coverage, mobility status, rehabilitation service utilization, SDoH, and donor site outcomes was retrospectively collected on all head and neck oncologic reconstruction patients who underwent anterolateral thigh (ALT) or fibula free flaps at the University of Missouri from 2015 through 2022. Morbidity was defined as donor site complications including infection, seroma, hematoma, skin graft failure, tendon exposure, and postoperative falls that were documented within the one year postoperative period. The Healthy People 2030 model from the US Department of Health and Human Services was used to define our SDoH categorizations, which included economic

stability, education access and quality, healthcare access and quality, neighborhood and built environment, and social and community context. Statistical analysis was performed using Chi squared, Fisher exact, and two-tailed T tests where appropriate.

Results: 116 patients (91 male and 25 female) met inclusion criteria. Thirteen (17.6%) of the 74 ALT patients and 22 (52.4%) of the 42 fibula patients developed any donor site complication within the one year postoperative period. 53.4% of the population had at least one documented SDoH. No individual SDoH was associated with an increase in adverse donor site outcomes compared to patients without documented SDoH. However, 14.3% patients with two or more SDoH experienced flap failure compared to 1.1% the those with one or zero SDoH (p=.012). Within the subpopulation that had further post-discharge physical therapy recommendations, 72.7% of patients with SDoH failed to complete this therapy compared to 0% of patients with no SDoH (p=.026).

Conclusion: The presence of social determinants of health may place patients at increased risk for flap failure and failure to complete recommended physical therapy. Future investigation may help elucidate particular patient characteristics that link risk factors and outcomes. Quality initiatives should focus on improving donor site and flap outcomes for these at-risk groups of patients.

Panel Discussion: Translational Advances in Thyroid Cancer

(Wednesday, May 15, 2024 | 3:15 PM - 4:00 PM)
Room: Grand Ballroom GHIJ

AHNS10: SURGICAL AND ONCOLOGIC OUTCOMES OF CONVERSION SURGERY VS IMMEDIATE SURGERY FOR PATIENTS WITH LOW-RISK PAPILLARY THYROID CARCINOMA - Helena Levyn, MD; Daniel W Scholfield, MChB; Alana Eagan, MPH; Ashok R Shaha, MD, FACS; Richard J Wong, MD; Jatin T Shah, MD, PhD, Dsc; Ganly Ian, MD, MS, PhD; Luc G Morris, MD, MS; Robert M Tuttle, MD; Memorial Sloan Kettering Cancer Center

Objective: To assess the safety and oncologic outcomes of patients undergoing conversion surgery (CS) due to concern for disease progression after a period of active surveillance (AS) for low-risk papillary thyroid cancer (PTC) vs a propensity matched cohort of patients who underwent immediate surgery (IS).

Methods: From a registry of 559 patients followed with AS for low-risk PTC, this study analyzed patients who underwent CS for their indication for surgery, intraoperative findings, surgical complications, pathologic characteristics, overall survival (OS) and any recurrence free survival, calculated using the Kaplan-Meier method. These parameters were compared to a propensity matched cohort of patients who underwent IS, matched by age, gender, tumor size, surgical procedure and length of follow up. FDR (False Discovery Rate) p-value was used to determine the significance value.

Results: Of 559 AS patients, 56 (10.3%) were referred to surgery. In 40 patients (7.5%) CS was performed due to suspected disease progression, while in 16 (2.9%) surgery was undertaken due to non-disease related reasons. The median duration of AS in the disease progression group was 40 months (IQR 18, 58, range

0-99). Tumor growth and suspected extrathyroidal extension (ETE) were equally the primary indication for CS (n=19, 45.3% for each), followed by metastatic/ suspicious lateral lymph nodes (n=4, 9.5%,). In 26 (65%) patients, CS consisted of lobectomy; and in 14 individuals (35%) total thyroidectomy with or without neck dissection. At the time of surgery, the cancer was found to be adherent to the recurrent nerve in 1 case (2.4%), with normal vocal cord function postoperatively. There was 1 separate case of postoperative vocal cord paresis, unrelated to the index cancer. There were no cases of permanent hypocalcemia, and 2 cases of seroma (5%). Of the cases with suspected ETE as the indication for CS (n=19), ETE was confirmed pathologically in 8 cases (42%). When compared with matched IS group, there were no differences in neither gross or microscopic ETE, positive margins, tumor encapsulation, vascular invasion, number of positive nodes or AJCC 8 stage (100% in IS group and 95% in CS group). There were no differences in rates of adjuvant radioactive iodine between the groups and 100% of patients were without evidence of disease at last follow up. There were no differences in OS or any recurrence free survival (p=1, p=0.13, respectively).

Discussion: In our prospective AS cohort, 7.5% of patients have undergone CS due to suspicion of disease progression. These patients underwent curative surgery without evidence of escalated risk of complications, adverse pathologic features, diminished survival or recurrence outcomes compared to IS.

Scientific Session 2: Cancer Biology/TME

(Wednesday, May 15, 2024 | 3:15 PM - 4:00 PM)
Room: Grand Ballroom EF

AHNS11: CIRCULATING TUMOR DNA KINETICS FOLLOWING INDUCTION CHEMOTHERAPY PREDICTS RESPONSE IN HPV+ OROPHARYNGEAL SQUAMOUS CELL CARCINOMA - Zachary M Huttinger, MD, PhD; Emile Gogineni, DO; Sujith Baliga, MD; Dukagjian Blakaj, MD, PhD; Prijanka Bhateja, MD; Marcelo Bonomi, MD; Stephen Y Kang, MD; Matthew O Old, MD; Nolan B Seim, MD; Kyle K VanKoevering, MD; Amit Agrawal, MD; Enver Ozer, MD; James W Rocco, MD, PhD; Catherine T Haring, MD; The Ohio State University James Cancer Hospital and Solove Research Institute
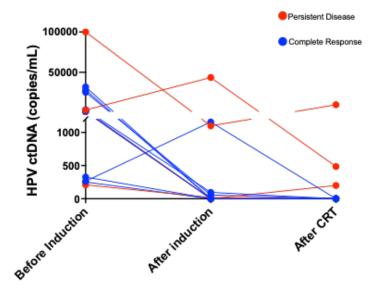
Background: There is an increasing number of patients with human papillomavirus (HPV) mediated oropharyngeal squamous cell carcinoma (HPV-OPSCC). A subset of patients present with locally aggressive disease. Several active clinical trials are investigating induction chemotherapy, immunotherapy, or combination approaches to reduce disease burden and prime the immune system prior to definitive therapy. There is a lack of biomarker data to guide definitive treatment following induction in this population.

Methods: Patients undergoing induction chemotherapy and definitive chemoradiation (CRT) therapy for HPV-related OPSCC at a tertiary academic medical center from 2022 and 2023 were reviewed. Patients with anatomic imaging and tumor tissue modified viral (TTMV)-HPV circulating tumor (ct) DNA testing before and after induction chemotherapy, and following completion of definitive CRT were included. Patient demographics, TNM classification, treatment details, ctDNA results, and imaging results were extracted. Primary and nodal disease volumes were calculated by RECIST criteria.

Results: A total of 13 patients were identified who had Stage III HPV- OPSCC were treated with induction chemotherapy (regimen of platinum-based, taxane, and either 5-fluorouracil or Cetuximab) followed by definitive CRT with platinum-based chemotherapy with or without addition of taxane, and 70 Gy radiation. Baseline ctDNA levels correlated strongly with volume of primary tumor (R^2=0.59), but did not correlate with nodal volumes (R^2=0.01) or total disease burden (R^2=0.18). Figure 1 demonstrates ctDNA kinetics in this cohort. After induction, 0/13 patients had complete response by PET imaging, whereas 7 patients (53.8%) had complete molecular response by ctDNA testing. After completion of CRT, 8 (61.5%) patients had complete imaging and molecular response. Of patients who had ctDNA clearance after induction, 6/7 (85.7%) remained disease free after definitive CRT, whereas one had progressive disease diagnosed by both imaging and post-treatment ctDNA tests. Three patients had elevated post-treatment ctDNA and all (100%) were found to have progressive disease on post-treatment imaging.

Conclusions: CtDNA testing may have a higher specificity than PET scans in assessing post-induction response. CtDNA clearance patterns following induction may predict disease control after definitive therapy. Additional prospective trials are needed. These data support including biomarker testing into clinical trial design.

Figure 1:

AHNS12: CANCER STEM CELLS RESIST TARGETING BY TUMOR INFILTRATING LYMPHOCYTES IN A THREE-DIMENSIONAL IN VITRO MODEL - John Henry Owen, MS; Colleen Hochfelder, MD; Brennan McMichael, MD; Jinelis Santiago, BS; Spring Gao, BS; Michael Allevato, PhD; Mark Prince, MD; Chad Brenner, PhD; Steven Chinn, MD; University of Michigan

Background: Head and neck squamous cell carcinomas (HNSCC) are heterogenous populations containing a subset of cancer stem cells (CSCs) that are resistant to chemotherapy and radiotherapy. The tumor microenvironment plays an important role in structuring and maintaining the stem cell population. Cancer-associated fibroblasts (CAFs) are stromal cells that are shown to result in a worse prognosis when present in high proportions in a tumor. Tumor-infiltrating lymphocytes (TILs), conversely, lead to more positive outcomes when found in higher numbers. The relationship between CAFs, TILs, and CSCs is explored in a three-dimensional in vitro spheroid model to better replicate in vivo conditions and assess multicellular interactions.

Materials/Methods: A new HNSCC cell line, UM-SCC-122, was established from a patient with a T2N1M0 cancer of the tongue. CAFs were isolated from tissue at the time of surgery, and blood draws from follow-up visits were used to isolate lymphocytes. UM-SCC-122 was transfected with either GFP or dsRed fluorescent proteins to allow for flow cytometry sorting of GFP+/ALDH+/CD44+ CSCs or dsRed+/ALDH-/CD44- non-cancer stem cells. CAFs were stained with a far red tracing dye while T cells were stained with a violet tracing dye to allow for all cell types to be visualized by fluorescence microscopy. Spheroids were grown for six days before introduction of CD3/CD28-activated T cells to represent TILs. Quantification of the spheroids and secreted cytokines was compared before and after the addition of TILs.

Results: GFP+/ALDH+/CD44+ CSCs grew larger spheroids and composed a higher initial proportion of a mixed cell spheroid when compared with dsRed+/ALDH-/CD44- cells. High numbers of TILs were efficient in reducing spheroid size within 48 hours and were more cytotoxic towards dsRed+ cells than GFP+ cells. In mixed GFP+/dsRed+ spheroids, TILs preferentially targeted the dsRed+ population. IL-2, a marker for active T cells in an immune response, was measurable only in the presence of dsRed+ cells, and this concentration was much higher in spheroids composed only of dsRed+ cells. Spheroids grown in coculture with CAFs secreted high levels of IL-6 and IL-8 while decreasing the level of IL-2 after introduction of TILs. These cocultured spheroids were more resistant to TIL cytotoxicity.

Conclusion: The tumor microenvironment is a complicated system involving interactions between multiple cell types. TILs are capable of killing cancer cells when present in high numbers although CSCs have an innate resistance to the immune response. CAFs secrete cytokines that confer further immune evasion to the cancer cell population. The composition of an individual tumor relating to proportions of CSCs, CAFs, and TILs can be predictive of outcome and sensitivity to therapies. We describe a three-dimensional in vitro model capable of altering the proportions of these different cell types to allow for a more clinically relevant exploration of these various interactions and identification of potential targets for improved treatment.

Figure 1. A) Fluorescent images of spheroids before and after introducing TILs. Spheroids were initiated either with GFP+/ALDH+/CD44+ CSCs, a 1:1 mix of GFP+ and dsRed+ cells, or dsRed+/ALDH-/CD44- non-cancer stem cells. B) Cancer cell viability 48 hours after added TILs. C) IL-2 supernatant concentrations 48 hours after added TILs.

Figure 2. A) 3D composite image of a spheroid initiated with equal numbers of CSCs(green), non-CSCs(red) and CAFs(pink) after introduction of TILs(blue) . B) IL-6 supernatant concentrations of spheroids initiated with varying proportions of CAFs. C) IL-8 supernatant concentrations of spheroids initiated with varying proportions of CAFs.

AHNS13: PROGNOSTIC UTILITY OF A GENE EXPRESSION PROFILE THAT QUANTIFIES ANTI-TUMOR IMMUNITY IN HPV+ OPSCC -

Dominick Rich, BS[1]; Lovely Raghav, PhD[1]; Malay Sannigrahi, PhD[1]; John N Lukens, MD[1]; Lova Sun, MD[1]; David Shimunov, MD[2]; Robert M Brody, MD[1]; Ahmed Diab, PhD[1]; Alexander Lin, MD[1]; Roger B Cohen, MD[1]; Phyllis A Gimotty, PhD[1]; Jianxin You, PhD[1]; Alexander T Pearson, MD, PhD[3]; Alexander C Huang, MD[1]; Jalal Jalaly, MD[1]; Devraj Basu, MD, PhD[1]; [1]University of Pennsylvania; [2]SUNY Stonybrook; [3]University of Chicago

Importance: Human papilloma virus-related (HPV+) oropharyngeal squamous cell carcinomas (OPSCCs) are highly immune-infiltrated and therapy-responsive relative to HPV-negative head and neck cancers and many other solid tumors. However, the variability in tumor immune microenvironment (TIME) among HPV+ OPSCCs and its relationship to oncologic outcomes are not well-defined.

Objective: To evaluate treatment-naïve HPV+ OPSCCs that later failed therapy for TIME features that are predictive of cancer recurrence and have potential to guide therapeutic decision-making.

Design, Setting, and Participants: A single institution retrospective cohort of 851 HPV+ OPSCC patients undergoing transoral robotic surgery from 2007 to 2020 was used to identify 50 tumors that later recurred locoregionally within the adjuvant radiation field (n=14) and/or at distant sites (n=43). We identified non-recurrent controls from the same cohort, selecting 49 tumors from patients with prolonged follow up and similar stage, smoking history, and adjuvant therapy. RNAseq was performed, and the transcriptional profiles of the two groups were compared for evidence of differing immune cell content using the xCell pipeline (two-tailed t-test <0.05) and distinct cytokine signaling using the CytoSig prediction model. Gene set enrichment analysis (GSEA) was used to compare activity in the immune-related Hallmark and Kegg pathways between cases and controls (p-adj. <0.05), and the genes in the differentially expressed pathways were used to create an immune suppression score. This score was evaluated for ability to stratify recurrence-free and overall survival (RFS and OS) of patients in two external cohorts.

Results: Based on xCell analysis, the tumors that subsequently recurred were significantly depleted of multiple anti-tumor immune cell compartments (e.g. naïve and central memory CD4+ T-cells, multiple B-cell subsets, dendritic cells, and M1 macrophages). By contrast, pro-tumorigenic CD4+ Th2 cells were increased in these tumors and inversely correlated with abundance of the anti-tumor cell types on a per-sample basis by Pearson coefficient (R=-0.51, p<0.001). CytoSig analysis showed significantly decreased pro-inflammatory cytokine signaling (e.g. IL-1α, IL-1β, IL-18) and increased anti-inflammatory cytokine signaling (e.g. CSF1, IL-4, and IL-6) in the tumors that later recurred vs. control tumors. Comparing activity of 24 immunity-related Hallmark and Kegg pathways by GSEA demonstrated that 20 of them were functionally suppressed in the tumors that recurred. The 930 unique genes contained in these 20 pathways were used to generate an immune suppression score for each tumor comprised of the number of genes downregulated by ≥1 S.D. below the mean. This novel score robustly stratified survival in two external cohorts that contain a mix of surgical and nonsurgical cases: TCGA (n=52, RFS p=0.0026, OS p=0.0142) and a single institution cohort (n=46, RFS p=0.0015, OS p=0.0040).

Conclusion and Relevance: HPV+ OPSCCs that are predisposed to cancer recurrence and lethal outcome contain a pro-tumor immune milieu that was characterized here based on transcriptional indicators of altered immune cell content and cytokine signaling. These findings support using features of the TIME to identify the HPV+ OPSCC patients at greatest risk of treatment failure and to guide application of emerging neoadjuvant approaches to reverse the suppression of anti-tumor immunity.

AHNS14: CHARACTERIZATION OF THE PRIMARY TUMOR-SENTINEL NODE IMMUNOMIGRATOME DEMONSTRATES A KEY ROLE FOR DENDRITIC CELL TRAFFICKING IN THE SUCCESSFUL RESPONSE TO IMMUNORADIOTHERAPY -

Robert Saddawi-Konefka, MD, PhD[1]; Riyam Al Msari[2]; Cynthia Tang[1]; Chad Phillips[1]; Lauren Clubb[1]; Farhoud Faraji, MD, PhD[1]; Riley Jones[1]; Andrew Sharabi, MD, PhD[1]; J. Silvio Gutkind, PhD[1]; Joseph Califano, MD[1]; [1]University of California, San Diego; [2]MIT

PD-1 inhibition (PD1i) has demonstrated no benefit when combined with chemoradiotherapy for locally advanced HNSCC, raising the possibility that standard therapies compromise the response to immunotherapy. To address this hypothesis, we previously demonstrated that ablating tumor draining lymphatics abolishes the response to immune-oncology therapy. Specifically, we defined that the response to immunotherapy is coordinated by interferon type-I signaling through the cDC1 population in tumor-draining lymph nodes.

ORAL PAPERS

These findings support the premise that successful tumor responses to immuno-oncology (IO) therapies is predicated upon intact and functional, locoregional anatomy. Accordingly, we hypothesize that lymphatic-preserving, tumor-directed immune oncology therapy will promote antitumor immunity by enhancing surveillance along the tumor-immune-lymphatic axis.

To explore this, we employed our recently characterized tobacco-signature, orthotopic murine oral squamous cell carcinoma models, one of which matches the immune infiltrate and PD1i response of human disease and the other of which is immune-cold with limited response to PD1i. In both models we define an immunoradiotherapy (IRT) scheme, using low-dose tumor-directed radiotherapy (tdRT), that achieves complete response and confers durable immunity. Mechanistically, we observe that successful tdIRT potentiates the response to PD1i by coordinating antitumor immunity across the tumor and regional lymphatics – specifically, the sentinel lymph node (SLN) – suggesting an active process of locoregional antitumor immunosurveillance.

To study surveillance across the tumor-SLN axis, we map the locoregional lymphatics joining the primary tumor to its SLN and develop models to selectively ablate these lymphatic channels. Interestingly, ablation of the lymphatic channels that link the tumor and SLN is sufficient to block the tumor IRT response, leading to a restriction of cytotoxic, tumor-antigen specific CD8 T cells from the TIME and an overall reduced antitumor T cell repertoire. To identify the requisite immune effectors that transit across tumor-SLN axis to mediate the tdIRT response, we employ tamoxifen-inducible reporter animal models in which we spatiotemporally label immune effectors during tdIRT. Using CITE-sequencing, we comprehensively profile the dynamics of locoregional antitumor immunosurveillance at single cell resolution, finding that activated, migratory dendritic cell populations transiting between the SLN and tumor are critical for T cell priming and clonotypic expansion and, ultimately, the successful tumor response to IRT.

We demonstrate that targeting tumors with stereotactic radiation and PD1i while sparing draining lymphatics enhances anticancer immunity by promoting locoregional immunosurveillance between the tumor and sentinel lymph node, resulting in significantly improved responses. Overall, this work represents a paradigm-shift in the design of IO therapies, which can immediately inform the design of next-generation immune oncology trials for HNSCC.

AHNS15: DURABLE ANTITUMOR IMMUNITY AFTER SUCCESSFUL PRIMARY TUMOR RESPONSES TO IO THERAPY IS CONFERRED BY CD8 TEX-STEM CELLS RESIDING WITHIN REGIONAL LYMPHATICS -

Robert Saddawi-Konefka, MD, PhD[1]; Cynthia Tang[1]; Riyam Al Msari[2]; Ravindra Uppaluri, MD, PhD[3]; Adam Luginbuhl, MD[4]; Joseph Califano, MD[1]; J. Silvio Gutkind[1]; [1]University of California, San Diego; [2]MIT; [3]Brigham and Women's Hospital and Dana-Farber Cancer Institute; [4]Thomas Jefferson University

While immune checkpoint inhibitor (ICI) therapy has demonstrated remarkable efficacy for treating solid cancers, achieving complete and durable immunity remains elusive. Understanding the mechanisms of immunologic memory after complete responses to ICI therapy is essential to achieve sustained anticancer responses and address the outstanding problem of recurrence for patients after successful primary tumor response – a particularly salient issue in the era of neoadjuvant immuno-oncology (IO). This study aimed to investigate mechanistic underpinnings of long-lasting immune memory following successful ICI therapy. In our previous work, we demonstrate that durable antitumor immunity is preserved following complete primary tumor responses even after ablation of tumor-draining lymphatics. Accordingly, we hypothesize that durable antitumor immunity is conferred peripherally but independently from tumor-draining lymphatics, which are routinely ablated with curative-intent oncologic therapies in HNC patients.

To address this hypothesis, we employed the tobacco signature HNSCC preclinical model, 4MOSC1, in which we have previously defined schemes to achieve durable immunity after ICI that are as robust as classical vaccination models. By leveraging this unique in vivo model of durable immunity after ICI, along with tamoxifen-inducible reporter animal models in which we can precisely and spatiotemporally label immune effectors, we elucidate the mechanistic underpinnings of durable anticancer responses. An analysis of key immunologic effectors in ICI-responder animals reveals a robust but regionally-restricted distribution of the Tex-stem CD8 T cell population. Moreover, by employing the OVA-expressing 4MOSC1 model, we find antigen-specific Tpex in a similar spatial distribution, suggesting that regional lymphatics are the key to durable antitumor immunity after successful IO therapy. To explore the role of tumor-draining lymphatics versus all regional lymphatics in conferring durable immunity, we performed a series of ablative surgeries that reflect the clinical scenarios of HNSCC patients. Surprisingly, removal of tumor-draining lymphatics alone while preserving other regional lymphatics following successful primary tumor response does not impair durable host immunity. Lastly, we find that adoptive transfer of these key effectors into naïve tumor-bearing animals is sufficient to mediate tumor rejection.

This study demonstrates that while successful primary tumor responses to ICI require intact tumor-draining regional lymphatics, durable antitumor immunity can be conferred independently from other non-tumor-draining reginal lymphatics. As the field moves closer to incorporating neoadjuvant IO treatments into standard therapies, these insights have critical and immediate implications for how to best manage tumor-draining lymphatics and implement elective ablative therapies.

AHNS16: DECREASED T-CELL REPERTOIRE AND LOWER DENSITY OF ANTIGEN-PRESENTING CELLS IN THE TUMOR MICROENVIRONMENT OF IMMUNOSUPPRESSED PATIENTS WITH NON-MELANOMA SKIN CANCER SUGGEST IMPAIRED INNATE IMMUNITY IS A KEY DRIVER OF IMMUNOSUPPRESSION -

Jennifer L Anderson, MD, PhD[1]; Shorook Na'ara, MD, PhD[1]; Xiayu Rao, MS[1]; Micah Castillo, BS[2]; Veena Kochat, PhD[1]; Emre Arslan, PhD[1]; Frederico O Gleber-Netto, DDS, MSc, PhD[1]; Shamima Akhter, PhD[1]; Adewale Abebayo, BS[1]; Tongxin Xie, MD, PhD[1]; Hinduja Sathishkumar, MS[1]; Kala Debnath, MPhil[1]; Shajedul Islam, PhD[1]; Preethi Gunaratne, PhD[2]; Pryadharsini Nagarajan, MD, PhD[1]; Jing Wang, PhD[1]; Kunal Rai, PhD[1]; Michael Migden, MD[1]; Neil Gross, MD[1]; Moran Amit, MD, PhD[1]; [1]University of Texas MD Anderson Cancer Center; [2]University of Houston

Background: Non-melanoma skin cancer is the most common malignancy, with basal cell carcinoma (BCC) being the most common and cutaneous squamous cell carcinoma (cSCC) the second most common. An increased incidence of non-melanoma skin cancer is observed in immunosuppressed

(IS) patients. These patients also have a worse prognosis than their immunocompetent (IC) counterparts despite equivalent treatment modalities. Immune checkpoint inhibition (ICI) has been successfully used for treatment of cSCC and select populations of BCC in IC patients, however use in IS patients has been limited due to the risk of adverse effects such as allograft rejection. Better understanding of the tumor immune microenvironment (TIME) is needed to determine if ICI can safely be employed in IS patients.

Objectives: To compare immune-cell populations, T-cell clonality, and T-cell diversity in IS and IC patients with non-melanoma skin cancer.

Methods: Cytometry by time-of-flight (cyTOF) was used to analyze 59,732 CD45^{+} immune cells derived from 24 non-melanoma skin cancer samples, including both cSCC and BCC, from 14 IC and 10 IS patients. Multispectral imaging was used to characterize tumor and stromal cells in 103 cSCC patients comprised of 61 IS and 42 IC patients. To measure T-cell activation, we used single cell sequencing to measure the frequency of individual rearranged T-cell receptor (TCR) genes, known as T-cell clonotypes, in 19 BCC and 15 cSCC samples isolated from 15 IS and 19 IC patients.

Results: Analysis of immune cells derived from non-melanoma skin cancer samples by cyTOF did not reveal a significant difference in T-cell populations between IS and IC patients. In contrast, multispectral imaging demonstrated a higher density of CD68^{+} tumor-associated macrophages in both tumor and stoma in IC patients with cSCC compared to IS patients. Additionally, we showed that the IS cohort had significantly higher tumoral CD68^{+}PDL1^{+} cell density. Single cell TCR sequencing revealed that there is a lower percentage of unique clonotypes in IS patients compared to IC patients. We also observed decreased T-cell diversity in IS patients compared to IC patients. Additionally, we observed a higher percentage of unique clonotypes and increased T-cell diversity in patients with BCC compared to SCC.

Conclusions: Overall, we demonstrated that a lower density of tumor-associated macrophages in the TIME of IS patients is associated with decreased T-cell clonotypes and diversity. We also showed that macrophages present with the TIME of IS patients have higher PD-L1 expression, which indicates a more immunosuppressive phenotype. This suggests an impaired innate immune response leads to decreased T-cell activation in IS patients and may contribute to their worse outcomes compared to IC patients. Our results support the rationale for use of anti-PD-L1 therapy and agents such as TLR (Toll-like receptor) agonists to augment the innate immune system in IS patients.

Panel Discussion: Rare Tumors: Update on Translational Biology and Clinical Management

(Wednesday, May 15, 2024 | 4:00 PM - 5:00 PM)
Room: Grand Ballroom GHIJ

AHNS17: PRMT5 INHIBITION HAS A POTENT ANTI-TUMOR ACTIVITY AGAINST ADENOID CYSTIC CARCINOMA OF SALIVARY GLANDS - Vasudha Mishra[1]; Alka Singh[1]; Michael Korzinkin[2]; Xiangying Chen[1]; Claudia Wing[1]; Viktoria Sarkisova[2]; Alexandra Ozerova[2]; Oksana Glushchenko[2]; Manu

Sundaresan[1]; Koichi Ito[3]; Peggy Scherle[3]; Ivan Ozerov[2]; Thomas Cyberski[1]; Frank Pun[2]; Le Shen[1]; Alexander T Pearson[1]; Ari J Rosenberg[1]; Mark W Lingen[1]; Alex Zhavoronkov[2]; Bruce Ruggeri[3]; Nishant Agrawal[1]; Evgeny Izumchenko[1]; [1]University of Chicago; [2]Insilico Medicine; [3]Prelude Therapeutics

Purpose: Adenoid cystic carcinoma (ACC) is a rare glandular malignancy, commonly originating in salivary glands of the head and neck. Given its protracted growth, ACC is usually diagnosed in advanced stage. Treatment is limited to surgery and/or adjuvant radiotherapy, which often fails to prevent disease recurrence, and no approved targeted therapies are currently available. We propose protein arginine methyl transferase 5 (PRMT5) as a potential therapeutic target for ACC and demonstrate potent antitumor activity of small molecule inhibitors of PRMT5.

Experimental Design: We applied PandaOmics (an AI-driven target discovery platform) on the transcriptomic dataset of 87 primary ACCs (62 sequenced internally and 25 obtained from Gene Expression Omnibus) to predict novel therapeutic targets. Identifying PRMT5 as a putative candidate, we next determined the applicability of PRMT5 inhibitors (PRT543 and PRT811) using ACC cell lines, organoids, and patient derived xenograft (PDX) models. Molecular changes associated with response to PRMT5 inhibition and anti-proliferative effect of the combination therapy with lenvatinib was then analyzed.

Results: PRMT5 was predicted among potential therapeutic targets for ACC. Treatment with PRT543 induced significant growth inhibition in ACC cell lines, organoids, and PDX models, paralleled by downregulation of global symmetric dimethylarginine (a substrate of PRMT5), MYC, MYB and other genes associated with ACC tumorigenesis. Notably, PRT811 (a brain penetrant PRMT5 inhibitor) displayed similar anti-proliferative effects. Given that a subset of genes targeted by lenvatinib were upregulated in ACC, addition of lenvatinib enhanced the growth inhibitory effect of PRMT5 blockade in vitro.

Conclusion: Our study underscores the role of PRMT5 in ACC and supports PRMT5 blockade as a promising strategy for treating this rare disease.

Scientific Session 3: Mucosal

(Thursday, May 16, 2024 | 9:00 AM - 9:45 PM)
Room: Grand Ballroom GHIJ

AHNS18: INVESTIGATION OF THE EARLY NEOPLASTIC TRANSFORMATION OF ORAL SQUAMOUS CELL CARCINOMA USING GENETICALLY ENGINEERED MOUSE ORGANOIDS - Casey A Collet, BS[1]; Hua Zhao, MD[2]; Stephanie Wong, MD[1]; Boyan Hu, BS[2]; Uttam K Sinha, MD[1]; De-Chen Lin, PhD[2]; [1]Department of Otolaryngology, Keck School of Medicine, University of Southern California Los Angeles, USA; [2]Center for Craniofacial Molecular Biology, Herman Ostrow School of Dentistry, and Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, USA

Objective: Modeled the neoplastic transformation of oral squamous cell carcinoma (OSCC) using genetically engineered mouse organoids in order to explore the genetic, epigenetic, and transcriptomic changes of carcinogenesis.

Methods: Organoids were established from mouse oral tongue and oropharyngeal tissue. Trp53/Cdkn2a double knock out (DKO) was introduced using CRISPR-Cas9 genome editing via electroporation. Trp53/Cdkn2a mutations were confirmed by TOPO cloning and Sanger sequencing. To further model premalignant changes, DKO organoids were transduced with a retroviral vector to induce PI3KCAE545K overexpression or exposed to the drug DAPT to induce Notch inhibition. Organoids were analyzed for structural and growth properties at different time points by measuring organoid size using photomicrographs under phase-contrast microscopy and cell viability using WST-1 assays. Tumorigenicity was validated using xenograft transplantation assays.

Results: Mouse oral tongue DKO organoid size was significantly larger (p <0.0001) and cell viability significantly greater (p<0.0001) on day 4 and 7 compared to control organoids. Similarly, mouse oropharyngeal DKO organoid size was significantly larger (p <0.0001) and cell viability greater (p<0.0001) on days 4, 7, 10, and 13 compared to control organoids. Oral cavity DKO organoids induced with PIK3CA overexpression demonstrated greater size (p <0.0001) and viability (p <0.0001) compared to DKO organoids. Meanwhile, Notch inhibited oral cavity DKO organoids demonstrated greater viability (p <0.0001), but not significantly greater growth. Oral cavity DKO and PIK3CA overexpressed groups demonstrated tumor growth during xenotransplantation assays, while control organoids exhibited no growth.

Conclusions: Considering our phenotypic data, we conclude that we have successfully modeled premalignant changes of oral cavity and oropharyngeal tissue. Tumorigenicity was confirmed using xenotransplantation assays. We will analyze epigenomic changes using CUT&Tag sequencing and transcriptomic changes using RNA sequencing. We will further explore differentially expressed genes identified via these sequencing techniques.

AHNS19: DNA DAMAGE PRECEDES VIRAL INTEGRATION IN HPV-TRANSFORMED TONSILLAR KERATINOCYTES

- Kimberly Chan, MD[1]; Christopher Tseng, MD[1]; Emily Milarachi, MD, MSCI[1]; David Y Goldrich, MD[1]; Kathryn Sheldon, PhD[2]; Lisa Schneper, PhD[2]; Lijun Zhang, MS, PhD[3]; Brandon LaBarge, MD[1]; Max Hennessy[1]; Craig Meyers, PhD[2]; James R Broach, PhD[2]; David Goldenberg, MD, FACS[1]; [1]Department of Otolaryngology - Head and Neck Surgery, Penn State Hershey Medical Center; [2]Institute for Personalized Medicine, Penn State College of Medicine; [3]Case Western University

Introduction: Approximately 70% of oropharyngeal squamous cell carcinomas (OPSCC) are caused by human papillomavirus (HPV). Among patients with HPV-associated OPSCC, patients in which HPV remains episomal in their tumor tend to have better outcomes compared to patients in which HPV integrates into the host genome. Moreover, HPV-positive OPSCC tumors in which the virus has integrated exhibits extensive accumulation of structural variants, not only at the site of integration but also throughout the entire genome. In contrast, tumors in which HPV remains episomal accumulate relatively few structural variants. Whether HPV integration is a consequence of genomic instability or the cause of genomic instability remains unknown.

Methods: Six different tonsillar keratinocyte cell lines were infected by HPV16 through transformation and were cultured for over 100 passages. Using the Bionano Saphyr® protocol, we performed optical genome mapping (OGM) on each cell line at six different time points spaced over the first fifty passages to evaluate genomic structural changes as a function of number of passages and integration status of the virus. We performed whole-genome sequencing (WGS) on cells taken at the fortieth cell passage of each cell line to identify whether HPV had integrated and, if so, where. To gain greater insight regarding the site of integration, we used targeted anchor polymerase chain reaction (PCR) to amplify the region of integration coupled with long-read sequencing on a Pacific Biosciences (PacBio) instrument.

Results: We found that HPV integrated into the genome in five of the six lines and remained episomal in the sixth. Integration occurred by the fortieth passage and as early as the eighteenth. In the five cell lines in which HPV integrated, structural variants increased in number up to the time of integration and very few appeared after integration. In the episomal cell line, structural variant accumulation continued throughout the course of the experiment. Anchored PCR followed by long range PacBio sequencing provided a detailed characterization of the site of integration.

Conclusion: These results suggest that genome instability occurs during HPV transformation of primary keratinocytes and precedes HPV integration. Genome rearrangement then declines, concurrent with viral integration and remains low during subsequent growth of the transformed cells. Accordingly, we conclude that genome instability in this in vitro system causes viral integration rather than being a consequence of integration. Finally, targeted anchor PCR provides a facile method to determine the state of HPV in the cell and, if integrated, the structural changes that occurred at the site of integration.

AHNS20: IS PATHOLOGICAL COMPLETE RESPONSE (PCR) A SURROGATE ENDPOINT OF OVERALL SURVIVAL IN PATIENTS WITH TECHNICALLY UNRESECTABLE ORAL CAVITY CANCERS? A REAL WORLD DATA OF 900 PLUS PATIENTS -

Shatabdi Chakraborty; Vijay Patil; Vanita Norhona; Nandini Menon; Ajay Singh; Pankaj Chaturvedi; Prathamesh Pai; Kumar Prabhash; Tata Memorial Hospital

Background: Technically unresectable oral cavity squamous cell cancers (OCSCC) are non-amenable for upfront surgery. Neo-adjuvant chemotherapy (NACT) can downstage the tumor and facilitate surgical resection. Pathological complete response (PCR) post-NACT is a surrogate endpoint of overall survival in rectal and breast cancers. However, its importance in patients with borderline resectable OCC is unknown.

Methods: This was an institutional review board-approved retrospective analysis of a prospectively collected dataset of borderline resectable OCSCC patients who received NACT. Adult patients with an eastern cooperative oncology group (ECOG) performance status (PS) 0-2 who were deemed as technically unresectable in a multi-disciplinary clinic (MDC) were included. These patients received 2-3 cycles of NACT (3-weekly) and underwent a response assessment. Depending on response and general condition, they were re-assessed in MDC and further therapy was decided. Patients with good general condition who became resectable underwent surgery followed by appropriate adjuvant therapy. Overall survival (OS) was calculated from the date of diagnosis to the date of death. Kaplan-Meier method was used for the estimation of OS. The impact of pathological response on OS was assessed using the log-rank method.

Results: Nine hundred twenty-seven patients underwent surgery followed by adjuvant CTRT in 94.0% of patients or adjuvant RT in 4.4% of patients. Seventy-six (8.2%) patients attained a pathological complete response. 869 (93.7%) achieved negative margins. Three thirty-eight (36.5%) patients had pT4 disease. The lympho-vascular invasion was seen in 53 (5.7%) while perineural invasion was seen in 186 (20.1%) patients and 337 (36.4%) had extranodal extension. The median OS of the entire cohort was 17 months (95% CI: 14.7 – 19.3 months). The median OS of patients who attained PCR was 55 months (95% CI: 22.9 – 87.1 months) vs 16 months (95% CI: 13.9–18.1 months) for those who did not attain PCR (p=0.004). The corresponding 10-year OS were 40.5% (SE-7.4%) and .21.1% (SE-3.2%).

Conclusion: Pathological complete response is a surrogate marker of long-term overall survival in patients of technically unresectable oral cavity cancers.

AHNS21: RATES OF RECURRENCE IN PATIENTS WITH EARLY-STAGE ORAL TONGUE CANCER MANAGED WITH SURGERY WITHOUT POSTOPERATIVE RADIATION - Mae Wimbiscus, BA; Jaclyn Lee, MD; Robert Sinard; Kyle Mannion; Sarah Rohde; Michael Topf, MD; Vanderbilt University Medical Center

Background: Patterns of failure among participants with early-stage oral tongue cancer remain understudied. The objective of this study is to determine the incidence of local, regional, and distant rates of recurrence in patients with early-stage, low risk oral tongue squamous cell cancer (OTSCC) in a large cohort who underwent partial glossectomy alone or glossectomy and ipsilateral elective neck dissection, without any further adjuvant therapy.

Study Design: Retrospective cohort study at single tertiary care center.

Methods: A database of patients with OTSCC who underwent partial glossectomy with or without elective neck dissection without adjuvant radiation therapy from 2000 to 2022 was queried. Only patients with early-stage oral tongue cancer (pT1 to pT2) without clinical or pathological nodal disease (cN0 and pN0) were included. Patient-related, tumor-related, and treatment-related characteristics were recorded. Local recurrence-free survival, regional recurrence-free survival, and disease-specific survival were calculated by the Kaplan-Meier method. Predictors of recurrence were analyzed by univariate and multivariate analysis.

Results: In total, 293 patients with pathologic T1-T2N0 OTSCC underwent partial glossectomy with (170 patients, 58%) or without (123 patients, 42%) elective neck dissection during the study period. No patients received adjuvant radiation therapy. These patients were 57.2% male, with a median age of 58.8 (IQR 49-68). Pathologic T staging included 164 patients that were T1 and 96 patients that were T2. Median depth of invasion was 3.0 mm (IQR 1-7). At a median follow-up of 55 months (range 1-203 months), the 3-year rates of local recurrence-free survival, regional recurrence-free survival, and disease-specific survival were 83.3%, 88.4%, and 92.5%, respectively. Regional recurrence was ipsilateral in 73.5% of patients, contralateral in 14.7%, and bilateral in 8.8%. On multivariable logistic regression, the only predictor of recurrence was close or positive margins (p < .001). Patients who developed recurrence in the neck had a significantly poorer disease-specific survival compared with those who did not (60.6% vs 97.67%; P <.0001).

Conclusions: In this single institution study, patients with low risk, pT1-2N0 OTSCC treated with surgery alone had excellent locoregional control. Almost a quarter of regional recurrences are in the contralateral neck. In this early stage population, close or positive margins was the only risk factor associated with recurrence.

AHNS22: SURVIVAL OUTCOMES IN RECURRENT ORAL CAVITY AND OROPHARYNGEAL SQUAMOUS CELL CARCINOMA - Isaac Solomon, BA[1]; Joshua Lee, BS[2]; Farhoud Faraji, MD, PhD[1]; Theresa Guo, MD[1]; [1]University of California San Diego; [2]New York Medical College
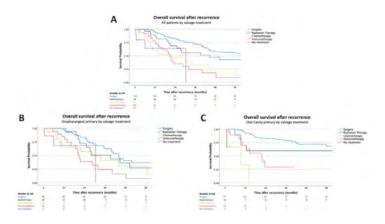
Introduction: While definitive treatment of primary oral cavity (OC) and oropharyngeal (OP) squamous cell carcinoma (SCC) confers favorable survival outcomes, the prognosis for recurrent disease remains poor. Surgical salvage has conventionally been the preferred approach for recurrent OC/OPSCC; however, the emergence of immune checkpoint inhibitors has kindled interest as a potential alternative therapeutic intervention. In this study, we compare the survival outcomes between salvage treatment modalities, with a specific emphasis on assessing the efficacy of immunotherapy in the context of recurrent disease.

Methods: This retrospective study, approved by the Institutional Review Board, analyzed data from patients aged ≥18 with recurrent oral cavity or oropharyngeal squamous cell carcinoma treated at a single institution between 2016 and 2022. Demographics, tumor details, primary/salvage treatments, and recurrence/survival outcomes were collected. Recurrence was defined as local, regional, and/or distant metastasis post-primary treatment, with a ≥3-month disease-free interval and clear margin surgical resection. Overall survival was measured from time of recurrence. Statistical analyses included Pearson's chi-squared test for comparing categorical data between OC and OP patients. Univariate and multivariate analyses were conducted using Cox regression, and recurrence and survival analyses were performed using Kaplan-Meier estimation and the log-rank test.

Results: A total of 220 (OCSCC [n=111] and OPSCC [n=109]) with recurrent SCC were included. The oral cavity patients were more likely to be female, present with lower primary N stage, experience locoregional recurrence and undergo surgical treatment (in both primary and salvage setting) (p<0.001 for each). Median time to recurrence from primary treatment was 15.0 months; no significant difference was found between primary OCSCC and OPSCC (12.6 vs. 16.2 months, respectively; p=0.29). Evidence of perineural invasion independently predicted shorter time to recurrence (HR 1.6; p<0.05). The overall two-year survival after recurrence was 57% (median: 43.8 months). Univariate analysis identified better ECOG performance status, favorable T and N classifications, primary surgery, absence of distant metastases, and surgical salvage as predictors for improved survival after recurrence (p<0.05). For recurrent OCSCC, two-year survival after recurrence was 49%, and this was significantly improved in those undergoing surgical salvage (79%) compared to immunotherapy (29%; p<0.001), chemotherapy (0%; p<0.001), and no treatment (0%; p<0.001), but not compared to radiotherapy (60%; p=0.84). OCSCC patients undergoing immunotherapy had statistically significant longer overall survival after recurrence compared to those undergoing chemotherapy (p<0.05). Recurrent OPSCC had a two-year survival of 66% (median survival: 79.9 months), with surgical salvage (two-year survival: 63%) outperforming immunotherapy (25%; p<0.001), chemotherapy (39%; p<0.05),

and no treatment (p<0.01), and similar to radiotherapy (52%; p=0.39). HPV status did not confer a statistically significant difference on two-year survival after recurrence (positive: 54%, negative: 39%; p=0.89). Recurrent OCSCC demonstrated superior two-year survival compared to OPSCC (p<0.01).

Conclusion: Our study reaffirms the pivotal role of surgical salvage as the preferred therapeutic modality for recurrent OC/OPSCC, yielding superior survival outcomes compared to systemic treatment, even in the era of immunotherapy. The retrospective design offers insights but limits generalizability, underscoring the need for prospective validation studies.

AHNS23: CHARACTERIZATION OF THE ORAL CAVITY MICROBIOME IN PATIENTS WITH OCSCC AND LEUKOPLAKIA

- Ann Powers, MD; Daniel Dickstein, MD; Adam Cantor, BS; Sida Chen, MD; Joshua Barlow, MD; Susmita Chennareddy, BS; Brandon Gold, MD; Tanvir Queraishi, BS; Nina Rodriguez; Diana Kirke, MD; Marita Teng, MD; Scott Roof, MD; Ilaria Mongo, PhD; Jeremiah Faith, PhD; Jose Clemente, PhD; Eric Genden, MD; Richard Bakst, MD; Icahn School of Medicine at Mount Sinai

Purpose/Objectives: Known risk factors for oral cavity squamous cell carcinoma (OCSCC) include history of tobacco and/or alcohol use. Some individuals develop OCSCC without any known risk factors, suggestive of another source contributing to these malignancies. The oral microbiome has been hypothesized to contribute to the development and progression OCSCC through metabolic, inflammatory, and/or immune-modulating effects. Previous studies have shown an association between poor oral hygiene and tooth loss with cancer, potentially implicating the oral microbiome in the development of tumors. Our aim is to characterize and investigate the role of the microbiome in OCSCC and leukoplakia. Here, we present results from the first 91 patients with OCSCC, pre-malignant lesions (leukoplakia) and healthy controls enrolled in our study.

Materials/Methods: From 2020 to 2023, we swabbed the buccal mucosa, tongue and tumor of patients with OCSCC and controls. The microbiome samples were analyzed using 16S ribosomal RNA gene sequencing. Dual barcode paired-end microbiome sequencing data was demultiplexed and processed using MMEDS and QIIME 2. Reads were denoised using DADA2 and mapped to GreenGenes for taxonomic assignment. Rarefaction was performed at 1,150 reads per sample. Alpha diversity was measured using Faith's phylogenetic diversity, and beta diversity was estimated using Bray-Curtis distances after correcting for batch differences.

Differential abundance analysis was performed using LEfSe.

Results: 91 patients (45 patients with OCSCC, 13 with pre-malignant lesions, 33 controls) were included in our analysis. Patients with OCSCC had significant differences in alpha diversity compared to controls (p=0.002) and compared to pre-malignant patients (p=0.013). There were no significant differences in alpha diversity in patients with OCSCC with known risk factors and without risk factors (p=0.626). Beta diversity was also significant between OCSCC and controls (p=0.016) and OCSCC and pre-malignant (p=0.008). Compared with controls and pre-malignant, patients with OCSCC were more likely to harbor Fusobacterium and Enterobacteriaceae taxa, and had lower levels of Rothia, Bacteroides and Blautia.

Conclusion: This is the first study to date to compare the oral microbiome in patients with OCSCC, pre-malignant lesions (leukoplakia), and controls. We found that OCSCC patients have significantly lower diversity than those with pre-malignant lesions and healthy controls, as well as significant differences in microbial composition. Specifically, we observed an enrichment in bacteria that enhance proliferation and promote a tumorigenic immune environment, such as Fusobacterium, with a parallel reduction in anti-inflammatory taxa such as Blautia. Overall, our results point to oral microbial dysregulation as a potential driver of tumor growth/progression. Further study is needed and patient accrual is ongoing to determine if pre-malignant samples lose diversity, given only 13 patients have been enrolled in this arm.

Jatin Shah Symposium: Genomic Landscape of HNSCC: Where We Are and Where We Are Going

(Thursday, May 16, 2024 | 10:15 AM - 12:00 PM) Room: Grand Ballroom GHIJ

AHNS38: ASSOCIATION OF NOVEL TUMOR-IMMUNE MICROENVIRONMENT MEASUREMENTS WITH RECURRENCE OUTCOMES IN HEAD AND NECK CANCER PATIENTS RECEIVING DEFINITIVE ORGAN PRESERVATION THERAPY.

- William J Benjamin, MPH[1]; Santhoshi Krishnan, PhD[2]; Michael Allevato, PhD[1]; Chamila Perera, PhD[3]; Jeremy Taylor, PhD[3]; Gregory T Wolf, MD[4]; Arvind Rao, PhD[2]; Nisha D'Silva, BDS, MDS, PhD[5]; Maureen A Sartor, PhD[2]; Laura S Rozek, PhD[6]; Steven B Chinn, MD, MPH[4]; [1]University of Michigan Medical School; [2]University of Michigan Department of Computation Medicine and Bioinformatics; [3]University of Michigan Department of Biostatistics; [4]University of Michigan Department of Otolaryngology - Head and Neck Surgery; [5]University of Michigan School of Dentistry; [6]Georgetown University Department of Oncology

Introduction: Tumor-infiltrating lymphocytes (TILs) play an important role in the prognosis of head and neck squamous cell carcinoma (HNSCC). However, TILs are both difficult and time-intensive to measure, which has limited their clinical utility. Seeking to remedy this, our team developed a machine learning classifier capable of computing a rapid and automated assessment of the tumor immune microenvironment that incorporates TIL infiltration and tumor-TIL spatial relationships. We previously reported that GScore is correlated traditional

markers of TIL infiltration and is associated with survival among HNSCC from all sites. Herein, we seek to investigate whether GScore is associated with recurrence outcomes among patients with oropharyngeal, hypopharyngeal, or laryngeal SCC who were treated with definitive organ preservation therapy.

Methods: This study is a retrospective analysis of prospectively collected oropharyngeal, hypopharyngeal, and laryngeal SCC patients managed with definitive radiation, chemoradiation, or induction selection protocols from the University of Michigan SPORE cohort. A machine-learning classifier trained on pathologist labeled samples was used to identify tumor cells and TILs across digitized H&E slides from the tumor samples. The extent of TIL infiltration within a tumor was assessed using the G-cross function comparing the coordinates of lymphocytes to tumor cells within a slide. Levels of spatial infiltration within tumors were outputted as G-cross(r) curves, and the area-under-the-curve was used as a metric for measuring TIL spatial infiltration (GScore) (Figure 1). GScore was categorized into tertiles for analysis. Our primary outcome of interest was recurrence-free interval, which was calculated from the date of diagnosis to the date of recurrence, patients were censored at date of last follow up or death. Survival estimations were completed using Kaplan-Meier analysis and Cox-Proportional Hazard modeling.

Results: A total of 158 patients were included in our study including 89 (56.3%) with HPV-positive oropharyngeal cancer, 24 (15.2%) with HPV-negative oropharyngeal cancer, 9 (5.7%) with hypopharyngeal cancer, and 36 (22.8%) with laryngeal cancer. Within the cohort, 133 (70.9%) patients had Stage III or IV disease. For definitive management, 24 (15.2%) patients received radiation therapy, 126 (79.8%) patients received chemoradiation, and 8 (5.0%) patients were treated with an induction chemotherapy followed by chemoradiation. A higher tertile of GScore was significantly associated with a higher 60-month recurrence-free interval (87.8% vs. 78.3%, vs 52.5%, p<0.01) (Figure 2). In multivariable models adjusting for age, stage, site, HPV, pack years, and comorbidities, the highest tertile of GScore was associated with a significantly lower hazard of recurrence compared to the lowest tertile (T3 vs. T1: 0.30 [0.1, 0.8], p=0.02).

Conclusion: Higher GScore's appear to be associated with lower recurrence in oropharyngeal, hypopharyngeal, and laryngeal squamous cell carcinoma patients treated with definitive organ preservation therapy, which supports that GScore may serve as a potential prognostic biomarker in this patient population. Further study investigating associations between GScore and treatment response may enhance the it's translational applications in the future.

Figure 1: Workflow for identification of TIL locations, density, and distances; involving image analysis of slides and subsequent machine learning to identify TILs on tissue.
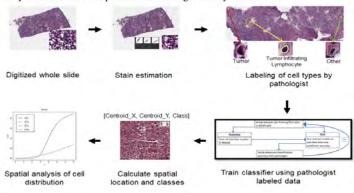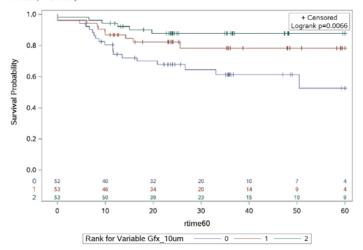

Figure 2: Analysis of 60-month recurrence-free interval stratified by GScore tertile. (2=Highest, 1=Middle, 0=Lowest).

Reconstructive Challenges in Special Populations

(Thursday, May 16, 2024 | 1:00 PM - 1:45 PM) Room: Grand Ballroom EF

AHNS24: FINITE-ELEMENT ANALYSIS OF OPTIMAL MANDIBULAR OSTEOTOMY ANGLES TO OPTIMIZE RECONSTRUCTIVE PLATE STRESS FOR PATIENTS UNDERGOING SIMULATED MANDIBULAR BODY RECONSTRUCTION. - Hugh A Kim, MD[1]; Michael De Biasio, BASc[1]; Ralph W Gilbert, MD[1]; John R de Almeida, MD, MSc[1]; David P Goldstein, MD[1]; Douglas B Chepeha, MD, MSPH[2]; Vito Forte, MD[1]; Thomas Looi, PhD, MASc[1]; Christopher M Yao, MD[1]; [1]University of Toronto; [2]University of Michigan

Background: Mandibular resection is used to treat oral cavity malignancy when there is bone invasion. Reconstruction is performed with a titanium plate and an osseous autogenous transplant. However, the rates of plate fracture are as high as 45% in the literature, and this creates an unacceptable medical burden for the patient because reoperation is required. Traditional mandibular osteotomies are perpendicular to the inferior boarder of the mandible, which results in a heavy reliance

on the titanium plate to overcome the vertical shear forces generated by mandibular loading before bony union is complete. We modeled different geometry for mandibular resection to optimize stability of a reconstruction plate post-operatively.

Methods: Computed tomography images of an adult male human mandible were downloaded from the Visible Human Project, a public domain library. The cortical bone and muscle masks were segmented in Mimics (Materialise, version 26.0) and imported to SOLIDWORKS (Dassault Systemes, release SP5.1) for finite-element analyses. Four posterolateral mandibular resections and fibular transplants with an osseointegrated molar implant were modeled following 1) vertical, 2) angled, 3) stair-shaped, and 4) sagittal cuts (Figure 1). Mastication was simulated under 1) incisal, 2) ipsilateral implanted molar, and 3) contralateral molar loading conditions. Three screws were placed on each native mandible segment, with two in the transplanted segment. In the sagittal cut scenarios, one screw on each side penetrated both transplanted and native mandible segments. Screw extrusion was modeled to be negligible during simulation, and frictional contact was defined between bone segments. Material properties of the mandible were simplified as homogeneous cortical bone, and the plate and screws as titanium alloy. The mandible was constrained with a fixed hinge joint at each condyle and fixed geometry at the incisor, ipsilateral molar implant, or contralateral molar based on the loading condition. 200N forces were applied at the insertions of the masseter and temporalis muscles in the direction of the segmented muscle bellies. Our simplifying assumptions are based on a methodological review of similar finite-element analysis studies (Merema, 2020).

Results: The location of maximum von Mises stress was between the two screws bordering the anterior osteotomy in incisal and ipsilateral molar loading, and posterior osteotomy in contralateral loading, in all but the vertical cut incisal loading scenario (Figure 2). Across the cuts, the vertical cut resulted in the highest plate stresses with incisal (2.83x108 MPa) and ipsilateral molar loading (7.97x108 MPa). The lowest plate stresses were seen with angled cut in incisal loading (2.10x108 MPa) and sagittal cut across ipsilateral (2.86x108 MPa) and contralateral molar loading (2.68x108 MPa, Table 1).

Conclusions: The traditional vertical cut resulted in less favorable plate stresses, especially compared to angled and sagittal cuts, in all loading scenarios. The next phase of our study will vary different parameters for sensitivity analyses and validate these results in vitro.

Figure 1. Mandibulectomy cut designs including vertical (top left), angled (top right), stair-shaped (bottom left), and sagittal (bottom right) cuts.
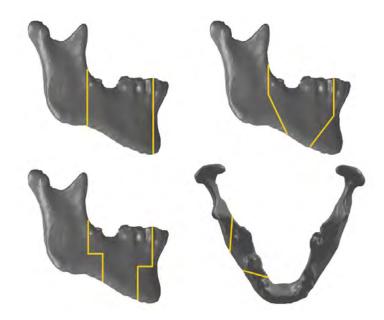

Figure 2. Von Mises stress plot in angled cut.

Table 1. Maximum von Mises stress (in MPa) on plate.

Load	Vertical cut	Angled cut	Stair cut	Sagittal cut
Incisal	2.83×10^8	2.10×10^8	2.45×10^8	2.25×10^8
Ipsilateral molar	7.79×10^8	4.63×10^8	4.33×10^8	2.86×10^8
Contralateral molar	3.57×10^8	3.60×10^8	1.21×10^9	2.68×10^8

Panel Discussion: New Technologies in Head and Neck Cancer

(Thursday, May 16, 2024 | 1:30 PM - 2:45 PM)
Room: Grand Ballroom GHIJ

AHNS25: SWALLOW WATCH: AN AUTOMATED DYSPHAGIA ALERT PROGRAM FOR PATIENTS WITH HEAD AND NECK CANCER TREATED WITH RADIOTHERAPY - Yue Ma, MD[1]; Joseph Kidane, MD[2]; Claire E Perrin, BS[1]; Jason W Chan, MD[3]; Inderpreet Kaur Khalsa, MS[4]; VyVy N Young, MD[1]; Clark A Rosen, MD[1]; William R Ryan, MD[1]; Cara Evans, MM, MS, CCCSLP[1]; James J Lappin, BA[1]; Tyler W Crosby, MD[1]; Sue S Yom, MD, PhD[3]; Sky Yang, MS, CCCSLP[1]; Brittany Mitchell, MS, CCCSLP[1]; Erik Steele, MFA, MA, CCCSLP[1]; Lois Chen, MS, CCCSLP[1]; Desi Guitterrez, MA, CCCSLP[1]; Trina Sheedy, MMS, PAC[1]; Mary Xu, MD[1]; Kathryn Wai, MD[1]; Jonathan George, MD[1]; Chase Heaton, MD[1]; Ivan El-Sayed, MD[1]; Andrea Park, MD[1]; P. Daniel Knott, MD[1]; Hyunseok Kang, MD[5]; Alain Algazi, MD[5]; Amelia Komp, NP, MSN[3]; Christine Kim, MS, RN[5]; Brittany Dingler, MHS, PAC[5]; Sarah L Schneider, MS, CCCSLP[1]; Patrick Ha[1]; [1]University of California San Francisco, Department of Otolaryngology-Head and Neck Surgery, San Francisco, CA; [2]University of Southern California, Caruso Department of Otolaryngology-Head and Neck Surgery, Los Angeles, CA; [3]University of California, San Francisco, Department of Radiation Oncology, San Francisco, California; [4]University of California San Francisco, School of Medicine, San Francisco, CA; [5]University of California, San Francisco, Department of Medicine, San Francisco, California

Introduction: Dysphagia is a common side effect of head and neck cancer (HNC) radiotherapy. Timely detection and proactive management of dysphagia are vital for improving outcomes in head and neck cancer survivors. Effective, cost-efficient, and sustainable care delivery models that allows long-term dysphagia surveillance and proactive treatment are currently lacking. We report the results of a prospective study examining the feasibility of an automated patient-reported dysphagia alert program, called Swallow Watch (SW), to enable timely detection and management of dysphagia.

Methods: A multidisciplinary team of physicians (head and neck surgery, laryngology, medical and radiation oncology, and facial plastic and reconstructive surgery), speech-language pathologists (SLP), and HNC survivors developed SW. HNC patients with tumors involving the oral cavity, oropharynx, hypopharynx, and larynx and treated with radiotherapy were invited to participate in SW. A brief swallow function check-in survey was sent to patients before cancer treatment and every 3 months thereafter. Based on patient answers, SW was programmed to detect significant weight loss (>10 lbs in 3 months), hospitalization for aspiration pneumonia and IV hydration, and clinically meaningful deterioration in swallow function (M.D. Anderson Dysphagia Inventory score < 60 or decrease > 10 points). SW was programed to send automated dysphagia alerts to the administrative team who then followed a standardized workflow (Figure 1) to connect patients with appropriate clinicians for timely dysphagia management. Descriptive statistics were used to summarize SW data.

Results: Between 2021 and 2023, 459 HNC patients treated with radiotherapy were invited to participate in SW via email. 230 patients (51%) actively engaged with the program, with 65% male and 72% White. Notably, 44% of patients consistently responded to 80-100% of the SW check-ins. During this period, the SW system generated a total of 242 dysphagia alerts from 1125 survey responses: 156 alerts for significant weight loss, 38 for IV hydration, 8 for aspiration pneumonia, and 40 for swallow function deterioration (Table 1). After triage workflow, 23% of these alerts led to clinical appointments, with a median appointment time of 16 days from the date the dysphagia alert was generated.

Conclusions: The deployment of an automated dysphagia surveillance and alert program for head and neck survivors led to prompt identification and proactive treatment of dysphagia by efficiently allocating clinical resources to patients in need. SW is easily translatable across various healthcare delivery models and can enhance coordination among multidisciplinary teams in dysphagia care.

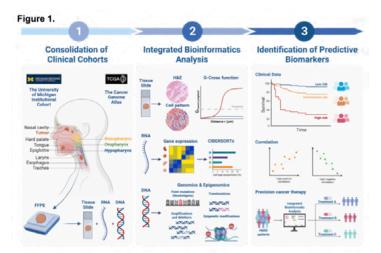| Time after Initiation of Radiotherapy (month)	Survey Responses	Weight loss (>10lbs within 3 months)	Requirement of IV Hydration	Aspiration Pneumonia	Drop in Swallow Function	Total
Baseline	182	25	0	0	0	25
3	216	61	15	1	27	104
6	181	27	6	1	5	39
9	132	12	2	1	2	17
12	110	10	5	0	1	16
15	83	3	3	2	1	9
18	69	6	3	1	1	11
21	61	4	2	2	0	8
24	62	3	1	0	1	5
27	13	0	1	0	1	2
36	5	2	0	0	0	2
39	4	2	0	0	0	2
45	3	1	0	0	0	1
57	4	0	0	0	1	1
Total	1125	156	38	8	40	242

Table 1. Swallow Watch Alerts Distribution

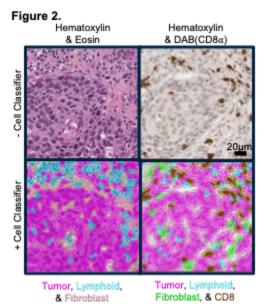Figure 1: Swallow Watch Alerts Clinical Workflow for the Administrative Team

AHNS26: UNLOCKING PREDICTIVE BIOMARKERS IN ORAL CANCER THROUGH INTEGRATED BIOINFORMATICS AND SPATIAL PROFILING - Michael M Allevato, PhD[1]; Leanne Henry[1]; Santhoshi N Krishnan, PhD[1]; Lisa Chionis[1]; Josh D Smith, MD[1]; Janice L Farlow, MD, PhD[1]; Gregory T Wolf, MD[1]; Laura S Rozek, PhD[2]; Jonathan B McHugh, MD[1]; Arvind Rao, PhD[1]; Maureen A Sartor, PhD[1]; Steven B Chinn, MD[1]; [1]University of Michigan; [2]Georgetown University

Background: Oral cavity squamous cell carcinoma (OCSCC) has an unpredictable response to immunotherapy, and standard biomarkers evaluating the tumor immune microenvironment (TIME) lack widespread translational applicability. Defining the microenvironment is critical to understanding mechanisms and allows the development of reproducible and accurate prognostic and predictive biomarkers based on immune profiles. To further study and deconstruct the TIME within OCSCC, we integrated our previously developed computational spatial analysis (CSA) with in-silico deconvolution analyses to comprehensively study the TIME in OCSCC.

Figure 1.

Methods: As illustrated in Figure 1, our research pursued data integration by leveraging paired bulk RNA-Seq datasets (n= 965) from two independent sources: the University of Michigan (UM) and The Cancer Genome Atlas Head-Neck Squamous Cell Carcinoma (TCGA-HNSC) cohorts. This diversity empowered us to explore correlations between genetics, phenotypes, clinical aspects, and OCSCC's immune landscape. Analyses included determining tumor mutational burden (TMB), neoantigen load, and deconvolution using CIBERSORTx for in-silico immune profiles. CSA, including the GCross function (GFx), assessed tumor-infiltrating lymphocyte (TIL) density and distribution relative to cancer cells/fibroblasts, generating immune scores. GFx scores were correlated with WES and RNA-Seq-derived cell-type deconvolution results, immune cell activation expression signatures, and gene expression-based radiosensitivity index scores. Pearson's correlation coefficient and associated p-values were calculated, followed by Cox proportional hazards multivariate regression for the survival and recurrence analysis cohort.

Figure 2.

Results: We found consistent cell counts and G-function scores across diverse tumor samples by validating our H&E cell characterization models in TCGA-HNSC and UM cohorts via CIBERSORTx analysis and CD8 staining (Figure 2). Subsequently, approximately 1000 unique OCSCC samples (472 from TCGA and 493 from UMICH) were characterized for immune cells and quantitatively assessed for TIL density and spatial relationships with cancer cells and fibroblasts. High G-function scores were valuable for predicting lymph node metastasis and decreased metabolism, potentially aiding resource-constrained predictive models based on H&E-stained slides. Integrating spatial relationships with immunogenomics data strengthened our prognostic capabilities, revealing a significant link between lymphocyte-infiltrated regions enriched with CD8+ T-cells and critical factors such as tumor mutational burden, neoantigen load, and improved overall survival. These findings provide critical insights into the impact of the tumor immune microenvironment on OCSCC prognosis.

Conclusion: In conclusion, our study presents an integrated dataset with the potential to generate insights and immunomodulatory therapies to address the challenge of OCSCC's poor immunogenicity. We demonstrate the applicability of computational spatial analysis and in-silico deconvolution across diverse patient populations and pathology images, yielding clinically actionable predictions. Our findings suggest the pivotal role of digital pathology profiling in predicting immunotherapy responses, paving the way for informed and personalized treatments for oral squamous carcinoma patients.

ORAL PAPERS

Panel: Evolution of Immunotherapy in Head and Neck Cancer

(Thursday, May 16, 2024 | 1:45 PM - 2:45 PM)
Room: Grand Ballroom EF

AHNS27: IMMUNOGENICITY AND EFFICACY OF AN E6/E7-TARGETED PROPHYLACTIC MRNA LIPID NANOPARTICLE VACCINE FOR OROPHARYNX CANCER - Radhika Duggal, MA[1]; Jin Dai, PhD[2]; Jessica Geiger, MD[2]; Emrullah Yilmaz, MD[2]; Daniel McGrail, PhD[2]; Travis Kerr, MSc[2]; Jonathan Ligon, MD[3]; Jonathan Chardon-Robles, MS[3]; Hector Mendez Gomez, PhD[3]; Paul Castillo, MD[3]; Jessica Altemus, MS[2]; Frances Weidert, MS[3]; Duane Mitchell, MD, PhD[3]; Elias Sayour, MD, PhD[3]; Natalie Silver, MD, MS[2]; [1]Cleveland Clinic Lerner College of Medicine; [2]Cleveland Clinic; [3]University of Florida

Intro: HPV-associated oropharyngeal squamous cell carcinoma (OPSCC) is rapidly rising. While response to definitive treatment is excellent, most patients with recurrent/metastatic OPSCC do not respond to immune checkpoint inhibitors (~80%). Our group has developed a patented mRNA lipid nanoparticle vaccine platform (mRNA-LP) that can reprogram the systemic and tumor immune microenvironment to unlock antigen specific T cell immunity. In this study, we used preclinical models to understand the immunogenicity and efficacy of a targeted E6/E7 mRNA-LP designed to prevent tumor recurrence after salvage surgery or for high-risk patients after definitive treatment.

Methods: We treated C57/B6 mice with 4 weekly doses of E6/E7 mRNA-LP vaccine formulations intravenously (IV) or intramuscularly (IM) vs nanoparticle (LP) control. Splenocytes were analyzed to assess vaccine immunogenicity and ELISPOT/interferon (IFN) gamma staining was performed after E6/E7 peptide stimulation to demonstrate antigen specificity. A cohort of mice were implanted with MEERL cancer cells after 4 weeks of vaccine (or LP) pre-treatment and tumor growth was assessed.

Results: At 20 days post tumor implantation, there was a significant reduction in MEERL tumor growth in the mRNA-LP vaccine treated mice vs controls, across all treatment groups (P<0.05). After E6/E7 peptide stimulation, IFN-gamma was significantly increased in CD4+ T cells, relative to stimulation with peptide controls, indicating antigen specific immunity in the IV and IM formulations. ELISPOT demonstrated increased IFN-gamma production in IV mRNA-LP formulation after E6/E7 peptide stimulation. IV administration caused increased CD4 effector memory T cell percentages and shifts from M2 to M1 macrophages in splenocytes. As expected, the IM formulation did not induce significant immune cell changes within the spleen.

Conclusion: This study demonstrates initial immunogenicity, efficacy, and antigen specificity of a prophylactic cancer vaccine for HPV-associated cancers, using our patented mRNA-LP platform targeted to E6/E7. Further studies are needed prior to clinical translation; however, this targeted vaccine may be used as prophylaxis for cancer recurrence after salvage surgery or definitive therapy in high-risk HPV-positive OPSCC patients.

**AHNS28: NEOADJUVANT CYTOKINE (IRX-2) IMMUNOTHERAPY FOR RESECTABLE ORAL CAVITY CARCINOMA: FINAL RESULTS OF THE INSPIRE TRIAL - ** <u>Gregory T Wolf, MD</u>[1]; Emily Bellile, MS[1]; Siyu Liu, PhD[1]; Sartor A Maureen, PhD[1]; Laura S Rozek, PhD[1]; Jonathan B McHugh, MD[1]; INSPIRE Trial Clinical Investigators[2]; [1]University of Michigan; [2]INSPIRE trial clinical investigators

Oral cavity squamous cell carcinoma (OSCC) is characterized by multiple alterations in cell mediated tumor immunity especially involving the tumor microenvironment that is often described as an "immune desert" due to the lack of immune reactive tumor infiltrating lymphocytes (TILs). To determine if a novel neoadjuvant regional injection of physiological concentrations of a cell derived, multi-cytokine biologic (IRX-2) can restore immune reactivity, increase TILs and enhance patient survival, an international multi-institutional randomized Phase II clinical trial was conducted in patients with Stage II-IV OSCC undergoing surgical resection (NCT 02609386).

Intention-to-treat (ITT) enrollment was 105 previously untreated patients however a total of 9 patients were excluded for wrong histology, no treatment or patient refusal. A total of 96 patients were randomized (2:1) to receive the IRX regimen 3 weeks prior to surgery. This regimen consisted of an initial dose of cyclophosphamide (300mg/m2) followed by 10 days of regional perilymphatic IRX-2 cytokine injections and daily oral indomethacin, zinc and omeprazole (IRX) compared to the identical regimen without IRX-2 cytokines (Con). The trial also called for similar 5-day adjuvant regimens monthly x 4. Safety, toxicity, tumor and immune responses, event-free (EFS) and overall (OS) survival were determined. Age, sex, TNM class did not differ significantly among the 64 IRX and 32 Con patients. Kaplan-Meier estimates for OS and EFS, inferential comparisons and asymptotic log-rank testing between the two regimens were determined. Previously reported biomarkers, immune and tumor responses were explored with respect to survival outcomes.

The IRX regimen was well tolerated with no grade 3 toxicities and all patients were able to undergo planned surgery at a mean of 29 days from randomization. 72% of patients went on to planned postoperative radiation and all patients received neoadjuvant immunotherapy, however early in the trial it was evident that 80% of patients did not accept the adjuvant regimen and the trial was amended to delete this requirement. For both treatment arms, 97% underwent complete tumor resection. In prior preliminary analysis significant increases in TILs were noted for the IRX arm. For the ITT population (n=105) there were no significant differences in OS or EFS by treatment arm. Among patients with more advanced disease (Stage III/IV) clear trends for improved OS and EFS were observed for the IRX arm. OS at 48 mo. was 70.4 vs 66.3 mos. (IRX vs Con) and median EFS of 45.6 vs. 21.6 mos. and particularly for patients receiving postop chemoXRT (median EFS of 49.5 vs. 33.1 mos.). Subset analyses of outcomes by tumor response, TILs and nanostring immune response genes will also be presented.

Conclusions: Although survival outcomes did not reach statistical significance, the trial demonstrated the safety and feasibility of neoadjuvant cytokine immunotherapy that was associated with significant increases in TILs and a strong trend for improved outcomes in patients with advanced (Stage III/IV) disease. The lack of toxicity or serious adverse events support future combination therapy with other neoadjuvant

immunotherapy or chemotherapy regimens. Patient acceptance of adjuvant immunotherapy regimens is a challenge.

Scientific Session 4: Potpourri

(Thursday, May 16, 2024 | 3:15 PM - 4:00 PM)
Room: Grand Gallroom GHIJ

AHNS29: USING ARTIFICIAL INTELLIGENCE TO AUTOMATE THE EXTRACTION OF STAGING CRITERIA FROM THE ELECTRONIC HEALTH RECORDS OF OROPHARYNGEAL CANCER PATIENTS. -

Elif Baran[1]; Aaron W Li[2]; Steven Aviv[2]; Jessica Weiss[2]; Chris Pettengell[2]; Irene Karam[3]; Andrew Bayley[3]; Ian Poon[3]; Kelvin Chan[4]; Ambika Parmar[4]; Martin Smoragiewicz[4]; Danny J Enepekides[1]; Kevin M Higgins[1]; Hagen Klieb[5]; Tra Truong[5]; Antoine Eskander[1]; [1]Department of Otolaryngology-Head & Neck Surgery, University of Toronto, Toronto, ON, Canada; [2]Pentavere Research Group Inc, Toronto, ON, Canada; [3]Department of Radiation Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON, Canada; [4]Department of Medical Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON, Canada; [5]Department of Pathology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada

Background: Accurate and timely staging of cancers is crucial for patient prognosis and treatment decisions, yet documentation is often poor and data from our site illustrates a 25-54% staging documentation rate within 6 weeks of initial assessment. Given the rapid advancements in Artificial Intelligence (AI) and its applications in healthcare, this study aimed to develop a novel approach using the AI engine DARWEN™ to extract essential information from the electronic health record (EHR) of oropharyngeal cancer patients and assign a TNM stage according to 8th AJCC guidelines.

Methods: A team of expert reviewers manually assessed the records of 803 patients diagnosed with oropharyngeal squamous cell carcinoma between January 1, 2010, and August 1, 2020. They created a ground truth dataset and developed a comprehensive rulebook for staging, which consisted of 135 rules: 17 for p16 status, 60 for T stage, 40 for N stage, and 18 for M stage. Due to the rulebook's complexity and the limited data available relative to the number of rules, a novel approach was needed.

We focused on the core concepts within the rulebook, including size, location, state, metastases, and p16 status and trained four distinct models: Model T (entity relationship extraction model) for anatomical location and invasion state, Model S (numerical extraction model) for lesion size, Model M (sequential classification model) for metastasis detection, and a p16 model for p16 status. T stage and N stage were determined using Model T and Model S, with upstaging applied when necessary due to the size of the lesion. M stage involved Model M to identify metastases and then Model T providing the specific anatomical location. p16 status was determined solely by the p16 model.

To validate our approach, the results were compared against the ground truth established by expert reviewers and accuracy reported.

Results: The process of training and testing models required significantly less time than manual data abstraction from all 803 patient records. For binary outcomes like p16 status

and M stage, DARWEN™ achieved accuracy of 92% for p16 (F1=0.92) and 88% for M stage (F1=0.90). Accuracy was lower for T and N staging at 56%. Error analysis showed that there was inadequate training data coverage for the additional rules. When combining p16 status and TNM to predict early vs. advanced stage cancers, the overall accuracy reached 82%.

Conclusion: Our innovative approach leveraging AI significantly reduced data abstraction time compared to manual methods, achieving impressive accuracy for p16 status and M stage. While T and N staging accuracy was comparatively lower due to limited training data, the overall accuracy in predicting early vs. advanced stage cancers highlighted the clinical relevance of our approach.

Clinical documentation is incredibly varied, with conflicting and inconsistent information found throughout EHR. Tailoring AI to address these challenges is complex but essential. This research not only provides a practical solution to staging challenges but also underscores the potential of AI technologies in enhancing patient care and oncological decision-making. Further model refinement and research are warranted to improve accuracy and clinical applicability.

AHNS30: DOES CENTRAL NECK DISSECTION NEGATIVELY INFLUENCE HYPOPARATHYROIDISM AFTER ANGIOGRAPHY-GUIDED THYROIDECTOMY? -

Pablo Moreno Llorente, PHD, MD, FEBS[1]; Arantxa Garcia-Barrasa, MD[1]; Mireia P Pascua, MD[1]; José Luis Muñoz-De-Nova, MDPHD[2]; [1]Hospital Universitari de Bellvitge; [2]Hospital Universitario De La Princesa, Madrid (Spain)

Background: It is well known that central neck dissection (CND) performed during thyroid surgery may be a potential risk of hypoparathyroidism. Indocyanine green angiography (ICG) has been used to assess the viability of parathyroid glands (PGs) immediately after thyroidectomy, and it has been demonstrated that the presence of only one well-vascularized gland is sufficient to maintain normal calcium levels postoperatively. Recently, angiography-guided thyroidectomy (A-GT) has been shown to significantly reduce postoperative hypoparathyroidism episodes. The objective of the study was to assess the effect of CND on postoperative hypocalcemia in patients undergoing A-GT, as well as to determine the influence of PG position.

Methods: Prospectively-maintained database including consecutive patients undergoing total thyroidectomy + CND between April 2016 and September 2023. The control group included patients in which ICG-angiography was used to assess PG perfusion between April 2016 and September 2020. The study group included patients undergoing A-GT since September 2020 up to the present time.

Perfusion of the PGs was evaluated in every single PG after lobectomy and after CND. The 0-1-2 scoring system was used (0: not vascularized [black], 1: traumatized [grey], 2: well-vascularized [white]). Patients in the study group were injected ICG after medialization of each thyroid lobe in order to enhance the PGs vascular feeding pattern, which was used for guiding thyroid lobe resection on in each side. Thyroidectomy was performed after previous preservation of the PGs and their feeding vessels.

Results: Ninety-seven patients out of 181 underwent total thyroidectomy + CND; bilateral CND was performed in 71 patients (73.2%) and unilateral CND in 26 (26.8%), therefore 168 "sides" (lobectomies-CND) were included in the study.

There were 54 patients and 97 "sides" in the control group, and 43 patients and 71 "sides" in the study group. As shown in Table 1, superior PGs were significatively better preserved than the inferior ones after A-GT, (p = 0.026). Although inferior PGs were at higher risk for devascularization after CND in both groups, CND did not significantly reduce the perfusion of well-preserved PGs after thyroidectomy, which was independent of the position of the glands (superior or inferior PGs) and the control or the study group.

A-GT patients showed a significant reduction of hypoparathyroidism episodes minimizing the deleterious effect of CND on PGs function.

Table 1.- Results

PGs	Control group 97 sides	A-GT 71 sides	P
Superior			
- Identified	87 (89.7)	67 (94.4)	0.423
- Score 2 post-thyroidectomy	30 (34.5)	36 (53.7)	0.026
- Score 2 post-CND	24 (80)	32 (88.9)	0.510
Inferior			
- Identified	67 (69.1)	55 (77.5)	0.303
- Score 2 post-thyroidectomy	31 (47)	24 (43.6)	0.914
- Score 2 post-CND	21 (67.7)	18 (75)	0.773
Hypocalcemia (%)	31.5	7	0.007

Conclusion: Well-perfused inferior PGs are at a higher risk of devascularization after CND. However, A-GT significantly better preserved superior PG perfusion and may help minimize the deleterious effect of CND on PGs viability and hence reducing the rate of postoperative hypoparathyroidism episodes.

AHNS32: A NOVEL TECHNIQUE FOR IN-OFFICE SECONDARY TRACHEOESOPHAGEAL PROSTHESIS PLACEMENT WITH IMMEDIATE VOICING IN POST-LARYNGECTOMY PATIENTS

- Abdullah Adil, MD[1]; Joshua D Smith, MD[1]; Teresa Lyden[1]; Anna Blakely[1]; Madison Blair[1]; Keith Casper[1]; Kelly M Malloy[1]; Chaz Stucken[1]; Mark Prince[1]; Steven B Chinn[1]; Andrew J Rosko[1]; Molly E Heft-Neal[1]; Tiffany Glazer[2]; Matthew E Spector[3]; [1]University of Michigan; [2]University of Wisconsin; [3]University of Pittsburgh

Background: Tracheoesophageal prosthesis (TEP) placement is the preferred method for rehabilitation of voice in patients after total laryngectomy (TL). Most described techniques for secondary TEP placement require general anesthesia or conscious sedation. In-office techniques have traditionally been limited by patient discomfort, inability to precisely visualize and perform TE puncture, and need for return visit for delayed prosthesis placement. In 2016, we described a novel method for in-office, secondary TE puncture with immediate prosthesis placement using a transnasal esophagoscope (TNE) and Seldinger technique. We have now used this technique in over 300 patients and provide an updated report on its utility and outcomes.

Methods: Patients return to clinic 2 – 6 weeks post-laryngectomy for TE puncture and immediate prosthesis placement. The nasal cavities, oropharynx, and laryngectomy stoma are anesthetized and the TNE is used to visualize the planned puncture site approximately 10 – 12 mm superior to the stoma. An Arrow multi-lumen central venous catheter kit (Teleflex, Morrisville, NC) is used for TE puncture under direct visualization and prosthesis is sized and placed using a gel capsule insertion method. The esophageal lumen is visualized throughout the entire procedure to avoid iatrogenic trauma. After prosthesis placement, patients and caregivers are instructed on TEP care and use. Herein, we retrospectively reviewed all patients who underwent this procedure at our institution from 2012 – 2023. We report rate of TEP dislodgement, need for re-puncture, and intelligibility outcomes.

Results: From 2012 – 2023, we used our technique for TEP placement in 342 patients post-laryngectomy. Patients had a median (range) age of 68 (29 – 99) years (n = 307, 89.8 % male). The median (range) time between TL and first TE puncture was 36 (7 – 6334) days. The median (range) length and diameter of prostheses placed was 10 (6 – 22) mm and 16 (14 – 20) Fr, respectively. All patients undergoing this technique were able to vocalize immediately after TEP placement. There were no false passages or bleeding complications. Eleven (3.2 %) patients required re-puncture due to TEP dislodgement.

Conclusion: Our technique for in-office secondary TEP placement via TNE and Seldinger technique is safe, effective, and well tolerated by patients.

AHNS33: IMPACT OF SECOND TOUCH VISITS BEFORE SURGICAL INTERVENTION ON POSTOPERATIVE RADIATION THERAPY (PORT) DELAYS - Sarah F Wagoner, BA[1]; Antonio Bon Nieves, BS[1]; Rohit Nallani, MD[1]; Emma Rea, PAC, MPH[1]; Colleen Sommer, PAC[1]; Amelia S Lawrence, BS[1]; Kevin J Sykes, PhD, MPH[2]; Andrés M Bur, MD[1]; Kiran Kakarala, MD[1]; Yelizaveta Shnayder, MD[1]; Chelsea Hamill, MD[1]; [1]The University of Kansas Medical Center; [2]Baylor Scott and White Health and Wellness Center

Importance: Patients with head and neck squamous cell carcinoma (HNSCC) can experience significant barriers to care, including access to subspecialists, distance from the treating facility, financial toxicity, issues with employment or childcare, access to dental care, and limited social support. Previous studies have demonstrated that patients who face barriers to care may experience delays in postoperative radiotherapy (PORT) initiation, resulting in worse oncologic outcomes. Solutions, such as an additional informational pre-treatment visit with an advanced practice provider (APP) following the initial visit with the oncologic and reconstructive surgeons, i.e. a "second touch" visit, could help reduce delays.

Objective: To investigate PORT initiation times amongst HNSCC patients who received a second touch visit versus those who did not.

Design: Prospective cohort study from June 2021 to July 2022.

Setting: Single tertiary academic medical center.

Participants: Adults with a newly diagnosed primary HNSCC undergoing free flap surgery and PORT between 6/30/2021 and 7/1/2022 who were offered a second touch visit.

Main Outcome(s) and Measure(s): This study assesses the effect of a second-touch clinic visit on delays in PORT initiation, defined as receiving PORT greater than 42 days after surgery.

Results: A total of 47 patients were included. The mean age at diagnosis was 62.3 (±12.1); most patients were male (59.2%) and White (91.8%). The most common primary tumor site was the oral cavity (93.9%). More than half of patients who were offered a second touch visit attended it (N=29, 61.7%). Patients who did and did not have a second touch visit did not differ in adjuvant treatment received (chemoradiotherapy vs.

ORAL PAPERS

RT; p=0.11) or primary tumor site (p=0.177). On univariable analysis, patients who received a second touch visit experienced PORT delays in lower proportions, although this difference was not statistically significant (58.6% vs. 83.3%, p=0.077). On multivariable logistic regression, patients who received a second touch visit had 50% lower odds of experiencing a PORT delay compared with their counterparts who did not attend a second touch visit (aOR= 0.469, CI 95% 0.27 - 0.81, p=0.018).

Conclusions and Relevance: Patients who attended a second touch clinic visit were less likely to experience delays in PORT initiation. This demonstrates the potential for advanced practice provider-driven second touch visits to reduce delays in care. Future studies should examine whether these visits can improve clinical outcomes in patients with HNSCC requiring PORT.

AHNS34: IMPACT OF TIMELY POSTOPERATIVE RADIATION THERAPY (PORT) ON SURVIVAL OUTCOMES IN HEAD AND NECK CANCER PATIENTS - <u>Niketna Vivek</u>; Rahul K Sharma, MD; Kavita Prasad; Kyle Mannion, MD; Natalie Lockney; Vanderbilt University School of Medicine

Background: The Commission on Cancer (CoC) and American Head and Neck Society (AHNS) have instituted a quality metric that time to initiation of postoperative radiation therapy (PORT) should be less than six weeks for patients with surgically managed head and neck cancer. We aim to assess the 2-year survival implications of receiving PORT within or after the suggested 42-day timeframe at our institution and to identify factors predicting PORT delay.

Methods: We conducted a retrospective review of patients receiving postoperative radiation therapy over a three-year period (January 2018 to December 2020). Delay in PORT was defined as greater than 42 days to treatment after surgery. Survival outcomes included both overall survival (OS) and disease-free survival (DFS). Cox regression was used to analyze survival outcomes while controlling for age, stage, p16 status, anatomic subsite, PORT delay, and location of radiation therapy (outside hospital (OSH) vs. institutional). Multivariate logistic regression was used to investigate predictors of PORT delay.

Results: Our analysis included 263 patients who met the study criteria. Notably, 73.0% of patients experienced delays in PORT, with a median time to treatment initiation of 52 days. OSH radiation treatment trended towards a higher number of delays (79% vs. 67%, p=0.060). Those experiencing delays on average lived further from treatment facilities (28 mi vs. 20 mi, p=0.036). Patients with PORT delay displayed a 2-year OS of 76.1% (95% CI 65-88%) compared to 83.3% (77-89%) for those without delay (log-rank; p=0.68), and a 2-year DFS of 75.7% (65-87%) and 73.2% (67-81%) (log-rank p=0.81). On multivariate logistic regression, institutional treatment (vs. OSH) was associated with lower likelihood of delay (OR 0.24, 95% CI 0.09-0.63, p=0.005). Delay in treatment and location of RT did not impact OS or DFS.

Conclusion: In this single institution study, a substantial proportion of patients experienced PORT delays. Patients that were treated at OSH radiation facilities were more likely to experience a delay. However, PORT delay did not result in statistically significant difference in OS and DFS.

Panel Discussion: HPV+Oropharyngeal Squamous Cell Carcinoma

(Thursday, May 16, 2024 | 4:00 PM - 5:00 PM) Room: Grand Ballroom EF

AHNS35: SALIVA COMPARED TO BLOOD-BASED CELL-FREE TUMOR DNA IN HPV-NEGATIVE HEAD AND NECK SQUAMOUS CELL CARCINOMA - <u>Liyona Kampel, MD, PhD</u>; Leonor Leider Trejo, MD; Shlomo Tsuriel, PhD; Narin Neiderman Carmel, MD; Anton Warshavsky, MD; Gilad Horowitz, MD; Jobran Mansour, MD; Dov Hershkovitz, MD, PhD; Nidal Muhanna, MD, PhD; Tel Aviv Sourasky Medical Center

Background: Liquid biopsy has recently emerged as a non-invasive surrogate biomarker in various cancers. Non blood sources, such as saliva samples, can be more easily accessible with minimal risks compared to traditional tissue biopsies. Saliva may be particularly useful in mucosal head and neck squamous cell carcinoma (HNSCC), as tumors may shed DNA fragments directly to saliva fluids. In this study, we utilized next-generation sequencing (NGS) to detect patient-specific somatically altered TP53 in cell free DNA (cfDNA) in plasma and saliva samples of HPV-negative HNSCC patients.

Materials and Methods: NGS was utilized to detect somatic alterations in the coding regions of TP53 gene in HPV-negative HNSCC samples. Once a significant TP53 mutation was detected, cfDNA extracted from plasma and saliva were scrutinized for the presence of the tumor-specific mutation. Clinical disease features and outcomes were analysed in relation to cfDNA detectability.

Results: Overall, TP53 gene was sequenced in 72 tumor specimens, revealing somatic mutations in 55 (77%) samples. Thirty patients were selected for deep targeted sequencing of cfDNA to identify the tumor-specific TP53 alteration. Cases represented various sites and clinical stage of HNSCC. DNA extraction from body fluids yielded comparable concentration of cfDNA in plasma and saliva samples. The fraction of detectable mutant DNA alleles was also comparable between saliva and plasma (mean, 0.95% ± 1.2 vs. 0.77% ± 0.9, respectively). Interestingly, detectable patient-specific somatically altered TP53 in plasma cfDNA, did not necessarily correlate with its detection in the saliva, and vice versa. Saliva cfDNA was detected in locally advanced laryngeal cancer (mostly T4 disease), while in oral cavity – saliva cfDNA was also detected in early-stage cancers.

Conclusion: Detection of tumor derived DNA in saliva seems to be site- and T stage-dependent compared to plasma cfDNA. Saliva liquid biopsy may be complementary to detection of blood derived cfDNA. Larger scale studies should be conducted to better define the role of saliva cfDNA for prognostication and surveillance of HNSCC patients.

AHNS36: IMPACT OF INDUCTION CHEMOTHERAPY ON CIRCULATING TUMOR DNA IN HPV-ASSOCIATED OROPHARYNGEAL CANCER - <u>Christopher J Hughes, MBBS</u>[1,2]; Thom R Loree, MD[1,2]; John T Loree, MD[3]; Mark S Burke, MD[1,2]; Michael Y Nagai, DDS, MD[1,2]; Saurin R Popat, MD[1,2]; Naheed Alam, MD[4]; Daniel Ford, PAC[4]; Dwight

Patterson, MD[5]; [1]Department of Head and Neck Surgery, Erie County Medical Center/Department of Otolaryngology-Head and Neck Surgery, SUNY Buffalo; [2]Temple University Health System, Department of Surgery; [3]Erie County Medical Center Department of Medical Oncology; [4]Department of Surgery, Buffalo Department of Veteran Medical Affairs

Background: Circulating HPV tumor DNA assays (ctDNA) are increasingly establishing a role in the diagnosis, treatment and after-care of patients with HPV-associated oropharyngeal cancer (HPV-OPC). Using a de-escalation paradigm of neoadjuvant chemotherapy followed by surgery, we have previously observed high and durable cure rates, particularly in non-smokers, with few patients subject to adjuvant radiation and its attendant morbidity. In this study, our aims were to correlate ctDNA, before and after both induction chemotherapy and subsequent definitive treatment.

Methods: A prospective enrolment of 21 patients with HPV-OPC documented by histology, p16 positivity and ISH confirmed HPV status was undertaken between February 2021 and October 2023. The patients were consented to IRB-approved protocol, assaying ctDNA both before and after induction chemotherapy (Cisplatin and Docetaxyl) and thirdly, following definitive curative treatment (surgery or chemo-radiation). HPV ctDNA assays were conducted by Naveris Laboratory, Boston, USA.

Results: 21 patients were enrolled, 19 male and 2 female, presenting with Stage I to Stage IV disease. Of primary lesions, 13 originated in the tonsil, 7 in the tongue base and one remains unknown. All patients had HPV ctDNA assays before and after three cycles of neoadjuvant chemotherapy, in addition to serial assays commencing two weeks beyond completion of definitive therapy. Definitive therapy consisted of chemoradiation in two patients only, while the remaining 19 underwent surgery. Surgery consisted of transoral resection of the primary lesion in 18 (excluding one with unknown primary) and modified radical neck dissection in 19. Only three of 19 patients managed with definitive surgery subsequently required post-operative radiation (16%), two tonsillar resections with a positive deep margin and one patient with residual extra-nodal disease in the neck dissection specimen. 19 of 21 patients had a detectable HPV ctDNA at diagnosis (Sensitivity 90%). The two patients with undetectable assays had their tumor specimens confirmed positive to HPV 16 by Naveris Laboratory. Of two patients managed with chemoradiation, one ctDNA was rendered negative following induction chemotherapy, but both remain negative in follow-up. Of the remaining 17 patients managed with definitive surgery, 12 patients had HPV ctDNA rendered negative by induction chemotherapy, however 6 of these patients were found to have minimal residual disease in their pathology specimens (Specificity 50%). Finally, of 5 patients who were still HPV ctDNA positive despite neoadjuvant chemotherapy, all were confirmed to have minimal residual disease in their surgical specimens (Sensitivity drops to 45% following neoadjuvant therapy). Overall survival is 95%, at follow-up ranging from 7 to 33 months (median 22 months). 19/20 survivors remain NED with negative ctDNA, while one patient is alive with a metachronous soft palate primary, diagnosed following a newly positive ctDNA.

Conclusions: A complete response to induction chemotherapy cannot be reliably predicted by a negative HPV ctDNA assay, but a persistently positive ctDNA is highly predictive of persistent or recurrent HPV-OPC.

AHNS37: SURVIVAL OUTCOMES FOR SUBJECTS ENROLLED IN A SINGLE ARM, OPEN LABEL TRIAL OF THERAPY DE-ESCALATION IN PATIENTS WITH STAGE I-III HPV+ OROPHARYNGEAL SCC - <u>Herschel Patel, MD</u>; Aru Panwar, MD; William Lydiatt, MD; Andrew Coughlin, MD; Andrew Holcomb, MD; Angela Osmolak, MD; Oleg Militsakh, MD; Robert Lindau, MD; Head and Neck Surgical Oncology, Methodist Estabrook Cancer Center, Nebraska Methodist Hospital, Omaha, Nebraska

Importance: Therapy de-escalation for patients affected by human papilloma-virus mediated oropharyngeal carcinoma (HPV+ OPSCC) may alleviate burden of treatment-related short-term and late side-effects. Reporting outcomes from prospectively conducted therapy de-escalation clinical trials may be critical to ensuring oncologic safety of such approaches.

Objective: To assess the overall and disease-free survival outcomes (OS and DFS, respectively) for subjects with stage I-III HPV+ OPSCC enrolled in a therapy de-escalation trial.

Methods: Single arm, open label, therapy de-escalation clinical trial in adult subjects with stage I-III HPV+ OPSCC (ClinicalTrials.gov Identifier: NCT04638465). The main outcome measures included probability estimates for (a.) 2-years OS and (b.) 2-years DFS.

De-escalated adjuvant therapy was delivered for subjects with intermediate or high risk features on surgical pathology, per summary provided in table 1. A nearly 17% reduction in cumulative dose of radiotherapy was observed for subjects with intermediate risk features on surgical pathology. Subjects with high risk features experienced a nearly 9% reduction in cumulative dose of radiotherapy to primary site and nodal basins with concurrent weekly cisplatin (40mg/m2 weekly x 6 cycles). Patients with more extensive disease at the primary site, those who were technically ineligible for surgical resection, or with bilateral or bulky nodal disease were treated with concurrent chemotherapy and radiotherapy at dose level 1 (60 Gy radiation over 6 weeks combined with weekly cisplatin 40mg/m2 x 6 doses) (a nearly 14% reduction in cumulative dose of radiotherapy). Patients who presented with T4 primary neoplasm or N3 nodal disease received treatment at dose level 2 (70 Gy over 7 weeks combined with weekly cisplatin 40mg/m2 x 7 cycles).

Subject deaths and recurrence events were prospectively recorded and Kaplan-Meier analyses were performed. Median values with ranges are provided for events including death and recurrence during study follow-up. Survival probabilities are presented with 95%CI.

Results: One hundred fifty subjects completed a median follow-up of 26.4 months (range 0-57 months). Eight deaths were observed at a median interval of 12.3 months (range 0-24.8 months). The 2-year OS probability was 93.4% (95% CI, 88.1-98.6%). Eleven subjects experienced disease recurrence at a median of 14.0 months (range 4.2-36.5 months). The 2-year probability of DFS was 94.4% (95% CI, 89.6-99.2%).

Conclusion and Relevance: Survivors of HPV+ OPSCC receiving curative intent therapy in this single arm, open label, therapy de-escalation trial experienced lower cumulative dose of radiotherapy (dose reduction range 9-17%), and experienced OS and DFS outcomes that are comparable to historical cohorts treated with conventional regimens. These results may

inform and reassure clinicians and subjects involved in therapy de-escalation trials for HPV+ OPSCC regarding safety, and facilitate larger comparative effectiveness trials in the field.

TABLE 1: Summary of therapy options available to subjects in the clinical trial (ClinicalTrials.gov Identifier: NCT04638465)

Therapy Option	Primary Site & TNM classification			
	Tonsil	Base of Tongue/ Non-tonsil primary neoplasm	Unidentified primary site	Comments
Surgery only[+i]	T1-3*, N0-1 (single node)	Laterally situated T1-2, N0-1 (single node)	T0, N1 (single node)	Adjuvant therapy for intermediate[α] or high[β] risk features
Surgery with adjuvant therapy[Ω]	T1-3, N1 (2-4 nodes)	T1-2, N1 (2-4 nodes) or N2		
Concurrent chemo-radiotherapy, *Dose level 1*	T1-3, N2		T0, N2	*Radiotherapy:* 60 Gy/ 6 weeks (2Gy/fraction, 5 fractions/week) *Chemotherapy:* Weekly Cisplatin 40mg/m^2, 6 cycles
Concurrent chemo-radiotherapy, *Dose level 2*	T1-3, N3 T4, any N	T3-4, any N Any T, N3	T0, N3	*Radiotherapy:* 70 Gy/ 7 weeks (2Gy/fraction, 5 fractions/week) *Chemotherapy:* Weekly Cisplatin 40mg/m^2, 7 cycles

+ Surgery: Trans-oral resection of primary site, and ipsilateral neck dissection (levels II-IV)

i Single modality radiotherapy available to patients technically ineligible for curative intent surgery

* Only selected exophytic T3 tumors eligible

α Intermediate risk features: Extra-nodal extension (ENE) ≤2 mm, extensive per-neural invasion (PNI) or lympho-vascular invasion (LVI), 2–4 histologically positive nodes. Postoperative radiotherapy: 50 Gy/ 5 weeks (2Gy/fraction, 5 fractions/week) to primary site and nodal basin.

β High risk features: ENE >2 mm, positive margins, >4 histologically positive nodes. Postoperative radiotherapy: 60 Gy/ 6 weeks (2Gy/fraction, 5 fractions/week) to primary site and nodal basins with concurrent weekly Cisplatin 40mg/m^2, 6 cycles.

Ω Chemo-radiotherapy available to patients technically ineligible for curative intent surgery

Gy, Gray

mg/m^2, milligram/meter^2

POSTER LISTINGS

B001: INVESTIGATING THE ASSOCIATION BETWEEN HASHIMOTO'S THYROIDITIS AND PAPILLARY THYROID CANCER AGGRESSIVENESS - <u>Adriana I Baez Berrios, BS</u>; Mathilda Alsen, MPH; Margaret Brandwein-Weber, MD; Maaike van Gerwen, MD, PhD; Icahn School of Medicine at Mount Sinai

Background: The ~20% coexistence rate of Hashimoto's thyroiditis (HT) and papillary thyroid carcinoma (PTC), along with conflicting findings on the potential correlation between HT and less aggressive PTC, warrants further examination. This study aimed to compare pathological tumor aggressiveness indicators between PTC +/- HT to understand their interplay and impact on patient outcomes. This study adds a novel dimension by investigating aggressive lymph node (ALN) status, previously unexplored in this context.

Methods: Retrospective chart data was collected for PTC patients at a NY academic medical center's Department of Otolaryngology-Head and Neck Surgery from 2018-2020. A diagnosis of HT was determined through pathologic criteria. Pathology reports were reviewed for pathological indicators of cancer aggressiveness that included angioinvasion, lymphatic invasion, perineural invasion, extrathyroidal invasion, margin of resection, tumor focality, TNM staging, and ALN status. Positive ALN status is defined as either > 5 positive lymph nodes, or ≥ 1 positive lymph node > 3 cm, and/or ≥ 4 positive lymph nodes with extranodal extension. Univariate analyses were used to compare demographic and histopathological characteristics between PTC+HT and PTC only groups. Multivariable logistic regression models were used to compare PTC aggressiveness pathological markers between groups, while adjusting for sex, age, race, smoking status, and BMI.

Results: Among the 533 patients with PTC, 102 (19.1%) had HT. PTC+HT patients were often female (81.4% vs 62.4%, p = 0.0002), younger (48.82 vs 52.62 years, p = 0.034), non-smokers (78.4% vs 68.7%, p = 0.035), and had N0 stage tumors (46.1% vs 24.8%, p < 0.0001). PTC+HT was associated with significantly lower odds of N1 stage (ORadj, 0.50; 95% CI, 0.29-0.86) and lymphatic invasion (ORadj, 0.53; 95% CI, 0.29-0.97) versus PTC alone. There was no significant difference in positive ALN status (ORadj, 0.87; 95% CI, 0.45-1.69) and decrease in the odds of a positive resection margin (ORadj, 0.64; 95% CI, 0.33-1.25) between groups. Multivariable logistic regression revealed no significant increase in the odds of T2/3/4 stage versus T1 (ORadj, 1.12; 95% CI, 0.69-1.80), angioinvasion (ORadj, 1.37; 95% CI, 0.55-3.37), perineural invasion (ORadj, 1.59; 95% CI, 0.55-4.64), extrathyroidal extension (ORadj, 1.23; 95% CI, 0.76-2.00), or multifocality (ORadj, 1.18; 95% CI, 0.76-1.84) when comparing PTC+HT to PTC alone.

Conclusion: We find no evidence that PTC in the setting of HT is more aggressive than without HT. Although PTC+HT patients seem to have a lower odds of positive lymph nodes, binary lymph node status is not a meaningful prognosticator. ALN, which considers cumulative metastatic burden, is an important prognosticator, and there was no difference found between groups. Medical surveillance of HT patients potentially contributed to earlier PTC detection and thus less advanced tumors in relation to N stage. These findings are noteworthy to clinicians consulting HT patients and contribute to the discussion regarding surveillance and early PTC detection.

B002: HIERARCHICAL AND T-SNE CLUSTER ANALYSIS SHOW DIFFERENTIAL GENE MUTATIONS IN LOCAL VS METASTATIC ANAPLASTIC THYROID CARCINOMA - Richard D Hammer[1]; Naiwei Chen, PhD[1]; Dean C Pavlick[2]; Matthew Hiemenz, MD[2]; <u>Laura M Dooley, MD</u>[1]; [1]University of Missouri; [2]Foundation Medicine

Introduction: Anaplastic thyroid carcinoma (ATC) is an uncommon and aggressive thyroid cancer with rapid progression and poor survival. Our studies of the molecular characteristic of 727 cases of ATC, the largest study of this disease to our knowledge, have given insights into this aggressive cancer, showing 6 groups of ATC by t-SNE cluster analysis defined by characteristic genetic mutations. However, little has been done in comparing mutations in primary vs metastatic ATC. In this study, we perform cluster analysis and identify distinct differences in mutations in primary vs metastatic sites of ATC.

Design: Deidentified NGS results on 727 cases of ATC were obtained from Foundation Medicine. The data set consisted of 481 cases of local thyroid ATC and 205 cases of ATC to distant sites. 41 cases designated as "lymph node" without further designation were excluded to prevent inclusion of locally invasive tumor. Cluster analysis by Jaccard distance metric to calculate distances for sparse binary genomic profiles for pattern recognition was used. Hierarchical clustering was evaluated by Ward's linkage rule. The determination of the number of clusters combined the Dunn index, clinical rationale and the number of significant principal components based on the Bayesian method of Auer and Gervini. For further visualizing the resulting similarity data of characteristic mutations, through the dimensionality reduction (DR) in 254 characteristic mutations, the t-distributed stochastic neighbor embedding (t-SNE) algorithm was applied to visualize and interpret the classes of pathogenic mutations. The characteristic mutations in both groups were compared by Fisher's exact test for each individual testing and the multiple testing with the Benjamini-Hochberg procedure, respectively.

Results: Analysis of groups by site of thyroid vs distant metastasis showed 6 clusters similar to our prior study. The top mutated genes by site in each category are shown in table 1. However, there was significant differences in distribution of *BRAF, NRAS, NF1, CCNE1* and *KMT2D*. *BRAF* showed significant increase in metastatic sites (p=8.5×10-6), while *NRAS*, *NF1*, *CCNE1* and *KMT2D* were significantly decreased in metastatic sites (p=0.0235, 0.0029, 0.0210, 0.0222, respectively) (Tables 1-2, Figure 1). With accounting for the multiple testing, the results showed a significant difference for *BRAF* (Table 2).

Conclusions: Comparison of local vs metastatic ATC showed 6 groups defined by genetic mutations with enrichment of *BRAF* in metastatic sites, and a decrease in *NRAS* and *NF1* clusters compared to local thyroid tumors. The molecular cluster defined by *BRAF* comprises approximately 30% of primary ATC yet defines 48.8% of metastatic tumors. This implies classification of ATC by molecular groups carries biological and prognostic significance, as well as potential treatment options with targeted therapy for multiple targets. Molecular classification of ATC should be performed on all cases to guide treatment and prognosis.
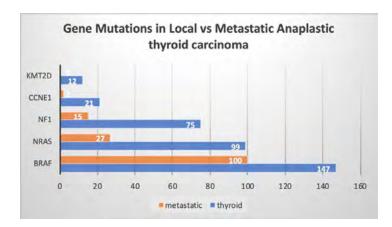
Gene Mutations in Local vs Metastatic Anaplastic thyroid carcinoma

Table 1. Topmost frequent mutations

Gene	Metastatic (n=205)	%	Thyroid (n=481)	%
TP53	135	66.0	324	67.4
TERT	131	64.0	317	65.9
BRAF	100	48.8	147	30.6
CDKN2A	58	28.3	132	27.4
CDKN2B	41	20.0	87	18.1
NRAS	27	13.2	99	20.6
PTEN	28	13.7	76	15.8
PIK3CA	33	16.1	62	12.9
NF1	15	7.3	75	15.6
NF2	28	13.7	52	10.8
MTAP	15	7.3	43	8.9
RB1	13	6.3	44	9.2
DNMT3A	21	10.2	35	7.3
ATM	11	5.4	22	4.6
JAK2	11	5.4	13	2.7
CD274	10	4.9	12	2.5
PDCD1LG	10	4.9	11	2.3

Table 2

Gene	Thyroid (n=481)	Metastatic (n=205)	p value	Adjusted p value[‡]
BRAF	147 (30.6%)	100 (48.8%)	$8.5×10^{-6}$	0.0022
NRAS	99 (20.6%)	27 (13.2%)	0.0235	1
NF1	75 (7.3%)	15 (15.6%)	0.0029	0.3682
CCNE1	21 (4.4%)	2 (0.98%)	0.0210	1
KMT2D	12 (2.5%)	0 (0%)	0.0222	1

[‡]The multiple testing with the Benjamini-Hochberg procedure for 254 characteristic mutations was considered.

B003: HIERARCHICAL AND CLUSTER ANALYSIS OF ANAPLASTIC THYROID CARCINOMA SHOWS DISTINCT MOLECULAR SUBGROUPS AND PATHWAYS OF CARCINOGENESIS - Richard D Hammer, MD[1]; Naiwei Chen, PhD[1]; Dean C Pavlick[2]; Matthew Heimenz, MD[2]; Laura M Dooley, MD[1]; [1]University of Missouri; [2]Foundation Medicine

Introduction: Anaplastic thyroid carcinoma (ATC) is an uncommon and aggressive thyroid cancer. Early studies of ATC were composed of relatively small groups, and showed no pathognomonic mutation, with mutations of both *BRAF* and *RAS* pathways. The largest prior single study of ATC in 2018 included 196 cases and identified novel genetic events with characteristic genetic groups. The corresponding result showed groups of ATC with cluster analysis defined by

1. *BRAFV600*

2. *CDKN2A* loss of function

3. *NRAS*

4. *PTEN +NF1 and RB1 (KIT/PDGFR, CD274, JAK2)*, higher tumor mutational burden and microsatellite repair gene mutations

This has been used to postulate the mechanism of evolution of this tumor as one of sequential gain of mutations and ultimately acquiring mutations of *TP53* and *TERT* promoter resulting in ATC. However, clinical experience suggests the existence of a "de novo" pathway which is not characterized. This is supported by the fact that the majority of ATCs do not have mutations in *BRAF* or *RAS* yet show an aggressive clinical pattern with *TP53* mutations.

Design: Deidentified NGS results on 727 cases of ATC were obtained from Foundation Medicine. To explore and identify classes of mutations, we applied the hierarchical clustering using Ward's linkage rule. The determination of the number of clusters combines Dunn index, clinical rationale and the number of significant principal components based on the Bayesian method of Auer and Gervini. The t-distributed stochastic neighbor embedding (t-SNE) algorithm was further applied to visualize and interpret the clusters of pathogenic mutations through the dimensionality reduction in 254 characteristic mutations. Descriptive statistics was used to summarize the findings.

Results: t-SNE projected the distribution of mutation characteristics from 6 identified clusters that confirms distinct groups previously identified (Table 1, Figure 1). t-SNE analysis shows further discrimination of *BRAF* negative pathways (groups 3-6) with the largest group predominated by *PTEN* (group 6, 220 pts) and group 3 showing *RET+TERT* co-mutation predominant (85.7% vs TP53 9.5%). Group 4 involved *NRAS* but was *TP53* predominant (85.7%). A *KIT* predominant group 5 (combined with group 4 of the prior) appeared to be a distinct group. Group 6 with *PTEN* also showed frequent mutations in *DNMT3A*, *ATM*, *TET2*, and *ASXL1* suggesting a role for clonal hematopoiesis. *ARID1A* also clustered with group 6, while *PIK3CA*, *BCOR* and *CHEK2* clustered in group 2 along with *BRAF*.

Conclusions: Hierarchical clustering analysis along with t-SNE analysis of 727 cases of ATC shows distinct groups defined by molecular mutations and may provide a classification for diagnosis. This study confirms prior defined molecular subgroups of ATC. Our results also show clusters involving *RET+TERT* and

KIT. The largest group of ATC with *PTEN+NF1* may result in de-novo ATC with no significant contribution from *BRAF*, *NRAS* or *RET*. Further studies to assess the clinical impact, targeted therapies, and if there is survival and/or response to treatment differences will require prospective analysis of additional cases.
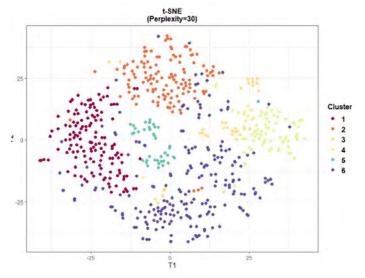

Table1. Clusters of Characteristic Mutations in 727 cases of Anaplastic thyroid carcinoma

	Clusters (top genes)	# PTS	TERT > 75%	TP53 >75%
1	CDKN2A, CDKN2B (NF2, MTAP)	144	+	
2	BRAF (PIK3CA, CHEK2)	187	+	
3	RET, RAC1	42	+	
4	NRAS, CCNE1, EPHA3	91		+
5	KIT,PDGFR, JAK2, CD274, PDCD1LG2, KDR	39		+
6	PTEN, NF1, RB1	220		+

B004: CORRELATION BETWEEN IMMUNOHISTOCHEMISTRY ASSESSMENT OF YAP EXPRESSION AND CLINICAL OUTCOMES OF HEAD AND NECK CANCER PATIENTS

- Alexandra Dorman; Liyona Kampel; Leonor Trejo; Nidal Muhanna; Tel-Aviv Sourasky Medical Center

Background: Squamous cell carcinomas (HNSCC) represent the most prevalent pathology among head and neck cancers, displaying escalating incidence and mortality rates in recent decades.One of cellular pathways contributing to HNSCC progression is the Hippo – YAP (Yes Associated Protein) pathway. YAP plays a crucial role in regulating cell proliferation, tissue stability, and organ size. It has been identified as a promoter of tumorigenic phenotypes and transcriptional changes associated with tumor progression.

Objective: We aimed to evaluate whether outcomes of HNSCC patients can be predicted based on a simple and readily available histologic assessment of the YAP expression.

Materials and methods: Patients with pathologically confirmed HNSCC were identified and immunohistochemistry was used to assess YAP protein expression.

Results: A total of 30 HNSCC specimens arising at the oral cavity (25), larynx (3) and lip (2) were histologically assessed. All of the specimens exhibited high cytoplasmic expression of YAP in tumor tissues compared to adjacent normal tissue. Notably, fourteen samples displayed elevated nuclear expression of YAP, oral cavity (12), larynx (1) and lip (1). We observed that positive nuclear YAP expression significantly correlated with better overall survival (OS) compared to negative nuclear YAP expression (Kaplan Meier estimate of 5-year OS 55% vs. 9% respectively, P = 0.0158), and with higher rates of progression free survival (PFS) Kaplan Meier estimate of 5-year OS 40% vs. 7% respectively, P = 0.033).

Conclusion: Immunohistochemistry assessment of YAP expression can predict clinical outcomes of HNSCC patients. This observation underscores the complexity of YAP's role in HNSCC progression and warrants further evaluation in a larger scale study and maybe ultimately integrated into a clinicopathologic risk model for patients with HNSCC.

B005: CHARACTERIZING INTRA-TUMORAL BACTERIA IN OROPHARYNGEAL SQUAMOUS CELL CARCINOMA -

Radhika Duggal, MA[1]; Jin Dai, PhD[2]; Kristiana Fredenburg, MD, PhD[3]; Jessica Altemus, MS[2]; Travis Kerr, MSc[2]; Daniel McGrail, PhD[2]; Natalie Silver, MD, MS[2]; [1]Cleveland Clinic Lerner College of Medicine; [2]Cleveland Clinic; [3]University of Florida

Intro: Ororpharyngeal squamous cell carcinoma (OPSCC) has been rapidly increasing due to Human Papilloma Virus (HPV)-associated disease. While the response rates to definitive treatment are excellent in this population, identifying factors that may contribute to treatment resistance and disease recurrence are needed. The oral microbiome is an important component of the tumor microenvironment that can influence therapeutic responses. This study aimed to profile intratumoral bacteria in OPSCC using the Cancer Genome Atlas Program (TCGA) and an institutional cohort of patients with aggressive oropharynx cancer.

Methods: Using established microbial computational pipelines (Pathseq) from whole exome/genome data extracted from the TCGA, we profiled oncobacteria (cancer-associated bacteria) abundance in OPSCCs (n=76). For the institutional patient cohort, 26 patients with HPV-positive OPSCC and available pre-treatment biopsy specimen were retrospectively identified. Of the 26 patients, 14 HPV-positive OPSCC patients had disease recurrence/metastasis and were selected to represent an aggressive cohort. DNA was extracted from patient FFPE blocks and 16S rRNA gene sequencing and qPCR for bacterial abundance was performed to identify bacterial composition and abundance. mRNA expression profiling was performed using the HTG molecular platform and GSEA immune cell profiling was performed. Bacterial sequencing data and mRNA expression profiling were correlated with clinicopathologic outcomes.

Results: In the TCGA cohort, HPV-positive OPSCC was associated with decreased oncobacteria abundance when compared to HPV-negative OPSCC (p < 0.01). A lower abundance of oncobacteria was found to correlate positively with both progression free survival and overall survival in HPV-positive OPSCC in this cohort. In the institutional cohort, within the HPV-positive OPSCC population (n=26), increased oncobacteria burden was associated with worse overall survival (p<0.05). mRNA expression profiling demonstrated increased polymorphonuclear myeloid derived suppressor cell (PMN-MDSCs) signatures in the aggressive HPV-positive cohort (p<0.05).

Conclusion: In this study, we demonstrate that increased oncobacteria burden is associated with HPV-negative OPSCC and more aggressive HPV-positive OPSCC. Intratumoral bacteria may serve as a potential prognostic marker for OPSCC, but more studies are needed for clinical translation.

B006: CRENOLANIB IMPROVES PD-1 RESPONSE AND OVERALL SURVIVAL IN IMMUNE CHECKPOINT INHIBITOR RESISTANT MURINE MODELS OF ORAL SQUAMOUS CELL CARCINOMA - Katherine Gonzalez, BS; Xiangfeng Shen, PhD; Tammara Watts, MDPhD; Duke University

Background: Present line indications for pembrolizumab are for patients with metastatic or unresectable recurrent (i.e. incurable) head and neck squamous cell carcinoma (HNSCC). However, only a minority of patients on immunotherapy will realize a durable survival benefit because >80% of patients with metastatic HNSCC do not respond to PD-1 blockade. Tumor microenvironment mesenchymal stem cells (MSCs) and cancer associated fibroblasts (CAFs) have been reported significantly contribute to chemotherapy and radiation resistance. Moreover, MSCs have been shown to contribute to an immunosuppressive tumor microenvironment by upregulating PD-L1 in breast cancer models. We have previously shown crenolanib improves MSC mediated cisplatin resistance in vitro through modulation of MSC-mediated activation of AKT signaling, therefore we hypothesize that targeting MSCs may be of therapeutic benefit alone and in combination with anti-PD1 immunotherapy.

Methods: Oral cancer was induced in the buccal space of C56/BL6 mice with the murine oral cancer cell lines MOC1 or PD-1 resistant cell line, MOC2. When tumors reached approximately 5 x 5 mm, mice were treated with 15 mg/kg (low dose) or 30 mg/kg crenolanib (high dose) for five consecutive days over 3 weeks. Tissue were harvested for immunohistochemistry and immunofluorescence analysis and ex vivo cell cultures prepared for analysis by western immunoblotting and flow cytometry.

Results: There was a significant reduction in tumor volume in mice bearing MOC1 and MOC2 tumors (p<0.03) treated with either low or high dose crenolanib compared to vehicle control. Overall survival was also significantly improved in mice bearing MOC1 tumors treated with high dose crenolanib compared to mice treated with vehicle control (p<0.04) and approached significance in MOC2 mice treated with low dose crenolanib. Tumor sections were imaged by immunofluorescence microscopy. There was a decrease in expression of PDGFR-α on MOC1 tumor cells and α-SMA on tumor microenvironment stromal cells in mice treated with crenolanib compared to vehicle control, suggesting crenolanib targets both cell types. There was a significant reduction in tumor volume (p<0.0001) and improved overall survival (p<0.0004) in mice bearing MOC2 tumors treated with combination crenolanib plus pembrolizumab compared to vehicle plus pembrolizumab.

Conclusions: Preliminary in vivo data suggests crenolanib may be efficacious when used in combination with anti-PD1 immunotherapy by inhibiting the immunosuppressive effects of tumor microenvironment MSCs.

B007: ACTIVATION OF AKT SIGNALING IN MESENCHYMAL STROMAL CELLS INDUCES POOR OVERALL SURVIVAL AND RADIATION RESISTANCE IN MURINE MODELS OF ORAL CANCER. - Katherine Gonzalez, BS; Xiangfeng Shen, PhD; Tammara Watts, MDPhD; Duke University

Background: An abundant stromal infiltrate has been associated with poor overall survival in patients with head and neck squamous cell carcinoma. Mesenchymal stromal cells (MSCs) and cancer associated fibroblasts (CAFs) comprise a large component of the stromal cell infiltrate. While MSCs and CAFs have been reported to induce therapeutic resistance in cancer, how oral squamous cell carcinoma (OSCC) cells activate tumor promoting mechanisms in MSCs that potentiate worse survival outcomes and radiation resistance has not been well described in the context of OSCC.

Methods: MSCs were grown in MOC1 conditioned media and activation of AKT measured by western immunoblotting. To recapitulate the stroma rich desmoplastic reaction characteristic of OSCC in vivo, MSCs were grown in 1:1 co-culture with the murine oral cancer cell line MOC1. Tumors were induced in the buccal space of C56/BL6 mice using previously established inoculums of MOC1 cells alone or MOC1/mMSC co-cultures. Following the development of tumors measuring ~5 mm, mice were administered a single fraction of 10Gy radiation to the buccal space.

Results: Flow cytometry analysis of MOC1/mMSC co-cultures demonstrated 3:1 ratio of MOC1:mMSC cells, as measured by the selection markers EpCAM and CD106, respectively. Histologically tumors derived from mice bearing MOC1/mMSC tumors were consistent with a stromal infiltration surrounds nests of tumor cells compared to tumors derived from MOC1 alone. The median overall survival in mice bearing MOC1/mMSC tumors (24 days) compared to MOC1 alone (42 days) was reduced by 57% (n= 10; p<0.003). Following the single administration of 10Gy radiation to the buccal space, the median overall survival of mice bearing MOC1/mMSCs tumors (45 days) compared to MOC1 alone (56 days) was reduced by 20% and approached significance in this small initial pilot of mice (n=3; p<0.06). We observed a 2.5-fold increase in pAKT (S473) and a 3.3-fold increase p-AKT (T308) in MSCs following 4-hour exposure to MOC1 conditioned media (n>3; p<0.001), suggesting MOC1 induces complete activation of p-AKT at both S473 and T308.

Conclusions: MSCs and MOC1 induce bi-directional effects resulting in activation of AKT in MSCs, significant reduction in overall survival and radiation resistance, in vivo. These data suggest therapeutic strategies targeting cross-talk between MSCs and OSCC cells may be of therapeutic benefit to improve radiation sensitivity in the oral cavity.

B008: CANCER-ASSOCIATED FIBROBLASTS INDUCE STEM-CELL-LIKE BEHAVIOR IN HEAD AND NECK CANCER CELL LINES. - Colleen G Hochfelder, MD[1]; John Henry Owen, MS[1]; Prashant Puttagunta, BS[1]; Spring Gao, BS[1]; Michael Allevato, PhD[1]; Joshua Smith, MD[1]; Mark E Prince, MD[2]; J Chad Brenner, PhD[2]; Steven B Chinn, MD[2]; [1]Department of Otolaryngology-Head and Neck Surgery, University of Michigan, Ann Arbor, MI; [2]Department of Otolaryngology-Head and Neck Surgery, Rogel Cancer Center, University of Michigan, Ann Arbor, MI

Background: Cancer-associated fibroblasts (CAFs) are a group of fibroblasts which are induced out of quiescence by head and neck squamous cell carcinomas (HNSCCs). Cancer stem cells (CSCs) are a subset of tumor cells with unique stem-cell-like properties that are hypothesized to be responsible for a tumor's capacity to grow, spread, and resist treatment. CSCs are identified by surface cell markers, including CD44 and ALDH. CSCs and CAFs are thought to be major drivers of tumoral plasticity, heterogeneity and tumor metastasis are CAFs and cancer stem cells (CSC). Here, we assess the ability of CAFs to induce a stem-cell-like state and in vitro spheroids.

Materials/Methods: We explored the relationship between CAFs and the ability to induce spheroids in patient-derived HNSCC lines (UM-SCC-103, UM-SCC-122, UM-SCC-124, and UM-SCC-125). Cells were either treated with increasing percentages of FGF or co-cultured with patient-derived, matched CAFs and rates of spheroid formation were assessed. Cell lines were transfected with GFP and dsRED. Cells were sorted in flow cytometry and populations bearing surface CSC markers CD44 and ALDH were isolated (GFP: CD44+ALDH+, dsRed:CD44-/ALDH-). Different ratios of thesesorted cells were then incubated with and without CAFs and with increasing amounts of FGF2. Spheroids were assessed using fluorescent microscopy at days 1, 3, and 7. Supernatants were frozen for future analysis of secreted cytokines from co-cultures at each time point, data pending. Means were compared using T-tests using STATA 15.1 SE.

Results: Multiple cells lines demonstrated formation of spheroids by day 7 of treatment with either EGF or FGF2. Use of FGF2 in cell line media produced higher amounts of spheroid formation compared to EGF. Tumor cells did not demonstrate spheroid formation spontaneously and required either supplementation with FGF2 or co-culture with CAFs. Co-culture of HNSCC cell lines with CAFs resulted in increased number of spheroids. The difference was significant at each time point (p<0.0001 for each). Spheroids formed with CAFs present were significantly larger in diameter at days 3 and 7 (p=0.008, p=0.007). In the CD44-/ALDH- cell population, FGF2 supplementation did not induce spheroids, but the addition of CAFs was able to induce spheroid formation. Spheroids demonstrated organized architecture, with an outer shell of CAFs (blue), surrounding a core of CD44+/ALDH+ cells (green) and CD44-/ALDH- cells (red) (Figure 1). The creation of spheroids was modifiable using two FGFR inhibitors. In co-culture with HNSCC cells and CAFs, the number of spheroids created was significantly reduced when treated with FGFR inhibitors (p=0.003).

Conclusion: CAFs appear to be a key regulator of in vitro stem-cell-like behavior in HNSCC cell lines able to induce and maintain spheroids. Inhibition of FGF2Rs was able to significantly reduce the number of spheroids induced by CAFs suggesting this relationship is modifiable.

Figure 1. Architecture of HNSCC cell line spheroid. Green cells are CD44+/ALDH+. Red cells are CD44-/ALDH-. Blue cells are CAFs. A. CD44+/ALDH+ cells cultured with CAFs. B. Mix of CD44+/ALDH+ and CD44-/ALDH- cells cultured with CAFs. C. CD44-/ALDH- cells cultured with CAFs. All images are 20X.

B009: PDCD10 IS A PROMISING NOVEL THERAPEUTIC TARGET FOR HEAD AND NECK SQUAMOUS CELL CARCINOMA - Manu Sundaresan; Alexander von Kumberg; Xiangying Chen; Claudia Wing; Lucas Huang; Elena Jochum; Elena Jochum; Mark W Lingen; Alka Singh; Vasudha Mishra; Alexander T Pearson; Ari J Rosenberg; Nishant Agrawal; Le Shen; Evgeny Izumchenko; University of Chicago

Oral cavity squamous cell carcinoma (OCSCC), the most common subtype of head and neck squamous cell carcinoma (HNSCC), is a devastating disease, causing substantial morbidity and mortality. Consumption of alcohol and tobacco products increases the risk of OCSCC. Prevalence of human papilloma virus (HPV) infection outside of oropharyngeal cancer is low, and its significance remains debatable. Only a handful of targeted therapies are available for patients with HPV-negative HNSCC (which include many OCSCCs), and the 5-year overall survival remains ~50%. While strategies are being designed to improve risk assessment, detection, and therapeutic intervention, these approaches are limited by our incomplete understanding of HNSCC biology, particularly in its early development. Thus, it is crucial to identify novel targets of therapeutic interest.

PDCD10 is a multifaceted protein shown to be overexpressed in several solid malignancies. It was reported that PCDC10 regulates numerous oncogenic pathways and may contribute to tumorigenesis and chemoresistance by promoting cell proliferation, anti-apoptosis, epithelial-mesenchymal transition, and inhibiting anti-tumor immune responses. Recently it was suggested that PDCD10 is involved in regulating cancer stem cells (CSCs) maintenance in breast and lung cancers. While PDCD10 is being actively studied in several preclinical settings, there is limited data on its role in head and neck tumorigenesis.

In this study we first showed that stable PDCD10 knockdown in human OCSCC cell lines decreases tumor cell proliferation, DNA replication, migration, and invasion, both *in vivo* and *in vitro*. We next used murine tongue organoid models with 4-OHT inducible PCDC10 expression to demonstrate that PDCD10 is a prerequisite for the 4NQO-induced malignant transformation and acquisition of oncogenic behavior. Finally, we will use 4-NQO induced mouse model of oral carcinogenesis to assess the ability of the site-specific Cre-mediated deletion of Pdcd10

to avert the onset of oral neoplasms and to prompt anti-tumor effect after 4-NQO induced oral tumors are formed. Taken together, our studies suggest that PDCD10 plays an important role in promoting oral tumorigenesis and provides a strong rationale for the clinical development of PCDC10 inhibitors as a potential targeted therapeutic approach for patients with ACC.

Given the devastating nature of HPV- HNSCC and dearth of effective treatment approaches, providing new insights into the cancer driving molecular mechanisms regulated by PDCD10 and using this knowledge for developing therapeutic approaches targeting its activity may ultimately improve patient prognosis.

B010: COMPARATIVE ANALYSIS OF SPATIAL TRANSCRIPTOME EVALUATION OF EARLY STAGE TONGUE CANCER WITH OR WITHOUT METASTASIS. - Doh Young Lee; Seoul National University

Introduction: Decision making on performing neck dissection on the patients with early tongue cancers is still based on the clinicoradiologic characteristics. Several studies have demonstrated that certain genomic biomarkers can be applied and give valuable information with regard to the possibility of neck metastasis of early tongue cancers. This study aimed to anlayze the spatial transcriptomic evaluation of early tongue cancers and reveal the difference between patients with neck metastasis and without metastasis.

Methods: Eight patients with early tongue cancer was included in spatial transcriptomic analysis, and they were distributed into two gropus: grous with neck metastasis (4 patients) and without metastasis (4 patients). FFPE samples of primary tumors of each patients were sectioned on positive charged slide, and 20 regions of interest for spatial transcriptomics were marked. CosMx SMI (NanoString) single cell in situ analysis was performed on the 8 samples and a total of 160 regions of interest (FOV). Differentially expressed genes were anlyzed and compared between the group with neck metastasis and without metastasis. RNAseq using the bulk tissue was also performed for the reference and comparison.

Results: Leiden clustering revealed there was 5 types of cancer cell clusters. Among them, cluster 8 was significantly abundant in group without neck metastasis, while clusters 6 and 14 were predominant in group with neck metastasis. DEGs with adjusted p-value lower than 0.01 and log2FC greated than 1.5 were as follows: CXCL14, EGFR, COL17A1, MMP1, TPM2, KRT15, TGFBI, IGFBP6, MT2A, ITGA6, CAV1, FN1, and ITM2B. David pathway analysis revealed that DEGs were assoiated with extracellular matrix organization, focal adhesion, basemembrane, and integrin binding. In the stromal area, there was significant prominent cell type of M2 macrophage in group without neck metastasis.

Conslusions: Spatial transcriptome analysis on the neck metastasis of early tongue cancer revealed that invasive front of primary tumor showed differently expressed genes associated with tumor adhesion.

B011: A UNIQUE SUBSET OF TISSUE-RESIDENT NATURAL KILLER CELLS ISOLATED FROM HEAD AND NECK SQUAMOUS CELL CARCINOMA PRODUCES ALLERGY-ASSOCIATED CYTOKINES - Sainiteesh Maddineni, BS; Krishna Sharma; Imran A Mohammad, PhD; John B Sunwoo, MD; Stanford School of Medicine

Type 1 immune responses are typically associated with an IFNy-dominant effector response and are associated with clearance of intracellular pathogens and tumors, while type 2 immune responses are associated with the production of IL-4, IL-5, and IL-13 which play a role in extracellular pathogen clearance and allergy. Natural killer (NK) cells and group 1 innate lymphoid cells (ILC1s) are normally associated with type 1 responses in the context of cancer, and NK cells have been increasingly explored as a possible cellular therapy for solid tumors. Recently, intraepithelial ILC1-like (ieILC1-like) NK cells have been recognized as a subset of tissue-resident NK cells with a type 1 phenotype and strong cytotoxicity in the microenvironment of head and neck squamous cell carcinoma (HNSCC). However, the heterogeneity of this population of ieILC1-like NK cells remains unexplored. Here, we characterize a subset of ieILC1-like NK cells that produce a strong type 2 immune response with stimulation.

Ex vivo differentiation of CD49a+CD103+ ieILC1-like NK cells was achieved by co-culturing peripheral blood NK cells from healthy donors with IL-15 and irradiated HNSCC feeder cells. These ieILC1-like NK cells had high cytolytic activity against tumor cell targets as assessed by xCelligence impedence-based killing assays. To characterize the ieILC1-like NK cells better, a Luminex analysis of the cytokines produced in the cultured supernatants of either ieILC1-like NK cells or conventional NK cells, following stimulation by K562 tumor cells, revealed IL-13 as a cytokine selectively produced by ieILC1-like NK cells. Moreover, ieILC1-like NK cells did not produce IL-13 without stimulation. These findings were validated at the mRNA and protein level by quantitative reverse transcription-polymerase chain reaction and intracellular flow cytometry. Specifically, we found that a subset of ieILC1-like NK cells produces both IFNy and IL-13 in response to stimulation with either K562 tumor cells or PMA and ionomycin. Flow cytometry analysis also confirmed that these cells produce the type 2 cytokines IL-4 and IL-5, in addition to IL-13. These cells did not express canonical ILC2 markers such as CRTH2, KLRG1, or high levels of GATA-3, and they maintained expression of the canonical NK cell transcription factors T-bet and EOMES.

Thus, our findings indicate that there is a distinct subset of tissue-resident natural killer cells capable of producing both type 1 and type 2 cytokines in the microenvironment of head and neck cancer. Further studies are focused on understanding markers of this distinct subset, the physiologic roles of these novel cells, the prevalence of this subset in patient tumors, and the possible impact they have on the prognosis of head and neck squamous cell carcinoma.

B012: EXAMINING DOWNSTREAM SIGNALING PATHWAYS IN RESPONSE TO CDK4/6 INHIBITION IN ORAL CAVITY SQUAMOUS CELL CANCER - Jing Zhu[1]; Layla Maria[1]; Nitisha Shrivastava[1]; Stelby Augustine[2]; Nicole Kawachi[1]; Vikas Mehta[2]; Michael Prystowsky[1]; Shanye Yin[1]; Thomas J Ow[2]; [1]Department of Pathology, Albert Einstein College of Medicine; [2]Department of Otorhinolaryngology - Head and Neck Surgery, Montefiore Medical Center

Background: CDKN2A is one of the most commonly altered genes in oral cavity squamous cell carcinoma (OCSCC), resulting in loss of CDK4/6 regulation by p16 and unchecked cell cycle progression from G1 to S. CDK4/6 inhibitors are thus a logical treatment option, and our group has demonstrated potential efficacy in preclinical studies. While CDK4/6 inhibitors work to arrest cell cycle progression via canonical Rb signaling, the impact of signaling via alternative CDK4/6 targets is not fully understood. This report explores global cell signaling changes and proteasomal regulation pathways in OCSCC in response to the CDK4/6 inhibitor, palbociclib.

Methods: RNAseq analysis was used to identify differentially expressed genes in 2 HNSCC cell lines (HN5 and Cal27) and 2 conditionally reprogrammed (CR) cell cultures (CR15 and CR18) after treatment with the CDK4/6 inhibitor, palbociclib. Paired t-test was conducted to analyze changes in gene expression in senescent markers. 7 OCSCC lines were treated with palbociclib and protein expression of senescence-related markers and known CDK4/6 targets FOXM1 and SENP3, was assessed. Co-immunoprecipitation assays were performed in HN5 cells before and after palbociclib treatment. Presence of binding of inhibitory regulator, Ecm29, to proteasome 26S was examined in response to treatment.

Results: Gene expression data revealed that 62 genes were consistently downregulated in all 4 OCSCC models. While the majority of pathways involved cell cycle regulation, preliminary evaluation revealed that 17 downregulated genes were involved in alternative pathways including DNA replication and repair, reactive oxygen species damage, histone modification, and ubiquitination. 3 genes—CENPU, CEP55, and TROAP— are regulators of the PI3K/AKT pathway that is commonly involved in tumorigenesis. Additionally, 4 genes—HJURP, FAM111B, WDR76, and EZH2—were found to be implicated in either apoptosis or senescence when suppressed in other cancers. Consistent with our previous results, one of the genes consistently downregulated is FOXM1, whose protein degradation mediates cellular senescence. Other mediators of senescence, specifically SENP3, was not found to have significant transcriptional downregulation (p=0.244). Western blotting revealed that SENP3 protein levels were significantly reduced in all OCSCC cells after treatment with palbociclib, suggesting a post-transcriptional degradation mechanism. Our current study explored the role of proteasome 26S activity and regulation in the degradation of senescence markers. Ecm29, an inhibitory binding partner of 26S, was shown to dissociate and activate 26S in response to palbociclib in other cancer types and confirmed in control experiments. However, co-immunoprecipitation of proteasome 26S with Ecm29 demonstrated that levels of Ecm29-26S binding was not significantly reduced after palbociclib treatment, suggesting that Ecm29 is not associated with palbociclib-induced proteasome activation in OCSCC cells.

Conclusion: CDK4/6 inhibitors impact cell cycle progression in OCSCC as expected. However, we demonstrate that multiple alternate pathways are impacted that may have therapeutic implications. Ongoing studies are examining methods to optimize therapeutic combinations leveraging the effect of CDK4/6 inhibition in OCSCC.

B014: INTEGRIN ?1 REGULATES PERINEURAL INVASION AND RADIORESISTANCE OF ORAL SQUAMOUS CARCINOMA CELLS BY MODULATING CANCER CELL STEMNESS -
Sung Joon Park[1]; Sei Young Lee[2]; [1]Chung-Ang University Gwangmyeong Hospital; [2]Chung-Ang University Hospital

Objective: Perineural invasion and radioresistance are one of the main adverse features of treatment outcomes in oral squamous cell carcinoma (OSCC), but the exact mechanism is still unknown. We conducted an in vitro experiment to evaluate the role of integrin β1 (ITGB1) in the perineural invasion of radioresistant OSCC.

Methods: Two OSCC cell lines (SCC25, SCC15), radiation-induced radioresistant OSCC cell lines, and human non-neoplastic Schwann cell line (HEI-286) were used in this study. The association between expression of ITGB1 and adhesion to neural cell was evaluated using control and radioresistant OSCC cell lines. ITGB1 was inhibited by small hairpin RNA, and then the adhesion to neural cell and aggressiveness of both radioresistant OSCC cell lines were evaluated.

Result: Adhesion to neural cell was significantly increased in radioresistant cell lines than in control cell lines. In addition, the expression of ITGB1 was increased in radioresistant cell lines than in control cell lines, and ITGB1 expression was more prominent in cancer stem cell-like cells. When the expression of ITGB1 was inhibited, the adhesion to neural cell and invasion and migration of radioresistant OSCC were significantly reduced. Moreover, the expression of cancer stem cell markers and the size of spheroid formations were also significantly attenuated by inhibiting ITGB1.

Conclusion: These findings suggest that ITGB1 may be a significant contributor to the perineural invasion of radioresistant OSCC cells, and is associated with cancer stem cell-like cells. More detailed research is warranted to evaluate the role of ITGB1 as a novel emerging therapeutic target for radioresistant OSCC.

B015: TIMP1 AND CD63 PROGNOSTIC AND MECHANISTIC CONSIDERATIONS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA - Prashant Puttagunta, BS[1]; Kimberly Oslin, MD[2]; John H Owen[1]; Colleen Hochfelder, MD[1]; Chad J Brenner, PhD[1]; Steve B Chinn, MD[1]; [1]University of Michigan; [2]Detroit Medical College

Introduction: Tissue inhibitor of matrix metalloproteinases-1 (TIMP-1) and its receptor, CD63 are poor prognostic biomarkers in various cancers, secondary to cell proliferation, metastasis, and treatment resistance. We are currently studying the prognostic value of TIMP-1 and CD63 expression in HNSCC and evaluating potential mechanisms of this ligand-receptor pair and its relationship to expression of known epithelial-mesenchymal transition (EMT) markers and PI3K-AKT pathway genes.

Methods: TIMP1 and CD63 associations with survival and clinical variables were analyzed using normalized mRNA expression data from 519 HNSCC primary tumors and 43 matched adjacent normal tissue. siRNA transfections in HNSCC cell lines derived from patient tumors were then used to evaluate the effect of TIMP1 and CD63 knockdown on transcription of downstream EMT and PI3K-AKT genes through qPCR analysis. Survival analysis was then validated through immunohistochemistry (IHC) staining for TIMP1 and CD63 of patient tumor microarrays

(TMA);150 tumor samples from a single institution were stained for high or low expression of TIMP1 and CD63 then evaluated for associations with clinical outcomes.

Results: High expression of TIMP-1 and CD63 are associated with decreased OS and PFI, both independently and through a TIMP1-CD63 interaction, by Kaplan-Meier survival analysis. Nodal status was significantly associated with high TIMP-1 and CD63 expression [odds ratio (OR)=1.77, p=0.004; OR=1.65, p=0.01, respectively], and perineural invasion was significantly associated with high CD63 expression (OR=1.68, p=0.01). TIMP-1 mRNA is overexpressed in HNSCC tumors relative to normal tissue with TIMP-1 and CD63 expression having significant positive correlation in HNSCC (r=0.68, p<0.0001). TIMP-1 and CD63 expression are significantly associated with expression of epithelial-mesenchymal transition (EMT) markers and PI3K-AKT pathway genes of which we selected the most significantly co-expressed for further analysis. siRNA transfections reduced transcription of TIMP1 and CD63 by 85% and 80% respectively, and knockdown of TIMP1 significantly reduced transcription of AKT3 (p < 0.01) and PIK3CA (p < 0.05), while significantly increasing transcription of SNAI1 (p < 0.01) and VIM (p < 0.01). CD63 knockdown also significantly decreased transcription of AKT3 (p < 0.01) and PIK3CA (p < 0.05), and significantly increased expression of SNAI1 (p < 0.01), with no effect on VIM.

Discussion: This analysis provides additional evidence that TIMP-1 and CD63 are prognostic biomarkers in HNSCC. Co-expression of these genes with the mesenchymal phenotype of EMT and clinical associations between TIMP1/CD63 with nodal metastasis and PNI provide evidence that this pathway may contribute to metastases. The reduction of AKT3 and PIK3CA transcription, known contributors to cell growth and proliferation, as well as increases in transcription of EMT genes SNAI1 and VIM suggest TIMP1 and CD63 play a role in downstream regulation of cell growth, proliferation, and epithelial-mesenchymal transition, either through direct promotion or through a feedback mechanism. We are further characterizing these effects with promising preliminary data through western-blot analysis, rescue experiments with exogenous TIMP1, and functional spheroid assays.

Figure 1. High expression of TIMP1 and CD63 are associated with worse overall survival in HNSCC. Kaplan Meier analysis of overall survival by TIMP1 and CD63 expression in 519 patients with oral squamous cell carcinoma.

Figure 2. Proposed interaction between TIMP1/CD63 with downstream cell behavior pathways and epithelial mesenchymal transition. Silencing of TIMP1/CD63 may further elaborate on the complex interactions between downstream mediators and their effect on EMT genes and cell behavior.
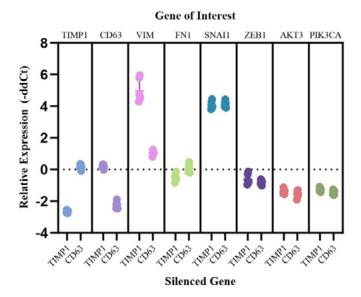
Figure 3. Effect of siRNA silencing of TIMP1 or CD63 on mRNA expression of downstream EMT and PIK3CA pathway genes. qPCR quantification of mRNA expression in cells treated with either TIMP1 or CD63 siRNA, compared to expression under mock transfection conditions with change in expression of Actin and GAPDH genes used as reference. Values represented as −ddCt, difference in number of qPCR cycles required to reach the same level of expression compared to mean number of cycles for mock transfection control; higher/lower ddCt represents increased/reduced expression by factors of approximately 2 per ddCt.

B017: PROGNOSTIC IMMUNE SIGNATURE AS A PREDICTOR OF DEVELOPMENT OF DISTANT METASTASIS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA - Justina S Shafik[1]; James R Barnett[1]; Han Yu, PhD[2]; Surui Hou, PhD[2]; Jianhong Chen, PhD[3]; Thomas J Belbin, PhD[4]; Bradley A Schiff, MD[1]; Richard V Smith, MD[1]; Gregory Rosenblatt, PhD[5]; Michael B Prystowsky, MD, PhD[5]; Pawel Kalinski, MD, PhD[6]; Nicolas F Schlecht, PhD, MSc[3]; Thomas J Ow, MD, MS[1]; [1]Department of Otorhinolaryngology, Albert Einstein College of Medicine, Bronx, NY, USA; [2]Department of Biostatistics and Bioinformatics, Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [3]Cancer Prevention and Control, Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [4]Memorial University of Newfoundland, Canada; [5]Department of Pathology, Albert Einstein College of Medicine, Bronx, NY, USA; [6]Department of Immunology, Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA

Background/Objective: Distant metastasis (DM) occurs in approximately 15% of patients with advanced head and neck squamous cell carcinoma (HNSCC) and is largely incurable. While several clinical factors are associated with DM development, their predictive utility is limited. Immune-related gene expression profiles from tumor tissue have been studied as potential prognostic biomarkers in several cancers, including HNSCC. Our group has recently demonstrated that a 32-gene expression immune signature is associated with survival in HNSCC. The current study investigates the prognostic value of immune-related gene expression signature as a biomarker for DM.

Methods: We conducted a secondary analysis of gene expression data from patients treated for HNSCC at our institution. A panel of 32 immune-related genes were previously trained and validated on disease-specific survival to stratify patients into high- and low-risk groups. T-Tests, Mann-Whitney U-Tests and Chi-squared analysis were used to compare the clinical and pathological variables between individuals with DM and without DM. Kaplan-Meier survival analyses and log-rank tests were used to compare time to DM between high-risk and low-risk immune signature groups. Additionally, cox regression analysis was used to examine relative risk of DM associated with the immune panel status adjusting for nodal disease status.

Results: A total of 174 patients with HNSCC – 27 with DMs and 147 without – were analyzed. The median age was 63 years (IQR 56,70), 123 (71%) were male, 116 (67%) were White, 52 (30%) were Black, and 2 (1%) were Asian. 85 (49%) had a high-risk immune signature and 89 (51%) had a low-risk immune signature. Median follow up time was 50.9 months (IQR 17.7,110). Individuals with DM were significantly younger than those without (58 IQR 54,65 vs 64 IQR 57,71). Additionally, there was a significantly higher proportion of individuals with N1, N2, and N3 stage compared to those without DM (P=0.007). The high-risk immune signature group contained a greater proportion of patients with DM; however, the association was not statistically significant (P=0.11). Notably, the immune signature proved significant in stratifying patients by time to DM (P=0.038). In our cox regression model, we found that individuals with a high-risk immune signature had a 2.72 (95% CI 1.22,6.08 P=0.015) fold higher hazard risk of DM compared to those with a low-risk immune signature when adjusting for nodal stage.

Conclusion: Our 32-gene immune signature has potential to predict time to DM in HNSCC patients. High-risk individuals demonstrated an accelerated progression to DM, underscoring the need for further validation and exploration of immune profiles in managing HNSCC.

B018: IDENTIFICATION OF A MOLECULAR IMMUNOPHENOTYPE FOR CLINICALLY AGGRESSIVE PAPILLARY THYROID CARCINOMAS - Wesley H Stepp, MD, PhD; Jason Tasoulas, MD, DMD; Trevor G Hackman, MD; Sid Sheth, DO; Jeff M Blumberg, MD; University of North Carolina

Papillary thyroid cancer (PTC) is generally considered an indolent neoplasm, but has the ability to demonstrate clinically aggressive features in certain patients. Understanding which of these tumors are clinically more aggressive earlier in diagnosis can lead to more effective treatment strategies and better overall survival for patients with PTC. In this study, we identified a molecular phenotype for a subset of papillary thyroid cancers that are clinically aggressive, and have significantly decreased overall (OS) and disease-free survival (DFS) than tumors that were less clinically aggressive.

Twenty-four patients with pathologically diagnosed papillary thyroid cancer were screened for a total of 770 genes using a targeted mRNA immuno-oncology panel. mRNA was isolated from formalin fixed, paraffin-embedded tumor blocks and gene expression was analyzed using NanoString nCounter technology.

Unguided hierarchical clustering of the twenty-four patient's gene expression profiles revealed two explicitly discrete genetic profiles amongst our cohort that was controlled for age, sex and tumor stage. Patients with overexpression of MHC class II related pathways and under expression of Wnt and Tor (i.e. immunologically "active" cluster) had a OS and DFS (100%, 95%, 87% at 1, 2 and 5 years for OS; 100%, 89%,

89% for DFS, respectively) compared to those who had a high expression of MAP-K and anti-apoptosis pathways (i.e. immunologically "suppressed" cluster) (100%, 93%, 77% at 1, 2 and 5 years for OS; 100%, 84%, 84% for DFS, respectively.)

In conclusion, we have identified two genetically distinct variants of PTC based on unique immunophenotypes. Patients with tumors in the immunologically "active" subgroup had significantly improved OS and DFS compared to those in the immunologically "suppressed" subgroup. Our study highlights a new and exciting avenue allowing future surgeons to tailor patient therapy for papillary thyroid carcinoma based on gene expression.

B019: PRIMING A NON IMMUNOGENIC HNSCC CELL LINE WITH EVEROLIMUS TO IMPROVE RESPONSE TO ANTI-PD-1 IMMUNOTHERAPY - Rhodee Ric G Toledo[1]; Tara Moore-Medlin[2]; Chun Li, MD[2]; Dauren Adilbay[2]; Christopher Chen[2]; Emily Daniel[2]; Alok Khandelwal, PhD[2]; Cherie-Ann Nathan, MD, FACS[2,3]; [1]School of Medicine, LSU-Health Science Center, Shreveport, LA, USA; [2]Department of Otolaryngology-Head and Neck Surgery, LSU-Health Sciences Center, Shreveport, LA, USA; [3]Feist-Weiller Cancer Center, LSU-Health Sciences Center, Shreveport, LA, USA

Background: TP53-mutant head and neck squamous cell carcinoma (HNSCC) is associated with 50-60% recurrence rates due to resistance to treatment, necessitating additional therapy. Immunotherapies with blockade of the PD-1 pathway are approved and widely used for recurrent and metastatic HNSCC. Unfortunately, only 15-20% of patients ultimately benefit from anti-PD-1 therapy, highlighting the need to improve checkpoint inhibitors' efficacy. Mutant p53 causes persistent activation of the PI3K/mTOR oncogenic cell-signaling pathway, the most dysregulated signaling mechanism in TP53 mutant HNSCC, suggesting a potential role of mTOR inhibitors for the treatment of mutant TP53 HNSCC. In our phase II multi-institutional clinical trial, adjuvant treatment with Everolimus significantly improved progression-free survival in TP53 mutated patients compared to placebo (Log-Rank P=0.027; HR=0.24, 95% CI: 0.06-0.95). Our preliminary studies demonstrated that treatment with mTORi attenuated tumor growth in the TP53 mutant tumor cell xenografts and failed to elicit resistance after prolonged treatment, unlike that seen with cetuximab. Resistance to targeted agents is well known and hence if patients fail the mTORi regimen, immunotherapy could potentially be utilized as adjuvant therapy to prevent recurrence.

Methods: C57BL/6 mice received tongue implantations with syngeneic 50,000 ROC-1 cells and then randomized into 6 groups: Control, Everolimus (Ev), anti-PD-1, combination treatment (Ev+ant-PD-1), and sequential treatment groups (Everolimus followed with anti-PD-1 and anti-PD-1 followed with Everolimus). To mimic minimal residual disease, interventions were started three days post-implantation. Mice were either administered with Everolimus (5mg/kg/b.w) by oral gavage daily or received intraperitoneal injections with anti-PD-1 (200 μg) three times per week. Tumor volume and body weight were measured twice weekly through Day 70 or until humane endpoint criteria were met.

Result: At 50 days post-implantation, mTORi followed by anti-PD-1 immunotherapy demonstrated 78% progression-free survival (PFS) compared to 56% in the control group (p=0.019). Treatment with Everolimus alone also exhibited significant PFS at 76% compared to the control group (p=0.038). The remaining groups a trend towards an increase

of PFS at 50 days post-implantation (anti-PD-1 alone at 66%, anti-PD1+Ev at 38%, and anti-PD1-Ev at 69%); however, no statistically significant difference was determined (p=0.23).

Conclusion: Our studies suggest that mTORi sensitizes non-immunogenic HNSCC cell lines to anti-PD-1 treatment. Ongoing research is aimed to determine the mechanism for mTORi-induced sensitization of anti-PD resistant HNSCC cell line.

B020: INVESTIGATING THE MECHANISMS OF A CXCL12 LOCKED DIMER AGAINST HPV(-) HEAD AND NECK CANCER. - Oscar Villarreal Espionsa; Medical College of Wisconsin

Intro/Background: Head and neck cancer (HNC) exceeds 66,000 cases per year resulting in over 14,000 deaths annually in the United States. Radiation therapy (RT) is central to HNC management, but 5-year survival remains under 50% using current approaches. To improve HNC outcomes, novel agents are required which can synergize with RT to limit disease recurrence. To this end, we have recently identified synergistic effects against HNC between RT and a modified version of the chemokine CXCL12, locked in its dimerized state. CXCL12 exists in a monomer-dimer equilibrium in human physiology. However, through site-directed mutagenesis, CXCL12 can be produced which is either locked in its dimerized (LD) or monomeric (LM) state. CXCL12 primarily works through its receptor CXCR4, and the CXCR4-CXCL12 signaling axis has been implicated in proliferation, invasion, and metastasis in several malignancies. The purpose of this study was to evaluate the mechanisms underlying the observed anti-neoplastic properties of LD CXCL12 in HNC.

Methods: HNC cell lines (Detroit 562 and FaDu) were treated in vitro with 500nM LD CXCL12 every other day, with or without 8Gy radiation. Proliferation was measured via automated hemocytometer with Trypan blue exclusion. Apoptosis was measured via annexin staining. CXCR4-expression was evaluated by immunocytochemistry, flow cytometry, and RT-PCR. Apoptotic markers were evaluated via a preformed RT-PCR TaqMan Array plate. A FaDu cell line over-expressing CXCR4 was creating through lentivirus transduction.

Results: LD CXCL12 demonstrated anti-proliferative effects across HNC cell lines but did not adversely affect benign CXCR4-expressing cell lines. LD CXCL12 further induced synergy with 8Gy radiation, leading to decreased HNC proliferation, increased apoptosis, and decreased clonogenic survival. However, LM CXCL12 and a full CXCR4-antagonist (AMD3100) demonstrated no anti-proliferative effects nor synergy with RT in these HNC lines, suggesting biased agonism as the LD CXCL12 mechanism of action. Next, we validated the anti-neoplastic importance of CXCR4 modulation in HNC by demonstrating increased growth and radioresistance in CXCR4-overexpressing FaDu compared to the wild-type line. Via a RT-PCR Taqman Array plate, we saw an upregulation trend of apoptotic markers in both Fadu and Fadu CXCR4 overexpression cell lines. In particular, at days 3 and 5 TNF was upregulated in both LD and RT and then synergistically more upregulated in LD/RT. The consistency of this finding supports its potential biological relevance.

Conclusion: This study highlights the potential of using LD CXCL12 in combination with RT to improve outcomes for HNC patients. Future studies are needed to further dissect the cellular signaling mechanisms of LD CXCL12 and investigate its efficacy in vivo.

B022: SALIVA-BASED DETECTION OF ORAL HPV AND ORAL CANCER - Vasudha Mishra[1]; Claudia Wing[1]; Xiangying Chen[1]; Alka Singh[1]; Chetan Bettegowda[2]; Nishant Agrawal[1]; Evgeny Izumchenko[1]; [1]University of Chicago; [2]Johns Hopkins University

Head and neck cancers (HNC) consist of a group of biologically and clinically diverse malignancies arising from the oral cavity, pharynx, larynx, paranasal sinuses, nasal cavity, and salivary glands. Oral cavity squamous cell carcinoma (OCSCC) and oropharyngeal squamous cell carcinoma (OPSCC) are the most common subtypes, together comprising the majority of HNC cases. While these cancers are associated with tobacco use and alcohol consumption, infection with human papilloma virus (HPV) is also etiologic to HNC, with OPSCC known to harbor higher HPV positivity rates relative to OCSCC, which is largely HPV-negative (HPV-). This distinction is clinically relevant as HPV-positive (HPV+) tumors are more responsive to therapy and associated with a better prognosis. While early-stage OCSCC/OPSCC has favorable 5-year relative survival rates of >80%, diagnosis typically occurs at more advanced disease stages, where the survival rate drops precipitously to ~20-40%. Compounding this grim outlook is the growing incidence of HNC in patients that do not smoke or drink alcohol, as well as the startling rise in HPV+ OPSCC incidence, thus increasing the affected population and burden on the healthcare system. Currently, painful incisional biopsies are the standard clinical method to diagnose HNC, and there are no accepted non-invasive screening options available for early disease detection or serial assessment of treatment efficacy. There is thus an urgent need to develop non-invasive diagnostic solutions that accurately identify disease at an early stage, as well as to develop faithful methods to quickly discern HPV status to inform effective treatment decisions and improve patient outcomes.

We have recently developed a novel salivary liquid biopsy screening method for early detection of OCSCC, which relies on targeted Next Generation Sequencing (NGS) of 7 commonly mutated genes associated with OCSCC tumorigenesis. Demonstrating the utility of this approach, we have shown that it is able to accurately and reproducibly identify ~93% of patients with OCSCC, including early stage cases. To enhance the capabilities of this screening platform we have incorporated probes targeting high-risk HPV strains (HPV16/18) into the sequencing panel. Applying this multi-functional assay to a cohort of primary OCSCC tumors, driving somatic mutations were detected in all cases. Furthermore, using the 5% alignment cutoff, all OCSCC specimens were HPV-. We next sequenced HPV+ OPSCCs using the same criteria, detecting 93% of the cases as HPV positive by our combined assay. We next applied this updated assay to saliva specimens collected from 30 OCSCC patients and 10 healthy individuals. Somatic mutations were detected in all OCSCC saliva specimens, while no actionable aberrations were found in healthy controls. As expected, most of the OCSCC saliva samples (27 of 30) were HPV-, with the remaining 3 samples being inconclusive.

While additional analytical validation is needed to accurately assess the performance of this dual panel in saliva specimens, such multi-functional (mutational drivers/HPV) detection assay may expand its clinical utility to patients with HPV+ disease, facilitating personalized treatment decisions based on tumor biology (mutations) in addition to clinical risk factors (presence of high-risk HPV).

B023: THE UTILITY OF RADIOMICS IN THE PROGNOSTICATION OF OROPHARYNGEAL SQUAMOUS CELL CARCINOMA - A SYSTEMATIC REVIEW - Ameen Amanian, MD, MSE[1]; Sarah Adams, BSc[2]; Keshinisuthan Kirubalingam, MD, MClSc[3]; Ricky Hu, MD[1]; Connor Holmes, MD[1]; Carole Fakhry, MD[4]; Masaru Ishii, MD, PhD[4]; Francis Creighton, MD[4]; Eitan Prisman, MD, MS[1]; [1]University of British Columbia; [2]College of Medicine, University of Cincinnati; [3]Western University; [4]Johns Hopkins University School of Medicine
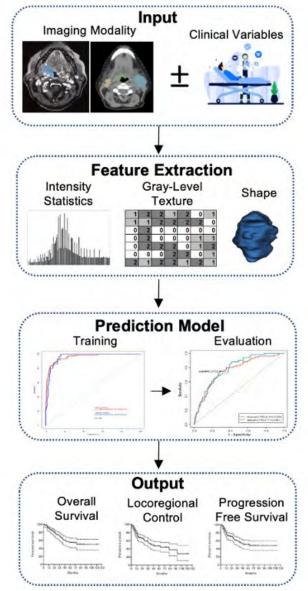
INTRODUCTION: Human papillomavirus (HPV)-related oropharyngeal squamous cell carcinoma (OPSCC) has significant prognostic advantages compared to HPV-unrelated disease. Although it typically harbors favorable cure rates, it is difficult to predict which patients are at risk of recurrence using TNM staging alone. Clinicians have turned towards imaging to see if imaging biomarkers may provide clues pertaining to patient prognosis. Radiomics is a quantitative approach to imaging, which aims to enhance the existing data by mathematically characterizing shape, texture, and pixel distributions (Figure-Radiomics Workflow). Radiomic algorithms have the capacity to discriminate potentially meaningful phenotypic differences in imaging for prognostic evaluation of OPSCC. However, the utility of radiomics within the clinical setting remains to be seen due to the recent introduction of this technology. The objective of this study is to systematically review the application of radiomics in prognostication of patients with OPSCC within the current literature.

METHODS: The Pubmed/MEDLINE and Embase databases were comprehensively searched from the date of inception until October 31, 2022. All original English studies reporting on the use of radiomics through any imaging modality (e.g., CT, MRI, PET) for prognostication of patients with OPSCC were included. Two independent authors reviewed and selected studies in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA). From a total of 662 abstracts, 11 studies met inclusion criteria and were selected for data extraction and analysis. The Radiomics Quality Score (RQS) was used for study quality assessment. The risk of bias of each study was determined using the Prediction model Risk of Bias Assessment Tool (PROBAST).

RESULTS: Of the 11 studies included in the systematic review, 10 were retrospective and 1 was prospective for a total of 2338 patients. Six studies utilized radiomics features alone and five utilized combined radiomics and clinical features. CT was the most common imaging modality used (n = 6) followed by MRI (n = 3) and PET/CT (n = 3). Three studies utilized an imaging dataset from multiple institutions. Shape, volume and textures were the most predictive radiomic features in prognostication. Models using a combination of both clinical and radiomic features were predictive of locoregional control (LRC), overall survival (OS) and progression-free survival (PFS). The average RQS score was 7.9 (std 4.9). The inter-reader reliability for the total RQS score amongst both reviewers was deemed excellent with a Pearson correlation coefficient of 0.962. Overall, there was a low risk of bias for 5 and 11 of the studies within the 'risk' and 'applicability' domains respectively.

CONCLUSION: This systematic review illustrates the application of radiomics in the prognostication of OPSCC patients. The results showed that combined radiomics and clinical models to be most successful in predicting LRC, OS and PFS in OPSCC patients. Additionally, radiomic features

pertaining to tumor shape, volume and texture were the most significant variables in prognostication. However, current models are difficult to reproduce to due to the lack of external validation. Future studies should therefore incorporate larger sample sets to enhance the translational potential of radiomics in the management of OPSCC.

B024: THE EFFICACY AND SAFETY OF RADIO-FREQUENCY ABLATION ON PAPILLARY THYROID CARCINOMA - Clarissa Cheong, MBBS, MRCS, Edin; Joy Xin Yi Au, MBBS; Jereme Yijin Gan, MBBS, Hons, Monash, FAMS, ORL; Ernest Weizhong Fu, MBBS, YLL, FAMS, ORL; Hao Li, MBBS, YLL, FAMS, ORL; Ming Yann Lim, MBBS, Melbourne, FAMS, ORL; Tan Tock Seng Hospital

Objectives: The 2021 CIRSE/ETA clinical practice guidelines proposed active surveillance (AS) and US-guided minimally invasive treatment (MIT) for suitable cases of PTC.

RFA avoids complications of general anesthesia, reduces length of hospitalisation, and reduces morbidity from surgery. This presents a strong alternative treatment choice for patients who are not surgical candidates due to the presence of comorbidities.

However, there have only been 1 systematic review and 3 combined systematic review meta-analyses on this topic to date.

This systematic review and meta-analysis seeks to evaluate the efficacy and safety of RFA in the treatment of PTC, with the aim of updating the information presented in previous studies.

Methods: Pubmed, Embase and Cochrane databases were searched for relevant studies from 1990 to 2021. 14 studies with a total of 1366 patients were included. Pooled volume reduction rates (VRRs) from 1 to 48 months after HIFU, complete disappearance rates (CDR) and complications were assessed.

Results: RFA proved to be an effective treatment in reducing the volume of PTCs.

Pooled VRRs were 92.23 (95% CI 81.61-102.86, I2=0%) at 6 months, 96.59 (95% CI 91.05-102.13, I2=0%) at 12 months and 99.31 (95% CI 93.74-104.88, I2=NA). 5 studies showed an eventual CDR of 100%.

No life threatening complications were recorded. The most common complications included pain, transient voice hoarseness, fever, and less commonly first degree burn.

Conclusion: RFA may be an effective and safe alternative to treating PTCs. Larger clinical trials with longer follow-up are needed to evaluate the effectiveness of RFA in treating PTCs.

B025: BEYOND THE PATIENT'S EXPERIENCE: THE FINANCIAL TOXICITY OF CANCER ON CAREGIVERS - Maria Armache, MD; Nadia L Samaha, BS; Madison Hearn, BS; Rachel Stemme, BS; Carole Fakhry, MD, MPH; Leila J Mady, MD, PhD, MPH; Department of Otolaryngology - Head & Neck Surgery, The Johns Hopkins School of Medicine

Introduction: The financial implications of cancer diagnosis and treatment are a significant concern for patients. Up to 75% of patients with cancer struggle with copayments, with approximately 20% improperly taking prescribed medications to defray costs. Patients with HNC have disproportionately higher treatment-related financial toxicity than other patients with cancer. This toxicity has direct implications on patient outcomes, including higher symptom burden, poorer quality of life, and worse psychological well-being. Caregivers play a critical role in supporting cancer patients' illness trajectories. Caring tasks may, however, be time-consuming, difficult, and potentially disruptive. Caregivers share finances and take time off work hours to provide care, potentially leading to lost wages. While most research has focused on describing financial toxicity in patients, fewer studies have examined its extension to caregivers and its potential impact on patients. The aim of our study is to systematically describe the FT of caregivers of patients with cancer.

Methods: A systematic review was performed according to PRISMA guidelines. PubMed, Embase, CINAHL, and Web of Science were queried using the terms "financial toxicity", "screening", "cancer," and all relevant synonyms. Peer-reviewed studies that measured the self-reported financial impact of cancer treatment in caregivers of adult patients met inclusion

criteria. Citations were excluded if they were a review or editorial, included caregivers of patients < 18 years or were in a foreign language. Outcomes evaluated included FT measures/tools, FT prevalence, and sociodemographic factors associated with FT.

Results: Among 1086 identified studies, eleven described the financial burden in 2201 caregivers of patients with cancer. Different tools were used to screen for FT: the Comprehensive Score for Financial Toxicity (COST), the financial subscale in Zarit Burden Instrument (ZBI) and in the Caregiver Reaction Assessment Tool (CRAT), the Financial problems subscale in Caregiver Quality of Life Index Cancer Scale (CQOLC), the Economic Hardship Questionnaire (EHQ), the Personal Financial Burden Scale, the measure of financial distress in the Edmonton Symptom Assessment Scale (ESAS), the NCCN Distress Thermometer, and the Economic Burden measure from the Family Impact Survey. Overall 10% to 63% of caregivers experienced at least some form of financial burden. High FT was found in 44% of HNC caregivers, and in 32% of caregivers of patients with advanced lung or brain tumors. Individual-level factors associated with increased financial distress in caregivers were younger age, being employed, having a lower educational attainment, having children at home, being single, experiencing greater lost income and missed work, and high levels of helping the patient financially. Lower FT in caregivers was associated with lower patient FT and earlier cancer stages (I-III). Caregivers' FT was associated with patient care non-adherence.

Conclusion: Despite the heterogeneity of screening tools used to assess financial burden, our study underlines a noteworthy prevalence of high FT in caregivers of patients with cancer. Our findings highlight the ripple effect of FT on caregivers with implications on treatment adherence for patients. These results provide important first steps in understanding the importance of integrating caregivers in the development of multipronged approaches for mitigating FT in cancer care.

B026: ASSESSING THE EFFICACY OF PREOPERATIVE PROCEDURAL PATIENT EDUCATION AS AN INTERVENTION TO MITIGATE STRESS AND ANXIETY AMONG OTORHINOLARYNGOLOGY SURGERY PATIENTS: A RANDOMIZED CONTROLLED TRIAL - Ranny Assaf, MD, PhD[1]; Chia-Jung Busch, Prof, Dr, MD, PhD[1]; Tina Brzoska, Dr, med, MD, PhD[1]; Marcus Vollmer, Dr, rer, nat[2]; Britta Buchold, Dr, rer, med[3]; [1]University Hospital Greifswald; [2]Institute of Bioinformatics Greifswald Germany; [3]Institute of Clinical Psychology of Greifswald University Hospital

Background: Patients awaiting ENT surgery typically experience significant physical and psychological stress. However, although there is evidence that preoperative education interventions can lead to positive perioperative outcomes for surgical patients in general, less is known about the effectiveness among patients undergoing ENT surgery.

Objective: This study investigated whether, preoperative procedural patient education designed for ENT surgery patients, as a time- and cost-efficient intervention, can reduce patient stress and anxiety.

Design: Randomized controlled trial.

Methods: We employed a randomized parallel-group design with 2 study arms to compare a procedural patient education to the standard preoperative preparation procedure. The study comprised 164 patients who underwent inpatient ENT surgery under general anesthesia. An externally validated inventory (State-Trait Operation Anxiety, STOA) was used to assess perioperative state anxiety days before (T1), on the day of (T2, T3) and a day after (T4) surgery. In addition, the perioperative stress and anxiety levels were further evaluated using the numeric rating scale for stress (NRS) as well as the vital parameters blood pressure (BP), respiratory rate (RR) and heart rate (HR). Moreover, user ratings on the usefulness of the patient education were assessed with an evaluation questionnaire. The study arms were subjected to a comparison of perioperative state anxiety through two-tailed independent samples t-tests, utilizing a 95% confidence interval. Subjective ratings were correlated with STOA values to investigate possible associations between perioperative anxiety with perceived usefulness.

Results: Of 164 participants randomized, 152 completed the trial. Participants who received preoperative education experienced a significantly lower increase in the state anxiety on the day of operation (mean difference +2,15, P=0.03) compared to those who did not receive an educational intervention (mean difference 3.09, P=0.04). Furthermore, participants who perceived a potential preoperative education as helpful (Helpfulness between 6 – 10) showed significantly lower stress increase (M=+2.80) compared to the control group (M=+4.04, P=0.05). There was no significant difference between groups regarding a change in vital parameters. Based on the results using the NRS, female patients randomized to the preoperative education group showed significantly lower stress levels postoperatively (M=-2.95) compared to female patients of the control group (M=-2.19; P=0.04). There was some evidence to suggest similar but non-significant effect for male patients (P=0.10).

Conclusions: This type of preoperative education has demonstrated its effectiveness in alleviating stress and anxiety among patients undergoing ENT surgery. Considering the existing body of evidence and prevailing international norms, it is advisable to integrate preoperative education as a standard practice, with a particular emphasis on offering it to patients who perceive the educational intervention as valuable, as our study indicates that they derive substantial benefits from it.

B027: TRENDS AND PREDICTORS OF COST IN HEAD AND NECK CANCER RECONSTRUCTION - William J Benjamin, MPH[1]; Rosh K Sethi, MD, MPH, FACS[2]; [1]University of Michigan Medical School; [2]Harvard Medical School Department of Otolaryngology - Head and Neck Surgery

Introduction: Pedicled and free flap reconstruction of complex head and neck defects is an important aspect of surgical care for head and neck cancer patients. However, few data are available on contemporary trends or factors associated with inpatient cost. This study seeks to define trends in the cost of inpatient head and neck reconstructive surgery between 2016 and 2020, and identify predictors of increased cost.
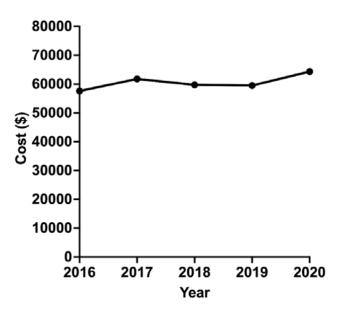
Methods: A population-based cross-sectional study between 2016 and 2020 utilizing the Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS) was performed. 2020 was chosen as the end point as it was the most recent year available for analysis. Hospital admissions where an ablative head and neck procedure followed by pedicled or free flap reconstruction for head and neck cancer were identified using International Classification of Disease-10 procedural codes. The primary outcome of interest was total admission cost,

inclusive of procedural and post-procedural care. Hospital-specific cost-to-charge ratios, as defined by HCUP, were utilized. Cost data were adjusted to 2016 dollars using the consumer price index to normalize for inflation. Temporal trends in the cost of reconstruction and predictors of cost in patients undergoing reconstruction were assessed using survey-weighted regression models and Cochrane-Armitage testing.
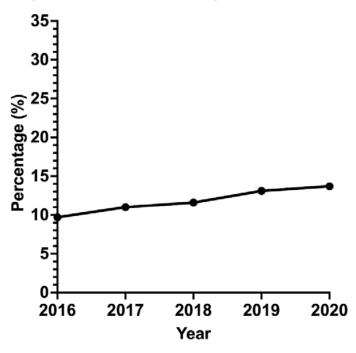
Results: A weighed total of 57,765 cases of ablative surgery for head and neck cancer were performed during the study period. Of these cases, 6,905 (12.0%) included pedicled or free flap reconstruction. Among patients treated with a concurrent ablative and reconstructive surgery, the average age was 63.6 years (S.D. 11.5), 88.1% were male and 76.9% were white. Average cost of head and neck reconstruction increased from $57,592 in 2016 to $64,371 in 2020 (Figure 1). The number of ablative cases with a flap reconstruction increased significantly from 1,025 (9.7%) in 2016 to 1,670 (13.8%) in 2020 (p<0.01, Figure 2). Mean length of stay was 11.9 days (S.D. 8.0). There was no significant increase in cost from 2016 and 2020 (β: 1,144 [-205 - 2,493, p=0.10). Length of stay was identified as a significant predictor of increased cost, with each additional day of admission costing $2,947 (β: 2,947 [2,585 – 3,308], p<0.01).

Conclusions: Flap reconstruction following ablative surgery for head and neck cancer increased by 4.1% between 2016 and 2020 without a significant increase in inpatient costs. Among major patient and hospital-level variables, length of stay was significantly associated with increased costs following head and neck reconstruction. In the setting of rising healthcare costs, the promotion of healthcare value is of increasing importance. Our study identified length of stay at a potentially targetable factor for mitigating costs among patients receiving concurrent ablative and reconstructive surgery for head and neck cancer. Further study aimed at identifying drivers of increased length of stay and costs may enable the development of interventions aimed at improving the value of care for this patient population.

Percentage of ablative head and neck procedures with a flap reconstruction

Trends in Cost of Flap Reconstruction for Head and Neck Cancer in the United States

B028: RACIAL DISPARITIES IN DIAGNOSIS AND TREATMENT OF ANXIETY AND DEPRESSION IN HEAD AND NECK CANCER SURVIVORS - Tyler J Gallagher, BS; Matthew E Lin, BS; Niels C Kokot, MD; Keck School of Medicine of USC

Introduction: Head and neck cancer (HNC) survivors are particularly susceptible to anxiety and depression, however the impact of racial status on rates of diagnosis and treatment of mental health conditions among HNC survivors has rarely been explored. We utilized a large database of electronic medical record data to understand racial and ethnic differences in diagnosis and treatment of anxiety and depression in HNC survivors.

Study Design: Cross-Sectional

Methods: The TriNetX database, a network of globally federated, deidentified electronic medical record data, was utilized for analysis. Cohorts were created by racial and ethnic groups for adults (³18 years) with diagnosis of HNC and no previous anxiety and/or depression diagnosis per ICD-10 codes (n=180,346). Incidence of new depression and/or anxiety within 2 years of HNC diagnosis was reported, then compared after 1:1 propensity score matching for demographic characteristics. Subsequently, cohorts were created for racial and ethnic groups including adult HNC survivors with diagnosis of depression or anxiety within 2 years of HNC diagnosis. Rates of medication treatment (per RxNorm codes) recommended for depression or anxiety by the American Psychiatric Association as well as rates of psychotherapy utilization (per ICD-10-PCS, CPT, and SNOMED codes) any time after depression/anxiety diagnosis were reported then compared between each racial and ethnic group after 1:1 propensity score matching.

Results: Rates of newly diagnosed anxiety and/or depression within 2 years of HNC diagnosis were highest (n, %) among white individuals (4,316; 4.1%) and non-Hispanics (3,971; 4.1%), followed by Native Americans/Native Hawaiians (22; 4.1%), African Americans (488;4.0%), Hispanics (334; 3.8%), any minority individual (648; 3.6%), and Asians (138; 2.6%). After propensity score matching, white individuals had higher rates of diagnosis of anxiety and/or depression after HNC diagnosis compared to any minority (OR:1.35[95%CI:1.22-1.49]) and Asians (OR:1.89[95%CI:1.54-2.32]). Simple rate of treatment with medication for anxiety and/or depression after diagnosis among HNC survivors was highest (n, %) among non-Hispanics (2,926; 59.3%), followed by whites (3,065; 57.6%), African Americans, (309; 53.9%), Native Americans/Native Hawaiians (14; 53.9%), any minority individual (406; 52.6%), Hispanics (198; 49.8%), and Asians (83; 48.0%). After diagnosis of anxiety and/or depression, utilization of medication for treatment was higher among white individuals compared to any minority (OR:1.10[95%CI:1.01-1.50]), Asians (OR:1.72[95%CI:1.14-2.60]), and native Americans and native Hawaiians (OR:5.11[95%CI:1.88-13.93]). Simple rate of treatment with psychotherapy for anxiety and/or depression after diagnosis among HNC survivors was highest (n,%) among Hispanics (30; 7.5%), followed by Asians (10; 5.8%), African Americans (28; 4.9%), non-Hispanics (199; 4.0%), any minority individual (31; 4.0%), and white individuals (195; 3.7%). After diagnosis of anxiety and/or depression, utilization of psychotherapy for treatment was not significantly different between whites and any minority (OR:1.32[95%CI:0.81-2.14]) or non-Hispanics and Hispanics (OR:0.54[95%CI:0.28-1.03]).

Conclusions: Here, we describe higher rates of diagnosis of anxiety and/or depression among white individuals compared to any minority and Asian individuals, raising concern for lack of identification of anxiety and depression among minority survivors of HNC. Additionally, we demonstrate lower rates of medication usage for anxiety and depression among minority HNC survivors with anxiety and/or depression, suggesting need for further study of this disparity.

B029: PREVALENCE AND PREDICTIVE FACTORS FOR HPV VACCINATION AMONG OLDER ADULTS IN THE UNITED STATES - Tyler J Gallagher, BS; Matthew E Lin, BS; Niels C Kokot, MD; Keck School of Medicine of USC

Introduction: In 2018, the Food and Drug Administration expanded approval age for the HPV vaccine to individuals aged 27-to-45 years old. Investigation of vaccination prevalence and factors association with vaccination in this older age cohort are rare but important given the rise in HPV+ oropharyngeal squamous cell carcinoma. Thus, we sought to explore predictive factors for vaccination among older adults after FDA approval.

Study Design: Cross-sectional

Methods: Cohort included adults aged 30-44 years [TG1] [TG2] from 2018-2022 Behavioral Risk Factor Surveillance System (BRFSS) who completed the HPV vaccination survey module with interview year 2019-2023 (n=26,470). Participants self-reported HPV vaccination status. 3 vaccinations were considered complete vaccination, as all in the cohort were ineligible for initial 2-dose vaccination eligibility upon initial vaccine approval. Prevalence of any HPV vaccination and complete vaccination were analyzed with BRFSS survey weighting. Multivariable regression with survey weighting was utilized to explore predictive factors for HPV vaccination.

Results: On unweighted analysis, the cohort was primarily aged 40-45 years (n=9,476; 35.8%), white (14,580; 56.1%), and female (14,593; 44.7%). The weighted prevalence of any HPV vaccination and full-series vaccination was 15.9% [95%CI:15.2-16.7%] and 6.4% [95%CI:6.0-7.0%], respectively. Upon multivariable regression, relative to those in the 30-34 years age group, those 35-39 years (OR:0.39[95%CI:0.32-0.49]) and 40-44 years (OR:0.17[95%CI:0.13-0.23]) were less likely to receive complete vaccination. Those aged 35-39 years (OR:0.44[95%CI:0.38-0.51]) and 40-45 years (OR:0.23[95%CI:0.19-0.29]) were less likely to have any vaccination. Females were more likely to receive complete (OR:5.17[(95%CI:3.84-6.96]) and any (OR:2.61[95%CI:2.23-3.05]) HPV vaccination than males. Black/African-American (OR:0.75[95%CI:0.56-0.99]), Asian-only (OR:0.48[95%CI:0.31-0.75]), and Hispanic (OR:0.59[95%CI:0.42-0.82]) individuals were less likely to receive complete vaccination compared to white-only individuals. Asian-only (OR:0.64[95%CI:0.46-0.88]) individuals were less likely to receive any HPV vaccine, while mixed race individuals (OR:1.56[95%CI:1.09-2.25]) were more likely. Compared to those in the South, those in the Midwest (OR:2.54[95%CI:1.75-3.69]) and Northeast (OR:1.95[95%CI:1.54-2.47]) were more likely to be completely vaccinated. This was also true for any HPV vaccination, as relative to the South, those in the Midwest (OR:2.34[95%CI:1.85-2.95]) and Northeast (OR:1.88[95%CI:1.60-2.20]) were more likely to receive any HPV vaccine. High school graduates (OR:2.21[95%CI:1.75-3.69]), those with some college (OR:2.62[95%CI:1.28-5.39]]), and college graduates (OR:4.75[95%CI:2.30-9.79]) were more likely to be completely vaccinated than those with only some high school education. Compared to those with some high school education, those with some college education (OR:1.53[95%CI:1.01-2.33]) and college graduates (OR:2.27[95%CI:1.49-3.46]) were more likely to have any HPV vaccine, though high school graduates (OR:1.29[95%CI:0.84-1.97]) were not more likely. Compared to those who are married, those previously but not currently married (OR:1.65[95%CI:1.18-2.29] and OR:1.76[95%CI:1.41-2.19]), those who have never been married (OR:1.56[95%CI:1.19-2.04] and OR:1.58[95%CI:1.31-1.90]), and those in unmarried partnerships (OR:1.80[95%CI:1.26-2.54] and OR:1.40[95%CI:1.06-1.83]) were more likely to have complete or any HPV vaccination, respectfully. Additionally, those with a personal doctor were more likely to receive full vaccine series (OR:1.79[95%CI:1.24-2.60]) and any vaccine (OR:1.29[95%CI:1.03-1.61]). Those with any cancer history (OR:1.15[95%CI:0.75-1.75]) or history of head and neck cancer (OR:1.11[95%CI:0.21-5.81]) did not have increased likelihood of complete vaccination or any HPV vaccination (OR:1.29[95%CI:0.94-1.76] and OR:0.40[95%CI:0.08-2.09], respectively.

Conclusions: This study demonstrates low overall HPV vaccination in US Adults aged 27-45 years. While much of this is explained by personal situation, such as marital status, this study reveals that educational and access issues continue to significantly affect vaccination status in this cohort.

B030: ASSOCIATION OF CANNABIS USE AND HEAD AND NECK CANCER: A RETROSPECTIVE CROSS-SECTIONAL STUDY - Tyler J Gallagher, BS; Matthew E Lin, BS; Neils C Kokot, MD; Keck School of Medicine of USC

Introduction: The literature has demonstrated links between cannabis use and development of some head and neck cancers on a genetic and molecular level. Additionally, individuals who consume cannabis by smoking may be

exposed to an additional cancer risk via the inflammatory effects of smoke inhalation. Here, we utilized a large database of electronic medical record data to explore the clinical association between cannabis use and laryngeal cancer.

Study Design: Cross-Sectional Study

Methods: We queried TriNetX, a globally federated database of deidentified electronic medical record data. Two cohorts were created, each defined by an arbitrary index event "Outpatient Hospital Clinic Visit" (HCPCS: G0463) to allow for comparison of cancer incidence after an index event with the largest possible sample while also allowing for propensity score matching on the TriNetX platform. One cohort was defined by individuals with the index event and presence of a cannabis related disorder (ICD-10: F12), and the other was defined by individuals with the index event without a cannabis related disorder. Additionally, patients with head and neck cancers in anatomic regions analyzed in this study before the index event were excluded. New diagnosis of malignant neoplasm of the oral cavity (ICD-10: C01-C05), oropharynx (ICD-10: C09-C10), nasopharynx (ICD-10: C11), larynx (ICD-10: C32), and salivary gland (ICD-10: C08) were analyzed in each group. Then, TriNetX Advanced Analytics were utilized to perform 1:1 propensity score matching between groups for current age, age at index event, sex, ethnicity, race, alcohol related disorders, and tobacco use. Subsequently, incidence of new head and neck cancer diagnosis was analyzed.

Results: Rate of new malignancy in all analyzed anatomic locations was higher in the cannabis related disorder group (n=103,786) compared to the group without cannabis related disorder (n=4,537,923), including for oral (0.085% and 0.018%, respectively), oropharyngeal (0.091% and 0.012%), nasopharyngeal (0.011% and 0.003%), laryngeal (0.102% and 0.014%), and salivary gland (0.016% and 0.003%) cancers. After 1:1 propensity score matching (n=103,718 per group), individuals in the cannabis related disorder group had a higher risk of new oral (OR: 4.69 [95% CI: 2.86-7.69]), oropharyngeal (OR: 6.34 [95% CI: 3.68-10.93]), and laryngeal (OR: 4.08 [95% CI: 2.66-6.27]) cancer but not nasopharyngeal (OR: 1.20 [95% CI:0.52-2.78]) or salivary gland (OR: 1.60 [95% CI: 0.73-3.53]) cancer.

Conclusions: This study demonstrates a significant association between cannabis use and oral cancer, oropharyngeal cancer, and laryngeal cancer via a large population-based study. This study is limited by potential inconsistency of diagnosis, inability to assess dose-response, limited ability to control for covariates, and limited assessment of temporality. Further research should examine the mechanism of this association and search for dose-response with strong controls to further support evidence of this association.

B031: COMORBID DEPRESSION IN HEAD AND NECK CANCER PATIENTS - Marina C Martinez; Andrey Finegersh, MD, PhD; Fred M Baik, MD; Floyd C Holsinger, MD, FACS; Heather Starmer, MA, CCCSLP, BCSS; John B Sunwoo, MD; Davud Sirjani, MD; Vasu Divi, MD; Michelle M Chen, MD, MHS; Stanford University

Importance: Depression is more prevalent in individuals with cancer than in the general population and is correlated with increased mortality in cancer patients. Head and neck cancer (HNC) patients are particularly vulnerable, and prior studies have shown that these patients are twice as likely to die from suicide as other cancer patients.

Objective: To determine whether there is a difference in the prevalence of depression in head and neck cancer patients compared to patients with other cancers.

Design: Retrospective cohort study of a population-level database

Setting, Participants, and Exposures: A weighted analysis of 23,001,196 adult patients in the 2019 National Health Interview Survey database with a diagnosis of cancer who completed the PHQ-9 questionnaire.

Main Outcome(s) and Measure(s): Depression based on the PHQ-9 questionnaire.

Results: Of 364,524 adult patients with HNC (22.3% female, 77.8% male), the prevalence of depression on the PHQ-9 questionnaire (mild, moderate, or severe) was 40.1% in HNC patients and 22.3% in all other cancer patients (P=.008). Among patients with other cancers, the cohorts with the highest proportion of depression were lung cancer (38.6%), gynecological cancers (32.7%), and non-colorectal gastrointestinal cancers (28.7%). However, relative to patients with other cancers, patient with HNC were equally likely to screen positive for anxiety (23.6% vs 16.0%, P=.20), take medication for depression (13.9% vs 10.1%, P=.37) and state that they never feel depressed (59.7% vs 53.7%, P=.71). There was also no difference in age, marital status, race, and urban/rural location between our HNC cohort and patients with other cancers. On multivariable logistic regression analysis of factors associated with depression among patients with cancer, having HNC was associated with increased likelihood of depression (OR, 5.7; 95% CI, 2.2-14.7). Other factors associated with depression included being unmarried or not living with a partner (OR, 1.6; 95% CI, 1.2-2.0) and anxiety (OR, 10.0; 95% CI, 7.4-13.5).

Conclusions and Relevance: Patients with head and neck cancer are twice as likely to screen positive for depression than those with other cancers, despite having similar rates of self-reported depression and depression medication utilization. This suggests that depression may be largely underreported and undertreated in this population and further research is needed to develop interventions to improve identification and optimize treatment for this vulnerable population.

B032: HARNESSING ARTIFICIAL INTELLIGENCE TO IMPROVE THE READABILITY OF PATIENT EDUCATIONAL MATERIALS IN HEAD AND NECK CANCER SURGERY - Andrew Meci, MPH[1]; Andrew J Rothka, BS[1]; Madison Hearn, BS[1]; F. Jeffrey Lorenz, MD[2]; Neerav Goyal, MD, MPH, FACS[2]; [1]Penn State College of Medicine; [2]Penn State Health

Introduction: According to the American Medical Association (AMA) and the National Institute of Health (NIH), educational materials provided to patients should not exceed a 6th-7th grade reading level. The goal of this study is to 1) determine the reading level of patient education materials for head and neck cancer procedures and 2) determine the feasibility of the use of artificial intelligence (AI) to improve the readability of these materials.

Methods: Patient materials for common head and neck cancer treatments and procedures were obtained from the American Academy of Otolaryngology – Head and Neck Surgery (AAO-HNS) and the American Cancer Society (ACS). Topics included were laryngeal cancer, thyroid nodules,

thyroid cancer, fine needle aspiration, skin cancer, salivary glands, oral lichen planus, nasopharyngeal cancer, neck mass in adults, head and neck cancer, human papillomavirus, Mohs surgery, glossectomy, mandibulectomy, maxillectomy, transoral robotic surgery, laryngectomy, neck dissection, reconstructive surgery, and tracheostomy. ChatGPT 3.5 (OpenAI) was used to modify texts to a lower grade level and create de novo texts on the same topics at a desired lesser than 6th-grade reading level. Characters, word count, and Flesch-Kincaid reading ease and grade level were recorded for source texts and texts modified or generated by ChatGPT. T-tests were used to determine statistical differences in grade levels and Pearson Correlations were used to compare data.

Results: AAO-HNS texts and ACS patient informational material on head and neck cancer surgery and topics averaged a reading grade level of 9.1 (SD 1.2). Texts modified by ChatGPT resulted in a significantly reduced mean reading level of 6.5 (SD 2.0) (p < 0.01) and texts generated by ChatGPT also had a significantly reduced reading level compared to source material of 5.5 (SD 0.8) (p <0.01). There was a medium strength correlation between a greater number of words and greater ease of translating text to a lower grade level (Pearson Correlation = 0.36).

Conclusions: Accessibility of patient education materials is vital to the shared decision-making process between patient and provider. Patient informational materials that are currently available were consistently above the recommended reading levels. AI can be utilized to successfully improve the accessibility of patient informational materials regarding head and neck cancer surgical interventions.

B033: RACIAL DISPARITIES IN QUALITY OF CARE AMONG HEAD AND NECK CANCER PATIENTS -

Uchechukwu C Megwalu, MD, MPH; Vasu Divi, MD; Yifei Ma, MS; Stanford University School of Medicine

Background: Significant racial disparities exist in head and neck cancer (HNC) outcomes. Racial/ethnic minority patients (especially Black patients) have worse survival outcomes than non-Hispanic White patients, even after adjusting for disease stage and other clinically important factors. Some of the racial/ethnic differences in survival may be explained by differential access to high-quality care.

Objective: To examine racial/ethnic differences in use of high-quality hospitals and quality of care among patients treated for HNC in California.

Methods: Data were extracted from the California Cancer Registry dataset linked with discharge records and hospital characteristics from the California Department of Health Care Access and Information. The study cohort comprised adult patients with HNC (oral cavity, oropharynx, hypopharynx, or larynx) diagnosed between January 1, 2010, and December 31, 2019. Patient-level compliance with the following recommendations from the National Comprehensive Cancer Network (NCCN) guidelines were assessed: 1) Adjuvant radiotherapy (RT) for surgically-resected T3-4, and N2-3 disease, and 2) dual modality therapy for T3-4, and N2-3 disease. Principal component analysis was used to generate a composite HNC-specific hospital quality score, incorporating the following hospital-level factors: case volume, cancer center accreditation status, NCCN guideline compliance, and Agency for Healthcare Research and Quality (AHRQ) Patient Safety

Indicators. The impact of hospital quality on overall survival (OS) was assessed using Cox regression models with robust standard error using sandwich variance estimators. Logistic regression was used to assess the association between race/ethnicity and use of high-quality hospitals, and the associations between race/ethnicity and NCCN guideline compliance.

Results: Patients treated in hospitals ranked in the top tertile for quality had improved OS [Hazard ratio (HR) 0.85, 95% Confidence Intervals (CI) 0.79 to 0.90], after adjusting for site, tumor stage, Charlson comorbidity score, surgical resection, neck dissection, radiotherapy, chemotherapy, age, and sex. Black patients (odds ratio [OR] 0.87, 95% CI 0.78 to 0.98) and Hispanic patients (OR 0.82, 95% CI 0.76 to 0.89) were less likely to be treated in top-quality hospitals compared with non-Hispanic White patients. This association disappeared for Black patients, but persisted for Hispanic patients, after adjusting for insurance status. Black patients with advanced-stage disease were less likely to be treated with dual-modality therapy (OR 0.81, 95% CI 0.68 to 0.97), however, this association disappeared after adjusting for neighborhood socioeconomic status, insurance status, and hospital quality. There was no association between race/ethnicity and adjuvant RT among patients with surgically-resected advanced tumors.

Conclusion: Treatment in high-quality hospitals is associated with improved survival for patients with HNC. However, Black and Hispanic patients are less likely to be treated in high-quality hospitals compared with non-Hispanic white patients. This disparity appears to be partly mediated by insurance status. Black patients with advanced-stage disease are less likely to be treated with dual-modality therapy. This disparity appears to be mediated by socioeconomic status, insurance status, and hospital quality.

B034: TOWARDS GENDER AND RACIAL PARITY WITHIN REPUTABLE OTOLARYNGOLOGY JOURNAL EDITORIAL BOARDS AND LEADERSHIP ROLES, 2018-2023 -

Neil Parikh, BS, BA; Amina Khan, BS; Mitchell Figueroa, BA; Benjamin Tam, BS; Kevin Herrera, BS; Tamara Chambers, MD; University of Southern California

Objectives: To assess the representation of traditionally underrepresented populations, including racial minorities and females, on otolaryngology journal editorial boards.

Introduction: As of 2020, females comprised greater than 50% and racial minorities approximately 49% of all medical students. However, similar strides towards gender and racial parity are not as pronounced within otolaryngology journal editorial boards. Prior studies found that while females were appropriately represented among mid-level editorial board members (EBMs), they were underrepresented on the overall editorial board and there were no female editor-in-chiefs. Furthermore, to our knowledge, no similar analysis stratifies editorial board composition by race.

Methods: Thirteen high-impact clinical otolaryngology journals were selected based on a 5-year impact factor > 2.0 and the availability of data from at least 2018 onwards. Editorial board members were grouped by position, journal, and journal year. Position was further consolidated into Editor in Chief, Associate Editor (Associate, Section, Deputy, and Assistant Editor), Editorial Board, and Resident Editor. Race and gender were inferred based on individuals' name and photo and confirmed via Google Search of surname origin in ambiguous cases. This

methodology has been utilized by multiple studies published in reputable otolaryngology journals, however, we acknowledge the inherent limitations of assuming an individual's gender and race. The proportion of female and non-white editorial board members was calculated. Chi-squared tests were conducted to ascertain the statistical significance in difference in editorial board composition between 2018 and 2023.

Results: From 2018-2023, female membership on editorial boards increased from 21.4% (range 4.5% - 46.0%) to 27.5% (5.9% to 54.3%) (P = .015). Contemporaneously, non-white membership on editorial boards increased from 22.8% (range 4.5% - 39.0%) to 26.9% (range 2.9% to 40.4%) (P = .099). The greatest increase in non-white membership was for Asian American Pacific Islanders who underwent an increase of 1.9% from 17.7% to 19.6%. Black and Latinx board members remain particularly underrepresented in 2023, at 1.4% and 2.9% of editorial board members respectively. Broken out by board position, female membership increased from 8.3% to 15.4% at Editor in Chief, 17.8% to 21.6% at Associate Editor, 21.5% to 28.1% at Editorial Board, and decreased from 66.7% to 61.9% at Resident Editor. Similarly, non-white representation increased from 8.3% to 23.1% at Editor in Chief, 25.2% to 31.6% at Associate Editor, 22.8% to 25.7% at Editorial Board, and 8.3% to 28.6% at Resident Editor.

Discussion: While significant progress towards gender parity has been made between 2018-2023, progress towards racial parity has been more muted. Black and Latinx editorial board members remain disproportionately underrepresented compared to the broader population. Interestingly, the proportion of non-white Editors in Chief is outpacing the percentage of female Editors in Chief. Since editorial board positions are one component of professorship at academic institutions, a diverse editorial board may hasten the diversification of otolaryngology faculty and thereby provide likeminded mentors for prospective otolaryngology applicants in the long-term. Finally, more diverse editorial boards may be more likely to support and accept innovative, understudied research, such as on health disparities within otolaryngology.

B035: PATIENT COMMUNICATION AFTER PAROTIDECTOMY TRENDS AND ASSOCIATIONS WITH COMPLICATIONS -
Andrew Prince[1]; Kimberly Oslin[2]; David Forner[1]; Josh Smith[1]; Emma Hershey[1]; Lisa Chionis[1]; Michael Allevato[1]; Mark Prince[1]; Steven Chinn[1]; [1]University of Michigan; [2]Henry Ford Health

Background: Parotidectomy is a common procedure and understanding the rationale for why patients communicate with the treating team post-operatively may allow for better pre-operative education, post-operative discharge planning, and improved satisfaction among patients and providers. We therefore reviewed post-operative patient communications to identify trends and candidate associations with surgical complications.

Methods: Retrospective study of patients who underwent parotidectomy from 2018-2022 in a single tertiary-care institution was performed. All patient communications were immediately documented within the electronic medical record by health care professionals, and we reviewed them with 6 months of follow-up. We categorized patient communications as requiring an action by the surgeon (procedure, antibiotics, or non-planned evaluation), instructions by support staff (conservative wound and pain management) or reassurance

(normal postoperative expectations and clarification of discharge instructions). Patients with neck dissection and free flap were included in the cohort, while communications about drain removal or pathology results were excluded.

Results: A total of 779 parotidectomies were identified. Most patients were men 59.3% (n=461), Caucasian 87.4% (n=681) and had an average age of 62.4yrs ±16. We found 37.4 % (n=291) of patients had post-op communications. There was no significant difference between patients with post-op communication and those without when evaluating demographics, comorbidities, surgical approach, inpatient vs outpatient status, or tumor pathology. Trends within post op communications included wound concerns 37.1% (n=108), swelling 36.4% (n=106), pain management 16.8% (n=49), post-op instructions 11.3 % (n=33), other medical concerns 11.3% (n=33), and drain concerns 6.2% (n=18). We found 20.3% (n=59) of post-op communication required an action by the surgeon, 26.1% (n=76) required instruction by the support staff, and the other 53.6% (n=156) required reassurance or clarification of post-op discharge information. In a multivariate model, the odds of an action required by the surgeon were significantly higher for post-op communication about swelling (OR=4.9, 95% CI= 2.3-9.9) and wound concerns (OR= 4.7, 95% CI= 2.3-9.7).

Conclusions: Post operative patient communication within 6 months after parotidectomy occurs over 33% of the time. Only about 50% of that communication requires an action by the surgeon or instructions from support staff, while the other half need reassurance or discharge instruction clarification. Post-op swelling and wound concerns increase the odds of an action required by the surgeon 4 fold. A majority of patient concerns could be reduced with improved patient discharge information and communication on the day of surgery. Our findings will help guide institutions on appropriate discharge instructions, responses to patient concerns, and improve patient/physician post-op satisfaction.

B036: DEVELOPMENT OF A VIRTUAL SIMULATION TOOL FOR LOCAL AND REGIONAL FLAP RECONSTRUCTION IN THE HEAD AND NECK - Fatemeh Ramazani, MD, MMEd; Robert Hart; Jessica Henley; Shamir Chandarana; Wayne Matthews; Christiaan Schrag; Jennifer Matthews; David Mackenzie; Court Cutting; Justin Lui; University of Calgary

Background: Simulation based learning poses an opportunity to provide surgical trainees with high fidelity learning environments where they can deliberately practice technical skills. Local and regional reconstructive techniques are commonly used for closure of cutaneous defects in the head and neck. The three-dimensional visualization and design of these local flaps poses a challenge for trainees across various subspecialties. By offering a controlled yet realistic environment for practice, simulation platforms address the crucial need for enhanced exposure, allowing trainees to develop and refine their skills in handling the complexities of local flap reconstructions.

Objective: The objective of this study was to develop and validate an educational curriculum, integrated within a virtual simulation tool, specifically tailored to facilitate the training of surgical residents in the domain of local and regional flap reconstruction.

Methods: This was a two phase, prospective study set at a single centre. In Phase I, an extensive literature review of pertinent

texts and educational benchmarks in Otolaryngology (Oto-HNS) and Plastic Surgery was undertaken. This comprehensive review informed the development of a structured curricular framework for three common local reconstructive techniques (Z-Plasty, Rhomboid flap, and Bilobed flap). Phase II was dedicated to validating the developed curriculum using survey methodology. Six fellowship trained head and neck reconstructive surgeons were asked to assess and validate the content, organization, and flow of the proposed curriculum. Expert consensus was achieved following two rounds of participant surveys. The refinement of the curriculum's readability and its applicability to learners was achieved through survey feedback obtained from Oto-HNS and Plastic Surgery trainees.

Results: This study resulted in the development of an dedicated curriculum, implemented via a virtual simulation platform, focusing on three frequently utilized local reconstructive techniques. Curricular objectives include reconstructive indications, key flap measurements, pre-operative considerations, potential complications, and post-operative care. Detailed procedural steps were intricately integrated into the curriculum, complemented by annotated video demonstrations showcasing the techniques executed on an innovative local flap simulator.

Conclusions: The implementation of this digital simulation curriculum stands to significantly enhance the acquisition of a fundamental procedural skill, bridging gaps in clinical exposure and substantially augmenting competence and confidence in local and regional flap reconstruction during residency training. The utilization of this curriculum represents a pivotal step towards addressing the challenges associated with limited hands-on experience, offering an innovative and immersive learning approach that fosters a deeper understanding and proficiency in these intricate surgical techniques.

B037: THYROID TALK ON TIKTOK: A SOCIAL MEDIA ANALYSIS OF THYROIDECTOMY INFORMATION ON TIKTOK - Janisah Amirah I Saripada, BS; Arianna V Ramirez, MD; Ogechukwu Anwaegbu, BS; Orly M Coblens, MD; Sepehr Shabani, MD; Viran J Ranasinghe, MD; University of Texas Medical Branch at Galveston

Objective: This study aims to explore the landscape of public perception on thyroid surgery through the lens of the popular social media platform TikTok. Our objectives include evaluating social media posts related to thyroid surgery to examine perceptions, types of content, types of content creators, post-operative complaints, content accuracy, and understandability.

Study Design: A mixed-methods approach incorporating qualitative and quantitative analyses.

Setting: The TikTok social media platform.

Methods: In October 2023, a comprehensive search on TikTok was conducted for the top 100 public posts for the following search terms "thyroidectomy," "thyroid removal," and "thyroid surgery." The selected videos were then subjected to analysis, involving quantification of likes, comments, shares, video length, and views. Video engagement was further assessed using the Video Popularity Index. The type of account posting the videos, the medical provider's role, and the content accuracy in alignment with the American Thyroid Association Guidelines were also considered. Patient experiences, symptoms, and complaints both before and after surgery were documented.

Additionally, videos categorized as providing medical advice or educational content were evaluated for understandability and patient actionability using the Patient Education Materials Assessment Tool (PEMAT), and their accuracy was scrutinized against the American Thyroid Association (ATA) Guidelines.

Results: Among the top 100 videos analyzed, a predominant portion (63%) was generated by personal patient accounts, with the remainder being contributed by physicians (27%), Non-MD/DO Medical accounts (8%), and non-medical health practitioners (2%). A noteworthy percentage (39%) of posts depicted thyroidectomies negatively, primarily emanating from personal patient accounts (100%). The most common post-operative complaints included neck pain (19%), followed by low energy (9%), hormone imbalance (7%), weight gain (7%), difficulty swallowing (7%), and poor cosmesis (7%). The most prevalent themes included postoperative experiences (36%) and medical education (36%), followed by pre- and post-operative experiences (14%), physician/healthcare advice (7%), and preoperative experiences (6%). Content accuracy, when compared to ATA guidelines, was 100% for MD/DO medical accounts while only 65% for non-medical health practitioners. PEMAT scores were given for videos created by MD/DO accounts which revealed 78.69% in understandability while only 26.61% in actionability. Lastly, the most popular videos were from patient accounts with video popularity indices of 0.93 and 0.79.

Conclusion: Social media posts were predominantly shared by patients, specifically in the post-operative period highlighting a negative experience. This insight could inform otolaryngologists in optimizing their patient interactions and treatment plan in the postoperative period. Further, physicians could improve engagement in social media to increase medical advice content. Lastly, low PEMAT actionability scores indicate that there is room for improvement in creating content that can effectively engage patients that may need thyroid surgery.

B038: BECK DEPRESSION INVENTORY II RESPONSE FOLLOWING PARATHYROIDECTOMY FOR PRIMARY HYPERPARATHYROIDISM: A SYSTEMATIC REVIEW AND META-ANALYSES - Om Chitnis, BS[1]; Sabrina Wagner, BA[1]; John Caraway, BS[1]; Michael Orestes, MD[2]; [1]Uniformed Services University; [2]Walter Reed National Military Medical Center

Importance: Currently there is a lack of consensus regarding neuropsychiatric symptoms as an indication for parathyroidectomy in primary hyperparathyroidism (pHPT). Additionally, it is unclear as to which psychometric instruments or psychometric score cut offs could be used as indication for surgery in these patients.

Objective: The Beck Depression Inventory II (BDI-II) is a well studied psychometric instrument that is widely used, easy to administer, and highly sensitive/specific for depression. The purpose of this study is to perform the first ever systematic review and meta-analyses of pre- and post-operative BDI-II scores in patients with pHPT undergoing parathyroidectomy with the goal of determining if BDI-II scores significantly improve after surgery.

Data Sources: A comprehensive search of the literature was performed using PubMed, Embase, PsycINFO, Web of Science, and Ovid All EBM Reviews. All relevant literature published through August 1st, 2023, was included.

Study Selection: Study selection was guided by the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) strategy. Studies met inclusion criteria if they evaluated pre- and post- operative BDI-II scores in patients with pHPT undergoing parathyroidectomy. Bias was assessed via the validated Methodological Index for Non-Randomized Studies (MINORS) criteria.

Data Extraction and Synthesis: Three reviewers manually extracted data and a fourth reviewer cross-checked extracted data for accuracy. Data was pooled using a random-effects model.

Main Outcomes and Measures: Random effects (RE) meta-analyses were used to estimate overall standardized mean BDI-II score changes within parathyroidectomy and control cohorts at ≤1 month and at 6 months postoperatively. Additional RE meta-analysis estimated both the standardized mean difference in BDI-II scores and overall relative risk for the presence of depression before surgery in the parathyroidectomy versus control cohorts.

Results: The literature search returned 1553 articles for initial review of which 9 (746 participants) met criteria for inclusion and meta-analyses. Meta-analysis revealed that pHPT patients had significantly higher presurgical BDI-II scores when compared to control groups. Additionally, patients experienced a significant and sustained decrease in BDI-II scores following parathyroidectomy. Notably, there was a dramatic decrease in the percentage of patients with BDI-II scores ≥14 following parathyroidectomy.

Conclusions and Relevance: Patients with pHPT experience a significant and sustained improvement in BDI-II scores following parathyroidectomy. We propose that a BDI-II score ≥14 could potentially be used as an indication for parathyroidectomy in patients with otherwise asymptomatic pHPT.

B039: PAPILLARY THYROID CANCER SURGICAL TRENDS BEFORE AND AFTER THE 2015 AMERICAN THYROID ASSOCIATION GUIDELINE CHANGES -

Laura M Cogua[1]; Connor J Tupper, BA[1]; Peter T Silberstein, MD[1]; Kathryn E Coan, MD[1]; Ameya A Jategaonkar, MD[2]; [1]Creighton University School of Medicine; [2]Department of Otolaryngology, Barrow Neurological Institute

Introduction: The extent of surgical treatment for papillary thyroid cancer (PTC) has been widely debated. In 2006, the American Thyroid Association (ATA) advocated for total thyroidectomy for tumors over 1.0cm. In 2015, the ATA the updated guidelines recommended lobectomy for tumors <1.0 cm and total thyroidectomy for tumors >4 cm. The guidelines incorporated other factors, such as high risk pathologic features, for the treatment of Intermediate size nodules (between 1 and 4 cm in size) . There are few studies comparing the impact of the ATA guidelines on clinical practice. Here we evaluate the impact of the 2015 ATA guidelines on the surgical treatment of PTC.

Methods: Patients diagnosed with PTC between 2000-2020 were collected from the Surveillance, Epidemiology, and End Results (SEER) database. Patients were separated into two groups by year of diagnosis, either pre-ATA guideline changes (2000-2015) or post-ATA changes (2016-2020). Extent of surgery was separated into lobectomy or total thyroidectomy. Additional variables collected included age, gender, race, stage, tumor morphology, tumor size, chemotherapy, and radiation status, time to treatment, median household income,

and population size of the patient's home area. Logistic regression analysis was performed to assess for associations with diagnosis before or after the 2015 ATA guideline changes.

Results: A total of 162,636 patients were included, of which 116,273 patients (71.5%) were pre-ATA guidelines and 46,363 patients (28.5%) were post-ATA updates. The rate of lobectomy increased from 12.1% pre-ATA updates to 22.6% post-ATA updates (p<0.05). The increase in lobectomy was greatest in intermediate size tumors (1.0cm-4.0cm); the rate pre-ATA update was 6.4% pre-ATA changes compared to 23.5% post-ATA changes (p<0.05). Analysis of patient demographics and other variables demonstrated an increase in the frequency of age over 65 years, race Black, Hispanic, Asian, and American Indian/Alaskan Native, higher nodal stage, tumor size over 4.0cm, and need for chemotherapy in the post-ATA update cohort (p<0.05). There was a decrease in the frequency of female gender, distant metastasis, tumors under 1.0cm, and radiation therapy in the post ATA update subset (p<0.05).

Conclusions: Our results show that after the 2015 ATA guideline changes there has been a significant increase in the rate of lobectomy across all PTC tumors. This has been especially pronounced in the surgical treatment of tumors of intermediate size, i.e. between 1.0cm-4.0cm. This is further confirmed in our adjusted regression showing an increased rate of lobectomy in the post-2015 ATA guideline change period. This data suggests that the guideline update has been successful in driving de-escalation of surgery for PTC, especially intermediate sized tumors. Future research could benefit from assessing the impact of these trends on patient outcomes including, but not limited to, survival, hospital length of stay, and cost of treatment, and other post-operative outcomes.

B040: XENOGRAFT TRANSPLANTATION OF MACROENCAPSULATED HUMAN PARATHYROID TISSUE IN IMMUNOCOMPETENT MICE AND RAT MODELS -

Sophie S Jang, MD[1]; Mads K Larsen, BS[2]; Julie E Noel, MD[1]; Grace Wei, PhD[2]; Lisa A Orloff, MD[1]; [1]Stanford University, Department of Otolaryngology-Head and Neck Surgery; [2]Encellin
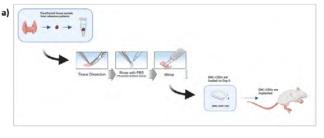
Introduction: Inadvertent removal or devascularization of parathyroid glands during thyroid and neck surgery can lead to permanent hypoparathyroidism, necessitating lifelong treatment with calcium and vitamin D supplements. These therapies provide suboptimal control of serum calcium levels, reduced quality of life, and frequent long-term complications. Allograft parathyroid transplantation, a promising alternative, offers the potential for restoration of normal PTH secretion, but has not warranted the associated risk of lifelong immunosuppression. This study utilized an immunoprotective nanoporous cell encapsulation device (CED) to transplant human parathyroid xenografts in immunocompetent animal models without immunosuppressive therapy to investigate parathyroid tissue viability and function.
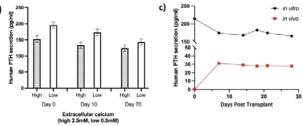
Methods: Seven human parathyroid adenoma samples were obtained during parathyroidectomy under IRB approved protocol. A total of two (2) C57BL/6 mice and fifteen (15) Lewis rats that were immunocompetent were used per IACUC approved protocol. Tissue homogenization methods - manual scalpel mincing or mechanical tissue chopping - were compared. Tissue homogenate was then loaded into the CED (**Figure 1a**). CEDs were transplanted into the flank or abdomen in animal models and human PTH levels were measured in blood after 30-70 days. Overall cell viability and response to 20min
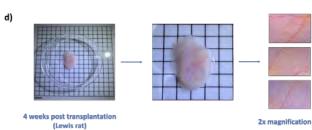
extracellular calcium exposure was assessed in explants at day 0, 10 and 70 post transplantation. Confocal microscopy was utilized to visualize cell viability and neovascularization.

Results: The mean weight of the surgically removed parathyroid glands was 206.7 mg (range, 17–894mg). Between the two methods of homogenization, similar functionality of PTH secretion was noted after 1hr incubation in vitro. However, mechanically chopped tissue had significantly lower cell survival and PTH secretion (12% decrease) compared to manually minced (3% decrease) at 24hr incubation. PTH diffusion across the nanoporous membrane of the CED achieved 90% at 100 minutes in vitro. Mass of parathyroid tissue loaded into CED had a linear correlation with PTH secretion after 1hr incubation (R^2=0.989). Following xenograft explant from the animal, functional response to high or low extracellular calcium levels in vitro was consistent with expected physiological response at day 0, 10 and 70 (**Figure 1b**). Sustained parathyroid tissue activity was assessed with PTH secretion in vitro (supernatant, 22% decrease from baseline) and in vivo (blood, 9% decrease) weekly for 28 days in rat (**Figure 1c**). A similar trend was seen in mice with PTH secretion decreasing 24% in vitro and 12% in vivo at day 70 compared to day 10. Encapsulated tissue showed revascularization at 4 weeks after transplant into an immunocompetent rat (**Figure 1d**).

Conclusion: Macroencapsulated human parathyroid xenograft had sustained PTH secretion, response to extracellular calcium, and revascularization in immunocompetent mice and rats up to 70 days after transplantation. Encapsulating the tissue in an immunoprotective CED decreases the likelihood of immune-mediated rejection without the use of immunosuppressants while allowing necessary nutrients to pass through the selectively permeable membrane and sustain parathyroid tissue viability and functionality. Future work includes bringing this method to human clinical trials and investigating the feasibility of allograft transplantation without immunosuppression.

B041: BITTER TASTE AGONISTS REGULATE APOPTOSIS IN MEDULLARY THYROID CANCER CELLS -
Kimberly Wei, BS; Zoey Miller, BS; Joel Thompson, BS; Robert Lee, PhD; Ryan Carey, MD; University of Pennsylvania

Introduction: There is a substantial need for translational thyroid cancer advances in rare and aggressive tumors such as medullary thyroid cancer (MTC). Arising from parafollicular cells of the thyroid, MTC constitutes <5% of all thyroid cancers in the US but is associated with worse survival compared to more common histologies like papillary and follicular. Bitter taste receptors (T2Rs) and their associated genes (TAS2Rs) have recently been studied in a variety of solid tumors including breast, ovarian, and head and neck squamous cell carcinomas. These receptors have been found to regulate multidrug resistance transporters and anticancer functions such as apoptosis and migration. The aim of this project is to characterize the expression, signaling, and function of T2Rs in response to bitter agonists in MTC cells with the hopes of generating potential therapeutic roles in the future.

Methods: Experimental work was performed in three MTC cell lines (MDA-T32, MDA-T68, MDA-T85). TAS2R expression was analyzed for all 25 TAS2Rs using quantitative reverse transcription PCR and immunofluorescence was performed in a subset of T2Rs. Live cell imaging was used to measure intracellular calcium signaling responses to agonists with a broad range of T2R targets (denatonium, diphenhydramine, flufenamic acid, quinine, thujone, and lidocaine). The effects of bitter agonists on proliferation and apoptosis were assessed using crystal violet and caspase 3/7 activation assays, respectively.

Results: TAS2R expression varied between MTC cell lines, but TAS2R14 was consistently one of the highest expressed TAS2Rs, with an expression level of ~2% relative to housekeeping gene UBC (Fig. 1A). Immunofluorescence demonstrated that T2R14 was mostly present intracellularly in all three cell lines (Fig. 1B). Five bitter agonists produced significant calcium responses across all cell lines, while thujone produced a more variable response ($p<0.05$) (Fig. 1C). All bitter agonists were found to significantly decrease proliferation and induce apoptosis over the course of 3-12 hours in one or more cell lines ($p<0.05$) (Fig. 1D-E).

Discussion: MTCs express T2Rs mostly intracellularly, including T2R14 which has been studied in multiple cancers. Bitter agonists induce calcium responses with downstream caspase activation, decreased proliferation, and apoptosis. These results suggest that activation of T2Rs by bitter agonists may have therapeutic applications in MTC, warranting further characterization of the involved signaling pathways.
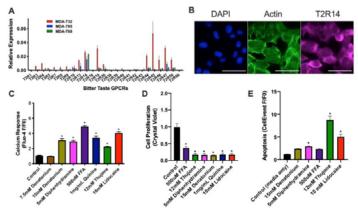
Figure 1. A) Relative expression (normalized to UBC) of 25 TAS2Rs via qPCR B) T2R14 expression in MDA-T32 cells via immunofluorescence stain with DAPI (nucleus) and phalloidin (actin) C) MDA-T32 Ca^{2+} peak responses to bitter agonists D) MDA-T32 proliferation response to bitter agonists via crystal violet assay E) MDA-T32 CellEvent (caspase 3 and 7 indicator) fluorescence at 12 hours with bitter agonists

decrease in efficiency (p=0.042 and p<0.001, respectively), while any resident involvement made microvascular cases significantly more efficient (p=0.001). The number of these specific head and neck surgeries has varied over the last two decades with peaks in 2010 (larynx), 2011 (oral cavity), 2018 (microvascular), although the complication rate has remained stable at an average of 29.1, 28.9, and 36.6%, respectively. In the VHA, resident participation in larynx procedures from 2001-2011 averaged 83% and declined to 72% from 2012-2021 (p<0.001). Similar trends can be seen for oral cavity (p < 0.001) and microvascular procedures (p < 0.001).

Conclusion: Resident participation in head and neck oncologic surgeries among veterans was linked to increased operative time in laryngeal and oral cavity surgeries but decreased operative time in microvascular surgery. Similarly, wRVU per hour decreased with resident involvement for laryngeal and oral cavity surgery, but significantly increased in microvascular surgery. Resident participation did not affect complication rates or return to the operating room. Despite these results, there has been a decline in resident involvement among head and neck oncologic surgeries at VAMCs over the last two decades.

B042: THE IMPACT OF RESIDENT INVOLVEMENT ON OPERATIVE TIME AND OUTCOMES FOR U.S. VETERANS IN HEAD AND NECK ONCOLOGIC SURGERY - John Anderson[1]; Xue Geng, MS[2]; Jessica Maxwell, MD, MPH[3]; [1]Georgetown University School of Medicine; [2]Georgetown University Medical Center; [3]University of Pittsburgh Medical Center

Background: Head and neck oncologic surgery at Veteran's Affairs Medical Centers (VAMC) nationwide has historically been a valuable aspect of resident surgical training. However, the impact of resident participation on patient outcomes and productivity in this setting remains unknown. The aim of this study was to determine the impact of resident involvement on complications, operative time, and productivity among veterans undergoing head and neck cancer surgery.

Study Type: Clinical Database Study

Study Design: Retrospective

Methods: Current procedural terminology codes were used to identify patients who underwent head and neck surgeries involving the larynx, oral cavity, and microvascular free tissue transfer in the Veterans Affairs Surgical Quality Improvement Program (VASQIP) database from 2001 to 2021. Operative time, work relative value units (wRVU) generated per hour, and occurrence of post-operative complications were compared among attendings with junior residents, attendings with senior residents, and attendings alone.

Results: Of 3,898 veterans who underwent head and neck surgeries of the larynx (n=1,786), oral cavity (n=1,749) and microvascular surgery (n=363), most cases were performed by an attending with a senior resident (58.8%). Resident involvement did not significantly affect complication or return to the operating room rates. Operative time was significantly longer when junior residents were involved in larynx procedures and senior residents were involved in oral cavity procedures (p=0.009 and p<0.001, respectively) but was significantly shorter in microvascular surgeries when any resident participated (p<0.001). Efficiency, or wRVU per hour, followed this trend in that junior resident involvement in laryngeal surgeries and senior resident involvement in oral cavity surgeries caused a significant

B043: GENDER DIFFERENCES IN RESEARCH ACTIVITY AMONG HEAD AND NECK FELLOWSHIP PROGRAM DIRECTORS - Anna Simone Andrawis, BS; Rita Vought, BA; Victoria Vought, BA; Ava Herzog; Ian Gorsen, BS; Jean Anderson Eloy, MD; NJMS

Purpose: Significant differences in career advancement and opportunities exist within academic medicine, especially in highly subspecialized fields. The objective of this study was to evaluate differences in research activity by gender among Head and Neck Fellowship program directors.

Methods: Head and Neck Fellowship directors were identified through the directory of Accredited Advanced Training in Head and Neck Oncologic and Endocrine Surgery Fellowships. There were 78 relevant programs evaluated for differences in gender among publications (h index, total publications, total citations, publication span, and mean and weighted Relative Citation Ratio (m-RCR and w-RCR). Publication information was extracted using Scopus and iCite.

Results: Seventy-eight program directors were evaluated, of which 15% were women. Female directors were distributed evenly by program focus (p=0.41), with 7 Endocrine programs (29% women), 33 Oncology programs (18% women), and 48 programs without a specific focus (11% women). Similarly, no differences in gender distribution were observed by location (p=0.45), with 20 programs in the Northeast (5% women), 24 in the South (17% women), 20 in the Midwest (25% women), 11 in the West (22% women), and 3 outside the United States (no women). An inverse relationship (p=0.45) was observed between female representation and years in practice, with the highest percentage of women with 0-9 years in practice (24%) and the lowest percentage with over 20 years in practice (11%). Female directors had on average fewer publications (114 vs. 66; p=0.028), and w-RCR (176.3 vs 75.7; p=0.026) compared to male peers. Male directors on average also had more citations (2,722 vs 139; p=0.38) over a greater span of publishing time (20.9 vs 15.2 years; p=0.070). Additionally, male directors had higher average h-index (26.4 vs 18.1; p=0.053), m-RCR (2.1 vs 1.6, p=0.92), and w-RCR (176.3 vs 75.7; p=0.026) compared to their female colleagues.

Conclusion: Head and Neck Fellowship program leadership has significant gender disparities (15% women), which is in line with other analyses of gender within academic medicine leadership. Female directors overall have lower measures of research activity compared to male peers. This may be indicative of an underlying inaccessibility for women to reach positions of authority among the head and neck specialty. However, the impact of the publications, or m-RCR, from male and female directors are similar which indicates the quality of research is comparable. Thus, among female fellowship directors, there may be a lack in support for prolonged research and publication funding in comparison to their male colleagues.

B044: USE OF VIRTUAL REALITY FOR MANAGEMENT OF ANXIETY DURING CHEMOTHERAPY - Ana V Araujo, BS[1]; Vivek C Pandrangi, MD[1]; Jason Y K Chan, MD, FRCSEd[2]; Ryan J Li, MD, MBA[1]; [1]Oregon Health and Science University; [2]Chinese University of Hong Kong

Background: Anxiety is a common symptom among cancer patients and may be heightened during chemotherapy infusions. Limited access to cognitive behavioral therapy and adverse effects of anxiolytic medications may place some limits on their usefulness. Non-pharmacologic point-of-care measures for anxiety reduction and improvement of patient satisfaction during cancer treatment may be effective amongst patients receiving chemotherapy. The purpose of this study was to explore the value of virtual reality (VR) for managing anxiety among patients undergoing chemotherapy infusions in the treatment of head and neck cancer, as well as other cancer types.

Methods: This was a prospective, two-arm randomized clinical pilot trial of adult patients undergoing chemotherapy or biologic treatment infusions at a tertiary academic medical center from April to September 2023. Patients with head and neck, breast, thoracic, and hematologic malignancies were included. Patients were randomized to the VR or control (smartphone) groups for use up to 30 minutes during their infusion, with a choice of game or meditation content. Patients completed surveys prior to intervention, immediately after intervention, and after their infusion, including the State Anxiety Inventory (SAI) and the Virtual Reality Sickness Questionnaire (VRSQ). Patient satisfaction was evaluated using two investigator-designed questions measured using a 5-point Likert scale. The primary outcome was post-intervention change in SAI anxiety score. The Mann-Whitney U non-parametric test was used to evaluate differences between groups.

Results: Out of 50 patients recruited, 46 patients were included in the final analysis (4 withdrawals). There were 25 patients in the VR group and 21 patients in the smartphone group. Mean (standard deviation) age was 58.7 (14.0) years, and the majority of patients were female (62%). There were no differences in median baseline anxiety levels between the two groups by the SAI (VR vs. smartphone: 37 vs. 33, p=0.45), or median device use time (30.0 vs. 30.0, p=0.34). The majority of patients had not previously used a VR headset (70%). Immediately after intervention, there was no significant difference in anxiety reduction between groups (median [interquartile range; mean rank]), (VR: 7 [8; 25.3] vs. Control: 2 [14; 21.4], p=0.34). After infusion completion, there also was no significant difference in anxiety reduction (VR: 9 [9; 21.4] vs. Control: 4 [18; 17.6], p=0.10). The mean VRSQ score (SD) was 8.02 (9.11) out of a total score of 133, indicating mild adverse symptoms associated with VR. Patients in the VR group also reported significant enjoyment of their audiovisual experience (5.0 [1.0]) as well as desire to use their audiovisual experience more often in their healthcare (5.0 [1.0]).

Conclusion: While there was no significant difference in anxiety reduction between VR and smartphone groups, the reductions in anxiety achieved across both groups may be clinically meaningful. These interventions were well tolerated and implemented with low technical complexity. Patients in this setting also appear to enjoy the use of VR and reported a high desire to use this technology in their future healthcare. The value of these simple interventions to treat anxiety among cancer patients undergoing chemotherapy or biologic infusions may be substantial.

B045: THE DEVELOPMENT OF AN AUTOMATED ALGORITHM TO IDENTIFY AND MANAGE POST-THYROIDECTOMY HYPOCALCEMIA - Diane Chernoff[1]; Lukasz Czerwonka, MD[2]; Daniel Waxman[3]; Petar Djuric, PhD[3]; Gabrielle Brite[1]; Lauren Langman[1]; Chiara Rabeno[1]; [1]Renaissance School of Medicine at Stony Brook University; [2]Stony Brook Medicine; [3]Stony Brook University Electrical and Computer Engineering

Importance: Post-thyroidectomy hypocalcemia has an incidence of 40%, with about 3% of patients experiencing permanent hypocalcemia[1]. The data from this study may be used to reduce the incidence of post-thyroidectomy hypo- and hypercalcemia and shorten hospital length of stay.

Objective: To develop a computerized artificial intelligence algorithm to quantitively prevent and treat post-thyroidectomy hypocalcemia based on patients' demographic factors and immediate post-operative parathyroid hormone (PTH) and calcium values.

Design: We conducted a retrospective chart review of 378 patients who underwent total or completion thyroidectomyies from July 2013 until June 2023.

Setting: University hospital

Participants: A random sample of all patients who were at least 18 years of age and received total or completion thyroidectomies. Patients who received simultaneous parathyroidectomies were excluded.

Main Outcome and Measurements: Prior to data collection, we hypothesized that patients with immediate post-operative PTH levels at or below 15pg/mL were at risk for developing hypocalcemia. We recorded patient demographic information and surgical pathology reports. We documented patient pre-operative and post-operative labs, including PTH and calcium levels. We recorded the frequency, dosage, and response to calcium and calcitriol supplementation. Lastly, we noted any emergency department visits or rehospitalizations in the three months following the procedure.

Results: Patients had a mean age of 52.5 and 72.4% were female. 58.2% of patients received post-operative calcium supplementation and 47.1% received calcitriol supplementation. 20.2% of patients became hypocalcemic at some point during their hospital stay, despite supplementation. FasterRisk was used to compute data-driven risk score for post-operative hypocalcemia (< 8 pg/mL)[2]. The algorithm processed patients' demographic, pathologic, and laboratory values and predicted that patient BMI, pre-operative calcium, and post-operative PTH and calcium were the most indicative of hypocalcemia. Across 4-way stratified cross-validation, we achieve an AUROC score

of 0.78 +- 0.06 with predictive accuracy of 82.53 +-5.47%.

Conclusions and Relevance: The data supports that both pre-operative patient factors as well as immediate post-operative labs contribute to the risk of post-operative hypocalcemia. Across a 4-way stratified cross validation, it appears that BMI below 20, pre-operative calcium ≤ 8.9mg/dL, post-operative calcium ≤ 8.1mg/dL, and post-operative PTH ≤ 10.7pg/mL added to patient risk scores. Immediate future analysis will include training the algorithm to quantitatively predict calcium supplementation dosage and frequency for patients who develop hypocalcemia.

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B046: LONGITUDINAL AND FUNCTIONAL OUTCOMES AFTER FIBULA FREE FLAP RECONSTRUCTION FOR MANDIBULAR OSTEORADIONECROSIS - Linda Chow, MD, FRCSC; Logesvar Balaguru, BS, BA; Peter Dziegielewski, MD, FRCSC, FACS; University of Florida

Background: Patients who undergo radiotherapy treatment for oral cavity and oropharyngeal malignancies may experience serious sequelae resulting in osteoradionecrosis (ORN). Symptoms of mandibular ORN include recurrent infections, inability to tolerate an oral diet, and pain, which may serve as the impetus to proceed with definitive surgical management via resection of the diseased bone and free bony reconstruction. While the viability of bony reconstruction for ORN has been well-investigated, longitudinal outcomes with a focus on patient function remain poorly studied. This study therefore seeks to characterize longitudinal and functional outcomes after fibula free flap reconstruction (FFF) for mandibular ORN following radiotherapy (XRT) treatment.

Methods: A retrospective chart review was performed from January 1st 2013 to January 1st 2022. All patients with mandibular ORN who underwent segmental mandibulectomy followed by FFF were included. Patients who had previous XRT treatment for an upper aerodigestive tract malignancy or received previous chemotherapy were included. Patients with bisphosphonate use were excluded. Demographics, comorbidities, complications, XRT and chemotherapy details, and long-term functional and nutritional outcomes were obtained.

Results: Among 33 patients included, there were 22 (67%) males and 11 females. Nineteen patients (57%) were ex-smokers with a mean 18.6 pack-year use; four (12%) were active smokers. Thirty-one patients (94%) had a history of oral cavity cancer and received adjuvant XRT, 17 of whom also underwent chemotherapy. The average XRT dose was 54.4 Gy with a mean of six years (0.44 to 20 years) from completion of XRT to ORN. Mean in-hospital post-operative course was 11 days. At discharge, ten (30%) patients had a tracheostomy with an average time to decannulation of 45 days. Of the 22 (67%) patients discharged with a gastrostomy tube, nine patients still had their gastrostomy tube at their most recent follow up visit, an average of 3 years (SD 1.9 years) post-gastrostomy tube placement. At discharge, six patients utilized a combination of enteral and oral nutrition; all

but one adopted oral nutrition by their six-month follow-up visit. At the one-year follow-up, four patients utilized a combination of enteral and oral nutrition; by their two-year follow up, three continued combination nutrition while the other switched to oral nutrition. The mean pre-operative DIGEST score was 1.15. Post-operatively, patients had an average DIGEST score of 2.47; at the one-year follow up, it was 2.80. The FFF remained viable for all patients, when seen at their most recent follow-up.

Conclusion: When focusing on long-term functional outcomes following fibula free flap reconstruction for ORN, initial analysis demonstrates persistent swallowing dysfunction. Further data analysis is warranted to characterize the impact of FFF for pain and infection rates in mandibular ORN.

B047: DRIVERS OF REDUCED SOCIAL COMMUNICATION AFTER LARYNGECTOMY IN TRACHEOESOPHAGEAL SPEAKERS - Barbara M Ebersole, MA, CCCSLP; Sheila Buoy, MPH; Kristofer Jennings, PhD; Miriam Lango, MD; Talia Schwartz, MS, CCCSLP; Carsyn Cunningham, MS, CCCSLP; Holly McMillon, MS, CCCMCD; Christine Porsche, MS, CCCSLP; Carly Barbon, PhD; Ryan P Goepfert, MD; Stephen Lai, MD; Katherine Hutcheson, PhD; University of Texas MD Anderson

Background: Total laryngectomy (TL) is a rare but functionally debilitating procedure, altering respiration and causing permanent aphonia. Tracheoesophageal puncture (TEP) consistently outperforms other methods of alaryngeal speech across a myriad of functional and quality of life (QOL) outcomes and is considered the gold standard of voice rehabilitation. Yet, there is little known about what factors influence communication amongst TEP speakers. Understanding these factors may facilitate patient selection for TEP, expectation setting during preoperative counseling, and strategies to optimize social functioning and QOL. This study aims to explore factors associated with patient-reported communication participation in TEP speakers after TL.

Methods: We conducted a sub-study analysis of prospectively collected data from the PATH Registry (NCT-05036330). Of the 130 patients with a TL who consented to PATH, 72 had a TEP and were included. Demographic, surgery, stomal supply, functional, and patient-reported outcomes (PRO), including selected items from the MD Anderson Symptom Inventory-Head and Neck Module [MDASI-HN], EQ-5D, and the Cough And Sputum Assessment [CASA-Q]) were analyzed for correlations with patient perceptions of their communication participation, as measured by the Communication Participation Item Bank (CPIB). Multiple linear regression models were performed.

Results: In this cohort of mostly older, male, longer-term TEP speakers, (mean age 67, 82% male, mean time since TEP 5.2 years) 79% reported abnormal communication participation (n=57, CPIB Tscore <57.5). The mean CPIB was 47.8, with moderately impaired communication participation most frequently reported (n=25, 35%, Tscore range 35-45) and the same proportion noting their condition interferes with being able to communicate with people they know. No stomal factors (e.g., attachment types, hands free valve usage) were associated with communication participation. Large negative mean differences in communication participation Tscores were seen in 6 domains, including persons who are Hispanic [-11.58, 95% CI (-2.7,-20.4), p=0.011], had anxiety/depression [-9.1, 95% CI (-4,-14.1) p=<0.000], had circumferential flap reconstruction [-13.4, 95% CI (-6.5,-20.3), p=<0.000], had non-fluent TE voice [-16.7, 95% CI (-32.9,-0.5) p=0.044], had

a displaced puncture [-9.62, 95% CI (-3.1,-16.2), p=0.005], or had a feeding tube [-10.43, 95% CI (-3.1,-23.9), p=0.128]. PRO measures associated with CPIB included CASA-Q phlegm interference with speech (p=<0.000), MDASI difficulty chew/swallowing (p<0.000), MDASI difficulty voice/speech (p<0.000), and the MDASI interference score (p<0.000). When controlling for the above clinically meaningful factors, only surgical factors of having a circumferential flap (p=0.035) and a displaced puncture (p=0.044); demographic factor of Hispanic ethnicity (p=0.013); and PRO measures of MDASI Interference (p=0.001) and CASA-Q phlegm interference with speech (p=0.007) were significantly associated with communication participation.

Conclusion: Impaired communication participation is prevalent among 79% of TEP speakers and interferes with participation in other aspects of daily life. Hispanic persons experienced disproportionately lower communication participation; this potential health disparity warrants further study. Patients with a circumferential flap or whose anatomy may necessitate a suboptimal puncture location may also be at higher risk for reduced social communication after TEP.

B048: DETERMINING PERFORMANCE INDICATORS FOR QUALITY DASHBOARD IN HEAD AND NECK SURGICAL ONCOLOGY SERVICE: A MIXED-METHODS ANALYSIS - Chibundum Ezenwukwa; Romaine F Johnson, MD, MPH, FACS; Andrew T Day, MD, MPH; Baran D Sumer, MD; University of Texas Southwestern Medical Center

Project Background: There is insufficient evidence to guide the design and development of a head and neck surgical oncology quality metric dashboard.

Objective: The aim of this study is to determine key performance indicators to measure quality in the head and neck surgical oncology service and establish the foundations for a departmental dashboard.

Methods: Semi-structured interviews were conducted to identify performance indicators to include in the dashboard. Stakeholders included 6 surgeons and 1 advanced practice provider with diverse emphases in head neck oncology, reconstruction, survivorship, quality, and administration. Participants drew on their own experiences to discuss the challenges regularly faced and which performance indicators they felt would best assess quality in the division. Interviews were video recorded and transcribed, coded and rapid thematic analysis was performed using Microsoft Excel by one member of the research team. Potential topical and specific performance indicators were identified. Stakeholders were surveyed and asked to identify the top three most important quality metrics from a list. Following this, comprehensive thematic analysis was performed by two members of the research team, and a final list of quality metric topics and specific performance indicators was identified. The research team then synthesized interview and survey data to identify the quality metrics deemed most important by stakeholders.

Results: Six providers underwent interviews and five responded to the survey. During interviews, providers identified 13 topics and 50 specific quality metrics; the research team derived 8 additional topics from the data. All topical and specific performance indicators were assigned to five overarching quality metric categories: perioperative (n=33), process (n=7), oncologic (n=4), function and quality of life (n=10), and other

survivorship (n=12). More providers identified potential quality metrics in the perioperative (n=6/6) and process (n=5/6) categories compared to the oncologic (n=2/6), function and quality of life (n=3/6), and other survivorship (n=3/6) categories. The most common topical quality metrics identified included postoperative: surgical complications (n=5/6), hemorrhage (n=5/6), wound healing complications (n=4/6), infection (n=3/6), medical complications (n=4/6); swallowing (n=3/6), and speech (n=3/6). The most common specific quality metric identified was free flap failure (n=4/6). After rapid thematic analysis, five providers identified their 3 most important potential quality metrics from a list of 22 topical and specific quality metrics. Two non-responders designated 2 and 4 top potential quality metrics during their interviews, respectively. The following topical or specific quality metrics were designated most important: postoperative hemorrhage (n=4/6), overall survival (n=2) or overall mortality (n=2; n=4/6), time from diagnosis to treatment (n=3/6), and overall wound healing complications (n=1), including free flap failure (n=1; n=2/6).

Conclusions: This study identified potential key performance indicators to measure quality in head and neck cancer. These measures represent the values of the department, the common challenges faced, and the elements necessary to provide quality care to these patients. Using these data, we plan to re-engage stakeholders and obtain additional feedback to guide the specific design and development of a quality dashboard for the department.

B049: APPLYING MACHINE LEARNING TO PREDICT SWALLOW OUTCOMES FOLLOWING A TOTAL LARYNGECTOMY - Aseem Jain, MSE[1]; Sarah Adams, BSc[1]; Ameen Amanian, MD, MSE[2]; Nimesh Nagururu, BS[3]; Francis Creighton, MD[3]; Brian Cervenka, MD[4]; [1]University of Cincinnati; [2]University of British Columbia; [3]Johns Hopkins University; [4]University of Colorado

Introduction: Total laryngectomy (TL) remains one of the primary treatment modalities for managing advanced laryngeal carcinoma. While the primary aim of TL is oncologic cure, preserving or improving swallow function is critical for the patient's quality of life. Previous literature has explored how various patient characteristics and surgical techniques impact post operative swallowing function. Our aim in this study is to expand upon their work and leverage machine learning (ML) methods to develop a novel predictive model for swallowing function following TL. To our knowledge, this application of ML has not been studied before in this patient subset.

Methods: A single institution database of 235 patients who had undergone TL was created that included patient demographic, surgical, postoperative, and swallow function data. One-year postoperative swallow function data was evaluated with the FOIS Scoring system. The FOIS score was dichotomized into requiring enteral nutrition (FOIS 1-3) and total oral diet (FOIS 4-7). Univariate analysis using chi-squared tests was performed for all study variables. One-year swallowing function was then predicted using various ML models including traditional methods such as multinomial logistic regression and newer methods, including support vector machine, random forest, and boosted classification models. Overall accuracy, sensitivity (SN), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), and area under the receiver operator curve (AUC) were used to evaluate model performance.

Results: A total of 171 patients or 72.7% of the cohort achieved oral diet; other study and surgical characteristics are shown in Tables 1 and 2 along with the univariate analysis. Patient and surgical variables associated with poor FOIS scores included prior chemoradiation (p=0.01), pre-operative dysphagia (p=0.02), presence of a post-operative fistula within 30 days (p<0.01), use of a myocutaneous flap (p=0.03), total pharyngectomy (p<0.01), and non-primary closure (p=0.02). Primary reconstruction with an overlay was associated with improved FOIS scores (p=0.02). As shown in Table 3, the boosted ML classification model outperformed other models for predicting a positive (FOIS>3) swallow outcome. The boosted model identified patients achieving an oral diet with 77.4% accuracy (SN=0.93, SP=0.37, PPV=0.80, NPV=0.67, AUC = 0.71), exceeding traditional multinomial logistic regression performance. Based on the variable weights from the boosted model shown in Figure 1, the three most important predictors of swallowing function were the presence of postoperative fistula, duration of postoperative fistula, and age. Other variables that significantly impacted the model were use of primary closure, exposure to prior radiation, and number of esophageal dilations.

Conclusion: ML enables the creation of accurate models to predict swallow outcomes for patients undergoing TL. Generally, ML models applied were highly sensitive but not specific, suggesting models could accurately rule out patients that did not achieve a positive swallow outcome. The presence and duration of a long-term fistula were the most critical variables for this model. This model has the potential to be clinically applied for improved patient counseling and post-operative management.

	Achieved Oral Diet (FOIS 4-7)	Percent/P-value
Total (n=234)	171	72.7%
Gender		
Males (74.0%)	130	74.7% (.25)
Females (26.0%)	41	67.2% (.26)
Diabetes (16.6%)	31	79.5% (.30)
Smoking (92.3%)	159	73.3% (.54)
Prior Treatment*		
No prior treatment (36.5.3%)	64	74.4% (.66)
Radiation (30.2%)	57	80.2% (.09)
Chemoradiation (30.2%)	44	**62.0% (.01)**
Surgery (10.2%)	20	83.3% (.21)
Pre-operative Dysphagia (40.9%)	62	**64.6(.02)**
Fistula within 30 days (28.5%)	32	**47.7(<.01)**

Table 1: Total Laryngectomy Patient Characteristics Summary

	Achieved Oral Diet (FOIS 4-7)	Percent/P-value
Total	171	72.7
Closure Type		
Primary Closure only (38.6%)	58	74.4 (.69)
Anterolateral (ALT) (18.0%)	34	82.4(.11)
Radial Free Forearm (RFFF) (10.6%)	15	60.0 (.13)
Latissimus (LAT) (21.2%)	42	72.4 (.95)
Pectoralis (PEC) (6.9%)	12	66.7 (.54)
Other (3.2%)	10	66.7 (.58)
Free Flap type		
Muscle (29.6%)	36	80.0 (.23)
Cutaneous (21.2%)	47	73.4 (.88)
Myocutaneous (15.9%)	29	**60.4 (.03)**
Pharyngectomy		
No Pharyngectomy (72.0%)	129	75.4 (.13)
Partial Pharyngectomy (18.0%)	34	79.1 (.30)
Total Pharyngectomy (10%)	8	**38.1 (<.01)**
Primary Closure w/ Overlay (40.7%)	79	**80.6 (.02)**
Non-Primary Closure (20.6%)	34	**57.6 (.02)**
Base of Tongue Resection (16.9%)	26	65.0 (.23)

Table 2: Total Laryngectomy Operative Technique Summary

	Logistic Regression	Support Vector Machine	Random Forest Classifier	Boosted Classifier
Overall Accuracy	74.00%	73.60%	71.10%	**77.40%**
Sensitivity	**94.70%**	93.60%	85.30%	93.00%
Specificity	18.80%	20.30%	32.80%	**37.5%**
Positive Predictive Value (PPV)	75.70%	75.80%	77.10%	**80.00%**
Negative Predictive Value (NPV)	57.10%	54.20%	45.70%	**66.90%**
Area under ROC Curve (AUC)	0.70	0.69	0.65	**0.71**

Table 3: Summary of various machine learning model performance for predicting swallow function after a total laryngectomy

Figure 1: Top six features important for predicting swallow function after total laryngectomy based on Boosted Classifier model

B050: IMPACT OF INTERNAL LYMPHEDEMA ON DYSPHAGIA MANAGEMENT OUTCOMES IN HEAD AND NECK CANCER (HNC) SURVIVORS: A RETROSPECTIVE REVIEW - Akhil Katragadda, BS; Andrew Peachman, BS; Mohammad Bilal Alsavaf, MD; Fahad Rind, MD; Mayuri Srikanth, MD; Jack Birkenbeuel, MD, MBA; Zachary Wykoff, BS; Veena Kallambettu, MA, CCCSLP; Jacqueline Tardif, MA, CCCSLP; Tulsi Patel, CCCSLP; Amy Compston, PT, DPT, CLTLANA; Apoorva T Ramaswamy, MD; The Ohio State University Wexner Medical Center

Introduction: Combined advanced treatment modalities for head and neck cancer (HNC) often lead to multiple morbidities including dysphagia and internal lymphedema (IL). Dysphagia can have a significant impact on patient health and quality of life through issues ranging from malnutrition to aspiration pneumonia. However, little is known about the association between internal lymphedema (IL) post-HNC treatment and dysphagia treatment. The objective of this study is to evaluate any predictors of internal lymphedema in HNC survivors with dysphagia and determine how the presence of internal lymphedema impacts esophageal dilation outcomes.

Methods: A retrospective analysis of 48 HNC patients with dysphagia who underwent esophageal balloon dilation (BD) at a tertiary medical center between 2020-2022 was conducted. Internal lymphedema severity was determined at eight anatomic sites on Fiberoptic Endoscopic Evaluation of Swallowing (FEES) recordings based on the Modified Patterson Lymphedema Scale and rated by two independent reviewers trained by a speech-language pathologist. IL was assessed for maximum severity across all sites and total number of affected sites as reported in previous literature. Balloon dilation surgery outcomes were assessed with Eating Assessment Tool-10 (EAT-10) scores and incidence of complications.

Results: Of the 48 patients reviewed, 13 (27.1%) experienced severe IL, 25 (52.1%) experienced moderate IL, 7 (14.6%) experienced mild IL, and 3 (6.3%) experienced no IL as a maximum level of IL at any site. No patients had IL at only 1 site. The oropharynx was the most common tumor site (n=27, 56.3%) followed by the oral cavity (n=8, 16.7%). BMI was negatively correlated with the maximum severity of IL at any site (p=0.029) and the number of affected sites (p=0.016). Number of affected sites significantly correlated with presence of xerostomia (p=0.013). For both maximum severity of IL and number of affected sites, no significant associations were noted in age, sex, tumor site, tumor stage, HNC treatment modality, deep connective tissue fibrosis, preoperative EAT-10 score, EAT-10 score improvement, number of dilation surgeries, and extent of dilation procedure. There was a significant difference between number of dilation surgeries and severity of IL at the pyriform sinuses (p=0.035). There were no significant differences in balloon dilation postoperative complications between patients with no to mild IL and moderate to severe IL.

Conclusion: Management of dysphagia in HNC survivors is important for long-term quality of life. Our findings suggest that HNC survivors with dysphagia are more likely to have concurrent development of internal lymphedema than the general HNC survivor population. Although maximum severity of IL at any site and number of affected sites were not associated with EAT-10 score improvements, there were significant differences noted in number of balloon dilation surgeries based on severity of IL at the pyriform sinuses. Thus, our data suggests that attention should be paid to evaluation of IL in HNC survivors with dysphagia and future studies should be completed to better understand these relationships.

B051: THEMATIC ANALYSIS OF HEAD AND NECK CANCER SURVIVOR SMALL GROUPS ON OTOTOXICITY EFFECTS ON QUALITY OF LIFE AND BARRIERS TO OTOTOXICITY MONITORING - David S Lee, MD[1]; Lauren Mueller, BA[1]; Susan K Wong, BA[1]; Emma Y Travis, BS[1]; Donna B Jeffe, PhD[1]; Angela L Mazul, PhD, MPH[2]; Kate McClannahan, AuD, PhD[1]; Judith E Lieu, MD, MSPH[1]; [1]Washington University in St. Louis; [2]University of Pittsburgh

Importance: Cisplatin-based chemoradiation therapy is commonly used to treat patients with head and neck cancer. Although it often causes irreversible dose-dependent ototoxicity, less than 10% of patients seek ototoxicity monitoring after 6 months of completing treatment. Understanding how treatment-related ototoxicity affects quality of life among cancer survivors and identifying barriers to ototoxicity monitoring remain open questions. Research on these topics enable the development and implementation of interventions to improve ototoxicity monitoring programs for cancer survivors and improve quality of life in survivorship.

Objective: To identify (1) quality-of-life domains that are affected by treatment-related ototoxicity among cancer patients and (2) barriers to ototoxicity monitoring adherence among cancer patients with treatment-related ototoxicity.

Design, Participants, and Setting: A qualitative study was performed using semi-structured small group sessions conducted from March 2023 to September 2023 with cancer survivors treated with cisplatin-based chemoradiation therapy at a National Cancer Institute-designated comprehensive cancer center. Questions focused on the impact of treatment-related side effects on participants' quality of life and perceived barriers to ototoxicity monitoring. Sessions were led by a doctoral candidate in audiology with no prior contact with participants. Verbatim transcripts of recorded sessions were distributed to four independent reviewers. Each reviewer performed inductive thematic analysis. Through discussions during coding of the narratives, the reviewers reached consensus regarding themes salient to quality-of-life domains affected by ototoxicity and barriers to ototoxicity monitoring.
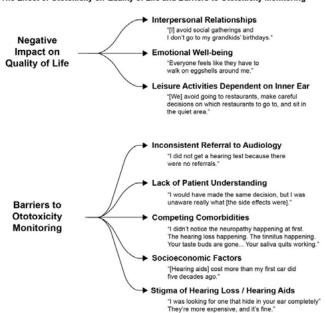
Main Outcomes and Measures: Participant perspectives on the effects of ototoxicity on quality of life and barriers to ototoxicity monitoring of head and neck cancer patients treated with cisplatin-based chemoradiation therapy.

Results: Seven small group sessions ranging from one to four participants were conducted on 18 total participants (median age = 58 [range 45-67]; 13 [72%] male; 16 [89%] white). Themes regarding the effects of ototoxicity on quality of life included negative impact on: 1) interpersonal relationships; 2) emotional well-being; and 3) leisure activities dependent on the inner ear. Themes identified as barriers to ototoxicity monitoring included: 4) inconsistent referral to audiology, 5) lack of patient understanding, 6) competing comorbidities, 7) socioeconomic factors, and 8) stigma of hearing loss/hearing aids.

Conclusions and Relevance: The adverse effects of treatment-related ototoxicity have long-term implications for reducing cancer patients' quality of life. Many participants desired audiology follow-up but lacked understanding of

both ototoxic side effects and guidance from healthcare providers regarding ototoxicity monitoring. Efforts to educate patients before, during and after cancer treatment and provide appropriate referrals may decrease undiagnosed and untreated ototoxicity among cancer survivors. Future research will focus on using these data to develop a new patient-reported outcome measure to evaluate treatment-induced ototoxicity on quality of life and whether an ototoxicity monitoring protocol embedded within head and neck cancer survivorship clinic will improve hearing-related quality of life.

Inductive Thematic Analysis of Head and Neck Cancer Survivor Small Groups: The Effect of Ototoxicity on Quality of Life and Barriers to Ototoxicity Monitoring

B052: DISPARITIES IN BASELINE PATIENT REPORTED QUALITY OF LIFE AND AREA LEVEL DEPRIVATION AMONG PATIENTS WITH HEAD AND NECK CANCER - Kyle Leonard, MD[1]; Samantha Tam, MD[1]; Amy Williams, PhD[1]; Courtney Rose[2]; Kimberly A Oslin, MD[1]; Veronica Bernacchi, PhD, RN[3]; Steven S Chang, MD[1]; Suhael Momin, MD[1]; Farzan Siddiqui, MD, PhD[4]; Vivian F Wu, MD, MPH[1]; Eric Adjei Boakye, PhD[1]; [1]Henry Ford Health System - Department of Otolaryngology-Head & Neck Surgery; [2]Henry Ford Health System - Department of Public Health Sciences; [3]Michigan State University; [4]Henry Ford Cancer Institute - Department of Radiation Oncology

Introduction: Low socioeconomic status is a significant predictor of poor outcomes, such as mortality and quality of life, for post-treatment head and neck cancer (HNC) patients. HNC patients with low socioeconomic status often live in resource-deprived communities with systemic disinvestment, which contributes to poor quality of life prior to cancer treatment. We hypothesize that HNC patients with low socioeconomic status have lower pre- treatment quality of life compared to HNC patients with high socioeconomic status. To test our hypothesis, we examined the association between area deprivation using the Area Deprivation Index (ADI) and pre-treatment quality of life using the Functional Assessment of Cancer Therapy – Head and Neck (FACT-HN) in patients with HNC.

Methods: This is a retrospective cohort study of patients undergoing treatment for HNC between November 2015 and September 2022. The FACT-HN Version 4 was administered to patients as part of routine pretreatment evaluation with psych-oncology prior undergoing treatment for HNC. The FACT-HN is a validated patient reported outcome measure used to assess the quality of life and functional status of patients with HNC based on patient report. The FACT-HN subscales of social/familial, emotional, functional, and physical well-being were used in this study as outcome variables. The ADI was created by the U.S. Health Resources and Services Administration to stratify socioeconomic disparity based on census data. Due to majority of patients residing in the state where the institution is located, this study used the state ADI. ADI was categorized into quintiles with the lowest quintile representing higher socioeconomic status and higher quintile representing lower socioeconomic status. Kruskal-Wallis tests were used to examine the association between ADI and the four FACT-HN subscales.

Results: A total of 376 patients were included in the study of whom 18.4% resided in areas in the first quintile, 21.8% in second quintile, 20.2% in third quintile, 19.7% in fourth quintile, and 20.0% in fifth quintile. The median physical well-being was (24.0, IQR=20.0-27.0), social score was (24.0, IQR=20.0-27.0), emotional was (18.0, IQR=15.0-21.0), and functional was (20.0, IQR=13.0-25.0). Patients who resided in areas in the fifth quintile (i.e., higher deprivation) reported worse physical well-being than those in the first quintile (median=23.0 compared to 25.0; P=0.0046). Similarly, patients who resided in areas in the fifth quintile reported worse functional well-being than those in the first quintile (median=18.0 compared to 21.0; P=0.0259). Finally, patients who resided in areas with higher deprivation reported worse social well-being than those with lower deprivation (median=23.0 compared to 26.0; P=0.0214).

Conclusions: These results suggest that patients with HNC residing in areas with higher levels of deprivation have a lower pre-treatment quality of life in physical, functional, and social domains than those residing in areas with less deprivation. This study highlights pre-treatment disparities between HNC patients with high and low socioeconomic status. These findings can be used to tailor clinical assessment and treatment planning for HNC patients with low socioeconomic status.

B054: IMPLICATIONS OF NON-SURGICAL FACTORS ASSOCIATED WITH INCREASED LENGTH OF HOSPITAL STAY IN HEAD AND NECK MICROVASCULAR RECONSTRUCTIVE PATIENTS - Lavanya Nagappan, MD; Marie-Ange Munyemana, BA, MSCl; Evan Snyder, BA; Sherrie Wang, BS; Brian P Swendseid, MD; Cooper University Health Care

Patients undergoing head and neck microvascular surgery can have particularly challenging post-operative needs, which may prolong hospitalization. We sought to understand the non-surgical determinants resulting in prolonged length of hospital stay (LOS) in the head and neck microvascular patients, in order to optimize postoperative care and resource allocation. The primary outcome of this study was 'prolonged LOS', defined as additional LOS (>1 day) after the patient was cleared for discharge from a surgical standpoint. A total of 62 patients from 2018 to 2023 were included in the analysis of this single-center retrospective cohort study; 17 female (27.4%) and 45 male (72.6%). 54 were English-speakers (87.1%), and the mean [SD] age at time of surgery was 62.29 [10.7] years. The average LOS of the entire cohort was 2.1 [3.4] days with a median of 1 day. 27

patients (43.5%) experienced prolonged LOS with an average of 4.33 [4.2] days and a median of 3 days. Lack of bed availability at rehab/skilled nursing facilities (SNF) (Odds Ratio (*OR*): 2.591 [95% CI: 1.867-3.595, *p* = .008), facility prohibiting tracheostomy and feeding tube requirements (*OR*: 2.522 [1.836-3.464], *p* = .019), medical comorbidities requiring additional treatment (*OR*: 2.121 [1.308-3.441], *p* = .039), and feeding tube issues (*OR*: 2.245 [1.428-3.529], *p* = .017) were significant predictors for prolonged LOS on univariate analysis. Delayed discharge was not associated with home supply delivery (*p* = .229), patient preference for rehab/SNF (*p* = .086), and transportation issues (*p* = .251). The multivariable model did not yield any statistically significant predictors. At an average cost of $4000 per day for step-down beds, the cumulative costs to a hospital system due to prolonged length of stay secondary to nonsurgical problems is substantial. Our hope is that, by recognizing these barriers and providing data about their impact, we can catalyze the development of prospective interventions that can be used to predict and minimize these delays and costs. This can contribute to improved patient outcomes, reduced healthcare costs, and enhanced efficiency in head and neck cancer management.

B055: SOCIOECONOMIC FACTORS IMPACTING EQUITY IN COMPLETION OF PATIENT REPORTED OUTCOME MEASURES AMONG PATIENTS WITH HEAD AND NECK CANCER - Oghenefejiro Okifo[1]; Eric Adjei Boakye[1]; Liam Hart[1]; Carl Wilson[1]; Kelly Hirko[2]; Nada Al-Antary[1]; Steven Chang[1]; Farrah Elsiss[1]; Michael Ryan[1]; Theresa Zatirka[1]; Samantha Tam[1]; [1]Henry Ford Health; [2]Michigan State University

Introduction: Routine monitoring of patient-reported outcome measures (PROMs) has been demonstrated to improve quality of life, decrease unplanned health care utilization, and improve overall survival. However, patients may face socioeconomic barriers when completing these instruments, potentially resulting in missed opportunities to improve outcomes in these already disadvantaged populations. Previous studies demonstrated that patients with orthopedic spinal pathologies completing PROMs were overwhelmingly White, non-Hispanic, and more likely to reside in wealthier communities. Meanwhile, other studies reported that patients with low health literacy, non-English speakers, and patients with learning disabilities may struggle to complete PROMs. The aim of this study was to investigate socioeconomic factors influencing PROMs completion among patients with head and neck cancer.

Methods: All patients with a prior history of head and neck cancer and an outpatient oncology visit were eligible for inclusion in this retrospective cohort study. In this routine implementation of PROMs, patients were offered PROMs one week prior to their appointment via their patient-facing portal or at the time of the visit on a tablet. Four domains of the National Institute of Health's Patient-Reported Outcome Measures Information System (PROMIS) computer adaptive instruments were used: pain interference, physical function, fatigue, and depression. Census tract based socioeconomic status indicators (median household income, proportion of residents having a high school education or higher) were used to define Area Deprivation Index (ADI). ADI is a composite measurement of socioeconomic disparity developed by the U.S. Health Resources and Services Administration. Patient-reported social determinants of health (SDoH) was collected using a modified Health Leads screening questionnaire during clinic visits. Chi-Square tests were used to investigate the association of socioeconomic factors and PROMs completion.

Results: A total of 226 patients were included in the analysis. Of these patients, 45.9% completed PROMs and 25% completed the SDoH screening. The average age was 65 (SD=13) years, 64.9% were male, 73.1% were White, 54.2% were married, 4.3% indicated they had transportation barriers, and 32.0% indicated their physical or mental health prevents them from doing things they need/want to do. There was a significant association between ADI and PROMs completion. The proportion of patients residing in areas with lower ADI (i.e., lower deprivation) had higher completion rate than those residing in higher ADI areas (i.e., higher deprivation; 54.0% versus 27.3%, P=0.0001). However, there was no significant association between the SDoH and PROMs completion. White patients also had higher PROMs completion compared to non-White patients (48.2% versus 29.0%, P=0.0111). Finally, patients who were married (52.4%) had higher proportion of PROMs completion compared to those who were divorced/separated/widowed (30.2%) or single (32.1%, P=0.0100).

Conclusion: This study demonstrated that some socioeconomic factors such as residence in an area with higher levels of deprivation, non-White race, and single marital status were associated with lower rates of PROMs completion. Understanding needs and developing targeted interventions to increase PROMs completion in vulnerable populations is necessary to ensure equitable distribution of the potential benefits of PROMs.

B056: CORRELATIONS BETWEEN THE DEVELOPMENT OF EXTERNAL AND INTERNAL LYMPHEDEMA IN HEAD AND NECK CANCER SURVIVORS WITH DYSPHAGIA - Akhil Katragadda*, BS; Andrew T Peachman*, BS; Mohammad Bilal Alsavaf, MD; Andrew Paik, BS; Mayuri Srikanth, BS; Jack Birkenbeuel, MD; Zachary Wykoff, BS; Veena Kallambettu, CCCSLP, MA; Jacqueline Tardif, CCCSLP; Tulsi Patel, CCCSLP; Amy Compston, PT, DPT, CLTLANA; Apoorva T Ramaswamy, MD; The Ohio State University Wexner Medical Center

Introduction: Internal lymphedema and external lymphedema are common complications seen in head and neck cancer (HNC) survivors who were treated with a combination of therapies that include surgery with or without chemoradiation. HNC survivors with dysphagia are a particularly unhealthy patient population that commonly experiences many comorbidities and are at risk for worse long-term outcomes compared to the general HNC survivor population. A previous study has shown that External Lymphedema (EL) has an impact on the management of dysphagia in HNC survivors. This study aims to explore patients with Internal Lymphedema (IL) and whether there is a correlation between IL and EL. Although common compilations, there are few studies that assess the prevalence of both IL and EL in HNC survivors with dysphagia.

Methodology: A retrospective analysis was conducted on 48 HNC survivors over the age of 18 who underwent dysphagia treatment at a single institution between 2020-2022. EL was classified as stage I, II, and III by a physical therapist utilizing the Foldi scale. IL was classified as mild, moderate, or severe by the presence of lymphedema at 8 anatomic sites based on the modified Patterson Lymphedema Scale. The rating for IL was determined based on the ratings of two independent, trained individuals. IL was assessed for maximum severity across all sites and the total number of affected sites as reported in previous literature.

Results: The demographics of this study were predominantly white (95.8%), male (77.1%), and with a mean age of 66.7. The mean BMI in this study was 26.2. Of the 48 patients in this study, 37 (77.1%) presented with EL while the maximum IL score at any site was found to be 7 (14.6%) scored mild, 25 (52.1%) scored moderate, and 13 (27.1%) scored severe. There were 3 (6.3%) patients who had no IL. On average, patients had 6 sites with some clinical evidence of IL. 31 (64.6%) developed both EL and had at least one site with moderate or severe IL. Only 2 (4.2%) patients were found to have neither EL nor IL. BMI was found to be negatively correlated with both the severity of IL at the maximum site (p=0.029) and the number of affected sites (p=0.016). EL was not found to have any correlation with BMI. The presence of EL was not found to be significantly correlated with the number of sites affected with IL. There was no significant association between the severity of EL and the maximum severity of IL at any site. Further analysis found that the presence of xerostomia (p=0.013) was significantly correlated with the number of sites affected with IL.

Conclusion: A majority of HNC patients with dysphagia and IL have concurrent EL. Clinicians should consider the presence of xerostomia in a patient with widespread IL. These findings should inform clinicians regarding the clinical management of comorbidities associated with HNC radiation therapy. This study highlights the need for prospective studies to look at IL and its relationship to complications in HNC survivors with dysphagia.

B057: ASSOCIATIONS BETWEEN SUBSTANCE USE, QUALITY OF LIFE, AND PAIN AMONG VETERAN SURVIVORS OF HEAD AND NECK CANCER - <u>Teyhana Rounsavill, BA</u>[1]; Felipe Rubim, MA[2]; Elizabeth R Hooker, MS, MPH[2]; Kara Winchell, MA[2]; Christopher G Slatore, MS, MD[2]; Benjamin J Morasco, PhD[2]; Shannon M Nugent, PhD[2]; [1]School of Medicine, Oregon Health and Science University, Portland, OR; [2]Center to Improve Veteran Involvement in Care, VA Portland Health Care System, Portland, OR

Objective: Head and neck cancer (HNC) survivors often suffer from undertreated pain. It is unclear if self-administered substances influence HNC survivors' pain or quality of life (QOL). We examined the association of self-reported substance use with pain interference, pain severity, and quality of life (QOL) among Veteran HNC survivors. We hypothesized that substance use would be positively associated with pain interference and severity while inversely associated with QOL.

Methods: We recruited Veterans from a national sample who were at least two years post clinically confirmed HNC diagnosis with documented chronic pain, defined as at least three Numeric Rating Scale (NRS) pain scores of four or more in their medical record. All participants completed a cross-sectional survey with measures of alcohol and substance use, quality of life, pain intensity and interference, and pain self-efficacy. Using linear regression models, controlling for relevant clinical and sociodemographic variables, we tested the associations between nicotine, alcohol, and cannabis use and four subscales of a QOL measure, pain interference, and pain severity. We examined pain self-efficacy as an interaction.

Results: We included 191 veterans, the majority aged 66 years or older (58.7%), male identifying (97.4%) and White/Caucasian (82.7%). One-third of participants had moderate (29.8%) or high (4.7%) nicotine use, one-quarter had moderate (21.5%) or high (2.7%) alcohol use, and less than one-third had moderate

(26.2%) or high (3.7%) cannabis use. Multivariate analysis found that Veterans with high alcohol use had a 25-point lower QOL communication score (39.9 (95% CI: 13.5, 66.3); 64.6 (59.1, 70.0); p= 0.07) and QOL eating score (38.4 (95% CI: 17.6, 59.2); 60.9 (95% CI: 56.7, 65.2); p= 0.03) compared to no/low alcohol use. No statistical significance was found between any substance use levels and average pain severity or interference scores in our multivariable analyses; however, those with high nicotine use were associated with clinically significant higher pain scores compared to the no/low use group (Interference: 5.3 (95% CI: 3.4, 7.2); 4.3 (95% CI: 3.8, 4.8); Severity: 6.1 (4.3, 7.8); 4.7 (95% CI: 4.3, 5.2)). In interaction models examining whether the association between substance use and pain differed by self-efficacy for pain management, Veterans with no/low nicotine use and low self-efficacy had clinically significant higher pain interference scores compared to those with high self-efficacy (5.8 (95% CI: 5.1, 6.6); 2.4 (95% CI: 1.6, 3.2), indicating that high self-efficacy is associated with decreased pain.

Conclusion: HNC survivors with high alcohol use had significantly lower eating and communication QOL. Those who had high nicotine use and lower self-efficacy had clinically significant higher pain severity. Programs focused on alcohol and nicotine cessation and improving pain management coping self-efficacy should be included in post-treatment plans to address factors affecting QOL and pain.

B058: CIGARETTES AND CENTS: EXPLORING TOBACCO DEPENDENCE AND CESSATION AS A MODIFIABLE RISK FACTOR FOR FINANCIAL TOXICITY IN PATIENTS WITH CANCER - <u>Nadia L Samaha</u>[1]; Stefany Lazieh, BS[2]; Brennan McMichael, MD, MBA[1]; Nicholas Scott-Wittenborn, MD[1]; Maria Armache, MD[1]; Carole Fakhry, MD, MPH[1]; Leila J Mady, MD, PhD, MPH[1]; [1]Department of Otolaryngology-Head and Neck Surgery, Johns Hopkins University School of Medicine; [2]Johns Hopkins University School of Medicine

Background: Tobacco use is the leading preventable cause and modifiable risk factor associated with head and neck cancer (HNC). Beyond the direct health hazards associated with its use, tobacco expenditures may supplant spending on health-promoting behaviors and have been associated with decreased spending on housing, food and clothing, and increased food insecurity. As such, tobacco use and associated spending may exacerbate financial toxicity (FT) related to cancer treatment, with implications on oncologic outcomes and mortality. However, no studies have investigated the relationship of tobacco use and FT in patients with HNC. In this study, we systematically reviewed the literature on the financial burden of tobacco use and cessation in smoking-related cancers.

Methods: A systematic review was performed according to PRISMA guidelines. Multiple databases were queried using the terms "tobacco dependence", "smoking cessation", "financial toxicity", "cancer" and all relevant synonyms. Peer-reviewed studies were included if they measured any financial cost related to tobacco use or cessation in populations with smoking-related cancers, including but not limited to lung and HNC. Citations were excluded if they were a review, abstract, editorial, or in a foreign language. All costs were converted to U.S. Dollars based on current exchange rates, and pooled descriptive statistics were obtained for similar measured outcomes.

Results: Among 518 identified articles, 22 met inclusion criteria, representing 14 countries across 5 continents [study types: economic model (n=13), retrospective cohort (n=6), prospective randomized (n=2), randomized control trial (n=1)]. Although most studies included patients who smoke with any type of cancer, 13.6% (n=3) focused on HNC and 9.0% (n=2) on lung cancer. Regarding tobacco use, outcomes were direct and indirect medical costs for treating smoking-attributable cancers, hospital expenditures, and additional treatment costs in cancer patients who continued smoking. For tobacco cessation, outcomes were healthcare cost savings, cessation intervention cost-effectiveness, and incremental cost-effectiveness ratio from cessation (ICER) for quality-adjusted life years (QALY) gained. Annual direct costs for treating smoking-related cancers ranged between $5,074–52,106/patient and $3.8 million–23.8 billion/country. Annual indirect costs amounted to $43,224/individual. Patients who continued smoking after their cancer diagnosis incurred an average of $7,507 (range $4,335–10,678) in total additional medical costs. One country's public health burden from a single hospitalization for smoking-associated oral cancer was estimated to reach $16.4 million ($32,817/patient) by 2026. The cost of cessation interventions ranged between $4–25,329/participant, the average cost/quit was $6,277 (range $2,688–9,866), and the average ICER (Δcost/ΔQALY) was $14,680 (range $3,903–52,067). Healthcare cost savings up to $470 million/year were realized in some countries due to smoking cessation. Providing financial incentives for smoking cessation in patients with HNC proved unsuccessful.

Conclusion: Tobacco use has a substantial financial impact on patients, health systems, and governments. Current cessation efforts vary dramatically by cost and design, yet they appear to be cost-effective both at the individual and societal level. Further work is needed to elucidate the role of tobacco spending on FT in cancer care to develop tobacco cessation interventions which reduce both the health and financial harms of tobacco dependence.

B059: PROVIDER PERSPECTIVES AND ACCESS TO PALLIATIVE CARE FOR PATIENTS WITH HEAD AND NECK CANCER: AN AMERICAN HEAD AND NECK SOCIETY (AHNS) SURVEY - Shreya Sriram, BS[1]; Akua Owusu-Boahene[1]; Anna Gersten, MD[2]; Christine G Gourin, MD, MPH[3]; [1]Johns Hopkins Department of Otolaryngology-Head and Neck Surgery; [2]Johns Hopkins Department of Medicine; [3]Johns Hopkins Department of Medicine and Department of Otolaryngology-Head and Neck Surgery

Objective: To explore provider perspectives about palliative care (PC) in head and neck cancer (HNCA) care.

Methods: A 25-question electronic survey was disseminated to the membership of the American Head and Neck Society (AHNS) from April 10, 2023 through June 13, 2023.

Results: The response rate was 5% (82/1,778) with 9% (76/848) of active fellows responding. The majority of respondents reported comfort assessing patient readiness for and acceptance of PC (94%), knowledge that PC and hospice are not synonymous (88%), and utilization of PC services (84%). Respondents were most likely to refer to PC at symptomatic disease progression (52%) or terminal diagnosis (29%) rather than at initial diagnosis (17%). Participants less likely to refer to PC were less likely to refer at symptomatic progression (8% vs 39%, P=0.0006) and less likely to agree that it is important to address advance directives in the outpatient HNCA clinic (62% vs 87%, P=0.0406). There was no difference in PC utilization rates by years in practice. Symptoms were monitored by 94% of respondents; however, only 29% utilized standardized symptom burden questionnaires and only 24% assessed quality of life (QOL), with great variation in questionnaires used. Discordance was identified between self-reported and actual access to local inpatient and outpatient PC services.

Conclusion: Most HNCA providers utilize PC and are comfortable discussing PC. Barriers to PC identified include a lack of established optimal timing for PC referral, perceived lack of local access to PC, and a lack of uniform standardized assessment of symptom burden and QOL.

B060: SAFETY OF HYPERBARIC OXYGEN THERAPY USE FOR RADIATION-INDUCED NECROSIS IN HEAD AND NECK CANCER PATIENTS: A SYSTEMIC REVIEW AND META-ANALYSIS - Wilhelmina Tan, MS[1]; Delaney E.S. Clark, BS[1]; Orly Coblens, MD[2]; Viran Ranasinghe, MD[2]; Sepehr Shabani, MD[2]; [1]UTMB John Sealy School of Medicine; [2]UTMB Department of Otolaryngology

Background: Hyperbaric oxygen therapy (HBOT) utilizes a pressurized chamber to delivery oxygen to patients. It has been a recognized adjuvant therapy options for tissue necrosis, owning to its ability to hyperxoygenate tissues, stimulate angiogenesis, improve leukocyte function, promote fibroblast proliferation, enhance collagen synthesis, and increase osteoclast activities, therefore promoting healing. However, when tissue necrosis results from radiation therapy–which is commonly employed in head and neck cancer treatment regimen–the pro-angiogenic and tissue growth effect have raised concerns, and questions are casted on its safety on being used in head and neck cancer patients. Over the years, randomized controlled trials or retrospective cohort studies assessing HBOT's safety and treatment outcomes in oncology patients have yielded conflicting results, often attributed to the limited sample sizes of individual studies.

Objectives: The systematic review and meta-analysis sought to evaluate the safety and efficacy of HBOT, emphasizing its influence on malignancy recurrence rates post-radiation therapy in head and neck cancer patients.

Study Design: Systemic review/meta-analysis

Methods: In October 2023, we searched for articles published in English between January 2000 and October 2023 using PubMed and Ovid MEDLINE. Two independent reviewers assessed the retrieved articles, excluding non-human studies, case reports, unpublished or terminated studies, abstracts, and review articles. Data from included studies were extracted and analyzed.

Results: Ten randomized controlled trials and retrospective cohort studies were included, comprising 314 patients (243 in the HBOT group and 71 in the non-HBOT group). HBOT sessions ranged from 13 to 62 maximum. Follow-up duration spanned from 12 months to five years. HBOT exhibited a marginal reduction in malignancy recurrence (relative risk 0.95, p = 0.84, number needed to treat = 88), with a chi-square value of 0.04 and a critical value of 3.841 at a 95% confidence level.

Conclusion: Although HBO showed a slightly decreased risk of malignancy recurrence in head and neck cancer patients, the difference was not statistically significant. However, there is also no substantial evidence that HBOT increases the recurrence risk of head and neck cancer comparing to patients receiving radiation therapy without HBOT. Based on the findings, the potential for malignancy recurrence should not preclude the consideration of HBOT for head and neck cancer patients with tissue necrosis.

B061: IMPACT OF DELAYED POST-OPERATIVE RADIOTHERAPY ON SURVIVAL IN HEAD AND NECK CANCERS - A SYSTEMATIC REVIEW AND META-ANALYSIS

- Noémie Villemure-Poliquin, MD, MSc, FRCSC[1]; Karolina Gaebe, MS[2]; Jin Kwon, MS[3]; Marc Cohen, MS[4]; Marianne Ruel[5]; Kennedy Ayoo, MD[6]; Julie Hallet, MD, MSc, FRCSC[7]; Antoine Eskander, MD, ScM, FRCSC[8]; [1]Institute of Health Policy, Management and Evaluation (IHPME) - Dalla Lana School Of Public Health, University of Toronto, Toronto, Ontario, Canada; [2]Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada; [3]Faculté de Médecine, Université de Montréal, Montréal, Québec, Canada; [4]Ruth and Bruce Rappaport Faculty of Medicine, Technion- Israel Institute of Technology, Haifa, Israel; [5]Université Laval, Québec, QC, Canada; [6]Division of Vascular Surgery, Peter Munk Cardiac Centre, University Health Network, University of Toronto, Toronto, Ontario, Canada; [7]Department of Surgery, University of Toronto, Toronto, Ontario, Canada; [8]Odette Cancer Centre-Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

Importance: Delays can occur at various timepoints throughout the continuum of care of Head & Neck cancers (HNC). The Commission on Cancer (CoC) has a single quality metric for HNC patients; an interval <6 weeks from surgery to postoperative radiotherapy (S-PORT). However, this metric is based on a systematic review with a meta-analysis (SRMA) published over two decades ago and primarily relied on data of limited quality.

Objective: The aim of this updated SRMA is to provide a timely and comprehensive assessment of the impact of delayed S-PORT greater than 6 weeks in patients with HNC.

Study selection: We conducted comprehensive searches on MEDLINE, Embase, CENTRAL, Web of Science, and CINAHL databases for trials and cohort studies evaluating the impact of delayed S-PORT in patients with HNC, covering their inception up to September 26th, 2023. We also searched the bibliographies of all relevant systematic reviews related to the study's topic and manually screened the grey literature, focusing on proceedings of major society conferences from the last three years.

Data extraction and synthesis: Data abstracted from each study included study characteristics, patient demographics, disease characteristics, definitions of S-PORT delays, treatment modalities, and criteria for all included outcomes. Two reviewers (N.V.P and K.G) independently extracted the data, and any discrepancies were resolved by a third party (A.E.). The data was pooled from individual studies using the Der Simonian and Laird random effect model to estimate overall pooled effects. We tested for heterogeneity among studies using the I^2 test and conducted prespecified subgroup analyses based on anatomic subsite to evaluate sources of heterogeneity.

Main outcomes and measures: Our primary outcome was 5-year overall survival. Secondary outcomes

included local and locoregional recurrences.

Results: Our search strategy yielded a total of 10,380 titles and abstracts. After the removal of 7972 duplicates, 551 articles were assessed for full text eligibility and 48 were included in the final systematic review. Most of the included studies were conducted in the United States, with multiple using the National Cancer Database (NCDB). Pooled analysis revealed that patients who received S-PORT within 42 days exhibited a 4% increase in survival compared to those with delayed treatment (aHR: 1.04 [1.03 – 1.06]; P < 0.0001; I2 = 82%; N = 215,496; 14 studies). Upon excluding overlapping NCDB-based studies, a more significant increase in survival for the timely treatment group was observed at the latest time point (aHR: 1.10 [1.01 – 1.20]; P = 0.02; I^2 = 39%; N = 52,003; 5 studies).

Conclusion and relevance: Our findings provide robust evidence that delaying S-PORT beyond 6 weeks is associated with substantial increases in both overall mortality and locoregional recurrences in HNC patients. These findings are supported the most recent systematic reviews to date, thereby reinforcing the current recommendations of the CoC. To further inform clinical decision-making and enhance patient care, future research should explore the impact of treatment delays on patient-centered outcomes including psychological distress and QoL.

B062: FUNCTION SPARING ENUCLEATION OF VAGAL, SYMPATHETIC AND OTHER CERVICAL SCHWANNOMAS: AN ANALYSIS OF 100 PATIENTS TREATED OVER A 20 YEAR PERIOD

- Marina Aweeda, BS; Jaclyn Lee, MD; Austin T Hoke, MD; Ramez Phillips, MD; Michael C Topf, MD; James L Netterville, MD; Vanderbilt University Medical Center

Objectives: Complete surgical resection is the accepted standard of care for treatment of extracranial schwannomas of the head and neck. However, to spare neural function of the vagus, hypoglossal, and pharyngeal plexus nerves, we perform intracapsular enucleation of vagal schwannomas. This technique had excellent early outcomes and was extended to other extracranial schwannomas, including sympathetic, spinal accessory nerve, and brachial and cervical plexus. We present an extensive 20-year series of patients undergoing enucleation of extracranial schwannomas to evaluate postoperative outcomes and rates of recurrence.

Methods: A prospective cohort study was conducted to identify patients who underwent intracapsular enucleation of extracranial schwannomas between June 2003 and August 2023, at a single tertiary academic medical center and global health sites. Surgical pathology was used to determine final diagnosis of schwannoma. Vocal cord function was assessed on postoperative day (POD) 1, using nasolaryngoscopy, with weakness of the true vocal folds (TVF) defined as hypomobile or immobile. Dysphagia was assessed using functional oral intake scale (FOIS) scores. Physical examination was used to assess cranial nerve (CN) dysfunction and Horner's syndrome. Patients were assessed at 1 week, 6 months, and 12 months postoperatively. Recurrence was evaluated by surveillance imaging and clinical exam findings.

Results: In total, 160 patients received care for cervical schwannomas. In this cohort, 40 patients (25%) were observed annually due to advanced age or patient preference, while 120 patients (75%) underwent enucleation. Of the surgical cohort, 100 patients (83%) received appropriate follow up. These patients were predominantly White (n=88), female (n=67), with

a mean age of 50 years (range 16-75). Most had schwannomas of the vagus nerve (n=43), followed by sympathetic (n=39), cervical plexus (n=6), brachial plexus (n=3), hypoglossal (n=3), glossopharyngeal (n=2), and spinal accessory (n=1). The mean maximal tumor dimension was 4 cm (range 1.4 to 8.6 cm). In patients undergoing enucleation of vagal schwannomas, 53.5% (23/43) of patients had normal function of the ipsilateral TVF on POD 1. Nine patients (20.9%) had mild TVF dysfunction and adequate oral nutrition at discharge. Eleven patients (25.6%) had significant TVF paresis or paralysis and underwent injection laryngoplasty on POD 3 with collagen or hyaluronic acid for temporary medialization. At 1 year postoperatively, normal TVF function and adequate oral intake was achieved in 79% (34/43) of patients who underwent enucleation of vagal tumors. Of the 24 patients with first bite syndrome pain, the majority had sympathetic (n=10) and vagal (n=10) schwannomas. Following sympathetic schwannoma enucleation, 90% of patients experienced Horner's syndrome (35/39), of which 86% (12/14) of patients with follow up experienced improvement or complete resolution in an average of 9.5 months. Of the 66 patients with postoperative surveillance imaging, there were 0 recurrences, for a median follow-up period of 12.5 months (range 1-193 months).

Conclusions: Intracapsular enucleation of extracranial schwannomas is an effective and feasible approach that allows for preservation of the cranial nerves with strong functional outcomes and very low rates of recurrence. Prospectively, patients are being contacted to collect further long term follow up data regarding functional outcomes and recurrence.

B063: WHICH COMORBIDITY INDICES IDENTIFY PATIENTS WHO EXPERIENCE POOR OUTCOMES FOLLOWING SURGERY IN HEAD AND NECK CANCER PATIENTS? - Soraya Fereydooni[1]; Devesh Malik[1]; Daniel Jacobs, MD[2]; Benjamin L Judson, MD, MBA[2]; [1]Yale School of Medicine; [2]Yale New Haven Hospital

Background: Identifying patients at risk of postoperative adverse events and discharge to other than home after surgery in patients with head and neck cancer is of utmost importance. Comorbidity indices have been associated with worse patient outcomes. However, multiple indices exist and there is no consensus on which is the most reliable metric.

Objectives: We assessed associations of the modified 5-item frailty index (mFI-5), the modified Charlson comorbidity score (mCCI), the modified Elixhauser comorbidity score (mECI), and the American Society of Anesthesiologists (ASA) physical status classification system score with 30-day mortality, 30-day rate of major and minor complications, discharge disposition, and extended LOS in the hospital following reconstructive and head and neck surgery.

Methods: This retrospective study used the 2006-2020 National Surgical Quality Improvement Program (NSQIP). The comorbidity indices were modified for NSQIP based on prior literature. Multivariable logistic regressions, controlling for the available social determinants of health and the comorbidity indices, were conducted to determine the associations between the indices and the outcomes.

Results: This study identified 25,197 patients with HNSCC, of which 11% experienced a major complication, 15% a minor complication, hospital stay (mean: 2.0; SD [1.0, 7.0]), and 7% were discharged to a destination other than their home/permanent residence. Of the four indices, each point increase in ASA class

was most strongly associated with a major complication (Odds ratio: 2.07 [95% CI: 1.91, 2.24]), a minor complication (2.57 [2.39, 2.76]), and a prolonged length of hospital stay (2.50 [2.40, 2.70]). Each point increase in ASA class was also most strongly associated with discharge to a destination other than home/ permanent residence, as it had the strongest negative association with discharge to the patient's home/permanent residence (0.41 [0.37, 0.46]). Each point increase in mECI had the lowest association with the aforementioned outcomes (1.06 [1.05, 1.08]; 1.10 [1.08, 1.11]; 0.28 [0.25, 0.31]; 0.91 [0.89, 0.93], respectively).

Conclusion: Each point increase in ASA class was the strongest comorbidity index for association with major complications, minor complications, prolonged hospital stays, and discharge to destinations other than home/permanent residence. The mFI-5, mCCI, and then mECI were progressively less associated with all four adverse outcomes. ASA class should continue to be prioritized in HNSCC-associated clinical outcomes research as a proxy for controlling confounding comorbidity status.

B064: THE IMPACT OF THE COVID-19 PANDEMIC ON LARYNGEAL CANCER TIME TO TREATMENT INITIATION - Marina Aweeda, BS; Rahul K Sharma, MD; Carly Fassler, BS; Kyle Mannion, MD; Sarah L Rohde, MD; Robert J Sinard, MD; Michael C Topf, MD; Vanderbilt University Medical Center

Objectives: Socioeconomic status, race, and accessibility of care can contribute to delays in cancer diagnosis and treatment. The COVID-19 pandemic disrupted healthcare delivery and exacerbated existing disparities. This study sought to evaluate the effect of the COVID-19 pandemic on time to treatment initiation (TTI) for patients with laryngeal cancer and determine whether specific demographic characteristics were associated with overall treatment delays.

Methods: A retrospective analysis of the National Cancer Database (NCDB) was conducted to identify patients diagnosed with laryngeal cancer between 2017 and 2020. Patients were categorized based on their year of diagnosis as "non-COVID" (2017 to 2019) and "COVID" (2020). A linear regression was used to evaluate TTI. Multivariable logistic regression controlling for tumor characteristics was performed to explore the independent effects of COVID-19, race, and income on stage at diagnosis. Advanced stage at diagnosis was defined as Stage III and IV overall staging.

Results: In total, 30,729 patients were diagnosed with laryngeal cancer during non-COVID years and 8,961 during the COVID-19 pandemic (2020). There were no significant differences in median TTI (34d vs. 34d, p=0.70) during non-COVID and COVID, respectively. During non-COVID years, 63.4% (n=19,496) of patients received surgery compared to 64.7% (n=5796) of patients during COVID. There was no significant difference in median time to surgery (15d vs. 16d, p=0.80) during non-COVID and COVID, respectively. Patients diagnosed with laryngeal cancer during the COVID-19 pandemic were less likely (b=- 1.1, 95% CI -2.1, -0.08, p=0.034) to experience treatment delays but were more likely to present at an advanced stage at diagnosis (OR=1.14, 95% CI 1.08-1.21, p<0.001). Additionally, Black patients were more likely to present at an advanced stage at diagnosis (OR=1.17, 95% CI 1.09-1.26, p<0.001) and experience delays in treatment (b=2.9, 95% CI 1-7-4.1, p<0.001) compared to White patients. Higher income patients were less likely to present at a later stage at diagnosis (OR=0.67, 95% CI 0.63-0.72, p<0.001) and to experience treatment delays (b=-

3.1, 95% CI -4.3, -1.9, p<0.001) than lower income patients.

Conclusions: In this national database study, patients with laryngeal cancer were more likely to present with advanced stage disease during the COVID-19 pandemic, but once diagnosed were not more likely to experience delays in TTI. White patients and higher income patients were less likely to present with advanced stage and also less likely to experience TTI.

B065: PATTERNS OF CARE FOR T1 GLOTTIC SQUAMOUS CELL CARCINOMAS FROM 2004-2020 -

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Background: There exists uncertainty regarding surgery or radiation therapy (RT) as the first-line treatment for T1 glottic squamous cell carcinoma (SCC) patients, and treatment decision-making continues to be highly variable among these patients. The incidence and associated factors of receiving both treatments (considered overtreatment) has not been previously studied.

Objectives: Our objectives were: 1. to describe the national trends over time in both overall and initial treatment modality for T1 glottic SCC from 2004-2020; and 2. to identify factors independently associated with receiving dual-modality (over-treatment) therapy, and with initial treatment choice.

Methods: The National Cancer Database (NCDB) from 2004-2020 was queried for patients of all ages with a histologically confirmed new diagnosis of glottic cT1N0M0 SCC. The primary outcomes for this study were the trends in overall and initial treatment regimens used for patients in the cohort. All treatment patterns over time were analyzed using the Cochran-Armitage test for trend, and multivariable logistic regressions were used to determine the factors associated with dual-modality therapy and initial treatment choice.

Results: This study identified 22,414 patients, of which most patients received RT only (57%), 21% received surgery only, and 22% received both treatments. From 2004 to 2020, there was a decreasing trend in multimodality treatment for T1 glottic SCC (P < 0.001). Additionally, there was an overall decline in the utilization of RT only (P < 0.001), and an increase in surgery only (P < 0.001). When investigating initial planned treatment over the time period, there was an overall increase in surgery first (P < 0.001). Of note, assessment at a non-academic (OR: 1.662 [95% CI: 1.523 to 1.814]) vs. academic facility was associated with a higher likelihood of receiving dual-modality therapy, as well as year of treatment: 2016 - 2018 (Odds ratio (OR): 1.168 [1.004 to 1.359]), 2013 - 2015 (OR: 1.419 [1.221 to 1.648]), 2010 - 2012 (OR: 1.611 [1.388 to 1.871]), 2007 - 2009 (OR: 1.682 [1.450 to 1.951]), and 2004 - 2006 (OR: 1.795 [1.548 to 2.081]) vs. the 2019 - 2020 period. On the other hand, T1b tumors were less likely to be treated with both treatments (OR: 0.795 [0.707 to 0.894]) vs. T1a tumors. Notable factors associated with a lower likelihood of receiving surgery first include assessment at a non-academic (OR: 0.714 [0.666 to 0.766]) vs. academic facility, and T1b tumors (OR: 0.536 [0.485 to 0.592]) vs. T1a tumors.

Conclusion: Over the past two decades, there has been a consistent decline in the use of dual-modality treatment for T1 glottic SCC, with an increase in use of surgery first rather than RT. Nevertheless, most patients continue to receive RT first. Patients treated at non-academic centers were more likely to

receive dual-modality treatment and were less likely to receive surgery first. Finally, T1b staging was found to incur a decreased risk for dual-modality treatment and for receiving surgery first.

B066: SALIVARY FISTULA IN LARYNGECTOMY PATIENTS WITH CONTRAST IMAGING VS. WITHOUT IMAGING: A SYSTEMATIC REVIEW -

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Introduction: Post-laryngectomy management in head and neck patients varies, particularly regarding the utilization of contrast imaging for the early detection of pharyngeal leaks before oral refeeding. Practices differ between use of preemptive contrast imaging prior to initiating oral intake. Despite negative imaging findings, some patients still experience fistula formation upon the reintroduction of oral intake. This systematic review aims to evaluate the role and necessity of contrast imaging by comparing the incidence of fistulae in patients who underwent imaging to those who did not, before resuming oral intake. Through this, we aim to provide clinicians with valuable insights that could inform clinical decision-making, optimize the use of resources, and potentially reduce the incidence of post-laryngectomy complications.

Methods: A systematic search was conducted using PubMed, Scopus, and the Cochrane Library for studies published between January 2000 and October 2023. The search strategy was designed to identify all relevant literature on fistula formation post-laryngectomy, using keywords such as "laryngectomy," "fistula," "esophagram," "barium swallow," and "oral intake." Initially 1040 articles resulted, removal of duplicates and screening of titles resulted in 696 articles that were removed. Subsequent abstract and full-text review of the remaining 344 articles led to the exclusion of 323. Ultimately, 21 studies met the inclusion criteria, with 8 reported using contrast imaging for fistula detection prior to initiating oral intake and 13 not using contrast imaging studies.

Results: 1,094 patients received contrast imaging after laryngectomy and/or pharyngectomy, with 9.8% (107 out of 1,094) developing post-operative fistulas upon reintroducing oral intake. Contrast imaging was performed between 9 to 15 days post-operation, predominantly utilizing Barium or Gastrografin with esophograms or videofluoroscopy as the imaging modalities. The average onset of oral intake was between 9 to 13 days post-surgery in this group.

In contrast, among 1,862 patients who did not receive contrast imaging, 8.53% (159 out of 1,862) developed fistulas post-operatively. For these patients, oral intake commenced variably, ranging from as early as the first post-operative day to beyond the twelfth.

On average, 30.3% of patients in the cohort that utilized contrast imaging received radiation therapy prior to laryngectomy. In comparison, an average of 46.2% of patients in the cohort without contrast imaging underwent radiation therapy prior to laryngectomy.

Conclusion: While contrast imaging is an important diagnostic tool for evaluating salivary leakage and the potential extent of fistula formation, our study indicates that contrast imaging after laryngectomy may not significantly reduce the incidence of post-operative fistulae after initiating oral intake, with rates of 9.8% in the contrast imaged group versus 8.53% in the non-imaged group. These findings suggest that contrast imaging before oral refeeding may not be as critical as previously thought in preventing fistulae. Future guidelines could consider a more individualized approach to post-operative care, taking into account the patient's specific clinical context rather than relying solely on routine contrast imaging.

B067: IMPACT OF THE ENHANCED RECOVERY AFTER SURGERY (ERAS) PATHWAY ON POST OPERATIVE OUTCOMES FOR TOTAL LARYNGECTOMY PATIENTS

- Anjali Devgan, MS[1]; Chinmay Ghavat[1]; Lucy Xu, MD[2]; Mark Varvares, MD[2]; Jeremy Richmon, MD[2]; Jeremy Goldfarb, MD[2]; Allen Feng, MD[2]; [1]Harvard Medical School; [2]Massachusetts Eye & Ear Department of Otolaryngology

Importance: ERAS protocols have been shown to reduce length of stay and complications in multiple specialties and have become an increasing area of interest in otolaryngology. A recent meta-analysis highlighted the need for more rigorous outcomes analysis stratified by type of head and neck surgery. Total laryngectomy (TL) was selected for this study due to the operation's well-established complications and the extensive post-operative care required. Understanding the impact of this pathway allows for adjustments to the ERAS protocol to drive further improvements in patient outcomes.

Objectives: To investigate the impact of an ERAS pathway on post-laryngectomy outcomes.

Design, Setting, and Participants: We performed a retrospective, case-control study of patients undergoing a total laryngectomy (TL) at a single academic institution from January 2016 to June 2023. Patients were stratified into pre-ERAS (January 2016-December 2018) and post-ERAS (January 2019-June 2023) groups and were matched using inverse probability of treatment weighting, based on age, sex, history of prior chemo and/or radiation therapy, and reconstruction type. To assess the normality of the variables, a Shapiro-Wilk normality test was employed and subsequently Welch's test and Mann-Whitney U test were used to analyze the variables. Primary end points, specifically the 30-day readmission rate and 30-day unplanned return to surgery rate, were analyzed using Kaplan Meier curves and causal survival analysis. An adjusted logistic regression model was performed for LOS and secondary endpoints of the study. All statistical analysis was performed in R, version 2023.09.1. This study was granted exemption by the institutional Human Research Office.

Exposures: Enrollment in the ERAS pathway (January 2019-June 2023).

Main Outcomes and Measures: Hospital length of stay (LOS), 30-day readmission rate, 30-day unplanned return to surgery rate, duration to initiation of enteral tube feeds and oral diet, surgical site infection rate, and fistula rate.

Results: The study population consisted of 240 patients with no significant baseline differences between two groups (n=83 pre-ERAS, n=157 post-ERAS). Patients following the ERAS

protocol were less likely to have unplanned return to surgery (p = 0.045) and had earlier initiation of oral feeds (p=0.02). The inverse probability weighted analysis for readmission within 30 days estimated a risk of 41.6% in the pre-ERAS group and a 27.6% in the post-ERAS group, though the difference was not significant (p =0.07) There was no statistically significant difference for LOS, surgical site infection, and fistula formation.

Conclusions and Relevance: This retrospective analysis found that enrollment in the ERAS protocol for TL patients was associated with lower reoperation rates and faster initiation of enteral and oral feeds, as well as decreased risk of readmission within 30 days. This investigation allows for better characterization on the impact of the ERAS pathway and illuminates areas for future improvements.

B068: THE IMPACT OF SOCIOECONOMIC AND GEOGRAPHIC FACTORS ON ACCESS TO TRANSORAL LASER MICROSURGERY FOR EARLY-STAGE LARYNGEAL MALIGNANCY - Charles Gallego, BS; Matthew Groysman, MD; Shethal Bearelly, MD; University of Arizona College of Medicine

Transoral laser microsurgery (TLM) is a minimally invasive surgical intervention for early stage glottic tumors. Despite having treatment and functional outcomes similar to upfront radiotherapy (RT), not all eligible patients have equitable access to this surgical approach. We sought to investigate factors such as socioeconomic status, treatment or health characteristics, level of education and residing in a Medicaid expansion state that might predict access to TLM.

Using the National Cancer Database (NCDB), data was collected from a cohort consisting of 20,269 patients who underwent either TLM or RT for T1-T2, N0, M0 early-stage squamous cell carcinoma of the glottis. A multivariate analysis was performed to identify variables that predicted receiving TLM.

Gender, age, year of diagnosis and race did not seem to significantly predict receiving either TLM or radiotherapy. Patients with Medicaid (Odds Ratio (OR): 0.697, 95% Confidence Interval (CI) 0.576 – 0.844) or no insurance (OR: 0.559, 95% CI 0.426 – 0.733) were much less likely to receive TLM compared to those with private insurance. Patients living in areas with low educational attainment were less likely to receive TLM (OR: 0.674 (95% CI 0.571 – 0.795). However, patients who lived in a state that expanded Medicaid as part of the Affordable Care Act early in 2014 were much more likely to receive TLM compared to patients that resided in states that did not expand Medicaid (OR: 1.284, 95% CI 1.124 – 1.467). Patients who sought treatment at a non-academic medical center were significantly less likely to receive TLM compared to those who went to academic medical centers (OR 0.403, 95% CI 0.37 – 0.439)

Understanding the factors that affect access to TLM is crucial for improving healthcare equity and ensuring that patients receive the most appropriate treatment for early-stage glottic carcinoma. We highlight the need for targeted interventions, policy changes, and educational efforts to enhance access for all eligible patients. Ultimately, addressing these factors can lead to better outcomes and reduced healthcare disparities.

B069: COMPARISON OF RECONSTRUCTIVE TECHNIQUES FOLLOWING TOTAL LARYNGOPHARYNGECTOMY WITH ESOPHAGECTOMY: A NSQIP ANALYSIS -

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Background: Total laryngopharyngectomy with esophagectomy (TLPE) remains a viable treatment option for patients with locally advanced and recurrent tumors of the hypopharynx, larynx, and cervical esophagus. Reconstructive techniques for pharyngoesophageal defects have evolved over the past few decades, ranging from pedicled flaps to free tissue transfer and visceral transposition flaps. Several studies at the institutional level have examined outcomes of these reconstructive techniques with heterogeneous results. The objective of this study was to utilize the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database to compare the most common reconstructive techniques following TLPE.

Methods: The ACS-NSQIP 2005-2020 database was queried using current procedural terminology (CPT) codes for adult patients who had undergone both total laryngectomy or total laryngopharyngectomy and esophagectomy. Patients were then grouped based on the type of reconstruction—soft tissue free flap (STFF), gastric pull-up (GP), and jejunal free flap or colonic interposition (JF/CI). Patient characteristics were examined including gender, age groups, race/ethnicity, BMI groups, functional status, ASA scores, and preoperative comorbidities (Table 1). Thirty-day postoperative outcomes including medical and surgical complications, reoperations, readmissions, mortality, operative time (OT, minutes), and total hospital length of stay (LOS, days) were also analyzed. Univariate analysis was done utilizing the Kruskal–Wallis H test for continuous variables and Fisher's exact test or Chi-square for categorical variables. A multivariate regression analysis was done to determine reconstructive approach as a predictor for adverse postoperative outcomes controlling for patient characteristics (Table 1).

Results: Of the 102 patients identified who underwent TLPE between 2005-2020, 94 patients had the reconstructive approach specifically coded in NSQIP. The majority of patients underwent GP (51, 54.3%) while (24, 25.5%) patients underwent reconstruction with a STFF, and (19, 20.2%), patients with JF/CI. On univariate analysis age groups, race/ethnicity, and estimated probability of mortality were significantly different between groups (all, p<0.05). There was a significant difference in OT, H(2) = 15.390, p<0.001, and LOS, H(2) = 11.060, p = 0.004, between the different reconstruction groups. Post-hoc analysis showed that median OT [IQR] for GP [499.0 (206.0)] was significantly different than JF/CI [705.0 (279.0); p<0.001] and FF [568.5 (233.0); p=0.017]. Median LOS [IQR] for GP [17.50 (18.5)] was significantly different than STFF [12.0 (10.0); p=0.001] but approaching significance for JF/CI (12.0 [15.0]; p=0.060). Median OT (p=0.196) and LOS (p=0.369) for JF/CI and STFF were not significantly different. A multivariate regression analysis controlling for age groups, race/ethnicity, and weight loss showed STFF compared to GP had decreased odd ratios of pulmonary complications (OR: 0.14; 95%CI: 0.02–0.87; p=0.035). Otherwise, there were no additional significant differences amongst the groups with regard to other outcome variables.

Conclusion: Based on our analysis, outcomes following TLPE are similar among patients who undergo reconstruction via GP, STFF, or JF/CI. Our study suggests that patients who underwent GP had a shorter OT, however, there was an increase noted in pulmonary complications. GP may also be associated with an increased hospital LOS. Further prospective studies are needed to better delineate the advantages of each reconstructive option as well as speech/swallow outcomes.

Preoperative Variables	P-value
Gender	0.686 †
Race/ethnicity	0.009 *
Age groups	0.021 *
BMI groups	0.774
ASA groups	0.862
Functional Status	0.457
Diabetes Mellitus Requiring Therapy	1.000
Current Smoker Within One Year	0.129 †
Congestive Heart Failure	1.000
Hypertension Requiring Medication	0.827 †
Severe Chronic Obstructive Pulmonary Disease	0.333
Dialysis	1.000
Steroid/Immunosuppressive Therapy for a Chronic Condition	0.708
Bleeding Disorder	1.000
Estimated Probability of Morbidity	0.087
Estimated Probability of Mortality	0.019 *

Table 1: Univariate analysis between preoperative variables. Superscript † indicates that chi square was used instead of Fisher's exact test if ≤20% of expected cell counts are less than five. Superscript * indicated that preoperative variables in the univariate phase with a p-value that is significant or approaching significance (<0.1) were added to the multivariate logistic regression analysis.

Thirty-day Postoperative Outcome	GP	RI	P-value	FF	P-value
Adverse Event; N (%)	Ref	1.32 (0.24-7.10)	0.750	0.72 (0.16-3.23)	0.668
Severe Complications; N (%)	Ref	0.88 (0.17-4.48)	0.876	0.65 (0.15-2.84)	0.569
Wound Complications; N (%)	Ref	1.24 (0.18-8.66)	0.832	1.74 (0.29-10.37)	0.544
Pulmonary Complications; N (%)	Ref	3.12 (0.62-15.78)	0.169	0.14 (0.02-0.87)	0.035
Renal Complications; N (%)	Ref	0.00 (0.00-461.42)	0.359	NC	NC
Cardiac Complications; N (%)	Ref	NC	NC	0.44 (0.02-8.61)	0.591
Thromboembolic Complications; N (%)	Ref	0.76 (0.05-11.33)	0.843	NC	NC
Sepsis-Related Complications; N (%)	Ref	0.07 (0.00-13.52)	0.327	0.00 (0.00-3.59)	0.077
Any Reoperation; N (%)	Ref	1.97 (0.41-9.43)	0.397	1.84 (0.43-7.88)	0.412
Any Readmission; N (%)	Ref	NC	NC	NC	NC
Mortality; N (%)	Ref	NC	NC	12.59 (0.04-3554.07)	0.379

Table 2: Multivariate logistic regression on adverse postoperative outcomes within reconstruction groups controlling for gender, age groups, race/ethnicity, BMI groups, ASA groups, functional status, estimated probability of morbidity/mortality, and preoperative comorbidities listed in Table 1. Only calculable OR (95%CI), P-values were included (NC = non-calculable).

B070: THE PROGNOSTIC SIGNIFICANCE OF P16 IN LARYNGEAL SQUAMOUS CELL CARCINOMA -

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Importance: The traditional standard-of-care of laryngeal squamous cell carcinoma (LSCC) yields an estimated 5-year relative survival of 61%, with a decrease to 30% 5-year relative survival if cancer has metastasized. Management of patients with LSCC is based on patient factors, physical exam findings, and radiographic studies as there are no definitive prognostic or predictive biomarkers to guide clinical decision-making. Thus, there is an unmet need for predictive biomarkers that guide the use of less toxic therapies while maintaining or improving outcomes in LSCC. Expression of p16INK4A (hereafter called p16), a tumor suppressor protein expressed from the *CDKN2A* gene, has been reported as a positive prognosis in overall head and neck and its subsites, such as the oropharyngeal squamous cell carcinoma. Yet, there is continued controversy regarding the role of p16 in non-oropharyngeal cancer, like LSCC.

Objective: To assess the prevalence of p16/*CDKN2A* positivity and its association with survival outcomes in LSCC patients.

Design, Setting, and Participants: A total of 310 patients, aged 18 and older, who had a diagnosis of LSCC were included in this study. Of these patients, 117 patients were identified from The Cancer Genome Atlas Program (TCGA) and 193 patients underwent treatment between 2000 and 2017 at the University of Maryland Medical Center (UMMC). Patients' age and sex were similar between the two cohorts. UMMC had more black patients than TCGA cohort (37.8% and 16.2% of total patients, p < 0.0001).

Intervention: Standard-of-care LSCC treatment.

Main Outcomes and Measures: The primary outcome was the prevalence of p16 as assessed by p16 immunohistochemistry (negative to positive with strong intensity) and p16 reverse-phase protein array (0-2.6, higher scores reflect higher protein expression) and its association with overall and disease-free survival (DFS) outcomes.

Results: The mean patient's age was 60.4 ± 10.2 and 61.9 ± 9.1 in the UMMC and TCGA cohort, respectively. The majority of the cohort were males (76.2% and 82.9% in the UMMC and TCGA cohort, respectively) and current or former smokers (91.7% and 85.5% in the UMMC and TCGA cohort, respectively). Univariate analysis using Fisher's exact test showed the p16-negative group was more likely to have recurrence and/or deceased patients than the p16-positive group (p = 0.0369). In TCGA cohort, Kaplan-Meier plots showed the probability of 5-year DFS in high and low p16 protein groups were 89% and 51%, respectively (p = 0.0266). Similarly, the probabilities of 5-year DFS in low vs high *CDKN2A* expression groups were 84.7% and 42.8%, respectively (p = 0.0845). In the same patient cohort, the mean relative p16 protein expression on TNM stage II, stage III, and stage IV were 1.116, 1.075, and 0.6204, respectively (p = 0.0280).

Conclusions and Relevance: Our analysis of TCGA laryngeal cancer cohorts suggests that high expression of the p16 protein marker is associated with a lower risk of recurrence and lower TNM stage. To leverage p16 expression as a prognosis biomarker in LSCC, we are investigating the immunological and metabolism changes underlying the positive association between its expression and improved clinical outcomes.

B071: RADIATION VERSUS SURGERY IN EARLY-STAGE GLOTTIC CANCER: AN ANALYSIS OF FUNCTIONAL AND SURVIVAL OUTCOMES - <u>Ramez Philips</u>[1]; Pratyusha Yalamanchi[1]; Aarti Agarwal[2]; Dev Amin[2]; Eric Mastrolonardo[2]; Wenda Ye[1]; Kyle Mannion[1]; Robert Sinard[1]; Michael Topf[1]; Eben Rosenthal[1]; James Netterville[1]; Joseph Curry[2]; Sarah Rohde[1]; [1]Vanderbilt University Medical Center; [2]Thomas Jefferson University Hospital

Objective: To compare functional and oncologic outcomes between primary surgery versus radiation in patients with early glottic cancer.

Materials & Methods: This is a propensity-matched retrospective cohort study utilizing a large multi-institutional electronic healthcare registry, TriNetX. Patients with T1/T2 N0 glottic squamous cell carcinoma undergoing primary surgery versus radiation were reviewed. Patients were propensity score matched based on statically significant variables between the two cohorts using a 1:1 nearest neighbor regression analysis. Functional outcomes included dysphagia, pneumonia, weight loss, dysphonia, gastrostomy tube dependence, and tracheostomy tube dependence at 6 months, 1 year, 3 years, and at any time indexed after diagnosis. Oncologic outcomes included 3-year overall survival (OS) and laryngectomy-free survival.

Results: A total of 1,007 patients who underwent radiation or surgery for glottic squamous cell carcinoma during the study period met inclusion criteria. After propensity matching, 536 patients were included and were distributed equally amongst both cohorts. Patients undergoing surgery had lower odds ratio of dysphagia at 6 months (OR, 0.68; 95% CI, 0.47 – 0.98) and 1-year post surgery compared to radiation (OR, 0.49; 95% CI, 0.32 – 0.75) but equivalent rates of dysphagia at 3 years. There was no difference in gastrostomy and tracheostomy tube dependence at any time point. Patients undergoing surgery had an increased odds ratio of having dysphonia at 6 months (OR, 1.32; 95% CI, 1.15 – 1.46) but equivalents odds of dysphonia at 1 and 3-years post treatment. Three-year overall survival rates were 91.7% vs 78.0% in patients undergoing surgery and radiation, respectively. Patients undergoing surgery had a statistically significant improvement in 3-year OS when compared to patients undergoing radiation (log rank p < 0.001 (HR, 0.35; 95% CI, 0.22 – 0.55)). Three-year laryngectomy free survival rates were 94.5% and 90.8% in patients undergoing surgery and radiation, respectively. Patients undergoing surgery had a statistically significant improvement in 3-year laryngectomy free survival when compared to patients undergoing radiation (log rank p = 0.032 (HR, 0.51; 95% CI, 0.27 – 0.95)).

Conclusion: Patients undergoing surgery for early stage glottic carcinoma are less likely to have short-term dysphagia but more likely to have dysphonia compared to patients undergoing radiation. Long-term functional outcomes are equivalent. Patients undergoing surgery have improved 3-year overall and laryngectomy-free survival.

B072: ASSOCIATION OF PREALBUMIN AND ALBUMIN WITH WOUND HEALING COMPLICATIONS AFTER TOTAL LARYNGECTOMY WITH FREE FLAP RECONSTRUCTION - <u>Anthony Tang</u>[1]; Sophia Dang[2]; Isabella Lao[1]; Sumaarg Pandya[1]; Kevin J Contrera[2]; José P Zevallos[2]; Mario G Solari[3]; Robert L Ferris[2]; Seungwon Kim[2]; Shaum Sridharan[2]; Michael E Spector[2]; [1]University of Pittsburgh, School of Medicine; [2]University of Pittsburgh Medical Center, Department of Otolaryngology-Head and Neck Surgery; [3]University of Pittsburgh Medical Center, Department of Plastic Surgery

Introduction: Malnutrition is an important risk factor for patient surgical outcomes. This is especially true for head and neck cancer patients receiving a total laryngectomy (TL) with free flap reconstruction (FFR). Preoperative prealbumin and albumin values have both been used to indicate poor nutrition. While low albumin has been studied in head and neck cancer in general, laryngectomy patients have a unique set of wound healing complications that have significant morbidity and mortality. The aim of this study is to identify the prognostic value of preoperative prealbumin and albumin levels with wound healing complications and readmissions in head and neck cancer patients with TL and FFR.

Methods: A retrospective review was conducted in all patients who underwent head and neck oncologic surgery with TL and FFR from 2016-2022 at a tertiary-care institution. Only patients with either preoperative (within 1 month of surgery) prealbumin

or albumin lab values were included. Low prealbumin levels and low albumin levels were defined as < 20 mg/dL and <3.4 g/dL, respectively. Outcomes collected included any wound healing complications (e.g., wound dehiscence, fistula, and salivary leak), return to the operating room (RTOR), and readmission. Wound healing complications and nutritional markers were compared using chi-squared, t-test, fisher's exact test analysis, and multivariable logistic regression.

Results: A total of 83 patients met the inclusion criteria. The mean age at surgery was 61.6 ± 9.3. The majority of patients were male (70.4%) and Caucasian (90.5%). 34.5% of patients had radiation prior to TL and FFR. There were 64 patients (77.1%) with preoperative prealbumin lab values, 37/64 (44.6%) of these patients had a low prealbumin level. There were 82 patients (98.8%) with preoperative albumin lab values, 31/82 (37.8%) of these patients had low albumin levels. There was an association between low prealbumin levels and any wound healing complication, wound dehiscence, RTOR, and readmission on univariate analysis (p=0.033, p=0.004, p=0.089, p=0.076, respectively). Low albumin levels were associated with postoperative infection and fistula (p=0.014, p=0.065, respectively). On multivariate analysis, low prealbumin levels were associated with any postoperative wound healing complications (OR, 3.8; CI 1.1-13.1; p=0.034) controlling for age, smoking, and preoperative radiation.

Conclusions: TL patients with preoperative low prealbumin and albumin levels were associated with wound healing complications including dehiscence and fistula. In addition, low preoperative prealbumin levels were associated with higher rates of RTOR and readmission. Consideration of more frequent prealbumin testing in HNC patients with TL and FFR may lead to better mitigation of post-operative wound healing complications, reoperation, and readmission.

B073: ASSOCIATIONS BETWEEN INSURANCE COVERAGE, TREATMENT PATTERNS, AND OUTCOMES IN HYPOPHARYNGEAL SQUAMOUS CELL CARCINOMA PATIENTS - <u>Sharanya M Thodupunoori, BS</u>[1]; Vanshika S Narala, BS[1]; Samuel Auger, MD[2]; David Grande, MD[2]; Christopher Roxbury, MD[2]; Elizabeth A Blair, MD[2]; [1]The University of Chicago Pritzker School of Medicine; [2]The University of Chicago Medicine - Department of Surgery - Section of Otolaryngology

Importance: Squamous cell carcinoma of the hypopharynx (HSCC) accounts for 95% of malignant tumors in the hypopharynx and has one of the worst prognoses of all head and neck cancers. While surgery and radiotherapy can prolong life, there is significant financial morbidity associated with treatment which may act as a barrier to care for underserved populations, including the uninsured and underinsured. Understanding the relationship between insurance status, treatment modality, and survival outcomes will inform future initiatives to increase accessibility of care.

Objective: Determine whether insurance status for HSCC patients is associated with differences in treatment patterns and survival outcomes.

Design: Population-based retrospective cohort analysis.

Setting: The National Cancer Database (NCDB) is a clinical oncology database from hospital registry data from more than 1,500 Commission on Cancer-accredited facilities.

Participants: Patients aged 0-90 diagnosed with HSCC according to the International Classification of Diseases for Oncology (ICD-O) codes C129-C132 & C138-C139 and histology codes 8070-8076 from 2004-2020. Patients without a known insurance status were excluded.
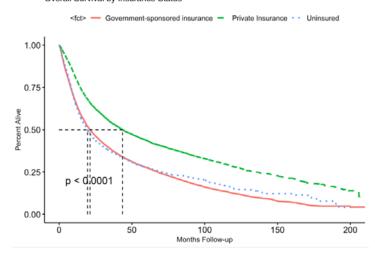
Exposures: Insurance status was classified as government-sponsored insurance, private insurance, and uninsured.

Main outcomes and measures: HSCC treatment modalities and overall survival (OS) were analyzed.

Results: A total of 23,788 HSCC patients were included; 66.2% had government-sponsored insurance, 28.9% had private insurance, and 5.0% were uninsured. Privately insured patients presented more frequently with early-stage cancer (17.3% T1, 33.6% T2). Those with government-sponsored or no insurance were more likely to present with advanced-stage cancer (government-sponsored: 24.3% T3, 30.9% T4; uninsured: 25.9% T3, 40.1% T4). Privately insured patients were more likely to undergo surgery (23.9%, p<0.001) and radiation therapy (78.8%, p<0.001). Privately insured individuals had higher OS (1-year OS 79.4%, 5-year OS 43.6%, and 10-year OS 28.2%) compared to patients with government-sponsored (64.7%, 27.6%, and 12.4%) and no insurance (63.5%, 27.9%, and 15.1%). Multivariable analysis controlling for age, sex, race, rurality, comorbidities, primary tumor site, disease grade and stage, and surgical margin status showed that privately insured patients had a 13% decreased risk of mortality (hazard ratio [HR]: 0.87, 95% confidence interval [CI]: [0.76-0.99], p<0.05) while patients with government-sponsored insurance had a 19% increased risk (HR: 1.19, CI: [1.05-1.35], p<0.01). T4 tumor stage was associated with double the risk of mortality compared to T1 (HR: 2.07, CI: [1.92-2.25], p<0.001). Surgery was associated with a 30% decrease in mortality risk compared to nonsurgical management (HR: 0.70, CI: [0.60-0.82], p<0.001). Radiation therapy was associated with a 42% decrease in mortality risk (HR: 0.58, CI: [0.55-0.62], p<0.001).

Conclusions and Relevance: HSCC Patients with private insurance were more likely to present with earlier stage disease, undergo definitive treatment, and have significantly better OS compared to those with government-sponsored or no insurance. These data suggest that health insurance impacts HSCC outcomes and supports national health care reform to increase accessibility and affordability of care.

Overall Survival by Insurance Status

B074: BETEL-NUT ORAL SQUAMOUS CELL CARCINOMA: A COLLECTION OF FALSE PET/CT LYMPH NODE AVIDITIES

- Adeeba Ghias, MD[1]; Kurtis Young, MD[2]; Karina Marcelo, MD[1]; Hyeong Ahn, PhD[3]; Kelly Anderson, MD[1]; Eric Wirtz, MD[4]; [1]Tripler Army Medical Center; [2]University Medical Center of Las Vegas; [3]University of Hawaii School of Medicine; [4]Brooke Army Medical Center

Background: The betel nut, a psychoactive substance commonly chewed in the Pacific islands, Guam, South and Southeast Asia, has been declared a human carcinogen by the International Agency for Research on Cancer. The prevalence of betel nut chewing in the Micronesian islands is as high as 94% in Yap or 76% in Palau. In these regions, it is often combined with slaked lime, tobacco, betel leaf, and mixed with alcohol, all of which have been proposed or confirmed to be carcinogenic. Betel nut chewers with oral squamous cell carcinoma (BNOSCC) were observed to frequently have PET avid lymph nodes that were benign on final pathology from lymph node dissection. In this population, false lymph node positivity is likely a result of metabolic disorders and inflammation resulting from betel nut chewing. Since nodal involvement is critical in determining prognosis and adjuvant therapy per the National Comprehensive Cancer Network (NCCN) guidelines, this discrepancy leads to uncertainty in predicting survival outcomes and is confounding when a patient presents with a unilateral tumor but bilateral cervical hypermetabolism. Previous studies demonstrated PET/CT to be 76.5% to 94.5% specific compared to CT or MRI at 79.4% relative to pathological staging, with a false positive rate ranging between 10% and 16.7%. The literature reports PET/CT scans in head and neck squamous cell carcinoma patients overall to have a sensitivity of 86% to 98%, specificity of 92% to 93%, and a positive predictive value of 91%.

Methods: To compare, a series of 25 patients from 2011-2018 with T3 and T4 stage oral cavity tumors were reviewed. In this cohort, a series of proportions tests were completed to determine accuracy, sensitivity, specificity, and positive and negative predictive values relative to PET/CT imaging.

Results: After initial analysis, 36% of nodes overall were falsely positive on imaging. Patient-to-patient variability was high, with 9 patients demonstrating a 100% false positive rate. Sensitivity was 62.5% and specificity was 21%. The positive and negative predictive values were both 40%. There was no statistically significant correlation between tumor staging and nodal avidity.

Conclusions: Although the study sample size was small, the percentage of patients with BNOSCC with false positive nodal avidity is greater than the previously reported rate of false positivity with PET/CT imaging. The data set also suggests that as such, PET/CT findings in patients with BNOSCC may not be reliable in surgical or systemic medical treatment planning. Ongoing study will further elucidate the degree of false nodal positivity and will help to determine if PET/CT can be reliable for treatment planning in advanced-stage BNOSCC versus other imaging modalities that could potentially have better sensitivity/specificity for this targeted patient population. As more individuals from betel nut endemic areas migrate to the West, it is likely that radiologists and head and neck surgeons will face these diagnostic dilemmas in patients with associated malignancies. Therefore, knowledge of the aforementioned paradigms is critical in providing quality care for this patient population.

B075: MUCOSAL MELANOMA OF THE HEAD AND NECK REGION

- Lilah Kahloon, BS; Tanya Gupta, BA; Zhanxu Liu, MS; Maiying Kong, PhD; Reema Ishteiwy, MD; Neal Dunlap, MD; Christina Albert, BA; Devaughn Crawford, BA; Elizabeth Cash, PhD; Melanie Townsend, MD; University of Louisville School of Medicine

Mucosal melanoma of the head and neck is a rare and deadly disease. Treatment paradigms are shifting to include systemic agents in the form of immunotherapy. The role and timing of local therapy considering these new agents needs to be investigated. Currently, there is no staging system for mucosal melanomas despite its poor prognosis in comparison to cutaneous melanomas of the head and neck. Consideration of patient outcomes across different sequences of treatment options may allow for development of a standardized staging system for mucosal melanomas of the head and neck region.

The National Cancer Database was queried for patients over 18 years of age with mucosal melanoma of the head and neck. Cases to be included in this study were extracted according to histology (ICD-O 2 melanoma codes M872–M879). Review focused on treatment parameters, surgical characteristics, clinical and pathologic staging, as well as postoperative adjuvant treatment and overall survival. Additional factors such as treatment at an academic institution vs. non-academic institution and payer status were also considered. 1,857 patients were included in the analysis which examined association between treatment combinations, specific to their sequence related to immunotherapy, as it related to the overall survival of patients. A multivariate Cox proportional hazards model was used to identify factors and treatments associated with survival. Propensity score matching and log-rank test were also employed to examine treatment effectiveness between groups receiving different treatment patterns which provided control for all confounding variables.

Among all patients, 6.4% received immunotherapy only, 0.75% underwent surgery following immunotherapy, and 8.72% received immunotherapy after surgery. Most patients (69.95%) received surgery alone. In addition, 3.02% received radiation therapy after immunotherapy, 1.83% received immunotherapy after radiation therapy, and 9.26% were treated with radiation therapy alone. Across patients, those who received surgery showed a significantly longer median survival time of 37.2 months compared to those who received combinations not including surgery. Patients treated with only radiation saw the shortest median survival time of 9.46 months. In contrasting the four groups receiving surgery and immunotherapy, alone or in combination, a higher risk of mortality was found in patients who received immunotherapy alone compared to patients who received surgery alone. In contrasting the four groups receiving radiation and immunotherapy, alone or in combination, no significant differences were found. After using a propensity score matching method to examine addition of immunotherapy onto radiation or surgery, immunotherapy following or preceding radiation therapy had a trend to improve survival time when compared to radiation alone.

Our study revealed important trends in the effects of different treatment options for mucosal melanomas of the head and neck on patient survival. Inclusion of surgery as part of the treatment sequence appears to be an important factor in overall survival. Furthermore, the use of radiation therapy in isolation as treatment appears to lower survival outcomes. Our review

supports consideration of immunotherapy addition to radiation therapies in cases where surgical intervention is not favored or contraindicated, in order to maximize overall survival.

B076: TOWARD QUANTITATIVE MRI BIOMARKERS OF HEAD AND NECK LYMPHEDEMA AND FIBROSIS IN ORAL AND SUBMENTAL REGIONS OF INTEREST: POST HOC ANALYSIS OF THE MANTLE TRIAL - <u>Shitong Mao, PhD</u>[1]; Holly McMillan[1]; Abdallah S Mohammed[1]; Sara Ahmed, MD[2]; Renji He[1]; Yao Ding[1]; Sheila Buoy[1]; Jihong Wang[1]; Clifton D Fuller[1]; Katherine A Hutcheson[1]; [1]The University of Texas M.D. Anderson Cancer Center; [2]Baylor College

Importance Quantifying Head and Neck Lymphedema and Fibrosis (HN-LEF) is crucial in the investigation and management of this highly prevalent treatment sequelae in head and neck cancer (HNC). The HN-LEF grading system classifies physically palpable soft-tissue change categorically. Imaging biomarkers from MRI may serve to complement or validate HN-LEF when assessing the effectiveness of therapeutic interventions for toxicity profiles of patients.

Objective: To explore the relationship between 1) physical HN-LEF classification in submental and oral regions of interest (ROI) and the MRI T1- and T2-weighted signal intensity (SI) in close proximity regions, and 2) a novel HN-LEF score and MRI T1 and T2 structural volumes.

Design: Post hoc analysis of pilot single arm MANTLE trial (NCT03612531).

Setting: Single institution, NCI-designated comprehensive cancer center.

Participants: A total of 16 individuals (mean [SD] age, 68.28 [6.98] years; 3 [19%] female) enrolled in the MANTLE trial underwent MRI. All participants were disease-free at least two years post-radiotherapy with grade ≥2 fibrosis (in any cervical ROI) and dysphagia. Over a 12-week period, participants engaged in manual therapy sessions accompanied by concurrent standardized multiparametric, serial MRI examinations and palpation-based HN-LEF evaluations at 3-time points: baseline, post-manual therapy, and post-washout.

Exposures: The independent variable HN-LEF included its categorical classification (No LEF, A/B = edema, C= edema + fibrosis, D=fibrosis) and a novel metric (10-point scale) derived from the HN-LEF categories (type/severity classification).

Main Outcomes and Measures: The T1- and T2 MRI SI as well as structural volume was examined by Kruskal-Wallis tests by HN-LEF categories and the novel HN-LEF score. We hypothesized higher T2 SI in edema states, higher T1 SI in fibrotic states, and decreasing structural volume as the HN-LEF score increased.

Results: We identified a statistically significant difference in mean ranks among HN-LEF categories in relation to the MRI SI ($p < 0.05$, A/B and C are higher than D and No LEF for T1, and A/B is the highest for T2). Furthermore, six pairs of FOM volumes on T2-weighted MRI demonstrated a strong negative correlation ($p<0.05$) with the HN-LEF score at those sites: digastric vs. submental left ($r = -0.42$; 95% CI, -0.70~ -0.03), digastric vs. Intraoral left ($r = -0.41$; 95% CI, -0.69~ -0.02), genioglossus vs. Intraoral left ($r = -0.50$; 95% CI, -0.75~ -0.10), mylohyoid vs. Intraoral left ($r = -0.51$; 95% CI, -0.76~ -0.12),

mylohyoid vs. Intraoral right ($r = -0.42$; 95% CI, -0.71~ -0.01), tongue base vs. Intraoral left ($r = -0.47$; 95% CI, -0.74~ -0.07).

Conclusions and Relevance: This exploratory analysis provides hypothesis-generating data supporting further study of T2 SI as an imaging biomarker of edematous soft tissue states after RT in HNC. The inverse correlation between the novel HN-LEF scores and structural volumes points to the potential validity of this metric assuming structural volume diminishes as patients move from edema to fibrotic states. This study highlights the potential for enhancing the LEF quantification using imaging metrics, which might further aid in the early detection and precise measurement of lymphedema and fibrosis severity in post-radiation HNC patients.

B077: A MULTI-INSTITUTIONAL FEASIBILITY LEAD-IN TRIAL OF LYMPHATIC MAPPING WITH SPECT-CT FOR EVALUATING CONTRALATERAL DISEASE IN LATERALIZED OROPHARYNX CANCER USING 99M-TECHNETIUM SULFUR COLLOID - <u>LM Sarkis</u>[1]; C Yao[1]; A Hendler[2]; S Tzelnick[1]; M Au[3]; H Zhang[4]; A Eskander[5]; K Higgins[5]; D MacNeil[6]; A Hosni[7]; D Goldstein[1]; J de Almeida[1]; [1]Department of Otolaryngology-Head and Neck Surgery, Princess Margaret Cancer Centre/ University Health Network, University of Toronto, Toronto, Ontario, Canada; [2]Department of Nuclear Medicine, University of Toronto, Toronto, Canada; [3]Department of Otolaryngology Head and Neck Surgery, Hamilton Health Science Center, Hamilton, Ontario, Canada; [4]Faculty of Health Sciences, McMaster University; [5]Department of Otolaryngology-Head and Neck Surgery, Sunnybrook Health Sciences Centre, Toronto, Ontario; [6]Department of Otolaryngology - Head & Neck Surgery, Schulich School of Medicine & Dentistry, Western University, London, ON, Canada; [7]Radiation Medicine Program, Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, ON, Canada

Introduction: The standard treatment paradigm for oropharyngeal squamous cell carcinoma is radiotherapy to both the primary and cervical lymph nodes. Bilateral neck radiotherapy is common and is associated with xerostomia, dysphagia, and reduced QOL. Lymphatic mapping with radiotracer injections followed by SPECT-CT may be used to identify at risk drainage patterns and thus to tailor contralateral neck radiotherapy. We evaluated the feasibility of surgeon performed radiotracer injections followed by SPECT-CT for patients with lateralized oropharyngeal cancers across multiple institutions as part of a lead-in trial into a larger phase 3 randomized trial (SELECT trial).

Methods: A total of twelve adult patients were selected with lateralised oropharyngeal carcinoma (T1-T3) across four tertiary referral head and neck cancer centers who were planned for definitive or adjuvant radiotherapy and had no contralateral nodes on clinical exam or cross-sectional imaging. Patients subsequently underwent injection of 99-m Technetium Sulfur Colloid in 4-6 standard locations approximately 5mm away from the visible edge of the tumor. Patients then underwent static planar lymphoscintigraphy to verify tracer migration, followed by SPECT-CT acquired at 30 min +/- 15 min (optional) and 3 hours (+/-1 hour) (mandatory time-point) after injections to allow transit time to the contralateral neck. NASA task load index was used to measure surgeon comfort with injections (workload measured across six dimensions of mental demand, physical demand, temporal demand, effort, performance and frustration level).

Results: Twelve patients were enrolled in the trial (mean age: 60 years, M:F 11:1) , 6 (50%) with tonsil and 6 (50%) with tongue base primary tumors. Injections were done with local anesthesia in 7/12 (58%) (four with tonsil and three with tongue base) and general anesthesia in 5/12 (42%) (two with tonsil , three with tongue base) . Ten patients underwent SPECT-CT at 30 minutes and all 12 patients completed SPECT-CT at 3 hours. All patients tolerated the procedure, and all patients had successful lymphatic mapping imaging with no failed radiotracer migrations. Four patients (33%) had contralateral drainage (3 tonsil, 1 tongue base). Two of those patients (50%) had contralateral drainage on the delayed (3 hr) SPECT that was not present on the immediate (30 min) SPECT. Drainage was noted to level Ib, II, III, IV, V of the ipsilateral neck in 2/12 (17%), 11/12 (92%), 9/12(75%), 2/12 (17%) and 1/12(8%). Of the four patients with contralateral drainage, drainage was noted to level II in 4/4 (100%), and level III in one patient (25%). The median NASA task load index across all 12 patients was 23. There were no patients with a NASA task load index >50. There were no adverse events with injections.

Conclusion: Lymphatic mapping with SPECT-CT of lateralised oropharyngeal squamous cell carcinoma can be performed safely across multiple institutions allowing determination of lymphatic drainage pathways without significant side effects. Future phase 3 RCT (SELECT Trial) will compare SPECT guided management of the contralateral neck vs. bilateral neck radiotherapy in patients with oropharyngeal cancers not involving midline.

B078: INTER-RATER AGREEMENT IN THE INTERPRETATION OF EXTRANODAL EXTENSION OF METASTATIC SQUAMOUS CELL CARCINOMA - A MULTI-INSTITUTIONAL STUDY - LM Sarkis[1]; R Ghossein[2]; N Katabi[2]; R Gupta[3]; B Perez-Ordonez[4]; I Weinreb[4]; B Xu[2]; M Richardson[5]; S Smith[6]; J de Almeida[1]; [1]Department of Otolaryngology-Head and Neck Surgery, Princess Margaret Cancer Centre/ University Health Network, University of Toronto, Toronto, Ontario, Canada; [2]Memorial Sloan Kettering Cancer Center, New York, USA; [3]Chris O'Brien Lifehouse, Sydney, Australia; [4]Univeristy of Toronto, Toronto, Canada; [5]Medical University of South Carolina; [6]Toronto General Hospital

Introduction: In patients with head and neck squamous cell carcinoma, extranodal extension (ENE) [synonyms: extracapsular spread (ECS) or extracapsular extension (ECE)] has been shown to be a negative prognostic factor and associated with poor overall survival, and increased risk of distant metastases.[i],[ii] Further to this, the presence of extranodal extension guides adjuvant therapy and generally confers the need for systemic therapy. There is however variability amongst pathologists in the interpretation of both the presence and extent of extranodal extension,[iii] and a paucity in the literature to provide diagnostic criteria for ENE. The purpose of this study is to assess inter-rater agreement in both diagnosis and extent of ENE in head and neck squamous cell carcinoma amongst head and neck pathologists.

Methods: Representative slides from 50 patients exhibiting various extents of ENE obtained from archived histopathology slides of patients who had undergone neck dissection for head and neck squamous cell carcinoma were selected and reviewed by eight head and neck pathologists across four tertiary head and neck institutions. Digital slides were de-identified, unmarked, shared electronically and scored by each rater into categories (no ENE, minor ENE, major ENE, ENE with undetermined extent) to determine inter-rater agreement. Agreement between raters was measured using the Fleiss Kappa statistic and classified as follows (< 0 : poor, 0-0.2 : slight, 0.2-0.4 : fair, 0.4 - 0.6 :

moderate, 0.6-0.8 : substantial, 0.8 -1.0 : almost perfect).

Results: Inter-rater agreement for the diagnostic presence of ENE was moderate (kappa=0.49). For minor ENE, the inter-rater agreement was only fair (kappa=0.36) and for the presence of major ENE the inter-rater agreement was moderate (kappa = 0.54). Excluding indeterminate cases and no ENE (n=27), agreement for minor and major ENE were both moderate (kappa = 0.42, 0.43, respectively). A unanimous decision regarding extent of ENE amongst all eight pathologists was obtained in 7/50 (14%) patients.

Conclusion: These findings of only fair to moderate consistency in the histopathological diagnosis and characterisation of ENE across multiple high volume tertiary Head and Neck centres suggest the imperative need for a consensus guideline amongst pathologists in both processing of lymph nodes and interpretation.

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B079: NOVEL IMMUNOTHERAPEUTICS AND ANAPLASTIC THYROID CARCINOMA: ANALYZING NATIONAL SURVIVAL OUTCOMES - Richard Bavier, MD; Bao Y Sciscent, BS; Mohamad Saltagi, MD; Neerav Goyal, MD, MPH, FACS; David Goldenberg, MD, FACS; Department of Otolaryngology-Head and Neck Surgery, Milton S. Hershey Medical Center

Importance: Recent developments in targeted immunotherapies have shown efficacy in treating patients with Anaplastic Thyroid Carcinoma (ATC). However, due to the rarity of the disease process and the limitations of immunotherapeutics, current literature has largely been limited to case series.

Objective: To determine if immunotherapeutic treatment is an independent predictor of survival in ATC and characterize which patients are receiving immunotherapy.

Design, setting, participants: The National Cancer Database was retrospectively queried to identify all cases of ATC from 2004-2017. Data analysis was performed from October 1, 2023 to November 1, 2023.

Main Outcomes and Measures: The primary aim was to assess whether use of immunotherapies is an independent predictor of survival in patients with ATC. The secondary aim was to characterize the socioeconomic and logistical factors associated with patients receiving immunotherapy.

Results: A total of 5,450 patients with ATC were identified of which 59.2% (n=3225) were female and the median age at

diagnosis was 70 years (11-90 years). Of the 5,450 patients, 52 received immunotherapy. Median survival for all patients was 4.3 +/- 0.11 months. Compared to patients who did not receive immunotherapy, patients who underwent immunotherapy had an increased median survival (6 +/- 1.83 months vs. 4.3 +/- 0.11 months, p= 0.006). Other independent predictors of survival on univariate analysis included younger age (p < 0.001), race (p = 0.012), Charlson Deyo Comorbidity Score (CDCC) (p <0.001), treatment with surgery, chemotherapy or radiation (p<0.001), treatment at a high-volume institution (p <0.001), and treatment at an academic/integrated care network institution. When controlling for all significant demographic and clinicopathologic factors, immunotherapy treatment was an independent predictor of survival (HR 1.71; 95% CI [1.23-2.39] p = 0.002). On evaluation of socioeconomic and logistical factors associated with immunotherapy treatment, the only predictor of immunotherapy treatment was treatment at a higher volume facility (p =0.024). A high-volume facility was defined as those seeing above the observed average – six cases during the study period. Race, gender, age, facility type, CDCC, or insurance status were not associated with receiving immunotherapy.

Conclusions and Relevance: Treatment of ATC with immunotherapy is an independent predictor of survival. With the availability of immunotherapy trials, referrals to higher volume centers may convey a survival advantage.

B080: DOES LYMPH NODES DISSECTION OR NECK IRRADIATION MITIGATE THE EFFECT OF IMMUNOTHERAPY FOR VERY ADVANCED OR METASTATIC HNSCC? - Liyona Kampel, MD, PhD; Daniel Halpern, MD; Gilad Horowitz, MD; Jobran Mansour; Inbal Finkel, MD; Nidal Muhanna, MD, PhD; Anton Warshavsky; Tel Aviv Sourasky Medical Center

Background: Immunotherapy has brought new hope to patients with very advanced head and neck squamous cell carcinoma (HNSCC), but recent trials have shown modest benefit to patients with recurrent or metastatic disease. Neck dissection (ND) or irradiation administered before or concurrently with immunotherapy were shown to impair its effectiveness in pre-clinical studies. In this study we aimed to evaluate real life experience by assessing whether ND or neck irradiation that preceded immunotherapy were related with poorer treatment response or survival outcomes.

Materials and Methods: The medical records of all patients with HNSCC who were treated with immunotherapy (pembrolizumab, nivolumab or cemiplimab) since July 2013 until July 2023 were retrospectively reviewed. Excluded were patients diagnosed with another malignancy other than HNSCC or cutaneous primary. Demographics and disease variables were recorded, including combined positive score (CPS) as well as all therapies administered since diagnosis. Outcome measures included response to immunotherapy (complete response, CR; partial response, PR; stable disease, SD or disease progression, DP), 2-year disease free survival (DFS) and 2-year overall survival (OS).

Results: Eighty patients were included in the study. All patients had locally advanced disease. Forty-one patients (51%) were not amenable to surgical resection or had metastatic disease. Nineteen patients were treated with immunotherapy as the first-line therapy, and 61 patients received immunotherapy as the second- or third-line. The group of patients who had previously undergone ND or treated with neck irradiation did not demonstrate worse outcomes in terms of treatment response,

DFS and OS compared to the group that did not receive any nodal treatment. These groups were similar in terms of disease extent and demographic characteristics except for younger age of patients who underwent ND or irradiation (mean: 64 years vs. 72 years, P=0.019). Cox regression analysis found older age as the only factor related to worse survival, when adjusting for metastatic disease and previous ND or irradiation. CPS<1 was predictive for DP, however only a trend toward worse OS was observed (mean survival 17 months compared to 30 months, P=0.156). Patients who received immunotherapy as the first-line therapy had significantly worse 2 years OS (37% vs. 56%, P = 0.016), but no difference in 2 years DFS was observed.

Conclusions: In this study we found that nodal dissection or neck irradiation that preceded immunotherapy for high risk, recurrent or metastatic HNSCC did not confer worse survival outcomes. Poorer outcomes were observed in patients treated with immunotherapy as first line and CPS<1.

B081: COMPLETE TUMOR RESECTION REVERSES NEUTROPHILIA-ASSOCIATED SUPPRESSION OF SYSTEMIC ANTI-TUMOR IMMUNITY - Amir M Kaskas; Paul Clavijo, PhD; Jay Friedman, PhD; Marco Craveiro, PhD; Clint T Allen, MD; Head and Neck Section, Surgical Oncology Program, National Cancer Institute, National Institutes of Health, Bethesda, MD

Neoadjuvant immune checkpoint blockade for head and neck squamous cell carcinoma (HNSCC) is yielding promising results. Neutrophilic cells that infiltrate HNSCC are immunosuppressive, and their increased frequency associates with a lack of pathologic response to neoadjuvant immunotherapy. Although increased peripheral neutrophilia also associates with lack of response to immune checkpoint blockade therapy in the relapsed setting, the contribution of peripheral neutrophils to systemic anti-tumor immunity is poorly understood. Here, we investigated whether the peripheral accumulation of neutrophils that occurs with tumor progression in immunocompetent mice contributes to systemic immunosuppression, and if complete primary tumor surgical resection could reverse neutrophil-induced systemic anti-tumor immune suppression. A syngeneic murine oral cancer model was used to study the role of neutrophils in systemic anti-tumor immunity in tumor-bearing and tumor-resected mice. Proteomic and functional immune assays studying plasma cytokine concentration, peripheral immune frequencies, and systemic anti-tumor immunity with and without complete primary tumor resection were used. We observed that Ly6G+ neutrophils accumulated in the periphery of mice as primary tumors progressed, and that this accumulation associated with plasma G-CSF concentration – a cytokine critical for mediating myelopoiesis. These circulating neutrophils were functionally immunosuppressive in ex vivo T cell suppression assays. Complete resection of the primary tumor reversed peripheral G-CSF accumulation and the observed peripheral neutrophilia and resulted in enhanced systemic anti-tumor immunity in mice. The observed enhancements of systemic anti-tumor immunity seen after tumor resection were reproduced by selectively depleting neutrophils in the periphery of tumor-bearing mice, validating the ability of peripheral neutrophils to mediate suppression of systemic anti-tumor immunity. Together, these data indicate that surgical resection itself may allow a more immune permissive periphery and directly improve a HNSCC patient's anti-tumor immunity following neoadjuvant immunotherapy. Our study provides critical context for the role of immunosuppressive neutrophils in the periphery and provides additional support for the

continued study of neoadjuvant immunotherapy, specifically for patients with newly diagnosed HNSCC unrelated to HPV.

B082: VALIDATION OF ARTIFICIAL INTELLIGENCE PREDICTION MODEL FOR HEAD AND NECK CANCER IMMUNOTHERAPY RESPONSE - Andrew S Lee, Medical Student; Karena Zhao; Cristina Valero, MD, PhD; Luc Morris, MD, MSc, FACS; Memorial Sloan Kettering Cancer Center

Introduction: Although immune checkpoint blockade (ICB) has improved outcomes in patients with recurrent and/or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC), identifying patients likely to benefit from ICB remains a challenge. A previously developed model using a random forest algorithm showed promising results to predict ICB response using 16 clinical, laboratory, and genomic features in a pan-cancer development cohort. However, its applicability in HNSCC is largely unknown due to the small proportion of HNSCC patients in the development cohort. In this study, we perform a validation of a machine learning ICB prediction model using a HNSCC-only cohort, measuring discrimination, calibration, and survival prediction.

Methods: A validation set of 96 patients with recurrent/metastatic HNSCC who had received at least 1 dose of anti-PD-1, anti-PD-L1, or anti-CTLA-4 ICB at our tertiary care center from 2015 to 2019 was retrospectively identified following IRB approval. Two random forest models were validated: RF16 and RF11, which use 16 and 11 input features, respectively (Figure). Features included in RF11 were age, sex, body mass index, tumor stage at time of first ICB infusion, cancer type, history of chemotherapy before ICB, ICB agent, blood albumin, platelets, hemoglobin, neutrophil-to-lymphocyte ratio, tumor mutational burden (TMB), fraction of copy number alterations, HLA-I evolutionary divergence, loss of heterozygosity status in HLA-I, and microsatellite instability status. Response to ICB was based on Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Patients who exhibited complete response or partial response were classified as responders; patients who experienced stable disease or progressive disease were classified as non-responders. Survival was estimated using the Kaplan-Meier method and Cox proportional hazards.

Results: In the validation cohort of 96 R/M HNSCC patients, the RF16 and RF11 classifiers were used to give ICB response probabilities. An optimal cutpoint was determined to classify patients into predicted responder (PR) or predicted non-responder groups. RF16 and RF11 achieved moderate discrimination, defined by area under receiver operating curve (AUROC) (RF16 AUROC=0.60, RF11 AUROC=0.65, TMB AUROC=0.57). The models' predictions show adequate 'weak calibration', assessed by calibration slope and intercept. (RF16 calibration slope=1.10, intercept=0.33; RF11 calibration slope=1.98, intercept = 0.17) A perfectly calibrated model would have a slope of 1 and intercept of 0.

The RF11 model was able to accurately predict OS and PFS in the validation cohort, with hazard ratios for OS and PFS of 0.53 (95% CI 0.29–0.99, p=0.045) and 0.49 (95% CI 0.27–0.87, p=0.016), respectively.[ML1]

Conclusion: Our data validates a model that could aid clinical decision making and patient risk stratification. As the availability of data improves and new markers of tumor immunology are discovered, similar prediction models are expected to improve upon this work to assist in providing personalized therapy.

Figure: Schematic representation of validation of prediction model.

B083: "THE PROGNOSTIC SIGNIFICANCE OF NEUTROPHIL-TO-LYMPHOCYTE RATIO IN HEAD AND NECK SQUAMOUS CELL CARCINOMA PATIENTS RECEIVING NEOADJUVANT IMMUNE CHECKPOINT INHIBITORS" - Pablo A Llerena; Kathryn Nunes; Praneet C Kaki; Eric Mastrolonardo, MD; Annie Moroco, MD; Joseph M Curry, MD; Jennifer M Johnson, MD, PhD; Adam J Luginbuhl, MD; Thomas Jefferson University
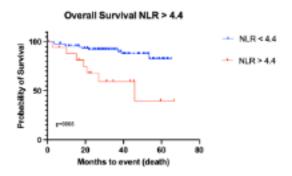
Introduction: The Neutrophil-to-Lymphocyte Ratio (NLR) is a well-known prognostic factor for patients with advanced cancers undergoing treatment with immune checkpoint inhibitors (ICI). NLR was derived from the concept of inter-relationship between inflammation and cancer immune surveillance. Neutrophils are associated with inflammatory response and inhibition of T-lymphocytes. However, there are limited studies that have investigated its prognostic role in patients with head and neck squamous cell carcinoma (HNSCC) who are undergoing immune checkpoint inhibitor (ICI) therapy. Our study aims to evaluate NLR as an independent predictor of Overall Survival (OS) and Progression-Free Survival (PFS) in HNSCC patients.
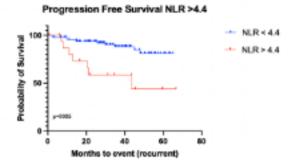
Method: We conducted a retrospective analysis of 110 patients from 2017 to 2022 who participated in three neoaduvant trials: durvalumab ± metformin (n=33), nivolumab ± tadalafil (44), or nivolumab ± indoleamine 2,3-dioxygenase (n=36). The pre-treatment NLR was calculated using absolute neutrophil and absolute lymphocyte counts obtained at neoadjuvant ICI initiation. Patients were treated definitive and adjuvant treatment based on standards of care. Overall survival (OS) and progression-free survival (PFS) were assessed with Kaplan-Meier analysis. Predictors of OS and PFS were assessed using multivariate cox regression and recursive partitioning tree, while accounting for pre- treatment clinical factors (NLR, age, sex smoking, BMI and P16 status, clinical T/N stage, AJCC status,)

Results: A total of 113 patients were included in this analysis at the initiation of ICI, patient demographics were as follows: the median age of patients was 61 years (32-86), the median BMI was 29 (19-50), 56% were P16+, 25% were smokers (continued or former), and a median NLR of 2.7 (1.0- 9.0). Through Kaplan-Meir analysis we found that patients with an NLR > 4.4 had a worse OS and PFS, 5 years after treatment: [p <0005,HR:4.6 (95% CI,1.1-19.6)], [p=.0005,HR:4.6 (95%, CI

1.0:12.0)], respectively. After adjusting for gender, age, P16 status, smoking history, clinical T and N stages, as well as the AJCC status, we observed that an NLR > 4.4 before induction was independently associated with worse OS [p < 0.0001, HR 1.3; (95% CI 1.44-1.5). Additionally, an NLR > 4.4 [p < 0.0001, HR:1.4 (95% CI 1.2-1.5)], advanced clinical T stage (T3/4) [p =0.02, HR 4.7; 95% CI 1.3-16.3)], BMI < 24 [(p = 0.04, HR 1.1 (95% CI1.0-1.2)] were also independently associated with worse PFS.

Conclusion: In the evolving era of checkpoint inhibition, we need to look for signals that could indicate response or overall event free survival. NLR is a readily available ratio that speaks to the fitness of the peripheral immune complement. These results suggest that high NLR is associated with worse OS and PFS in patients treated with neoadjuvant ICI followed by standard of care for HNSCC. Prospective analysis is needed to validate this peripheral signal and to establish its efficacy to predict an association with ICI treatment vs global response to all treatments.

Overall Survival NLR > 4.4

Progression Free Survival NLR >4.4

B084: ASSOCIATION BETWEEN SURVIVAL OUTCOMES AND PATHOLOGIC TREATMENT EFFECT FOR PATIENTS WITH HEAD AND NECK SQUAMOUS CELL CARCINOMA TREATED WITH NEOADJUVANT IMMUNE CHECKPOINT INHIBITORS - Annie Moroco, MD; Kathryn Nunes; Pablo Llerena; Angela Alnemri, MD; Jennifer Johnson, MD, PhD; Rita Axelrod, MD; Madalina Tuluc, MD; Stacey Gargano, MD; Tingting Zhan, PhD; David Cognetti, MD; Joseph Curry, MD; Adam Luginbuhl, MD; Jefferson

Introduction: The utilization of immune checkpoint inhibitors (ICI) in patients with head and neck squamous cell carcinoma (HNSCC) during the preoperative window of opportunity has been exploited as a means to evaluate response to treatment. Pathologic treatment effect (pTE) varies among patients

receiving ICI with cutoffs for nonresponders, partial responders and complete responders decided without significant clinical impact. We sought to assess survival outcomes related to pTE in our cohort of HNSCC patients undergoing neoadjuvant ICI.

Methods: A pooled analysis was performed on two neoadjuvant clinical trials from July 2017 to January 2022: NCT03238365 (nivolumab ± tadalafil) and NCT03854032 (nivolumab ± indoleamine 2,3-dioxygenase). pTE was calculated independently by two pathologists and scored as a percentage: area of treatment response relative to total tumor surface area. Overall survival (OS) and progression-free survival (PFS) were assessed with Kaplan-Meier analysis. The association of pTE was determined using recursive partitioning to build a regression tree for both OS and PFS, and these recursive partitioning leaves were used to plot Kaplan-Meier survival curves.

Results: A total of 79 patients were included in the analysis. At the time of trial initiation, patients were mean age of 62.6 years, with the cohort primarily white (94%), male (89%) and current/former smokers (62%). Over half (43 patients, 54%) had oropharyngeal primary tumors, of which 39 were HPV-mediated. The remaining primary sites included 35% oral cavity, 5% larynx, 4% hypopharynx, and 1% sinonasal. Mean follow-up length for the cohort was 3 years (range 1-5.7 years). Using recursive partitioning, a pTE cutoff of 55% and 57% was determined for OS and PFS, respectively. Patients with pTE ≥55% had the highest OS, with only 1 death recorded (p=0.041). Similarly, patients with pTE ≥57% had improved PFS, with no observed disease progression (p=0.012). Distribution of HPV-mediated disease was similar between cohorts.

Conclusion: These results suggest that pathologic response to neoadjuvant ICI in HNSCC patients is associated with improved OS and PFS. Survival curves assessing patients with clinical stage 4 disease were not significantly different in OS or PFS as compared to stage 1 disease. Although this study was not powered for this analysis, further investigation with combined cohorts of patients treated with neoadjuvant ICI may demonstrate improved survival in advanced disease.

B085: EVALUATING RACIAL DISPARITIES IN IMMUNE CHECKPOINT INHIBITOR SURVIVAL AND AUTOIMMUNITY IN HEAD AND NECK CANCER - Kathryn L Nunes, BA; Shreya Mandloi, BS; Pablo Llerena, BS; Annie Moroco, MD; Eric Mastrolonardo, MD; David M Cognetti, MD; Adam J Luginbuhl, MD; Joseph M Curry, MD; Thomas Jefferson University

Introduction: Over the past decade, immune checkpoint inhibitors (ICIs) have emerged as a promising treatment for head and neck cancer. Racial disparities surrounding ICI use, including access and treatment response, have been reported. Recent studies have suggested these racial inequities in ICI access and effectiveness also exist in head and neck cancer, however current literature is largely limited to retrospective studies with small population sizes. There is a paucity of literature comparing racial disparities in survival outcomes of head and neck cancer patients treated with ICI. This large database study seeks to understand racial inequities in ICI outcomes for head and neck cancer patients.

Methods: The TriNetX US Collaborative Network database was queried for patients >18 years-old with a diagnosis of head and neck cancer that were treated with ICIs (Durvalumab, Nivolumab, Ipilimumab, and Pembrolizumab). Cohorts were

defined by race: non-Hispanic White, Black, and Asian. Race cohorts were 1:1 propensity score matched (PSM) for comorbidities (hypertensive heart disease, ischemic heart disease, asthma, chronic obstructive pulmonary disease, diabetes, alcohol use and nicotine use), oncologic stage (AJCC stage and TNM stage) and chemoradiation treatment. Demographic differences in cohorts were evaluated prior to matching. Following cohort matching with PSM, overall survival and rates of autoimmunity were assessed at 5 years.

Results: 6,623 non-Hispanic White, 594 Black, and 303 Asian HNC patients treated with ICI were identified. At a baseline, the black patient cohort was significantly younger at index, with significantly higher stage disease as well as higher comorbid rates of ischemic heart disease, asthma, alcohol and nicotine use compared to the non-Hispanic White cohort (p<0.01). The geographic distribution of HNC patients receiving ICI therapy were as follows: White equally distributed, majority of Black patients were treated in the south (63%), majority of Asian patients were treated in the west (49%). With PSM, there was no significant difference in overall survival between non-Hispanic white and Asian patients ([OR: 1.1 (0.7-1.7)]. In contrast, black patients were associated with significantly lower survival rates compared to non-Hispanic white and Asian patients [HR: 1.3 (1.1, 1.5), 1.4 (1.1,1.8), respectively]. The white and Asian patient cohorts had significantly higher rates of autoimmune conditions after ICI therapy compared to black [OR: 2.0 (1.4,2.8), 2.2 (1.4,3.5), respectively].

Conclusion: This study represents the most extensive analysis of racial disparities on ICI outcomes in HNC patients. This study found that black patients treated with ICIs had decreased survival rates at 5 years compared to non-Hispanic White and Asian patients. This disparity persisted following PSM, which matched cohorts for comorbidities, oncologic stage and adjuvant therapy. After PSM, Black patients also had significantly lower rates of autoimmunity after ICI therapy. Further investigation is required to elucidate the underlying etiologies of these trends. Noted differences in survival may be a reflection of geographic practice differences, access to care and/or socioeconomic status. Understanding the barriers to head and neck cancer care is important to improve health equity and overall health of our population.

B086: DEVELOPMENT AND VALIDATION OF A PROGNOSTIC SIGNATURE FOR OVERALL SURVIVAL USING PERIPHERAL BLOOD BIOMARKERS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA TREATED WITH IMMUNE CHECKPOINT INHIBITORS - Cassie Pan[1]; Qian "Vicky" Wu[2]; Jenna Voutsinas[2]; Kevin Ng[2]; Armita Norouzi[1]; Jeffrey J Houlton[3]; Brittany Barber[1]; Zain Rizvi[1]; Emily Marchiano[1]; Neal Futran[1]; George E Laramore[1]; Jay J Liao[1]; Upendra Parvathaneni[1]; Neil Panjwani[1]; Renato G Martins[4]; Cristina P Rodriguez[1]; [1]University of Washington; [2]Fred Hutchinson Cancer Research Center; [3]Head and Neck Specialists, Charleston, SC; [4]Virginia Commonwealth University

Background: We previously showed that in head and neck squamous cell carcinoma (HNSCC) treated with immune checkpoint inhibitors (ICIs), pretreatment higher lactate dehydrogenase (LDH) and absolute (abx) neutrophils as well as lower percent (%) lymphocytes correlated with worse overall survival (OS). Using these peripheral blood biomarkers (PBBMs), we developed a prognostic signature for OS risk stratification in HNSCC treated with ICIs. We then validated our signature in an independent cohort.

Methods: We randomly split our institutional dataset of recurrent/metastatic HNSCCs treated with ICIs (n=151) into training (n=100) and testing (n=51) datasets. Using the training data, we built an OS multivariable Cox regression model with LDH, % lymphocytes, and abx neutrophils and adjusted for ECOG, p16-status, and smoking as confounders. Combined proportion score (CPS) was not included as it had not been routinely collected. The continuous risk score = $\beta1*X\_LDH + \beta2*X\_\%lymphocytes + \beta3*X\_abxneutrophils$ was calculated based on estimated coefficients from the Cox model and 3 PBBMs. We trichotomized patients into risk groups using a grid search maximizing score test statistics from the Cox model to identify optimal cutpoints ($\theta1$, $\theta2$) defining low-risk (risk score$\leq\theta1$), intermediate-risk ($\theta1$$\theta2$). Kaplan-Meier OS curves were generated by risk group. We validated the continuous risk score and trichotomized signature in the testing data by Cox regression. Using an independent cohort as the external validation set (n=54), we validated the trichotomized signature by Cox regression.

Results: Training and testing datasets showed no significant differences in age, sex, race, smoking, alcohol, Charlson comorbidity index, p16-status, ECOG, or PBBMs. From the training data, the OS risk score = $1.2431*log10(LDH) - 1.9464*log10(\%\_lymphocytes) + 0.473*log10(abx\_neutrophils)$. Optimal risk score cutpoints were $\theta1$=0.401 and $\theta2$=1.029, resulting in 21 low-risk, 44 intermediate-risk, and 35 high-risk patients, with Kaplan-Meier curves for the trichotomized signature shown in Figure 1A. Testing dataset risk scores were then calculated and trichotomized into risk groups, resulting in 7 low-risk, 24 intermediate-risk, and 20 high-risk patients; Kaplan-Meier curves showed clear separation of the high-risk group but some overlap between low and intermediate-risk groups (Figure 1B). Adjusting for ECOG, smoking, and p16-status in the testing group, higher risk scores correlated with worse OS (HR 2.08, [95%CI 1.17-3.68], p=0.012). The prognostic signature was then evaluated in an independent cohort. There were no significant clinicodemographic differences across the training, testing, and independent datasets, except that ICIs were more frequently first-line therapy in the independent dataset. Trichotomizing risk groups using the previously determined cutpoints was borderline significant (p=0.068), with Kaplan-Meier curves showing the low-risk group with best OS and some overlap between intermediate and high-risk groups (Figure 1C).
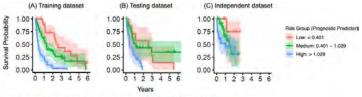

Figure 1. Kaplan-Meier estimates on OS by optimal cutpoints in each dataset

Conclusions: We developed a prognostic biomarker signature for OS based on previously identified PBBMs for HNSCC treated with ICIs. Validation of the prognostic signature in both the testing and independent cohorts were promising, although limited by sample size. This prognostic model may aid in identifying patients less likely to benefit from ICIs and warrants validation in a larger cohort receiving first-line ICIs as well as correlation with CPS biomarker.

B087: THE IMPACT OF NEOADJUVANT IMMUNOTHERAPY ON ADVANCED, RESECTABLE PERI-AURICULAR CUTANEOUS SQUAMOUS CELL CARCINOMA: A MATCHED COMPARISON

- David Z Allen, MD[1]; Neil D Gross, MD[2]; Marc-Elie Nader, MD[2]; Renata Ferrarotto, MD[3]; Moran Amit, MD, PhD[2]; Priya Nagarajan, MD[3]; Paul W Gidley, MD[2]; [1]The University Of Texas Health Science Center At Houston; [2]Department of Head and Neck Surgery, Division of Surgery, University of Texas MD Anderson Cancer Center, Houston, TX, USA.; [3]Department of Head and Neck Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX USA

Introduction: The standard-of-care for advanced periauricular cutaneous squamous cell carcinoma (CSCC) is surgery and adjuvant radiation therapy. Neoadjuvant immunotherapy has recently demonstrated high pathologic response rates in resectable CSCC, offering the potential for function-preserving surgery in selected cases. In this study, we aim to compare the oncologic outcomes of patients treated with neoadjuvant immunotherapy and surgery for advanced periauricular CSCC to those of age and stage-matched patients treated with standard-of-care up-front surgery.

Methods: Single-institution, retrospective review of patients with advanced periauricular cSCC treated with neoadjuvant immunotherapy followed by surgery versus historic controls treated with up-front surgery from the years 2005-2023. Patients with pathologically proven CSCC involving the external auditory canal treated with curative intent surgery were eligible for inclusion. Demographic, tumor, and treatment variables were extracted from the electronic medical record. The primary variables obtained were disease-free survival (DFS), recurrence-free survival (RFS) and overall survival (OS). Survival probabilities were estimated using the Kaplan-Meier estimate.

Results: The study included 79 patients, of which 20 received neoadjuvant immunotherapy and were age and stage-matched to 59 patients who underwent up-front surgery. Disease staging was as follows: T1/T2=37 (47%), and T3/T4=42 (53%). 20 patients had recurrent disease at presentation, equally distributed between the two groups. The up-front surgery group had a longer median follow-up (63.4 months) than the neoadjuvant immunotherapy group (26.4 months, p < 0.05). 52 patients (85%) in the up-front surgery group received post-operative radiation therapy, compared to 8 (40%) in the neoadjuvant immunotherapy group (p-value = 0.01). DFS favored the immunotherapy group at 2 years (77% vs. 62%) and 4 years (67% vs. 51%; both p-values < 0.05). RFS also favored the immunotherapy group at 2 years (77% vs. 63%) and 4 years (68% vs. 52%; both p-values < 0.05). Median OS was 5.5 years (4.59-11.5) with no significant differences between the two groups (HRadjusted 0.56, 95% CI = 0.17-1.88). Patients who presented with recurrent disease had worse OS (56 months v. 137 months, HRadjusted 2.23, 95% CI = 1.14-4.4, p-value < 0.05).

Discussion: Neoadjuvant immunotherapy has showed improved survival outcomes in patients with advanced, resectable peri-auricular cSCC. Additionally, this approach has significantly reduced the number of patients requiring radiation. These promising findings underscore the importance of including this patient cohort in upcoming randomized trials.
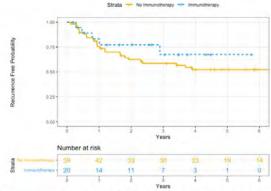

Figure 1. Kaplan-Meier estimates of Recurrence Free Survival in the total cohort of patients with advanced peri-auricular CSCC compared with those who were treated at MD Anderson with neoadjuvant immunotherapy and those who were not. Associated risk table is depicted.

B088: CHARACTERISTICS INFLUENCING DISTANT METASTASIS IN OLFACTORY NEUROBLASTOMA: A RETROSPECTIVE COHORT ANALYSIS -

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Introduction: Distant metastasis (DM) is a frequent occurrence in olfactory neuroblastoma, with a latency of up to 15 years. However, the risk factors are poorly understood. We aim to assess the long term incidence of DM, and to identify both predicative and ameliorative factors.

Methods: Patients with olfactory neuroblastoma treated at a tertiary institution from 1980-2023 were identified. Demographic information, along with patient, tumor, and treatment characteristics were analyzed. The primary outcome was Distant Metastasis-Free Survival (DMFS), and survival probabilities were obtained using the Kaplan-Meier method.

Results: A cohort of 99 patients were identified. The majority were male (64%), with a median age of 51 year. The overall incidence of DM was 32% at a median of 13.6 years after presentation. The majority of patients were T3-T4 (72%), which was associated with worse DMFS compared to T1-2 (Median DMFS 13.3 years v. median not reached; p < 0.05, Figure 1). Of the 77 patients with Hyams scores, 39% had a score of 3-4, and 61% had a score of 1-2. Patients with Hyams grades above 2 had a worse overall DMFS (Median DMFS 13.6 v. median was not reached; 1-4 years DMFS 86% v. 100%; 5-6 years DMFS 80% v. 100%; p < 0.05; Figure 2). Patients were Kadish A (12%), B (44%) and C (44%). Higher Kadish scores was associated with lower DMFS (5-year DMFS 100% v. 95% v. 63%, p < 0.05). Dural involvement was associated with shorter DMFS (DMFS 1-4 years 94% v. 79%; DMFS 5+ years 91% v. 79%; p < 0.05; HRadjusted 3.49, 95% CI 1.27-9.65, p < 0.05, Figure 3). Patients who received chemotherapy had lower DMFS (HRadjusted 3.32 1-11, p < 0.05). Patients treated with radiotherapy to the neck had a better DMFS throughout years 1-4 (100% v. 85%; p < 0.05) and years 5-6 (88% v. 71%; p < 0.05). However, the overall DMFS was not significantly different, possibly related to the small sample size (HRadjusted 1.57, 95% CI 0.46-5.36, p = 0.5).

Conclusions: Distant metastasis occurred in 32.6% of patients, with a longer median interval between initial diagnosis to recurrence than previously reported. Dural involvement, advanced T stage, higher Hyams and Kadish scores were associated with shorter DMFS. While radiation to the neck did not have an overall change in DMFS, there was a short term protective effect. These findings may stratify patients for long term follow up, and inform further studies that reduce the long term morbidity of this disease.

Figures:

Figure 1. DMFS compared to T stage.

Figure 2. DMFS compared to Hyams Grade

Figure 3. DMFS compared to Dural Involvement.

B089: MULTIFACTORIAL ASSOCIATIONS OF INDIVIDUAL-LEVEL AND COMMUNITY-LEVEL SOCIAL DETERMINANTS ON SKULL-BASE SQUAMOUS CELL CARCINOMA PROGNOSIS IN THE US - Rishabh Sethia, MD[1]; David J Fei-Zhang, BA[2]; Larry W Wang, BA, MSc[2]; Jill N D'Souza, MD[3]; Daniel C Chelius, MD[4]; Anthony M Sheyn, MD[5]; Jeffrey C Rastatter, MD, MS[1]; [1]Ann & Robert H. Lurie Children's Hospital of Chicago; [2]Northwestern University - Feinberg School of Medicine; [3]Louisiana State University Health Sciences Center - School of Medicine; [4]Texas Children's Hospital; [5]St Jude Children's Research Hospital

Introduction: Prior head-neck squamous cell carcinoma (HNSCC) literature have examined the roles of social determinants of health (SDoH) in promoting cancer disparities. These include socioeconomic status measures of income level and education, being of minoritized racial-ethnic groups, insurance status, individual behaviors, and others. However, these SDoH studies are constrained by low sample sizes while only assessing narrow scopes of SDoH, which limit their generalizability in understanding the confounding interactions of varied SDoH in real-world contexts. Furthermore, less inquiry has been made specifically within the context of skull-base squamous cell carcinomas (SBSC). Therefore, we sought to characterize how a nationwide, contemporary cohort of patients diagnosed with SBSC have differential outcomes through multifactorial analyses of widely varying SDoH, including the utility of the Yost Index, a robust, census-level composite of many SES-measures, alongside other varied community- and individual-level sociodemographic factors.

Methods: In this retrospective cohort study, adult patients (aged 20+ years) diagnosed with SBSC between 2010-2018 were obtained through the specially authorized head and neck cancer database from the National Cancer Institute-Surveillance, Epidemiology, and End Results Program (SEER). Age-adjusted, multivariate regressions were conducted with

covariates of individual sex & race-ethnicity (Non-Hispanic White as the reference against Black, Hispanic, Asian and Pacific Islander, Native American, and Unknown), alongside census-level rurality-urbanicity (where being of urban environments was the reference) and Yost-SES-index score (combination of 7 measures of education, housing, income, employment measures, separated into quintiles, with highest-SES-quintiles set as reference level) for outcomes of tumor staging (Stage I-III as reference), overall survival, 3-year & 5-year all-cause mortality, and disease-specific mortality.

Results: Across 6,700 SBSC adult patients, the most represented clinicodemographic characteristics were being of 45-64 years of age (n=3127, 46.7%), male sex (n=4943, 73.8%), and non-Hispanic White race/ethnicity (n=3669, 54.8%). For Yost-SES-Index, community-level low-middle-SES was well-represented (n=3256, 49%). A majority of SBSCs were primarily located in nasopharyngeal (n=4383, 65.4%) and orbital-base sites (n=1862, 34.4%). Overall, unique prognostic associations with different SDoH-factors were observed across multivariate regressional models. For overall mortality, poor Yost-SES was a markedly positive independent effector (HR, 1.44; 95%CI, 1.33-1.56; p<0.001). For combined AJCC-TNM staging, poor Yost-SES (OR, 1.28; 95%Cl, 1.13-1.45) and being of minority race/ethnicity (OR, 1.57; 95%CI, 1.39-1.79) were markedly positive predictors (all p<0.001). For 3-year all-cause mortality, poor Yost-SES was a markedly positive predictor (OR, 1.70; 95%CI, 1.51-1.93; p<0.001). For 5-year all-cause mortality, Yost-SES was a markedly positive predictor (OR, 1.66; 95%CI, 1.46-1.89; p<0.001) alongside being of minority race/ethnicity (OR, 1.20; 95%CI, 1.05-1.37; p=0.008). For disease-specific mortality, being of Female-Sex (OR, 1.40; 95%CI, 1.14-1.72; p=0.001) and minority race/ethnicity (OR, 1.92; 95%CI, 1.59-2.32; p<0.001) were both markedly positive predictors.

Conclusions: Comprehensive analyses of SDoH-factors demonstrated the strongest associations with worse SBSC-prognosis with poor community-level SES and individual-level minoritized race-ethnicity. In the context of SBSC clinical outcomes, this investigation presents quantifiable targets of disparities that should be addressed with prospective investigations and initiatives.

B090: CONTEMPORARY, INDIVIDUAL-LEVEL AND COMMUNITY-LEVEL SOCIAL DETERMINANT ANALYSES OF MENINGIOMA CARE AND PROGNOSTIC DISPARITIES IN THE US - David J Fei-Zhang, BA[1]; Rishabh Sethia, MD[2]; Larry W Wang, BS, MSc[1]; Jill N D'Souza, MD[3]; Daniel C Chelius, MD[4]; Anthony M Sheyn, MD[5]; Jeffrey C Rastatter, MD, MS[2]; [1]Northwestern University - Feinberg School of Medicine; [2]Ann & Robert H Lurie Children's Hospital of Chicago; [3]Louisiana State University Health Sciences Center - School of Medicine; [4]Texas Children's Hospital; [5]St Jude Children's Research Hospital

Introduction: Previous studies on social determinants of health (SDoH) have explored its contribution to exacerbating skull-base tumor disparities, including meningiomas. These factors have included measures of socioeconomic status, education, being of minoritized racial-ethnic groups, and insurance status. However, these studies have been greatly constrained by sample size, chronology of when patients were diagnosed and treated, and scant representation of social factors within large databases. From such limitations, past assessments have singly focused on one or a small subset of sociodemographic factors in their associations with poor outcomes. With such

narrow scopes of variables considered, these past investigations display decreased generalizability towards understanding real-world intersections between varied SDoH and their influence on meningioma outcomes. As such, we sought to further characterize meningioma care and prognosis disparities by employing modern, national patient datasets and multifactorial analyses of the Yost Index, a census-level composited measure for socioeconomic status (SES), and a variety of other census- and individual-level sociodemographic factors.

Methods: This retrospective cohort study analyzed adult patients (aged 20+ years) diagnosed with meningioma between 2010-2018 in the United States through the National Cancer Institute-Surveillance, Epidemiology, and End Results Program (SEER) database. Age-adjusted, multivariate regressions were conducted across 13 covariates of individual sex & race-ethnicity (reference level being of Non-Hispanic White race-ethnicity; comparators against composite of Black, Hispanic, Asian and Pacific Islander, Native American representation), along with census-level rurality-urbanicity and Yost-SES-Index score (composite 7 SES-measures of income, education, housing, and employment, separated by quintiles using the highest-SES-quintile as the reference level) for outcomes of all-cause mortality, primary surgery receipt, radiation therapy receipt, and delay in treatment after diagnosis (reference level being below or at 3 months and comparator at 3+ months) as the outcomes.

Results: From 110,042 adults diagnosed with meningioma, the most common clinicodemographic characteristics were being of 65-84 years of age (n=46,850, 42.6%), female sex (n=81,246, 73.8%), and non-Hispanic White race/ethnicity (n=74,280, 67.5%). Community-level poor SES was also well-represented based on the Yost-SES-Index (n=51,061, 46.4%). In general, female-sex was a common prognostic factor across multivariate regressional models. For overall mortality, Female-Sex was a markedly negative independent effector (HR, 0.69; 95%CI, 0.67-0.71; p<0.001) while poor Yost-SES was a markedly positive independent effector (1.31; 1.28-1.34; p<0.001). For primary surgery receipt, being of a minority race/ethnicity was an independent positive predictor (OR, 1.18; 95%CI, 1.15-1.22; p<0.001) while Female-Sex was a markedly negative predictor (OR, 0.70; 95%CI, 0.68-0.72; p<0.001). For radiation therapy receipt, both Female-Sex (OR, 0.79; 95%CI, 0.75-0.83; p<0.001) and being of minority race/ethnicity (OR, 0.83; 95%CI, 0.79-0.87; p<0.001) were negative predictors. Lastly, Female-Sex was a markedly positive predictor of treatment delays greater than 3 months (OR, 1.38; 95%CI, 1.34-1.43; p<0.001).

Conclusions: Through these modern, multivariate SDoH-analyses, adults with meningiomas showed differential care and prognostic outcomes most strongly associated with varied individual-level sex and minoritized race-ethnicity, as well as community-level SES. With these comprehensive quantitative approaches, this study elicits specific factors of disparities that should be mitigated through future investigations and initiatives.

in the diagnosis and management of skull base ORN.

B091: FEATURES AND MANAGEMENT OF OSTEORADIONECROSIS OF THE SKULL BASE: A SYSTEMATIC REVIEW - Ashton Huppert Steed[1]; Shawn M Stevens[2]; Ameya A Jategaonkar[2]; [1]University of Arizona College of Medicine-Phoenix; [2]Barrow Neurological Institute, Department of ENT and Skull Base Surgery

Background: Osteoradionecrosis (ORN) of the skull base is a rare but potentially devastating consequence of radiotherapy for cancers of the head and neck. While ORN of the mandible has been well studied, there is a paucity of data regarding both the unique presentation and management of skull base ORN (SBORN). Various treatment methods have been discussed ranging from medical management and hyperbaric oxygen (HBO) to free tissue transfer. Nevertheless, there is currently no universally accepted protocol for the treatment of SBORN

Objective: To synthesize the existing literature regarding skull base ORN and better inform surgeons on the management of this complex condition.

Methods: A systematic literature search was conducted in accordance with PRISMA guidelines. Studies were included if they described adult patients with skull base ORN and reported treatment modalities utilized. Case reports, review articles, and studies of pediatric patients were excluded. The search terms were: (Osteoradionecrosis OR "radiation-induced necrosis") AND ("Skull Base" OR "Sphenoid" OR "Occipital" OR "Temporal" OR "Frontal" OR "Ethmoid" OR "Clivus").

Results: 382 unique abstracts were identified and screened. Ultimately, 29 studies with 593 patients with SBORN were included. The most common site was the lateral skull base with 439 patients (70.1%), followed by anterior skull base with 178 patients (28.4%). Nine patients (1.4%) had involvement of less common sites including occipital and parietal bones. Of note, some patients presented with ORN of multiple skull base sites. The most common primary malignancy site was the nasopharynx (n=270), followed by the parotid gland (n=107). The mean time to presentation of ORN following completion of radiotherapy was 84.3 months (7 years) with a range of 1.1-672 months. Presenting symptoms varied based on location but primarily composed of pain, headache, foul odor, and abnormal bleeding or drainage. 239 (40.3%) patients were treated primarily with medical management, whereas 354 (59.7%) patients required surgical intervention. Conservative treatment varied but often included systemic antibiotics, local debridement, topical agents, and HBO. Reconstruction of defects was performed using local flaps in 109 patients, whereas free flaps were utilized in 87 patients. Types of free flaps used included: anterolateral thigh, latissimus dorsi, serratus anterior, fascia lata, gracilis, and radial forearm. While surgical procedures varied widely across studies depending on location and severity of ORN, patients treated surgically generally had improved survival rate and reduction of ORN symptoms as compared to medical management.

Conclusion: SBORN represents a unique and challenging complication of the treatment of head and neck cancers. The consequences can be catastrophic and include carotid blowout, therefore prompt identification and treatment are key. Here we show the varied treatment approaches that are discussed in the literature and how ultimately vascularized tissue transfer to either reconstruct or "rescue" the affected tissues remains a mainstay of treatment. In future work, we hope to pursue a consensus statement to guide clinicians

B092: INDUCTION CHEMOTHERAPY FOR SINONASAL SQUAMOUS CELL CARCINOMA: SYSTEMATIC REVIEW AND META-ANALYSIS - Nrusheel Kattar, MD[1]; Manish D Mair, MS, MCh, Head and Neck Consultant[2]; Ameya Asarkar, MD[1]; [1]LSU Shreveport Department of Otolaryngology - Head and Neck Surgery; [2]University Hospital of Leicester, NHS Trust, UK

Introduction: Locally advanced squamous cell carcinoma (SCC) of the nasal cavity and paranasal sinus (SCCNP) has classically been managed with extensive resection of large lesions, resulting in lack of orbital organ preservation, often with disfigurement, loss of visual function, and decreased quality of life. Induction chemotherapy (ICT) has a well-documented role in the treatment of certain locoregionally advanced head and neck cancers, but the use of ICT has not been systematically reviewed in the management of sinonasal SCC.

Methods: Using the National Institute for Health and Care Excellence (NICE) search domain, PubMed, Embase, and Medline databases were queried for original English articles without any restrictions on date. This review was conducted in accordance with the 2020 PRISMA guidelines. A meta-analysis of pooled success rate with an inverse variance statistical method and fixed effects analysis model was performed using RevMan software (Version 5.3.5; Cochrane Group, London, UK).

Results: Of 343 abstracts initially screened, 10 full-text articles were included in this review, consisting of 394 patients, 225 of whom were male (56.8%) with an average age of 54. Nine studies were retrospective and 1 was prospective. 99% of patients (389/393) had at least T3 disease with the majority (72%, 234/327) of patients having no clinical lymphadenopathy(N0).

In all included studies, induction chemotherapy was followed by either: 1) Definitive chemotherapy +/- radiation +/- salvage surgery or 2) Surgery with adjuvant therapy. Meta-analysis of 6 of 10 studies revealed a pooled partial response (PR) rate of 68% (95% CI 0.64-0.73, I2 97%); studies including heterogeneous data from pathology other than sinonasal SCC were not included in the meta-analysis. PR was defined as at least an 80% reduction of tumor volume on follow-up after ICT. In contrast, complete response (CR) rates to ICT as reported in 5 studies ranged from 0% to 25%; stable response ranged from 0% to 54% in 6 studies. Overall survival (OS) was reported in 4 studies, ranging from 59%-72%. Disease-free survival (DFS) was reported in 2 studies, ranging from 68%-76%. Orbital preservation rates were reported in 3 out of 10 studies and ranged from 78% to 82%.

Conclusion: Pooled evidence of retrospective data suggests that ICT may be an effective modality in producing partial response for locally advanced sinonasal SCC. However, further study in the form of high-quality prospective trials with standardized regimens could help to further elucidate the optimal management of these patients.

Figure 1. Forest Plot of Meta-Analysis for Systematic Review of Induction Chemotherapy for Sinonasal Squamous Cell Carcinoma. Diamond, overall effect estimate; square, point estimate of the study; black line, 95% CI

B093: PATHOLOGICAL COMPLETE RESPONSE AFTER INDUCTION CHEMOTHERAPY AND PEMBROLIZUMAB AND NASOPHARYNGECTOMY FOR LOCALLY RECURRENT NASOPHARYNGEAL CARCINOMA

- Victor Ho-Fun Lee, MD[1]; Joseph Chung-Kit Chung, MS[1]; Stephanie Nga-Sze Wong, MS[1]; Sum-Yin Chan, FRCR[1]; Chi-Chung Tong, FRCR[1]; Raymond King-Yin Tsang, MS[2]; Dora Lai-Wan Kwong, MD[1]; [1]The University of Hong Kong; [2]National University of Singapore

Background: Despite aggressive intensive radical treatment, about 15-30% of patients developed relapse of their previously treated nasopharyngeal carcinoma (NPC). Among other available treatment options including radical surgery and 2nd course radiation therapy with or without adjunct chemotherapy, chemotherapy and targeted therapy, chemotherapy and immune checkpoint inhibitors (ICIs) as 1st line treatment for recurrent or metastatic NPC have led to a prolonged progression-free survival and better objective response compared to chemotherapy alone. Nevertheless, very little is known about the objective response and treatment outcomes for those confined to local recurrence only, and whether radical surgery could still be considered safe and effective in salvaging the local recurrence after initial chemotherapy and ICI therapy. We report the treatment outcomes of five patients with locally recurrent NPC after treatment with preoperative chemotherapy and pembrolizumab and subsequent radical resection.

Methods: Patients with histologically confirmed EBER-positive undifferentiated carcinoma and radiologically staged (T1W, T2W, T1W contrast-enhanced, and diffusion weighted magnetic resonance imaging [MRI] of the nasopharynx and neck and 18F-fluorodeoxyglucose positron-emission tomography with integrated computed tomography [PET/CT] locally recurrent NPC (rT3N0M0 for all patients who relapsed 7 months, 3.5 years, 9 years, 15 years and 27 years, respectively, after prior treatment for their initial NPC) were prospectively recruited. The median of their pretreatment plasma EBV DNA were 270 copies/ml (range 0 to 481 copies/ml). They received preoperative chemotherapy gemcitabine (1000mg/m^{2}) on day 1 and day 8 and cisplatin (100mg/m^{2}) on day 1 as well as immune checkpoint inhibitor pembrolizumab 200mg as a fixed dose on day 1 via intravenous infusion every 3 weeks for 4 to 6 cycles followed by reassessment magnetic resonance imaging and nasopharyngectomy.

Results: Five patients were prospectively recruited with an median age of 54 years (range 36 to 70 years). All patients completed preoperative chemotherapy and ICI therapy without any dose reduction or ≥grade 3 adverse events. MRI and PET/CT scan after preoperative therapy showed significant partial responses. Their plasma EBV DNA dropped to 0 copies/ml after preoperative therapy. They underwent radical nasopharynectomy (1 received maxillary swing nasopharyngectomy and 4 received endoscopic nasopharyngectomy) within 1 month after the last dose of chemotherapy and ICI therapy. All were discharged from hospital within a week of their operations. They could resume and tolerate full oral diet 1 month after their operations. Pathological examination of the resected specimens showed pathological complete response in all patients. All patients were still alive and free of disease relapse (median 12 months, range 1 to 17 months) after operation without significant long-term treatment-emergent complications. Their plasma EBV DNA remained undetectable. One developed transient grade 2 facial paresthesia which improved 1 month after operation and became a grade 1 event.

Conclusions: The treatment outcomes of our patients with locally recurrent NPC treated with preoperative chemotherapy and ICI therapy followed by radical resection were highly encouraging. Our results have paved the way for us to design further prospective multicenter studies to verify our findings and investigate the predictive tumor and immune biomarkers for tumor response.

B094: OUTCOMES FOR NEUROENDOCRINE CARCINOMAS OF THE HEAD AND NECK: 20 YEARS OF EXPERIENCE AT A SINGLE INSTITUTION

- Nathan Lu[1]; Anthony Tang[2]; Jessica Maxwell[1]; Kevin Contrera[1]; Matthew Spector[1]; Jose Zevallos[1]; Robert Ferris[1]; Seungwon Kim[1]; Shaum Sridharan[1]; Dan Zandberg[1]; [1]University of Pittsburgh Medical Center; [2]University of Pittsburgh School of Medicine

Background: Neuroendocrine tumors and carcinomas (NEC) are composite tumors of the nervous and endocrine systems and have the capability of releasing neuropeptides. NEC in the head and neck are rare, accounting for only 0.3% of all head and neck cancers, with heterogeneous clinicopathological and genomic features. This study provides the largest single institution review of patients with NEC of the head and neck. We aim to describe and elucidate the features of NECs that have been treated at our institution, with a focus on treatment modality and survival outcomes.
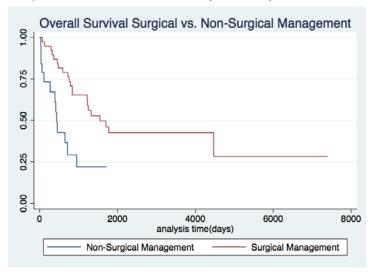
Methods: A retrospective review was completed on all patients with a diagnosis of neuroendocrine carcinoma of the head and neck at our institution between 2002 and 2023. Variables collected include demographics, comorbidities, cancer site, stage, differentiation, invasion, treatment type, recurrence, and survival.

Chi squared analysis, student t-test, and log-rank test were utilized for univariate analysis and survival analysis. Cox regression was used for overall survival and recurrence-free survival analyses.

Results: This study included 57 NEC patients (36.8% female, 65.2 ± 14.5 years old). Differentiation subtypes were reported in 30 patients; 21 of these patients (70%) had presented with poorly differentiated NEC, 8 (26.7%) with moderately differentiated NEC, and 1 (3.3%) with well-differentiated NEC. 21/30 patients with histology data were diagnosed with small cell NEC and 9/30 were diagnosed with large cell NEC. The most common primary sites were sinonasal (31.6%), larynx (29.8%), and parotid (8.8%).

Thirty-nine patients were treated with surgical management and 13 had non-surgical management with (chemo)radiotherapy. For the entire cohort, 2-year overall survival (OS) was 54.4% and two-year recurrence free survival (RFS) was 43.9%. Two-year RFS (55.26% vs. 21.05%, p=0.014) and OS (68.42% vs 26.32%, p =0.003) were improved in patients with surgical management compared to non-surgical management. Cox regression demonstrates improved survival with surgery when controlling for age, grade, histology, and primary site (HR 0.21, p = .011). Amongst surgical patients, RFS and OS were not associated with primary site, grade, nor histologic subtype.

Conclusion: In this case series, we present histological and survival findings for 57 NECs of the head and neck at a single inst?itution. The majority of these malignancies were poorly differentiated and located in either the sinonasal space or the larynx. Treatment strategies varied, however, patients who underwent surgical treatment had significantly improved OS compared to those who had non-surgical management.

Overall Survival Surgical vs. Non-Surgical Management

B095: THE CRANIOCERVICAL NERVE PLEXUS: A MICRODISSECTION STUDY - Nicole Starke, MS[1]; Brittany Puebla, MS[1]; Andrew Schleffer, BS[1]; Roham Hadidchi[2]; Mohammadali M Shoja, MD[1]; [1]Nova Southeastern University Dr. Kiran C. Patel College of Allopathic Medicine; [2]Nova Southeastern University College of Psychology and Neuroscience
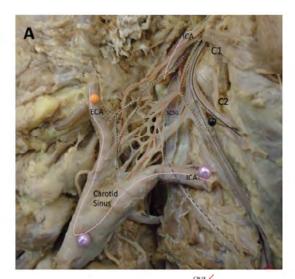
Introduction: The parapharyngeal space (PPS) is a complex anatomical region adjacent to the pharynx, housing critical neurovascular structures. This space encompasses the last four cranial nerves (CN), upper cervical spinal nerves, the superior cervical sympathetic ganglion (SCSG), jugular vein, and the internal carotid artery. The intricate network of nerves within this space establishes a series of anastomoses that have received limited attention in existing literature. This study aims to elucidate the formation and anastomotic patterns within the neural plexus of the PPS, which we refer to as the craniocervical nerve plexus (CCP).

Methods: We performed gross and stereomicroscopic dissection of nine bisected heads to expose the PPS, three of which are still in progress. The dissection involved a lateral approach to the parapharyngeal space by removing the ramus of the mandible and muscles of mastication. The connective tissue was removed under gross dissection and stereomicroscopic dissection was performed to trace nerves and their anastomoses. A composite drawing of the CCP was constructed based on the observed patterns of neural anastomoses.

Results: In all nine specimens, a fusion of cranial nerves X and XII was observed at or above the level of the C1 transverse process (Figure 1). Gross examination of cranial nerve X revealed the presence of a ganglion distal to the jugular foramen in four out of the nine specimens. Connections were also noted between the C1/C2 nerves and SCSG and cranial nerve XII. The carotid sinus received a variable number of branches, with up to eight branches in one specimen, including contributions from cranial nerves IX and X, the SCSG, and the superior laryngeal nerve. In six fully dissected specimens, a connection between the pharyngeal branches of cranial nerves IX and X was present (Figure 1A and B). The exploration of the carotid sinus plexus is ongoing in the remaining three out of the nine specimens.

Discussion: This study provides a comprehensive anatomical description of the CCP, elucidating a more complex anatomy than was previously thought. The neural interconnections within the PPS are extensive and variable, creating a plexus that supplied multiple branches to the carotid sinus and pharynx. Within this variability, reproducible patterns could be ascertained. Fusion of cranial nerves X and XII has been reported sporadically as a rare finding but was found in all specimens of this study. Understanding the microanatomy of the CCP can be valuable for surgeons operating in this area and improves upon our understanding of pathologies in the skull base and neck. Further research is required to fully elucidate the functional importance of the anastomoses within the CCP. Histological studies could offer insight into the nerve fiber composition of the identified branches, potentially shedding light on their significance.
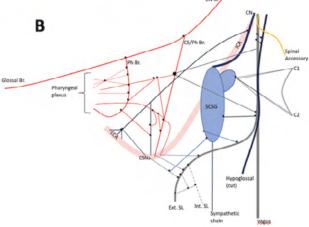
Figure 1: Craniocervical nerve plexus of one specimen. (A) Annotated cadaver (B) Drawing with nodes representing anastomoses

B096: THE IMPACT OF ADJUVANT RADIATION THERAPY ON SURVIVAL IN SINONASAL TUMORS FOLLOWING SURGICAL RESECTION: A RETROSPECTIVE MULTI-INSTITUTIONAL, MULTI-NATIONAL ANALYSIS - <u>Cameron P Worden, MD</u>[1]; Jason Tasoulas, MD, DMD[1]; Saima J Wase, MD[1]; Vasileios Chatzinakis, MD[2]; Iacopo Dallan, MD[3]; Thibaut Van Zele, MD, PhD[4]; Steven M Johnson, MD[5]; Siddharth H Sheth, DO, MPH[6]; Christos Georgalas, MD, PhD[2]; Brian D Thorp, MD[1]; [1]University of North Carolina - Department of Otolaryngology/Head and Neck Surgery; [2]Endoscopic Skull Base Centre Athens, Hygeia Hospital, Athens, Greece; [3]First Otorhinolaryngologic Unit, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy; [4]Department of Otorhinolaryngology, Ghent University Hospital, Ghent, Belgium; [5]Department of Pathology and Laboratory Medicine, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; [6]Division of Oncology, Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Background: Sinonasal neoplasms (SNN) are a rare and histologically heterogeneous subset of head and neck cancers.

Resultingly, clinical and pathological data and the association with survival is typically limited to single institution experiences. The use of adjuvant radiation therapy (aRT) following maximal surgical resection in SNN has been shown to improve locoregional control, disease-free survival, and overall survival (OS) dependent on patient and pathology-specific factors. However, aRT utilization can vary based on institutional practice patterns. We aimed to determine if aRT following primary surgical resection conferred survival benefits across various sinonasal tumor histological subtypes within a multi-institutional, multi-national cohort.

Methods: We retrospectively analyzed a multi-institutional, multi-national (US, Greece, Italy, Belgium) cohort of SNN patients who received primary surgical resection between 1998-2023. Demographic information, TNM staging, tumor histology, primary and adjuvant treatment results, and follow-up and survival data were recorded. Univariable and multivariable analyses of OS were performed using a Cox regression model adjusted for patient age, sex, tumor histology, T-stage, and N-stage. A directed acyclic graph was used to inform the adjustment set variable selection. Survival curves were generated utilizing the Kaplan-Meier method and compared using the Gehan-Breslow-Wilcoxon test.

Results: 329 patients (Belgium: 137, USA: 101, Greece: 47, Italy: 44) were included. The mean age was 60 years (standard deviation, 15 years) with 63% being male. SNN histological subtypes treated included intestinal-type adenocarcinoma (33%), squamous cell carcinoma (SCC; 29%), sarcoma (7%), chordoma (7%), esthesioneuroblastoma (6%), adenoid cystic (5%), other (5%), mucosal melanoma (4%), sinonasal undifferentiated carcinoma (SNUC; 2%), and non-intestinal type adenocarcinoma (2%). The majority of patients were T3-4 (54%) and N0 (91%), with nodal positivity being highest in SCC (21%) and SNUC (17%). Following surgical resection, 79% of patients had negative margins and 80% of the total cohort received aRT. The median OS across all histologies was 39 months (5-year OS: 68%, 10-year OS: 55%). Five-year OS ranged from 39% for mucosal melanoma to 89% for chordoma. In the pooled multivariable analysis, aRT was not associated with improved OS (HR=0.45, 95% CI: 0.19-1.09). When stratified by histology, aRT was associated with improved OS (HR=0.08, 95% CI: 0.02-0.28) in SCC. Similarly, Kaplan-Meier analysis showed an improvement in OS in SCC patients who received aRT following surgery compared to those who underwent surgical resection alone (p < 0.008). Among SCC patients, practice patterns for aRT use differed across centers in this study. In the Belgium cohort, all SCC patients received aRT following surgical resection, including those with T1-2 tumors. Comparatively, 71% and 56% of SCC patients in the USA and Italy cohorts received aRT.

Conclusions: The addition of aRT following surgical resection was independently associated with improved overall survival in SCC patients, however similar trends were not seen in the combined SNN cohort. Institutional practice patterns regarding the utilization of aRT in SCC patients varied among centers in this study.
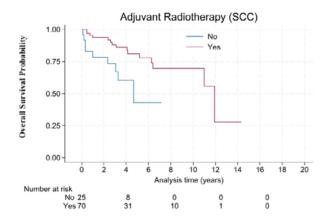
Figure 1. Kaplan-Meier curve displaying improved OS for SCC patients who underwent primary surgical resection with aRT compared to surgical resection alone (p value < 0.008).

B098: MEASURE, MARK, THEN CUT: SYSTEMATIC USE OF MARGIN MARKING IMPROVES SURGICAL OUTCOMES FOR T1, T2 ORAL AND OROPHARYNGEAL SCC -

Nikita Bedi, BS[1]; Sohei Mitani, MD[2]; Michael C Jin, BS[1]; Ryan K Orosco, MD[3]; Michael C Topf, MD[4]; F C Holsinger, MD, FACS[1]; [1]Stanford University; [2]Ehime University Graduate School of Medicine Shitsukawa, Toon Ehime Japan.; [3]University of New Mexico; [4]Vanderbilt University

Objective: Despite advancements in preoperative surgical planning and intraoperative guidance, the positive margin rate in oral cavity and oropharyngeal cancers remains high, particularly when compared to other solid malignancies. To better educate surgeons-in-training about margin management, a systematic approach to measuring surgical margins around oral cavity and oropharyngeal lesions prior to surgical excision termed "measure, mark, then cut" (MMC) was implemented at an academic medical center.

Methods: Patients with T1-2 oral cavity and oropharyngeal squamous cell carcinoma (SCC) treated with surgical resection. Clinicopathologic factors and outcomes of local recurrence (LR) and survival were assessed.

Results: 192 patients were identified of which 66% had oral cavity SCC and 34% oropharyngeal SCC. MMC was used for margin planning and documented in 85 patients (44%). The rate of involved margins was significantly lower in the cases utilizing MMC (14.3% vs. 44.3%, p < 0.001).The closest margin distance was double for patients having surgery with MMC (3.5 mm vs. 1.4 mm, p < 0.001). Survival rates, including overall survival, disease-free survival, LR-free survival were significantly improved in the cases with pre-excision MMC. Using multivariable Cox proportional hazards regression modeling, LR for patients with MMC was significantly lower with a hazard ratio (HR) of 0.252

Conclusion: Surgical planning using a simple pre-excision technique to measure, mark, then cut decreases the rate of positive mucosal margins and increases mean closest margin distance. Most importantly, this correlates with reduced risk of LR in patients and improved survival for patients with early-stage oral cavity and pharynx SCC.

Key words: surgical margins, oral cavity, oropharynx, measure

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B099: SURVIVAL ESTIMATIONS IN SURGICAL MANAGED ORAL CAVITY CANCER PATIENTS USING NOVEL TUMOR-IMMUNE MICROENVIRONMENT MEASUREMENTS. -

William J Benjamin, MPH[1]; Santhoshi Krishnan, PhD[2]; Michael Allevato, PhD[1]; Chamila Perera, PhD[3]; Jeremy Taylor, PhD[3]; Gregory T Wolf, MD[4]; Arvind Rao, PhD[2]; Nisha D'Silva, BDS, MDS, PhD[5]; Maureen A Sartor, PhD[2]; Laura S Rozek, PhD[6]; Steven B Chinn, MD, MPH[4]; [1]University of Michigan Medical School; [2]University of Michigan Department of Computational Medicine and Bioinformatics; [3]University of Michigan Department of Biostatistics; [4]University of Michigan Department of Otolaryngology - Head and Neck Surgery; [5]University of Michigan School of Dentistry; [6]Georgetown University Department of Oncology

Introduction: The oral cavity is the most prevalent site for head and neck squamous cell carcinoma (HNSCC) and is primarily managed surgically, therefore resulting in it being a commonly managed condition for head and neck specialists. While there is evidence of survival outcomes improving in oral cavity squamous cell carcinoma (OSCC), there is hope that the application of new biomarker-based technologies may improve treatment outcomes among OSCC patients. The tumor-immune microenvironment has been identified as an impact prognostic marker in HNSCC, with immune- "hot" tumors demonstrating improve survival compared immune-"cold" tumors. While meaningful for prognosis, current methods of measuring tumor-immune infiltration are limited due to inefficiencies and an inability to measure the spatial relationship between tumor cells and tumor-infiltrating lymphocytes, the latter of which is important given a tumor immune synapse is required for cytotoxic effects. In this study, we seek to investigate whether a rapid, automated measure of immune infiltration and tumor-TIL spatial relationships is associated with survival outcomes in patients managed surgically for OSCC.

Methods: Patient data and digitized H&E slides were obtained from the University of Michigan Head and Neck SPORE Cohort. A machine-learning classifier trained on pathologist labeled samples was used to identify tumor cells and TILs. The extent of TIL infiltration within a tumor was assessed using the G-cross function comparing the coordinates of lymphocytes to tumor cells within a slide. Levels of spatial infiltration within tumors were outputted as G-cross(r) curves, and the area-under-the-curve was used to calculate GScore. (Figure 1). GScore was categorized into greater than or equal to or less than the median for analysis. Our primary outcomes of interest were overall and disease-specific survival. Survival estimations were completed using Kaplan-Meier analysis and Cox-Proportional Hazard modeling.

Results: A total of 202 patients were included in our study of which the average age was 62 (S.D. 13) and 115 (56.9%) were male. Within the cohort, 114 (56.4%) patients had Stage III or IV disease. All 202 patients received upfront surgery after which 61 (30.2%) completed adjuvant radiation and 36 (17.8%) completed adjuvant chemoradiation. Patients with a GScore ≥ the median had significantly improved 60-month overall survival (66.0% vs. 53.6%, p<0.01) and disease-specific-survival (82.3% vs. 67.4%, p<0.01) compared to those from below the median (Figure 2). In multivariable models adjusting for age, stage, pack years, and the ACE comorbidity index, a GScore less than the median was associated with a significantly higher hazard of death (HR: 1.8 [1.1, 2.9], p=0.01) and disease-specific death (HR: 2.2 [1.2, 4.3], p=0.01) compared to a GScore ≥ the median.

Conclusion: A higher GScore appears to be associated with improved overall and disease-specific survival in fully adjusted models among OSCC patients treated with upfront surgical resection. This finding provides support for GScore's utility as a potential prognostic biomarker in this patient population, however further study is needed to better characterize its translational utility.

Figure 1: Workflow for identification of TIL locations, density, and distances; involving image analysis of slides and subsequent machine learning to identify TILs on tissue.
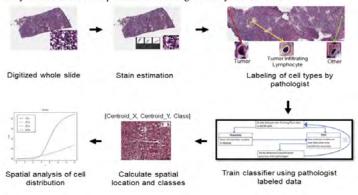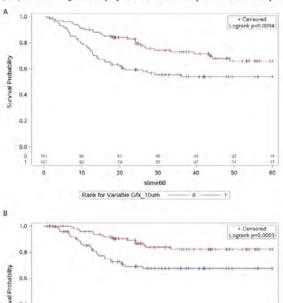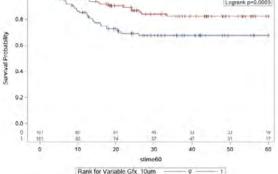

Figure 2: Overall survival (A) and disease-specific survival (B) stratified by ≥ median (red) or < median (blue) GScore among oral cavity squamous cell carcinoma patients treated with upfront surgical resection.

B100: RECENT INCIDENCE AND MORTALITY OF ORAL TONGUE SQUAMOUS CELL CARCINOMA IN THE YOUNG POPULATION: A SEER STUDY. -

Antonio A Bon-Nieves; Sarah Wagoner; Celina Virgen; Jamie Oliver; Rahul Alapati; Amelia Lawrence; Andres M Bur; Kiran Kakarala; Yelizaveta Shnayder; Chelsea S Hamill; University of Kansas Medical Center

Importance: Head and neck squamous cell carcinoma (SCC) is a considerable public health concern worldwide, with its incidence steadily rising in recent years. While traditionally associated with older age groups and well-established risk factors such as tobacco and alcohol consumption, an alarming trend has emerged in young adults. This shift in demographics highlights the need to comprehensively examine this population's unique characteristics and challenges. While previous studies have examined rising trends of oropharyngeal SCC amongst young men and others at oral cavity SCC in young women, no studies to date have comprehensively examined trends of oral tongue SCC (OT-SCC) in both cohorts.

Objective: This study aims to assess the incidence and changes in mortality of OT-SCC in the young adult population using the Surveillance, Epidemiology, and End Result (SEER) database.

Design: Retrospective cohort study from 2010 to 2020.

Setting: Population-based on the SEER database.

Participants: Patients under 40 years old with primary oral tongue cancer diagnosed between 2000-2020, were identified in the SEER database. Patient variables included demographics, tumor characteristics, treatments, and survival.

Main Outcome(s) and Measure(s): The outcomes of interest include incidence, overall survival (OS) and disease-specific survival (DSS) in young women diagnosed with OT-SCC.

Results: A cohort of 949 eligible patients was identified in SEER from 2010 to 2020. Most patients were aged 35 to 39 (41.0%) or 30 to 34 (30.9%), were predominantly White/Caucasian (81.0%), and 44.4% female. In women, the incidence of OT-SCC increased from an average of 8.1 to 11.4 per 100,000 yearly between 2000-2010 and 2010-2020, with a relative change of 40.6%. Similarly, men exhibited a steeper rise in incidence compared to women, where it increased from 11.9 to 15.1 per 100,000, with a relative change of 26.9%. Mean length of follow up was 45.3 months (±38.0), with a range of 0 to 131 months. Young OT-SCC female patients had a significantly higher 5-year OS rate compared to males (74.6% vs 66.9%, p=0.009). Similarly, 5-year DSS was significantly higher in young women (85.4%) compared to young men (78.7%, p=0.01).

Conclusions and Relevance: This study highlights the rising incidence of OT-SCC among young women over the past two decades. While the majority of current studies focus on this increase amongst young women, our study shows a pronounced increase amongst young men as well. Despite these incidence variations, the DSS for young OT-SCC patients is higher amongst women compared to men. This increasing incidence of OT-SCC in young patients highlights a need to promote awareness and education amongst physicians; physicians should consider a lower threshold to biopsy oral tongue lesions in this population.

B101: SEX-SPECIFIC DIFFERENCES IN DIETARY PATTERNS AND RISK OF ORAL SQUAMOUS CELL CARCINOMA - Luis Gomez Castillo, BA; Kara Cushing-Haugen, MS; Emily Marchiano, MD; Neal Futran, DMD; Holly Harris, ScD, MPH; Brittany Barber, MD, MSc; University of Washington/Fred Hutch Cancer Center

Intro: The incidence of oral squamous cell carcinoma (OSCC) has shown an alarming increase in young, non-smoking individuals globally. This trend is rapidly accelerating among White females, where it has increased by 4% annually in the United States, with similar trends observed worldwide. Emerging evidence from other alimentary site cancers suggest an association between Western diets and carcinogenesis, particularly among early-onset cases. Thus our objective was to investigate sex-specific differences between dietary patterns and development of OSCC.

Methods: We conducted a prospective cohort study using data from the Nurses' Health Study (NHS, 1980-2016) and the Health Professionals Follow-up Study (HPFS, 1986-2016) among 121,700 female nurses and 51,529 male health professionals, respectively. Diet was assessed via food frequency questionnaire (FFQ) every four years. In each cohort we examined the three dietary patterns: prudent, Western, and the Alternative Healthy Eating Index (AHEI) as well glycemic index, red meat consumption, refined grains, and sugar-sweetened beverage (SSB) intake. Cox proportional hazards adjusted for age, caloric intake, tobacco pack-years, alcohol intake and BMI, were used to calculate hazard ratios (HR) and 95% confidence intervals (CIs) for the association between each dietary factor and OSCC incidence.

Results: 90,839 women and 45,790 men with a mean age of 46.3 and 54.1 years at baseline, respectively, were included in the analysis. A total of 245 (146 women and 99 men) incident OSCC cases were reported over 36 years of follow-up for NHS and 30 years of follow-up for HPFS. Notably, after controlling for age, tobacco, alcohol, caloric intake, and BMI, adherence to the AHEI (i.e. a healthier dietary pattern) was associated with a lower risk of OSCC only among female participants in the NHS. Specifically, those in the highest (healthiest) quintile of the AHEI had a 50% lower risk of OSCC compared to the lowest (least healthy) quintile (95% CI, 0.28-0.89; P trend = 0.033[HKL1]). In contrast, no association was observed with the AHEI or any other dietary patterns among the male HPFS cohort.

Discussion: Our study highlights the significance of dietary patterns in modifying the risk of developing OSCC in females, but not males. Higher AHEI dietary score, reflecting a diet rich in fruits, vegetables, and whole grains, was associated with a lower risk of OSCC in females only, highlighting the potential interplay between diet and OTSCC carcinogenesis.

B102: MARGINAL MANDIBULECTOMY INCREASES THE RISK OF OSTEORADIONECROSIS COMPARED TO SEGMENTAL MANDIBULECTOMY IN THE SURGICAL MANAGEMENT OF ORAL SQUAMOUS CELL CARCINOMA WITH ADJUVANT RADIATION THERAPY - Hossein Jazayeri, MD, DMD[1]; Madison LeBlanc, DDS[1]; Wyatt Spresser, DDS[1]; Kevin Lee, MD, DDS[2]; Jonathan Troost, PhD[1]; Justine Moe, MD, DDS[1]; [1]University of Michigan; [2]University of Buffalo

Purpose: Ablative surgery is the primary treatment modality for oral squamous cell carcinoma (OSCC). Historically, greater depth of invasion in the mandibular cortex may necessitate segmental resection for disease-free survival while noninvasive disease may be managed with marginal resection, preserving form and function (1,2). Mandibulotomy similarly serves as a technique to gain access to anatomic sites affected by cancer. While any of the three modalities may be necessary to treat disease, the risk of developing osteoradionecrosis (ORN) in irradiated subjects with OSCC undergoing these techniques is poorly understood. As such, the purpose of the study was to elucidate this phenomenon.

Methods: Institutional Review Board approval at Michigan Medicine was acquired for the completion of this study. Subjects who had a diagnosis of OSCC from 2002 until 2022 treated by the University of Michigan Department of Oral and Maxillofacial Surgery were included. Patient demographics, tumor characteristics and location, chemoradiotherapy were characterized. Primary predictor variables were method of mandibular osteotomy: marginal or segmental mandibulectomy, or mandibulotomy. Primary outcome variables were whether the subject developed ORN. Descriptive statistics were computed for the cohorts. Two-sample t-tests were used to compare all continuous data while Fisher's exact tests were computed for comparison of categorical data. A p-value of < 0.05 was deemed statistically significant.

Results: There were 1,168 subjects who presented to the University of Michigan Department of Oral and Maxillofacial Surgery for evaluation and treatment of their OSCC. Of these, 375 subjects underwent segmental mandibulectomy, marginal mandibulectomy, or mandibulotomy (32.1%). Further, 206 of these subjects also completed adjuvant radiation therapy (17.6%). Age, sex, immunocompromised status, and smoking status did not significantly alter their treatment modality. T stage was statistically significant with treatment modality, with 84.8% of segmental mandibulectomy, 49.2% of marginal mandibulectomy, and 54.6% of mandibulotomy patients presenting with a T4 tumor. N stage was not statistically significant among treatment modality (p = 0.55). Development of ORN was much more likely among subjects undergoing marginal mandibulectomy as 20.3% of subjects experienced this complication compared to 7.6% of segmental mandibulectomy subjects (p = 0.03).

Conclusions: Adjuvant radiation, while many times necessary in cancer care, carries the deleterious risk of altering bone remodeling. Among the three techniques investigated in this study, marginal mandibulectomy is accompanied by the highest likelihood of developing ORN.

References:

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2. Renda, L., et al. (2020). "A nomogram to predict osteoradionecrosis in oral cancer after marginal mandibulectomy and radiotherapy." Laryngoscope 130(1): 101-107.

B103: SENTINEL LYMPH NODE BIOPSY IN ORAL TONGUE SQUAMOUS CELL CARCINOMA: A NCDB EVALUATION OF TREATMENT MODALITIES UTILIZED AND OUTCOMES - Samuel Auger, MD; Nicholas Oberhelman, MD; Nishant Agrawal; University of Chicago

Introduction: Squamous cell carcinoma (SCC) of the oral cavity is one of the most common head and neck cancers, with oral tongue being one of the most common subsites. Surgery remains the mainstay of treatment of early-stage oral tongue SCC with elective neck dissection (END) often preferred by surgeons for tumors with greater than 2 to 3 millimeters depth of invasion. END has been shown to reduce recurrence rate and improve survival in early-stage tongue SCC, though it carries an increased risk of overall surgical morbidity. Sentinel lymph node biopsy (SLNB) is an established practice in the management of several cancer types. SLNB has been selectively utilized as an alternative to END in the surgical management of early-stage tongue SCC. Given its selective use, there is limited data on outcomes in patients undergoing END versus SLND for early-stage tongue SCC. In this study, we utilized The National Cancer Database (NCDB) to evaluate treatment outcomes in patients with early-stage tongue SCC who underwent SNLB.

Methods: Use of The National Cancer Database (NCDB) was deemed exempt from review by the University of Chicago Institutional Review Board. The NCDB was queried for both male and female patients of all ages diagnosed with squamous cell carcinoma of the oral tongue between 2004 and 2020. Patients were included if they had T1 or T2 disease, N0 neck at diagnosis, underwent surgery of the primary site, and END or SNLB. Patients were grouped into END or SLNB. SLNB was captured starting in 2012. Descriptive, univariate, multivariate, and survival analysis was performed in R version 4.3.0.

Results: We identified 8907 patients with T1 or T2 oral tongue SCC in the NCDB. 189 (2.1%) of these patients underwent SLNB and 8718 (97.9) underwent END. The mean age was 62.4 years. 3202 of the cohort had tumors arising from the border of tongue (35.95%), with the next most common site being the anterior 2/3 of tongue (30.9%). All included patients underwent resection of the primary tumor, 7396 received adjuvant radiation (83.04%), and 241 received adjuvant chemotherapy (2.706%). Overall survival of our cohort at 1, 5, and 10 years was 96.0%, 79.1% and 60.37% respectively. Overall survival was significantly worse in T2 compared to T1 stage and in patients with positive margins on initial resection. There was a statistically significant increase in 5-year overall survival among patients who underwent SLNB compared to END (Figure 1). Patients who underwent adjuvant radiation or adjuvant chemotherapy had worse survival[AN[1] .

Conclusion: SLNB has been used in a sparring manner in patients undergoing surgery or oral tongue SCC. Our retrospective analysis suggests that in patients who underwent SLNB, survival is improved compared to those undergoing END, possibly related to selection bias. Radiation and chemotherapy are markers for worse overall survival and likely suggest adverse features regarding tumor pathology and/or resection status. Our study adds to evidence supporting prospective evaluation of SLNB in early-stage oral tongue squamous cell carcinoma. Further work, as is ongoing nationally, is required to standardize patient selection criteria for SLNB.

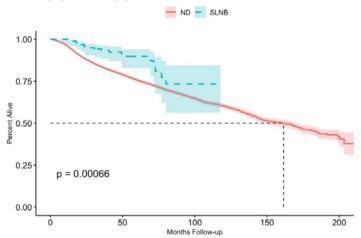Figure 1 – Comparison of Overall Survival Between Elective Neck Dissection and Sentinel Lymph Node Biopsy.

Figure 1 – Overall survival was significantly higher among SLNB patients in the first five years after diagnosis than the END patients. Green line and shading represents SLNB survival and red line and shading represents ND survival.

B104: SOCIOECONOMIC DEPRIVATION IS ASSOCIATED WITH INCREASED INCIDENCE OF HEAD AND NECK CANCERS - Henrique Ochoa Scussiatto, MS, MD[1]; Kerstin Stenson, MD[2]; Samer Al-Khudari, MD[2]; Vanessa Stubbs, MD[2]; Jayant M. Pinto, MD[1]; Mihir K. Bhayani, MD[2]; [1]The University of Chicago; [2]Rush University Medical Center

Introduction: Socioeconomic deprivation is associated with increased head and neck cancer (HNC) mortality in cross section, but how it affects HNC incidence is underexplored. We determined whether Area Deprivation Index (ADI) predicts HNC incidence-rate in a nationally representative ecological sample.

Methods: We obtained HNC incidence-rates from 608 US counties from 2011-2019 using the Surveillance, Epidemiology and End Results (SEER) program from the National Cancer Institute, along with sociodemographic information. ADI was collected from the Center for Health Disparities at University of Wisconsin. Data on smoking and alcohol intake was linked using CDC data frames (county level). Flexible, semi-nonparametric regression models were used to test the relationship between ADI and HNC incidence-rate, adjusting for demographics, urbanicity, smoking, and heavy alcohol intake.

Results: Counties with high deprivation indices had higher incidence-rates of oral cavity and pharyngeal cancers controlling for age, sex, race, education, household income, unemployment, heavy alcohol intake and smoking in primary analyses (IRR=1.03, 95% CI 1.01, 1.06, p=0.02 per 5 units increase in ADI score). This relationship was robust after adjusting for multiple testing (Holm`s method, p=0.04; FDR, p=0.03) and using other analytic methods (ordinary least squares [OLS] regression: β=0.29, 95% CI 0.01, 0.57, p=0.04). Specific subsites of HNC were also associated with higher deprivation: tongue (IRR=1.11, 95% CI 1.07, 1.14, p<0.01; Holm`s, p=0.01; FDR, p<0.01) and tonsil (IRR=1.05, 95% CI 1.01, 1.09, p=0.02; Holm`s, p=0.05; FDR, p=0.03). Salivary gland, oropharynx, and hypopharynx subsites had a significant association in our primary analysis, but did not demonstrate a significant association when accounting for multiple testing and/or in OLS regression.

Conclusions: This nationally representative ecological study shows that socioeconomic deprivation is associated with increased incidence-rate of oral cavity and pharyngeal cancers. Identifying a relationship between social context and HNC incidence could allow targeted interventions that reduce the burden of this disease on vulnerable communities.

B105: TUMOR BED MARGIN ASSESSMENT IS ASSOCIATED WITH INCREASED USE OF ADJUVANT THERAPY IN PATIENTS WITH EARLY ORAL SQUAMOUS CELL CARCINOMA -

Jamie R Oliver, MD[1]; Rahul Alapati, BS[1]; Andrew J Holcomb, MD[2]; Mark A Varvares, MD[3]; Marisa R Buchakjian, MD, PhD[4]; Andrés M Bur, ND[1]; [1]University of Kansas Medical Center; [2]Nebraska Methodist Health System; [3]Massachusetts Eye and Ear; [4]University of Iowa Hospitals and Clinics

Introduction: Positive margins and close margins are associated with worse prognosis among patients with oral cavity squamous cell carcinoma. However, variation exists in margin sampling technique with recent literature suggesting a higher frequency of positive and close margins when intraoperative margins are taken from the tumor bed versus from the resected specimen. It has been suggested that these closer margins may in turn lead to increased use of adjuvant therapy, however this has yet to be established in the literature.

Methods: A retrospective multi-institutional study was conducted at three high volume tertiary care centers investigating 637 patients who underwent surgical resection of cT1-2N0 oral cavity squamous cell carcinoma. Patients were grouped for analysis based on intraoperative margins assessment technique: specimen-based margins (SBM) vs. tumor bed-based margin (TBBM). Positive margin rates and distance from closest margins between cohorts were compared. Outcomes of re-resection, adjuvant therapy use, and recurrence rates were evaluated. Univariable and multivariable analyses were performed investigating factors associated with adjuvant therapy use.

Results: Most patients had tumors of the oral tongue (412, 64.7%) and had clinical T1 classification tumors (369, 57.9%). Most underwent resection with TBBM (530, 83.2%) while fewer patients underwent resection with SBM (107, 16.8%). The TBBM and SBM cohorts had no significant differences in clinical or pathologic factors including oral cavity subsite, clinical and pathologic staging, rates of perineural invasion, lymphovascular invasion, and extranodal extension. Compared to SBM cases, TBBM resections had a significantly narrower closest margin distance (average case closest margin 2.92mm (IQR 1.0-4.0mm) vs 3.69mm (IQR 1.75-5.0mm), p=0.02). In contrast to closest margin distances, positive margin rate did not significantly differ between SBM (8, 7.6%) and TBBM cases (55, 11.3%, p=0.35). Patients with resection using SBM had a significantly higher rate of re-resections (25, 23.4%) compared to TBBM cases (77, 14.5%, p=0.04). Following surgical resection, 25.5% of SBM cases (n = 27) and 31.9% of TBBM cases (n = 168) received adjuvant treatment, most frequently radiation. In multivariable regression controlling for age, institution, tumor size, pathologic nodal staging, perineural invasion, lymphovascular invasion, and extranodal extension, margin assessment using TBBM was associated with increased rates of adjuvant therapy use (odds ratio = 2.1, 95% CI 1.12-4.28, p=0.027). Rates of local recurrence (SBM: 13, 12.1%, TBBM: 90, 17.0%, p=0.26), regional recurrence (SBM: 14, 13.1%, TBBM: 68, 12.8%, p=1.0) and distant metastasis (SBM: 8, 7.5%, TBBM: 24, 4.5%, p=0.32) did not significantly differ based on margin sampling technique.

Discussion: Tumor bed-based margin sampling is significantly associated with higher rates of narrow margin clearance in patients with early oral squamous cell carcinoma. This in turn is associated with higher utilization of adjuvant therapy which confers additional morbidity to patients with similar disease control.

B106: THE POTENTIAL PROGNOSTIC VALUE OF TUMOR CONFIGURATION IN EARLY-STAGE ORAL CAVITY CANCER -

Fahad Rind, MD; Catherine T Haring, MD, PhD; Stephen Y Kang, MD; Kyle K VanKoevering, MD; Amit Agrawal, MD; Ricardo L Carrau, MD, MBA; Enver Ozer, MD; Nolan B Seim, MD; James W Rocco, MD, PhD; Matthew O Old, MD; The Ohio State University

Introduction: The depth of invasion is an important prognostic marker that was added to the American Joint Committee on Cancer (AJCC) Tumor (T) staging for oral cavity squamous cell carcinoma (OCSCCC) in the AJCC 8th edition Staging Manual. However, it is not always available before ablative surgery and is more commonly only measured at the time of postoperative surgical pathology analysis. This study aims to measure the effect of tumor configuration on overall survival in Stage I & II OCSCC.

Methods: Institutional Review Board approval was granted. A manual retrospective electronic medical record chart review was conducted on surgically treated oral cavity cancer cases between January 2012 and December 2019 at a tertiary medical center. Inclusion criteria included patients that were adults (>18 years old) and had oral cavity cancer of AJCC Stage 1 & 2 (early-stage). The tumor configuration was gathered from pathology reports. Notably, some tumors showed multiple configurations. Descriptive data analysis was utilized to analyze baseline demographics, social history, comorbidity status, perioperative factors, pathology, and long term follow up. The primary outcome of interest was the effect on overall survival. Covariates of overall survival were assessed using Cos Proportional-Hazards models.

Results: A total of 180 cases of early-stage oral cancer were included, and the majority of included patients were male (n=114). The mean age of patients was 62.3 years. The cohort consisted of 121 stage I OSCCC and 59 stage II OCSCC. In total, 126 tumors showed endophytic features, 35 showed ulcerative features, 23 showed exophytic features, 4 were well-circumscribed, two showed polyploid features, two showed flat and one was poorly circumscribed. Some tumors exhibited multiple configurations i.e. 22 showed ulcerative & endophytic (U&E) features and 10 showed exophytic & endophytic feature. The only variables to have a significant effect on 5-year overall survival were U&E tumor configuration (p<0.01), ulcerative tumor configuration (p=0.02), and depth of invasion (p=0.03). When controlling for depth of invasion, the significance of U&E (Hazard ratio 3.12, p<0.01) remained but ulcerative configuration did not (p=0.06).

Conclusion: In early-stage OCSCC, the ulcerative & endophytic tumor configuration showed a significantly poorer overall survival, even when controlling for the depth of invasion. This may be evidence to the importance of clinical examination in prognosticating early stage OCSCC, when the depth of invasion is not available.

B107: DENTAL REHABILITATION OF THE SCAPULAR TIP IN MIDFACE RECONSTRUCTION: AN INSTITUTIONAL EXPERIENCE - <u>LM Sarkis</u>; K Cuddy; R Gilbert; D Goldstein; J de Almeida; Department of Otolaryngology-Head and Neck Surgery, Princess Margaret Cancer Centre/ University Health Network, University of Toronto, Toronto, Ontario, Canada

Introduction: Defects of the maxilla after surgical resection of malignant tumors result in severe functional impairment and problems with facial appearance, mastication and a lack of midfacial support. Recently there has been a paradigm shift towards complete functional oromandibular reconstruction with dental implants after resection to achieve functional rehabilitation. Traditionally, the free fibula flap has been utilised given the availability of bone stock however there is a paucity in the literature assessing dental and prosthetic restoration of the midface using the scapula free flap. The purpose of this study is to present our experience with dental implantation of the scapula tip free flap in midface reconstruction of the maxilla.

Methods: This is a retrospective review of 12 patients who underwent midface reconstruction using the scapula tip between January 2013 and December 2020 at a tertiary referral Head and Neck cancer unit. All patients underwent dental implant placement by an oral and maxillofacial surgeon (K.C) using the 4.1mm Straumann internal hexagon model dental implant system. Follow up of dental implants was conducted both clinically and radiologically with cross sectional imaging. Implant success was defined as both osseointegration and prosthetic rehabilitation.

Results: The mean age of the patients was 52.5 years with two thirds (8/12) of the patients being male. A total of 36 implants were placed into 12 scapula free flaps. The total number of implant failures was 4/36 (11%). Primary stability achieved was <15nM in all dental implants placed. 5/12 (42%) of patients development hypergranulation around the dental implants. There were no flap failures. All patients were able to be restored with a removable implant overdenture.

Conclusion: Dental implantation can be achieved in the scapula tip following maxillectomy utilising the scapula tip for reconstruction, however its use in immediate restoration is limited by the difficulty in obtaining primary stability at the time of implant placement.

B108: PREDICTING TREATMENT DELAYS AMONG PATIENTS WITH ORAL CAVITY CANCER: A RETROSPECTIVE COHORT STUDY - <u>Khara Sauro</u>; Steve Nakoneshny; Wayne Matthews; Shamir P Chandarana; Robert Hart; Daniel Edwards; Joseph C Dort; University of Calgary

Importance: Treatment delays in patients with oral cancer decrease survival and increase the risk of recurrence. Therefore, understanding and predicting who is likely to have delayed treatment provides an opportunity to reduce inappropriate treatment wait-times and improve outcomes for patients.

Objective: To identify factors that predict treatment delays in patients with oral cavity cancer.

Methods: This retrospective population-based cohort study used real-world health data, to identify adult patients diagnosed with oral ca was used to link the cohort to data from hospitals, emergency departments, and physician visits. The primary outcome variables were the wait-time from diagnosis to primary surgery and the wait-time from surgery to adjuvant radiation (continuous variables), which were dichotomized for analysis (delayed primary surgery was > 28 days and delayed adjuvant radiation was > 42 days). Logistic and linear regression explored the relationship between outcome variables and patient and cancer-related variables (age and stage at diagnosis, sex, comorbidities), and processes of care variables (hospital complications, length of hospital stay, emergency department visits) that may delay time from surgery to adjuvant radiation.

Results: There were 767 patients with an average age of 63 (SD=13) years old who had two or more comorbidities (54%). 48% of patients were diagnosed with stage IV cancer.

In the cohort 82% had surgery as their first treatment and 33% had adjuvant radiation (surgery and adjuvant radiation = 255 patients). The mean wait-time to primary surgery was 28 (SD=25) days, and the mean wait-time to adjuvant radiation was 56 (SD=21) days. When dichotomized, 81% of patients had surgery within the recommended time and 6% had adjuvant radiation within the recommended time.

Only pre-existing comorbidities was associate with wait-time to surgery; patients with two or more comorbidities were 0.65 (95%CI= 0.46, 0.90) times less likely to have surgery within the recommended wait time than those who had no comorbidities. Patients who were older were less likely (OR=0.96, 95%CI=0.94, 0.98) to receive timely adjuvant radiation, and patients diagnosed at stage III or IV were 16.15 (95%CI=3.84, 67.99) times more likely to have adjuvant radiation within the recommended time than those diagnosed with stage I or II. When considering process of care factors, none were associated with delays in adjuvant radiation. The two provincial cancer centres differed in time to adjuvant radiation; the odds of receiving timely adjuvant radiation was 2.12 (95%CI=1.02, 4.41) greater for one centre than the other, which persisted after controlling for age and stage at diagnosis (OR=2.28; 95%CI=1.0, 5.31).

Conclusion: The findings suggest that patients who are older and have complex comorbidities are more likely to have delays in treatments, which may not be inappropriate as these patients may be frail and not be physically ready for surgery. Strategies to prehabilitate patients prior to treatment can reduce frailty and improve patient outcomes after treatment. Healthcare system-level factors may also underpin treatment delays based on the finding of between centre differences in wait-times. Future research focusing on healthcare system barriers to timely treatment is needed.

B109: ORAL MICROBIOME DYSBIOSIS ASSOCIATED WITH METASTASIS AND MORTALITY IN ORAL SQUAMOUS CELL CARCINOMA - <u>Delaney Sheehan, MD</u>[1]; Kesava Asam, MS[2]; Juhi J Patel, BS[1]; Caitlyn B Tomblin, MD[3]; Manuel Lora Gonzalez, MD[4]; Harishanker Jeyarajan, MD[1]; Andrew Fuson, MD[1]; Benjamin Greene, MD[1]; Susan McCammon, MD, PhD[1]; Yedeh Ying, MD, DMD[5]; Anthony Morlandt, MD, DDS[5]; Gary Yu, PhD[6]; Chi T Viet, MD, PhD, DDS[7]; Brad Aouizerat, MAS, PhD[2]; Carissa M Thomas, MD, PhD[1]; [1]Department of Otolaryngology-Head and Neck Surgery, University of Alabama at Birmingham; [2]Department of Oral and Maxillofacial Surgery, New York University College of Dentistry; [3]Heersink School of Medicine, University of Alabama at Birmingham; [4]Department of Pathology,

University of Alabama at Birmingham; [5]Department of Oral Maxillofacial Surgery, University of Alabama at Birmingham; [6]Columbia University; [7]Department of Oral and Maxillofacial Surgery, Loma Linda University School of Dentistry

Background: The oral microbiome that exists with oral squamous cell carcinoma (OSCC) is altered compared to the normal oral cavity microbiome, and periodontal pathogens such as Porphyromonas gingivalis and Fusobacterium nucleatum, periodontitis, and poor dental hygiene are risk factors for OSCC. It is unclear how dysbiosis of the oral microbiome may be associated with clinical outcomes in OSCC.

Objective: To determine if OSCC oral microbiome differences exist prior to treatment based on metastasis and 3-year recurrence and survival.

Materials/Methods: Oral swabs of the mucosal microbiome (normal and tumor) were collected from patients with OSCC prior to treatment. Lymph node (LN) metastases were determined based on pathologic assessment of removed LNs during neck dissection. Outcomes including recurrence and survival were followed prospectively for 3 years. DNA was isolated from the oral swabs using Zymo Research DNA Fecal/Soil Microbe Kit and the 16S V4 region was sequenced. FASTQ files were imported into Qiime2. Qiime2 results (ASV table, taxonomy, tree) and Metadata were converted into a Phyloseq object. Environmental contaminants were removed based on negative controls, and appropriate quality control was performed. Alpha (InvSimpson, Shannon) and beta (Bray Curtis) diversity was calculated and ANCOMBC2 was used to generate differential abundances. Microbiome differences based on metastatic disease and 3-year recurrence and overall survival were analyzed.

Results: Ninety-eight patients were included with a mean age of 61 (std 13.4, min 26, max 83), 66% male (N=65) and 92% white (N=90). The rate of regional metastatic disease was 33.7% (N=33), rate of 3-year recurrence was 19.4% (N=19), and overall survival at 3 years was 81.6% (N=80). The oral microbiome associated with OSCC has higher alpha diversity (InvSimpson, p=0.0015; Shannon, p=0.00078) compared to the contralateral normal site. Beta diversity was also significantly different (PERMANOVA, p=9.999e-05). Samples collected from tumor demonstrate increased abundance of Fusobacterium, Selenomonas, Capnocytophaga, Peptococcus, Aggregatibacter, andPeptostreptococcus but decreased Streptococcus, Schaalia, Rothia, and Veillonella compared to the contralateral normal site. The mucosal microbiome associated with tumor was compared between metastatic (to regional LNs) (N=33) and nonmetastatic disease (N=56). No differences were seen in alpha or beta diversity. There were multiple taxa with a significant difference in relative abundance (Figure 1) including increased Prevotella, Peptococcus, Rothia, Kingella, Capnocytophaga and decreased Selenomonas, Veillonella, Catonella. Microbiome comparisons were also made based on recurrence (N=19) and overall survival (N=19). Genera with a significant difference based on recurrence include increased Porphyromonas, Prevotella, Rothia, Treponema, Fusobacterium, Streptococcus and decreased Prevotella, Selenomonas, Haemophilus, Streptococcus. Finally comparison of overall 3-year survival demonstrated significant differences with increased Prevotella, Rothia, Schaalia and decreased Haemophilus, Fusobacterium, Peptococcus, Kingella.

Conclusion: Pretreatment differences in the oral microbiome of OSCC exist based on the clinical outcomes of metastasis, recurrence and survival. Microbiome dysbiosis could be incorporated into risk stratification algorithms for OSCC.

Further research is needed to understand if the bacteria are simply passengers or contributing to disease progression.
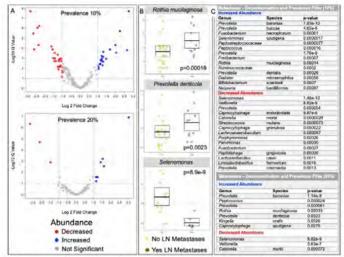

Figure 1. Oral Microbiome Changes Associated with Regional Metastatic Disease in OSCC. A) Volcano plots demonstrating significant changes in relative abundance with a prevalence threshold of 10% and a more stringent 20%. **B)** Box plots demonstrating increased *Rothia mucilaginosa* and *Prevotella denticola* and decreased *Selenomonas* in metastatic OSCC. **C)** Table of all significantly altered genera with a prevalence threshold of 10% and the more stringent 20% threshold.

B110: THE NEUTROPHIL-TO-LYMPHOCYTE RATIO IS ASSOCIATED WITH OUTCOMES ON PEMBROLIZUMAB IN ORAL CAVITY SQUAMOUS CELL CARCINOMA - Angeline A Truong, MS[1]; Rex H Lee, MD[1]; Xin Wu, MD[2]; Alain Algazi, MD[3]; Hyunseok Kang, MD[3]; Ivan H El-Sayed, MD[1]; Jonathan R George, MD, MPH[1]; Chase M Heaton, MD[1]; William R Ryan, MD[1]; Mary J Xu, MD[1]; Patrick K Ha, MD[1]; Katherine C Wai, MD[1]; [1]Department of Otolaryngology-Head and Neck Surgery, University of California San Francisco; [2]Department of Radiology and Biomedical Imaging, University of California San Francisco; [3]Department of Medicine, University of California San Francisco

Introduction: Treatment of advanced stage oral cavity squamous cell carcinoma (OCSCC) can lead to a high degree of morbidity with disappointing survival outcomes. Immune checkpoint inhibitors (ICIs) such as pembrolizumab have shown promising results for the treatment of head and neck cancer, though only in a small group of patients. It remains unclear what factors predict response. A high neutrophil-to-lymphocyte ratio (NLR) has been associated with poorer survival in OCSCC, though less is known about its association with outcomes in patients with OCSCC undergoing ICI treatment.

Objective: To determine the relationship between pre-treatment NLR and 6-month progression-free survival (PFS)/2-year overall survival (OS) in patients with recurrent/metastatic OCSCC on pembrolizumab.

Methods: Retrospective chart review was performed on patients with OCSCC receiving pembrolizumab at a tertiary care center between May 2016 – May 2022. Pre-treatment NLR was calculated from pre-infusion labs drawn on the day of the first ICI cycle. We evaluated pre-treatment NLR as a continuous variable. The primary outcome was 6-month progression-

free survival (PFS). The secondary outcome was 2-year overall survival (OS). Disease progression was defined radiographically as (1) appearance of a new metastatic lesion which was not present on baseline pre-ICI scan, or (2) >20% increase in the diameter of target lesions from baseline scan. These criteria were adapted from RECIST criteria and was confirmed by subspecialty radiologist review. We employed Cox proportional hazards models to analyze the relationship between pre-treatment NLR and 6-month PFS and 2-year OS. We decided a priori to adjust for age, concurrent systemic therapy, and presence of distant metastases at the start of ICI treatment.

Results: Fifty-two patients with OCSCC were included. Overall, 6-month PFS was 46%, and 2-year OS was 44%. The median pre-treatment NLR was 5.7 (IQR 3.6-7.6). Twenty-seven (51.9%) patients received pembrolizumab alone, 4 (7.7%) patients received concurrent radiation therapy (XRT), 18 (34.6%) patients received concurrent chemotherapy, and 3 (5.8%) patients received concurrent chemoradiation therapy. Nineteen (36.5%) patients had distant metastases at the start of ICI treatment. After adjustment, increased NLR was independently associated with lower 6-month PFS [HR 1.05 (95% CI 1.01-1.11), p=0.028] and lower 2-year OS [HR 1.12 (95% CI 1.05-1.20), p<0.001] (Table 1).

Discussion: In OCSCC patients receiving pembrolizumab, a higher pre-treatment NLR was associated with inferior 6-month PFS and 2-year OS. Pre-treatment NLR may represent a useful metric to identify patients most likely to benefit from ICI.

Table 1. Adjusted Cox proportional hazards model for 6-month PFS and 2-year OS with continuous NLR (N=52)

Variable	6-mo PFS			2-year OS		
	HR	95% CI	P-value	HR	95% CI	P-value
Age (years)	0.97	(0.94, 1.00)	0.027	0.98	(0.96, 1.01)	0.128
Concurrent systemic agent(s)						
No	Ref			Ref		
Yes	0.43	(0.18, 1.05)	0.064	0.25	(0.10, 0.62)	0.003
Distant metastases at start						
No	Ref			Ref		
Yes	1.63	(0.69, 3.81)	0.264	1.37	(0.61, 3.07)	0.448
Pre-treatment NLR	1.05	(1.01, 1.11)	0.028	1.12	(1.05, 1.20)	<0.001

HR, hazard ratio; OS, overall survival; PFS, progression-free survival

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B111: INTRAOPERATIVE ULTRASOUND IN ORAL TONGUE CANCER RESECTION - Kevin Higgins, MD, MSC, FRCSC[1]; Joaquin I Ulloa, MD[1]; Danny Enepekides, MD, MPH, FRCSC[1]; Eskander Antoine, MD, Msc, FRCSC[1]; Yan Bernie[2]; Kayaniyil Baldwin[2]; Lauren Lewis[2]; Eva Pellegrino[2]; Veronica Kus[2]; [1]University of Toronto; [2]Sunnybrook Research Institute

Introduction: Between 2003 and 2013, intraoral cavity cancer saw a 3.4% annual increase, with males experiencing a higher incidence. Squamous cell carcinoma, affecting the tongue and floor of the mouth, often requires surgical intervention, where positive surgical margins significantly impact survival rates. Intraoral ultrasound has shown promise in providing accurate preoperative insights.

Objectives: This study aimed to explore the effectiveness of intraoperative ultrasound mapping in reducing positive surgical margins for tongue cancer patients. Primary goals included assessing and comparing the incidence of positive surgical margins based on NCCN classification. Secondary objectives involved evaluating relapse-free and overall survival rates after 2-3 years.

Methods: A prospective cohort pilot study with 30 patients was conducted, dividing them into treatment and control groups. The treatment arm underwent surgery with intraoperative ultrasound mapping, while the control group relied on historical data without intraoperative ultrasound. Surgical procedures involved clinical evaluation, palpation, and intraoperative ultrasound assessment.
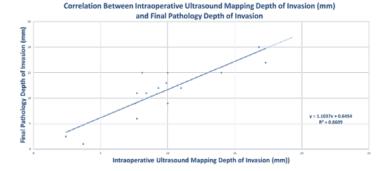
Results: In the intraoperative ultrasound arm, 60% exhibited negative margins, with no positive margins, and wider margins (5.19 mm) compared to the control group (2.80 mm) (p=0.0115 < 0.05). The control group showed 27% positive margins. Perineural invasion was observed in 53% of specimens across both arms. Patients in both arms displayed minimal lymph node involvement. The R^2 value of 0.86 highlights the consistent accuracy of intraoperative ultrasound in measuring the depth of invasion.

Survivorship in the treatment group was positive, with almost all patients showing no recurrence, while one patient in the control group succumbed to the disease.

Discussion: The study demonstrated promising advancements in achieving thorough clearance of deep resection margins with intraoperative ultrasound. Wider margins and the absence of distinctly positive deep margins in the treatment group underscored the efficacy of intraoperative ultrasound, aligning with metanalysis results. The R^2 value highlighted consistent accuracy in measuring the depth of invasion.

Conclusion: Intraoperative ultrasound emerges as a promising tool in tongue cancer surgeries, surpassing control group outcomes and reported literature. Its effectiveness in measuring depth of invasion, improving deep margin clearance rates, and cutting tumors positions it as a valuable asset for surgeons. Further exploration of intraoperative ultrasound's impact on enhancing surgical outcomes in tongue cancer patients is warranted based on these compelling results.

Ultrasound Depth of invasion (mm)	Final Pathology Depth of Invasion (mm)
7.7	11.0
3.7	1.0
17.3	17.0
8.1	15.0
7.6	9.0
11.0	12.0
8.4	11.0
16.8	20.0
9.9	13.0
2.4	2.5
9.3	12.0
14.0	15.0
10.0	9.0
7.7	6.0
15.0	10.0

Correlation Between Intraoperative Ultrasound Mapping Depth of Invasion (mm) and Final Pathology Depth of Invasion

$y = 1.1037x + 0.6454$
$R^2 = 0.8609$

B112: ANALYSIS OF COMORBIDITY BURDEN AND TIME TO SURGERY IN ORAL CAVITY SQUAMOUS CELL CARCINOMA - Wenda Ye, MD; Rahul Sharma, MD; Jean-Nicolas Gallant, MD, PhD; Ramez Philips, MD; Pratyusha Yalamanchi, MD; Melanie Hicks, MD; Eben Rosenthal, MD; James Netterville, MD; Kyle Mannion, MD; Alexander Langerman, MD; Robert Sinard, MD; Michael Topf, MD; Sarah Rohde, MD; Vanderbilt University Medical Center

Background/Rationale: Prior studies have shown that treatment delays are associated with worse survival outcomes in oral cavity squamous cell carcinoma (OCSCC). However, patients with significant comorbidity burden may require optimization prior to treatment initiation to prevent perioperative morbidity and mortality. The objective of this study is to determine the impact of comorbidity burden on surgical treatment delay in a large national cancer database.

Study Design: Retrospective analysis of the National Cancer Database (NCDB)

Methods: Retrospective analysis of patients with OCSCC in the NCDB between 2004-2020. Charlson-Deyo Comorbidity Score (CCI) was extracted for all patients. Time to surgery (TTS) was investigated across CCI. Multivariable linear regression was used to investigate the independent effect of CCI on time-to-surgery adjusting for demographics (age, race, sex, insurance status) and tumor characteristics (stage). TTS was investigated

as a continuous outcome. Cox-regression analysis was used to examine the impact of TTS on 3-year overall survival (OS).

Results: For analysis, 83,664 patients were included. Most patients had a total CCI score of 0 (N=61,965, 74%), while 14,826 had a score of 1 (18%), 4,226 with a score of 2 (5%), and 2,647 with a score of 3 or greater (3%). The median time to surgery was 35 days (IQR 19-53). Time to surgery gradually increased with comorbidities, with a median TTS of 33 days (15-51) for those with a CCI of 0, and 36 days (21-55) for those with CCI score of 3+ (p<0.001). On multivariate linear analysis predicting TTS, a CCI score of 2 (beta = 2.9, 95% CI 1.2-4.6, p<0.001) and 3+ (beta = 2.2, 95% CI 0.04-4.4, p=0.045) was associated with longer TTS. On Cox-regression analysis, continuous TTS was independently associated with 3-year OS (HR 1.00, 1.00-1.00, p=0.003) but with marginal absolute effect.

Conclusions: In this large database study, increasing comorbidity burden in patients with OCSCC was associated with minor increased time to surgery. Delays in time to surgery only had marginal effects on 3-year overall survival. These findings suggest that patient comorbidity status in OCSCC may lead to delays in initiation of surgery. As there is a delicate balance between proceeding towards definitive therapy and pre-treatment optimization, further investigation into measures to expedite this process is warranted.

B113: LOCAL AND SYSTEMIC DETERMINANTS OF ORAL HEALTH AS RISK FACTORS FOR ORAL CAVITY SQUAMOUS CELL CARCINOMA IN NEVER-SMOKING ADULTS: A CASE-CONTROL STUDY USING THE NIH ALL OF US NATIONWIDE DATABASE - Peiran Zhou, MD, PhD[1]; Neeraja Konuthula, MD[2]; Cassie Pan, MD[1]; Rocco Ferrandino, MD[1]; Sarah Holte, PhD[3]; Zain Rizvi, MD[2]; Emily Marchiano, MD[1]; Neal Futran, MD, DMD[1]; Brittany Barber, MD, MSc[1]; [1]University of Washington; [2]University of Miami; [3]Fred Hutchinson Cancer Center

Introduction: Tobacco use has long been recognized as a prominent risk factor associated with the development of oral cavity squamous cell carcinoma (OCSCC). Despite a notable decline in smoking rates from 20.9% in 2005 to 11.5% in 2021, incidence rates for cancers of the oral cavity and pharynx combined have exhibited a concerning upward trend, ~ 0.6% per year 2007 to 2016, especially in young, never-smoking patients. Prior research suggested OCSCC is associated with poor oral health. This study utilizes the NIH All of Us Research Program, designed to facilitate inclusive precision medicine research within a large-scale cohort, to evaluate a range of local and systemic oral health determinants as risk factors associated with developing OCSCC in never-smoking patients.

Methods: A case-control study was conducted utilizing the NIH All of Us database. The case group included all never-smoking adults with a diagnosis of OCSCC, each with four age, gender, and race matched never-smoking controls. The database was queried for factors reflecting and/or affecting oral health, including periodontal disease, acquired absence of teeth, hyperlipidemia, hyperglycemia, HIV, oral-related autoimmune diseases, depression, antidepressant use, eating disorders, preterm labor (female only), and oral contraceptive use (female only). Odds ratios and 95% confidence intervals (CI) were calculated for each risk factor.

Results: Four hundred and five never-smoking adults with OCSCC and 1,620 age, gender, race matched never-smoking OCSCC-free controls were identified. The average age of OCSCC onset was 58.39 years, ranging from 18 to 88 years. The demographic distribution in both case and control groups showed a relatively even split between gender, with approximately 49.38% identifying as male, 49.14% as female, and 1.48% as others. In terms of racial composition, 69.63% were White, 10.86% were Black, 1.98% were Asian/Native Hawaiian/Pacific Islander, and 17.53% belonged to other racial categories. Logistic regression analysis revealed several independent predictors of OCSCC with odds ratios (95% CI) of 4.99 (2.79-8.92) for periodontal diseases, 1.53 (1.12-2.08) for hyperlipidemia, 2.96 (1.20-7.27) for HIV infection, 2.40 (1.21-4.74) for oral-related autoimmune diseases, 1.51 (1.01-2.24) for depression, 8.46 (1.55-46.14) for eating disorders, and 1.53 (1.05-2.22) for antidepressant use. Some risk factors did not exhibit statistically significance: 1.07 (0.37-3.08) for acquired absence of teeth, 1.46 (0.99-2.15) for hyperglycemia/diabetes mellitus, 3.17 (0.83-12.24) for a history of preterm labor (limited to females), and 3.26 (0.86-12.35) for oral contraceptive use (limited to females).

Conclusion: We identified several independent predictors of OCSCC in never-smoking adults, including periodontal diseases, hyperlipidemia, oral-related autoimmune diseases, depression, eating disorders, and antidepressant use. These findings underscore the complex nature of OCSCC etiology and emphasize the importance of a comprehensive approach to OCSCC risk assessment and prevention. Further statistical analysis is underway to generate composite risk scores for OCSCC in never-smoking adults.

B114: NASOGASTRIC FEEDING TUBE USAGE FOLLOWING TRANSORAL ROBOTIC SURGERY FOR OROPHARYNGEAL CARCINOMA -

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Background: Rates of perioperative nasogastric feeding tube (NGT) placement following transoral robotic surgery (TORS) for oropharyngeal carcinoma vary widely by tumor characteristics and institutional practices. This investigation aims to identify predictors of NGT placement after TORS and compare functional outcomes and complications among patients with and without NGT.

Methods: This is a retrospective review of patients who underwent TORS for oropharyngeal carcinoma between 2016 and 2023 at a single tertiary-care institution. During this study period, our institutional practice includes rare prophylactic NGT placement for only complex defects involving multiple subsites. Primary outcome includes NGT placement. Demographic, clinical, surgical, oncologic characteristics as well as complications and functional outcomes such as Functional Oral Intake Scale (FOIS) score were compared among groups. Univariable and multivariable logistic regression analyses were performed to identify predictors of perioperative NGT placement.

Results: Among 436 patients who underwent TORS for oropharyngeal carcinoma included in the study, 60 had an NGT placed post-operatively and required tube feeds. Among those who received NGT, 34% required NGT for less than 7 days, 18% required NGT for 7-13 days, and 47% required NGT dependent for 14 days or more. There were no differences in demographics between NGT-dependent and independent groups. Patients requiring NGT had a significantly increased Charleson Comorbidity Index (CCI) Score (4,2;p<0.001). NGT dependent patients had significantly greater pathologic T2 or larger tumors (71%,46%;p<0.0001); there was no difference in HPV mediated disease or N stage. There was no difference in tumor subsite or specific surgical resection subsites between groups. Significantly greater patients requiring NGT had tumors crossing midline (13%,3.3%;p=0.007) and histopathologic evidence of perineural invasion (41%,15%,p<0.001). Paired analysis demonstrated perioperative NGT dependence was associated with a greater decrease in BMI at 6 months (-2.02,-1.39,p=0.031). NGT dependence was associated with increased incidence of aspiration pneumonia (5%,0.5%,p=0.020) and length of stay (3 days,2 days;<0.001). There were no differences in readmission rates between groups. Patients who received NGT had a significantly lower FOIS upon discharge (2,5;p<0.001), which improved but remained significantly lower at 1 month (5,6;p=0.003), 3 months (5,6;p=0.004), and 1 year (5.5,7;p<0.001). Pre-operative and 3-year postoperative FOIS were not significantly different. Patient receiving NGT had significantly more inpatient speech language pathology sessions (2,1;p<0.001). There were no differences in gastrostomy tube or tracheostomy tube placement between groups at any time point. Multivariable logistic regression identified greater CCI (OR 1.37,95% CI 1.18-1.61;p<0.001), T2 or larger tumor (OR 2.04,95% CI 1.01-4.27;p=0.005), tumor crossing midline (OR 0.618, 95% CI 1.09-12.9; p=0.031), and perineural invasion (OR 0.364, 95% CI 1.66-6.97; p<0.001) as predictors of NGT placement.

Conclusion: NGT placement can be safely avoided in the majority patients undergoing TORS. Increased CCI, T2 or larger tumor, tumor crossing midline, and perineural invasion are risk factors for NGT placement. The majority who receive NGT utilize it for longer than 2 weeks. Specific subsites resected were not associated with nor predictive of NGT dependence. Patients requiring NGT had worse swallow function until 1 year postoperatively, associated with significantly higher weight loss. Additional multi-institutional data are being gathered for further analyses.

B115: ASSESSMENT OF TRI-MODALITY TREATMENT IN OROPHARYNGEAL SQUAMOUS CELL CARCINOMA: AN INSTITUTIONAL REVIEW -

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Introduction: Multi-modality treatment intensification is indicated for patients undergoing definitive surgical resection of head and neck cancer with high-risk pathologic features. Adjuvant radiation and chemotherapy following surgery or tri-modality therapy is recommended based on findings of extranodal extension (ENE) and positive margins for head and neck squamous cell carcinoma. However, tri-modality therapy for human papilloma virus (HPV) associated oropharyngeal squamous cell carcinoma (OPSCC) has not demonstrated significant improvement in survival compared to dual modality therapy such as surgery with adjuvant radiation or definitive chemoradiation. Avoidance of tri-modality therapy may reduce long-term functional side effects and toxicities in this

cohort. National cancer registry data has demonstrated the number of pathologic lymph nodes is associated with the high-risk feature of ENE and may be predictive of tri-modality care. The objective of this study is to assess the use of regional lymph node count to minimize rates of tri-modality therapy for OPSCC at the University of Maryland Medical Center.

Methods: Patients at the University of Maryland Medical Center who were diagnosed with OPSCC from 2018 through 2021 were extracted using the appropriate diagnostic ICD-10 code. Exclusion criteria included patients presenting with OPSCC recurrence or any patient that did not receive definitive treatment during this time interval. Demographic, radiographic, pathologic and survival variables were collected. Statistical analysis conducted included descriptive statistics, univariate and multivariate logistic regression as well as subset analysis for patients who were diagnosed with HPV-positive OPSCC and specifically those patients who underwent transoral robotic surgery.

Results: 252 patients met criteria and became the analytic cohort. The majority of the cohort was male (87%), former smokers (54%), with HPV-positive disease (87%). Subsite date demonstrated that most OPSCC cancers involved the palatine tonsil (53%) and/or the base of tongue (42.5%). Overall our institutional tri-modality rate was 14%. Our single modality rate was 19.4% and included those who underwent definitive surgery or radiation alone. The dual modality rate was 66% which includes those who underwent definitive chemoradiation or surgery with adjuvant radiation. Of the surgery cohort, pathologic extranodal extension was present in 28.9% of patients and in the transoral robotic surgery subset specifically the ENE rate was 25.5%. Multivariate logistic regression has demonstrated that the presence of pretreatment variables such as clinical ENE and number of lymph nodes are more likely to undergo tri-modality treatment (0.008, 0.01).

Conclusion: The institutional practice at the University of Maryland Medical Center has traditionally been to use pretreatment variables to stratify patients to definitive surgery versus chemoradiation in an attempt to avoid tri-modality care. Our data demonstrate that patients with a multiple lymph nodes or radiographic clinical ENE are more likely to have pathologic ENE that would indicate adjuvant chemoradiation and thus tri-modality care. Overall this demonstrates that the use of radiographic variables such as number of lymph nodes and clinical ENE can be used to predict whether a patient should undergo definitive chemoradiation even if the patient is a surgical candidate.

B116: TEMPORAL TRENDS IN HPV KNOWLEDGE AND HEAD AND NECK SQUAMOUS CELL CARCINOMA FOLLOWING EXPANDED VACCINATION ELIGIBILITY: A SEER-HINTS STUDY

- Oluwatobiloba Ayo-Ajibola, BS; Michelle Koh, BA; Catherine Julien, BA; Ryan J Davis, BS; Matthew E Lin, BS; Wendy J Mack, PhD; Daniel Kwon, MD; Keck School of Medicine of USC

Introduction: Human papillomavirus (HPV) is a critical precursor to a growing proportion of head and neck squamous cell carcinoma (HNSCC), especially oropharyngeal cancers. The approval of the Gardasil 9 vaccine for expanded age groups (up to 45 years old) in 2018 marked a significant stride towards curbing HPV-related neoplasms. This study delves into the impact of this policy shift on the public's comprehension of HPV, its vaccine, and its association with HNSCC.

Study Design: Cross-sectional survey waves

Methods: The National Cancer Institute Health Information National Trends Survey (2018 and 2020 cycles), a nationally representative survey of US adults, was queried. A sample of 7369 adults was assessed for knowledge of HPV, its vaccine, and its association with oral HNSCC and cervical cancer. Significance testing was used to assess variation between demographic subgroups as well as percent changes in awareness across the two years. Significance was set at p<0.05.

Results: Most respondents were aware of HPV (2018: 60.78%; 2020: 64.78%), and its vaccine (2018: 59.69%; 2020: 60.21). A significant decrease in the high awareness of the association with cervical cancer was seen (2018: 75.04%; 2020: 70.22%, p=0.028). Knowledge of HPV+ HNSCC was poor and did not change over time (2018: 29.96%, 2019: 29.52%). Caucasians (p=0.013), males (p=0.024), high school-educated individuals (p=0.009), and those making more than $200,000 (p=0.022) displayed an increased awareness of HPV. Bisexual individuals exhibited a decreased awareness (p=0.038). Possessing an annual income of $14,999 or less (p=0.038) and identifying as gay or lesbian (p=0.005) were associated with increases in vaccine awareness. While not significant (p=0.384), those identifying as gay, lesbian, or bisexual showed the highest increase in percent awareness of HPV+ HNSCC with increased educational attainment yielded stepwise increases in percent awareness for each year (2018: p= 0.036; 2020: p=0.108).

Conclusions: While awareness of HPV, the vaccine, and cervical cancer is high, that of the association with HNSCC remained poor despite expanded eligibility. Tailored public health educational endeavors elucidating the nexus between HPV and HNSCC may augment awareness among cohorts poised to reap substantial benefits from vaccination. This could potentially bridge the knowledge gap, fostering enhanced vaccination uptake and, subsequently, a downtrend in the incidence of HPV-associated HNSCC.

B117: MANAGEMENT OF HPV-RELATED HEAD AND NECK SQUAMOUS CELL CARCINOMA WITH UNKNOWN PRIMARY IN THE ERA OF TREATMENT DE-ESCALATION

- Thomas F Barrett, MD; Salma Ramadan; Patrik Pipkorn; Paul Zolkind; Jason T Rich; Richard A Harbison; Anthony J Apicelli; Wade Thorstad; Hiram Gay; Peter Oppelt; Douglas Adkins; Ryan S Jackson; Sidharth V Puram; Washington University School of Medicine in St. Louis

Background: Management of HPV+ head and neck squamous cell carcinoma with unknown primary (HNSCCwUP) remains controversial. A primary surgical approach involving transoral surgery (TOS) to search for the unknown primary and concurrent neck dissection (ND) has shown excellent rates of primary lesion detection. Furthermore, this approach has allowed for appropriate pathologic staging, directed adjuvant radiation therapy (RT) to high risk primary and nodal sites, reduced radiation dose to the pharynx, and decreased rates of patients receiving chemotherapy. Here, we report our long-term institutional experience with this approach in HPV+ HNSCCwUP.

Methods: We conducted a retrospective cohort analysis of patients who presented to our institution with p16+ cervical nodal metastasis with unknown primary between July 2012 and December 2021. Only patients who did not have evidence of a primary tumor on PET-CT or clinical

exam were included. Kaplan-Meier (KM) estimates were computed for both disease-free survival (DFS) and overall survival (OS). Details of adjuvant therapy, recurrence, and rates of gastrostomy tube placement were also analyzed.

Results: 66 patients met inclusion criteria (Table 1) with median follow-up of 5.5 years. The primary lesion was detected on final pathology in 57 patients (86.4%). 5-year KM-OS estimates for the undetected and detected groups was 100% and 95.2%, respectively (Figure 1). 5-year KM-DFS estimates were 88.9% and 95.2% in the undetected and detected groups respectively. One patient developed a regional recurrence at 13 months post-op, underwent salvage surgery, and showed NED at 19 months (Figure 2). Four patients (7%) developed distant metastases, two of whom died and two of whom underwent salvage metastectomy and subsequently with NED at 7.2 and 7.7 years respectively. Contralateral ND was performed in 25 patients (two with cN2 disease; 23 with tumors approaching midline), 7 of whom had bilateral disease on final pathology. 13 patients were treated with surgery alone (19.7%; Table 2). 25 patients (37.9%) did not receive RT to the primary site, 13 patients (19.7%) did not receive RT to the ipsilateral neck, and 49 patients (74.2%) did not receive RT to the contralateral neck. 16 patients (24.2%) received adjuvant chemotherapy. One patient required a gastrostomy tube during adjuvant treatment. There was a trend in de-escalation of adjuvant RT over time without change in 5-year DFS or OS (Figure 3).

Conclusion: TOS yields high rates of detection of the primary lesion in HPV+ HNSCCwUP. Both patients with detected and undetected primary lesions have excellent OS and DFS. Our single-institution experience suggests that a surgical approach with TOS and selective ND effectively directs adjuvant RT to high risk sites, allows for sparing radiation to low risk pharyngeal subsites and the contralateral neck, and avoids the need for chemotherapy in the majority of patients.

Figure 1. Kaplan-Meier curves for patients for overall and disease-free survival comparing patients whose primary lesion was found after surgery versus those whose were not.

	Primary Detected (N=57)	Primary Undetected (N=9)	Overall (N=66)
Adjuvant RT			
Yes	44 (77.2%)	8 (88.9%)	52 (78.8%)
Not recommended	5 (8.8%)	1 (11.1%)	6 (9.1%)
Refused	7 (12.3%)	0 (0%)	7 (10.6%)
Unknown	1 (1.8%)	0 (0%)	1 (1.5%)
Adjuvant Chemo			
Not indicated	39 (68.4%)	6 (66.7%)	45 (68.2%)
Cetuximab	3 (5.3%)	0 (0%)	3 (4.5%)
Cisplatin	10 (17.5%)	3 (33.3%)	13 (19.7%)
Refused	4 (7.0%)	0 (0%)	4 (6.1%)
Lost to follow-up	1 (1.8%)	0 (0%)	1 (1.5%)
RT to Primary			
No	19 (33.3%)	6 (66.7%)	25 (37.9%)
Yes	29 (50.9%)	1 (11.1%)	30 (45.5%)
Unknown	9 (15.8%)	2 (22.2%)	11 (16.7%)
Dose to Primary (Gy)			
0	12 (21.1%)	6 (66.7%)	18 (27.3%)
42	5 (8.8%)	1 (11.1%)	6 (9.1%)
60	24 (42.1%)	0 (0%)	24 (36.4%)
66	1 (1.8%)	1 (11.1%)	2 (3.0%)
70	1 (1.8%)	0 (0%)	1 (1.5%)
Unknown	14 (24.6%)	1 (11.1%)	15 (22.7%)
RT to Ipsilateral Neck			
No	12 (21.1%)	1 (11.1%)	13 (19.7%)
Yes	36 (63.2%)	7 (77.8%)	43 (65.2%)
Unknown	9 (15.8%)	1 (11.1%)	10 (15.2%)
Dose to Ipsilateral Neck (Gy)			
0	12 (21.1%)	1 (11.1%)	13 (19.7%)
42	5 (8.8%)	2 (22.2%)	7 (10.6%)
60	19 (33.3%)	4 (44.4%)	23 (34.8%)
60+52	12 (21.1%)	0 (0%)	12 (18.2%)
66	0 (0%)	1 (11.1%)	1 (1.5%)
Unknown	9 (15.8%)	1 (11.1%)	10 (15.2%)
RT to Contralateral Neck			
No	43 (75.4%)	6 (66.7%)	49 (74.2%)
Yes	5 (8.8%)	1 (11.1%)	6 (9.1%)
Unknown	7 (12.3%)	2 (22.2%)	9 (13.6%)
Missing	2 (3.5%)	0 (0%)	2 (3.0%)
Dose to Contralateral Neck (Gy)			
0	43 (75.4%)	7 (77.8%)	50 (75.8%)
42	1 (1.8%)	1 (11.1%)	2 (3.0%)
52	2 (3.5%)	0 (0%)	2 (3.0%)
60+52	2 (3.5%)	0 (0%)	2 (3.0%)
Unknown	9 (15.8%)	1 (11.1%)	10 (15.2%)
G-tube with RT			
No	53 (93.0%)	8 (88.9%)	61 (92.4%)
Yes	1 (1.8%)	0 (0%)	1 (1.5%)
Unknown	3 (5.3%)	1 (11.1%)	4 (6.1%)

Table 2. Details regarding adjuvant treatment.

	Primary Detected (N=57)	Primary Undetected (N=9)	Overall (N=66)
Gender			
Male	51 (89.5%)	9 (100%)	60 (90.9%)
Female	6 (10.5%)	0 (0%)	6 (9.1%)
Age (years)			
Mean (SD)	56.5 (8.13)	58.8 (7.81)	56.8 (8.07)
Median [Min, Max]	57.0 [39.0, 77.0]	57.0 [49.0, 72.0]	57.0 [39.0, 77.0]
Diagnosis Method			
FNA	31 (54.4%)	5 (55.6%)	36 (54.5%)
Core	6 (10.5%)	3 (33.3%)	9 (13.6%)
ELNB	17 (29.8%)	1 (11.1%)	18 (27.3%)
ND	3 (5.3%)	0 (0%)	3 (4.5%)
Surgical Approach			
MxLx	6 (10.5%)	0 (0%)	6 (9.1%)
TLM	22 (38.6%)	4 (44.4%)	26 (39.4%)
TORS	29 (50.9%)	5 (55.6%)	34 (51.5%)
Contralateral ND			
No	32 (56.1%)	8 (88.9%)	40 (60.6%)
Yes	25 (43.9%)	1 (11.1%)	26 (39.4%)
pT			
T0	0 (0%)	9 (100%)	9 (13.6%)
T1	48 (84.2%)	0 (0%)	48 (72.7%)
T2	9 (15.8%)	0 (0%)	9 (13.6%)
pN			
N1	44 (77.2%)	6 (66.7%)	50 (75.8%)
N2	13 (22.8%)	3 (33.3%)	16 (24.2%)
PNI			
No	54 (94.7%)	0 (0%)	54 (81.8%)
NR	1 (1.8%)	9 (100%)	10 (15.2%)
Yes	2 (3.5%)	0 (0%)	2 (3.0%)
LVI			
No	46 (80.7%)	0 (0%)	46 (69.7%)
NR	1 (1.8%)	9 (100%)	10 (15.2%)
Yes	10 (17.5%)	0 (0%)	10 (15.2%)
ECE			
No	28 (49.1%)	3 (33.3%)	31 (47.0%)
Yes	28 (49.1%)	6 (66.7%)	34 (51.5%)
Missing	1 (1.8%)	0 (0%)	1 (1.5%)
Follow-up (years)			
Mean (SD)	5.54 (2.79)	6.13 (2.72)	5.62 (2.77)
Median [Min, Max]	5.50 [1.09, 11.2]	6.45 [1.57, 9.99]	5.56 [1.09, 11.2]

Table 1. Patient characteristics. FNA = final needle aspiration; Core = Core needle biopsy; ELNB = excisional lymph node biopsy; ND = neck dissection; TLM = transoral laser microsurgery; TORS = transoral robotic surgery; PNI = perineural invasion; LVI = lymphovascular invasion; ECE = extracapsular extension
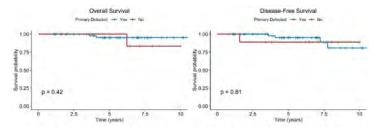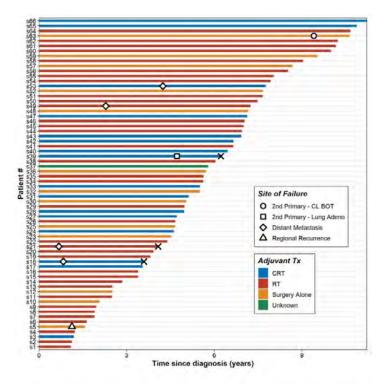
Figure 2. Swimmer plot including all patients included in the study. Bars extend to last known follow-up or death (marked with X). CL BOT = contralateral base of tongue.
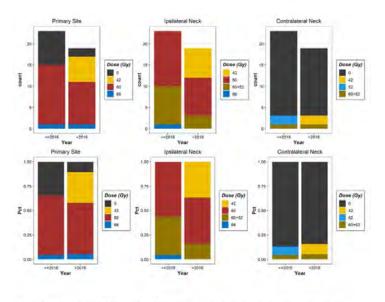

Figure 3. Barplots displaying number (top row) and proportion (bottom row) of patients receiving adjuvant radiation to the primary site, ipsilateral neck, and contralateral neck before and after the year 2017 at our institution. "60+52" refers to patients who received 60 Gy to the high risk nodal levels and 52 Gy to the elective neck levels.

B118: EVALUATING THE ACCURACY OF CHAT-GPT IN COMMON PATIENT QUESTIONS REGARDING HPV+ OROPHARYNGEAL CARCINOMA - Nikhil Bellamkonda, MD[1]; Janice L Farlow, MD, PhD[2]; Richard B Cannon, MD[1]; Marcus M Monroe[1]; Hilary C McCrary, MD, MPH[1]; [1]University of Utah; [2]Indiana University Health

Introduction: Large language model (LLM)-based chatbots such as Chat-GPT have been publicly available and increasingly utilized by the general public since late 2022. This study sought to investigate Chat-GPT responses to common patient questions regarding Human Papilloma Virus (HPV) positive oropharyngeal cancer (OPC). This cohort of patients has been found to have higher levels of education and socioeconomic status, making this patient population more apt to using LLMs to independently acquire information about their diagnosis and prognosis.
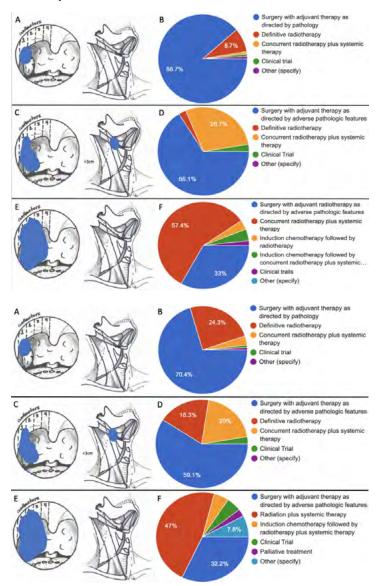
Methods: This was a prospective, multi-institutional study, with data collected from three high volume institutions that perform >50 transoral robotic surgery cases per year. The 100 most recent discussion threads including the term "HPV" on the American Cancer Society's Cancer Survivors Network's Head and Neck Cancer public discussion board were reviewed in September 2023. The 11 most common questions were serially queried to Chat-GPT 3.5; answers were recorded. A survey was distributed to fellowship trained head and neck oncologic surgeons at three institutions to evaluate the responses for clinical accuracy, comprehensiveness, and alignment with consensus in the head and neck surgical community. Study was IRB approved.

Results: A total of 8 surgeons participated in the study. All surgeons worked in an academic setting and had been practicing for an average of 10.4 years after fellowship. Five (62.5%) surgeons were male. For questions regarding HPV contraction and transmission, Chat-GPT answers were scored as clinically accurate and aligned with consensus 84.4% and 90.6% of the time, respectively. For questions involving treatment of HPV+ OPC, Chat-GPT was clinically accurate and aligned with consensus 87.5% and 91.7% of the time, respectively. Only 50% of surgeons thought that Chat-GPT responded accurately when asked about the timing of HPV vaccination. When asked about circulating tumor DNA testing, only 12% of surgeons thought responses were accurate or consistent with consensus in the head and neck surgical oncology community. The average comprehensiveness score for all responses was 4/5.

Discussion: The majority of the Chat-GPT 3.5's responses to common patient questions regarding HPV+ OPC were appropriate. However, it performed poorly with questions involving evolving therapies and diagnostics - thus, caution should be used when using a platform like Chat-GPT 3.5 to assess use of advanced technology. Patients should be counseled on the importance of consulting their surgeons to receive accurate and up to date recommendations, and use LLM's to augment their understanding of these important health-related topics. As this type of informational platform increases in use, it has great potential to provide the public with accurate and up-to-date health-related information.

B119: PRACTICE PATTERNS IN TREATMENT OF P16-NEGATIVE / HPV-NEGATIVE OROPHARYNGEAL SQUAMOUS CELL CARCINOMA: A SURVEY OF AHNS MEMBERSHIP - Mustafa G Bulbul, MD, MPH[1]; John DeAlmeida, MD, MSc, FRSCS[2]; Neil Gross, MD, FACS[3]; Meghan T Turner, MD, FACS[1]; [1]Department of Otolaryngology, West Virginia University; [2]Department of Otolaryngology Head and Neck Surgery, University of Toronto; [3]Department of Head and Neck Surgery, Division of Surgery, The University of Texas MD Anderson Cancer Center

Importance: Human papillomavurs (HPV)-negative oropharyngeal cancer has been shown to have worse overall survival in numerous clinical trials (RTOG 0129, RTOG 0234, TAX 423) compared to HPV-positive disease in spite of treatment intensification. Transoral robotic surgery (TORS) has been proposed as a way to intensify treatment, but is performed in so rarely that RTOG 1221 was forced to close.

Objective: To investigate practice patterns in the treatment of p16-negative / HPV-negative oropharyngeal squamous cell carcinoma (OPSCC) among head and neck surgeons (HNS), radiation oncologists (RO) and medical oncologists (MO).

Design and Participants: Cross-sectional survey of American Head and Neck Society (AHNS) membership.

Setting: Online electronic survey.

Methods: We designed an online survey that was tested by two experts, approved, and distributed via email to the AHNS membership list. Participation was voluntary and data was anonymously collected. Practice patterns with respect to HPV-negative disease were assessed.

Results: A total of 115 members (8.2% of AHNS members) responded (93.8% surgical, 3.5% radiation and 2.6% medical oncologists). Most (67%) had >5 years of experience in the field (43.5% had >10 years and 23.5% had 5-10 years) whereas 27.8% reported <5 years of experience and 5.2% were fellows-in-training. There was a relatively equal geographic distribution of the respondents (23.5% from Midwest, 22.6% from Northeast, 21.7% from South, 20% from outside the US and 12.2% from South). When asked about confirmation of HPV-negative status with HPV DNA/RNA in situ hybridization or PCR testing for p16-negative tumors, 21.7% reported never, 47% infrequently, 9.6% frequently, and 21.7% always. Most surgeons (60%) reported recommending TORS for identification of an unknown primary in a patient with p16- and HPV-negative neck mass. Similarly, at least half (50.9%) of surgeons indicated frequently treating resectable T1-T3 with TORS (5.6% always, 32.4% infrequently and 11.1% never). Results depicting what respondents would do in specific scenarios are presented in Figures 1 (healthy 60-year-old patient) and 2 (80-year-old patient with kidney disease). The majority (73.2%) of surgeons indicated infrequently (59.3%) or never (13.9%) treating T3/T4 with traditional open surgery as first line (21.3% frequently and 5.6% always). More than half of the surgeons (57.4%) believed survival is better with surgery compared to definitive non-surgical therapy for HPV-negative OPSCC. When asked about treatment intensification (dual modality adjuvant treatment for T1-2N0, or tri-modality treatment for T1-T2N1), there was wide variation in practice with 21.7% reported never and 36.5% infrequently, 32.2% frequently, and 9.6% always.

Conclusions: Most surgeons (57.4%) believe survival for HPV-negative OPSCC is better with surgery. The vast majority would treat T1-T2N1 tumors with surgery, while 73.2% would infrequently or never operate on T3/T4 tumors. There was wide variation in practice with respect to treatment intensification.

B120: PLASMA TUMOR TISSUE MODIFIED VIRAL HPV DNA AS A MARKER FOR DISEASE BURDEN IN OROPHARYNGEAL CARCINOMA OF UNKNOWN PRIMARY - Andre J Burnham, BS[1]; Nikhil T Vettikattu, BS[1]; Georges E Daoud, MD[2]; Nicole C Schmitt, MD[2]; Brian Boyce, MD[2]; Jennifer Gross, MD[2]; Harry M Baddour, MD[2]; Mark El-Deiry, MD[2]; Conor E Steuer, MD[3]; Nabil F Saba, MD[3]; James E Bates, MD[4]; William A Stokes, MD[4]; Mihir R Patel, MD[2]; Azeem S Kaka, MD[2]; [1]Emory University School of Medicine; [2]Winship Cancer Institute of Emory University, Department of Otolaryngology-Head and Neck Surgery; [3]Winship Cancer Institute of Emory University, Department of Hematology-Oncology; [4]Winship Cancer Institute of Emory University, Department of Radiation Oncology

BACKGROUND: Tumor tissue modified viral (TTMV)-human papillomavirus (HPV) deoxyribonucleic acid (DNA) has recently been shown to be a reliable marker of disease burden in patients with HPV-associated oropharyngeal squamous cell carcinoma (OPSCC), including nodal disease and clinical staging. However, few studies have investigated TTMV HPV DNA in patients with carcinoma of unknown primary (CUP) with presumed OPSCC. Here, we compare TTMV HPV DNA titers with radiographic and clinicopathological factors in patients with HPV-positive CUP.

METHODS: This retrospective chart review was approved by the Institutional Review Board (IRB00104979). The institutional database was queried for patients with presumed OPSCC who have undergone transoral robotic surgery (TORS) and neck dissection for HPV/P16+ CUP between 2019 and 2022 at a tertiary referral center. Patients met inclusion criteria if they had completed our institutional CUP protocol (preoperative cross-sectional imaging, physical and fiberoptic examination) and had both pre- and post-operative TTMV HPV DNA testing. A total of 28 patients met inclusion criteria. TTMV HPV DNA was quantified using NavDx®, by Naveris (Waltham, MA, USA). For included patients, clinicopathologic and radiographic information was abstracted from the medical record. Statistics were generated using linear regressions, student T-tests, and one-way ANOVA.

RESULTS: Twenty-five (89%) patients had detectable TTMV HPV DNA prior to TORS, and one patient (3.6%) had detectable DNA levels following surgery (median 163; SD ± 1608 fragment/mL). The number of positive cervical lymph nodes (median 2; SD ± 2.4) on final pathology (p = 0.0122) and nodal SUVmax on PET-CT (median 8.7; SD ± 5.6) (p = 0.0436) were positively correlated with TTMV HPV DNA titers. The median number of nodes collected per patient was 23 (SD ± 9.5). Radiographic lymph node diameter (median 3; SD ± 1.2 cm) was inversely associated with TTMV HPV DNA titers (p = 0.021). No significant association was observed between TTMV HPV DNA and pathological T- or N-classification.

CONCLUSION: To our knowledge, this is the largest case series to date investigating TTMV HPV DNA in OPSCC patients with CUP. Our results suggest TTMV HPV DNA may be helpful in refining treatment algorithms for patients with CUP.

B121: ONCOLOGIC AND FUNCTIONAL OUTCOMES OF TRANSORAL SURGERY IN HPV-NEGATIVE OROPHARYNGEAL CANCER - Katherine Chang, MD; Andrew Peterson, MD; Patrik Pipkorn, MD; Sidharth Puram, MD, PhD; Ryan Jackson, MD; Washington University

Introduction: The advent of transoral robotic surgery (TORS) and laser microsurgery (TLM) has been widely adopted for treatment of oropharyngeal carcinoma. There is a paucity of data on oncologic and functional outcomes in patients with human papillomavirus (HPV)-negative oropharyngeal squamous cell carcinoma (OPSCC).

Methods: A retrospective study of patients at a single institution with a pathologic diagnosis of HPV-negative OPSCC who underwent primary definitive TORS or TLM surgery with pathology-guided adjuvant therapy (1998-2020). The primary outcomes of interest were overall survival (OS) and disease-free survival (DFS). Secondary outcomes included rates of postoperative gastrostomy tube (G-tube), tracheostomy, and functional outcome swallowing scale (FOSS) scores.

Results: We identified 94 patients treated with transoral surgery for HPV-negative OPSCC. The majority of patients presented with late stage disease (stage III/IV, 70%); 79% presented with early T-stage (T1/T2) and most patients had positive nodal disease (71%). Of patients with nodal disease, the majority (66%) had ENE. Forty-four percent of patients received surgery alone, 28% received adjuvant radiation, and 29% received adjuvant chemoradiation. A total of 36 patients (39%) developed recurrent disease; 22% with locoregional and 15% with distant recurrence. Five-year overall survival and disease-free survival were 75% and 48% for stage I/II disease and 48% and 42% for stage III/IV disease. Early T-stage (T1/T2) was associated with improved 5-year OS (64% vs 24%, p<0.01) and DFS (50% vs 21%, p<0.01) when compared to late T-stage (T3/T4). Nodal disease and ENE were not significantly associated with OS or DFS. Five-year DFS was worse with positive margins [22% vs 50%, p<0.01] and perineural invasion (PNI) [25% vs 52%, p=0.01]. There was a trend towards worsened OS with positive margins and PNI, however this did not reach statistical significance. Patients with stage III/IV disease had higher rates of postoperative G-tube placement, tracheostomy, and higher FOSS scores (4-5) than patients with stage I/II disease: 31% vs 0% (G-tube), 21% vs 0% (tracheostomy), and 31% vs 0% (FOSS 4-5) respectively.

Conclusion: In patients with HPV-negative OPSCC undergoing transoral surgery, advanced T-stage was a poor prognostic factor associated with worse OS and DFS while nodal disease and ENE were not as predictive. We observed significantly improved OS with early stage disease and low rates of long-term G-tube and tracheostomy dependence. Transoral surgery for HPV-negative OPSCC appears to have acceptable oncologic outcomes while reducing functional morbidity in early stage disease.

B122: ASSESSING RISK OF POSTOPERATIVE HEMORRHAGE WITH NSAID USE AFTER TRANSORAL ROBOTIC SURGERY (TORS) - John Dewey, MD; Ryan Ziltzer, MD, MPH; Meghan Turner, MD; West Virginia University

Objective: To evaluate the risk of postoperative hemorrhage (POH) requiring operative intervention in patients receiving non-steroidal anti-inflammatory drugs (NSAIDs) for pain control after transoral robotic surgery (TORS) resection of oropharyngeal squamous cell carcinoma (OPSCC).

Methods: The TriNetX database, a database containing deidentified patient information from 80 healthcare organizations, was queried in November 2023 for patients undergoing TORS for the treatment of OPSCC. A cohort of patients who received perioperative NSAIDs and a comparison cohort of those who did not were identified. One-to one propensity score matching was used to create two cohorts matched for age, sex, race, ethnicity, preoperative anticoagulant use, and preoperative antiplatelet use. Outcomes were the rates of primary POH (up to and including 7 days after surgery) and secondary POH (8 to 30 days postoperatively) requiring operative control. Rates of primary and secondary POH were compared between cohorts using chi-square testing.

Results: A total of 1,167 patients who underwent TORS oropharyngectomy for OPSCC were identified; 338 patients received NSAIDs in the perioperative window and 829 did not. The rate of primary POH was 4.73% in those receiving NSAIDS vs. 3.86% in those not receiving NSAIDS (OR=1.238, 95% CI=0.670-2.287). The rate of secondary POH was 3.25% in those receiving NSAIDS compared to 1.68% in those not receiving

NSAIDS (OR=1.958, 95%CI=0.880-4.358). After propensity score matching, there were 331 patients who received an NSAID in the perioperative time period and 331 matched patients who did not. After propensity score matching the rate of primary POH was 4.53% in both groups (OR=1, 95% CI=0.481-2.080). The rate of secondary POH in the matched cohorts was 3.32% in patients receiving NSAIDS and 3.02% in patients not receiving NSAIDs (OR=1.103, 95% CI=0.462-2.635). Based on relative risk differences, there were no statistically significant differences in risk of primary POH or secondary POH between those patients who did and did not receive NSAIDs perioperatively.

Conclusion: NSAID use was not found to be associated with increased risk of POH after TORS resection of OPSCC. NSAIDs may be a safe and useful non-narcotic analgesic option in following TORS.

with PNI were 3.4 times more likely to develop recurrence (95% CI 1.4-8.1, p=0.006). Of patients with ENE, 10 underwent adjuvant chemoradiation. For PNI, 6 patients completed adjuvant chemotherapy while 9 completed adjuvant radiation. There was no difference in recurrence rates based on margin status.

Conclusion: This study demonstrated that presence of ENE and PNI pose the greatest risk for recurrence in those with oropharyngeal malignancies who undergo resection of primary tumor with TORS. No significant changes in recurrence were noted based on additional factors such as T stage, adjuvant therapy, smoking history, or margin status. This information plays a critical role in patient observation to safely monitor for recurrence. In addition, these factors may serve as markers for prognostication in oropharyngeal malignancies and TORS outcomes.

B123: RISK FACTORS FOR LOCOREGIONAL AND DISTANT RECURRENCE IN TRANSORAL ROBOTIC SURGERY - Taylor E Freeman, MD; Ryan Judd, MD; Fahad Rind, MD; Lauren Miller, MD; Stephen Kang, MD; Nolan Seim, MD; Matthew Old, MD; Amit Agrawal, MD; Enver Ozer, MD; Michael Li, MD; Catherine Haring, MD; The Ohio State University Wexner Medical Center

Background: In recent years, the incidence of oropharyngeal squamous cell carcinoma (OPSCC) has increased with nearly 20,000 cases diagnosed in the United States annually. Approximately 75% of these cases are caused by human papilloma virus (HPV). For those with early-stage disease, upfront surgical resection with concurrent neck dissection and pathology guided adjuvant therapy is an option. Extranodal extent (ENE) is an indication for receipt of adjuvant chemoradiation in oropharyngeal and head and neck squamous cell carcinoma treatment. However, some studies have shown that ENE in HPV related OPSCC may not carry the same negative prognostic significance as it does in HNSCC as a whole. This study sought to investigate pathologic risk factors associated with locoregional and distant recurrence for those with oropharyngeal SCC undergoing upfront surgical resection and quantify their impact.

Methods: This was a retrospective review of patients who underwent TORS for oropharyngeal SCC at a single institution between 2008 and 2022. Variables of interest included margin status, history of smoking, T stage, upfront neck dissection, presence of ENE, lymphovascular invasion, or perineural invasion, and receipt of adjuvant therapy. Univariate logistic regression and multivariate regression were used for data analysis and factor comparisons.

Results: Two-hundred and twenty-four patients underwent TORS for oropharyngeal SCC with or without adjuvant treatment. The cohort consisted of 85.5% men and 14.5% women. The majority of patients had T1 (110 patients) or T2 (112 patients) malignancies and N2 nodal involvement. Median follow-up was 5.4 years (IQR 2.8-8.3), during which there were 30 recurrences. Of the recurrences 14 were local, 7 were regional and 9 were distant recurrences. On univariate analysis, T stage (p=0.137), receipt of adjuvant therapy (p=0.915), and smoking status (p=0.547) were not found to be significantly associated with recurrence. On multivariate analysis, perineural invasion (PNI) and extranodal extension (ENE) were significantly associated with recurrence including locoregional and distant. Among the recurrences, 12 had evidence of ENE and 13 had PNI. Patients with ENE were 2.9 times more likely to develop recurrence (95% CI 1.2-6.8, p=0.017) compared to patients without ENE. Those

B124: IN-OFFICE OROPHARYNGEAL BIOPSIES SIGNIFICANTLY IMPROVES TIME-TO-TREAT - David Ludlow, MD[1]; Richard G Muller, MD[2]; Stephen Politano, MD[2]; Alec Bonifer, MD[2]; Emily Georgiadi[3]; [1]MetroHealth Medical Center; [2]Case Western/University Hospitals Cleveland Medical Center; [3]The Ohio State University

Background: Historically, operative biopsies have dominated cancer diagnostics for oropharyngeal (OP) lesions given the location of these masses and the challenges of performing in the office. However, limitations with operating room (OR) scheduling, block time, and patient-specific factors can lead to delayed time to OR and ultimately longer time-to-treat (TTT). Recent work from our institution has shown that avoiding the OR by performing PET/CT has decreased TTT as well as been more sensitive compared to historic methods of cancer diagnosis of the OP such as triple endoscopy (i.e., direct laryngoscopy, bronchoscopy, and esophagoscopy). That work has shown that only direct laryngoscopy with PET/CT was necessary to accurately diagnose cancer. At our institution, we prioritize biopsies of oropharyngeal lesions in clinic to decrease time-to-diagnosis (TTD) and TTT. Thus, the goal of our study was to determine if in-office biopsies significantly improved TTD and secondarily assess costs for patients.

Methods: We performed a single institution retrospective review comparing operative biopsies to in-office biopsy for patients with OP lesions. Descriptive statistics and student t-tests were performed using Microsoft Excel.

Results: Our cohort included a total of 46 patients who had an in-office biopsy and 42 who had operative biopsy with average ages of 58.5 and 58.6 years, respectively. Majority were male (i.e., 74 versus 24 females). The average time to biopsy for the in-office group was 3.4 days compared to 17.5 for the OR group (p<0.001). The average time to treatment for the in-office group was 33.7 days compared to 42.4 (p<0.05). Secondarily, total charges for the in-office group were $170,890 with an average of $5,892 per patient compared to the OR group with $387,526 of total charges and $176,614 per patient. When looking at total cost per patient, the total for the in-office group was $50,653 and $1,746 per patient compared to the OR group with a total cost of $58,452 and $2,656 per patient.

Conclusions: In-office biopsies significantly improve TTT for patients with oropharyngeal lesions. If an OP biopsy can be performed safely in the office, then a provider should do so to improve TTD and TTT. Cost should also be a consideration

when discussing in-office versus OR, and this should be balanced with one's own schedule and institutional availability.

B125: DE-ESCALATION INDUCTION CHEMOTHERAPY IN TREATMENT OF PATIENTS WITH HPV-POSITIVE OROPHARYNGEAL SQUAMOUS CELL CARCINOMA. -
Pavel Golubev, PhD[1]; Larisa Bolotina, PnD[2]; Artem Gevorkov, PhD[2]; Tatiana Deshkina[2]; Evgenya Kuzmina[1]; Ilya Pokataev[1]; Vsevolod Galkin[1]; [1]Oncology Center No1 - Branch Moscow State Budgetary Healthcare Institution, "Moscow City Hospital named S.S. Yudina, Moscow Health Department", Moscow, Russian Federation; [2]P. Hertsen Moscow Oncology Research Institute - Branch of the National Medical Radiology Research Centre, Moscow, Russian Federation

Relevance: According to Globocan in 2020 were identified 98 412 new cases of oropharyngeal squamous cell carcinoma in the world. At the same time, about 80% patients have a locally advanced cancer at the time of diagnosis

It was proved that the human papillomavirus (HPV) is a favorable prognostic factor. Patients with HPV-positive oropharynx cancer have higher indicators of progression-free survival (PFS) and overall survival (OS). HPV-associated tumors are high sensitive to conservative methods of treatment, one of the options is the use of induction chemotherapy (IC) with subsequent chemoradiation therapy (CRT). As induction chemotherapy, the only TPF regimen (cisplatin 75 mg/m2 + docetaxel 75 mg/m2 + 5-fluorouracil 1000 mg/m2/day 96 hours infusion every 21 days) has been approved which has high toxic profile.

Published results of randomized trials demonstrate the possibility of de-escalation CRT without reduction OS and PFS, but there is no data about safety of de -escalated IC regimen. Given the high toxicity of the standard regimen, as well as the presence of a favorable prognostic factor (HPV infection), in MNIOI P. Hertsen since 2021 has started a prospective trial, investigating the possibility of use the dual -component IC regimen according to the TP scheme (cisplatin 75 mg/m2 + docetaxel 75 mg/m2 every 21 days).

Objective: Improve the results of treatment of patients with locally advanced HPV- positive squamous cell carcinoma of the oropharynx by optimizing the scheme IC.

Materials and methods: Since 2021, 34 patients with locally advanced P16-positive squamous cell carcinoma of the oropharynx have been enrolled in the trial who received 3 cycles of IC to the TP scheme.

To carry out a comparative assessment of effectiveness and toxicity, a control arm was formed: 34 patients who received IC according to the standard three -component TPF scheme.

After completion IC patients of both groups had a standard CRT 70 Gy with carboplatin AUC 1.5-2.0 weekly.

The primary endpoints were the assessment of objective response rate after the IC and toxicity. The Secondary endpoints: 1-year OS and PFS

Results: Control disease is reached in all patients of both arms.

Complete response (CR) was achieved in 3 patients (8,8%), a partial response (PR) in 22 (64,7%), stable disease (SD) in 8

(23,5%) patients in the research arm. In the control arm: CR 4 patients (11,8%), PR 24 (70,6%), SD 6 (17,6%) patients. Both IC regimens demonstrated high efficacy rates, and there was no statistically significant ORR in the group (p=0.2133). Toxicity assessment was carried out on the CTC scales - NCIC V5.0.

Toxic manifestations were often observed in the arm of standard IC.

The higher incidence of mucositis in the control group was statistically significant (p=0.025).

1 year - PFS 94%, 1 year - OS 100% in the research group and 91% and 100% in the control arm.

Conclusions: The research scheme of IC demonstrated high results of an objective response, 1-year OS and 1 year - PFS, comparable to the standard TPF scheme, against the background of better tolerance.

B126: CLINICAL FEATURES, TREATMENT AND OUTCOMES FOR OROPHARYNGEAL ADENOID CYSTIC CARCINOMA: A SYSTEMATIC REVIEW -
Gabriel A Hernandez-Herrera[1]; Katelyn S Rourk[2]; Eric J Moore, MD[1]; Daniel L Price, MD[1]; Kendall K Tasche, MD[1]; Linda X Yin, MD[1]; Kathryn M Van Abel, MD[1]; [1]Department of Otolaryngology - Head and Neck Surgery, Mayo Clinic, Rochester, MN, United States; [2]Mayo Clinic Alix School of Medicine, Rochester, MN, United States

Purpose: Adenoid cystic carcinoma (ACC) is a slow growing neoplasm arising from salivary gland tissue and makes up 1% of head and neck cancer. Within the head and neck, primary ACC of the oropharynx (OPACC) is rare (1%). A thorough understanding of natural history, management, risk factors and oncologic outcomes is lacking.

Methods: A systematic review of the literature was performed following PRISMA guidelines by a trained medical librarian using MEDLINER, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews and Scopus via Elsevier. Publications from January 1, 1960 through July 11, 2023 were included. All reports that described symptoms, treatment modalities and outcomes for OPACC were reviewed by two independent reviewers and conflicts were reviewed by the senior author. National database studies, review papers, or studies that did not differentiate OPACC from other anatomic sites were excluded.

Results: A total of 195 cases from 44 studies were included. Demographics, findings and symptoms, pathologic features, treatment modalities, and oncologic outcomes are reported in Table 1. There was a female predominance within the cases that reported sex. The most common oropharyngeal subsite was the base of the tongue, followed by the soft palate. Patients most commonly presented with pain followed by mass or swelling. The most common histological pattern was cribriform, followed by combination of cribriform with either tubular or solid components. Staging was often T3 or greater, and close to a quarter of patients had positive nodes on pathology. Most patients underwent surgery with adjuvant radiotherapy, a quarter underwent radiotherapy only, 2 underwent chemoradiotherapy, and only 1 underwent surgery and chemoradiation. Open surgical approach was more commonly reported than transoral-robotic surgery (TORS), and almost a third of patients underwent neck dissections. No study reported on extranodal extension

and surgical margins were positive in 8 patients out of 27 that reported on them. Mean reported follow up was 22.4 months and overall survival ranged between 47.6% to 79% at 5 years.

Conclusion: There is a lack of high-quality studies on OPACC. It occurs more commonly in females and most common finding at diagnosis is pain. Unlike ACC of other head and neck subsites, OPACC is associated with regional nodal metastasis in nearly a quarter of cases. Overall survival appears moderate to good, however, more specific oncologic outcomes and long term follow up beyond five years are needed.

Table 1. Study Summary	
Demographics	**n (%)**
Studies	44
Patients	195
Mean age (range)	57 (25-79)
Sex (n= 91)	
Female (%)	57 (62.3%)
Male (%)	34 (37.7%)
Findings and Symptoms at Presentation	**n (%)**
Total (n=59)	
Mass or swelling	19 (32.2%)
Dysphagia	12 (20.3%)
Pain or discomfort	31 (52.5%)
Movement limitation	10 (16.9%)
Otalgia	3 (5%)
Odynophagia	3 (5%)
Facial numbness	1 (1.7%)
Pathologic Features	**n (%)**
Subsite (n=195)	
Base of tongue	144 (73.8%)
Palatine tonsil	5 (2.6%)
Soft palate	27 (13.8%)
Pharyngeal wall	1 (0.5%)
Unspecified	17 (8.7%)
Histological pattern (n=21)	
Cribriform	9 (42.9%)
Cribriform + tubular or solid	6 (28.6%)
Tubular	3 (14.3%)
Solid	3 (14.3%)
Tumor stage (n=56)	
T1/T2	16 (28.6%)
T3/T4	40 (71.4%)
Node involvement (n=130)	
Positive nodes	29 (22.3%)
Negative nodes	101 (77.7%)
Surgical margin status (n=27)	
Positive	8 (29.6%)
Negative	19 (70.4%)
Treatment Modality	**n (%)**
Treatment (n=49)	
Surgery + adjuvant RT	34 (69.4%)
Surgery + chemoRT	1 (2%)
RT only	12 (24.5%)
ChemoRT	2 (4%)
Surgical Approach (n=46)	
Open	17 (36.9%)
Robotic surgery	12 (26.1%)
Undisclosed	17 (37.0%)
Neck dissection	14 (30.4%)
Oncologic Outcomes	
Mean follow-up (range)	22.4 months (4-72)
5-year overall survival (range)	47.6% - 79%

B127: LONG-TERM FUNCTIONAL AND QUALITY OF LIFE OUTCOMES IN OROPHARYNGEAL SQUAMOUS CELL CARCINOMA PATIENTS: ASSESSING SURGICAL AND NON-SURGICAL THERAPIES - Justin K Joseph; Michelle Yoon; Jun Yun; Vivian Su; Ricardo J Ramirez, MD, MSCI; Cindy Ganz, MS; Raymond L Chai, MD; Mohemmed N Khan, MD; Mark L Urken, MD; Mount Sinai

Introduction: Incidence of oropharyngeal squamous cell carcinoma (OPSCC) has risen due to the increased incidence of human papillomavirus (HPV). HPV(+) disease portends a better prognosis compared to HPV(-) OPSCC. Favorable survival outcomes have given rise to the prevalence of long-term treatment-associated sequelae, including oropharyngeal dysfunction and diminished quality of life (QOL). We investigate functional and QOL outcomes using long-term follow-up data in a cohort of OPSCC patients.

Methods: Using a prospectively maintained institutional outcomes database, we characterize long-term swallowing and QOL trajectories. We included adults diagnosed with OPSCC who underwent surgery with adjuvant therapy or definitive (chemo)radiotherapy and had a minimum of 36-month follow-up. Patients were assessed using validated instruments: MD Anderson Dysphagia Inventory (MDADI), Quality Life Questionnaire (QLQ-35), and Vocal Tract Function (VTF). We performed ANOVA testing for univariate analyses, which examined longitudinal trends among surgical and non-surgical groups. We compared the pre-treatment patient scores with follow-up data at intervals to assess changes over time.

Results: We included 53 patients with OPSCC with a median age of 64 years (range 44-85 years), median follow-up of 48 months (range 36-72 months). Thirty-five patients were HPV(+) and 18 patients were either HPV(-) or unknown. Twenty-two patients (42%) received (chemo)radiotherapy while 31 patients received surgery with adjuvant therapy. The surgical group had no meaningful change from preoperative baseline for MDADI (n=17), QLQ-35 swallowing (n=18), or VTF jaw opening (n=20) scores. Nonoperative patients demonstrated a decline from baseline to one and three-month follow-up for MDADI scores (-26.1, 95% CI: -38.0 to -14.1, p=0.001 and -15.9, 95% CI: -26.5 to -5.3, p=0.002; points, respectively), with improvement at six months (-8, 95% CI: -24.4 to 8.1, p=0.7), and 60 months of follow up (-11, 95% CI: -24.3 to 2.5, p=0.1). Non-surgical patients demonstrated a decline in swallowing, represented by increased QLQ-35 scores. Swallowing was most impaired at one-month (+22.7, 95% CI: 37.9 to 7.6, p=0.002), with less impairment at three-month (+11.0, 95% CI: 20.9 to 1.1, p=0.02), and continued improvement through six and 72 months (+10.5, 95% CI: -5.1 to 26.0, p=0.3, and +3.2, 95% CI: -53.0 to 59.5 p>0.99, points respectively). VTF Jaw opening for the non-operative group demonstrated decline from baseline at one- and 60-month follow-up (-7.7mm 95% CI: -2.709 to -12.70, p=0.001 and -8.9mm 95% CI: -5.471 to -12.34, p<0.0001; respectively). with improvement at 72-month (-3.1 mm 95% CI: -17.28 to 23.45, p=0.99).

Conclusion: Our study reveals divergent functional and QOL trajectories between surgical and non-operative management of OPSCC, with better functional and QOL outcomes among patients undergoing surgery with adjuvant treatment. Factors such as advanced stage disease may limit candidacy for treatment modality and will be considered in future analyses.
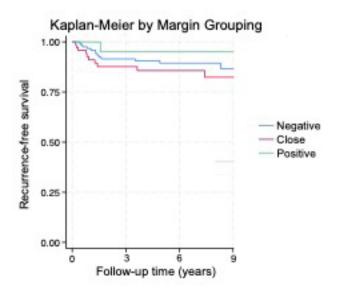
B128: SURGICAL MARGINS IN HPV+ PATIENTS UNDERGOING TRANSORAL ROBOTIC SURGERY - Ryan T Judd, MD; Taylor Freeman, MD; Fahad Rind, MD; Lauren Miller, MD; Stephen Kang, MD; Matthew Old, MD; Nolan Seim, MD; Amit Agrawal, MD; Enver Ozer, MD; James Rocco, MD; Michael Li, MD; Catherine Haring, MD; The Ohio State University

Background: Surgical margins are one of the most important prognostic factors in head and neck squamous cell carcinoma (SCC), with a negative margin of 5mm typically considered a truly "negative" margin. With the increasing prevalence of HPV+ SCC in the oropharynx and the advent of transoral robotic surgery (TORS), the need for widely negative surgical margins and their impact on survival have been called into question. Prior studies are limited by sample size, inclusion of HPV- patients, and heterogeneity in reporting margin status. We sought to determine the impact of involved surgical margins on recurrence-free survival in our cohort of patients.

Methods: This was a retrospective review of patients who underwent TORS for HPV+ oropharyngeal SCC at a single institution between 2008 and 2022. Patients with no residual carcinoma in the TORS pathological specimen were excluded. A positive margin was defined as tumor at the inked edge of the specimen without targeted re-resection at the positive margin. A close margin was defined as tumor 1) within 1mm of the inked edge or 2) at the inked edge with negative targeted re-resection. Our primary outcome measure was recurrence-free survival. Univariate logistic regression was performed to determine if there was an association of margin status with recurrence. Kaplan-Meier plots and log rank tests were performed to determine if margin status was associated with recurrence-free survival.

Results: 224 patients met inclusion criteria. 191 (85.2%) were male, and 129 (57.6%) were current or former smokers. There were 21 (9.4%) positive and 74 (33.0%) close margins. 68 (30.4%) patients underwent adjuvant chemoradiation, and 39 (17.4%) underwent adjuvant radiation alone. Median follow-up was 5.4 years (IQR 2.8-8.3), during which there were 27 (12.0%) recurrences. Of the positive margins, 15 (71.4%) involved the deep margin. Only one of 21 patients with a positive margin recurred. Only one patient with positive margins did not undergo adjuvant radiation or chemoradiation, and they did not have recurrence. There was no difference in recurrence rates based on margin status (close vs negative margin odds ratio [OR] 1.6 (95% CI: 0.7-3.6), p=0.27; positive vs negative OR 0.41 (0.1-3.3), p=0.40). Of the 24 patients with close margins who did not undergo adjuvant treatment, 4 (16.7%) recurred. A Kaplan-Meier plot for recurrence-free survival did not show a significant relationship between margin status and recurrence (p=0.19, Figure 1). Surgeries performed after 2015 were significantly less likely to have a positive margin (3.2 vs. 13.7%, p=0.015).

Conclusion: In patients with HPV+ OPSCC managed with upfront surgery, recurrence rates are very low even with positive or close main specimen margins. Adjuvant therapy likely mitigates any increased risk of recurrence with involved margins in this population. Unlike oral cavity cancer, wide main specimen margins may not be required for disease control in HPV + OPSCC patients managed with surgery.

Kaplan-Meier by Margin Grouping

B129: EARLY EXPERIENCE USING OF INDOCYANINE GREEN (ICG) FLUORESCENCE AS AN AID IN TRANSORAL ROBOTIC SURGERY - Omar A Karadaghy; Charlie Meyer; Jeremy Richmon; Massachusetts Eye and Ear

Importance: Carcinoma of Unknown Primary (CUP) presents a clinical challenge for practitioners. The current diagnostic approach often involves extensive imaging and examinations, with variable success. We aimed to evaluate the effectiveness of Indocyanine Green (ICG) injection using the Da Vinci robot to aid in intra-operative detection of primary tumors.

Objectives: To evaluate the diagnostic utility of ICG use during robotic surgery to aid in either the identification of the primary tumor or delineate the extent of disease to guide ablation

Methods: This study involved a retrospective review of patients treated at the Massachusetts Eye and Ear who underwent robotic surgery with the utilization of Indocyanine Green (ICG) for the identification of a primary tumor since November 1, 2022. All patients in the study were operated on using the SP model of the Da Vinci robot. Basic demographic and pathologic data were recorded. Intraoperative data points included assessing the presence of an identifiable primary tumor using white light only and documenting the confidence level of ICG localization.

Results: In total, 21 patients were identified who underwent robotic surgery using ICG. The mean age of the cohort was 59.9 years. Nineteen patients were male, and the primary diagnosis was HPV related squamous cell carcinoma (SCC) in 16 cases, HPV negative SCC in 3 cases, atypia in 1 case, and metastatic papillary thyroid carcinoma in 1 case. Five patients had either PET localizing or visually identified primary tumor, and ICG was used to guide surgical extent of resection and localize a retropharyngeal lymph node in a single case.

The remaining 16 patients had CUP in whom the primary was ultimately identified in 10 (62.5%) cases. ICG fluorescence was localized to a discrete focal area in 13 (81.3%) of cases, and correctly identified the primary tumor in 8 (50%) of cases of CUP. In the three cases where ICG was used without focal fluorescence localization, no primary tumor was identified following ipsilateral tonsillectomy and bilateral lingual tonsillectomies. Based on the results above, intra-operative

ICG fluorescence use yielded a sensitivity of 100% (CI 63.1% to 100%) with a specificity of 37.5% (CI 8.5% to 75.5%). The positive predictive value was 61.5% (CI 48.3% to 73.2%) and negative predictive value of 100.0% (CI 29.2% to 100.0%). Overall, the accuracy of ICG was 68.8% (CI 41.3% to 88.9%).

Conclusion: The integration of ICG fluorescence with the Da Vinci SP robot's real-time imaging capabilities is a valuable adjunct for enhancing primary tumor identification in CUP patients as well as guiding the extent of surgery in select patients.

B131: ROLE OF SALIVARY CIRCULATING TUMOR HPV DNA IN DIAGNOSING HEAD AND NECK CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS - Deepak R Lakshmipathy, BS; Aman Prasad, MD; Christian Fritz, MD; Karthik Rajasekaran, MD; University of Pennsylvania

Purpose: Circulating tumor human papillomavirus DNA (ctHPV DNA) are short fragments of DNA released by HPV-associated tumor cells upon exosomal release or cell death. Given its short half-life and cost-effectiveness, it has helped advance care for patients with anogenital cancers. These successes have spurred otolaryngologists to investigate its utility in diagnosing and managing head and neck (HN) cancer patients. Most studies have focused on plasma ctHPV DNA, but some have researched salivary ctHPV DNA in tandem given its reduced invasiveness and theoretic reduction of lead time. Herein we perform a meta-analysis focused on salivary ctHPV DNA to critically assess its diagnostic accuracy for HN cancer patients.

Methods: A systematic literature search was conducted across PubMed, Web of Science, Embase, and Cochrane Library databases. Two authors independently screened each article with a third author resolving conflicts. Inclusion criteria encompassed suspected HN cancer patients who underwent salivary ctHPV DNA testing at initial presentation. Non-English and review publications were excluded. Bivariate random effects meta-analyses calculated pooled sensitivities, specificities, positive likelihood ratios (LR+), negative likelihood ratios (LR-), and diagnostic odds ratios (DOR) with 95% confidence intervals (CIs); a summary receiver operating characteristic (SROC) curve was also generated.

Results: Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocols, 439 records were initially identified, and 6 studies met inclusion criteria. Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) scoring found the included works to have low risk of bias and low applicability concerns. These studies included 298 total patients consisting of 286 males (71%) with a mean age of 58.83 years. Regarding tumor characteristics, 204 patients were HPV+ (68%) with primary sites of oropharynx, oral cavity, unknown, larynx, and hypopharynx in descending order of prevalence. Most patients had late-stage tumors (i.e. T3-T4, N2-N3, M1, III-IV). Pooled sensitivity was 67% (39%-86% 95% CI) and pooled specificity was 78% (17%-99% 95% CI). Pooled LR+ was 8.67 (0.55-51.70 95% CI), pooled LR- was 0.72 (0.15-3.03 95% CI), and pooled DOR was 41.50 (0.18-282.00 95% CI). The I² estimate for these values was 41%. The area under the SROC curve (AUC) was 0.74.

Conclusions: Our results demonstrate that salivary ctHPV DNA is less sensitive and specific than plasma ctHPV DNA in diagnosing HPV-related HN cancer. Nevertheless, its relatively high LR+, DOR, and AUC values alongside low LR- value suggest

the modality should not be ruled out altogether. The findings presented here appear valid given the representativeness of the included patient population, low risk of bias, low applicability concerns, and moderate heterogeneity. Important limitations of this study include its small sample size. Subgroup analysis could consequently not be performed, potentially masking more pronounced diagnostic accuracy results. Additionally, per the nature of meta-analyses and by excluding non-English works, there is risk of publication bias. Overall, these findings provide valuable first insights into the current role of salivary ctHPV DNA in diagnosis, and we recommend repeating this analysis as more prospective, high-powered data becomes available.
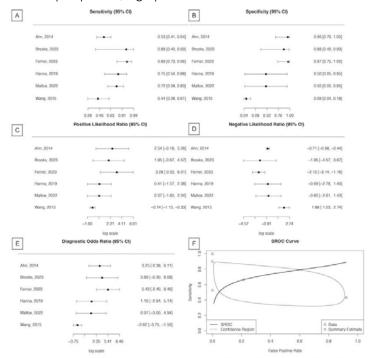

Figure 1: Forest plots showcasing A) sensitivity, B) specificity, C) positive likelihood ratio, D) negative likelihood ratio, and E) diagnostic odds ratio with 95 % confidence intervals (CI) of salivary circulating tumor HPV DNA testing in diagnosing HPV-related head and neck cancer alongside its associated F) summary receiver operating characteristic (SROC) curve.

B132: CUTTING THROUGH THE BIAS: EXTENDING THE INDICATIONS FOR TORS IN HPV-RELATED OROPHARYNX CANCER - Arnaud Lambert, MD, FEBORLHNS; Marco Mascarella, MD, MSc, FRCSC; Keith Richardson, MD, FRCSC; Jeffrey Chankowsky, MD, CM, FRCPC; Óscar Torres Nieto, MD, EDiNR; Nahid Golabi; Derin Caglar, MD; Nathaniel Bouganim, MD, CM; Nader Sadeghi, MD, FRCSC; McGill University Hospitals

Introduction: A paradigm shift has led to de-escalation trials for the treatment of HPV-related oropharynx cancer (HPV-OPC). These trials are subject to selection bias when comparing outcome to conventional concurrent chemoradiation (CRT). The objective of this study was to assess the favourability of TORS using magnetic resonance imaging (MRI) in patients with HPV-OPC who were enrolled in NECTORS or treated with CRT. It is hypothesized that neoadjuvant chemotherapy under NECTORS paradigm extends the indications for TORS while avoiding adjuvant RT/CRT
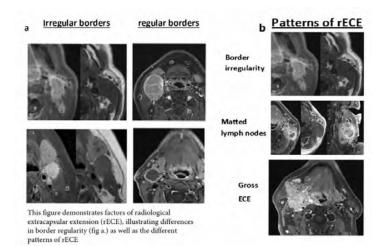
Methods: A retrospective cohort analysis of patients with HPV-OPC undergoing either neoadjuvant chemotherapy followed by TORS (NECTORS) or CRT was performed. The

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CRT group dates from 2010 until 30/01/2018, when NECTORS became an available treatment option. Favourability of TORS was based on pretreatment MRI tumor characteristics of the primary tumor (proximity to midline, hyoid bone, internal carotid artery, pterygoid musculature, tumor depth and extension into the parapharyngeal space). Neck disease was evaluated by the number of involved lymph nodes, the presence of retropharyngeal nodes and signs of radiological extracapsular extension (rECE): irregular border, matted lymph nodes, gross extension. Gross extracapsular extension (ECE) is an exclusion criteria for NECTORS. All images were separately evaluated by two head and neck surgeons and two neuroradiologists.

Results: A total of 111 patients undergoing NECTORS and 120 CRT were included in the study. Apart from proximity (<3mm, 2-5mm, >5mm) to the internal carotid artery (p= 0,0351), there was no significant difference in primary tumor characteristics on MRI between both groups. The indication for TORS was therefore equally unfavourable in both NECTORS and CRT treated groups (39% and 38%, respectively, p=0,531). Regarding neck disease burden, the presence of retropharyngeal nodes (p= 0,028) and gross ECE (p<0,0001) was significantly more present in the CRT group. There was no significant difference in number of neck nodes (p= 0,156), irregular borders (p=0,086) or matted lymph node metastasis (p=0,311).

Conclusion: While a selection bias has been described in selecting appropriate candidates for TORS given unfavourable primary tumor characteristics, patients with NECTORS had a similar rate of unfavourability on MRI as the CRT group. With regard to neck disease only patients with gross extracapsular extension into soft tissue or a high nodal burden of 6 or more involved nodes are excluded and unfavourable for NECTORS. For other neck disease characteristics, apart from the presence of retropharyngeal nodes, there was no significant difference between NECTORS and CRT.

Table 1	NECTORS		CRT		P-value*
	N=111	%	N=120	%	
Laterality					
Right	43	46,7	50	49,0	0,7509
Left	49	53,3	52	51,0	
Site					
BOT	37	38,1	33	32,0	0,3656
Tonsil	60	61,9	70	68,0	
Tumor depth: proximity to extrinsic tongue muscles (<3mm)					
Yes	12	12,1	13	13,3	0,8094
No	87	87,9	85	86,7	
Approaching midline (<3mm)					
Yes	16	16,2	15	15,2	
No	77	77,8	76	76,8	0,8502
Crossing	6	6,1	8	8,1	
Hyoid bone proximity (< 5mm)					
Yes	13	13,1	17	17,2	0,4279
No	86	86,9	82	82,8	
Parapharyngeal plane involvement					
Yes	14	14,1	17	17,2	0,5574
No	85	85,9	82	82,8	
Extensive soft palate involvement					
Yes	5	5,1	10	10,1	0,1793
No	94	94,9	89	89,9	
Internal carotid artery proximity					
<3 mm	3	3,1	10	11,2	
3 - 5 mm	7	7,3	11	12,4	0,0351
> 5 mm	86	89,6	68	76,4	
Pterygoid muscles proximity (<1mm)					
Yes	7	7,1	6	6,2	0,8034
No	92	92,9	91	93,8	
Number of suspicious nodes (Mean; SD)	2,20	1,37	2,64	1,87	0,1563
rECE					
Yes	40	40,4	52	53,6	0,0640
No	59	59,6	45	46,4	
Matted metastatic lymph nodes					
Yes	29	29,3	35	36,1	0,3109
No	70	70,7	62	63,9	
Irregular border of metastatic lymph nodes					
Yes	27	27,3	38	38,8	0,0860
No	72	72,7	60	61,2	
Gross extracapsular extension of metastatic lymph nodes					
Yes	0	0,0	13	13,5	<0.0001
No	99	100,0	83	86,5	
Retropharyngeal metastatic lymph nodes					
Yes	0	0,0	5	5,2	0,0281
No	98	100,0	91	94,8	

This figure illustrates factors of (un)favourability in relation to the extrinsic tongue muscles, midline and hyois bone (fig a), parapharyngeal space, soft palate and pterygoid muscle (fig b) and the proximity to the ICA (fig c.)

This figure demonstrates factors of radiological extracapsular extension (rECE), illustrating differences in border regularity (fig a.) as well as the different patterns of rECE

B133: PRESURGICAL INDUCTION CHEMOTHERAPY FOR HPV POSITIVE OROPHARYNGEAL SQUAMOUS CANCERS

- John T Loree, MD[1]; Mark S Burke, MD[2,3]; Naheed Alam, MD[4]; Daniel Ford, PAC[4]; Michael Y Nagai, DDS, MD[2,3]; Christopher J Hughes, MBBS[2,3]; Saurin R Popat, MD, MBA[2,3]; Joseph L Muscarella, DO[5]; Thom R Loree, MD[2,3]; [1]Temple University Hospital; [2]Department of Head & Neck Surgery, Erie County Medical Center (ECMC); [3]Department of Otolaryngology-Head & Neck Surgery,University at Buffalo-State University of New York (UB-SUNY); [4]Erie County Medical Center Department of Medical Oncology; [5]Department of Otolaryngology-Head and Neck Surgery, University of Buffalo-State University of New York (SUNY)

BACKGROUND: The predominance of Human Papilloma Virus (HPV) related tumors of the oropharynx have been associated with an increase in survival for patients suffering from these tumors. Pre-surgical chemotherapy is one method to de-escalate the morbidity of therapy. The aim of induction chemotherapy followed by surgery is to maintain survival in select oropharyngeal squamous cancers (OPSCC) while avoiding radiotherapy to reduce overall treatment morbidity. In this study, all patients underwent planned induction chemotherapy and surgery with selective use of adjuvant, postoperative chemoradiotherapy (CRT).

METHODS: From 2008 to 2020, sixty-nine patients with HPV positive oropharyngeal cancers were treated with induction chemotherapy followed by selective neck dissection and transoral resection of their primary disease. All patients were without distant metastasis at presentation. There were 64 men and 5 women with a mean age of 61 years. All patients were HPV+ via direct HPV immunohistochemistry (ISH). 51 patients were either never or long-term former smokers. 60 patients had primary disease in the tonsil, 8 in the base of tongue, 1 in the soft palate. 64 patients had nodal metastasis on presentation. All patients received induction chemotherapy inclusive of Cisplatin and Docetaxel (TP) of 2-4 cycles. 12 patients received either 5-FU or Cetuximab as well. Adjuvant chemoradiotherapy was deferred if patients had complete response (CR) to induction chemotherapy at the primary and neck, or with CR in the neck and partial response (PR) at the primary with negative surgical margins. Mean follow-up time was 4.2 years.

RESULTS: A CR to induction chemotherapy was achieved in 37/69 (54%) of patients. There were no treatment deaths or chemotherapy-related hospital admissions. 14/69 (20%) underwent adjuvant chemoradiotherapy. 19/32 (59%) patients with PR deferred chemoradiotherapy. 6 of these patients deferred chemoradiotherapy due to CR in the neck, 13 patients declined recommended chemoradiotherapy. 13/69 (19%) patients suffered recurrence of disease. Of these, 6 (46%) are currently free of disease (NED) as of most recent follow-up. Overall disease specific survival in this cohort was 93% (64/69), disease-free survival in this cohort was 81% (56/69). Cycles of chemotherapy, response, chemotherapy regimen, age, tumor TNM stage and treatment (CRT vs no CRT) were not predictive of survival on Fisher's exact testing. In total, 44/69 (64%) of patients were NED without undergoing chemoradiotherapy.

DISCUSSION & CONCLUSION: This is a select series of patients with limited follow-up. However, given HPV related tumors of the oropharynx have a more favorable prognosis regardless of treatment, radiotherapy was avoided in most patients without sacrificing survival. With the advent of newer chemotherapies and surgical techniques, radiation now has the highest treatment morbidity. Appropriate use of induction chemotherapy and surgical management of oropharyngeal cancers is dependent upon the resectability of the primary on initial presentation (lack of significant local invasion). Like previous studies, smoking status was the strongest predictor of overall survival. This study shows, for select HPV positive oropharyngeal cancers, induction chemotherapy followed by selective, trans-oral surgery allows for improved survival while avoiding the additional morbidity of (chemo)radiotherapy.

B134: THE LACK OF SEX-BASED STRATIFIED OUTCOMES IN HPV-ASSOCIATED OROPHARYNGEAL SQUAMOUS CELL CARCINOMA: A SYSTEMATIC SCOPING REVIEW -

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Importance: While the presence of HPV is known to affect the outcomes of oropharyngeal squamous cell carcinoma (OPSCC), there is a significant gap in research regarding the potential sex-based differences. Lack of sex-based stratification can lead to disparities in treatment response, prognosis, and overall patient experience.

Objective: The objective of this scoping review is to synthesize published studies and highlight the lack of research that includes sex-based stratification of outcomes.

Evidence Review: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension for Scoping Review guidelines were used to conduct this review. We performed a systematic search of terms to identify studies about HPV-associated OPSCC that included stratified results by sex. Cochrane Library, CINAHL, PubMed, SCOPUS, and Google Scholar were searched from inception through September 2023. Only English texts published in a peer-reviewed journal were considered. The quality and validity of studies were independently assessed by two reviewers (A.R.M. and E.S.C.). Conflicts were resolved by a third reviewer (S.A.N.). Data extraction was independently performed by two authors (A.R.M. and E.S.C.), and any discrepancies were mutually resolved. Extracted data included total study N value,

sex, age, overall survival, and recurrence-free survival. A meta-analysis of continuous measures (mean) and proportion (%) with 95% confidence interval (CI) was done when possible.

Findings: Twenty studies, including 13,312 patients, were reviewed in this article. The proportion of women in the included studies was 16.6% ([95%CI: 8.88% to 26.05%]). 30% (6/20) used the Surveillance, Epidemiology, and End Results (SEER) database. Of the studies included, 2 were specific to sex-based differences in HPV-associated OPSCC. Sex-based stratification of survival outcomes by stage and guideline adherence was reported in 5% of studies (1/20). Analysis of the 26 included studies demonstrated significant variation in survival assessment for our study's population of interest. 25% (5/20) of studies reported hazard ratios comparing the difference in overall survival between men and women. Other outcomes, such as recurrence-free survival, were reported in 10% (2/20) of studies. Of the studies that included data to analyze, the mean hazard ratio was .95 ([95%CI: .63 to 1.27]), and the mean recurrence-free survival was .80 ([95%CI: .08 to 1.52]), respectively.

Conclusions and Relevance: In conclusion, this scoping review addresses a significant research gap regarding sex-based stratification in HPV-associated oropharyngeal squamous cell carcinoma (OPSCC) outcomes.

Neglecting sex-based differences can impact treatment response, prognosis, and patient experience. Only a limited number of studies specifically examine these differences. Future research must address this gap to provide more tailored and effective treatments.

B135: MARGINS AND OUTCOMES AFTER TORS IN HPV-ASSOCIATED OROPHARYNGEAL CANCER -
Justin Choi, BS, MEd; Fasil Mathews, MD; Ofer Azoulay, MD; Richard M Rosenfeld, MD, MPH, MBA; Krishnamurthi Sundaram, MD; SUNY Downstate

Background: An acceptable margin after transoral robotic surgery (TORS) in patients with HPV-associated oropharyngeal squamous cell carcinoma (HPV+ OPSCC) varies between institutions and is often a consensus-based, rather than evidence-based, guideline with recent publications having incongruent definitions of "close" or "clear" margins. Clarifying margin cutoffs may help guide which patients can be successfully de-escalated.

Objective: To determine the effect of margin distance on outcomes in patients with HPV+ OPSCC after TORS.

Methods: Random-effects meta-analysis was used to pool data from studies obtained from a database search of PubMed, EMBASE, and Google Scholar using an a priori protocol with dual independent evaluation for inclusion, risk of bias assessment, and extraction of data for analysis. Articles that reported surgical margin distance and recurrence data after TORS in patients with HPV+ OPSCC were included. Rates of local, regional, and distance recurrences were compared across three groups: <1mm, 1-2mm, and >2mm.

Results: A total of 7 articles comprising 1150 patients were included in the analysis. The majority were tonsil primary (625, 54%), T1-T2 (1079, 94%), and N+ (891, 77%). Adjuvant radiation with or without chemotherapy was given to 846 patients (74%). Most patients had a >2mm margin after resection (804, 72%). Local, regional, or distant recurrence was observed in 14% (13/93) of patients with <1mm

margin, 10% (21/218) of patients with 1-2mm margin, and 6% (50/804) of patients with >2mm margin. There were no statistically significant differences in local recurrence, regional recurrence, or distant metastases based on margin status.

Conclusion: Low rates of recurrence were observed after TORS in patients with HPV+ OPSCC regardless of margin status. As most patients received radiation post-operatively, further investigation of de-escalation protocols in controlled clinical trials is needed.

B137: CORRELATION BETWEEN CIRCULATING TUMOR HPV DNA DETECTION AND CLINICOPATHOLOGIC FEATURES IN HPV-ASSOCIATED OROPHARYNGEAL SCC -
Shimrit Sharav, MD; Nicholas Kerl; Jeffrey J Houlton, MD; Terry A Day, MD, FACS; David M Neskey, MD, MSCR, FACS; South Carolina Head and Neck Specialists, Sarah Cannon Cancer Institute

Background: Circulating tumor tissue-modified viral (cTTMV) human papillomavirus (HPV) DNA is a dynamic, clinically relevant biomarker for HPV-positive oropharyngeal squamous cell carcinoma (OPSCC). With evolving research and accumulating data, clinical use has anecdotally started yet to be implemented as the standard of care. The reported sensitivity and specificity of cTTMV HPV DNA for detecting HPV-related Head and Neck Squamous Cell Carcinoma were 98.4% and 98.6%, respectively.[1] However, clinicians should be aware of its limitations, as a negative test does not necessarily indicate the absence of disease.[2]

Objective: To characterize clinicopathologic factors associated with a negative pretreatment cTTMV HPV DNA test with a pathology-proven HPV-related OPSCC, a false negative (FN) result.

Methods: This retrospective study included patients evaluated for HPV-related OPSCC between January 2022 and August 2023. All patients had a pretreatment cTTMV HPV DNA assay. Clinicopathologic characteristics collected from the electronic medical records include demographic variables, tumor and nodal staging, pathology, and imaging findings. Pretreatment cTTMV HPV DNA was assessed using a commercially available polymerase chain reaction-based assay, considered positive, indeterminate, or negative, and as a continuous score (fragments/mL). The study population was divided into two groups. Group 1 included patients who had a true positive (TP) test result, and group 2 included patients who had a false negative (FN) test result.

Results: Among 39 patients, 33 were men (85%), and 37 were Caucasian (95%), with a mean age of 66.5 years. Eight patients had a smoking history (20%). cTTMV HPV DNA was detected in 35 patients (90%) (group 1). All detectable cTTMV HPV DNA was genotype 16. Group 2 included four patients; three (7.6%) had a negative result, and one had an indeterminate result. Table 1 outlines the clinicopathologic characteristics of the study groups. Comparing the two groups, the mean size of the largest metastatic lymph node was 18 and 27 mm in the FN and TP, respectively (P value= 0.22). The difference in metabolic activity of the nodal disease detected by PET was borderline significant (P value=0.06), with 0.67 and 9.43 SUVmax in the FN and TP, respectively.

Conclusions: Several studies have reported a strong association between clinical cervical lymph node metastatic tumor burden and cTTMV HPV DNA.[1,3] Our study shows

a correlation trend between the metabolic activity of the cervical lymph node metastatic disease and the false negative cTTMV HPV DNA. The metabolic activity may improve the accuracy of evaluating the nodal disease burden and expected cTTMV HPV DNA results accordingly.

Table 1. The clinicopathologic characteristics of the study groups

Clinicopathologic Characteristics	Group 1 True Positive (%)	Group 2 False Negative (%)	P value
Total	N=35	N=4	
Gender			
Male	29 (83%)	4 (100%)	
Age (Mean)	66.5	66.5	
Race			
White	34 (97)	3 (75)	
Other	1 (3)	1 (25)	
Smoking status			
Never	27 (77)	4 (100)	
Former or current	8 (23)	0	
Tumor site			
Tonsil	16 (46)	2 (50)	
Base of tongue	12 (34)	2 (50)	
Unknown primary	3 (8.5)	0	
Overlapping	3 (8.5)	0	
Pharyngeal wall	1 (3)	0	
Clinical T stage			
T0	3 (8.5)		
T1	16 (46)	1 (25)	
T2	10 (29)		
T3	4 (11)	2 (50)	
T4	2 (5.5)	1 (25)	
Clinical N stage			
N0	4 (11)	2 (50)	
N1	16 (46)	2 (50)	
N2	13 (37)		
N3	2 (6)		
Radiographic Characteristics			
Largest node diameter (mm, Mean)	27.2	18	0.23
PET			
Primary SUV max (Mean)	8.6	13.12	0.23
Nodal SUV max (Mean)	9.43	0.67	0.06
Pathologic Features	N=12	N=3	
LVI	3	0	
PNI	2	1	
Positive margins	5	0	
Number of metastatic lymph nodes (mean)	1.83	0.67	0.22
ENE	4	0	

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B138: RETURN TO WORK AND FUNCTIONAL OUTCOMES FOLLOWING TRANSORAL ROBOTIC SURGERY VERSUS PRIMARY (CHEMO)RADIOTHERAPY FOR EARLY-STAGE P16+ OROPHARYNGEAL SQUAMOUS CELL CARCINOMA: A CASE-MATCHED RETROSPECTIVE COHORT STUDY - <u>Phillip Staibano, MD</u>[1]; Emily Oulousian[2]; Michael Xie, MD[1]; Michael K Gupta, MD[1]; Michael Au, MD[1]; Han Zhang, MD[1]; [1]McMaster University; [2]McGill University

Background: Oropharyngeal squamous cell carcinoma (OPSCC) mediated by human papillomavirus (HPV) continues to experience a rising prevalence. Current standard treatment for patients with early-stage p16-positive OPSCC is one, or a combination of, surgery, radiation, and chemotherapy. Current evidence indicates similar oncological outcomes after either transoral robotic surgery (TORS) or (chemo)radiotherapy ([C]RT). Since HPV-mediated OPSCC continues to affect young populations, treatment decision-making is largely based upon preserving function, activities of daily living, and return to work.

Objective: To determine the impact of primary TORS or (C)RT on return-to-work outcomes in patients with early-stage p16+ OPSCC.

Methods: We performed a 1:1 case-matched retrospective cohort study of adult patients who underwent primary TORS or primary (C)RT for cT1–T2 cN0–N2 OPSCC. Eligible patients included those undergoing primary curative treatment. All patients were matched based upon TNM staging, age, and cancer subsite. Our primary outcome was reason and time to return to work from start of primary treatment modality (in days). Our secondary outcomes included swallowing function as per MDADI and survival outcomes. We performed parametric analysis including multivariate regression analysis and t-tests. All analysis were performed using R statistical software.

Results: Overall, we included 69 patients. 27 patients within the TORS group and 42 patients within the primary (C)RT group. In the TORS group, the mean age (SD) was 61.5 and 73.3% were male. In this group, 73.3% were unilateral tonsillar SCC, 30% required adjuvant treatment, 10% developed recurrence, and 3.33% died of their cancer. In the primary CRT group, the mean age (SD) was 60.7 (9.66), 76.7% were males, 65.1% were unilateral tonsillar SCC, 23.3% developed recurrence, and 30.2% died of their cancer. The reason for returning to work was at least partially financial in both groups (73.3% vs. 50%). The most common profession in both groups was sales/manager. In patients matched for age and disease stage, the mean return to full/partial work duties from the first day of surgery/treatment was 46.3 days (SD: 21.1) for the TORS group and 269.8 days (SD: 75.4; p <0.001). TORS also performed significantly better for tonsil primaries (p <0.001). We found that mean MDADI scores 4-weeks, 3-months, 1-year, and 2-years post-treatment favoured the TORS group when compared to the primary (C)RT group (p < 0.001) and these significant differences were maintained in the tonsil group alone.

Conclusions: In age-, stage-, and subsite-matched early-stage p16+ OPSCC, we found that patients undergoing TORS faciliated return to work earlier than those undergoing (C)RT and wa associated with better swallowing function up to 2 years from the time of treatment. TORS may therefore help to maintain working status in young patients with early-stage p16+ disease.

B139: VOLUME OUTCOME RELATIONSHIPS IN OROPHARYNGEAL CANCER PATIENTS UNDERGOING TRANSORAL ROBOTIC SURGERY - Aaron Tucker, BA; Craig Bollig; Rutgers Robert Wood Johnson Medical School

Importance: High volume facilities (HVF) have access to advanced medical technology, experienced surgical faculty, and support staff that are thought to improve a variety of patient outcomes. Existing literature has suggested that surgical and radiation therapy based treatments of oropharyngeal squamous cell carcinoma (SCC) at HVF improved survival. Transoral robotic surgery (TORS) is a relatively novel and effective surgical approach for oropharyngeal cancers. There currently a lack of research that specifically addresses the influence of facility volume on TORS perioperative outcomes for oropharyngeal cancers.

Objective:

1) Further investigate the association between facility volume and perioperative outcomes in patients with oropharyngeal cancer undergoing TORS for using the national cancer database (NCDB)

Design: Retrospective analysis of patients aged >18 years old with oropharyngeal cancer using 2019 Patient User File of the NCDB.

Main Outcome and Measure: The number of TORS cases treated at each facility was determined. Facilities below the 75th percentile were considered Low Volume, those between 75th and 94th are Mid Volume, and those at or above 95th percentile are High Volume. Our perioperative outcomes included 30- and 90-day mortality and surgical margin status. Patient were stratified based on volume status and baseline charateristics were compared using univariate testing. Clincal variables associated with our outcomes of interest were analyzed using univariable and multivariable logistic regression. Odds ratios (OR) and 95% confidence intervals (CI) were generated.

Results: After exclusions, 4,294 patients were included in the analysis. Patients were distributed across Low, Mid, and High-Volume facilities as 24.3%, 35.7%, and 40.0% respectively. On univariable analysis, increases in facility volume were associated with decreasing positive margin rates (Low: 24.8%, Mid: 16.8%, High: 11.4%, p<0.001), decreasing 30-day mortality rates (Low: 1.9%, Mid: 1.0%, High: 0.4%, p<0.001), and decreasing 90-day mortality rates (Low: 2.8%, Mid: 1.7%, High: 0.8%, p<0.001). Lower facility volumes was associated with higher odds of positive margins on multivariable analyses (ref. High Volume, Mid-Volume OR: 1.4, 95%CI [1.2-1.8], Low Volume: OR 2.3 95%CI [1.9-2.9]); adjusting for non-academic facility status, clinical T stage, tumor histology, and tumor subsite. Lower facility volumes were also associated with greater odds of 30-day mortality (ref. High-Volume, Mid-Volume OR: 2.4, 95% CI [1.0-6.0], Low Volume OR: 4.6 95% CI [1.9-10.9]) and 90-day mortality (ref. High-Volume, Mid Volume OR: 2.1 95% CI [1.1-4.0], Low Volume OR 3.4 95% CI [1.8-6.5]), adjusting for Charlson Deyo Comorbidity Class.

Conclusions and Relevance: Our results confirm that higher facility volumes are associated with perioperative survival and margin status for oropharyngeal cancer treated with TORS, which is consistent with existing volume outcome literature. Future studies should aim to determine which driving factors within HVF are contributing to the observed outcomes in this patient population.

B140: SALIVARY BIOMARKERS FOR HPV(+) OROPHARYNGEAL SQUAMOUS CELL CARCINOMA (OPSCC): A SYSTEMATIC REVIEW - Tissiana G Vallecillo, MS[1]; Gabriel A Hernandez-Herrera, BS[2]; Kathleen R Bartemes, PhD[2]; John B Kisiel, MD[3]; Eric J Moore, MD[2]; Daniel L Price, MD[2]; Kendall K Tasche, MD[2]; Linda X Yin, MD[2]; Kathryn M Van Abel, MD[2]; [1]Mayo Clinic Alix School of Medicine, Rochester, MN, United States; [2]Department of Otolaryngology - Head and Neck Surgery, Mayo Clinic, Rochester, MN, United States; [3]Division of Gastroenterology, Mayo Clinic, Rochester, MN, United States

Background: Due to a lack of early symptoms, HPV(+) OPSCC is often diagnosed after nodal metastases, which may impact oncologic outcomes. Saliva offers a non-invasive and potentially low-cost advantage, which may aid in early diagnosis. Studies characterizing salivary biomarker detection tests have demonstrated a strong potential for monitoring disease response, especially after primary radiotherapy or induction chemotherapy. Further, in the context of multi-cancer early detection tests, salivary biomarker detection tests that are site specific may have utility for tumor localization. We aim to examine the performance of current salivary biomarker tests for the detection and localization of HPV(+)OPSCC.

Methods: A systematic review of the literature was performed following PRISMA guidelines by a trained medical librarian using MEDLINER, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews and Scopus via Elsevier. Publications from January 1, 2000 through July 12, 2023 were included. All studies that reported on performance of molecular tests on saliva samples for the detection of HPV(+)OPSCC using DNA, RNA or protein biomarkers were reviewed by two independent reviewers and conflicts were reviewed by the senior author. National database studies, review papers, studies that did not distinguished HPV(+) from HPV(-)OPSCC, and OPSCC from other anatomic sites within the head and neck were excluded. Essential results such as sensitivity and specificity were extracted, and studies were pooled based on the following four variables: method of tumor HPV status confirmation, saliva collection method, biomarker detection method and biomarker target.

Results: Among 170 eligible articles, 15 studies were included. The distribution of methods and techniques utilized across these studies are summarized in Table 1. Briefly, 27 tests targeted HPV DNA, 6 targeted proteins or antibodies, and 2 targeted mRNA. On pooled analysis, 9 experiments utilized p16 IHC to determine primary tumor HPV status, collected saliva by any method, performed any PCR on saliva samples, and targeted any HPV DNA. Of these, there were two sets of experiments that were comparable across studies. Three studies utilized p16 IHC to determine primary tumor HPV status, collected whole saliva, and performed PCR targeting the L1 region of HPV DNA. Two studies utilized p16 IHC to detect primary HPV status, collected saliva using oral rinses or gargles and performed qPCR targeting the HPV E6 and E7 oncoproteins. The median specificity and sensitivity of these biomarker tests are reported in Table 1.

Conclusion: To improve early detection of HPV(+)OPSCC and reduce morbidity associated with late-stage diagnosis and treatment, salivary biomarker detection tests offer a promising option. Existing tests most frequently utilize HPV DNA as a biomarker and can achieve high specificity for HPV(+)OPSCC. More studies are needed to better assess overall performance, including validation studies in larger prospective cohorts at

various stages of the disease process. Additional investigation is needed to understand utility in screening, primary diagnosis, site localization, treatment response, and surveillance.

Table 1. Study Summary		
Confirmation of HPV Tumor Status (n–44⁺)	**Number of studies**	**Number of Experiments**
p16 IHC	11	32
PCR	2	2
p16 IHC + HPV DNA ISH or PCR	1	4
HPV E6/E7 mRNA or DNA	1	3
p16 IHC +/- HPV DNA ISH	1	1
HPV DNA ISH	1	1
qPCR HPV E6 and E7	1	1
Saliva Collection* (n=44)		
Whole saliva	6	9
Oral rinse/gargle	5	25
Whole saliva and/or oropharyngeal swab	3	9
Oral rinse/gargle or whole saliva	1	1
Biomarker Detection (n=44)		
PCR	11	16
qPCR	5	21
q RT-PCR	2	3
ELISA	1	4
Biomarker Target (n=44***)**		
Methylated DNA	1	13
HPV L1 DNA	6	10
HPV E6 and E7 DNA	5	6
HPV E7 DNA	3	10
HPV E6 mRNA	2	2
HPV E6 DNA	1	1
HPV E6 protein	1	2
Salivary antibodies (E2, E6, E7)	1	4

Pooled Analysis						
Confirmation of HPV Tumor Status	Saliva Collection	Biomarker Detection	Biomarker Target	# of Experiments	Median Sensitivity % (range)	Median Specificity % (range)
P16 IHC	Any	Any PCR	Any HPV DNA	9	76 (40.3-100)	93.3 (69-100)
p16 IHC	Whole saliva	PCR	HPV L1 DNA	3	77.4 (76-100)	100 (69-100)
p16 IHC	Oral rinses	qPCR	HPV oncoproteins E6/7	2	75.0 (57-92.9)	95.5 (91-100)

⁺Number of total experiments
* Whole saliva is saliva only whereas oral rinses/gargles included a solution to collect saliva
** Any HR HPV
*** One study reported multiple targets in their experiments

B141: TRUE RECURRENCE OF HPV-ASSOCIATED OROPHARYNGEAL SQUAMOUS CELL CARCINOMA AND PATTERNS OF DISTANT METASTASIS LOCATION AND DETECTION - Rema Shah, BS; Sarah Wilkins; Saral Mehra, MD, MBA; Yale University School of Medicine

Objective: Despite the relative survival benefit conveyed by HPV positivity, recurrent HPV+ oropharyngeal squamous cell carcinoma (OPSCC) remains a challenging disease. While previous works have studied patterns of recurrence in HPV+ OPSCC, only one other study has focused specifically on "true" disease recurrence (recurrence >3months after primary treatment completion and image-established disease-free state) as opposed to persistence, and no work systematically analyzes how recurrences were detected.

Methods: A systematic review was conducted to understand current literature on HPV+ OPSCC recurrence patterns. For data on our own cohort, we collected demographic, tumor and recurrence information through our institutional Tumor Registry database and electronic medical record review for patients aged 18+ between 2012-2019. Statistical tests were performed in SPSS, with significance set at p<0.05.

Results: Out of the 367 patients that met inclusion criteria for the cohort, 37 (10.1%) experienced true disease recurrence. Within the true recurrence cohort, 18.9% of patients recurred locally, 29.7% recurred regionally, and 40.5% experienced distant metastasis. When investigating the location of distant metastasis, our cohort saw a large propensity towards the lung (87.5%). The brain had at 4 (25%) instances of metastasis, bone had 3 (18.8%) and liver had 2 (5.3%). The mean time to local and regional recurrence was not significantly different from time to distant metastasis (2.46 ± 0.42 years vs. 1.89 ± 0.22 years, p=0.28). Three-year post-treatment recurrence-free survival for patients with local/regional recurrence was 19.0% compared to 18.8% for distant metastasis (p=0.76). Three-year post-treatment overall survival for patients with local/regional recurrence was 76.2% compared to 68.8% for distant metastasis (p=0.62). The majority of patients identified their recurrence through symptom changes (81.1%) rather than through surveillance imaging (8.1%).

Conclusion: This study is the largest, most recent "true" recurrence cohort of HPV+ OPSCC to date and conducts the first known investigation into methodology of recurrence detection. By investigating the patterns, timeline and detection routes for HPV+ OPSCC recurrences, we present data that supports the establishment of post-treatment distant metastasis surveillance guidelines, in an effort to improve patient morbidity and access to palliative cancer care. Furthermore, by emphasizing the importance of standardizing persistence vs. recurrence terminology, we hope to more accurately counsel patients on expectations of recurrent disease in the future.

B142: COMPLICATIONS AFTER TRANSORAL ROBOTIC SURGERY FOR OROPHARYNGEAL CANCERS: AN EXPANDED ACS-NSQIP DATABASE STUDY - Stephanie Wong, MD; Liyang Tang, MD; Daniel Kwon, MD; Mark Swanson, MD; Niels Kokot, MD; Uttam K Sinha, MD; Albert Y Han, MD, PhD; University of Southern California

Background/Objective: Transoral robotic surgery (TORS) for OPSCC has provided an alternative primary treatment modality to chemotherapy and radiation for select patients and has reduced the need for aggressive open surgical approaches. Proponents of TORS emphasize lower treatment related morbidity and comparable oncologic outcomes. However, perioperative mortality due to catastrophic bleeding has been raised in some clinical trials. We sought to evaluate the overall safety of TORS for treatment of OPSCC using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database with the addition of recent data from the past decade.

Methods: A large, multi-institutional retrospective cohort analysis was conducted using the ACS-NSQIP database. We identified adult patients undergoing TORS for treatment of oropharyngeal cancer between 2010-2021 using a combination of CPT codes, ICD-9 and ICD-10 codes. The primary outcomes were 30-day perioperative mortality, morbidity, need for transfusions intraoperatively/postoperatively, and need for readmission or reoperation. Perioperative risk factors including smoking, diabetes, COPD, CHF, hypertension requiring medication, and bleeding disorders were also evaluated. Univariate analysis was used to identify independent perioperative risk factors associated with increased risk of readmission or reoperation. We also compared the outcomes from 2010-2017 and 2018-2021, when external carotid artery ligation was shown to prevent "severe" postoperative bleeding.

Results: A total of 1718 patients undergoing TORS for oropharyngeal cancer were identified. Of these, 43% (739) underwent surgery of the base of tongue (BOT), 46% (784) had surgery of the tonsil, and 11% (195) had surgery of an unspecified site of the oropharynx. Overall, there were 11 patient deaths identified, with a 30-day mortality rate of 0.6%. One mortality was related to postoperative hemorrhage. The overall rate of transfusions intraoperatively or postoperatively was 0.8%. The overall rate of readmission following TORS was 8.7%. Current smoking and severe COPD were associated with a significantly increased rate of readmission (14% in smokers vs 7.4% in nonsmokers, p < 0.001; 17.3% with COPD vs 8.3% without COPD, p = 0.023). The overall rate of reoperation for any reason was 7.0%. Current smoking (11% vs 5.8%, p = 0.001), severe COPD (15.4% vs 6.4%, p = 0.011), insulin dependent diabetes (16.3% vs 6.4%), and hypertension requiring medication (8.7% vs 5.2%, p = 0.007) were all factors that significantly increased the rate of reoperation. After 2017, the rates of readmission (8.5% vs 8.8%, p = 0.823) and reoperation (7.9% vs 6.3%, p = 0.196) were unchanged compared to 2017 and before. The rate of transfusions after 2017 (0.5%) was lower than before 2017 (1.1%), however this was not statistically significant (p = 0.21).

Conclusions: TORS continues to be a safe option for the treatment of oropharyngeal tumors, with improved safety the advent of external carotid ligation and newer models of robots, resulting in lower rates of all cause 30-day mortality and isolated catastrophic bleeding. This study provides insight on the risk factors associated with readmission and reoperation, which can guide proper patient selection for treatment of oropharyngeal cancer with TORS.

B144: SERUM HGF, VEGF-C, AND IL-17 CORRELATE WITH METASTASIS AND MORTALITY IN ORAL SQUAMOUS CELL CARCINOMA - Gabriela S Fonseca, BS[1]; Juhi J Patel, BS[2]; Patrick A Molina, PhD[1]; Caitlyn B Tomblin, MD[1]; Davide Botta, PhD[3,4]; Manuel Lora Gonzalez, MD[5]; Chi T Viet, MD, PhD, DDS[6]; Kesava Asam, MS[7,8]; Brad Aouizerat, MAS, PhD[7,8]; Hari Jeyarajan, MD[2]; Andrew Fuson, MD[2]; Benjamin Greene, MD[2]; Susan McCammon, MD, PhD[2]; Yedeh Ying, MD, DMD[9]; Anthony Morlandt, MD, DDS[9]; Gary Yu, PhD[10]; Carissa M Thomas, MD, PhD[2,11]; [1]Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL; [2]Department of Otolaryngology - Head and Neck Surgery, University of Alabama at Birmingham, Birmingham, AL; [3]Department of Microbiology, University of Alabama at Birmingham, Birmingham, AL; [4]Immunology Institute, University of Alabama at Birmingham, Birmingham, AL; [5]Department of Pathology, University of Alabama at Birmingham, Birmingham, AL; [6]Department of Oral and Maxillofacial Surgery, Loma Linda University School of Dentistry, Loma Linda, CA; [7]Department of Oral and Maxillofacial Surgery, New York University College of Dentistry, New York, NY; [8]Translational Research Center, New York University College of Dentistry, New York, NY; [9]Department of Oral Maxillofacial Surgery, University of Alabama at Birmingham, Birmingham, AL; [10]Columbia University, New York, NY; [11]O'Neal Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, AL

Background: Regional lymph node (LN) metastases is a poor prognostic factor in oral squamous cell carcinoma (OSCC), reducing survival by 50%. Tumor pathologic features are imprecise at predicting metastatic disease, therefore, novel biomarkers are needed to identify OSCC at risk for LN metastases. Vascular endothelial growth factor (VEGF) and associated angiogenesis mediators have been implicated in metastatic head and neck cancer.

Objective: To determine if serum angiogenic factors are predictive of tumor histology features, metastases, recurrence, and survival.

Materials/Methods: Serum collected from patients with OSCC prior to surgery was analyzed for HGF, VEGF-A, VEGF-C, VEGF-D, IL-6, IL-8, and IL-17 (human-specific Milliplex® multi-analyte Luminex panel kit) using a MagPix® instrument platform and related xPONENT® software (Luminex Corporation, Austin, TX, USA). Histologic grade, perineural invasion (PNI), lymphovascular invasion (LVI), depth of invasion (DOI), and extranodal extension (ENE) was collected from the pathology record, and a head and neck pathologist performed additional scoring based on Brandwein criteria (worst pattern of invasion (WPOI), lymphocyte infiltration, and PNI). Outcomes were followed prospectively for 3 years. The study population was characterized using descriptive univariate statistics. T test and chi square test were used to compare the study population based on regional metastatic disease and 3-year recurrence and survival.

Results: Ninety-nine patients were included with a mean age of 61 (std 13.4, min 26, max 83), 66% male (N=65) and 91% white (N=90). Most tumors were moderately-poorly differentiated (N=77, 81.1%) with 49% (N=48) with PNI and 27.6% (N=27) with LVI. The rate of regional metastatic disease was 37.1% (N=33), rate of 3-year recurrence was 19.2% (N=19), and overall survival at 3 years was 80.8% (N=80). Patients with regional metastatic disease had higher rate of moderately-poorly differentiated tumors (p=0.001), PNI (p=0.0001), LVI (p=0.0001), greater DOI (p=0.0001), and higher Brandwein scores (4.6 vs 3.1; p=0.008). Patients with recurrence were older (67.5 vs 59.5 years; p=0.019) and tumors had higher rate of PNI (p=0.004), ENE (p=0.001), greater DOI (p=0.030), augmented Brandwein scores (4.8 vs 3.3; p=0.017), and higher combined positive score (CPS) (5 vs 56.3; p=0.035). Patients alive at 3 years were younger (59.4 vs 67.9 years; p=0.012) and tumors had a lower rate of PNI (p=0.0001), ENE (p=0.031), less DOI (p=0.0166), and lower Brandwein scores (3.2 vs 4.9; p=0.002). Patients with regional metastatic disease had higher levels of preoperative HGF (232 vs 202pg/mL; p=0.046) and VEGFC (617.1 vs 433.7pg/mL; p=0.007) in their serum. On bivariate logistic regression, VEGFC was predictive of positive LN status (OR 1.002, 95% CI 1.001-1.004, p=0.012). Patients dead at 3 years had higher levels of preoperative HGF (239.9 vs 205.1pg/mL; p=0.05) and lower levels of IL17 (5.2 vs 6.7pg/mL; p=0.035). On multivariate logistic regression, HGF (OR 1.008, 95% CI 1.00-1.016; p=0.045) and IL17 (OR 0.744, 95% CI 0.551-0.946, p=0.030) were predictive of survival. Preoperative angiogenic serum markers were not associated with recurrence or tumor histologic features.

Conclusion: Select serum angiogenic factors correlate with metastasis and mortality in OSCC. These factors could be incorporated into effective risk stratification algorithms for management of OSCC.

B145: RISK OF SECONDARY CANCERS OF HEAD AND NECK FOLLOWING RADIATION THERAPY AMONG HPV+ OROPHARYNGEAL CANCER PATIENTS - Soroush Ershadifar, BS[1]; Ashar Brar, BS[1]; Shyam Rao, MD[2]; Arnaud Bewley[3]; Marianne Abouyared, MD[3]; Andrew Birkeland, MD[3]; [1]UC Davis School of Medicine; [2]UC Davis Department of Radiation Oncology; [3]UC Davis Department of Otolaryngology-Head and Neck Surgery

Background: Radiation induced malignancy is a late side effect of radiation therapy and can create a significant morbidity burden on patients. Radiation therapy has become part of the gold standard of treatment among patients diagnosed with HPV+ oropharyngeal cancers. In this study, we aimed to investigate the characteristics of head and neck second primary malignancies (SPMs) that can potentially be attributed to radiation therapy received as part of the treatment course for HPV+ oropharyngeal cancer.

Methods: The Surveillance, Epidemiology, and End Results (SEER) database, from 2010 to 2020, was queried for patients with a documented primary diagnosis of HPV+ HNC. Patients with subsequent SPMs documented were selected, and descriptive statistical analysis was conducted. SEER database HPV status field is limited only to 2010-2020.

Results: 24039 patients were identified to have been diagnosed with HPV+ HNC index tumors, and 22134 patients were documented to have received radiation as part of their treatment course. Amongst these patients, 1831 (8.27%) were diagnosed with subsequent malignancies, of which 351 (1.58%) patients were documented to have subsequent malignancies of the head and neck region. Among of the 351 identified individuals, 123 lesions with HPV+ status and 288 lesions with HPV-/unknown (not tested) status were documented. These 288 lesions were the primary data of interest in this study. Amongst these lesions, 140 were diagnosed within the same year of the index tumor, while the rest (n=148) were diagnosed at least a year apart that could hypothetically to be attributed as a late side effect of radiation therapy. The mean time to diagnosis of the SPMs from the index tumor was 4.32 years (SD = 2.48 years). Most common site of the SPMs among the 148 lesions was tongue anterior (n=57), followed by oropharynx (n=36, all documented to be HPV-), gum (n=12), pharynx (n=11), and other (n=36, including mucosal, salivary, laryngeal, hypopharynx, and nasopharynx).

Conclusion: Radiation therapy is a significant part of the treatment plan in patients with HPV+ oropharyngeal tumors. Despite its effectiveness, long term complications can cause significant morbidity amongst this patient population, especially given that this patient population presents at a younger age. Here, we report interesting cases of non-HPV related secondary lesions that could be attributed to radiotherapy in particular anatomical sub-sites. Such complications can alter patient's decision making and should be discussed prior to treatment initiation.

B146: A SURVIVAL ANALYSIS AND IDENTIFICATION OF PROGNOSTIC FACTORS AND IDEAL TREATMENT MODALITIES FOR MEDULLARY THYROID CARCINOMA OF THE HEAD AND NECK USING THE SEER DATABASE. - Heather Huo[1]; Megan K Lyden[1]; Earl H Harley, Dr[2]; Jonathan P Giurintano, Dr[2]; [1]Georgetown University School of Medicine; [2]Department of Otolaryngology-Head and Neck Surgery, Medstar Georgetown

Objectives: Analyze the association between demographic factors, tumor characteristics, and treatment modalities, particularly prophylactic central neck dissection, on overall survival (OS) and disease specific survival (DSS) of head and neck Medullary Thyroid Carcinoma (HNMTC).

Study Design: Retrospective database study

Methods: The 2000-2019 Surveillance, Epidemiology, and End

Results (SEER) dataset was queried for primary, histologically confirmed HNMTC. Only patients over the age of 18 and without distant metastases were included. Survival was estimated using weighted multivariable cox proportional hazards model.

Results: 2,683 patients met inclusion criteria. Negative predictors for DSS were age at diagnosis (HR 1.03, 95% CI:1.02-1.04, p<0.001) and regional (levels I-VI) nodal metastasis (HR 4.96, 95% CI:2.51-9.79, p<0.001). OS had the same predictors. In addition to poor and undifferentiated tumor grade, moderate tumor grade was also a negative predictor for DSS (HR 2.46, 95% CI:1.37-4.45, p=0.003). Tumor size was not a significant predictor. Any positive lymph node involvement was a negative predictor for DSS (HR 5.97, 95% CI:3.42-10.40, p<0.001) and OS (HR 6.147, 95% CI:3.91-9.66, p<0.001). The specific level of node involvement (lateral or central) resulted in similar OS (Levels I-V HR 0.543, 95% CI:0.384-0.859, p=0.002; Level VI HR 0.49, 95% CI:0.342-0.784, p=0.007). Race, sex, and the type of MTC (mixed medullary follicular or with amyloid stroma) were not significant predictors.

With regards to treatment modalities, surgery improved DSS (HR 0.359, 95% CI:251-0.514, p<0.001), but was not a significant predictor for OS (HR 0.841, 95% CI:0.23-3.34, p>0.05). The specific type of neck surgery performed (selective, modified radical, or radical) was not a significant predictor, nor was the number of regional lymph nodes removed. External beam radiation therapy was associated with worse DSS (HR 1.87, 95% CI:1.43-2.46) and OS (HR 1.58, 95% CI:1.25-2), as was chemotherapy (DSS: HR 2.38, 95% CI:1.76-3.21, p<0.001; OS: HR 2.152, 95% CI:1.64-2.81, p<0.001). The sequence of surgery and radiation was not significant.

Finally, in patients without positive nodal involvement, determined at time of diagnosis with pre-operative ultrasound exam, prophylactic central neck dissection was not a significant predictor. DSS at 1, 3, and 5 years was 95.85%, 91.12%, and 88.75%, respectively. OS at 1, 3, and 5 years was 94.17%, 87.98%, and 83.88%, respectively.

Conclusions: Age, tumor grade, and nodal involvement are important prognostic factors for HNMTC. For patients with nodal involvement, the number of lymph nodes removed was not a significant predictor. For patients without nodal involvement, as determined by pre-operative ultrasound exam, prophylactic central neck dissection was not a significant predictor of DSS or OS. Given the postoperative morbidities and risks associated with central neck dissection, this finding supports a conservative treatment approach for adult patients with HNMTC who are clinically N0 at time of diagnosis. Furthermore, both OS rates and DSS remained favorable, highlighting that the use of total thyroidectomy alone for clinically N0 adult patients with HNMTC is an effective and appropriate treatment option.

B147: POTENTIAL BENEFIT OF EFFECTIVE IMPLEMENTATION OF TIMELY POSTOPERATIVE RADIATION AS A QUALITY IMPROVEMENT METRIC ACROSS HEAD AND NECK SQUAMOUS CELL CARCINOMA PATIENTS - Peter Q Luong, MD[1]; Alexis L Hartman, BS[2]; Lisa M Velez-Velez, MD[1]; Sean T Massa, MD[1]; [1]Department of Otolaryngology-Head and Neck Surgery, Saint Louis University School of Medicine; [2]Saint Louis University School of Medicine

Introduction: The timely initiation of post-operative radiation therapy (PORT) within 6 weeks of surgery is the first national quality metric for head and neck cancer (HNC). Unfortunately,
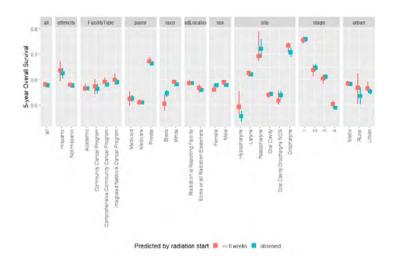
most HNC patients still experience PORT delays. In this study, we aim to quantify the potential benefits if all patients were to receive timely PORT regarding the average overall survival and survival disparities between subgroups.

Methods: The National Cancer Database was used to perform a retrospective cohort study of patients with a diagnosis of head and neck squamous cell carcinoma who received adjuvant radiation after initial surgery. Data from 2004-2016 was analyzed. The primary outcome was 5-year overall survival (OS). Inverse probability weighted models were used to estimate the overall survival of the cohort in the counter-factual scenario that all patients started adjuvant radiation within 6 weeks while adjusting for confounding. The observed OS was compared to the predicted OS with 95% confidence intervals (CI) reported. Survival analyses were replicated for the multiple demographic and clinical subgroups. All models were adjusted for or stratified by age, race, sex, ethnicity, Charlson comorbidity index, payor, urban/rural setting, site, stage, county-level high school graduation rate and income, and whether radiation was given at the reporting facility.

Results: 51551 patients were included in the final analysis. Patients were mostly male, white and non-Hispanic. 38.9% of patients received PORT within 6 weeks of surgery. The predicted average 5-year OS with all patients modelled as receiving timely PORT was not better than the observed OS (observed 0.58, 95% CI: 0.57-0.58; predicted 0.58, 95% CI: 0.57-0.59). Among sociodemographic variables, there was a significant difference in the observed and predicted OS for patients living in rural areas receiving PORT within 6 weeks (observed 0.54 , 95% CI: 0.53-0.63; predicted 0.58, 95% CI: 0.50-0.57). Predicted OS with timely PORT was better than observed for hypopharyngeal cancers (observed 0.46, 95% CI: 0.43 - 0.48; predicted 0.49, 95% CI: 0.47 - 0.54), as well as for stage IV disease (observed 0.49, 95% CI: 0.48 - 0.50; predicted 0.50, 95% CI 0.49 - 0.51).

Conclusions: We have demonstrated the largest potential survival benefits in the receipt of timely PORT are for patients living in rural areas, patients with hypopharyngeal cancers, and patients with stage IV disease. For the overall cohort and other subgroups, the benefit of PORT is modest. As more interventions are being developed to address delays in PORT and other emerging quality metrics, their impact on both overall survival and disparities should be assessed. These and other outcomes can be predicted with modelling to guide resources allocation to the most impactful interventions.

Figure 1. Predicted versus observed 5-year overall survival for head and neck cancer patients treated with surgery and adjuvant radiation including subgroups. Predicted survival based on inverse probability weight models for likelihood of receiving radiation within 6 weeks of surgery.

Predicted by radiation start ■ <= 6 weeks ■ observed

B148: DEVELOPMENT OF A PRECLINICAL MODEL OF OSTEORADIONECROSIS AND BONE REGENERATION ANALYSIS WITH BIOENGINEERED SCAFFOLD - Alessandra Ruaro[1]; Tiziana Mondello[1]; Stefano Taboni[1]; Harley Chan[2]; Jason Townson[2]; Luciana Sartore[3]; Piero Nicolai[1]; Ralph Gilbert[2]; Marco Ferrari[4]; Jonathan Irish[5]; [1]Padua University Hospital: Azienda Ospedaliera di Padova; [2]University Health Network, UHN; [3]University of Brescia: Università degli Studi di Brescia; [4]University of Padua Department of Neuroscience: Università degli Studi di Padova Dipartimento di Neuroscienze; [5]University of Toronto, UHN

Background: Osteoradionecrosis (ORN) is a serious burden for head and neck cancer patients, and it is one of the most challenging complications of radiotherapy, in particular mandibular ORN can have a profound impact on the quality of life.

The aim of this pre-clinical study is (i) to develop an irradiated/ORN model and (ii) to test the use of bioengineered scaffolds seeded with human mesenchymal stem cells (hMSCs), in this complex setting.

Methods: Nine male White New Zealand rabbits were used for this study. A radiation dose of 7 Gy was administered once every two days for a total of 5 fractions, using a single photon beam directed in a specific region of interest (ROI) of the body of the mandible, approximately below the first molar tooth, on the left side. The dose received on the contralateral side of the mandible was estimated to be 5Gy/fr.

The dose is estimated to be the biological equivalent to 115 Gy in humans, which corresponds to the dose used for a radical treatment approach in oncologic head and neck patients.

After the irradiation, rabbits were monitored clinically with daily examination, and radiologically both with CT (on week 4, 12, 16 after-scan) and MRI (on week 8 after-RT), in order to identify signs of ORN.

When 75% of the sample developed a radiological ORN, a bilateral marginal mandibulectomy was performed in the targeted area of irradiation. Hybrid core-shell combination of poly (L-lactic acid) and hydrogel chitosan (PLA-HyCh) scaffolds seeded with hMSCs has been used to reconstruct

the non-critical size (5x5mm) mandibular defects.

The bone regenerative properties of the bioengineered scaffolds were analyzed by in vivo radiological examinations and ex vivo radiological, micromorphological, and immunohistochemical analyses.

Results: During the post-RT monitoring, all rabbits showed signs of alopecia in the submandibular region after 4 months; at the radiological evaluation, all rabbits reported signs of unicortical erosion with loss of trabecular density, 75% had a bi-cortical erosion and 12.5% showed a bone sequestration at 16 weeks from RT.

The relative density increase (RDI) was significantly more pronounced in defects that were not reconstructed in respect to the reconstructed group (p-value <0.001) reaching 57,3% bone regeneration at 165 days from surgery. Among the reconstructed groups, the population with seeded scaffolds showed a significant RDI compared to the scaffold alone group, reaching 29,9% of bone regeneration.

No difference in RDI was observed on the two sides of the mandible that received a different dose of radiation (7Gy/fr on the left and 5Gr/fr on the right).

Conclusions: The irradiation planning with this study allowed to successfully create a double model: an irradiated model and an ORN model. The use of bioengineered scaffolds seeded with hMSC in a pre-clinical this setting did not show a significant improvement in bone regeneration. However, the application of regenerative medicine in ORN has proved to be a promising field of increasing interest in research. Therefore, our group is going to perform further studies to optimize this regenerative model.

**B149: PATIENT-SPECIFIC 3D SPECIMEN MAPS FOR ADJUVANT HEAD AND NECK RADIOTHERAPY PLANNING - ** Olivia L Prosak, BS[1]; Marina Aweeda, BS[2]; Kavita Prasad, BS[2]; Natalie A Lockney, MD[3]; Ryan M Whitaker, MD, PhD[3]; Michael C Topf, MD[2]; [1]Vanderbilt University School of Medicine, Nashville, Tennessee, U.S.A.; [2]Dept. of Otolaryngology-Head & Neck Surgery, Vanderbilt University Medical Center, Nashville, Tennessee, U.S.A.; [3]Dept. of Radiation Oncology, Vanderbilt University Medical Center, Nashville, Tennessee, U.S.A

Introduction: Numerous challenges exist in delineating adjuvant radiotherapy (RT) target volumes following primary surgical resection of head and neck cancer. Plans are created based on diagnostic imaging, operative and pathology reports, and discussions with the head and neck surgeon and/or pathologist. However, discerning target volumes for localization and radiation planning is difficult following postoperative anatomy changes. We have previously demonstrated the utility of three-dimensional (3D) scanning to improve intraoperative communication between pathologists and surgeons, but the potential benefits of this protocol to improve communication with the radiation oncologist have yet to be demonstrated.

Methods: This is an ongoing, non-interventional, prospective study to determine the feasibility and impact of incorporating 3D specimen maps into adjuvant RT planning (NCT05743569). Surgical specimens are 3D scanned and annotated with regard to sectioning and margin sites using computer-aided design (CAD) software. Radiation oncologists generate two postoperative RT plans for each case: one while blinded to a patient's 3D
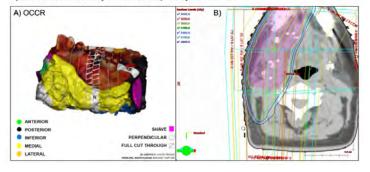
model (standard of care), and then the second utilizing the 3D specimen map. The primary outcome was the planned target volume (PTV) to the primary tumor bed (PTVp) +/- a boosted area to the tumor bed (PTVb) for patients with positive margins. Secondary outcomes included radiation doses to organs at risk (OARs), defined as critical structures near the treatment field on a case-by-case basis that served as a surrogate for radiation toxicity. Additionally, surveys were distributed among treating radiation oncologists to assess viability and perceived utility of the 3D specimen map. A series of 13 cases of mucosal head and neck cancer will be identified to appropriately power the study to detect a difference in treatment volumes.

Results: PTVs for the accrued cohort of patients (n=3) were slightly larger with 3D model derived volumes (+2.81%, NS) with no observable differences in target coverage. No clinically significant differences were observed in volumetric, mean, or maximum doses to OARs of interest including mandible, oral cavity, pharyngeal constrictors, or major salivary glands in this initial cohort. Initial survey respondents reported markedly improved confidence in treatment volumes created and improved ability to locate the site of positive margins with the addition of the 3D specimen map to current tools used for treatment planning. Respondents additionally reported improved communication and improved understanding of tumor size and characteristics with the 3D specimen map. All reported ease of use and that they would use the 3D specimen scan again during treatment planning.

Conclusions: 3D scanning and specimen mapping represents an innovative approach to postoperative radiotherapy planning with noted qualitative improvements in tumor characterization and surgeon–radiation oncologist communication. Trial results regarding changes in PTVs and OARs are ongoing.

Figure 1: Patient with pT4a N0 SCC of the R alveolar ridge and mandible s/p R oral cavity composite resection (OCCR)
A) 3D Specimen Map Annotated to Show Margin Sampling Location
B) External Beam Dosimetry and Contour Map for Adjuvant RT Plan

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**B150: ADJUVANT RADIOTHERAPY IS ASSOCIATED WITH IMPROVED OVERALL SURVIVAL IN PATIENTS WITH SPINDLE CELL CARCINOMA OF THE HEAD AND NECK - ** Nihar Rama, BS[1]; Samuel Auger, MD[2]; Christopher Roxbury, MD[2]; [1]Pritzker School of Medicine, University of Chicago; [2]Section of Otolaryngology, Department of Surgery, University of Chicago

Importance: Spindle cell carcinoma of the head and neck (HNSpCC) is a rare, aggressive form of head and neck carcinoma that originates in the mucous membranes of the upper aerodigestive tract and differs histologically and behaviorally from more common squamous cell carcinomas (SCC). HNSpCC has high rates of local recurrence and distant

metastasis with higher overall mortality compared to SCC of the head and neck. Management of HNSpCC involves surgical resection, but given the rareness of this tumor, the role of multimodal therapy in the management of HNSpCC remains incompletely understood. Therefore, detailed evaluation of the role of adjuvant radiation therapy (XRT) in HNSpCC can inform treatment decisions and guidelines.
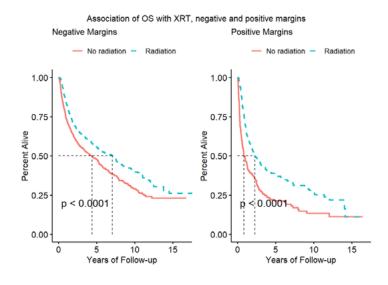
Objective: To assess the association between adjuvant XRT and overall survival (OS) in patients with HNSpCC.

Design, Setting, Participants: Retrospective cohort study of patients diagnosed with HNSpCC (*International Classification of Diseases for Oncology, Third Revision* codes 8033, 8032, and 8074) between 2004 and 2020 using the multicenter, hospital-based National Cancer Database (NCDB). All tumor sites were included. Exclusion criteria included missing staging and survival data.

Main outcomes and measures: The primary outcome was OS. Associations between adjuvant XRT and OS were analyzed using multivariable Cox proportional hazards regression. Subgroup analyses were performed based on margin status.

Results: Of 3502 patients (mean [SD] age 65.9 [12.9] years; 1037 [29.6%] female; 2931 [83.7%] White) with HNSpCC, 2578 [73.6%] underwent surgical resection. The most common site of HNSpCC was larynx (1023 [29.9%]) followed by oropharynx (515 [15.1%]) and tongue (475 [13.9%]). OS was 46.3% and 29.0% at 5 and 10 years, respectively. Subgroup analysis by margin status after surgery demonstrated that patients with negative margins had a 51.4% 5-year OS compared to 5-year OS of 32.6% for patients with positive margins (p<0.001). Adjuvant XRT following negative margin surgery was associated with a 5-year OS of 55.8% compared to 47.9% in patients receiving no adjuvant XRT (p<0.001). In patients with positive margins, adjuvant XRT was associated with a 5-year OS of 38.6% compared to 21.3% in patients receiving no adjuvant XRT. Multivariable Cox regression revealed that age > 70 (HR 1.65, 95% CI 1.36-1.99), positive nodal status (HR 1.41, 95% CI 1.27-1.57), T stage of T3/4 (HR 3.66, 95% CI 1.74-7.72), and Charlson comorbidity index of 1 or more (HR 1.22, 95% CI 1.11-1.35) were associated with poorer OS. Private insurance status (HR 0.66, 95% 0.59-0.75), receipt of adjuvant radiotherapy (HR 0.62, 95% CI 0.55-0.68), receipt of surgery (HR 0.61, 95% CI 0.55-0.69), and receipt of chemotherapy (HR 0.83, 95% 0.73-0.94) were associated with increased OS.

Conclusions and Relevance: Adjuvant XRT is associated with improved OS in patients with HNSpCC. Age greater than 70 years, Charlson comorbidity index ≥ 1, positive nodal disease, and positive margins following surgery are associated with poorer OS. Adjuvant XRT might play a critical role in improving the OS of HNSpCC patients following surgery, particularly in patients with positive margins following surgery. Further research is needed to understand the role of multimodal therapy in HNSpCC.

Association of OS with XRT, negative and positive margins

B151: OUTPATIENT BRIDGING SUPPLEMENTAL PARENTERAL NUTRITION: A NOVEL TREATMENT OF MALNUTRITION IN PATIENTS UNDERGOING RADICAL (CHEMO) RADIATION FOR HEAD AND NECK CANCER - Phillip Staibano, MD; Nhu-Tram Nguyen, MD; James Wright, MD; Han Zhang, MD; Karen Biggs, RD; McMaster University

Background: Approximately 80% of patients undergoing radical (chemo) radiation (C-RT) for head and neck cancer (HNC) require the support of a feeding tube during their treatments. Reactive gastrostomy tube (G-tube) insertion compared to prophylactic insertion provides needed nutritional support while avoiding unnecessary procedures. Patients experience physical and functional disability due to severe malnutrition while awaiting outpatient G-tube insertion. This necessitates home support with IV fluids, treatment interruptions, and hospital admission. As a result, we have instituted a program identifying high-risk patients for outpatient supplemental parenteral nutrition (SPN), providing daily 800 calories (i.e., 3 mL/kg/hr) over 4.5 hours/day, bridging them to G-tube placement. High-risk patients had intake of <60% of energy requirement over 3 days and/or 5% weight loss in month.

Objective: To investigate the impact of outpatient bridging SPN on patients' weight and muscle mass in patients with head and neck cancer waiting G-tube insertion.

Methods: We prospectively recruited 60 patients to undergo SPN from our tertiary-care cancer centre. Eligible HNC patients included any high-risk patient waiting G-tube insertion. Our primary outcome was the change in the muscle mass of patients, assessed with hand grip strength tests at initiation of SPN and after completion of SPN; the latter coincided with the timing of insertion of G-tube. Our secondary outcomes included serial weight measurements, pre/post albumin levels, incidence of hospital admissions, additional home care supportive visits for IV fluids, ED visits, and duration of G-tube dependency. We performed descriptive analyses. We performed t-test to compare pre- and post-SPN weight, hand grip strength, and albumin levels pre and post G-tube insertion. All statistics were performed using R software.

Results: A total of 60 patients met eligibility criteria to undergo SPN and be entered in this pilot study. 50 patients (83.3%) were male, and their mean age (SD) was 61.2 years. Forty-five patients were undergoing primary CRT for OPSCC staged cT1-T4 N0–N3. All patients underwent SPN bridging followed by G-tube insertion. The mean time to G-tube insertion from requisition date was 8.8 days (SD: 3.3 days). The mean time on SPN was 3.83 days (SD: 2.84 days). There was a significant improvement in mean hand grip strength following SPN when compared to before SPN (p = 0.04, 95% CI: -3.7, -0.16). There was no statistically significant change in the weight pre-SPN vs post-SPN vs last day of CRT (p = 0.243, 95% CI: -0.63, 2.2). There was no statistically significant pre- and post-SPN albumin levels (p = 0.127, 95% CI: -0.53, 3.9). The mean time from G-tube insertion to removal was 5.23 months (SD: 95 days). No patients required additional home care services for intravenous fluids while waiting for G-tube insertion. No patients required ED visits or hospital admissions for nutritional support.

Conclusions: In patients with HNC undergoing radical treatments with malnutrition, outpatient bridging SPN is associated with rapid stabilization of patients' weight loss and improvement of their muscle mass. Expansion of this initiative and systemic economic impact analysis of this program is underway.

B152: ADVERSE REACTIONS FROM RADIATION TREATMENT AMONG HEAD AND NECK CANCER PATIENTS WITH COLLAGEN VASCULAR DISORDERS

- Emily T Tran, BS[1]; Meng-Lun Hsieh, DO, PhD[2]; Christina Henson, MD[1]; J. Spencer Thompson, MD[1]; Nilesh Vasan, MD[1]; Ozer Algan, MD[1]; [1]University of Oklahoma Health Sciences Center; [2]UT Southwestern Medical Center

Purpose: Evaluation of radiation treatment toleration and toxicity in head and neck cancer patients undergoing radiation therapy.

Materials/Methods: This retrospective cohort study examined head and neck cancer patients with collagen vascular disorders (CVD) including lupus, scleroderma, rheumatoid arthritis, and Sjrogen's syndrome, or other non-specific CVD who underwent radiation therapy from 2005 to 2022 at a single institution. Additional inclusion criteria included a minimum follow up time of 3 months. Patient characteristics, diagnostics, and treatment information were extracted from institutional EMRs. CTCAE grading scale version 4 was used for assessment of symptoms.

Results: A total of 7 patients were found to fit study criteria. Table 1 details the patient demographics corresponding to their skin and subcutaneous reaction. Within this population, the median age was 63 with 4 males and 3 females. Median follow up time was 53 months. All patients were diagnosed with lupus, and 2 patients additionally had rheumatoid arthritis. All patients were diagnosed with squamous cell carcinoma, with primary locations including the floor of mouth, larynx, tonsil, tongue, and skin that metastasized to the parotid gland. One patient received concurrent chemotherapy with RT. Severe skin and subcutaneous toxicities were experienced by all patients, with 71% grade 2 reactions and 29% grade 3 reactions. Time to resolution of symptoms ranged from 42 to 348 days with grade 2 toxicities and 57 to 126 days with grade 3 toxicities. The most common toxicity was mucositis, with 71% of patients experiencing it severely. One patient did require a decrease in RT dosage due to skin and lupus exacerbation while another patient required a 1 week break in treatment.

Conclusion: CVDs have historically been considered a contraindication to RT due to high incidence of adverse effects, but more recent studies have found CVD patients tolerating contemporary RT techniques better than previously reported. Within a small sample of CVD patients diagnosed with head and neck cancer in a single institution, a majority of patients had symptoms lasting for greater than 3-4 months, requiring longer term close monitoring of patients. Special consideration and counseling should be given to patients diagnosed with CVD undergoing definitive radiation therapy to the head and neck region.

Table 1 – Patient Demographics and RT Dosage with Corresponding Skin/Subcutaneous Reaction

Age, Sex	CVD	Primary Site	Stage	Complete Dose (cGy)	# Fxn	RT Modality, Type	Symptom Grade	Symptom	Time to Resolution of Symptom (Days)
59, F	Lupus	Larynx	2	6600	30	Photon, 3D	2	Mucositis	42
74, M	Lupus	Tongue	3	6000	30	Photon, Rapid Arc	2	Mucositis	53
75, M	Lupus, RA	Skin with met to parotid gland	4	5855.3	30	Proton, IMPT	2	Moist Desquamation	120
50, F	Lupus	FOM	3	6565	35	Photon, IMRT	2	Erythema	205
63, M	Lupus	FOM	2	6600	33	Photon, IMRT	2	Mucositis	348
73, F	Lupus, RA	Tonsil	1	8090	38	Photon, IMRT	3	Mucositis	57
53, M	Lupus	Larynx	3	7140	34	Photon, IMRT	3	Mucositis	126

B153: SURVIVAL AND COMPARATIVE EFFICACY OF RADIOTHERAPY VS SURGERY FOR LOCOREGIONAL CONTROL IN HEAD AND NECK EXTRAMEDULLARY PLASMACYTOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

- Srivatsa Surya Vasudevan, MD, MS[1]; Sabry Babiker Sayed, MBBS[2]; Pratisksha Kapartiwar[3]; John Pang, MD[1]; Ameya A Asarkar, MD, FACS[1]; Lindsay Olinde, MD[1]; Katz Sanford, MD[1]; Kavitha Beedupalli, MD[1]; Cherie-Ann O Nathan, MD, FACS[1]; [1]Louisiana State University; [2]Faculty of medicine, international university of Africa; [3]Shree vasantrao Nike Government Medical college

Introduction: There are significant gaps in the literature pertaining to the locoregional control and survival rates of extramedullary plasmacytoma (EMP) with respect to various treatment approaches. Our objective is to systematically evaluate the differences in radiotherapy and surgical outcomes in EMP.

Methods: Databases, including PubMed, Scopus, Web of Science, Embase, and ScienceDirect, were systematically searched for articles reporting detailed information on the radiotherapy and surgical outcomes of extramedullary plasmacytoma from their inception up to November 2023. A random-effects model for meta-analysis was employed to obtain pooled estimates and calculate odds ratios (ORs) for survival, recurrence, and progression of EMP.

Results: We included 12 studies with a total of 742 patients in this meta-analysis. Of which, 505 (68%) patients received radiotherapy (RT)-only, while 237 (31.9%) patients underwent surgery (SX)-only treatment for EMP. All included patients had an initial diagnosis of EMP without multiple myeloma. The pooled overall survival (OS) rates at 2, 3, 5 and 10-year for RT-only treated EMP patients were 77%, 66%, 60% and 52%, respectively. Similarly, for SX-only treated EMP patients, the

pooled OS rates at 2, 3, 5 and 10-year were 83%, 65%, 53% and 56%, respectively. Comparable trends were observed in disease-free survival (DFS) rates at 2, 3, 5 and 10-year between RT-only and SX-only treated EMP patients (Table 1). Notably, there were no significant differences in recurrence rates (15% vs 25%, p = 0.46) and mortality rates (19% vs 16%, p = 0.30) between RT-only EMP and SX-only EMP, respectively. A substantial decrease in the odds of EMP progressing to multiple myeloma was observed in RT-only EMP [OR: 0.4 (95% CI: 0.1-0.9), p = 0.03] when compared to the SX-only EMP group (Figure 1).

Conclusion: This systematic review provides compelling evidence that EMP patients receiving radiotherapy have significantly lower chances of progression to multiple myeloma in comparison to surgery-only therapy. Furthermore, our analysis revealed comparable outcomes in terms of survival rates, recurrence and mortality rates between RT-only and SX-only EMP treatment groups.

Table 1. Survival and Locoregional control outcomes between RT and SX-only EMP

	Radiotherapy	Surgery	Radiotherapy vs Surgery (OR)
1-year OS	83% (95% CI: 67-92%)	84% (95% CI: 64-94%)	1.4 (95% CI: 0.2-9.5), p= 0.72
2-year OS	77% (95% CI: 59-89%)	83% (95% CI: 60-94%)	1.9 (95% CI: 0.1-19.9), p= 0.57
3-year OS	66% (95%CI: 51-79%)	65% (95% CI: 48-80%)	1.3 (95% CI: 0.3-4.5), p= 0.62
5-year OS	60% (95% CI: 44-74%)	53% (95% CI: 34-71%)	0.9 (95% CI: 0.4-1.7), p= 0.75
10-year OS	52% (95% CI: 38-65%)	56% (95% CI: 42-70%)	0.8 (95% CI: 0.4-1.5), p= 0.52
2-year (DFS)survival	77% (95% CI: 59-89%)	75% (95% CI: 63-84%)	1.7 (95% CI: 0.2-14.5), p= 0.62
3-year (DFS)survival	66% (95% CI: 52-79%)	65% (95% CI: 48-80%)	1.4 (95% CI: 0.4-4.6), p= 0.63
5-year (DFS)survival	56% (95% CI: 37-73%)	47% (95% CI: 32-62%)	2.6 (95% CI: 0.9-7.1), p= 0.07
10-year (DFS)survival	32% (95% CI: 20-48%)	33% (95% CI: 20-50%)	1.4 (95% CI: 0.4-5.4), p= 0.63
Local recurrence rate	15% (95% CI: 10-25%)	25% (95% CI: 12-44%)	0.6 (95% CI: 0.2-2.1), p= 0.46
Progression rate to MM	20% (95% CI: 13-28%)	40% (95% CI: 24-57%)	**0.4 (95% CI: 0.1-0.9), p= 0.037**
Overall mortality	19% (95% CI: 12-31%)	16% (95% CI: 6-38%)	1.4 (95% CI: 0.7-2.7), p= 0.30

Figure 1. Forest plot illustration of multiple myeloma progression odds between radiotherapy-only and surgery-only EMP

Plasmacytoma to Multiple Myeloma progression rate

Study name	Odds ratio	Lower limit	Upper limit	p-Value
Miller et al. 1998	0.5	0.0	6.9	0.576
Bachar et al. 2008	0.2	0.0	1.1	0.064
Veto et al. 2017	0.9	0.1	8.5	0.738
Wen et al. 2017	0.2	0.0	1.2	0.074
Zhu et al. 2020	1.0	0.1	16.0	1.000
Eriksen et al. 2023	2.1	0.1	54.2	0.644
Pooled 95% CI	0.4	(0.1 - 0.9)		0.037

B154: ZYGOMATIC IMPLANT-SUPPORTED OBTURATOR RECONSTRUCTION OF MAXILLECTOMY DEFECTS - Michael J Albdewi, BS[1]; Prashant Puttagunta, BS[1]; Noreen Khan[1]; John Hennessy[1]; Karthik Reddy[1]; Jonathan Troost, PhD[2]; Stephanie M Munz, DDS[3]; Joseph I Helman, DMD[4]; Justine S Moe, MD, DDS, FRCDC, FACS[3]; [1]University of Michigan Medical School; [2]The University of Michigan; [3]University of Michigan Medicine; [4]Case Western Reserve University

Introduction: Reconstruction of maxillectomy defects is crucial to restore facial form and function including speech and mastication. While prosthetic rehabilitation remains the standard of care, the use of obturator reconstruction is often limited to low level, unilateral maxillectomy defects at many institutions. Zygomatic implants are effective in the reconstruction of atrophic maxillary edentulism; however, the success rate and utility of zygomatic implants in supporting obturator prostheses following maxillectomy has not been validated.

Methods: A retrospective, single-institution review of patients undergoing maxillectomy surgery and zygomatic implantation due to benign or malignant disease of the head and neck was performed. Subjects were categorized into groups based on Okay and Brown classification (Low Complexity Brown [LB]: 1b, 1c, 1d, 2b. High Complexity Brown [HB]: 2c, 2d, 3d; Low Complexity Okay [LO]: 1b, 2, 2z, 2f. High Complexity Okay [HO]: 3, 3f, 3z). Implant survival estimates were completed using Kaplan Meier models. The impact of maxillectomy defect classification, demographic and treatment variables on implant survival, time to obturator reconstruction, and time to oral intake were analyzed using Cox proportional hazards models.

Results: 135 zygomatic implants in 78 patients were included with 40 females and an average age of 66.8 (33-89) years. The mean follow up duration was 125 (4-629) months. There were 40, 38, 34, and 44 patients in the LB, HB, LO, and HO groups, respectively. The overall zygomatic implant survival rate was 91.1%, with the most common reasons for failure being infection (8) and mobility (4). The mean times to obturator reconstruction and oral intake were 17.6 (0-649) days and 3.7 (0-85) days with most subjects achieving these endpoints on postoperative day 0. Maxillectomy defect complexity did not have a significant impact on overall implant survival, time to obturator reconstruction, and time to oral intake. Overall implant survival in the LB and HB groups were 94.0% and 91.5% at 1 year, 92.0% and 88.5% at 3 years, and 91.6% and 88.5% at 5 years, respectively. Overall implant survival in LO and HO groups were 91.3% and 90.0% at 1 year, 91.3% and 84.4% at 3 years, and 87.5% and 84.4% at 5 years, respectively.

Discussion: Patients undergoing implant-supported obturator reconstruction of maxillectomy defects demonstrated a high implant success rate and short times to oral intake and obturator reconstruction, in both low and high complexity maxillectomy defects. While high complexity maxillectomy defects traditionally undergo free flap reconstruction, these data support zygomatic implantation and obturator reconstruction as a viable alternative. As such, prosthetic rehabilitation with zygomatic implantation may be a safe and reliable rehabilitation option in a wider patient population than previously thought.

B155: SOCIAL DETERMINANTS OF HEALTH IN PATIENTS UNDERGOING MANDIBULAR FIBULA FREE FLAP RECONSTRUCTION FOR NEOPLASTIC DISEASE - Rohith M Bhethanabotla, MS[1]; Karolina Plonowska-Hirschfeld, MD[2]; P. Daniel Knott, MD[2]; [1]Drexel University College of Medicine; [2]University of California, San Francisco

Background: Social determinants of health (SDOH) are known to affect oncologic outcomes in head and neck cancer, including delay to diagnosis, disparity in access to care, and adherence to post-treatment surveillance. There is a paucity of data regarding how SDOH may impact access to and outcomes of microvascular free tissue reconstruction in oral cavity neoplasia.

Methods: Retrospective review of a tertiary academic medical center's free flap database was performed to identify patients with oral cavity malignancy undergoing segmental mandibulectomy and fibula free flap reconstruction between 2011 and 2023. Patients with prior history of free flap reconstruction or radiation therapy were excluded. Patient-level demographic information, including distance from hospital, primary language spoken, and insurance information, were abstracted from the patient's chart. Social Vulnerability Index, a metric from the Centers for Disease Control and Prevention, was used to provide county-level metrics of poverty by household income, unemployment, minority status, and English language proficiency. Clinical outcomes examined included 30-day readmission or reoperation rate, partial or total flap failure, tracheostomy decannulation at discharge, and medical complications during admission.

Results: One hundred thirty-five patients met criteria for study inclusion; the mean age of participants was 62 years at the time of surgery, and over half the cohort was male (72, 53%). Sixty-three patients (47%) identified as non-White [Asian: 36 (27%); Hispanic: 16 (12%); African-American/Black: 7 (5%); Other: 4 (3%)]. Non-White patients were more likely to come from counties with higher percentile of minority groups and households with non-English primary language (p=0.001 and 0.041, respectively), and 35% identified language other than English as their primary language compared to 0% among White patients (p<0.0001). Both groups had comparable household income by zip code (p=0.86) and insurance status (p=0.135). In multivariate analyses adjusting for sex, age, and primary language, patients identifying as White were more likely to live further from the hospital where their surgical treatment was performed than non-White patients (mean 105 miles versus 52 miles, respectively; p=0.008); however, non-White patients had longer wait time from reconstructive surgeon visit to surgery than White patients (mean 24.1 days versus 13.3 days, respectively; p=0.004). There were no differences in length of ICU or overall hospital stay, partial or total flap failure, 30-day readmission or reoperation rates, discharges to skilled nursing facility, time to tracheostomy decannulation, nor time to oral intake between the two groups (all p>0.10).

Conclusion: In this single institution experience, SDoH appear to primarily affect access to reconstructive surgery rather than complications or outcomes after fibula free flap for oral cavity neoplasms. Patients identifying as non-White had longer wait times from reconstructive surgeon consultation to surgery, which was not attributable to distance from household to hospital nor differences in county percentile of poverty, uninsured status, or unemployment. Additional investigation is needed to better understand factors influencing disparity in time to surgery experienced by non-White patients.

B156: IMPROVING ORAL INCOMPETENCE OUTCOMES USING DEPRESSOR ANGULI ORIS FLAPS IN THE SETTING OF MICROVASCULAR FREE TISSUE TRANSFER RECONSTRUCTION OF LARGE LOWER LIP DEFORMITIES - Whitney Jin, BA; Michael DiLeo, BS; David Hernandez, MD; Vlad Sandulache, MD, PhD; Eddie Liou, MD; Ray Wang, MD; Andrew T Huang, MD; Baylor College of Medicine

Background: Subtotal and total deformities of the lower lip secondary to oncologic treatments or trauma are a difficult reconstructive scenario due to the dynamic nature of the oral sphincter required for oral competence. Restoration of the epithelial and soft tissues of the lower lip can be achieved with microvascular free tissue transfer (MVFTT), but long-term functional outcomes on adjunct static or dynamic oral sphincter repair has been limited. Here, we describe our outcomes of MVFTT reconstruction of extensive lower lip deformities, specifically regarding oral competence following adjunct oral sphincter repair comparing static grafts and dynamic depressor anguli oris flaps.

Methods: Retrospective review at a tertiary care center between September 2017 and July 2023.

Results: Thirteen patients underwent subtotal or total lower lip resections during the study time period. The average age was 59 years with 85% being male. Ten (77%) patients were treated for lip squamous cell carcinoma, with the remainder due to trauma (8%) and oral incompetence following prior lower lip repair surgeries (15%). Three (23%) had prior lower lip surgery, with two having prior MVFTT and one a melolabial flap reconstruction. Two (15%) patients had prior lip radiation therapy. Nine (69%) patients underwent radial foream free flap reconstruction while four (31%) utilized the ulnar artery perforator free flap. There no flap failures. Six (46%) patients had concurrent static oral sphincter repair using tensor fascia lata (83%) and palmaris longus tendon (17%), while seven (54%) had dynamic repair using unilateral (71%) or bilateral (29%) depressor anguli oris flaps. Six (46%) patients required adjuvant radiotherapy, two in the static cohort and four in the dynamic group (p=1.0). Four (67%) patients in the static cohort developed oral incompetence post-treatment compared to none (0%) in the dynamic cohort (p=0.02). Of patients with oral incompetence in the static cohort, three (75%) required revision intervention using local flap repair (67%) or tensor fascia lata suspension (33%) with resolution of symptoms in one (25%) patient. All patients achieved a total oral diet, with two (33%) in the static cohort limited to a modified oral diet compared to no limitation in the dynamic group (p=0.19)

Conclusion: Concurrent dynamic repair using the depressor anguli oris flap can be an effective method in optimizing oral sphincter function following subtotal or total lower lip resection requiring MVFTT compared to more typical static repair methods such as tensor fascia lata or palmaris longus tendon suspension.

B157: SALVAGE NECK DISSECTION - A COMPARISON OF OUTCOMES FOR PATIENTS WITH VERSUS WITHOUT VASCULARIZED FLAP COVERAGE - Radhika Duggal, MA[1]; Cong Fan, BA[1]; Robin Davis, MS[2]; Michael A Fritz, MD[2]; Patrick J Byrne, MD, MBA[2]; Peter J Ciolek, MD[2]; Dane Genther, MD[2]; Jacob A Miller, MD, PhD[2]; Joseph Scharpf, MD[2]; Eric D Lamarre, MD[2]; Jamie A Ku, MD[2]; Natalie L Silver, MD, MS[2]; Shlomo A Koyfman, MD[2]; Shauna R Campbell, DO[2]; Neil M Woody, MD[2]; Brandon L Prendes, MD[2]; [1]Cleveland Clinic Lerner College of Medicine; [2]Cleveland Clinic

Introduction: Thirty percent of patients who undergo definitive treatment for advanced head and neck cancer experience local and/or regional recurrence. For years, surgery has been used for salvage of these recurrences, and recently re-irradiation and systemic treatment have become more common as adjuvant therapy after surgical salvage. A vascularized flap may provide multiple benefits for patients undergoing a salvage neck dissection, including the allowance of a more extensive neck dissection, improved contour of the neck, and protection from wound complications and great vessel exposure in the event of further adjuvant treatment. However, vascularized flaps are not widely reported for the reconstruction of standard

salvage neck dissection defects. This study compared the outcomes of patients undergoing salvage neck dissection with and without a vascularized flap reconstruction.

Methods: A retrospective cohort study was conducted including patients with primary oropharyngeal cancer who underwent a salvage neck dissection between 2010-2020. Patients undergoing major resections involving sites outside the neck as well as patients with vascularized flaps not utilized for reconstruction of the neck were excluded. Patients were compared based on whether reconstruction was performed with a vascularized flap. Fisher's exact, Wilcoxon rank-sum, and t-tests were utilized to compare the groups.

Results: We identified 39 patients undergoing a salvage neck dissection. 29(74%) were found to be HPV-positive. The mean age at salvage surgery was 62±10 years, and the median[IQR] years from primary diagnosis to salvage surgery was 1.1[0.6, 3.7]. The median length of follow up was 1.36[0.5, 3.6] years. 9(23%) of patients underwent a vascularized flap reconstruction while 30(77%) did not. Most vascularized flaps were from the anterolateral thigh(n = 5, 56%) and utilized the facial(n = 3, 33%) or superior thyroid(n = 2, 22%) artery. No flaps failed and 2(22%) required a reoperation. 30-day readmission was similar across groups with 1(11%) patient in the vascularized flap group requiring readmission(vs. 7%). Length of stay was significantly greater in the vascularized flap group with the median[IQR} being 6[2.5, 8] compared to 3[2, 4]. At 90 days, dysphagia, voice changes, trismus, and shoulder dysfunction were not significantly different between the groups. 100% of the vascularized flap and 83% of the non-vascularized flap reconstruction group ultimately received re-irradiation after salvage surgery.

Conclusions: Despite their potential benefits to the patient, vascularized flaps are not widely reported for routine reconstruction of neck defects following salvage neck dissections. Given the increasing long-term survival of patients with HPV-related head and neck cancer, this study aims to understand the role of vascularized flaps in improving outcomes of salvage neck dissection patients. This study did not find significant differences in functional outcomes at 90 days post-op between patients with and without a vascularized reconstruction. Given the low morbidity and established high success rate of modern free flap surgery, we believe that there may be a role for routine use of vascularized tissue for coverage of salvage neck defects. Future studies aimed at comparing long-term outcomes between these groups are needed.

B159: HEAD AND NECK FREE FLAP OUTCOMES FOLLOWING INTRAOPERATIVE ANASTOMOTIC REVISION - <u>Claudia N Gutierrez, MD, MS</u>[1]; Jeffrey Bellinger, BS[2]; Jessica M Pagel, BS[2]; Naushin Ali, BS[1]; David Shonka, MD[1]; Jonathan Garneau, MD[1]; Katherine Fedder, MD[1]; Eric Dowling[1]; [1]University of Virginia Department of Otolaryngology; [2]University of Virginia School of Medicine

Objective: Free tissue transfer is a highly reliable procedure for the reconstruction of head and neck defects. However, the most common cause of failure is secondary to microvascular compromise. As such, it's critical to understand the implications of intraoperative anastomotic revision on free flap survival. This study provides a detailed analysis of free-flap survival outcomes following intraoperative anastomotic revision and the implementation of additional salvage techniques during surgery.

Method: CPT codes were used to identify all patients who underwent free flap reconstruction at a single tertiary institution from January 2013 to August 2023. Retrospective chart review was performed to obtain demographics, history of radiation, nutrition status, comorbidities, tumor characteristics, surgical technique, and post-operative course.

Results: A total of 305 free flaps in 296 patients were identified and reviewed. A total of 32 out of the 305 free flaps (10.5%) required intraoperative revision of the anastomosis. Mean age of the 32 patients requiring intraoperative anastomosis revision was 62.5 ± 14.6 years old, 62.5 % male, and had a mean follow-up time of 24.6 ± 31.0 months. Indication for free flap reconstruction included reconstruction after oncologic resection (87.5%), repair of an esophageal perforation (3.1%), chronic wound infection (6.3%), and chondronecrosis of the larynx (3.1%). Table 1 summarizes the most common intraoperative indications for anastomotic revision and salvage techniques used. The most common indication for intraoperative anastomosis was arterial thrombosis (n = 22, 68.8%) followed by arterial spasm (n = 7, 21.9%). Most patients only required one revision (n = 20, 62.5%) and the maximum number was three (n = 2, 6.3%). The most frequently employed salvage techniques, in addition to revising the anastomosis, included using different recipient vessels (n = 14, 43.8%), initiating an intraoperative heparin infusion (n = 7, 21.9%), and administering TPA through injections into the flap (n = 4, 12.5%). Only 12.5% (n = 4) required a return to the operating room due to a free flap complication and the overall free flap survival rate was 93.8% (n = 30).

Conclusion: This retrospective review reveals that intraoperative revision is associated with a free flap failure rate of 6.2% (n = 2/32), which is notably lower than the failure rate reported in the literature for intraoperative anastomotic revision, which is as high as 20%. This study demonstrates the successful salvage of free flaps through strategic intraoperative techniques, offering promising ways to enhance and optimize free flap survival.

Table 1: Summary of intraoperative techniques

Characteristic	No.%
Indication for intra-op reanastamosis	
Arterial thrombosis	n=22(69)
Arterial spasm/congestion	n=7(22)
Venous congestion	n=2(6)
Number of revisions	
x 1	n=20(63)
x 2	n=10(31)
x 3	n=2(6.3)
Salvage technique in addition to re-anastamosis	
Different recipient vessels	n=14(44)
TPA	n=4(13)
Heparin infusion	n=7(22)

B160: COMPARING FUNCTIONAL OUTCOMES FOLLOWING TORS WITH FREE FLAP RECONSTRUCTION USING A RADIAL FOREARM VS ANTEROLATERAL THIGH FLAP -

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Introduction: Large defects of the oropharynx following transoral robotic surgery (TORS) require microvascular free flap reconstruction (FFR). This is commonly performed using a radial forearm (RF) free flap that provides thin, pliable fasciocutaneous tissue. However, anterolateral thigh (ALT) musculocutaneous flaps are occasionally utilized for large defects if an RF is contraindicated, including dorsal palmar arch insufficiency, need for radial artery preservation, previous surgery, or morbidity. We compared the functional outcomes of oropharyngeal cancer patients treated with TORS followed by FFR using RF or ALT flaps.

Methods: Retrospective cohort study of patients who underwent TORS with FFR between 2010 and 2022 identified from the electronic medical record. Patients were stratified by type of flap received: ALT or RF. A 1:4 ALT:RF propensity score match (PSM) was performed to match for demographics, tumor characteristics, and adjuvant treatment. The Functional Oral Intake Scale (FOIS), graded from 1 (no oral intake) to 7 (no restrictions), was used to characterize functional swallowing outcomes. ANOVA and chi-squared statistical analyses were conducted in R Studio.

Results: Following PSM, 100 patients met inclusion criteria (mean age=61.3 years, 82% White, 85% male, 60% smoking history, mean CCI=1.22), of which 80% received an RF and 20% ALT free flap. 72% of oropharyngeal cancers were HPV-associated. 55 patients had pathologic T1-2 stage tumors. 20 patients received chemoradiotherapy (CRT) or radiotherapy (RT) to the head and neck prior to TORS, and 60 patients received adjuvant CRT or RT. There were no statistically significant differences in these characteristics between matched cohorts. ALT flaps had a larger average surface area than RF flaps (ALT: 62.95 cm2[SD=20.25] vs RF: 51.17[15.11], p=0.014).

Both cohorts demonstrated similar preoperative median FOIS (mFOIS) scores (ALT: 7[IQR: 5,7] vs RF: 7[6,7], p=0.6) and at the first follow-up 2 weeks post-TORS (2[1,2] vs 2[1,4], p=0.4). After 3 weeks, RF patients had higher mFOIS scores than ALT patients (2[2,2] vs 4[2,5], p=0.01). While both groups progressively improved with increased mFOIS at 6 months (3.5[2,5]vs 5[2,6], p<0.05) and 1 year (5[2,6] vs 6[5,6], p<0.05), RF patients had overall better swallowing outcomes throughout this period. PEG tube insertion rate was higher in the ALT cohort (52% vs 28%, p=0.031), although there was no difference in percent weight loss at one-year follow-up (-4.77[8.24] vs -6.31[7.90], p=0.7). There were no differences in the time to decannulation, rates of trismus, xerostomia, velopharyngeal insufficiency, aspiration, flap takebacks, or flap failures.

Conclusion: FFR using ALTs leads to a relatively slower recovery in nutritional intake with higher rates of PEG insertion with no difference in risk of major functional complications and is a reasonable choice for reconstruction in those with contraindications to RF.

B161: LIVER DISEASE PREDICTS 30-DAY POSTOPERATIVE COMPLICATIONS IN HEAD AND NECK MICROVASCULAR SURGERY -

Anish R Kosanam, BS[1]; James R Xu, BS[1]; Danielle Bottalico, MD[2]; Eric D Lamarre, MD[2]; [1]Case Western Reserve University School of Medicine; [2]Head and Neck Institute, Cleveland Clinic

Introduction: The implication of liver disease in head and neck cancer patients remains underexplored. Notably, liver function plays an indispensable role in producing clotting factors and albumin, both critical for the success of microvascular free tissue transfer surgeries. Diagnosis of liver disease is challenging, as many cirrhotic patients are asymptomatic. Metrics like the aspartate amino-transferase-to-platelet ratio index (APRI) and Model of End-stage Liver Disease (MELD) score have been employed to assess liver disease severity and surgical risk. This study aims to understand the influence of liver disease, as determined by APRI and MELD scores, on head and neck microvascular free tissue transfer surgeries.

Methods: This retrospective cohort study queried the 2005 to 2021 American College of Surgeons National Surgical Quality Improvement Program databases. Reconstructive cases performed by otolaryngologists (CPT: 15756, 15757, 15758, 15842, 20955, 20956, 20957, 20962, 20969, 20970, 20972, 20973, 43116, 43496, 49006, and 49906) with available age values and preoperative laboratory data were included. Patients were classified as having mild liver disease if they had an APRI score ≥ 0.7 with a MELD-Na score, a modified MELD score which has been shown to have greater prognostic ability, that is < 10. Advanced liver disease was defined as patients with an APRI score ≥ 0.7 with a MELD-Na score of ≥ 10. We compared the rate of postoperative complications using multivariable logistic regression.

Results: A total of 5459 cases met the inclusion criteria, of which 93 (1.7%) had mild liver disease, and 105 (1.9%) had advanced liver disease. The mild liver disease cohort was significantly younger and exhibited a dependent functional status compared to the no liver disease and advanced liver disease cohorts. Patients with evidence of liver disease had a significantly higher American Society of Anesthesiology classification. Comorbidities such as smoking, bleeding disorders, and significant weight loss were significantly associated with both mild and advanced liver disease stages. Furthermore, the advanced liver disease cohort showed a significant association with hypertension requiring medication and preoperative hypoalbuminemia. Postoperatively, the advanced liver disease cohort experienced extended durations from operation to discharge, prolonged hospital stays, and were more likely to return to the operating room post-surgery. Complications, both surgical and medical, were significantly elevated for advanced liver disease patients. Surgical complications included occurrences of superficial surgical site infections and the need for bleeding transfusions. Medical complications included pneumonia, unplanned intubation, extended ventilator use, systemic sepsis, and acute renal failure. On multivariable analysis, patients with advanced liver disease experienced a significantly higher rate of unplanned return to the operating room in 30-days (Odds Ratio (OR) 1.8; 95% Confidence Interval (CI) 1.2-2.9), any reoperation (OR 1.7; 95% CI 1.0-2.7), any complication (OR 1.6; 95% CI 1.0-2.5), and medical complication (OR 1.97; 95% CI 1.2-3.1).

Conclusion: Advanced liver disease significantly increases postoperative complication risks in microvascular free tissue transfer surgeries. Therefore, it is critical for ENT surgeons to collaborate with internal medicine specialists to ensure comprehensive liver disease assessment prior to these procedures, enhancing patient safety and surgical outcomes.

B163: THE EFFECT OF FRAILTY ON TOTAL TREATMENT PACKAGE TIME IN HEAD AND NECK CANCER PATIENTS UNDERGOING MICROVASCULAR FREE FLAP RECONSTRUCTION - <u>Javier K Nishikawa</u>[1]; Nicolaus D Knight, MS[2]; Sumanth Chandrupatla[3]; Jake Morgan, MD[2]; Benjamin Greene, MD[2]; Andrew Fuson, MD[2]; Hari Jeyarajan, MD[2]; Kirk Withrow, MD[2]; Susan McCammon, MD, PhD[2]; Carissa M Thomas, MD, PhD[2]; [1]Heersink School of Medicine, University of Alabama Birmingham, Birmingham, AL; [2]Department of Otolaryngology - Head and Neck Surgery, University of Alabama Birmingham, Birmingham, AL; [3]Science and Technology Honors Program, University of Alabama Birmingham, Birmingham, AL

Background: Microvascular free flap reconstruction for head and neck cancer (HNC) are major surgeries with a high risk of complications. HNC patients are often older, have co-morbidities, and suffer from malnutrition–factors that contribute to frailty. Frailty has been associated with higher rates of postoperative complications, longer hospital length of stay and increased care needs, which can delay adjuvant treatment and increase total treatment time. Delays in treatment have a significant negative impact on recurrence and survival. The effect frailty has on treatment package time in patients undergoing microvascular free flap reconstruction is unknown.

Objective: To determine if frailty predicts delays in time to surgery, time to adjuvant treatment, and total treatment package time (consultation to completion of adjuvant treatment).

Methods: A retrospective chart review was performed of all patients undergoing microvascular free flap reconstruction for HNC defects(2014-2020) at a single institution. Clinicodemographic information and treatment times were collected. A modified frailty index (mFI-5) was calculated using diagnoses of diabetes(DM), chronic obstructive pulmonary disease(COPD), hypertension(HTN), congestive heart failure(CHF), and dependent functional status. Data analysis was done in R studio. Linear regression was used to predict treatment time based on the mFI-5. Logistic regression compared actual treatment times to ideal times where values greater than 28 and 42 days for time to surgery and to adjuvant radiation were considered delays. A Pearson Chi-Squared test was used to determine an association related to age. Significance was defined as p<0.05.

Results: 620 patients were included with a mean age of 62.9 (std 11.4) years and 79(N=488) were male. The frequency of DM, COPD, HTN, and CHF ranged from 2.4%(N=15) to 58.7%(N=364) with HTN being most common. Table 1 displays the distribution of mFI-5s and Table 2 displays treatment times. When comparing mean treatment times to ideal, time to surgery was not significantly different from ideal (27 vs 28 days), but the average time from surgery to adjuvant treatment was higher (65 vs 42 days). No significant correlation was found between frailty and any treatment period (p>0.05) on linear or logistic regression analysis. When looking at treatment times only in patients with an mFI≥2, there was a trend towards significance for the total treatment package time(p=0.052). Pearson chi-squared test

demonstrated a strong dependency between age and frailty scores(P<0.0005), suggesting that older patients are more frail.

Conclusion: Frailty does not appear to be a significant predictor of treatment times or an indicator of treatment delay when calculated using the mFI-5 in patients undergoing microvascular reconstructive surgery. Alternative methods of calculating frailty incorporate additional clinicodemographic factors and laboratory values, and these measures may be indicative of prolonged treatment times.

MFI	Frequency(%)
0	51(8.2%)
1	216(34.8%)
≥2	353(56.9%)
	620(100.0%)

Treatment Period	Time(Days)
Initial Visit to Surgery	27.1±14
Surgery to Adjuvant Radiation	64.9±30
Total Treatment Package	88.7±32

B165: EVALUATION OF A 3-D PRINTED, HIGH-FIDELITY SIMULATOR FOR REHEARSAL OF FREE FLAP OSTEOTOMIES FOR RECONSTRUCTION OF SEGMENTAL MANDIBULECTOMY DEFECTS - <u>Joshua D Smith, MD</u>[1]; Allen Feng[2]; Shaum Sridharan[3]; Kevin Contrera[3]; David Zopf[1]; Zahra Nourmohammadi[1]; Kelly M Malloy[1]; Matthew E Spector, MD[1]; Molly E Heft-Neal[1]; [1]University of Michigan; [2]Massachusetts Eye and Ear; [3]University of Pittsburgh

Background: For osseous free flap reconstruction of segmental mandibulectomy defects, precisely planned and executed osteotomies are essential for optimal post-operative form and function. Prerequisite knowledge and skills to perform such osteotomies proficiently may be aided by simulators. We designed manufactured a high-fidelity, 3-D printed osteotomy simulator and evaluated its performance as a realistic, useful rehearsal tool for trainees.

Methods: We created custom segmental mandibular defects on 3-D printed mandibular templates (KLS Martin) and plated these with custom bent 2.0 mm reconstruction bars. Separate models were printed for fibula and scapular tip free flaps. Templates were scanned using an Artec Space Spider 3-D Scanner (Luxembourg) and printed in polylactic acid with an Ultimaker S5 printer (Netherlands). 3-D models of scapula and fibula bone were similarly generated using de-identified DICOM data and printed in polylactic acid. Participants were then asked to generate single segment scapular tip and three-segment fibula reconstructions. Likert-based surveys (scale 1 – 4) were then administered for participants' self-rating of our simulator's physical attributes, realism, ease of use, and utility for resident and fellow training.

Results: Our simulator was rated for physical attributes, realism, ease and utility of use by four head and neck oncologic and microvascular reconstructive surgery fellows and two otolaryngology chief residents. Ratings for physical attributes and realism are shown in the *Table*. All participants rated the simulator as "somewhat easy to perform" (n = 2) or "very easy to perform" (n = 4) for both fibular and scapular tip osteotomies. Additionally, all participants rated the simulator as having "some value" (n = 1) or "a great deal of value" (n = 5) as a training and evaluation tool for residents and fellows.

Conclusion: Our 3-D printed, high-fidelity simulator for rehearsal of free flap osteotomies for fibula and scapular tip free flap reconstruction of segmental mandibulectomy defects appears to have significant value as a training and evaluation tool for reconstructive head and neck surgeons. However, additional trials with larger numbers of participants are necessary.

Table. Evaluation results of simulator from six trainees in the domains of physical attributes and realism. Scale: 1: Not at all realistic; 2: Lacks too many key features to be useful; 3: Adequate realism as is, but could be improved; 4: Highly realistic, no changes needed.

-	Mean Rating (n = 6)
Physical Attributes	
Anatomical Landmark: Accuracy of Curved Plate	3.83
Anatomical Landmark: Accuracy of Straight Plate	4.0
Anatomical Landmark: Accuracy of Scapula	4.0
Anatomical Landmark: Accuracy of Fibula	4.0
Plate Quality	3.5
Defect Size	4.0
Realism of Experience (or how the "tissue" responds to "action")	
Rehearsal of Exposure	3.25
Fibular Osteotomy	3.33
Scapular Osteotomy	3.5
Maintenance of Periosteum	3.0
Miter Cut	3.2

B166: UNDERSTANDING THE IMPACT OF FRAILTY ON MORTALITY, FUNCTIONAL STATUS AND COMPLICATIONS FOR ELDERLY PATIENTS UNDERGOING FREE FLAP RECONSTRUCTION

- John J Sykes IV[1]; Alexandria Danyluk[1]; Peter T Dziegielewski, MD, FRCSC, FACS[2]; [1]University of Florida College of Medicine; [2]Department of Otolaryngology, University of Florida

Background: Frailty has been defined as a syndrome of age-related loss of physical, cognitive, social, and psychological functioning with the inability to compensate for increased stress, leading to decreased physiologic reserve. The 5-Factor Modified Frailty Index (MFI-5) was developed from the Modified Frailty Index (MFI-11) as a strong predictor of mortality and postoperative complications. These 5 factors include Functional status, Type 2 Diabetes, Chronic Obstructive Pulmonary Disease, Congestive Heart Failure, and Hypertension with Medication. This scale can play a crucial role in pre- and peri-operative planning for aging patients as the incidence of head and neck cancer has increased with the aging population and therefore there is an increased prevalence of comorbidities. Age was thought of as a key indicator of risk, but studies have shown the prognostic value of frailty in geriatric oncology.

Methods: Retrospective cohort study of patients over the age of 70 who underwent head and neck cancer resection with subsequent free flap reconstruction at our institution between 2014-2022. Patient frailty level was determined by using Modified Frailty Index 5 (MFI-5), categorized as the absence of frailty, mild frailty, and moderate to severe frailty based on a 0-5 score. Patients' demographic information, medical history, pre-operative and peri-operative clinical data, post-surgical outcomes, admission/re-admission rates/Length-of-stay, discharge location/length-of-stay, cancer type/staging, post-

operative RT timing, 30-and 90-day mortality were collected. Statistical analysis was conducted using SPSS version 28, significance was determined with a p<.05, determined by Fisher's exact test or Wilcoxon rank sum test. Univariate and multivariable logistic regressions were performed, and odds ratio (OR) and 95% confidence intervals (CI) were calculated and reported.

Results/Discussion: Prior studies have shown the usefulness of MFI-5 as a pre-operative risk stratification tool in head and neck surgery for a heterogeneous population of patients across a large age range. These have found relationships between increased MFI and outcomes such as medical complications, discharge to nonhome, reoperation, length of hospitalization, and others. We sought to evaluate this tool in a more homogenous patient population of elderly patients all undergoing cancer resection and free flap reconstruction. Additionally, we evaluated outcomes for 90-day mortality as most other studies were limited to 30-day outcomes. Increased MFI Score was associated with an increase in 90-day mortality (p=.038) but was not significantly associated with increased 30-day readmission, return to OR, or medical/surgical complications. Patients with MFI ≥1 were more likely to be older compared to those with MFI=0 (p=.018). There was no difference in overall length of stay and discharge location between patients with MFI 0 vs ≥1. Limitations of our study include our small sample size as this was a single institution, retrospective study. Future multi-institutional studies should investigate larger sample sizes of this specific population to further extrapolate relationships seen in our results that while clinically significant were not statistically significant in our population.

B167: PREDICTORS FOR 30-DAY READMISSION AFTER HEAD AND NECK MICROVASCULAR RECONSTRUCTION

- Siddhant Tripathi, MD; Grace Zhang; Jack Garcia; Abigail Haslinger; Nicholas Hutchins; Eugene Cho; Mohamed Yakub, MD; Kattia Moreno Giraldo, MD; Dustin Silverman, MD; Alice Tang, MD; Chad Zender, MD; Yash Patil, MD; University of Cincinnati Medical Center

Objective: To identify factors affecting 30-day readmission rates in patients who undergo head and neck free tissue reconstruction.

Methods: Single institution consecutive retrospective review. The medical records of 324 consecutive free tissue flaps performed by a single reconstructive surgeon between 2007 and 2012 at an academic institution were reviewed. Multivariable logistic regression models were used to identify demographic and clinical factors associated with 30 day readmission.

Results: There were 46 patients (12.3%) that were readmitted within 30 days of postoperative discharge. Use of vascularized bone-containing donor flap, tracheostomy, fistula, wound infection, and increasing units of RBCs received were independently associated with a 30-day readmission. Our multivariable regression model indicated that patients with wound infections had 2.8 times greater odds of being readmitted within 30 days (OR= 2.80, 95% CI [1.20 to 6.56]). Patients with a tracheostomy had 2.7 times greater odds of being readmitted within 30 days. For every unit of PRBCs, patients had 1.19 greater odds of 30 day readmission (95% CI [1.06 to 1.33])

Conclusion: Tracheostomy, wound infection, and receiving greater units of RBCs during the surgical admission were all risk factors for readmission within 30 days.

B168: FASCIOCUTANEOUS RADIAL FOREARM FREE FLAP WITH SCAFFOLD FOR RECONSTRUCTION OF HIGH-RISK TRACHEAL RESECTION DEFECTS: A CASE SERIES. - Parker Tumlin, MD; Jeffson Chung, MD; William Stokes, MD, FACS; West Virginia University

Importance: Primary tracheal reconstruction for defects larger than 4 cm or in a previously radiated field caries a high risk of anastomotic failure. The fasciocutaneous radial forearm free flap (RFFF) with implanted costal cartilage or external mesh offers a tension free option for reconstruction of these high risk tracheal defects.

Objective: To report our experience on tracheal reconstruction with the fasciocutaneous radial forearm flap and describe outcomes and complications.

Design: Retrospective case series of two patients across a 13-month time period.

Setting: Single tertiary care referral center

Participants: Two patients with malignancies of the trachea who underwent resection and reconstruction with a fasciocutaneous radial forearm free flap.

Main Outcome(s) and Measure(s): Overall survival, functional outcomes, perioperative complications and hospital length of stay.

Results: Patient 1 was a 66-year-old male with a primary adenocarcinoma of the thoracic trachea causing airway obstruction. He underwent resection of his thoracic trachea with a 12 cm anterior and 4 cm posterior tracheal defect. A suprahyoid and carinal release was performed to allow for primary anastomosis of the posterior tracheal wall. The anterior reconstruction was performed with a RFFF with previously implanted sub-cutaneous cadaveric rub cartilage. Surgery was performed via a median sternotomy on extracorporeal life support with coordination from cardiac surgery, thoracic surgery, and otolaryngology. Total operative time was 454 minutes. The patient was extubated at the conclusion of the case to a Montgomery T-tube. This was converted on POD 2 to a 6-0 distal XLT shiley tracheostomy tube due to dyspnea and problems with mucus plugging. The patient's stay was complicated by surgical site infection from an intra-thoracic hematoma with drainage from the sternotomy requiring mediastinal washout. Tumor resection required sacrifice of bilateral recurrent laryngeal nerves and the patient remained tracheostomy and gastrostomy tube dependent at discharge. Patient was discharged on postoperative day (POD) 28 with a speaking valve in place and had strong intelligible speech. Unfortunately, the patient developed local disease recurrence and expired 8 months postoperatively on palliative radiation and immunotherapy.

Patient 1: Pre-op verses 4 months post-op

Patient 2 was a 58-year-old female with history of cT2 N0 M0 squamous cell carcinoma of the epiglottis treated with primary radiation therapy who presented with a rT2 N0 M0 squamous cell carcinoma of the anterior tracheal wall. Patient underwent resection of the cervical anterior tracheal wall (5 cm anterior defect) and reconstruction with a radial forearm free flap supported by a 0.6 mm thick titanium mesh. Patient's tracheostomy was decannulated on POD 13 and discharged on POD 14. She did require temporary gastrostomy tube placement postoperatively which was removed on POD 36. Her last follow up was at 13 months postoperatively and has been without evidence of recurrent disease.

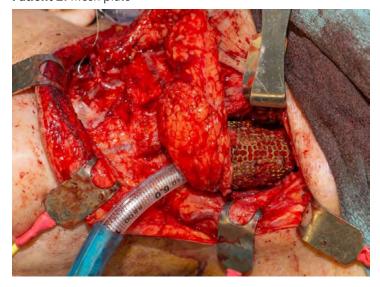**Patient 2:** Pre-op verses 4 months post-op

Conclusions and Relevance: We present two cases of tracheal resection where primary reconstruction would have been high risk or impossible. We were able to obtain adequate reconstruction with a radial forearm free flap with two different options to incorporate structural support into the neotrachea.

Patient 1: SubQ cadaveric rib

Patient 2: Mesh plate

that are managed and treated by a variety of medical and dental specialties. These may represent a non-surgical treatment option that may act as a bridge to more invasive or permanent solutions. While previous studies have evaluated the off-label use of filler for treating specific pathologies, a review summarizing the widespread non-cosmetic uses of filler for treating diseases of the head and neck has yet to be conducted.

Objective: This study aims to identify and summarize both common and novel non-cosmetic uses of injectable fillers in treating head and neck pathologies across a variety of disciplines.

Methods: A structured search was conducted in two electronic databases: Medline (Ovid) and Embase. Studies reporting the use of injectable fillers in the context of head and neck pathologies published up until October 2022, were included. Synthetic and autologous filler materials were included, while permanent materials or implants were excluded. Data was organized by indication and type of filler used. Pathologies were grouped according to anatomical location by 8 categories: laryngeal, oropharyngeal, sinonasal, oral cavity, dermatologic, orbital, craniofacial, and other. Both established and novel uses were recorded and themes were identified and qualitatively assessed.

Results: Two-hundred and ninety studies (N=10,316 patients) including relevant case reports were ultimately included. Thirty-five distinct indications for use of non-cosmetic filler in the head and neck were identified. The medical specialties most often reporting functional uses of filler were otolaryngology, ophthalmology, dermatology, dentistry, and plastic surgery. The most commonly used filler material was hyaluronic acid. The most common indications for treatment were vocal fold pathologies (N=97 studies, 4,052 patients), facial dysmorphia corrections (N=57 studies, 1,560 patients), temporomandibular joint disorder (N=30 studies, 1,760 patients), orbital pathologies (N=20 studies, 185 patients), velopharyngeal insufficiency (N=18 studies, 1,062 patients), and scar revisions (N= 12,655 patients). Many novel uses of filler were also identified across various disciplines.

Conclusion: Non-cosmetic uses of filler in the head and neck are being performed by a number of different types of specialists to treat a wide array of pathologies. Moreover, there are emerging uses of filler that are not well described in the literature. Knowledge of well-established and novel indications of filler often exist within one discipline but are not necessarily disseminated outside of a particular specialty; this study contributes a cross-discipline comprehensive current update of non-cosmetic and predominantly off-label uses of filler in the head and neck.

B169: NON-COSMETIC APPLICATIONS OF INJECTABLE FILLER IN THE HEAD AND NECK: A SYSTEMATIC REVIEW

- Jenny Xiao, MSc[1]; Laura Allen, MD[1]; Emily C Deane, MD, FRCSC[2]; Neil K Chadha, MD, MBChB, MPHe, FRCS[1]; [1]University of British Columbia; [2]University of Pennsylvania

Background: The use of injectable filler in cosmetic medicine and surgery is a popular means of correcting facial volume loss. Types of filler have evolved to include biosynthetic and autologous materials with varying properties, durations of effect, and potential risks. The application of injectable filler has expanded to include the numerous head and neck pathologies

B170: A NOVEL TECHNIQUE AND SYSTEM TO IMMEDIATE DENTAL IMPLANT REHABILITATION IN MALIGNANCY:
A CASE REPORT - Cheryl Yu, MD; Emma West, MD; Daniel Hawkins, DMD; Thomas Lee, MD; Christopher J Kandl, MD; Virginia Commonwealth University Health System

Introduction: Oncologic resection of maxillary and midface malignancies often entail extensive ablative and reconstructive surgeries that lead to significant aesthetic and functional compromise. Dental rehabilitation remains a challenging process within this population given multiple inherent variables of cancer, including the complexity of reconstruction, availability and integrity of implantable bone, need for adjuvant therapy, and risk of recurrence. While there appears to be a paradigm shift from secondary to primary implant placement, immediate

implant placement at time of tumor resection and reconstruction, the intricacies to optimally executing this continue to evolve. We present the first reported case of concurrent immediate dental reconstruction using the IPS preprosthetic system (IPS Implants Preprosthetic®, KLS Martin Group) in malignancy during resection of a recurrent maxillary alveolus cancer.

Methods: Case report and literature review.

Results/Case: A 62 year-old male, with a past medical history of pT2NxM0 squamous cell carcinoma of the right upper maxillary alveolus, presented to our Head and Neck Oncology clinic with biopsy proven recurrence (Figure 1). Oncologic history included initial primary treatment with prior surgical resection, including radical resection of the right upper alveolus and retromolar trigone, followed by adjuvant radiation therapy. He was subsequently noticed on surveillance visits to have a progressively enlarging defect in his right hard palate, ultimately revealing to be recurrence. After preoperative evaluation and discussion amongst the head and neck surgery, dental, and oral and maxillofacial teams, decision was made to proceed with simultaneous oncologic resection and implant (IPS Implants Preprosthetic®, KLS Martin Group) rehabilitation. Virtual planning was performed preoperatively to generate the patient-specific implant. The patient then underwent surgery as planned without complication. Ablative partial maxillectomy was first performed with use of the custom cutting guide to perform final osteotomies (Figure 2). This was then followed by implant placement with securing of the IPS scaffolding base to the remaining zygoma, piriform aperture, and maxilla (Figure 3). Radial forearm fasciocutaneous free flap was then harvested for reconstruction and inset, positioned over the implant with the posts traveling through the soft tissue of the flap (Figure 4). The temporary denture prosthesis was then finally placed with appropriate fit and occlusion (Figure 5).
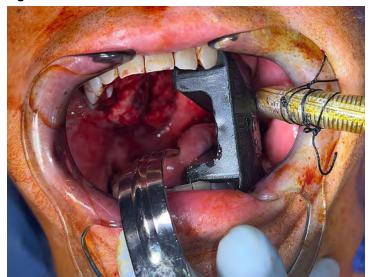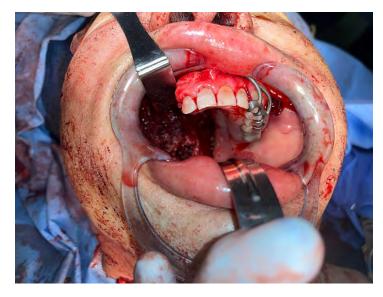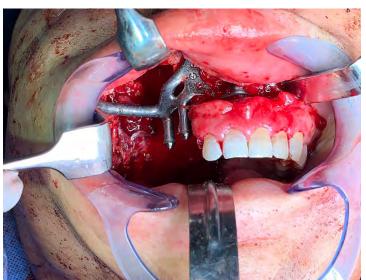
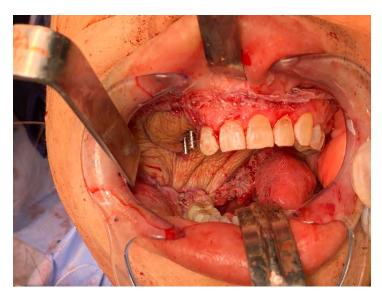**Figures**

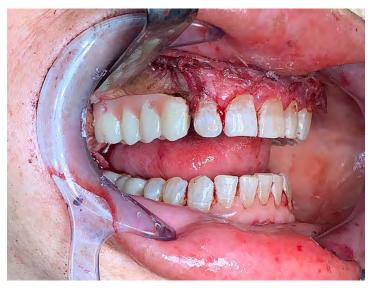Figure 2

Figure 3

Figure 1

Figure 4

Figure 5

Conclusion: Dental reconstruction remains a demanding and challenging process in the realm of head and neck malignancy, with no universally adopted algorithm or timeline for implantation. New techniques and options continue to arise, each tailoring towards varying characteristics and situations. The IPS Implants Preprosthetic® has proven to be a functionally reliable prosthetic framework in maxillary dental reconstruction in the secondary setting in this population; however its similar use in the primary setting, requires further investigation. Our case supports viable application of this system in this setting, which may provide high utility given perpetuating demand and desire for immediate dental rehabilitation.

B171: FACTORS ASSOCIATED WITH RESPONSE TO SIALENDOSCOPY IN PATIENTS WITH RADIOIODINE INDUCED SIALADENITIS - Xiaoxuan Emily Chen, BA[1]; Eseosa Odigie, MD[2]; Ashutosh Kacker, MD[3]; David I Kutler, MD[3]; [1]Department of Otolaryngology-Head and Neck Surgery, Weill Cornell Medical College; [2]Department of Head and Neck Surgery & Communication Sciences, Duke University Hospital; [3]Department of Otolaryngology-Head and Neck Surgery, Weill Cornell Medicine

Objective: Radioiodine therapy is frequently used after thyroidectomy for the treatment of thyroid cancer to ensure that all compromised remnant thyroid tissue is destroyed. After radiation therapy, some patients experience radioiodine induced sialadenitis (RIS), or salivary inflammation. Sialendoscopy, a minimally invasive procedure, is used to treat RIS that is refractory to conservative management such as salivary gland massages, sialagogues, antibiotics, or hydration. However, studies show there is an estimated recurrence rate of 0-40% of sialadenitis after sialendoscopy. Our objective is to assess demographic and medical factors that may predict response to treatment, which could help guide expectations on treatment outcomes.

Study design: Retrospective single-center study

Methods: We identified 315 patients who underwent sialendoscopy between January 2010 and June 2022. Patients with a diagnosis of radioiodine induced sialadenitis after radioiodine therapy for thyroid cancer were included. Utilizing the electronic medical record, patient demographics, comorbidities and post-operative outcomes were reviewed.

Results: 22 patients met inclusion criteria. Their mean age was 51.5 (SD=14.3) years (range 22-86 years). 41% (n=9) of patients were male. A total of 35 glands were treated with the sialendoscopy procedure. 73% (n=16) of patients had symptoms arising from the parotid glands, 23% (n=5) from submandibular glands, and 4.5% (n=1) from both glands. The mean time between symptom onset and their first sialendoscopy was 8.2 months (range 1-72 months). The dose of iodine (mCi) ranged from 50-153 mCi. Ductal stenosis (77%) was the most common ductal pathology. Sialadenitis involving the right parotid gland was significantly associated with reduced clinical improvement (p=0.03). Age, gender, number of sialendoscopies undergone, and procedures (duct dilation, Kenalog injection, sialodochoplasty) performed during sialendoscopy were not associated with clinical improvement (p>0.05). The majority of patients 82% (n=18) reported complete resolution or minimal residual symptoms following sialendoscopy.

Conclusion: Sialendoscopy is an effective treatment for patients with radioiodine induced sialadenitis refractory to conservative management. Patients in our cohort reported robust improvement in symptoms after intervention.

B172: A PERSONALIZED PREDICTIVE MODEL FOR SALIVARY GLAND CANCER USING ARTIFICIAL INTELLIGENCE - Andrew G Girgis, BS[1]; Bishoy M Galoaa, BS[2]; Anand Devaiah, MD[3]; [1]Boston University Chobanian & Avedisian School of Medicine; [2]College Of Engineering Electrical and Computer Engineering Department, Northeastern University; [3]Department of Otolaryngology Head and Neck Surgery, Boston Medical Center, Boston University Chobanian & Avedisian School of Medicine

Background: In the realm of healthcare, the integration of artificial intelligence (AI) into clinical settings has promise for marked improvements. The application of AI in surgical settings, particularly in managing complex conditions like head and neck tumors, remains relatively untapped. Recognizing the vast opportunities that AI offers in enhancing patient outcomes, we developed an AI model capable of predicting the optimal treatment regimens and applied this to salivary gland tumors to maximize patient survival. This approach aims not only to bridge an existing gap in the application of AI in medicine but also to significantly enhance patient survival outcomes through tailored treatment strategies.

Objective: To augment clinical decision-making for salivary gland malignancies to personalize treatment. The present study uses AI to harmonize data and recommend optimum treatment based on the patient's unique radiology, pathology, histology, and demographics.

Design, Setting, and Participants: We utilized the comprehensive SEER cancer database, selecting a cohort of 25,286 patients diagnosed with salivary gland malignancies. We then developed an AI model capable of proposing a treatment regimen optimized for maximizing patient survival. This was achieved by adopting a regression model equipped with an automatic feature selection module that diminishes the impact of data outliers, thereby mitigating biased result predictions due to the dataset's nature, which contains missing and incomplete information. To rigorously validate the model's effectiveness, we conducted post-training tests on a randomly chosen subset of 2,529 patients, representing 10% of the total dataset.

Results: In the study cohort of 25286 patients, 57.9% were men; 81.6% were white and 18.4% were of other races. Most of the patients are older adults with a mean age of 63.1 years. The model produced a highly effective output as seen through a Coefficient of Determination (R^2) of 0.99, Mean absolute error of 0.048 months, a mean square error of 0.0085, and a root mean square error of 0.092.

Conclusions and Relevance: The present study shows how a novel AI system can be a tool to help formulate optimal treatment plans that maximize patient survival through utilizing a personalized approach. An innovation of our AI model lies in the harmonization, utilization of the data, and interference of the dataset provided in order to provide optimized recommendations for treating salivary gland malignancies. Our AI model is also auto scalable to accommodate other clinical datasets, as demonstrated in the present study through use of different SEER datasets.

B173: TRANSORAL ROBOTIC SURGERY OF PRESTYLOID PARAPHARYNGEAL SPACE SALIVARY TUMORS: A 15-YEAR SERIES - Jake J Lee, MD, MSCI[1]; Christopher H Rassekh, MD[1]; Amy E Schettino, MD[1]; J W Rosenthal[1]; Anusha G Naik, BS[1]; Karthik Rajasekaran, MD[1]; Ara A Chalian, MD[1]; Robert M Brody, MD[1]; D G Farwell, MD[1]; Steven B Cannady, MD[1]; Devraj Basu, MD, PhD[1]; Ryan M Carey, MD[1]; Bert W O'Malley, MD[2]; Gregory S Weinstein, MD[1]; [1]University of Pennsylvania; [2]University of Maryland Medical Center

Importance: With the adoption of transoral robotic surgery (TORS), the TORS approach to parapharyngeal space (PPS) tumors has been increasing in frequency as an alternative to the conventional transcervical or transparotid approaches. Its feasibility and overall safety have been documented in small case series and systematic reviews. However, follow-up duration was less than 2 years, thereby limiting the assessment of long-term outcomes like local recurrence rates.

Objectives: To assess intraoperative characteristics, histologic variables, complications, and recurrence rates in this 15-year series of patients who have undergone TORS approach to PPS tumor resection.

Design: Retrospective case series.

Setting: Tertiary referral center.

Participants: Consecutive patients with prestyloid PPS salivary gland pathology who underwent TORS approach for resection from May 1, 2007 to August 30, 2022 were included. Patients who underwent a combined transoral and external approach, such as transcutaneous and transparotid, and those with non-salivary PPS pathology, were excluded.

Main Outcomes and Measures: The primary outcome was local recurrence. Secondary outcomes included intraoperative events, such as tumor rupture and cut-to-close time; histologic factors; and complications, including postoperative intubation, major wound dehiscence, first bite syndrome, intraoral hemorrhage, cranial neuropathy, and length of stay.

Results: Of 87 patients who underwent TORS for PPS resection at our institution, 52 patients (mean age 56.5 [SD 13.0] years, 36 [69%] females) with prestyloid salivary pathology were included. Median tumor size based on pathology was 3.5 (range 1.2-8.0) cm. Pathologic diagnoses included pleomorphic adenoma (41/52, 79%), other benign salivary tumors (5/52, 10%), and salivary malignancy (6/49, 11%). Malignant pathology included carcinoma ex pleo (n=3), mucoepidermoid carcinoma (n=2), and myoepithelial carcinoma (n=1), and all were only discovered on final pathology after resection. The intraoperative tumor rupture rate was 23% (12/52), which included fragmentation of the specimen. Positive and close margins were found in 2 (4%) and 22 patients (42%), respectively. Median cut-to-close time was 1.49 (range 0.48-3.60) hours.

The local recurrence rate was 4% (2/52), one related to pleomorphic adenoma and the other to carcinoma ex pleo. There were 0 cases of first bite syndrome. The rate of postoperative intubation was 8% (4/52), which all occurred in the first few years of adopting this surgical technique. The rates of major wound dehiscence, intraoral hemorrhage, and cranial neuropathy were each 2% (1/52). Median resumption of liquid and pureed/soft diet was postoperative day 1.0 (range 0-16) and day 2.0 (range 0-16), respectively, and all patients resumed an oral diet after their first postoperative visit. Median length of stay was 2.0 (range 1-9) days. Median follow-up duration with office visits and/or imaging was 844 (range 3-5731) months.

Conclusions and Relevance: The transoral robotic approach to prestyloid PPS salivary tumors is safe and associated with very low long-term local recurrence risk, even with capsule rupture. There was 0% incidence of first bite syndrome and very low incidence of wound dehiscence, hemorrhage, cranial neuropathy, and prolonged NPO status in this case series, which is the largest to date of this surgical modality.

B174: TRENDS IN THE EXTENT OF SURGICAL MANAGEMENT FOR LOW GRADE PAROTID MALIGNANCIES: A SEER ANALYSIS FROM 2004-2020 - Katelyn S Rourk, BS[1]; Gabriela A Calcano, BS[2]; Amy E Glasgow, MHA[3]; Elizabeth B Habermann, PhD[3]; Daniel L Price, MD[2]; Kendall K Tasche, MD[2]; Kathryn M Van Abel, MD[2]; Eric J Moore, MD[2]; Linda X Yin, MD[2]; [1]Mayo Clinic Alix School of Medicine; [2]Mayo Clinic Department of Otolaryngology- Head and Neck Surgery; [3]Mayo Clinic Robert D and Patricia E Kern Center for the Science of Health Care Delivery
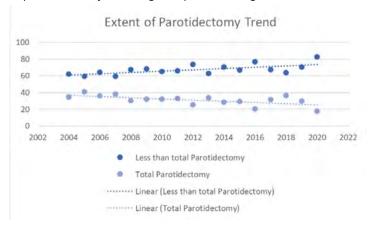
Introduction: Low grade parotid malignancies have high overall survival rates, with studies showing >90% 5-year disease specific survival in low grade acinic cell carcinoma (ACC) and mucoepidermoid carcinoma (MEC).1,2 However, controversy remains about the appropriate extent of surgery for these tumors. We explore the trends in extent of parotidectomy performed over the past decade and a half in low grade parotid malignancies in the United States (US). We hypothesize that there has been a national trend towards less aggressive parotidectomy for these pathologies.
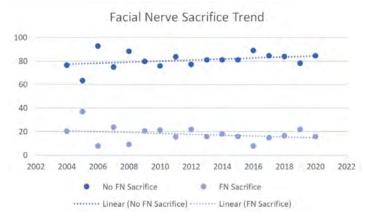
Methods: This is a retrospective cohort study of all low-grade (Grade I) ACCs and MECs in the Surveillance, Epidemiology, and End Result (SEER) set of cancer registries from 2004 to 2020. Extent of parotidectomy, demographics, TNM stage, presence or absence of facial nerve sacrifice, and overall and cancer-specific survival were assessed. Tumor staging was reported as either clinical or pathological. Less than total parotidectomy was defined as superficial parotidectomy, selective deep lobe parotidectomy, and any combination of the above that is less than a total parotidectomy using SEER site-specific surgical codes 30-38 for parotid gland (C079) and major salivary glands (C080-C089). Trends in surgical extent and facial nerve sacrifice were assessed using Cochran-Armitage tests. Kaplan-Meier survival curves were used to analyze overall and cancer-specific survival.

Results: 1288 patients were identified with low grade parotid malignancies (916 MEC; 372 ACC). Most patients (n=836, 65%) presented at age 45 or greater with a slight female predominance (1.58:1). Most patients were non-Hispanic White individuals (n=722, 59.9%), with the next most common group being Hispanic individuals (n=198, 15.4%). Most of the cohort presented with tumor stage T1 or T2 (n=1083, 84%), N0 (n=1161, 90.1%), and M0 (n=1248, 96.9%). Among the cohort, 21 patients (1.7%) did not undergo surgical treatment, 830 (67.6%) had less than a total parotidectomy, and 377 (30.7%) had a total parotidectomy. Over a 17-year period, treatment with less than total parotidectomies increased significantly (61.8 vs. 82.4%, p=0.02), while treatment with total parotidectomies decreased significantly (34.6 vs. 17.7%, p=0.02). During this same time, the surgical choice to spare the facial nerve slightly increased (76.4 vs 84.3%, p=0.08), although this was not statistically significant. Cancer-specific survival by surgical extent was excellent for both less than total and total parotidectomy groups, 99% and 98.2% respectively. There were 11 cancer deaths in the cohort with a median follow-up time of 82 months (range: 0-203 months). Given the extremely low overall event rate oncologic outcome comparisons between groups were not made. Overall survival by surgical extent was similarly high, with 89% and 92.3% for less than total and total parotidectomies, respectively.

Conclusion: Over the last decade and a half, there has been a significant de-escalation in the extent of parotidectomy for low grade parotid malignancy in the US and decreasing rates of facial nerve sacrifice. This data supports the need for future studies to investigate de-escalation in the extent of parotidectomy for low-grade parotid malignancies.

Extent of Parotidectomy Trend

Facial Nerve Sacrifice Trend

B175: ONCOLOGIC EFFICACY AND POSTOPERATIVE OUTCOMES OF LOW GRADE MUCOEPIDERMOID CARCINOMA TREATED WITH PARTIAL PAROTIDECTOMY - Katelyn S Rourk, BS[1]; Hawa M Ali, MD[2]; Jamie J O'Byrne, MAS[3]; Kendall K Tasche, MD[2]; Daniel L Price, MD[2]; Kathryn M Van Abel, MD[2]; Linda X Yin, MD[2]; Eric J Moore, MD[2]; [1]Mayo Clinic Alix School of Medicine; [2]Mayo Clinic Department of Otolaryngology- Head and Neck Surgery; [3]Mayo Clinic Department of Quantitative Health Sciences

Introduction: Low grade mucoepidermoid carcinoma (LGMEC) of the parotid gland has historically yielded excellent oncologic outcomes with low rates of recurrence. Surgery alone can be curative. However, the extent of parotidectomy required for cure in LGMEC remains controversial. Surgical approaches include partial parotidectomy (PP), superficial parotidectomy (SP), and near-total/total parotidectomy. Given the indolent nature of LGMEC, it is imperative to explore whether these tumors are amendable to less invasive surgical intervention without compromising oncological outcomes. In this study, we aim to assess the impact of extent of parotidectomy on surgical and oncologic outcomes in LGMEC.

Methods: This is a single tertiary care institution retrospective cohort study, from 2000-2022. All patients undergoing primary curative intent surgical treatment were included. Clinical

features collected included demographics, preoperative symptoms and facial nerve function, operative techniques, postoperative complications/facial nerve function, and recurrence. Extent of parotidectomy was defined in accordance with European Salivary Gland Society (ESGS) levels. PP was defined as level I, II, III, IV, or V. SP was defined as levels I-II. Total parotidectomy was defined as levels I-IV. Near-total parotidectomy was defined as levels I-III or I, II, & IV. Postoperative complications included hematoma, sialocele, seroma, Frey syndrome, First bite syndrome, and ear numbness.

Results: 59 patients with LGMEC were included. Most patients presented with a palpable parotid mass (n = 43, 73%). All participants had normal preoperative facial nerve function and none had cervical lymphadenopathy. 11 patients underwent PP, 37 underwent SP, and 10 underwent near-total/total parotidectomy. Tumor size was significantly smaller in the PP (1.4 cm) and SP (1.4 cm) groups compared to the near-total/total parotidectomy group (2.1 cm) (p = 0.02). PP and SP patients were more likely to have negative margins (100%) compared to near-total/total parotidectomy patients (70%) (p < 0.01). Neck dissection was more frequently performed on the near-total/total parotidectomy patients (20%) vs 9% for PP and 3% for SP patients. The near-total/total group was more likely to have positive intraparotid nodes (30% vs 0%) on final pathology (p = 0.02). 2 patients in the near-total/total parotidectomy group had invasion of the upper division of the facial nerve, requiring transection and simultaneous placement of an eyelid weight, compared to 0% of PP and SP patients. 30% of near-total/total parotidectomy patients required placement of an abdominal fat graft for reconstruction compared to 11% of SP and 0% of PP patients (p=0.1). There were no significant differences in postoperative complication rates between the groups. Postoperative facial nerve function was significantly better among PP patients (67% HB I) compared to SP (44% HB I) and near-total/total parotidectomy patients (0% HBI) (p < 0.01). Patients were followed for a median of 2.68 (0.003-17) years, during which only 1 patient (total parotidectomy) had a recurrence. No difference was observed in recurrence rates among the 3 groups (p = 0.46).

Conclusions: PP is a safe and oncologically efficacious surgical management strategy for smaller LGMEC tumors amenable to margin-negative resection. Compared to near-total/total parotidectomy, it has superior postoperative facial nerve outcomes and minimal post-operative complications.

B176: OUTCOMES OF SALVAGE SURGERY FOR RECURRENT CUTANEOUS SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK FOLLOWING DEFINITIVE SURGERY AND RADIATION THERAPY - Nikhil Bellamkonda, MD; Marcus M Monroe, MD; University of Utah
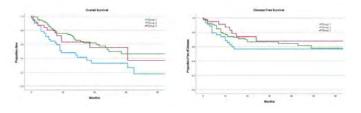
Objective: To better characterize outcomes of patients with a history of cutaneous squamous cell carcinoma (cSCC) of the head and neck previously treated with definitive surgery and radiation therapy (RT), who undergo salvage surgery for disease recurrence. There is minimal published data analyzing this category of patients.

Methods: This was a single institution retrospective case series. All patients evaluated for advanced cSCC between 2003-2022 within our department were reviewed. Patients were included if they had a history of surgical excision and adjuvant radiation therapy and then underwent salvage surgery for cancer recurrence (Group 1). Comparisons were made

to patients with recurrence who had salvage surgery after previous surgery without adjuvant RT (Group 2), and to patients undergoing primary surgery and adjuvant RT (Group 3).

Results: Of the 579 patients reviewed, a total of 49 met inclusion criteria (Group 1). Average length of follow up was 22 months (range: 0 – 90 months). A total of 19 patients (38.8%) experienced recurrence. All recurrences occurred within 14 months of salvage surgery. Among patents staged BWH T2b or T3, there was a 50% recurrence rate. Average overall survival following surgery was 35.6 months (95% CI: 24.7 – 46.4). This was significantly worse than patients in Group 2 (p = 0.006), who had an average overall survival of 61.3 months (95% CI: 50.8 – 71.8). T3 patients in Group 1 had significantly worse overall survival than those in Group 2 (p < .001) and Group 3 (p = .022), and significantly worse disease-free survival than in Group 2 (p = .005).

Conclusion: Patients who undergo salvage surgery for cSCC of the head and neck who have previously had surgical resection and RT have a high rate of recurrence and an overall survival of approximately three years. Further multi-institutional studies will be necessary to better characterize this category of patients and establish optimal treatment protocols.

B177: ROLE OF SOCIOECONOMIC STATUS IN PATIENTS WITH MELANOMA OF THE HEAD AND NECK - Nina Gallo, MD; Meghana Chanamolu, MD; William Stout, BS; Sofia Torres-Small, BS; Okenwa Okose, MD; John P Gleysteen, MD; Burton Wood, MD; University of Tennessee Health Science Center

Introduction: Melanoma incorporates extensive anatomical regions. Of particular concern are melanomas affecting the head and neck regions, constituting 10-20% of all cases. We sought to assess the effects of socioeconomic status (SES) on the prognosis of head and neck melanoma patients and their outcomes.

Methods: Using the Surveillance, Epidemiology, and End Results (SEER) database, we identified patients diagnosed with melanoma of the head and neck from 2006-2018. SES stratification was accomplished through the US (United States) Yost index, resulting in quintile categorizations from Group 1 (lowest SES) to Group 5 (highest SES). Statistical methodologies, including ANOVA, Kaplan-Meier Curves, and Cox Regression analyses, were applied to analyze patient demographics, disease extent at diagnosis, and survival metrics.

Results: A cohort of 53,967 patients were included in the study. The population revealed a male predominance (74%) and a majority white population (99%). Males comprised 74% of the cohort and 99% of patients were White. There were significantly more people living in urban areas than rural areas (p<0.001). Those of the lowest SES quintile were diagnosed on average 2 years later than those of the highest SES. Those with a lower SES were found to have tumors that were significantly larger in size and greater in Breslow Thickness (p<0.001). They were also found to have a shortest duration of survival and a higher mortality

when compared to those of higher SES groups (p<0.001).

Discussion: Low SES can have a profound impact on the prognostic outcomes of patients with head and neck melanoma. Despite remarkable strides in melanoma diagnosis and treatment, disparities persist among individuals of lower SES, manifesting in delayed diagnoses, aggressive tumor profiles, and compromised survival. It is paramount to encourage efforts that bridge the healthcare accessibility gap and ensure equitable care for all head and neck melanoma patients, irrespective of their socioeconomic background.

B178: INTRAOPERATIVE MOH'S HISTOLOGIC VS. STANDARD FROZEN SECTION ASSESSMENT IN DEFINITIVE SURGICAL TREATMENT FOR ADVANCED CUTANEOUS SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK - <u>Cong Fan, BA</u>[1]; Shlomo Koyfman, MD[2]; Allison Vidimos, MD[2]; Michael Fritz, MD[2]; Brian Gastman, MD[2]; Peter Ciolek, MD[2]; Jennifer Lucas, MD[2]; Jon Meine, MD[2]; Alok Vij, MD[2]; Eric Lamarre, MD[2]; Joseph Scharpf, MD[2]; Brandon Prendes, MD[2]; Natalie Silver, MD[2]; Neil Woody, MD[2]; Jacob Miller, MD[2]; Shauna Campbell, DO[2]; Jamie Ku, MD[2]; [1]Cleveland Clinic Lerner College of Medicine; [2]Cleveland Clinic

Introduction: Patients with skin cancer of the head and neck who have larger tumors, aggressive pathological features, and involvement of aesthetically important locations often receive surgical excision and reconstruction. The current standard of care is to perform gross margin assessment and inoperative frozen section analysis. However, this method can be limited by surgeon and pathologist selection, with a prior study finding an estimated 72% accuracy rate for assessing basal cell carcinoma (BCC). Our institution has developed a multidisciplinary approach using an intraoperative Moh's micrographic surgery (iMMS) technique that allows 100% of the peripheral and deep margins to be examined and mapped. This study sought to compare patient and disease characteristics and outcomes between patients who had received either the iMMS vs. standard frozen gross margin assessment for cutaneous squamous cell carcinoma (cSCC) of the head and neck.

Methods: This retrospective cohort study included patients at our institution who had undergone definitive surgery between 2014 and 2021 for cSCC of the head and neck, with a tumor size > 3cm, and who had received either intraoperative Moh's histologic or frozen section gross margin assessment. T-test and chi-squared test were used to compare continuous and categorical variables, respectively.

Results: A total of 68 patients were included: 32 in the iMMS group and 36 in the standard frozen section group. Baseline demographics did not differ between groups in terms of age (average 74 years), sex (85% male), race (98.5% white), smoking history (19.1% current smoker), or immunosuppressed/compromised status (26.5%). Disease and treatment characteristics, including anatomic site, BWH T stage, N stage, and treatment modalities (neck dissection, radiation therapy, systemic therapy) did not differ significantly between the groups. In the iMMS group, the average number of layers taken was 2.25. Additional margins were sent to pathology in 7 patients (21.9%): 2 for rule out of perineural invasion, 3 for deep margin analysis (including of bone/periosteum), 1 for lymph node analysis, and 1 for re-resection margin analysis. Overall, 6/32 (18.8%) of patients had a positive final margin status, similar to those in the standard frozen group (16.7%). The largest dimension of tumors in the iMMS group was significantly larger

than the frozen section group (7.9 vs. 4.7cm, p = 0.002). Regional recurrence, distant recurrence, and overall survival rates did not differ significantly between the groups. However, the number of patients with a local recurrence was significantly higher in the iMMS group (7 patients, 21.9%) vs. the standard frozen group (1 patient, 2.8%; p = 0.039) on univariate analysis (p = 0.039).

Conclusions: Intraoperative Moh's histologic margin assessment can be a valuable tool for patients with more complex disease who are undergoing definitive treatment for cSCC of the head and neck.

B179: REGIONAL LYMPH NODE METASTASIS IN SEBACEOUS CARCINOMA OF THE HEAD AND NECK: SYSTEMATIC REVIEW AND META-ANALYSIS - <u>Marta Kulich, MD</u>; Alison Yu, MD; Daniel Kwon, MD; Mark Swanson; University of Southern California

Introduction: Sebaceous carcinoma (SC) is a rare but aggressive malignant neoplasm most frequently originating in the periocular adnexa. Management of regional lymph nodes in SC, including the role of sentinel node biopsy, has been debated. We aim to synthesize published SC lymph node data to help inform clinical protocols.

Methods: Pubmed/MEDLINE and EMBASE searches were conducted to systematically find original articles published before October 2023 reporting regional lymph node status in adults with SC of the head and neck. Data on primary tumor site and size, among other clinical characteristics, was extracted. Meta-analysis was conducted to determine the pooled rate of lymph node metastasis and contributing factors.

Results: Of 1,011 screened abstracts, 197 underwent full text review, and 38 studies were included for final analysis. There was a total of 2,337 patients. Periorbital SC accounted for 97.3% of cases. The overall rate of regional lymph node involvement was 16% (95% CI, 14 – 19%, I[2] 57%). Among the 25 studies (1,432 subjects) which specified the time course of regional metastasis, 4% had nodal disease on presentation, while 12% were diagnosed with regional metastasis during recurrence. Twelve studies, comprised of 651 patients, reported the T-stage of the subjects with nodal metastasis; the rate of lymph node spread was 4% (3 out of 69) in T1 tumors, 8% (31 out of 379) in T2 tumors, 36% (62 out of 172) in T3 tumors, and 58% (18 out or 31) in T4 tumors (p <.001).

Conclusion: Lymph node metastasis in SC is common and warrants routine evaluation with imaging. Sentinel lymph node biopsy or elective neck dissection/parotidectomy should be considered for high T-stages.

B180: 40-GENE EXPRESSION PROFILING OF CUTANEOUS SQUAMOUS CELL CARCINOMA PREDICTS LYMPH NODE INVOLVEMENT AND HIGH-RISK FEATURES - <u>Marna A List, MD</u>[1]; Ramazan Gun, MD[1]; Rodrigo Martinez Monedero, MD, PhD[1]; Lindsay Olinde, MD[1]; Ameya Asarkar, MD[1]; Janine Hopkins, MD[2]; Cherie-Ann O Nathan, MD[1]; John Pang, MD[1]; [1]Louisiana State University Health Sciences; [2]Hopkins Dermatology

Objective: As diagnoses of cutaneous squamous cell carcinoma (cSCC) continue to rise, there is a push for improved methods of metastatic risk stratification beyond current staging systems and known clinicopathologic risk factors. Recently, molecular profiling

of cSCC has enabled risk stratification beyond TNM AJCC v8 staging paradigm. DecisionDx-SCC's 40-gene expression profile (40-GEP) has been validated as an augmentation to traditional risk stratification methods for metastasis-free survival in high risk cSCC. However, the relationship between risk category and clinicopathologic features remains unclear. Therefore, the objective of this study is to investigate the relationship between risk category from 40-GEP, nodal metastasis, high-risk pathologic features, and patient factors in an institutional cohort of patients diagnosed with cSCC.

Study design: Multicenter retrospective cohort study.

Patients and Methods: 37 patients with NCCN-defined high-risk cSCC were analyzed as part of an IRB-approved study at the Louisiana State University Shreveport Health along with 31 patients from a local community dermatologist. Tumor stage was defined according to the AJCC 8th edition guidelines. 40-GEP was performed on all tumors and risk was designated by the DecisionDX-SCC grading scale (1=low risk, 2a=moderate risk, 2b=high risk). Deidentified data was collected though comprehensive review of the patient's medical record, including operative and pathology reports. Data was analyzed via chi2 and multivariable regression with a designated significance value of 0.05.

Results: In our institutional cohort, male patients made up 91% (n=32) with a mean age of 77. A smoking history was present in 21 patients (59%). There were 18 patients with a history of cSCC, and of those 6 patients (33%) had previously been treated for cSCC in the same location. According to the AJCC 8th edition guidelines, 32.5% were T1, 22.5% were T2, 37.5% were T3, and 7.5% were T4. After treatment, 6 patients had locoregional recurrence (16%). On 40-GEP analysis of the combined cohorts, 49 tumors were low risk (Class 1), 18 were moderate risk (Class 2a), and 2 were high risk (Class 2b). Nodal metastases were noted in 10 patients (15%) at the time of diagnosis. Patients who were class 2a or 2b versus 1 were more likely to have smoked (76% vs. 40%, p=0.0256), and have high risk-pathologic features (poor differentiation, perineural invasion, or lymphovascular invasion; 44% vs. 13%, p=0.049). In our combined cohort data, patients who were category 2a or 2b were more likely to have lymph node involvement (35% vs. 6%, p=0.002). On logistic regression, category 2a or 2b was more significant than either T category, PNI, LVI, and grade for being predictive of lymph node involvement (OR 8.1, CI95 1.8-35.7, p=0.006).

Conclusion: Smoking history correlates with higher molecular risk profile in cSCC. Gene expression profiling of cSCC appears to have prognostic value beyond current risk stratification paradigms, specifically regarding nodal metastasis risk. Further research into the role of 40-GEP in the management of cSCC is warranted to deliver improved patient-centric care.

are well defined for body and limb subsites. However, due to the density of lymph nodes and the complexity of lymphatic drainage patterns, recurrence patterns based on depth of invasion are less well defined in the head and neck subsite.

Objective: The aim of this study was to investigate the prognostic factors that predict the pattern of treatment failure in head and neck melanoma.

Methods: A retrospective cohort study was performed based on a prospective database of consecutive head and neck melanoma patients at a tertiary care centre (St. Joseph's Hospital, Hamilton, Ontario). All patients were enrolled consecutively into the database by one of six fellowship-trained head and neck surgeons from 2009–2022. We included patients diagnosed with first-time primary cutaneous head and neck melanoma of any stage. Exclusion criteria included patients under 18 years of age, treatment refusal, melanoma in-situ, and any non-melanoma skin cancer or head and neck mucosal melanoma. For patients with more than one cutaneous head and neck melanoma, we only analyzed the lesion with the highest staging. We performed descriptive analyses for all included patients. We performed tests of proportionality and regression analysis to evaluate the effect of predictor variables on early-stage (i.e., T1/T2) vs. late-stage (i.e., T3/T4) cutaneous head and neck melanoma. All statistical tests were performed using R software.

Results: Overall, 374 patients met eligibility criteria. There were 273 males (73%) with a mean age of 69.3 years (SD: 13.6). The most common type of melanoma was nodular (22.9%), and the most common subsite was the face (31.4%). Moreover, 230 (61.5%) underwent SLNB with a positive SLNB rate of 7.4%. Most lesions (51.9%) were T3/T4. In patients who underwent SLNB, we found that T3/T4 lesions were significantly associated with recurrence (X2 = 10.49, p <0.001) and location of metastasis, but not overall survival (X2 = 2.65, p = 0.104). T1/T2 lesions were associated with locoregional recurrence and T3/T4 were associated with distant metastasis (Fisher's exact p = 0.003, OR: 6.6, 95% CI: 1.68, 29.8). A multiple regression model demonstrated a significant effect of the ulceration status (p = 0.023), age (p = 0.037), and T3/T4 lesions (p =0.021) as predictors of distant metastasis[S1] [S2] .

Conclusion: We have identified that in patients undergoing SLNB for cutaneous head and neck melanoma: age, ulceration status, and T3/T4 primary lesions are associated with distant metastasis, but necessarily worsened survival.

B181: PATTERNS OF FAILURE IN PATIENTS WITH CUTANEOUS HEAD AND NECK MELANOMA WHO HAVE UNDERGONE SENTINEL LYMPH NODE BIOPSY: A RETROSPECTIVE COHORT STUDY - Phillip Staibano, MD; Zahra Abdullah; Sofia Nguyen; Emily Oulousian; Michael Gupta; Michael Au; David Choi, MD; Trevor Lewis, MD; JEM (Ted) Young, MD; Han Zhang; McMaster University

Background: Depth of invasion continues to be the most important prognostic factor in melanomas. Well defined lymphatic drainage patterns coupled with recurrence patterns

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2025

AHNS 2025 ANNUAL MEETING AT COSM

May 14-18, 2025

Hyatt Regency New Orleans
New Orleans, Louisiana

2026

AHNS 12TH INTERNATIONAL CONFERENCE ON HEAD AND NECK CANCER

July 18-22, 2026

Boston Convention and Exhibition Center
Boston, Massachusetts