

**Opportunities for Research in the
Department of Otolaryngology-Head and Neck Surgery
Medical University of South Carolina**

Sinus Center

Chronic rhinosinusitis (CRS) is a heterogeneous group of disorders resulting in inflammation and infection of the paranasal sinuses. Because of the differences in the pathophysiology of CRS we are investigating a variety of mechanisms and treatments targeting CRS-related inflammation. Our research team includes both basic scientists and clinicians thus providing a variety of research opportunities including projects focusing on molecular and cellular mechanisms of adult and pediatric CRS, translation/animal model based investigation and numerous clinical trials to assess novel therapeutics and instruments. Laboratory techniques available are automated cell sorting, ELISA, immunohistochemistry, flow cytometric analysis, ciliary beat analysis, PCR and a number of cell based assays (e.g., migration, phagocytosis assays, proliferation, etc.) as well as use of a murine model of atopic CRS. Human tissues available includes sinus and turbinate, plasma, peripheral blood mononuclear cells, frozen tissue explants (for RNA and protein based assays), primary sinonasal epithelial cells (submerged and ciliated air/liquid interface cultures), primary fibroblast cultures and adenoid tissue and nasal mucus. In addition, we are actively investigating clinical outcomes for medical and surgical treatments of CRS. This also includes a number of industry sponsored studies and retrospective reviews. Ongoing projects and investigators are:

Impact of Medical and Surgical Treatments upon Clinical Outcomes in CRS

Investigators: Zachary Soler, M.D., Rodney Schlosser, M.D., Jennifer Mulligan, Ph.D.
Department of Otolaryngology-Head and Neck Surgery

Olfactory-specific Outcomes in CRS

Investigators: Zachary Soler, M.D., Rodney Schlosser, M.D., Jennifer Mulligan, Ph.D.
Department of Otolaryngology-Head and Neck Surgery

Role of Vitamin D3 metabolism in CRS

Investigators: Jennifer Mulligan, Ph.D., Rodney Schlosser, M.D.
Department of Otolaryngology-Head and Neck Surgery

Epithelial cell complement production in the pathogenesis of CRS

Investigators: Jennifer Mulligan, Ph.D., Carl Atkinson, Ph.D.
Department of Otolaryngology-Head and Neck Surgery, Department of Microbiology and Immunology

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Facial Plastics and Reconstructive Surgery

Clinical Research in Craniofacial Surgery

Investigator: Krishna Patel, M.D., Ph.D.

Department of Otolaryngology-Head and Neck Surgery

Current opportunities for clinical research in the areas of craniofacial surgery are underway. These studies investigate the socioeconomical, clinical, and physiological aspects of children with craniofacial anomalies.

Clinical Research in Microvascular Reconstruction

Investigator: Judith M. Skoner, M.D.

Department of Otolaryngology-Head and Neck Surgery

Current opportunities for clinical research in the area of microvascular reconstruction of complex head and neck defects.

Pediatric Otolaryngology

Endoscopic Treatment of Subglottic Stenosis

Investigators: David White, M.D., Clarice Clemmens, M.D., Christopher Discolo, M.D.

Department of Otolaryngology-Head and Neck Surgery

Opportunities in database-driven clinical research include analysis of national databases (Healthcare Cost and Utilization Program Kid's Inpatient Database, American College of Surgeons National Surgical Quality Improvement Program, AudGen database, and others) as well as regional and hospital data to identify areas of disparity and potential quality improvement in the administration of healthcare for ear, nose and throat disorders in children. Recent projects have evaluated tonsillectomy and adenoidectomy, craniofacial/cleft palate surgery, and cochlear implantation outcomes. Outcomes or disparities in special populations (Down syndrome, the morbidly obese, and others) have also been evaluated.

Clinical Research in Pediatric Dysphagia

Investigators: Clarice Clemmens, M.D., Katlyn McGrattan, Ph.D.

Department of Otolaryngology-Head and Neck Surgery

Current opportunities for clinical research in the area of pediatric dysphagia are ongoing. These studies are investigating the physiologic attributes and relationships of sucking, swallowing, and respiration in infants evaluated for dysphagia, and testing the association between objective measures of oropharyngeal swallowing physiology, cross-system comorbidities, and clinical presentation among infants evaluated for dysphagia.

Pediatric Sleep Disordered Breathing

Investigators: Clarice Clemmens, M.D., Phayvanh Pecha, M.D.

Department of Otolaryngology Head and Neck Surgery

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Opportunities are available in retrospective clinical research in the area of pediatric sleep disordered breathing. These studies investigate all aspects of pediatric sleep disordered breathing, from the effect of payer mix on outcomes to post-operative management through a large database of pediatric sleep disordered breathing patients.

Maxillofacial Prosthodontics

Functional Outcome Center

Investigator: Betsy K. Davis, D.M.D., M.S.

Department of Otolaryngology-Head and Neck Surgery

This ongoing project is focused on collecting and analyzing functional outcomes data from patients with head and neck cancer as related to oral health and function.

Evaluation of the Potential for 3D Imaging and Virtual Planning in Nasoalveolar Molding Appliance for Cleft Palate Babies

Investigator: Betsy K. Davis, D.M.D., M.S.

Department of Otolaryngology-Head and Neck Surgery

This research project focuses on using 3D imaging and virtual planning to capture the impression and fabrication of the nasoalveolar molding appliance for cleft palate babies.

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Head and Neck Oncology

Ceramidase and Head and Neck Squamous Cell Carcinoma

Investigators: Besim Ogretman, Ph.D., Terry Day, M.D., Keisuke Shirai, M.D.

Department of Biochemistry and Molecular Biology, Department of Otolaryngology-Head and Neck Surgery, Department of Medicine

Ceramidase is a lipid mediator that has been suggested to play a critical role in cell growth differentiation and apoptosis. The potential relationship of ceramidase to head and neck cancer has yet to be determined. This is a laboratory project that is developed to determine the role of ceramidase and sphingosine kinase-1 in activation and inactivation of head and neck cancer cell lines. Additionally, a recent clinical trial that resulted from mechanisms of action of ceramide compounds in head and neck cancer from our laboratory revealed that LASS gene and its product, C-18 ceramide, may play a role in chemotherapy induced cell death. Ongoing projects involve the role of HPV, PI3K/mTOR/Akt pathways in head and neck cancers.

Cell Signaling to Invasion and Metastasis

Investigators: Steven A. Rosenzweig, Ph.D., Terry Day, M.D.

Department of Cell and Molecular Pharmacology and Experimental Therapeutics, Department of Otolaryngology-Head and Neck Surgery

We are studying the function of the scaffolding protein NEDD9 (neural precursor cell expressed, developmentally downregulated 9) in head and neck squamous cell carcinoma cell invasion and metastasis. NEDD9 is part of the metastatic signatures of melanoma, glioblastoma, lung, breast and now head & neck cancer. Our goal is to carry out studies on human specimens in order to develop a prognostic signature for the development of metastatic disease.

Tobacco and Head and Neck Cancer

Investigators: Terry Day, M.D., Graham Warren, M.D., Ph.D.

Department of Otolaryngology-Head and Neck Surgery, Department of Radiation Oncology, Department of Cell and Molecular Pharmacology and Experimental Therapeutics, Hollings Cancer Center, Cancer Control Program

Our laboratory research is focused on two primary areas. The first primary research area involves investigation into the effects of tobacco products on cancer treatment outcomes. We span a spectrum of research activities including: (1) Evaluating the effect of tobacco products on fundamental cancer biology, *in vitro* and *in vivo* response to radiotherapy and/or chemotherapy, activation of signal transduction primarily through the PI3K/Akt and Ras/Raf/MAPK axes, and mechanisms to prevent the adverse effects of tobacco on therapeutic response; (2) Assessing tobacco use in cancer patients, providing tobacco cessation support, and evaluating mechanisms to increase cessation efficacy for cancer patients; (3) Evaluating the effects of tobacco use and cessation on clinical treatment outcomes for cancer patients following surgery, chemotherapy, and/or radiotherapy; (4) Assessing the cost effectiveness of tobacco cessation in cancer patients and addressing public policy to improve cancer outcomes. The second primary research area relates to identifying modulators of radiotherapeutic response *in vitro* and *in vivo* by activation of endogenous neurochemical and adrenergic

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signaling pathways, modulation of immune response, and administration of potential radiosensitizers and radioprotectors.

Evaluation of Nodal Involvement in High Grade Salivary Gland Carcinoma

Investigators: Anand K. Sharma, M.D., Terry Day, M.D.

Department of Radiation Oncology, Department of Otolaryngology-Head and Neck Surgery

This retrospective study evaluates incidence of positive lymph nodes in a variety of high grade salivary gland malignancies at MUSC over the past ten years. The rate of lymph node involvement in high grade salivary tumors varies from 20-60%. At our institution, all patients with high grade salivary tumors undergo ipsilateral neck dissection at the time of primary tumor resection. The aim of this study is to identify the incidence of nodal involvement, association with tumor histology, site, stage and presentation (primary vs. recurrent). The study will also look at patterns of local, regional and distant failure.

The CARE (Cancer and Relationship Experiences) Study

Investigators: Katherine R. Sterba, Ph.D., Terry Day, M.D.

Department of Public Health Sciences, Department of Otolaryngology-Head and Neck Surgery, Hollings Cancer Center

The overall goal of this pilot study was to characterize quality of life in head and neck cancer patients and their caregivers at the Hollings Cancer Center over a two year period (at diagnosis, during treatment, and after treatment) to inform the development of future interventions for head and neck cancer survivors and caregivers. The study included patients with HNSCC, salivary, thyroid and cutaneous malignancies with surveys at diagnosis and every 6 months for two years. Specific aims were to: (1) describe quality-of-life over two years in head and neck cancer patients and their caregivers and characterize similarities and differences in patient and caregiver quality-of-life at each study timepoint; (2) describe differences in quality-of-life in patients and caregivers by sociodemographic and clinical characteristics; and (3) examine the relationships among quality of life and clinical variables. This study has completed accrual and analysis is underway within an existing REDCAP database.

Transitions after Treatment in Head and Neck Cancer Patient-caregiver Dyads

Investigators: Katherine R. Sterba, Ph.D., Terry Day, M.D.

Department of Public Health Sciences, Department of Otolaryngology-Head and Neck Surgery, Hollings Cancer Center

The specific aims of this study are: 1) to develop and pretest a specialized survivorship care planning intervention for head and neck cancer patients and their primary caregivers and 2) to conduct a pilot randomized controlled trial (N=80 dyads) to test the efficacy of the dyadic end-of-treatment survivorship care planning intervention on patient symptom distress and adherence to care and dyad unmet needs, satisfaction with care, quality of life and dyadic coping.

Oropharyngeal Cancer Outcomes in Head and Neck Cancer

Investigator: Terry Day, M.D.

Department of Otolaryngology-Head and Neck Surgery

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It is well known that HPV-related oropharyngeal cancers are on the rise and that their incidence is expected to surpass cervical cancer by the year 2020. Additionally, it has been shown from our database that presentation, diagnosis and outcomes are different from traditional oropharyngeal cancer that is tobacco related. We aim to assess the early presentation of oropharyngeal cancer and compare symptoms, signs, and radiographic criteria to determine its impact on stage and prognosis. Over 600 patients are currently listed in the MUSC database and HPV testing and analysis is ongoing.

Epidemiological Studies in Head and Neck Cancers Using the SEER Database

Investigator: Eric J. Lentsch, M.D.

Department of Otolaryngology-Head and Neck Surgery

Although most common head and neck cancers have been well studied from an epidemiological point of view, many less common cancers have only been described in the literature in case studies and/or small single institution series. We have been using the Surveillance, Epidemiology and End Results (SEER) database for the last 2 years to study these rare tumor types. Publications have been achieved on topics such as head and neck sarcomas, uvular carcinoma, plasmacytoma, basaloid squamous cell carcinoma, and merkel cell carcinoma. We have also used SEER to take a new look at some more common tumors as well, such as melanoma and thyroid cancer. There remains a multitude of cancers to study in this fashion and it is ideal for someone looking for a meaning clinical research project that can be productively done in a short time block (i.e., 3 months).

Integrative Transcriptomic and Mutational Profiling of non-HPV and HPV Related Oropharyngeal Squamous Cell Carcinoma

Investigators: David M. Neskey, M.D., M.S.C.R., Viswanathan Palanisamy, Ph.D., Terry A. Day M.D., Elizabeth Hill, Ph.D.

Department of Otolaryngology-Head and Neck Surgery, Department of Biochemistry and Molecular Biology, Department of Public Health Sciences

In contrast to other head and neck subsites, oropharyngeal squamous cell carcinoma (OPSCC) has increased in incidence in recent decades due to a higher incidence of human papilloma virus (HPV) infection and it is anticipated by 2030, 47% of all HNSCC will originate from the oropharynx. Recent studies have identified unique mutational patterns for HPV related disease but this research did not address the impact of HPV status on gene expression in OPSCC. The objective of this study is to correlate variations in survival for non HPV and HPV associated OPSCC with differences in expression of HNSCC related genes. Our hypothesis is patients with poor overall survival and HPV associated OPSCC will have tumors with a distinct gene expression pattern. To test of hypothesis we will use the following specific aims: 1) to establish variations in expression of 48 HNSCC associated genes for HPV- and HPV+ samples, and 2) to validate the mRNA predictions of key genes in HPV related disease in both preclinical models and patient samples. It is anticipated HPV+ OPSCC will have a distinct gene expression pattern from HPV- OPSCC and furthermore, patients with poor outcomes in HPV+ disease will have a distinct gene expression signature. These outcomes will have a positive impact by delineating

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the genes associated with HPV related diseases and poor clinical outcomes, leading to novel treatment strategies that target these altered genes.

A Role for Myosin IIA in Regulating Mutant p53 Mediated Invasion of Head and Neck Squamous Cell Carcinoma

Investigators: David M. Neskey, M.D., M.S.C.R., Steven Rosenzweig, Ph.D.

Department of Otolaryngology-Head and Neck Surgery, Department of Cell and Molecular Pharmacology and Experimental Therapeutics

Head and neck squamous cell carcinoma (HNSCC) accounts for over 45,000 new cancer diagnoses annually in the United States. *TP53* is the most frequently mutated gene in HNSCC and some mutations (mutp53) termed gain of function (GOF) are associated with increased cell invasion and decreased patient survival. The mechanisms responsible for GOF mutp53 remain elusive, however, Myosin IIA (MyoIIA) has recently been identified as candidate. The objective of this proposal is to correlate the GOF characteristics of mutp53 with MyoIIA dysfunction. Our hypothesis is the oncogenicity of mutp53 is due to decreased MyoIIA function and these effects can be abrogated through MyoIIA reactivation. To test our hypothesis, we will use the following specific aims: 1) Establish oncogenic features of mutp53 are due to decreased function of MyoIIA and 2) Determine if re-expression of MyoIIA will suppress cell migration and invadopodia formation in wildtype and mutant p53 cells. It is anticipated GOF mutp53 will suppress MyoIIA activity leading to increased invasion and invadopodia formation. Additionally, reactivation of MyoIIA will rescue the oncogenic features associated with MyoIIA depletion. These outcomes will have a critical impact in delineating the roles of MyoIIA and GOF mutp53 in HNSCC invasion, leading to novel therapeutic targets specific to MyoIIA-depleted cells.

Novel Mechanisms Driving the Oncogenic Phenotype Observed in Gain of Function p53 Mutations in Head and Neck Cancer

Investigators: David M. Neskey, M.D., M.S.C.R., Steven A. Rosenzweig, Ph.D.

Department of Otolaryngology-Head and Neck Surgery, Department of Cell and Molecular Pharmacology and Experimental Therapeutics

Head and neck squamous cell carcinoma (HNSCC) is the 6th most common cancer worldwide and accounts for over 45,000 new cases annually in the United States. Since *TP53* is the most frequently mutated gene in HNSCC, occurring in 60-72% of cases, genomic alterations in this gene are key events in the development and progression of this disease. A novel computational method has been developed and validated that can identify a subset of high-risk mutations associated with decreased patient survival and increased development of distant metastases. Preliminary data suggests this oncogenic phenotype of high risk p53 mutations may be due in part to mutant-specific promoter binding sites that are significantly enriched with *FOXH1* motif leading to a large number of uniquely bound genes that are distinct from wild type p53 target genes. *FOXH1*, is a forkhead protein coding gene that is part of a transcriptionally active complex containing FOXH1/SMAD2/SMAD4. Interactions with the SMAD family of genes and mutant p53 have been implicated to contribute to the gain of function phenotype by forming a

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complex that increases TGF-beta induced metastases. Based on this, we hypothesize that mutant p53 with oncogenic properties activates cellular pathways and genes that are distinct from wild type p53. More specifically, high risk mutant p53 can modulate the *TGFB1* pathway and therefore up-regulate a mesenchymal gene signature which will lead to an increased rate of metastases. The studies proposed are designed to further examine *TGFB1* pathway regulation by mutant p53 and to extend these findings by identifying additional novel pathways targeted by mutant p53 leading to HNSCC.

Improving the Timeliness and Equity of Adjuvant Therapy Following Surgery for Head and Neck Cancer

Investigators: Evan M. Graboyes, M.D., Katherine R. Sterba, Ph.D., M.P.H, Elizabeth Hill, Ph.D., Terry Day, M.D., Graham Warren, M.D., Ph.D., Chanita Hughes Halbert, Ph.D.
Department of Otolaryngology-Head and Neck Surgery, Department of Public Health Sciences, Department of Psychiatry and Behavioral Sciences, Department of Radiation Oncology

Our multi-disciplinary research team is focused on understanding and addressing the determinants of treatment delays for patients with head and neck cancer (HNC) undergoing sequential multimodal therapy. The objectives of this project are to test the preliminary clinical impact and underlying behavioral mechanism of action of NDURE (Navigation for Disparities and Untimely Radiation thErapy), a novel theory-based navigation intervention developed to decrease delays and racial disparities in starting guideline-adherent postoperative radiation therapy (PORT) among patients with head and neck cancer (HNC). In this pilot randomized clinical trial (RCT), HNC patients will be randomized to NDURE or usual care. This project will have a significant clinical impact through the development of a scalable and practical intervention to decrease delays and racial disparities in starting PORT, thereby improving survival for HNC patients and decreasing racial disparities in mortality. Ongoing projects suitable for a three-month research project include assisting with the conduct and analysis of this ongoing RCT, preparation for future multi-site implementation studies, as well as additional projects related to geocoding, nomogram development, and conceptual model development.

Novel Treatment Strategies for Body Image Disturbance in Head and Neck Cancer Survivors

Investigators: Evan M. Graboyes, M.D., Katherine R. Sterba, Ph.D., M.P.H., Stacey Maurer, Ph.D., Brett Froeliger, Ph.D., Kenneth Ruggiero, Ph.D.
Department of Otolaryngology-Head and Neck Surgery, Department of Public Health Sciences, Department of Psychiatry and Behavioral Sciences, and Department of Neurosciences

Our multi-disciplinary research team focuses on developing new preventative and therapeutic interventions for head and neck cancer (HNC) survivors with body image disturbance (BID). The objectives of this project are to test the preliminary clinical impact and underlying behavioral mechanism of action of BRIG**H**T (Building a Renewed ImaGe after Head & neck cancer Treatment), a novel, manualized tablet-based tele-cognitive behavioral therapy (CBT) intervention to treat BID in HNC survivors. In this pilot RCT, HNC survivors with BID will be randomized to BRIG**H**T or active control. Ongoing projects suitable for a three-month research project include assisting with the conduct and analysis of this RCT, preparation for future multi-

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site implementation assessment, as well as projects related to scale development, telemedicine-based psychosupportive interventions, and the development of novel preventative interventions targeted to high-risk patients.

Association of Connectivity Dysregulation with Image Disturbance in Head and Neck Cancer Survivors

Investigators: Evan M. Graboyes, M.D., Yeonhee Park, Ph.D., Katherine R. Sterba, Ph.D., M.P.H., Brett Froeliger, Ph.D.

Department of Otolaryngology-Head and Neck Surgery, Department of Public Health Sciences, Department of Psychiatry and Behavioral Sciences, Department of Neurosciences

Our research team studies the underlying mechanisms and drivers of body image disturbance (BID) in head and neck cancer (HNC) survivors. The objectives of this project are to evaluate the neurobiological and cognitive mechanisms underlying BID in HNC survivors using resting state (rsFC) functional MRI (fMRI). In this cross-sectional study of disfigured HNC survivors, we will measure disfigurement and BID using validated tools and evaluate their association with 1) rsFC aberrations on fMRI, and 2) cognitive moderators of image disturbance on validated measures. Ongoing projects suitable for a three-month research project include assisting with the accrual and analysis of fMRI data and preparation for larger investigations into the neurobiological and cognitive mechanisms underlying BID in HNC survivors.

Molecular Mechanisms Underlying Racial Disparities in Head and Neck Squamous Cell Carcinoma

Investigators: Evan M. Graboyes, M.D., John Pearce, Ph.D., Cynthia Timmers, Ph.D., Marvella Ford, Ph.D.

Department of Otolaryngology-Head and Neck Surgery, Department of Public Health Sciences

We propose a collaborative partnership among members of a transdisciplinary team to determine whether race-associated polymorphisms in genes implicated in head and neck squamous cell carcinoma (HNSCC) initiation, growth and progression underlie the observed racial disparities in health outcomes for African Americans with HNSCC. The study is directed toward the long-term highly translational research goal of testing whether polymorphisms in genes involved in HNSCC tumor growth and progression, and potentially associated with prognostic features, contribute to the profound and persistent racial disparities in HNSCC incidence and mortality.

Relationship of Patient Priorities to Function and Health-Related Quality of Life (HRQOL) in Head and Neck Cancer

Investigators: Evan M. Graboyes, M.D., Katherine R. Sterba, Ph.D., M.P.H, Elizabeth Hill, Ph.D., Terry Day, M.D.

Department of Otolaryngology-Head and Neck Surgery, Department of Public Health Sciences, Hollings Cancer Center, Cancer Control Program

Because HNSCC occurs in critical areas for cosmesis and function, treatment results in significant morbidity related to disfigurement, swallowing and speaking, and often forces

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patients to prioritize certain functional outcomes over others. Thus, knowing how patients prioritize amongst different functional outcomes is critical to patient-centered care. Systematic use of patient-reported outcomes (PROs) in cancer care is associated with improved outcomes (including survival). Knowledge gaps in PROs for HNSCC exist related to the temporal stability of patient priorities and the relationship of priorities to function over time. These knowledge gaps prevent optimal patient-centric care that matches patient needs over time. The overall objective of this preliminary study is to examine how patient priorities relate to PRO measures of function and HRQOL over time. This will be accomplished in the following two ways: 1) characterize how patient functional priorities change over time and 2) use PRO measures to examine the relationship between patient functional priorities and patient function and HRQOL over time. These preliminary data will inform future work with the long-term goal of improving care by 1) facilitating pre-treatment counseling about prioritized outcomes, 2) guiding treatment decision-making to minimize morbidity in a patient-centric way, and 3) directing provision of patient-centered supportive care resources. We are conducting a prospective, single-center pilot study including 80 patients with HNSCC to examine the relationship between patient priorities and function/HRQOL over time. The overarching goal is to develop comprehensive patient-centered strategies to improve the quality of care for HNSCC patients.

Health Services Research in Head and Neck Cancer

Investigator: Evan M. Graboyes, M.D.

Department of Otolaryngology-Head and Neck Surgery

Measures of quality are used at individual physician and hospital-wide levels to determine ratings, accreditation, and reimbursement. However, there remains disagreement about how to define and measure quality in a pragmatic and actionable manner, as well as how current metrics correlate with outcomes that reflect high quality care. To date, no nationally endorsed, validated quality measures exist for patients with HNC. Using a variety of research tools including administrative datasets (e.g., National Cancer Database, SEER-Medicare, Healthcare Cost and Utilization Project) and multi-institution collaborations, this study seeks to 1) identify determinants of patient-centered quality HNC care; (2) develop interventions to address these determinants; and (3) disseminate and implement evidence-based quality improvement strategies into practice. This research program will consist of multiple smaller projects that can be completed within three-month timeframes.

Free Flap Outcomes in Patients with Head and Neck Cancer

Investigators: Evan M. Graboyes, M.D., Judith Skoner, M.D., Terry A. Day, M.D., Eric J. Lentsch, M.D., David M. Neskey, M.D., M.S.C.R., Joshua D. Hornig, M.D.

Department of Otolaryngology-Head and Neck Surgery

The objectives of this study are to characterize short and long-term outcomes for patients with head and neck cancer undergoing microvascular reconstruction. This research utilizes a prospectively maintained institutional database to address questions related to risk-stratification and clinical and functional outcomes for this high-risk patient population that can be addressed during a three-month research project.

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Laryngology – Voice, Airway, and Swallowing

Evelyn Trammell Institute for Voice and Swallowing

The MUSC Evelyn Trammell Institute for Voice and Swallowing provides opportunities in the study of speech, language, voice and swallowing physiology in children and adults. State of the art acoustic, aerodynamic, and imaging methods are geared toward the measurement of functional treatment outcomes across the age spectrum.

Use of High Resolution Pharyngeal Manometry as Biofeedback for Muscle Tension Dysphagia

Investigators: Ashli O'Rourke, M.D., Angelina Schache, M.S., CCC-SLP

Department of Otolaryngology-Head and Neck Surgery, Evelyn Trammell Institute of Voice and Swallowing

In this study, high resolution pharyngeal manometry will be used to measure the pressures generated by the pharynx during swallowing and identify physiologic swallowing characteristics. We hypothesize that biofeedback relaxation techniques will help decrease pharyngeal contractility.

The Effect of Cricopharyngeal Obstruction on Pharyngeal Swallowing

Investigators: Ashli O'Rourke, M.D., Kate Davidson, M.S., CCC-SLP

This study evaluates the effect of increasing obstruction in the cricopharyngeal region or pharyngoesophageal segment (PES) on pharyngeal swallowing function. An external device designed to apply pressure to the anterior cricoid ring is used to produce different pressures in the PES as measured by pharyngeal high resolution manometry. Simultaneous manometry and flexible endoscopic evaluation of swallowing are used to evaluate pharyngeal changes in normal adult volunteers.

The Efficacy of Superior Laryngeal Nerve Block for Refractory Chronic Cough and Globus

Investigators: Ashli O'Rourke, M.D., Courtney Tipton, M.D.

Refractory idiopathic throat sensations can be particularly bothersome to patients. This retrospective (and eventually prospective) study seeks to evaluate the efficacy of decreasing superior laryngeal nerve sensation in alleviating symptoms in patients for whom all other testing has been negative.

Recurrent Respiratory Papillomatosis (RRP) Viral Typing and its Association with Malignant Degeneration

Investigators: Lucinda Halstead, M.D., Mary Richardson, M.D., D.D.S.

Department of Otolaryngology-Head and Neck Surgery, Evelyn Trammell Institute of Voice and Swallowing, Department of Pathology and Laboratory Medicine

The goal is to identify specific RRP viral strains, review past pathologies, and evaluate for previously unrecognized potential for malignant transformation.

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Surface EMG and Laryngeal Video Characterization of Belting and Classical Singing Styles

Investigator: Lucinda Halstead, M.D.

Department of Otolaryngology-Head and Neck Surgery, Evelyn Trammell Institute of Voice and Swallowing

This study utilizes video surface EMG synched with laryngeal video examination of belting and classically trained amateur and professional vocalists to determine the muscles needed to sustain healthy belting technique.

Quality of Life Rating of Patients with Various Vocal Conditions and the Correlation of their Impairment to Other Disease States

Investigator: Lucinda Halstead, M.D.

Department of Otolaryngology-Head and Neck Surgery, Evelyn Trammell Institute of Voice and Swallowing

This study is currently examining patients with chronic cough and spasmodic dysphonia, and expanding to other vocal conditions, including paralysis, papilloma, and laryngopharyngeal reflux (LPR).

Communication and Swallowing Laboratory

The mission of the Communication and Swallowing Laboratory in the MUSC College of Health Professions is to improve the diagnostic accuracy and treatment effectiveness in communication and swallowing problems. The laboratory works closely with the MUSC Evelyn Trammell Institute for Voice and Swallowing and utilizes the following equipment and techniques: laryngeal endoscopy with stroboscopy, high-speed videoendoscopy, magnetic resonance imaging, videofluoroscopy, acoustic analysis, and aerodynamic analysis to improve the diagnostic accuracy and treatment effectiveness of communication and swallowing disorders.

Dysphagia after Stroke

Investigators: Heather Bonilha, Ph.D., CCC-SLP, Bonnie Martin-Harris, Ph.D., CCC-SLP, BCS-S

Department of Health and Rehabilitation Research, College of Health Professions and Department of Otolaryngology-Head and Neck Surgery, Evelyn Trammel Institute of Voice and Swallowing

Dysphagia, a term used to denote difficulty in swallowing, affects up to 78% of all stroke survivors. Dysphagia not only restricts patients' quality of life, but also leads to serious post-stroke complications, such as pneumonia, malnutrition and dehydration. Some dysphagic stroke patients recover spontaneously, while others never recover even with therapy. Currently, it is largely unknown why some patients recover while others remain with debilitating deficits. The objective of our study is to gain a better understanding of the neurobiological mechanisms leading to dysphagia recovery after stroke that could be directly translated into clinical practice. Our objective is to contribute to an explanatory neuroanatomical model of swallow disturbances and recovery after brain lesions. Our findings will translate to clinical practice by stratifying patients, improving counseling, informing therapists on treatment responders and guiding the development of new interventions, thus

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reducing costs and improving quality of life for patients with post-stroke dysphagia.

Dysphagia Post-anterior Cervical Discectomy and Fusion (ACDF)

Investigator: Heather Bonilha, Ph.D., CCC-SLP

Department of Health and Rehabilitation Research, College of Health Professions, Department of Otolaryngology-Head and Neck Surgery, Evelyn Trammel Institute of Voice and Swallowing

Dysphagia is defined as difficulty or discomfort swallowing. The occurrence of dysphagia post-cervical spine surgery is well known. There have been multiple prospective studies and numerous retrospective studies that have investigated dysphagia in patients after ACDF. Three prospective studies used an instrumental assessment of swallowing function. Patient-reported swallowing symptoms did not correlate with swallowing function on modified barium swallowing studies (silent aspiration). Detailed timing and kinematic measures revealed that decreased upper esophageal sphincter (UES) opening and delayed pharyngeal response time were the main physiologic impairments. This research seeks to determine the incidence of dysphagia pre- and post-ACDF in our clinical population and create optimal screening, diagnostic and treatment processes.

Impact of Pulse Rate on Swallowing Impairment and Radiation Exposure

Investigators: Heather Bonilha, Ph.D., CCC-SLP, Bonnie Martin-Harris, Ph.D., CCC-SLP, BCS-S, Maureen Lefton-Grief, Ph.D., CCC-SLP, Sameer Tipnis, Ph.D., Walter Huda, Ph.D., Paul Nietert, Ph.D.

Department of Health and Rehabilitation Research, College of Health Professions, Department of Otolaryngology-Head and Neck Surgery, Evelyn Trammel Institute of Voice and Swallowing, Department of Radiology, Department of Public Health Sciences

Modified Barium Swallow Studies (MBSS) are the key diagnostic test to identify abnormalities in the structures and functions of swallowing. However, MBSSs are a type of fluoroscopic study that uses ionizing radiation. Radiation exposure from medical tests are mandated to be as low as reasonable achievable. Pulse rate is a MBSS setting that is a main target for reducing radiation exposure. Unfortunately, decreasing pulse rate also decreases the information available from which to judge swallowing impairment. This research seeks to provide critical evidence needed to weigh the risk of erroneous judgments of swallowing impairment from reduced pulse rate against the benefits of decreasing radiation exposure. This evidence will serve as a guide for speech-language pathologists, radiologists, and hospital safety boards when evaluating MBSSs procedures and will inform patient care decisions.

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Hearing Research Program

Brain Imaging of the Aging Auditory System

Investigators: Mark A. Eckert, Ph.D., Kenneth I. Vaden, Jr., Ph.D., Jayne B. Ahlstrom, M.S., Judy R. Dubno, Ph.D.

Departments of Otolaryngology-Head and Neck Surgery, Pathology and Laboratory Medicine

We are using neuroimaging methods to examine age-related changes in the function and structure of the aging auditory system and attention systems that support hearing and communication. Ongoing projects include examinations of: 1) how different types of hearing loss occur with patterns of brain function and structure changes; and 2) speech recognition benefit from the engagement of attention systems. This research experience will provide training opportunities in the areas of experimental design, neuroimaging data acquisition and analysis, manuscript preparation, and an opportunity to develop expertise in the areas of communication and hearing loss as they relate to the brain.

Brain Systems for Decision Making and Cortical Speech Representation

Investigators: Kenneth I. Vaden, Jr., Ph.D., Jayne B. Ahlstrom, M.S., Judy R. Dubno, Ph.D., Mark A. Eckert, Ph.D.

Department of Otolaryngology-Head and Neck Surgery

Older adults demonstrate poorer auditory perception and speech recognition in noise, although changes in response caution can influence auditory task performance. This research uses functional neuroimaging measures to investigate how speech recognition in noise is affected by decision-making processes for middle-aged and older adults. We are also interested in examining how age-related structural declines relate to auditory perceptual variation later in life.

Behavioral and Electrophysiologic Studies of Human Auditory Function

Investigators: Judy R. Dubno, Ph.D., Kelly C. Harris, Ph.D., Mark A. Eckert, Ph.D., Kenneth I. Vaden, Jr., Ph.D., Jayne B. Ahlstrom, M.S.

Department of Otolaryngology-Head and Neck Surgery

Studies of the human auditory system include the ability to use frequency and temporal information in simple sounds and in speech, and how these abilities change in adverse listening conditions, with age, and with hearing loss. Behavioral measures include detection thresholds, the ability to detect small changes in frequency, intensity, or duration, and the ability to understand speech in realistic environments. Studies with hearing aids assess improved speech recognition in realistic environments for older adults and benefits of speech-perception training. Electrophysiologic studies include the use cortical potentials to assess age-related changes in temporal processing.

Neurobiology of Speech Recognition Impairments in Older Adults

Investigators: Mark A. Eckert, Ph.D., Kenneth I. Vaden, Jr., Ph.D., Jayne B. Ahlstrom, M.S., Judy R. Dubno, Ph.D.

Department of Otolaryngology-Head and Neck Surgery

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Older adults experience impaired speech recognition, particularly in challenging listening conditions. These impairments persist even when accounting for speech audibility and are thought to be due to declines in the central auditory system, as well as declines in attentional and intentional neural systems that support task performance and perception. We use neuroimaging methods to characterize brain structure and function to explain speech recognition impairments in older adults. This research includes the study of how cueing can help listeners prepare for and improve speech recognition in challenging listening conditions when there declines in the auditory system and the degree to which benefit from cueing might be limited by declines in attention and intention networks.

Cochlear Pathophysiology

Investigators: Kelly C. Harris, Ph.D., Richard A. Schmiedt, Ph.D., Judy R. Dubno, Ph.D.
Department of Otolaryngology- Head and Neck Surgery

Age-related hearing loss in humans is complex because many factors in addition to aging can produce hearing loss in older persons, such as the accumulated effects of a lifetime of exposure to noise, ototoxic drugs, or otologic disease. Thus, targeted treatments for age-related hearing loss must address the multiple sources of pathology and their complex impact on communication. Experiments employ physiologic measures of cochlear and auditory nerve function to characterize primary sites of pathology in the cochlea and auditory nerve. The impact of these changes in cochlear function on speech recognition and auditory processing are then assessed. Results from these experiments are expected to help move clinical assessment beyond the audiogram to identify the underlying pathophysiology associated with age-related hearing loss, important in the development of targeted therapeutic treatments.

Auditory System Plasticity

Investigators: Kelly C. Harris, Ph.D., Judy R. Dubno, Ph.D.
Department of Otolaryngology-Head and Neck Surgery

Cortical plasticity is a fundamental property of the brain and is the primary means by which the adult brain adapts to changing environments and enables new behavior. Aging is thought to reduce neural plasticity in the cortex, restricting the aging brain's response to change and adaptation. Neural presbycusis, or an age-related loss or inactivity of auditory nerve fibers, may compound these effects by reducing input to the higher auditory centers, including the cortex. We use neuroimaging methods, including electrophysiology, structural MRI, and magnetic resonance spectroscopy, to examine how the aging auditory cortex reacts to a gradual loss of input from the periphery in combination with wide-spread cortical changes. Ongoing studies examine how differences in neural plasticity relate to experience and hearing handicap, and affect auditory processing.

Human Otopathology Research on Age-Related Hearing Loss

Investigators: Judy R. Dubno, Ph.D.; Hainan Lang, M.D., Ph.D.; Paul R. Lambert, M.D., Ted A. Meyer, M.D., Ph.D., Mark A. Eckert, Ph.D., Bradley A. Schulte, Ph.D.
Departments of Otolaryngology-Head and Neck Surgery, Pathology and Laboratory Medicine

Significant progress has been made in understanding auditory and vestibular disorders using

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animal models. However, little is known about the specific physiologic, genetic, molecular, and cellular defects responsible for these disorders in humans, which is essential for advancing diagnosis and treatment. With the living human inner ear and auditory nerve inaccessible for examination, comparisons of structure and function of normal and pathological conditions depend on data obtained from examinations of human temporal bones from donors with well-characterized clinical histories and functional assessments. Temporal bones are collected at autopsy from patients in the MUSC Hospital System, especially those over 60 years of age, and from patients with auditory disorders identified by otolaryngologists in our department and from our longitudinal study of age-related hearing loss. The next phase of this project focuses on processing of existing and newly acquired human temporal bones to define the cellular and molecular changes in sensory hair cells and cells in the cochlear lateral wall and auditory nerve. These experiments will lead to further investigations of the molecular mechanisms in sensorineural hearing loss, including various subtypes of presbycusis (age-related hearing loss).

Audiologic and Genetic Studies of Age-related Hearing Loss

Investigators: Judy R. Dubno, Ph.D., Bradley A. Schulte, Ph.D., Mark A. Eckert, Ph.D., Lois J. Matthews, M.S.

Departments of Otolaryngology-Head and Neck Surgery, Pathology and Laboratory Medicine

Audiologic and biologic results from an ongoing study of older human subjects include cross-sectional data from ~1,500 subjects and longitudinal data from ~600 subjects. This database on age-related hearing loss contains audiologic data such as hearing levels, multi-frequency tympanometry, speech recognition in quiet and in noise, otoacoustic emissions, auditory brainstem responses, hearing handicap, and hearing-aid use and success. Biologic/medical data include clinical blood chemistries, medical and medication history, and family pedigree. Blood serum and DNA samples have been collected from more than 500 subjects. Studies include correlational analyses of hearing loss and other variables, longitudinal changes in auditory function, genotype-phenotype association studies, and identification of single nucleotide polymorphisms (SNPs) that are associated with specific age-related hearing loss phenotypes.

Morphology of the Dyslexic Brain

Investigators: Mark A. Eckert, Ph.D., Mulugeta Gebregziabher, Ph.D., Kenneth Vaden, Jr., Ph.D.
Departments of Otolaryngology-Head and Neck Surgery and Public Health Sciences

We are developing methods for multi-site studies on complex disorders using dyslexia as a model. Neuroimaging, behavioral, and demographic data have been collected for over 2000 cases from 21 international studies on reading disability. We have research opportunities to examine neuroanatomical predictors of reading disabilities. Projects can focus on neuroanatomical characterization, statistical analysis of retrospective data, and data sharing.

Neurobiology of Dyslexia

Investigators: Mark A. Eckert, Ph.D., Kenneth Vaden, Jr., Ph.D.
Department of Otolaryngology-Head and Neck Surgery

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Dyslexia is a common learning disability that has significant educational, social, and economic impacts but we have limited neurobiologic understanding for this complex disorder. A longstanding hypothesis suggests that people with dyslexia have atypical structural cerebral asymmetries. Ongoing research tests this hypothesis in a large multi-site sample and the degree to which genetic markers for dyslexia are observed in people with atypical cerebral asymmetries.

Expected Value in Hearing Aid Decision-Making

Investigators: Mark A. Eckert, Ph.D., Lois Matthews, M.S.; Judy R. Dubno, Ph.D.

Understanding when and why patients make hearing health care decisions can be critical for understanding when and how to provide the best clinical care. The varied subjective experiences and reasons patients have for their hearing health care choices can be difficult to measure. Behavioral economic measures provide objective and quantitative approaches for assessing the expected value that patients may have about their hearing health care. This project examines the contribution of effort and delay discounting measures for predicting if hearing aid candidates own hearing aids and how often hearing aid users wear their hearing aids. The results are expected to provide clinicians with a tool to understand the motivations of their patients and likely outcomes.

Cellular and Molecular Mechanisms of Sensorineural Hearing Loss

Investigators: Hainan Lang, M.D., Ph.D., Bradley A. Schulte, Ph.D., Judy R. Dubno, Ph.D.
Department of Pathology and Laboratory Medicine, Department of Otolaryngology-Head and Neck Surgery

Genetically modified mouse models and human inner ear tissues have been used for understanding the cellular and molecular mechanisms of auditory nerve survival and degeneration in several pathologies, including aging, exposure to noise and ototoxic drugs and genetic defects. We focus on the functional roles of neural crest cell associated transcription factors, RNA binding proteins, complement system, and their related regulatory networks for enhancing remyelination, preventing or protecting the auditory nerve from degeneration and promoting auditory nerve survival and functional recovery after cochlear injury. This translational research program provides an outstanding training opportunity for (1) collection and preparation of mouse and human temporal bone tissues; (2) contemporary histopathological and high-resolution imaging techniques to assay human and animal inner ear specimens; (3) cutting-edge cellular and molecular procedures such as molecular imaging of living cochlear cells, 3D cell culture assay, RT-qPCR, NanoString and RNA-seq analysis of the degenerative auditory nerve; and 4) evaluation of auditory nerve function using electrophysiological techniques including auditory nerve compound action potentials, spontaneous activities of single auditory nerve fibers, and auditory brainstem responses.

Adult Stem/Progenitor Cell and Auditory Nerve Regeneration and Repair

Investigators: Hainan Lang, M.D., Ph.D., Jeremy L. Barth, Ph.D.
Departments of Pathology and Laboratory Medicine, Regenerative Medicine and Cell Biology

Our recent research on isolation and characterization of adult neural stem/progenitor cells

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from adult mouse auditory nerve is aimed at replacing damaged spiral ganglion neurons (SGNs), preventing SGN degeneration and promoting auditory functional recovery. Several lines of studies are ongoing with a focus on remyelination and de-differentiation of adult glial cells after acute auditory nerve injury resulting from noise-exposure or ototoxic drug-exposure. A variety of advanced methods are employed to 1) isolate and expand neural stem/progenitor cells using neurosphere culture assay and auditory nerve micro-dissection; 2) purify and characterize neural stem/progenitor cells using transgenic mouse models and fluorescence-activated cell sorting; 3) identify the molecular characteristics of neural stem/progenitor cells using next generation sequencing, gene expression profiling at the single cell level (e.g., single cell RNA-seq), complementary proteomics assays and super resolution imaging analysis; and 4) direct evaluation of functional integration of the transplanted stem cells using microsurgery and well-established mouse models of auditory nerve degeneration.

Otology and Neurotology Research – Cochlear Implant Center

Surgeon Competency During Mastoid Surgery

Investigator: Ted A. Meyer, M.D., Ph.D.

Department of Otolaryngology-Head and Neck Surgery

Teaching surgery to residents and determining competency in the operating room is challenging. We are measuring surgeon movements during otological surgery, and analyzing the results with tracking software, surveys, and newly developing technology. Numerous opportunities exist to evaluate questions related to training, performance, and competency.

Childhood Hearing Loss Database Research

Investigator: Ted A. Meyer, M.D., Ph.D.

Department of Otolaryngology-Head and Neck Surgery

Over the past few years, we have analyzed a Pediatric Audiology-Otolaryngology-Genetics database called Audgen. As of September 2019, MUSC is the only center in the country using this database to answer questions about hearing loss in children. We have published 10 papers and have numerous ongoing projects.

Obesity and Skullbase Measurements

Investigator: Ted A. Meyer, M.D., Ph.D.

Department of Otolaryngology-Head and Neck Surgery

At MUSC, we have seen a tremendous increase in the number of patients presenting with CSF otorrhea and encephaloceles of the temporal bone. Several algorithms have been developed to measure the thickness and density of the skullbase. We continue to refine our methodology, and numerous projects involving this methodology remain. In addition, with the obesity epidemic, we have noticed changes to our clinical practice. We have evaluated effects of obesity on skullbase and other otological surgeries on thickness in terms of outcomes in patients undergoing repair of CSF leaks, length of time for cochlear implant surgery, and even generalized outcomes in ear surgery. Numerous opportunities exist to further our knowledge in these areas.

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Factors that Influence Quality of Life in Adult Cochlear Implant Users

Investigator: Ted R. McRackan, M.D., M.S.C.R., Judy R. Dubno, Ph.D.

Department of Otolaryngology-Head and Neck Surgery

The manner in which cochlear implant (CI) outcomes have been measured has not fundamentally changed in the past 30 years. The development of new cochlear implant quality of life (CIQOL) instruments provide the opportunity to perform a more comprehensive assessment of the impact of cochlear implantation beyond changes in speech recognition ability. This project focuses identifying novel factors that influence domain-specific changes in QOL after cochlear implantation

Clinical Research in Vestibular Disorders

Investigator: Habib Rizk, M.D.

Department of Otolaryngology-Head and Neck Surgery

Vertigo and dizziness are very common complaints across all demographic groups and are responsible for frequent ER visits, absenteeism, and increased health care spending. In the aging population, they are associated with an increased risk of falls. These disorders typically require a multidisciplinary team of otolaryngologists, neurologists, physical therapists, and audiologists. Our clinical research projects include: (1) defining the cognitive impact of various vestibular disorders and comparing these to other chronic disorders; (2) defining new quality-of-life metrics that are symptom specific and disease specific and address all domains of disability, including the cognitive disability; (3) analyzing the effect of pharmacologic and non-pharmacologic interventions on quality of life in patients with vestibular migraines; (4) defining electrophysiologic and vestibular function test characteristics in patients with vestibular migraines; (5) reviewing the role of physical therapy in the treatment of episodic vestibular disorders; (6) identifying physical and mechanical limitations associated with chronic rocking dizziness to establish functional outcome measures; (7) identifying patient factors affecting quality of life improvement in vestibular migraines and Meniere's disease; and (8) validating the English version of the Neuropsychological Vertigo Inventory, a disease specific cognitive self-assessment tool.