Rhinology Division/Sinus Center

Olfactory loss has dramatic impacts upon quality of life. Main causes include aging and chronic rhinosinusitis (CRS). Because of the differences in the pathophysiology of olfactory loss we are investigating a variety of mechanisms and treatments. 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 olfactory loss, imaging of patients with various causes of olfactory loss and numerous clinical trials to assess novel therapeutics and instruments. Laboratory techniques available are automated CT/MRI image analysis, cell sorting, ELISA, immunohistochemistry, flow cytometric analysis, and PCR. In addition, we are actively investigating clinical outcomes for medical and surgical treatments of OD due to viral and CRS causes. 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. Department of Otolaryngology-Head and Neck Surgery

Olfactory-specific Outcomes in CRS

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

Olfactory dysfunction in aging adults

Investigators: Rodney Schlosser, M.D., Zachary Soler, M.D., Judy R. Dubno, Ph.D., Mark Eckert, Ph.D.

Department of Otolaryngology-Head and Neck Surgery

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

Outcomes in Pediatric Otolaryngology

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

Outcomes in Pediatric Mandibular Distraction Osteogenesis

Investigators: William Carroll, M.D., Phayvanh Pecha, M.D. Department of Otolaryngology-Head and Neck Surgery Opportunities are available in retrospective clinical research in the area of pediatric mandibular distraction osteogenesis.

Pre-operative echocardiography in pediatric OSA

Investigators: William Carroll, M.D., Phayvanh Pecha, M.D. Department of Otolaryngology-Head and Neck Surgery Opportunities are available in retrospective clinical research in the area above.

Head and Neck Oncology

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 (<u>N</u>avigation for <u>D</u>isparities and <u>U</u>ntimely <u>R</u>adiation th<u>E</u>rapy), 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 BRIGHT (<u>B</u>uilding a <u>R</u>enewed <u>ImaG</u>e after <u>H</u>ead & neck cancer <u>T</u>reatment), 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 BRIGHT 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 multisite implementation assessment, projects related to identifying the determinants and contextual factors affecting the implementation of mental health interventions for patients with cancer, 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 BID in HNC survivors.

Cancer Care Delivery 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.

<u>Laryngology – Voice, Airway, and Swallowing</u> <u>Evelyn Trammell Institute for Voice and Swallowing</u>

The MUSC Evelyn Trammell Institute for Voice and Swallowing provides opportunities in the study of voice, swallowing and airway disorders. Ongoing clinical research projects are available for participation. Please contact Dr. Ashli O'Rourke or Dr. Lucinda Halstead if you are interested.

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.

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).

Hearing Research Program

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. 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.

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 presbyacusis, 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. Department of Otolaryngology-Head and Neck Surgery Department of Pathology and Laboratory Medicine

Significant progress has been made in understanding auditory and vestibular disorders using 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 wellcharacterized clinical histories and functional assessments. Our program has a large archive of human temporal bones collected from donors of all ages and has developed unique tissue processing procedures for cellular and molecular studies of human cochlear hair cells, stria vascularis, and spiral ganglion neurons. Training will be provided in the following specialized techniques: whole mount preparations and sectioning using human cochlear tissue, quantitative immunohistochemical analysis, 3D confocal imaging, and other cellular and molecular assays. Enhancing knowledge of human temporal bone anatomy and temporal bone drilling and dissection skills is another benefit.

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.

Department of Otolaryngology-Head and Neck Surgery Department of Pathology and Laboratory Medicine

Audiologic and biologic results from an ongoing study of older human subjects include crosssectional 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.

Cellular and Molecular Mechanisms of Sensorineural Hearing Loss

Investigators: Hainan Lang, M.D., Ph.D., Kelly Harris, Ph.D., Jeremy L. Barth, 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 Department of Regenerative Medicine and Cell Biology

Genetically modified mouse models and human inner ear tissues have been used for

understanding the cellular and molecular mechanisms of cochlear cell survival and degeneration in several pathologies, including aging, exposure to noise and ototoxic drugs, and genetic defects. We focus on the functional roles of cochlear immune response and neural crest cell-associated transcription factors, RNA binding proteins, complement system, and their related regulatory networks for enhancing regeneration/repair of the non-sensory cells in the cochlear lateral, preventing or protecting the auditory nerve from degeneration and promoting auditory functional recovery after cochlear injury, or aging. This translational research program provides an outstanding training opportunity for (1) mastering the basic knowledge related to inner ear biology, auditory physiology, otopathology, and cellular and molecular of deafness; and (2) the classic techniques of hearing research including collection and preparation of mouse and human temporal bone tissues, contemporary histopathological and high-resolution imaging techniques, molecular procedures such as molecular imaging of living cochlear cells, 3D cell culture assay, RT-qPCR, and NanoString assay, together with auditory physiological measures with in vivo mouse models. In addition, our ongoing experiments have developed several cutting-edge technologies to investigate how dysregulation of the cochlear immune cell contributes to the disruption of the cochlear lateral wall and auditory nerve declines, resulting in age-related hearing loss. These new technologies include functional proteomics, single-cell multi-omics, and in situ RNA sequencing.

Cochlear Cell Regeneration/Repair and Hearing Restoration

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

Our research on isolation and characterization of adult neural stem/progenitor cells from adult mouse auditory nerve is aimed at replacing damaged spiral ganglion neurons, preventing auditory nerve degeneration, and promoting hearing 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, 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.

Peripheral auditory system deficits and autism-like behaviors

Investigators: Hainan Lang, M.D., Ph.D., Kelly Harris, Ph.D., Judy R. Dubno, Ph.D., Christopher Cowan, Ph.D.

Department of Pathology and Laboratory Medicine

Department of Otolaryngology-Head and Neck Surgery

Department of Neuroscience

This is an exciting and newly developed project, which addresses a novel hypothesis that

abnormal macrophage-related activities, resulting from gene deficiency, leads to hearing loss and that these changes may be associated with communication impairment in Autism Spectrum Disorder (ASD) and other neurodevelopmental disorders. For example, mutations or deletions in the *MEF2C* gene have recently been linked to ASD. Our experiments revealed that Mef2c is highly expressed in cochlear macrophages in postnatal mice and that Mef2c hypofunction results in auditory nerve functional decline and hearing loss. This research provides training opportunities for animal models of ASD, neuroimmunology, evaluation of mouse communication and social interaction behavior, and central auditory processing and perception.

Neurobiology of Speech Recognition Impairments in Older Adults

Investigators: Mark A. Eckert, Ph.D., Kenneth I. Vaden, Jr., Ph.D., Carolyn McClaskey, Ph.D., Judy R. Dubno, Ph.D. Department of Otolaryngology-Head and Neck Surgery

Older adults experience speech recognition difficulties, particularly in challenging listening conditions. Ongoing brain imaging research is designed to test hypotheses that atypical structure and function in auditory and performance monitoring systems explain these speech recognition difficulties. Research and training opportunities are available involving structural and functional brain imaging.

Neurobiology of Dyslexia

Investigators: Mark A. Eckert, Ph.D., Kenneth Vaden, Jr., Ph.D., Zijun Wang, Ph.D. Department of Otolaryngology-Head and Neck Surgery Clemson University School of Computing

Dyslexia is a common learning disability that has significant educational, social, and economic impacts but we have limited understanding about the neural bases 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. Research and training opportunities involving structural imaging and novel data analysis approaches are available for this project, as well as for collaborative research with collaborators in the Clemson University School of Computing to establish deep learning classifiers for reading disability.

Brain Systems for Decision Making and Cortical Speech Representation

Investigators: Kenneth I. Vaden, Jr., Ph.D., 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.

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.

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 qualityof-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 nonpharmacologic 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 selfassessment tool.