NEWS FROM THE HARVARD MEDICAL SCHOOL
Department of Otolaryngology–Head and Neck Surgery

HARVARD Otolaryngology

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HIDDEN HEARING LOSS:
A 10-Year Journey

A decade after the discovery of cochlear synaptopathy, scientists uncover a new potential cause

(page 12)

HARVARD MEDICAL SCHOOL | Department of Otolaryngology Head and Neck Surgery

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News from the Harvard Medical School Department of Otolaryngology–Head and Neck Surgery

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Dear colleagues and friends,

This year marks my five-year anniversary as Chief of Otolaryngology–Head and Neck Surgery at Harvard Medical School. As I reflect on the past five years, I am grateful for the opportunities we have been given and for the progress we've seen.

Building upon our foundation in medical education, research, and clinical care, our faculty base and residency program have grown, new fellowship programs have been introduced, many high-level National Institutes of Health (NIH) grants have been awarded, new research endeavors have begun, and our affiliate hospitals have continued to be recognized by *U.S. News & World Report* as leaders. It's been a wonderful five years, and I am looking forward to what the next five will bring.

Also celebrating a milestone year is the discovery of cochlear synaptopathy. It's been 10 years since M. Charles Liberman, PhD, and Sharon G. Kujawa, PhD, of the Eaton-Peabody Laboratories at Massachusetts Eye and Ear/Harvard Medical School, described this phenomenon, which is commonly known as "hidden hearing loss." In our cover story starting on page 12, we discuss the progress that has been made in understanding this condition, including a recent study that reveals that conductive hearing loss may be a potential cause of cochlear synaptopathy.

In this issue, we also highlight an NIH P01 grant awarded to our head and neck team to explore immunotherapy as it relates to head and neck cancer, a new silk-based product for voice restoration, and a study questioning if tongue-tie surgery is always the best option for improving breastfeeding.

We're excited to share with you more about our research advances and current progress across the field. Thank you for your interest in and support of the department's activities.

Sincerely,

D. Bradley Welling, MD, PhD, FACS

Walter Augustus Lecompte Professor and Chair
Department of Otolaryngology–Head and Neck Surgery
Harvard Medical School

Chief of Otolaryngology–Head and Neck Surgery
Massachusetts Eye and Ear
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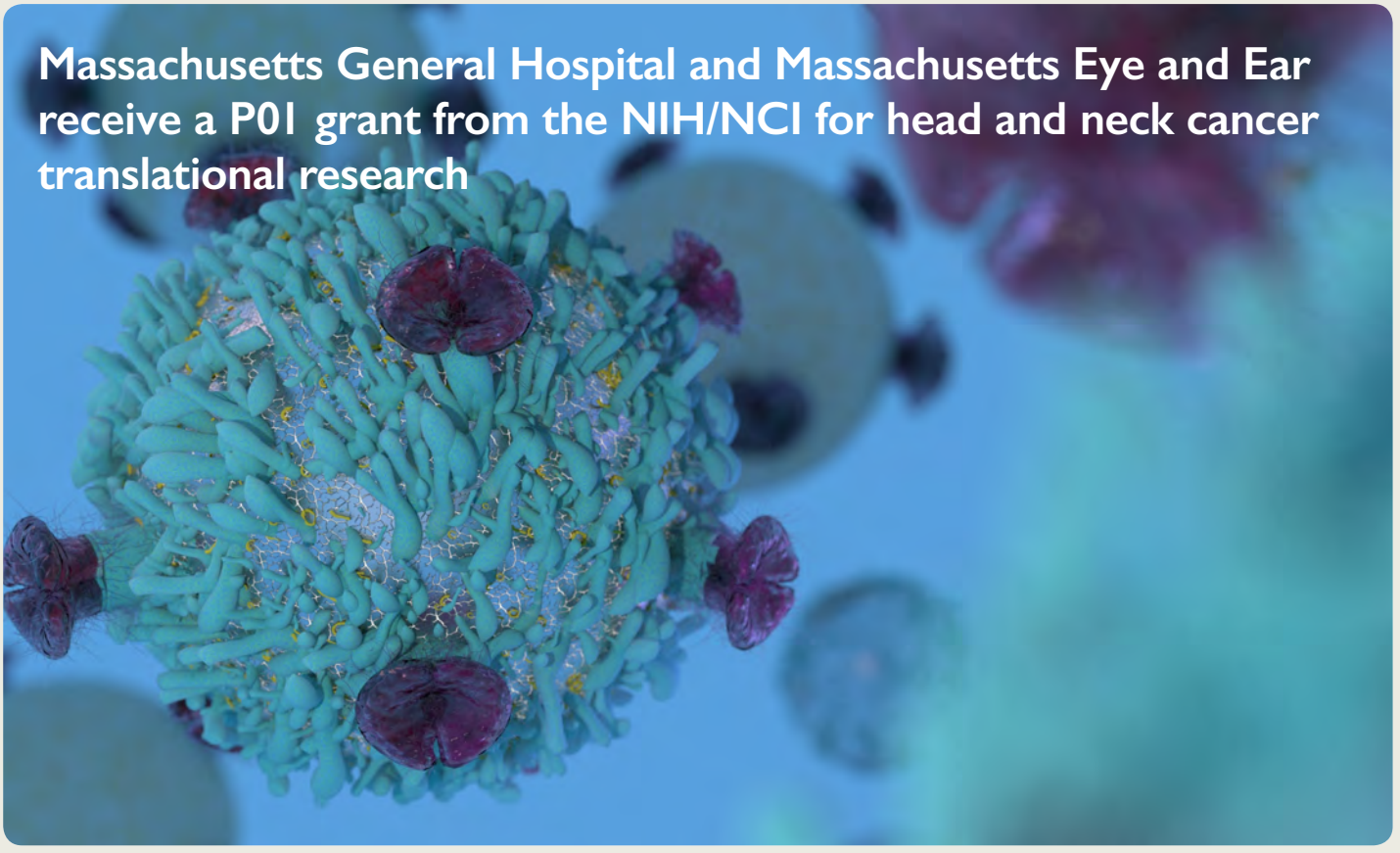
P01 Grant Awarded for Head and Neck Cancer



Massachusetts General Hospital and Massachusetts Eye and Ear receive a P01 grant from the NIH/NCI for head and neck cancer translational research

The head and neck cancer program at Massachusetts General Hospital and Massachusetts Eye and Ear has received its first Program Project (P01) grant from the National Institutes of Health (NIH) and National Cancer Institute (NCI). This $10.9M grant aims to better understand how cancer cells in the head and neck evade recognition by the immune system and, in turn, use that knowledge to develop novel therapies that reactivate an immune response against cancer cells.

Head and neck squamous cell carcinomas (HNSCCs) are a worldwide public health problem—they're the sixth most common malignancy in the world. The standard treatment is a combination of surgery, radiation, and/or chemotherapy. While these can be successful, current survival rates range anywhere from 30 to 70 percent. When primary therapies fail and disease recurs, HNSCC patients then have limited effective treatment options.

For decades, clinicians have sought ways to improve survival rates and have recently found promise in immunotherapy, a treatment that uses the body's natural defenses to fight off diseased cells.

"Your immune system is the first line of defense that protects you from harmful infections and the growth of abnormal cells," said Sara I. Pai, MD, PhD, FACS, Associate Professor of Surgical Oncology at Harvard Medical School and Director of Translational Research in Head and Neck Cancer at Mass General. "Immunotherapy harnesses the body's natural cells to eradicate cancer. It's one of the most personalized forms of cancer care available."

As a result of new immunotherapy drugs, the overall survival rate of HNSCC has recently been impacted for the first time in 50 years. On June 10, 2019, the U.S. Food and Drug Administration (FDA) approved immunotherapy as a first-line treatment for

recurrent and/or metastatic head and neck cancer based on the promising results of the phase III KEYNOTE-048 clinical trial.

"Immunotherapy is one of the biggest breakthroughs in head and neck cancer," said Derrick T. Lin, MD, FACS, Daniel Miller Associate Professor of Otolaryngology–Head and Neck Surgery at Harvard Medical School and Director of Head and Neck Surgical Oncology at Mass. Eye and Ear.

Although the approval of this treatment is an exciting step forward, just a small subset of HNSCC patients benefit from it at this time. Today's success rate with immunotherapy is only 15 to 20 percent because some patients develop resistance to the therapy while others have no response at all.

Bringing together a multidisciplinary team of experts, Paul M. Busse, MD, PhD, and Lori J. Wirth, MD, of Mass General, are leading a group alongside Dr. Lin and Dr. Pai with plans to tackle the two main barriers to achieving clinical response with immunotherapy: (1) the tumor's overall poor antigenicity, which limits the generation of antitumor immunity, and (2) innate and adaptive immune suppressive mechanisms that can lead to immune tolerance.

"By gaining further insight into both of these mechanisms of immune resistance, we have the potential to overcome them through the rational design of novel combinatorial strategies, which can ultimately increase the number of head and neck cancer patients who respond to immunotherapy," said Dr. Pai.

The team will address these barriers through three interrelated projects. The first project, led by Dr. Pai, will investigate epigenetically reprogramming head and neck cancers to improve their recognition by the immune system. The second project will focus on redirecting pre-existing viral-specific T cells to tumors through antibody-peptide epitope conjugate (APEC) molecules, co-led by Robert M. Anthony, PhD, and Thorsten R. Mempel, MD, PhD, of the Mass General Cancer Center.

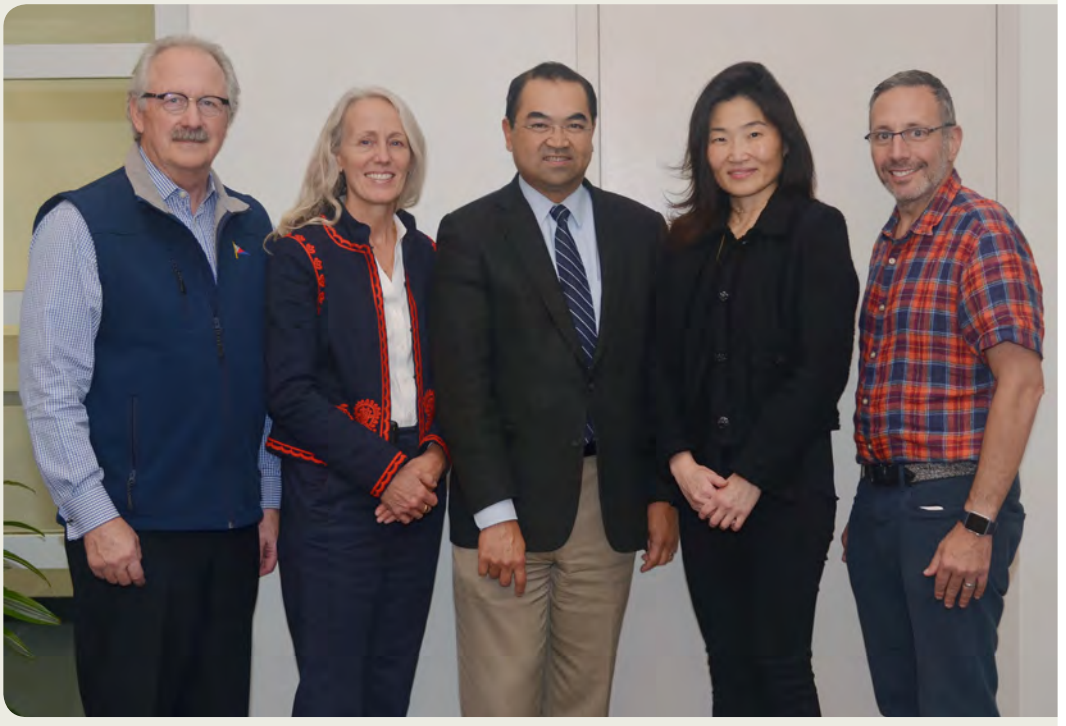
Lastly, a project led by Mikael J. Pittet, PhD, of the Mass General Center for Systems Biology, will define the relevant crosstalk needed between macrophages and T cells, which translates into improved clinical responses.

Two cores, led by Dr. Lin, Peter M. Sadow, MD, PhD, and William C. Faquin, MD, PhD, of Mass General, and Maureen A. Sartor, PhD, of the University of Michigan Medical School, will support these three projects.

These projects will leverage Mass General and Mass. Eye and Ear expertise in head and neck oncology, cancer immunology, genomics, epigenomics, and bioinformatics. This knowledge, in combination with the high patient volumes and innovative technology at both institutions, uniquely positions the team to find ways to better utilize immunotherapy in patients with head and neck cancer.

"We are so grateful for this opportunity," said Dr. Lin. "With our systematic approach, we strongly believe our team will be able to increase survival rates for head and neck cancer patients. Immunotherapy may only work for one in five HNSCC patients now, but we don't intend to stop until all patients derive benefit."

The generosity of patients, the Mike Toth Head and Neck Cancer Research Center at Mass. Eye and Ear, and other grateful donors helped support the infrastructure for the tissue collection and subsequent translational investigation and discovery that competitively positioned this group to apply for and secure such a prestigious grant.



From left to right: Drs. Paul Busse, Lori Wirth, Derrick Lin, Sara Pai, and Peter Sadow.

Saving Voices with SILK

A new FDA-approved silk-based product may offer hope for long-term voice restoration

Silk microparticles (red) serve as scaffolding for new collagen production (blue), providing the opportunity for long-lasting remediation.

The highly porous, sponge-like micro-particles are engineered for cellular integration, a process that is critical for long-term voice restoration and for mitigation of product migration tendency.

Engineered to reflect the unique biomechanics of vocal fold tissue, silk microparticles offer a novel approach to treating vocal cord insufficiency.

Artwork provided by Sofregen

Patients who suffer from vocal fold insufficiency, or incomplete closure of the vocal folds during speech, currently have limited long-term treatment solutions. The only permanent options available to them involve invasive procedures in the operating room.

Other treatment options include temporary injections into the vocal folds, usually performed in an outpatient setting. Often using materials such as carboxymethylcellulose, hyaluronic acid, or calcium hydroxylapatite, these injections are successful at restoring the voice, but in most cases, wear off in 18 months or less.

"Once the effect fades, patients must return to the doctor for more injections or opt for surgery," said Thomas L. Carroll, MD, Assistant Professor of Otolaryngology–Head and Neck Surgery at Harvard Medical School and Director of the Voice Program at Brigham and Women's Hospital. "For some patients, this is a reasonable option. However, for most, a permanent option that does not require a trip to the operating room is desired."

Clinicians and scientists are seeking a more permanent solution to treating vocal fold insufficiency, but most biologically relevant materials present two types of challenges. Typically, they either do not stay in the body long enough, or they cannot inherently promote tissue growth in or around the material—both key contributors to longer lasting effects.

Over the past decade, Dr. Carroll has collaborated with David L. Kaplan, PhD, of the Kaplan Laboratory at Tufts University School of Engineering, to test silk proteins, the constituents to the natural silk fibers used in textiles, as a possible material to restore lost volume in the vocal fold. Working with Dr. Kaplan's students, Dr. Carroll has helped explore the properties and potentials of silk as a vocal fold augmentation scaffold.

"Silk proteins incorporated into a novel vocal fold injection augmentation material may provide the longevity and tissue integration that can afford permanent voice restoration through an 'off-the-shelf' material."

—Dr. Carroll

Silk, which silkworms and spiders produce, is most commonly known for its use in clothing. In nature, it begins as a liquid before turning into a thread to make a protective cocoon. In this native form, the silk fibers demonstrate high tensile strength and ductility, permitting fibers to stretch without breaking. As a result, silk fibers have traditionally been used in medicine, most commonly as a suture material due to their natural toughness and biocompatibility.

Unlike other materials, silk can be manipulated to change with applied outside stimuli such as heat, electricity, or, in cases involving the voice, vibration. It makes it an attractive material for many applications for the voice. Because silk proteins create an optimal environment for the tissue support and regeneration required in patients with a loss of vocal fold tissue volume or movement, silk demonstrates promise.

"The medical field is typically looking for longevity in treatments that previously were temporary and did not offer a cure," said Dr. Carroll. "It's the same desire for those of us treating vocal fold insufficiency. Silk proteins incorporated into a novel vocal fold injection augmentation material may

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Dr. Thomas Carroll demonstrates what an injection will look like for a single surgeon operator.

provide the longevity and tissue integration that can afford permanent voice restoration through an 'off-the-shelf' material."

Introducing Silk Voice

Through his collaboration with Dr. Kaplan, Dr. Carroll was introduced to Sofregen Medical, Inc., a bio-engineering startup based in Medford, Massachusetts. This firm is focused on leveraging the regenerative properties of silk protein to restore tissue volume. Their goal is to reintroduce lost tissue volume in minimally invasive ways.

With similar goals in mind, Dr. Carroll, who is now on the Scientific Advisory Board of Sofregen, combined his efforts with them. Together they have developed Silk Voice, an injectable silk protein and hyaluronic acid mixture. Although this product has yet to be introduced to humans, the team found that Silk Voice remained without migration at the site of the injection in the vocal folds in a series of animal studies published in *The Laryngoscope*, which allowed local integration of regenerative cells and collagen within the silk matrix.[1]

To make Silk Voice, Sofregen takes traditional, medical grade silk and reverse engineers it into a liquid state. Once the thread is dissolved, it is turned into spherical, porous silk particles. These particles are then completely cleaned and purified to ensure they are not immunogenic. Finally, the particles are mixed with hyaluronic acid, a common substance used for vocal fold and cosmetic facial injections.

"We designed the silk particles to be porous and have optimal dimensions for cellular attachment," said Anh Hoang, PhD, Co-Founder and Chief Science Officer at Sofregen. "With other products, a significant portion of the solution moves away from the injection site. Our product doesn't do that, which allows for tissue volume to grow."

As a result of this investigational work, the U.S. Food and Drug Administration (FDA) cleared this product for augmenting vocal fold tissue to improve phonation in humans in January 2019. This marked the first—and currently only—FDA-approved product made from solubilized silk protein for medical use.

"Our team is extremely pleased to have achieved FDA clearance for our Silk Voice product. This milestone provides us with the opportunity to serve clinicians and their patients who seek novel and effective treatment for vocal fold insufficiency," said Jonathan Hartmann, Sofregen's incoming Chief Executive Officer.

The innovation team behind Silk Voice (from left to right): Drs. Thomas Carroll, Anh Hoang, Joseph Brown, and Christopher Gulka.

From bench to bedside

With FDA clearance, the product will soon be introduced to human patients through a multicenter clinical study. Although Dr. Carroll and the Sofregen team are not involved in the study design or execution to ensure data integrity, they are excited to see its results.

In collaboration with Sofregen, Dr. Carroll is also working on a novel delivery system for injecting Silk Voice into the vocal folds in the office setting. This now-patented device, which is shared between Dr. Carroll and Sofregen, is a new kind of catheter that allows a single surgeon to inject materials into a patient's vocal folds through the channel of a flexible scope passed through the nose and into the throat without the help of an assistant.

"Our hope is that this device provides an opportunity for laryngologists, as well as general otolaryngologists, to treat vocal fold insufficiency. The idea is that clinicians will be able to deliver this substance using flexible laryngoscopy skills, which could increase access to this procedure in both the outpatient and inpatient settings. This could ultimately restore voice function sooner and in more patients," said Dr. Carroll.

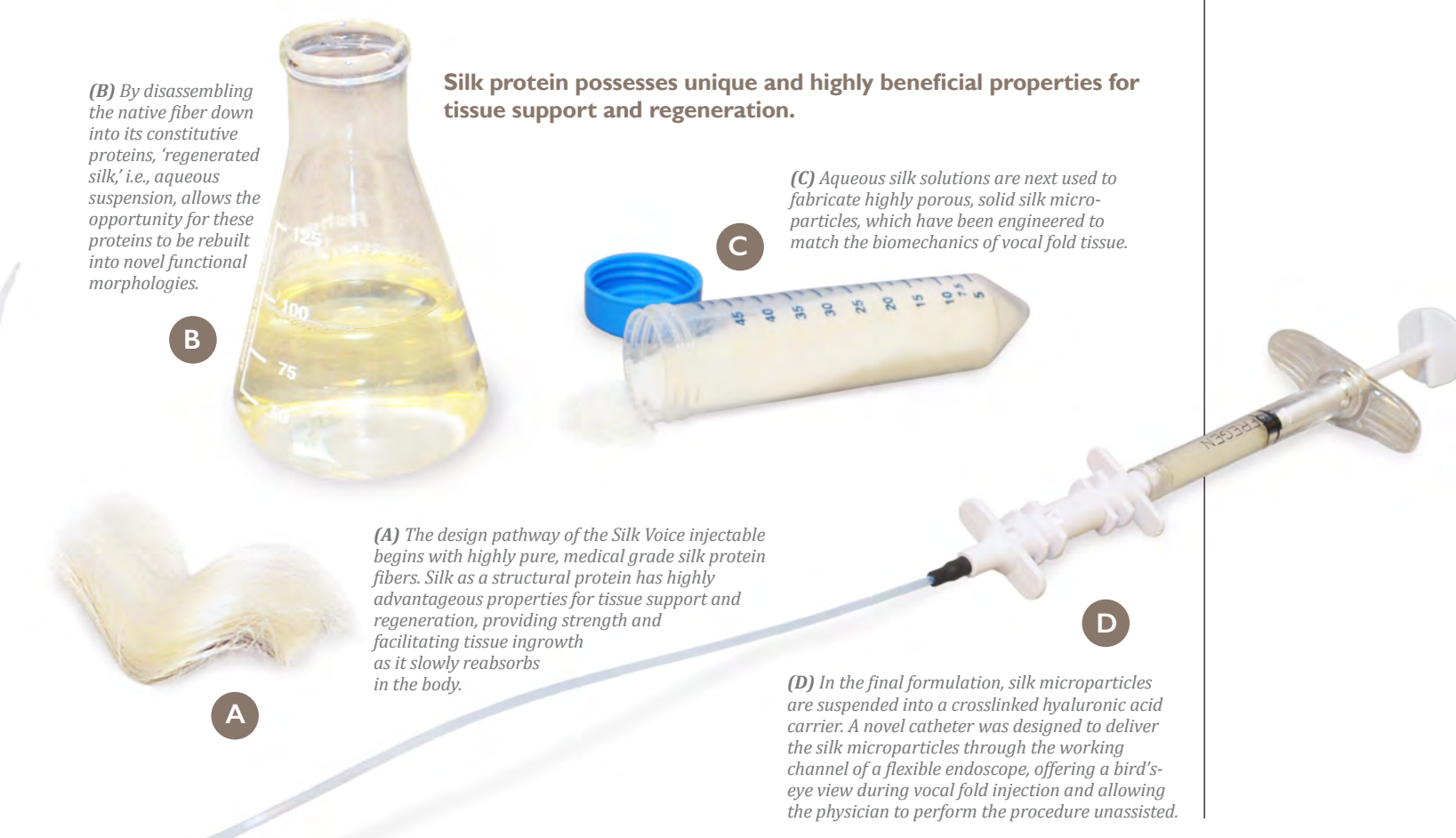
The combination of Silk Voice and its novel delivery system has the potential to make vocal cord injection augmentation more accessible. A procedure that currently requires a trained laryngologist and an assistant may soon be able to be performed by solo laryngologists and general otolaryngologists. In addition, the hope is that Silk Voice's tissue integration effect will lead to long-term volume recovery, providing patients with a functioning voice without the need for surgery.

"The idea of using silk for vocal fold augmentation stemmed from an academic basic science laboratory and is now being translated into the clinic where it can have an important impact on patients," said Dr. Carroll. "Silk Voice is a great example of science moving from 'bench to bedside.' We may have an opportunity to improve the access to treatment and overall care of patients with vocal fold insufficiency. I am hopeful when I consider future applications of silk in treating more complicated laryngeal conditions." ●

DISCLOSURE
Dr. Thomas Carroll shares a patent with Sofregen for the injection catheter, is a shareholder in Sofregen, and serves on Sofregen's Scientific Advisory Board.

[1]*Gulka CP, Brown JE, Giordano JEM, et al. A novel silk-based vocal fold augmentation material: 6-month evaluation in a canine model. Laryngoscope. 2019 Aug;129(8):1856-1862. doi:10.1002/lary.27618.*

Silk protein possesses unique and highly beneficial properties for tissue support and regeneration.



(A) *The design pathway of the Silk Voice injectable begins with highly pure, medical grade silk protein fibers. Silk as a structural protein has highly advantageous properties for tissue support and regeneration, providing strength and facilitating tissue ingrowth as it slowly reabsorbs in the body.*

(B) *By disassembling the native fiber down into its constitutive proteins, 'regenerated silk,' i.e., aqueous suspension, allows the opportunity for these proteins to be rebuilt into novel functional morphologies.*

(C) *Aqueous silk solutions are next used to fabricate highly porous, solid silk micro-particles, which have been engineered to match the biomechanics of vocal fold tissue.*

(D) *In the final formulation, silk microparticles are suspended into a crosslinked hyaluronic acid carrier. A novel catheter was designed to deliver the silk microparticles through the working channel of a flexible endoscope, offering a bird's-eye view during vocal fold injection and allowing the physician to perform the procedure unassisted.*

Is Tongue-Tie Surgery Always Necessary?

New research questions whether too many infants are receiving tongue-tie surgery to improve breastfeeding

Breastfeeding is developmentally important for newborns, but it doesn't come easy for all. Although it is recommended by several health organizations worldwide as the preferred infant feeding method, many mother-newborn dyads are having difficulty making breastfeeding successful due to latching trouble, limited weight gain, and mothers experiencing pain during the process.

Tongue-tie and/or lip tether might be one of the causes of such difficulties. Both are conditions present at birth that restrict the tongue's and lip's range of motion, which can affect how a child eats and swallows.

New parents often seek consultation if tongue-tie or lip tether are reported, as surgery to release tissue restriction is typically suggested. Known as a frenulectomy, this standard procedure removes the tissue bands that keep the tongue from moving freely or the lip from optimal position for latching. Many children have tissue that connects too tightly from the tongue to the floor of the mouth, while others have a tight tissue under the lip connected to their upper gum.

Some doctors recommend newborns receive corrective surgery right away. Others prefer to wait, as some cases of feeding issues resolve unrelated to the visible tongue-tie and/or lip tether. However, recent studies have shown an increase in the number of surgeries despite limited medical evidence supporting the procedure.

"We have seen the number of tongue-tie and upper lip tether release surgeries increase dramatically nationwide without a high level of evidence to show that these procedures are effective in the improvement of the breastfeeding process," says Christopher J. Hartnick, MD, MS, Director of Pediatric Otolaryngology at Massachusetts Eye and Ear and Professor of Otolaryngology–Head and Neck Surgery at Harvard Medical School.

Instituting a multidisciplinary approach

Despite a lack of medical literature linking surgery to improved breastfeeding, Dr. Hartnick notes that the U.S. Kids' Inpatient Database estimated a ten-fold increase in tongue-tie surgeries from 1,279 in 1997 to 12,406 in 2012.

Prompted by these rising rates and an influx of parents seeking second opinions, Dr. Hartnick and colleagues formed a multidisciplinary feeding evaluation program at Mass. Eye and Ear and Massachusetts General Hospital. It consists of clinicians from different medical specialties, including pediatric otolaryngology, pulmonology, gastroenterology, and speech-language pathology.

"We have seen the number of tongue-tie and upper lip tether release surgeries increase dramatically nationwide without a high level of evidence to show that these procedures are effective in the improvement of the breastfeeding process."

—Dr. Hartnick

A subset of this team recently performed a preliminary study to determine how many patients actually need tongue-tie surgery. This team, which included Dr. Hartnick, Christen L. Caloway, MD, Gillian R. Diercks, MD, MPH, Cheryl J. Hersh, MS, CCC-SLP, Rebecca Baars, MS, CCC-SLP, CLC, and Sarah Sally, MS, CCC-SLP, CLC, of the Mass. Eye and Ear Pediatric Airway, Voice, and Swallowing Center, examined 115 newborns who were referred in for tongue-tie surgery.

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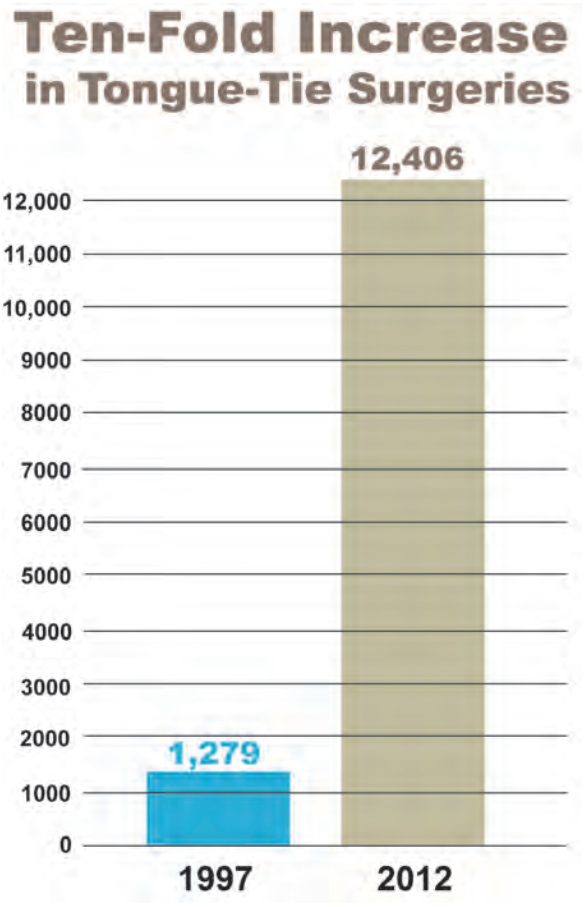


Because it can be difficult to predict which infants will benefit most from surgery, each mother-newborn pair met with a pediatric speech-language pathologist first. The speech-language pathologists performed comprehensive feeding evaluations that included clinical history, oral exam, and assessment of breastfeeding with each patient. They then offered real-time feedback and strategies to address the hypothesized cause of their breastfeeding challenges.

Published in *JAMA Otolaryngology–Head and Neck Surgery*, the study found that 63.5 percent of children who were referred in for surgery ended up not receiving it as determined by the comprehensive evaluation. Instead, parents chose not to select a surgical procedure to support successful breastfeeding of their newborns.

For the other 36.5 percent of patients, 10 (8.7 percent) underwent lip tie surgery alone and 32 (27.8 percent) underwent both lip and tongue-tie surgery, although all of the referrals were for tongue-tie surgery specifically.

"We've shown that the pathway of a multidisciplinary feeding evaluation is helping prevent babies from getting this procedure," said Dr. Hartnick. "A feeding evaluation program implemented on a wider scale may help identify

The Pediatric Airway, Voice, and Swallowing Center team from left to right: Jessica Sorbo, Sarah Sally, Dr. Stephen Hardy, Rebecca Baars, Dr. Christopher Hartnick, Dr. Shannon Fracchia, and Cheryl Hersh.

An example of an infant with tongue-tie.

the underlying cause of their breastfeeding difficulty and prevent infants from getting a surgery that might not be beneficial to improved breastfeeding."

A new way of thinking

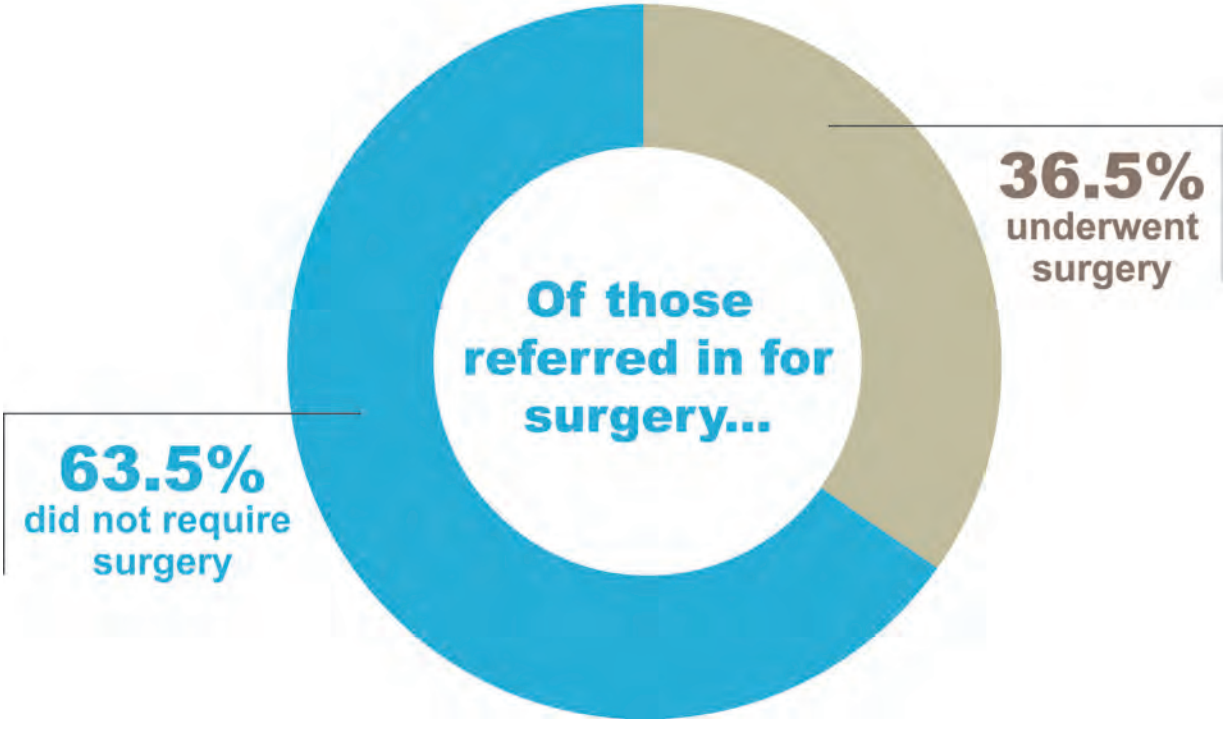
Standard tongue-tie and upper lip tether release surgeries are relatively safe outpatient procedures performed with local anesthetic, with risks, including pain and infection, being similar to any surgical procedure.

"Although the risks are low, many parents report experiencing guilt for not being able to provide the basic role of the parent in feeding their baby and worry about making the decision about having their newborn undergo surgery," said Dr. Hartnick. "There can also be significant out of pocket costs for the procedure that parents need to take into consideration."

Having the child undergo a feeding evaluation identifies strategies that can help with breastfeeding based on the baby's difficulties. If trialed for several days without improvement, parents can feel more confident in selecting the procedure for their infant.

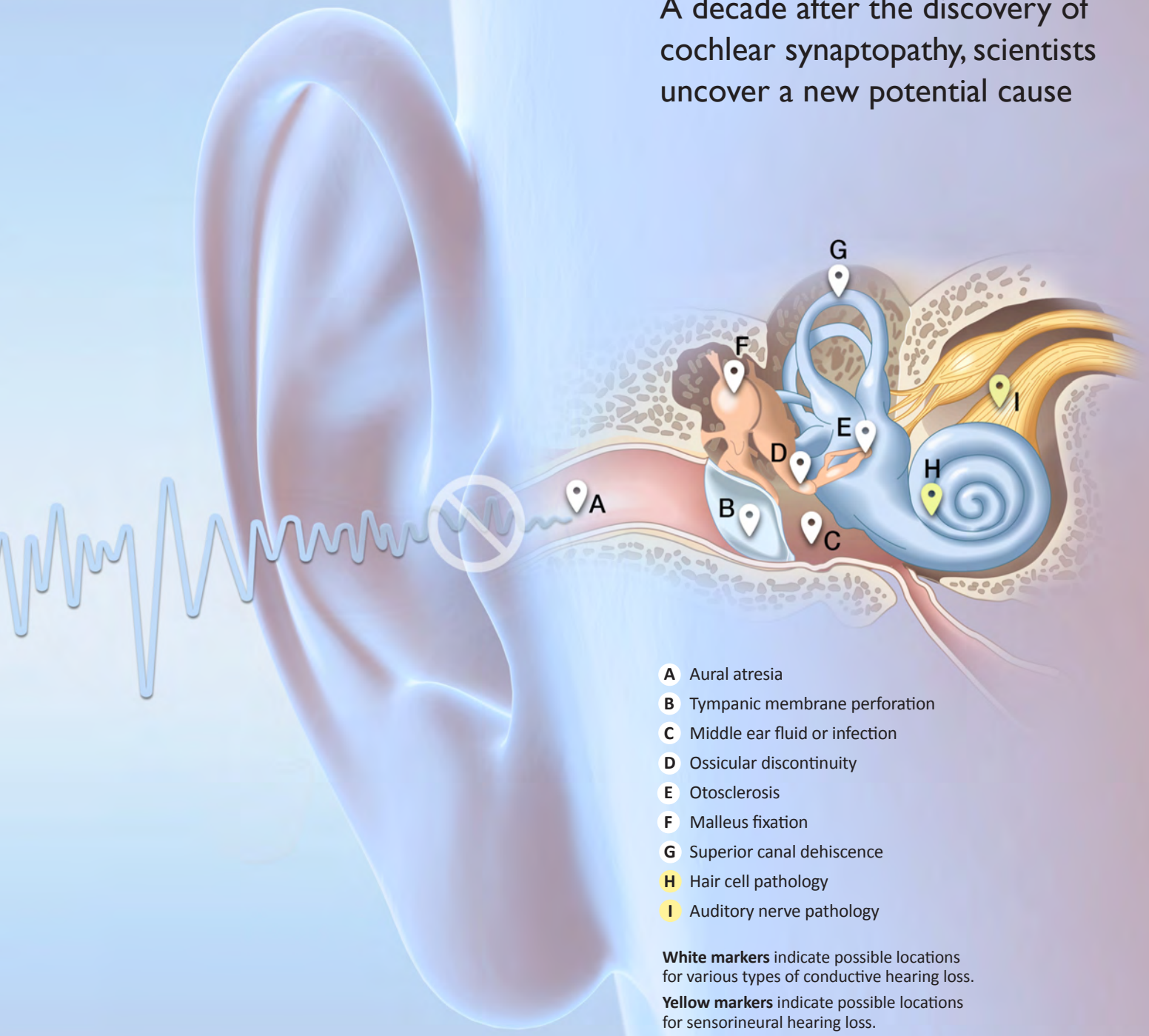
Future multicenter trials are planned and the researchers are now working on follow-up outcomes studies comparing infants who did and did not undergo tongue-tie surgery longer term. In the meantime, the study's authors call for the development of best practice guidelines to help with decision-making throughout the medical community.

"We've learned that an interdisciplinary collaboration is key to a thorough feeding evaluation," said study co-author and speech-language pathologist Cheryl Hersh. "This is still a work in progress, but we have learned a great deal about what we can do differently to help our patients and their families. In doing so, we have been able to identify many babies who are having breastfeeding problems that are not related to their lip and tongue anatomy and are able to improve their feeding with clinical strategies." ●



HIDDEN HEARING LOSS:
A 10-Year Journey

A decade after the discovery of cochlear synaptopathy, scientists uncover a new potential cause



- **A** Aural atresia
- **B** Tympanic membrane perforation
- **C** Middle ear fluid or infection
- **D** Ossicular discontinuity
- **E** Otosclerosis
- **F** Malleus fixation
- **G** Superior canal dehiscence
- **H** Hair cell pathology
- **I** Auditory nerve pathology

White markers indicate possible locations for various types of conductive hearing loss.

Yellow markers indicate possible locations for sensorineural hearing loss.

A common complaint heard in otology and audiology clinics is that patients have difficulties understanding speech in noisy environments. However, when their hearing sensitivity is measured and plotted on an audiogram, many of their hearing thresholds are in healthy ranges.

For years, clinicians and investigators questioned the efficacy of the audiogram in revealing such issues, as they suspected more had to be happening in the inner ear than an audiogram could measure.

In 2009, a team of investigators led by Sharon G. Kujawa, PhD, and M. Charles Liberman, PhD, of the Eaton-Peabody Laboratories (EPL) at Massachusetts Eye and Ear/Harvard Medical School, uncovered a new type of inner ear damage that could explain these poorly understood hearing complaints.

In a study published in the *Journal of Neuroscience,* they described that the neural synapses responsible for the communication between the ear and the brain are actually the most vulnerable structures in the inner ear. With age or noise exposure, many of these synaptic connections disappear and decrease the fidelity of the auditory information sent to the brain.

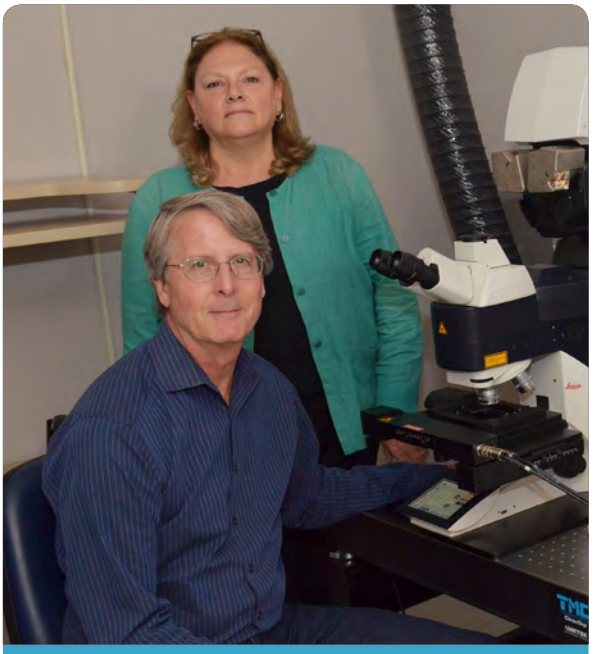
"This finding changed the landscape of how we look at patients with hearing loss," said Dr. Kujawa. "Conventional wisdom would suggest that sensorineural hearing loss is largely attributed to the loss of hair cells, the sensory cells of the inner ear that audiograms measure. But this study indicated something different."

Dr. Kujawa and Dr. Liberman showed that noise and aging first damage the synapses connecting the hair cells to the nerve fibers carrying neural signals to the brain, even when the hair cells are not damaged. This is now known as cochlear synaptopathy. Since hair cell function is what audiograms measure, this synaptic loss is typically undocumented, inspiring the popular term "hidden hearing loss."

A decade of discoveries

This year marks the 10-year anniversary of the discovery of cochlear synaptopathy. Throughout the past decade, investigators around the world have aimed to uncover the prevalence, diagnosis, and functional consequences of the condition.

Dr. Kujawa and Dr. Liberman note that over the past 10 years, the phenomenon of hidden hearing loss, which they originally demonstrated in noise-exposed and aging mice, has been documented in noise-exposed chinchillas, rats, guinea pigs, monkeys, and, most importantly, aging humans. Furthermore, several EPL investigators have developed techniques based on gene therapy and drug delivery that can protect the ear against noise exposure and even regenerate the neural connections after damage.



"Over the past 10 years, the phenomenon of hidden hearing loss, which we originally demonstrated in noise-exposed and aging mice, has been documented in noise-exposed chinchillas, rats, guinea pigs, monkeys, and, most importantly, aging humans."

—Drs. Liberman and Kujawa

"Although much work remains to be done, including the challenge of accurately diagnosing the degree of neural degeneration in human ears, the development of cures for this key aspect of hearing impairment is now a real possibility," said Dr. Liberman.

In 2017, this work led to the National Institute on Deafness and Other Communication Disorders, part of the National Institutes of Health, funding a team that includes Dr. Liberman and Dr. Kujawa, as well as

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"People with hearing loss in one ear are often reluctant to engage in rehabilitation as they still can rely on their better ear. Our study suggests that, in absence of treatment, speech perception may worsen in time."

—Dr. Maison

Stéphane F. Maison, PhD, and Daniel B. Polley, PhD, of the EPL, with a P50 grant to combine their efforts and tackle the condition from multiple angles.

Through four projects, including one studying donated human temporal bones, one focusing on animal models, and two working with human subjects, their goal is to work toward the refinement of diagnostic measures in human populations for cochlear synaptopathy, which could also lead to the development of future therapies.

One of the most recent discoveries of this team is the work of Dr. Maison and Dr. Liberman alongside D. Bradley Welling, MD, PhD, FACS, of Mass. Eye and Ear/Harvard Medical School, and Masahiro Okada, PhD, of Ehime University Graduate School of Medicine, who have found a connection between cochlear synaptopathy and sound deprivation. Their work suggests ear infections and conditions that cause chronic conductive hearing loss may lead to nerve degeneration when left untreated.

With cochlear synaptopathy, noise exposure, 'normal' aging, and use of ototoxic drugs have been identified causes of the condition. This study, however, is the first to suggest that underuse of the ear might also have similar damaging effects.

The effects of sound deprivation

In healthy ears, sound waves travel through the ear canal, reaching the eardrum and the tiny bones of the middle ear before getting to the inner ear where they are converted into electrical signals that are transmitted to the brain to interpret sound. When conductive hearing loss occurs, the sound transmission through the middle ear is impaired, leading to a reduction in sound levels and an inability to hear soft sounds.

In a study recently published in *Ear and Hearing*, this team retrospectively reviewed the hearing profiles of 240 patients who visited an audiology clinic at Mass. Eye and Ear with either an acute or chronic conductive hearing loss, but normal sensorineural function on hearing tests. They found that patients with longstanding conductive hearing impairments of moderate to moderately severe degrees had lower speech recognition scores on the affected side than the healthy side, even when the speech was loud enough to be clearly audible.

"Our results suggest that chronic sound deprivation can lead to speech recognition difficulties consistent with cochlear synaptopathy," said Dr. Maison. "The findings are especially important considering that children with asymmetric hearing loss have higher rates of academic, social, and behavioral difficulties."

This work validates previous research led by Dr. Maison in adult mice in 2015, showing that longstanding conductive impairment leads to loss of the synaptic connections between the inner ear's sensory cells and the auditory nerve that relays the electrical signals to the brain.

"People with hearing loss in one ear are often reluctant to engage in rehabilitation as they still can rely on their better ear. Our study suggests that, in absence of treatment, speech perception may worsen in time," said Dr. Maison. "If what we have observed in mice is

applicable to humans, there is a possibility that unilateral sound deprivation may affect the good ear as well. I would recommend that clinicians consider providing amplification in the management of unilateral conductive hearing loss."

Looking toward the next 10 years

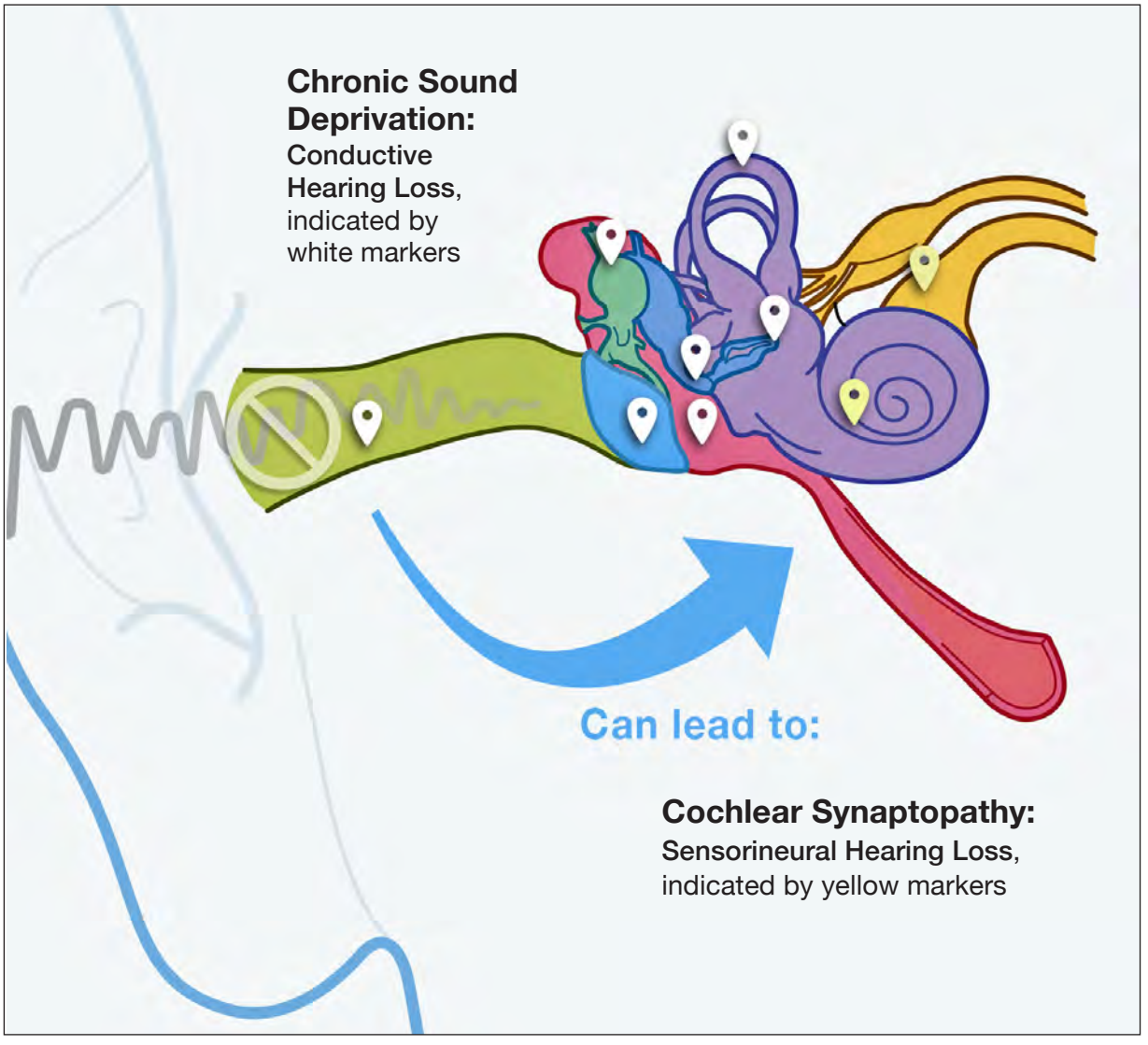
Ten years after the landmark discovery of cochlear synaptopathy, investigators are getting closer to understanding what hidden hearing loss is, what causes it, and how to identify it in patients. They even continue to describe possible causes as seen with Dr. Maison's and Dr. Liberman's recent study.

As these P50 projects continue to expand, the investigators hope to use their findings to improve the sensitivity and specificity of hearing tests in order to identify hidden hearing loss and define how this condition evolves in time.

"Establishing diagnostic indicators for hidden hearing loss in humans is important as recent animal research suggests that reconnecting the nerve to the sensory cells of the inner ear is possible," said Dr. Maison.

Additional insights and the establishment of a reliable diagnosis will also help clinicians choose the right candidates for clinical trials and determine the efficacy of a treatment.

"With our work, we have the potential to help a lot of people and that's encouraging," said Dr. Maison.



Harvard Medical School Celebrates 2019 Otolaryngology Graduation and Seventh Annual Meeting

Faculty and staff from the Department of Otolaryngology–Head and Neck Surgery at Harvard Medical School gathered in the Meltzer Auditorium at Massachusetts Eye and Ear on Friday, June 21, to celebrate the 2019 graduating class of residents and fellows.

Five chief residents and 11 clinical fellows graduated from a program led by Harvard Medical School's Vice Chair of Otolaryngology Education Stacey T. Gray, MD, Associate Otolaryngology Residency Director Kevin S. Emerick, MD, and Walter Augustus Lecompte Professor and Chair of Otolaryngology–Head and Neck Surgery D. Bradley Welling, MD, PhD, FACS.

"We are so proud of what our graduating residents and fellows have accomplished during their time with us," said Dr. Gray. "We are excited to see where they are headed next and proud to have them representing our program worldwide."

The Joseph B. Nadol, Jr., MD, Graduation Lectureship was given by Carol R. Bradford, MD, FACS, Executive Vice Dean for Academic Affairs at the University of Michigan Medical School. In her talk, she expressed the importance of work-life balance. In order to succeed in the field of medicine, she advised that one must "take care of themself in order to take care of others."

At the end of the ceremony, graduating resident Yin Ren, MD, PhD, was awarded the Jeffrey P. Harris, MD, PhD, Research Prize for his FOCUS research project, "Towards personalized precision medicine for vestibular schwannoma and hearing loss."

Prior to the graduation ceremony, the day began with the department's seventh annual meeting, an event that brings together faculty, residents, and fellows from each of our institutions.

The meeting featured Chief Resident research talks on topics from discovering biomarkers for chronic rhinosinusitis to the impact of hospital market competition on the adoption of transoral robotic surgery. These talks were followed by a poster session highlighting the work of all of our residents.

The annual meeting was concluded with faculty presentations by Jeffrey R. Holt, PhD, Professor of Otolaryngology–Head and Neck Surgery at Harvard Medical School, and Jeremy D. Richmon, MD, Associate Professor of Otolaryngology–Head and Neck Surgery at Harvard Medical School.

Awards and Honors

Annual Poster Session

Anuraag Parikh, MD
1st Place Poster Award
"Multiplexed immunofluorescence and multispectral imaging-based quantification of tumor and immune cell populations reveals spatial relationships in oral cavity SCC"

Yin Ren, MD, PhD
2nd Place Poster Award
"Tumor penetrating delivery of nanoparticles to human vestibular schwannomas"

Jeffrey P. Harris, MD, PhD, Research Prize

Presented to one of the graduating chiefs for their FOCUS research project.

Yin Ren, MD, PhD
"Towards personalized prevision medicine for vestibular schwannoma and hearing loss"

Clinical Fellow Teaching Award

Jennifer A. Brooks, MD, MPH

Chief Resident Teaching Award

Katie M. Phillips, MD, and
Rosh K. V. Sethi, MD, MPH

William W. Montgomery, MD, Faculty Teaching Award

Carleton Eduardo Corrales, MD

Harvard Otolaryngology Resident Well-Being Award

Mark A. Varvares, MD, FACS

Dr. Yin Ren receives the Jeffrey P. Harris, MD, PhD, Research Prize from Dr. Brad Welling.

Dr. Carol Bradford gives the graduation address.

Graduating Class of 2019

Residents

Ashton E. Lehmann, MD, is known for her ability to balance an earnest demeanor with a sunny disposition. As a clinician and surgeon, she is dedicated and thorough. She fully understands the weight and responsibility that comes with being a surgeon. Anyone can see how deeply she cares for her patients. From a research perspective, she immersed herself in the world of basic science during her residency. She worked with Ralph B. Metson, MD, on seeking a biomarker for chronic rhinosinusitis. Her work resulted in multiple national presentations and publications. She is now a rhinology and endoscopic skull base surgery fellow at Mass. Eye and Ear/Harvard Medical School.

Known for his ability to deeply connect with patients, **Brian M. Lin, MD, ScM**, excels as a clinician and surgeon. The devotion he has for each of his patients shines through his passionate, honest, and supportive nature. He joined our program as a seven-year research track resident. Working with Gary C. Curhan, MD, and Konstantina M. Stankovic, MD, PhD, FACS, he spent his dedicated research time looking into risk factors for hearing loss. This work resulted in many national presentations and publications. He additionally won the Academy Humanitarian Resident Travel Grant for a medical mission trip to Tamatave, Madagascar. He is now at Johns Hopkins University pursuing a fellowship in neurotology.

A natural leader, **Katie M. Phillips, MD**, is the definition of responsible and mature. She's respectful and thoughtful in how she leads a team, and these qualities are exemplified in the care she provides her patients. Early on in her residency, she developed a research interest in chronic rhinosinusitis (CRS). Working alongside Ahmad R. Sedaghat, MD, PhD, FACS, she measured quality of life in CRS patients for her resident FOCUS project. She has presented nationally and internationally, published several publications, and won many awards, including the John J. Conley, MD, Resident Research Award at the Triological Society for this work. She is now pursuing a rhinology/anterior skull base fellowship at Stanford University.

Photo by Aram Boghosian

The 2019 graduating class of residents from left to right: Drs. Katie Phillips, Yin Ren, Rosh Sethi, Ashton Lehmann, and Brian Lin.

Starting his residency with a background in developing nanotechnology tools to study the cancer genome, **Yin Ren, MD, PhD**, explored the personalization of precision medicine for vestibular schwannoma and hearing loss for his resident FOCUS project. Under the guidance of Konstantina M. Stankovic, MD, PhD, FACS, this work led to an Academy CORE grant and a New England Otolaryngological Society Research Grant along with several first author publications and national presentations. As a clinician, he is always prepared and approachable. He is also known for being organized and efficient. He is now continuing his work as the neurotology fellow at the University of California, San Diego.

Praised for his consistent professionalism, **Rosh K. V. Sethi, MD, MPH**, is known for being a team leader and educator. During his residency, Dr. Sethi explored a full range of research initiatives, including examining the impact of hospital market competition on the adoption of medical technology. All of his initiatives led him to be involved in a multitude of presentations and publications. He is known for being generous with his knowledge, often offering mentorship to medical students and other trainees. He is thoughtful and kind toward his patients, and a team player in the operating room. He is now at the University of Michigan pursuing a fellowship in head and neck oncologic surgery.

Clinical Fellows, Mass. Eye and Ear

Catherine G. Banks, MBChB, FRACS

Rhinology

Fellowship Directors: Ralph B. Metson, MD, Stacey T. Gray, MD, Eric H. Holbrook, MD
Future Plans: Department of Otolaryngology and Head and Neck Surgery, The Prince of Wales Hospital and Sydney Eye Hospital, University of New South Wales Sydney, Australia

Jennifer A. Brooks, MD, MPH

Thyroid and Parathyroid Surgery

Fellowship Director: Gregory W. Randolph, MD, FACS, FACE
Future Plans: Faculty, Boston Children's Hospital/Harvard Medical School

Christen L. Caloway, MD

Pediatric Otolaryngology

Fellowship Director: Christopher J. Hartnick, MD, MS
Future Plans: Director of Pediatric Otolaryngology, Rutgers New Jersey Medical School

continued on page 18

The 2019 graduating class of Mass. Eye and Ear fellows from left to right: Drs. Christen Caloway, Qasim Husain, Catherine Banks, Joel Fontanarosa, Nicholas Dewyer, and Jacqueline Greene. Not pictured: Dr. Jennifer Brooks.

Nicholas A. Dewyer, MD

Neurotology

Fellowship Director: Daniel J. Lee, MD, FACS
Future Plans: Director of Otology, Neurotology, and Skull Base Surgery, University of Arizona, Department of Otolaryngology–Head and Neck Surgery

Joel Fontanarosa, MD, PhD

Head and Neck Oncology/ Microvascular Surgery

Fellowship Directors: Daniel G. Deschler, MD, FACS, Jeremy D. Richmon, MD
Future Plans: Faculty, University of Rochester and the Wilmot Cancer Center

Jacqueline J. Greene, MD

Facial Plastic and Reconstructive Surgery

Fellowship Director: Tessa A. Hadlock, MD
Future Plans: Assistant Professor, Division of Otolaryngology–Head and Neck Surgery, University of California, San Diego

Qasim Husain, MD

Rhinology

Fellowship Directors: Ralph B. Metson, MD, Stacey T. Gray, MD, Eric H. Holbrook, MD
Future Plans: Coastal Ear, Nose, Throat, Private Practice, New Jersey

Clinical Fellows, Pediatric Otolaryngology, Boston Children's Hospital

Fellowship Director: Reza Rahbar, DMD, MD

Jaime Doody, MB, BCh

Future Plans: Clinical Assistant Professor in Pediatric Otolaryngology, University North Carolina, Chapel Hill

Joshua Gurberg, MD

Future Plans: Pediatric Otolaryngologist, Montreal Children's Hospital, Assistant Professor of Otolaryngology and Pediatric Surgery, McGill University

Rounak B. Rawal, MD

Future Plans: Attending Otolaryngology/ Head and Neck Surgeon, Connecticut Pediatric Otolaryngology, Clinical Instructor, Department of Surgery (Otolaryngology), Yale University School of Medicine

Cher Xue Zhao, MD

Future Plans: Faculty, Pediatric Otolaryngology, Mass. Eye and Ear/ Harvard Medical School

The 2019 graduating class of Boston Children's Hospital fellows from left to right: Drs. Jaime Doody, Rounak Rawal, Cher Xue Zhao, and Joshua Gurberg with Otolaryngologist-in-Chief Dr. Michael Cunningham (center).

The Otolaryngology–Head and Neck Surgery Residency Program at Harvard Medical School

Meet our PGY-1 Residents

Originally from Las Vegas, Nevada, **Ryan A. Bartholomew, MD**, is a graduate of Duke University. There, he studied neuroscience and philosophy, and was a member of the Yin Laboratory for an additional year. He then earned his medical degree from Harvard Medical School. Dr. Bartholomew has published several articles investigating the contributions of the basal ganglia to modulating behavior using optogenetic and 3D motion capture techniques in mice. During medical school, he was involved in clinical research in otolaryngology. He has interests in translational research, surgical innovation, and medical education.

Elliana Kirsh DeVore, MD, grew up in Cincinnati, Ohio, and graduated *summa cum laude* from the University of Cincinnati, College-Conservatory of Music with a degree in voice performance. Following her undergraduate work, she pursued a career as a professional opera singer, performing internationally in opera productions, concerts, and music festivals. During this time, her desire to understand the physiologic processes underlying the voice transformed her passion for performance to that of science. She returned to the University of Cincinnati to earn a second degree in neurobiology. She was awarded the University of Cincinnati Presidential Leadership Medal of Excellence. She then went on to receive her medical doctorate from Harvard Medical School. Dr. DeVore's research is dedicated to improving outcomes for patients with complex airway problems, including those with voice disorders.

Hailing from Dallas, Texas, **Krish Suresh, MD**, received his undergraduate and medical education in Chicago at Northwestern University. Graduating *magna cum laude*, he studied biology and computer science. He gained early acceptance to the Northwestern University Feinberg School of Medicine, where he received a fellowship for his basic science research in cancer epigenetics and also conducted clinical research in head and neck cancer. Dr. Suresh graduated from medical school *summa cum laude* and with honors for outstanding performance in otolaryngology and in his junior clerkships. He was also elected to Alpha Omega Alpha and the Gold Humanism Honor Society.

A native of Edina, Minnesota, **Michael Pei-hong Wu, MD**, graduated *summa cum laude* from Harvard College with a degree in molecular and cellular biology. He subsequently attended Harvard Medical School, where he completed the Harvard-Massachusetts Institute of Technology joint MD program within the Division of Health Sciences and Technology. During medical school, Dr. Wu spent a year examining the presence and role of cilia in human cancers. He has participated in multiple research projects, with primary interests in the cancer microenvironment, highly multiplexed imaging modalities for analysis of pathologic specimens, and surgical outcomes. An avid cellist, he is also interested in the intersection between music, health, and quality of life.

Originally from Montgomery, New Jersey, **Roy Xiao, MD**, attended Princeton University for his undergraduate studies in chemistry and computer science. His senior thesis resulted in a patented catalytic system for water purification and the American Chemical Society Division of Inorganic Chemistry Award. He then attended the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University for his medical and master's degrees. There, he worked on numerous studies investigating clinical outcomes for patients with head and neck cancers. He also completed a one-year fellowship at the National Institute on Deafness and Other Communication Disorders, part of the National Institutes of Health, through the Medical Research Scholars Program. His research interests include the efficiency of healthcare systems, immunotherapy for head and neck cancers, and surgical quality improvement.

New Clinical Fellows

Mass. Eye and Ear

Head and Neck Oncology/ Microvascular Surgery
Andrew J. Holcomb, MD

Facial Plastic and Reconstructive Surgery
Matthew Q. Miller, MD

Neurotology
Divya Chari, MD

Pediatric Otolaryngology
Asitha Jayawardena, MD, MPH

Rhinology
Aria Jafari, MD

Rhinology
Ashton E. Lehmann, MD

Thyroid and Parathyroid Surgery
Ayaka J. Iwata, MS, MD

Boston Children's Hospital

Pediatric Otolaryngology

Andrew E. Bluher, MD

Sara Gallant, MD

Erika Mercier, MD

Aiden (Eliot) Shearer, MD, PhD

Alumni Profile

Paul E. Hammerschlag, MD, FACS, HMS Otolaryngology Resident, Class of 1977

Building a career as an ear surgeon

For **Paul E. Hammerschlag, MD, FACS**, his journey to becoming an otologist is somewhat unique. While he grew up watching his father care for patients as an obstetrician, he has also had a bilateral sensorineural hearing loss (SNHL) from a young age.

Now a semi-retired ear surgeon and cochlear implant patient himself, Dr. Hammerschlag reflects on his career in otolaryngology.

"Between my hearing loss and my father being a physician, pursuing a career in medicine was always a natural thought for me," said Dr. Hammerschlag, an Associate Professor of Otolaryngology at New York University (NYU).

"When I was in high school, I had the opportunity to watch a well-known New York surgeon perform stapes surgery. That was the moment I knew I was attracted to the field of otolaryngology. In an inchoate way, I contemplated that I might have an intrinsic and possibly insightful connection to those with hearing loss."

A native of New York, Dr. Hammerschlag's studies began at NYU for his undergraduate degree, followed by becoming a Doctor of Science candidate at the Johns Hopkins Bloomberg School of Public Health. He then attended medical school at the Albert Einstein College of Medicine. It was there that he first heard of the Massachusetts Eye and Ear/Harvard Medical School residency program and was encouraged by his professors to apply.

Before he began his residency at Mass. Eye and Ear, however, he completed a pediatric internship at the University of Washington in Seattle, followed by a one-year general surgery residency with Virginia Mason Hospital.

"At the onset of my residency at Mass. Eye and Ear, I was able to see from first-hand experience how prominent and important the institution was," Dr. Hammerschlag commented. "It was an incredibly remarkable experience for me. I remember it being some of the busiest, most exciting, and fastest years of my life."

During residency, Dr. Hammerschlag spent his time studying with Harold F. Schuknecht, MD, former Harvard Medical School Chair of Otolaryngology, and other faculty. He is still very grateful to Dr. Schuknecht for embracing his hearing loss in ways others hadn't.

"After a bout of fluctuating SNHL during my general surgery residency, there were questions by others about how it might interfere with my ability to perform in residency," Dr. Hammerschlag explained. "Dr. Schuknecht indicated that it should not be an issue for me at Mass. Eye and Ear. Moreover, in his own inimitable way, Dr. Schuknecht was the best teacher I was fortunate enough to encounter. I hasten to add that there were other terrific faculty as well, resulting in a broad and meaningful training experience for those of us in the program."

"I will always have an intangible connection to Mass. Eye and Ear. It gave me a superb foundation to build on in terms of my professional career," he added.

Following his residency, Dr. Hammerschlag completed a general otolaryngology fellowship at Mass. Eye and Ear and remained on faculty until 1978. After an additional year in Seattle on the faculty at the University of Washington, Dr. Hammerschlag established his roots in New York.

Throughout his nearly 40-year tenure at NYU, he has devoted his practice to treating multiple otologic and neurotologic problems. Today, he covers a fellow and resident otology/neurotology clinic. His esteemed career has also included regular contributions to articles, textbooks, and periodicals, sharing his insights in roundtable discussions with colleagues, and lecturing across the country and around the world.

Dr. Hammerschlag has additionally spent much of his career teaching and mentoring the next generation of otolaryngologists.

"Over time, I have been humbled by the opportunity to care for patients and their families," said Dr. Hammerschlag. "I have also enjoyed and been challenged by teaching residents and fellows."

Now, he is adjusting to semi-retirement with nonmedical ventures, which include traveling, reading, renovating a New York townhouse, enjoying family, attending university courses, and completing subspecialty journal peer reviews.

Over the years, Dr. Hammerschlag has been able to connect with patients on a level most doctors aren't. He believes that being a cochlear implant user himself has enabled him to bring more understanding to his hearing loss patients and their families.

"My story isn't much different than those of others, but possibly understanding more of what some of my patients have gone through and helping them has been truly rewarding," Dr. Hammerschlag said. ●

Lara A. Thompson, PhD, Jenks Vestibular Physiology Laboratory of Massachusetts Eye and Ear/Harvard Medical School, Class of 2013

Finding the right balance between research and medicine

Photo by John Spaulding

For **Lara A. Thompson, PhD**, her interests in the arts and sciences began at a young age. It came by no surprise when she chose to study mechanical engineering at the University of Massachusetts Lowell.

"My childhood interests in creative endeavors didn't equate to engineering when I was growing up, but now looking back, those interests definitely shaped my career," said Dr. Thompson.

Now the Director of the Center for Biomechanical and Rehabilitation Engineering (CBRE) Laboratory and Associate Professor of Mechanical Engineering at the University of the District of Columbia (UDC), Dr. Thompson has found a way to apply her engineering background to advancing balance and gait research.

After earning her bachelor's degree, Dr. Thompson studied aeronautical and astronautical engineering at Stanford University. She then worked at the Charles Stark Draper Laboratory, Inc. for two years as a mechanical engineer, working on several Department of Defense (DoD) projects and creating models for various applications.

Wanting to do more with medicine, she then returned to school for her doctorate degree, enrolling in the joint Harvard Medical School-Massachusetts Institute of Technology Health Sciences and Technology (HST) program.

"I wanted to do something where I could apply my engineering background toward medicine," said Dr. Thompson. "I had an interest in medicine but wanted to work in academia and remain an engineer. That is how I found the HST program. It was the right balance between research, medicine, and engineering."

As an HST student, Dr. Thompson explored implants and prostheses of the inner ear, specifically vestibular implants. She was drawn to the vestibular implant because it affects a different part of the inner ear than one typically hears about. Most often, hearing aids and cochlear implants are discussed. However, vertigo and disequilibrium tied to the vestibular system are major concerns and fit well with her previous training and interests.

Dr. Thompson began working in the Jenks Vestibular Physiology Laboratory at Massachusetts Eye and Ear/Harvard Medical School under the guidance of Richard F. Lewis, MD. She worked on investigating postural control tied to the development of prototype prosthesis in non-human primates. She also investigated postural responses for balancing tasks of increasing difficulties and characterized the effects of an invasive vestibular implant on posture.

"Working with Dr. Lewis and being a witness to his ideas really made this program special in my mind," said Dr. Thompson. "There were also only three institutions nationwide working with vestibular prostheses at the time. We were treading on new ground, which both challenged and prepared me."

In 2013, Dr. Thompson earned her doctorate in biomedical engineering and immediately joined UDC to build a biomedical engineering program. She was responsible for writing the initial program proposal and got full board approval in 2014. Of approximately 100 Historically Black Colleges and Universities (HBCUs) nationwide, UDC is one of only three HBCUs to offer an undergraduate degree in biomedical engineering.

Dr. Thompson was also asked to initiate and build the CBRE Laboratory at UDC, which is a research laboratory focused on balance and gait, particularly in the aging population. This laboratory utilizes sensor technology and engineering principles to provide clinical diagnostics on individuals whose gait and motion have been impaired due to age, injury, or stroke.

"At one point growing up, I enjoyed working with living things in addition to wanting to have a career that allowed me to build and create," Dr. Thompson remarked. "Now I get to do both."

To date, Dr. Thompson has been a lead investigator of several grants from the National Science Foundation (NSF), including a research initiation award, an early-concept grant for exploratory research award, and a targeted infusion project award. She is also a co-investigator on two DoD grants and the lead investigator on a project sponsored by the Department of Aging and Community Living.

In recognition of her contributions, Dr. Thompson was honored as an HBCU STEM Innovator at the annual Black Engineer of the Year Awards conference and was a featured scientist in NSF's *Science Nation* in early 2019. She was also acknowledged nationally as a Diverse Issues of Higher Education Emerging Scholar in 2017.

"In many ways, my career is still just getting off of the ground, and that is exciting," said Dr. Thompson. "My goal is to really leave a footprint on the field from both a research and education perspective. I'm proud of the programs I've helped build and am looking forward to seeing how they grow." ●

HARVARD MEDICAL SCHOOL | Department of Otolaryngology Head and Neck Surgery

The Alumni Giving Society of the Department of Otolaryngology–Head and Neck Surgery at Harvard Medical School

The Department of Otolaryngology–Head and Neck Surgery at Massachusetts Eye and Ear/Harvard Medical School established the Alumni Giving Society in 2015 to recognize faculty and alumni who make gifts of $1,000 or more during the fiscal year (October 1–September 30). Participation is a way to stay connected and to help deliver the finest teaching experience for today's otolaryngology trainees.

Our alumni know from firsthand experience that support of the vital work of our students and faculty in the Department of Otolaryngology–Head and Neck Surgery helps drive continued achievement across all areas of education, research, and patient care. To date, we have 31 members whom we thank for their generosity and for partnering with us to achieve our department goals and institutional mission.

If you are not a member, please consider joining your colleagues today by making a gift with the enclosed envelope. As a member, you may designate your gift in the way that is most meaningful to you.

To learn more, please contact Julie Dutcher in the Development Office at 617-573-3350.

Alumni Giving Society Leadership

D. Bradley Welling, MD, PhD, FACS
Walter Augustus Lecompte
Professor and Chair of Otolaryngology–Head and Neck Surgery,
Harvard Medical School
Chief of Otolaryngology–Head and Neck Surgery,
Mass. Eye and Ear/
Massachusetts General Hospital

Mark A. Varvares, MD, FACS, '91, '92
Associate Chair of Otolaryngology–Head and Neck Surgery,
Harvard Medical School
President, Harvard Otolaryngology Alumni Association

Alumni Leaders

Daniel G. Deschler, MD, FACS
Richard E. Gliklich, MD, '93, '94
Donald G. Keamy, Jr., MD, MPH
Paul M. Konowitz, MD, FACS
John B. Lazor, MD, MBA, FACS, '95, '96
Jon B. Liland, MD, '72
Derrick T. Lin, MD, FACS, '98, '02
Leila A. Mankarious, MD
William W. McClerkin, MD, '73
Ralph B. Metson, MD, '87
Michael M. Paparella, MD
Herbert Silverstein, MD, FACS, '66

Harvard faculty, alumni, and residents at the 2019 American Academy of Otolaryngology–Head and Neck Surgery meeting.

Current Alumni Giving Society members for fiscal year 2019 from October 1, 2018, to September 30, 2019, are listed below. With your gift of $1,000 or more, you will be included in the 2020 Alumni Giving Society.

CHAMPION:
Gifts of $25,000 or higher
Ralph B. Metson, MD

VISIONARY:
Gifts of $10,000 to $24,999
Michael S. Cohen, MD
Eric H. Holbrook, MD
Michael B. Rho, MD, FACS

INNOVATOR:
Gifts of $5,000 to $9,999
Wade W. Han, MD, OD, FAAO
John B. Lazor, MD, MBA, FACS
Derrick T. Lin, MD, FACS
Edward J. Reardon, MD

PIONEER:
Gifts of $2,500 to $4,999
Barry J. Benjamin, MD
Samir M. Bhatt, MD
Nicolas Y. BuSaba, MD, FACS
Terry J. Garfinkle, MD, MBA
Richard E. Gliklich, MD
Christopher J. Hartnick, MD, MS
Daniel J. Lee, MD, FACS
Leila A. Mankarious, MD
Cliff A. Megerian, MD
Joseph B. Nadol, Jr., MD
Steven D. Rauch, MD
Jeremy D. Richmon, MD
Phillip C. Song, MD
D. Bradley Welling, MD, PhD, FACS

FRIEND:
Gifts of $1,000 to $2,499
Megan E. Abbott, MD
James P. Hughes, MD
William W. McClerkin, MD
Eugene N. Myers, MD, FACS, FRCS Edin (Hon)
Adrian J. Priesol, MD
Sunil Puria, PhD
Herbert Silverstein, MD, FACS
Feodor Ung, MD
Mark A. Varvares, MD, FACS

News from every corner of the Harvard Medical School Otolaryngology–Head and Neck Surgery Department.

New Faculty

Iván Coto Hernández, PhD, is an Instructor in Otolaryngology–Head and Neck Surgery at Harvard Medical School and investigator at Mass. Eye and Ear. Dr. Coto Hernández completed his doctoral studies in nanoscience at the Italian Institute of Technology and the University of Genoa, followed by postdoctoral training at the University of Paris-Sud and Mass. Eye and Ear/Harvard Medical School. His research focuses on super-resolution microscopy development and its application to the study of cranial and peripheral nerve disorders.

Shmuel Erez Davidi, MD, has joined Mass. Eye and Ear, Braintree to care for patients with balance disorders. He earned his medical degree from the Ruth and Bruce Rappaport Faculty of Medicine in Haifa, Israel before completing his internship at Sheba Medical Center and otolaryngology–head and neck surgery training at Kaplan Medical Center in Rehovot, Israel. He then completed a vestibular disorders fellowship at Mass. Eye and Ear/Harvard Medical School. His clinical interests include diseases of the ear, general adult otolaryngology, and balance disorders.

Karl R. Koehler, PhD, has joined the F.M. Kirby Neurobiology Center research staff at Boston Children's Hospital/ Harvard Medical School. With a doctorate in medical neuroscience and postdoctoral fellowship training from the Indiana University School of Medicine, his research focuses on using the organoid culture system as a platform to develop regenerative therapies for the inner ear and various craniofacial tissues. The overall aim of his work is to create new tools to study human sensory organ development, function, and regeneration.

Hamid Motallebzadeh, PhD, is an Instructor in Otolaryngology–Head and Neck Surgery at Harvard Medical School. With a doctorate degree in biomedical engineering from McGill University and postdoctoral training from Stanford University and Mass. Eye and Ear/Harvard Medical School, his research focuses on acoustics, hearing mechanics, and newborn hearing screening. Specifically, his research approach includes multi-physics and multi-scale biomechanics of auditory systems and artificial intelligence in medicine.

George A. Scangas, MD, is an Instructor in Otolaryngology–Head and Neck Surgery whose practice will join Mass. Eye and Ear, Emerson Place this winter. He earned his undergraduate and medical degrees from the University of Pennsylvania, before pursuing otolaryngology residency and rhinology fellowship training at Mass. Eye and Ear/ Harvard Medical School. An expert in rhinology and endoscopic skull base surgery, Dr. Scangas combines his clinical interest of caring for patients with diseases of the nose and sinuses with his research on medical and surgical outcomes to help improve quality of life for his patients.

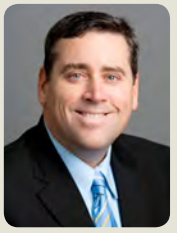
David A. Wolraich, MD, will join Mass. Eye and Ear, Longwood in December as a comprehensive otolaryngologist. A graduate of Harvard University, he earned his medical degree from the Albert Einstein College of Medicine before completing his otolaryngology training at the University of Pennsylvania. Joining our department from DuPage Medical Group in Chicago, Dr. Wolraich will see patients with a wide range of ear, nose, and throat conditions. His clinical interests include minimally invasive surgery, head and neck surgery, robotic surgery, sinus disorders, thyroid and parathyroid disorders, parotid masses, obstructive sleep apnea, snoring disorders, and airway and voice disorders.

New Leadership

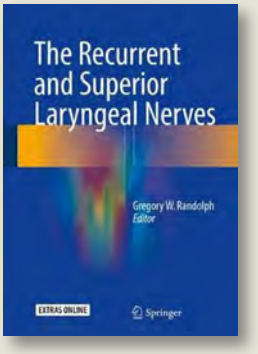
David H. Jung, MD, PhD, FACS, has been named the Medical Director of the Joseph B. Nadol, Jr., MD, Otolaryngology Surgical Training Laboratory at Mass. Eye and Ear.

Alice Z. Maxfield, MD, has been named the Otolaryngology Residency Site Director for Brigham and Women's Hospital.

HMS Promotion



Craig A. Jones, MD, FAAOA, Instructor in Otolaryngology–Head and Neck Surgery, Part-Time



The Recurrent and Superior Laryngeal Nerves textbook, authored by **Gregory W. Randolph, MD, FACS, FACE**, was recently translated into Russian, widening its reach to new surgeons worldwide.

Awards, Grants, and Honors

Dunia E. Abdul-Aziz, MD, is the recipient of the 2019 American Academy of Otolaryngology–Head and Neck Surgery Foundation Bobby R. Alford Endowed Research Award for her proposal, "Regulation of hair cell differentiation by histone demethylase Lsd1." She also recently received the Hearing Health Foundation Emerging Research Grant for her work, "Targeting epigenetics to restore hair cells," and an American Neurotology Society grant for her work, "Targeting epigenetic modifying enzymes for hair cell regeneration."

Donald J. Annino, Jr., MD, DMD, completed his 10th face transplant this summer at Brigham and Women's Hospital. Mass. Eye and Ear/Harvard Medical School otolaryngology residents **Allen L. Feng, MD**, **Nicholas B. Abt, MD**, and **Alessandra Colaianni, MD**, were on the surgical team and **Natalie Justicz, MD**, **Eric R. Barbarite, MD**, **Lauren E. Miller, MD, MBA**, and **Krish Suresh, MD**, were instrumental in the postoperative care.

Thomas L. Carroll, MD, was named an honorary member of the Mexican Voice Foundation and editor of *Chronic Cough*.

Jenny X. Chen, MD, Mass. Eye and Ear/Harvard Medical School otolaryngology resident, has been appointed a resident member of the Accreditation Council for Graduate Medical Education (ACGME) Review Committee for Otolaryngology–Head and Neck Surgery.

Michael J. Cunningham, MD, FACS, was invited to be the Percy Ireland Orator at the 28th Annual Percy Ireland Academic Day for the Department of Otolaryngology–Head and Neck Surgery at the University of Toronto in May. His topic was "Juvenile nasopharyngeal angiofibroma: Etiologic conundrum, surgical challenge, and recidivism risk."

Adeeb Derakhshan, MD, Mass. Eye and Ear/Harvard Medical School otolaryngology resident, was awarded the 2019 American Academy of Facial Plastic and Reconstructive Surgery Leslie Bernstein Resident Research Grant for his proposal, "The effect of electrical stimulation of Schwann cell states along nerve grafts." The work will be conducted in the Mass. Eye and Ear Berthiaume Surgical Photonics and Engineering Laboratory with mentor **Nate Jowett, MD, FRCSC**, and co-investigator and fellow resident **Suresh Mohan, MD**.

Daniel G. Deschler, MD, FACS, has been appointed co-chair of the Thesis Committee for the Triological Society and to the Salivary Malignancy Guidelines Panel of the American Society of Clinical Oncology.

Allen L. Feng, MD, Mass. Eye and Ear/Harvard Medical School otolaryngology resident, received a 2019 American Academy of Otolaryngology–Head and Neck Surgery Foundation CORE Resident Research Grant for his work, "Biomechanical analysis of force loadings during suspension microlaryngology."

Shekhar K. Gadkaree, MD, Mass. Eye and Ear/Harvard Medical School otolaryngology resident, has been awarded a Sections for Residents and Fellows-in-Training (SRF) Leadership Grant from the American Academy of Otolaryngology–Head and Neck Surgery.

Graduate students of the Speech and Hearing Bioscience and Technology (SHBT) program, **Janani Iyer** and **Kameron Clayton**, received the 2019 Amelia-Peabody Scholarship. This scholarship is given annually to SHBT students to support their research initiatives at Mass. Eye and Ear.

Nate Jowett, MD, FRCSC, has been awarded the American Academy of Facial Plastic and Reconstructive Surgery Research Scholar Award through the Academy CORE program. This funding will help advance work on a neuroprosthetic device for hemifacial reanimation. Alongside **Luk H. Vandenberghe, PhD**, Dr. Jowett has also been awarded a Charles H. Hood Foundation Child Health Research Award. This funding will support research into gene therapy for peripheral nerve repair.

David H. Jung, MD, PhD, FACS, has been awarded a Department of Defense Hearing Restoration Research Program Translational Research Award for his work, "Novel small molecule TrkB and TrkC agonists for cochlear synaptic regeneration." This project is a collaboration between Mass. Eye and Ear, the University of Southern California, Vanderbilt University Medical Center, and Akouos.

Vivek Kanumuri, MD, Mass. Eye and Ear/Harvard Medical School otolaryngology resident, was awarded third place at the New England Otolaryngological Society meeting for his talk, "Novel approaches to inner ear gene delivery."

Margaret A. Kenna, MD, MPH, FACS, FAAP, was awarded the 2019 USH Foresight Award from the Usher Syndrome Coalition at the Annual USH Connections Conference in July. This award is presented to esteemed honorees for their dedication and commitment to the Usher syndrome community.

Elliott D. Kozin, MD, the Mass. Eye and Ear Neskey-Coghlan Fellow in Neurotology, was named a 2019 star reviewer for the *Journal of Otolaryngology–Head and Neck Surgery*. He was also recently nominated for the Politzer award at the Politzer Society Meeting in Warsaw, Poland and was asked to serve as a member of the steering committee for the Procedural Learning and Safety Collaborative.

Richard F. Lewis, MD, has been awarded a National Institutes of Health R56 grant through the National Institute on Deafness and Other Communication Disorders. This grant will help fund Dr. Lewis' human vestibular implant work.

Greg R. Licameli, MD, is the recipient of the 2019 Trevor McGill Excellence in Teaching Award at Boston Children's Hospital.

Robin W. Lindsay, MD, was named associate editor of facial plastic and reconstructive surgery for *The Laryngoscope*. She also co-chaired the facial plastics section of COSM this past May in Austin, Texas.

Ronit Malka, MD, of the Berthiaume Surgical Photonics and Engineering Laboratory at Mass. Eye and Ear, received a 2019 American Academy of Otolaryngology–Head and Neck Surgery Foundation CORE Resident Research Grant for her proposal, "Quantitative model for decompression surgery in Bell's palsy."

Suresh Mohan, MD, Mass. Eye and Ear/Harvard Medical School otolaryngology resident, received the 2019 Plastic Surgery Foundation/American Society for Peripheral Nerve Combined Research Grant for his proposal, "Neuronal and Schwann cell transcriptional states in peripheral nerve regeneration."

Gregory W. Randolph, MD, FACS, FACE, recently chaired the World Congress on Thyroid Cancer 3.5 in Rome, Italy.

Edward J. Reardon, MD, received the Lira Award for Clinical Excellence from Beth Israel Deaconess Hospital-Milton. This award recognizes one outstanding physician each year for their commitment to medicine and compassion toward patients.

The Remenschneider Laboratory at Mass. Eye and Ear has received a Department of Defense Phase 1 SBIR grant for their work on 3D-printed tympanic membranes. Titled "Innovative solution to tympanic membrane repair," this work involves **Aaron K. Remenschneider, MD, MPH**, Neskey-Coghlan Neurotology Fellow **Elliott D. Kozin, MD**, and Harvard University PhD candidate **Nicole Black**.

The Pathologist has named **Peter M. Sadow, MD, PhD**, one of the top 100 influential people internationally in the field of pathology. The listing is based on a coalition of reader nominations and expert panel opinions.

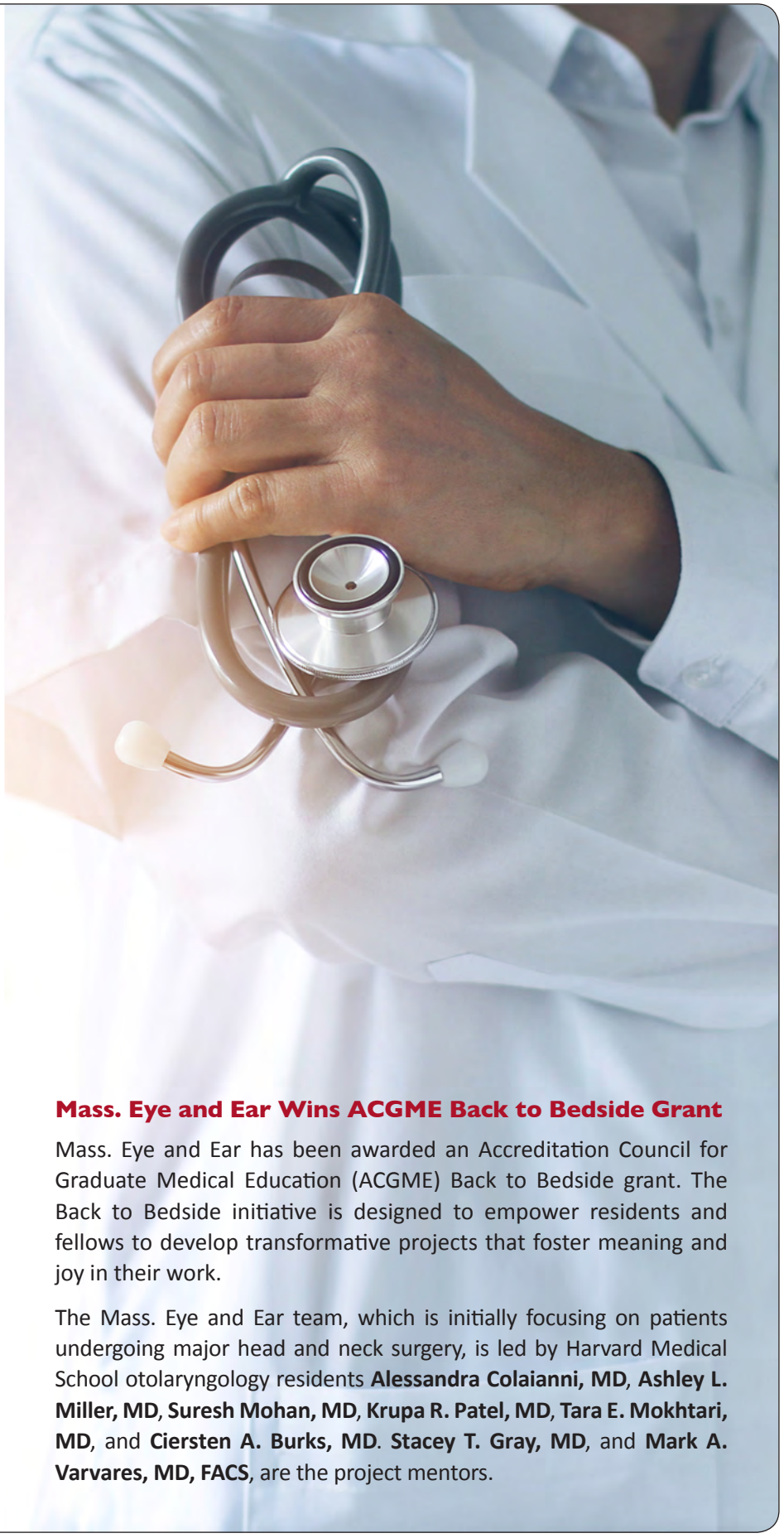
Howard C. Shane, PhD, is the 2019 recipient of the Frank R. Kleffner Lifetime Clinical Career Award from the American Speech-Language-Hearing Association. This award recognizes an individual's outstanding contributions to communication sciences and disorders over a period of at least 20 years. The award is given in honor of Frank R. Kleffner, a former American Speech-Language-Hearing Association president, who worked tirelessly over his lifetime to professionalize and expand the foundation's charitable goals.

David A. Shaye, MD, MPH, FACS, has been awarded the 2019 Arnold P. Gold Foundation Humanism in Medicine Award by the American Academy of Otolaryngology–Head and Neck Surgery.

Jennifer J. Shin, MD, SM, is the recipient of the Outstanding Award of Citizenship, Professionalism, and Service at Brigham and Women's Hospital.

Carolyn Sweeney, PhD, of the Takesian Laboratory at Mass. Eye and Ear, has been awarded an F32 Ruth L. Kirschstein National Research Service Award from the National Institute on Deafness and Other Communication Disorders for her proposal, "Serotonin regulation of VIP interneurons and auditory learning."

Lucas G. Vattino, PhD, of the Takesian Laboratory at Mass. Eye and Ear, has been selected as a Pew Latin American Fellow by the Pew Charitable Trusts. This honor is given to 10 postdoctoral fellows from six Latin American countries and provides two years of funding to conduct research in the U.S. Dr. Vattino will explore the neural circuitry that allows the brain to interpret and respond appropriately to sound.



Mass. Eye and Ear Wins ACGME Back to Bedside Grant

Mass. Eye and Ear has been awarded an Accreditation Council for Graduate Medical Education (ACGME) Back to Bedside grant. The Back to Bedside initiative is designed to empower residents and fellows to develop transformative projects that foster meaning and joy in their work.

The Mass. Eye and Ear team, which is initially focusing on patients undergoing major head and neck surgery, is led by Harvard Medical School otolaryngology residents **Alessandra Colaianni, MD**, **Ashley L. Miller, MD**, **Suresh Mohan, MD**, **Krupa R. Patel, MD**, **Tara E. Mokhtari, MD**, and **Ciersten A. Burks, MD**. **Stacey T. Gray, MD**, and **Mark A. Varvares, MD, FACS**, are the project mentors.

The following are select research advances from the Harvard Medical School Department of Otolaryngology–Head and Neck Surgery.

Basic Science

Coat protein PKHD1L1 required for normal hearing in mice

In a study recently published in *Nature Communications*, a team of Harvard Medical School investigators including **Artur A. Indzhykulian, MD, PhD**, discovered that the coat protein of hair cell stereocilia, known as Polycystic Kidney and Hepatic Disease 1-Like 1 (PKHD1L1), is required for normal hearing in mice. The bundle of stereocilia on inner ear hair cells responds to subnanometer deflections produced by sound or head movement. Stereocilia are interconnected by a variety of links and also carry an electron-dense surface coat. The study shows that PKHD1L1 mediates the surface coat at the surface of stereocilia. This coat may contribute to stereocilia adhesion or protect from stereocilia fusion, but its molecular identity remains unknown.

From a database of hair cell-enriched translated proteins, the investigators identified PKHD1L1, a large, mostly extracellular protein. Using serial immunogold scanning electron microscopy, they showed that PKHD1L1 is expressed at the tips of stereocilia, especially in the high-frequency regions of the cochlea. PKHD1L1-deficient mice lacked the surface coat at the upper, but not lower, regions of stereocilia and developed progressive hearing loss. Therefore, the investigators concluded that PKHD1L1 is a component of the surface coat and is required for normal hearing in mice.

Wu X, Ivanchenko MV, Al Jandal H, Cicconet M, Indzhykulian AA, Corey DP. PKHD1L1 is a coat protein of hair-cell stereocilia and is required for normal hearing. Nat Commun. 2019 Aug 23;10(1):3801.

Research questions similarity of cochlear mechanics between mammals

Research led by **Hideko Heidi Nakajima, MD, PhD**, featuring **Stefan Raufer, PhD**, and **John J. Guinan, Jr., PhD**, of Mass. Eye and Ear/Harvard Medical School, reveals newly discovered mechanics in human hearing. Published in *PNAS*, the study calls into question the classic view that cochlear mechanics are similar in most mammals.

Basic properties of hearing, such as its sensitivity and frequency tuning, arise from the mechanical responses in the cochlea. Such responses have been measured extensively in the cochlear base of laboratory mammals. Our understanding of human cochlear mechanics is largely founded on the assumption that cochlear mechanics are similar in all mammals.

In this study, the researchers show that the anatomy and motion of the human cochlear partition differ in crucial ways from the generalized, classic view of mammalian cochlear mechanics. The results are important for understanding human hearing and comparing results from laboratory animals.

Raufer S, Guinan JJ Jr, Nakajima HH. Cochlear partition anatomy and motion in humans differ from the classic view of mammals. Proc Natl Acad Sci USA. 2019 Jul 9;116(28):13977–13982.

Allele-specific gene editing prevents deafness in a model of dominant progressive hearing loss

Genetic hearing loss can arise from either dominant or recessive mutations in more than one hundred genes. To explore strategies for overcoming the consequences of dominant hearing loss mutations, a team of scientists led by **Jeffrey R. Holt, PhD**, from Boston Children's Hospital/Harvard Medical School, explored gene editing using a novel CRISPR/Cas9 approach.

The team screened 14 unique combinations of guide RNAs and Cas9 enzymes to disrupt a dominant mutation, known as Beethoven, in the gene for Transmembrane channel-like 1 (Tmc1). They identified a Cas9 enzyme and guide RNA combination that selectively disrupted the Beethoven mutation but not the correct, healthy Tmc1 gene.

Dr. Holt and colleagues then used the approach in the ears of heterozygous mice who carried one copy of the Beethoven gene and one healthy Tmc1 gene. The approach silenced the Beethoven mutation, left the healthy gene intact, promoted survival of sensory hair cells, and prevented progressive hearing loss. Further analysis revealed that the same strategy could be used to target more than 20 percent of dominant mutations that cause inherited human disease, including 15 additional deafness mutations.

György B, Nist-Lund C, Pan B, Asai Y, Karavitaki KD, Kleinstiver BP, Garcia SP, Zaborowski MP, Solanes P, Spataro S, Schneider BL, Joung JK, Géléoc GSG, Holt JR, Corey DP. Allele-specific gene editing prevents deafness in a model of dominant progressive hearing loss. Nat Med. 2019 Jul;25(7):1123–1130. *corresponding author*

A novel otoprotectant against cisplatin-induced ototoxicity

Cisplatin chemotherapy can induce a permanent, irreversible hearing loss in cancer patients. This potential side effect is a major concern for patients, oncologists, and otolaryngologists because it necessitates changing treatment. To date, there are few options available to treat or reverse the hearing loss induced by cisplatin.

James G. Naples, MD, of Beth Israel Deaconess Medical Center/Harvard Medical School, has demonstrated in previous work that repurposing the cardiovascular therapy diltiazem as an intratympanic (IT) therapy in solution reduces auditory threshold shifts in murine and guinea pig models. His most recent work has further explored repurposing diltiazem, a calcium-channel blocker, for single IT dose administration in a chitosan glycerophosphate (CGP) hydrogel.

CGP-diltiazem hydrogel allows for a more consistent, prolonged delivery of the therapy. This work has confirmed reduced auditory thresholds in a murine model. New histological findings from this work suggest that diltiazem may offer protection from ototoxic effects at the level of the ribbon synapse. This has potential to offer a novel,

translatable, and readily accessible therapy to patients who experience cisplatin-induced hearing loss.

Naples JG, Ruckenstein MJ, Cox BC, et al. Intratympanic diltiazem-chitosan hydrogel as a novel otoprotectant against cisplatin-induced ototoxicity in a mouse model. Otology & Neurotology. Accepted for publication, July 2019.

Differences in how the brain processes body translation for perception and eye movements

When our heads translate through space, our eyes move in the opposite direction to keep gaze stable. However, to completely compensate for head movements, larger eye movements are needed when the eyes are fixating on an object closer to the head. Past studies have shown that the brain correctly performs this computation via the translational vestibulo-ocular reflex (VOR).

Since perception of motion shares many anatomic pathways with the VOR, a team led by **Faisal Karmali, PhD**, of Mass. Eye and Ear/Harvard Medical School, asked whether the same computations might also affect motion perception. They found that perception of translation did not scale with fixation distance, while the VOR did. Thus, despite shared neuroanatomical pathways, the brain processes signals appropriately for the respective functional constraints. Specifically, eye movements require a transformation from a linear coordinate system to the angular motion of the eye, whereas perception occurs in a linear coordinate system.

These findings further clarify our understanding of neural processing, highlighting that differences between perception and action arise from clear differences in functional goals.

King S, Benoit C, Bandealy N, Karmali F. The influence of target distance on perceptual self-motion thresholds and the vestibulo-ocular reflex during interaural translation. Prog Brain Res. 2019;248:197–208.

Clinical Practice

Cochlear implant listener experience is different for early-implanted children and late-implanted adults

Cochlear implant (CI) programming is similar for all CI users despite limited understanding of the electrode-neuron interface (ENI), or the ability of each CI electrode to effectively

stimulate target auditory neurons. Recognizing this, a team of investigators led by **Julie G. Arenberg, MS, PhD**, of Mass. Eye and Ear/Harvard Medical School, examined whether ENI quality differed between early-implanted children and late-implanted adults.

The team found that children exhibited lower average auditory perception thresholds and most comfortable levels (MCLs) compared to adults, particularly with focused stimulation. Lower detection levels suggest a higher density of neurons for the early-implanted children. However, neither dynamic range nor channel-to-channel threshold variability differed between groups, suggesting that children's range of perceptible current was shifted downward. Children also demonstrated increased intracochlear resistance levels relative to the adult group, possibly reflecting greater ossification or tissue growth after CI surgery.

These results illustrate physical and perceptual differences related to the ENI of early-implanted children compared with late-implanted adults. Evidence from this study demonstrates a need for further investigation of the ENI in CI users with varying hearing histories.

DiNino M, O'Brien G, Bierer SM, Jahn KN, Arenberg JG. The estimated electrode-neuron interface in cochlear implant listeners is different for early-implanted children and late-implanted adults. J Assoc Res Otolaryngol. 2019 Jun;20(3):291–303.

Dysphagia after treatment for advanced head and neck cancer

Dysphagia, or swallowing difficulties, is a frequent and debilitating symptom of radiotherapy-based treatments for head and neck cancer, including chemoradiotherapy (CRT). Although the true extent of this problem is unknown, it has been estimated that at least 50 percent of long-term head and neck cancer survivors treated with an organ preservation approach have troubles with swallowing.

A Mass. Eye and Ear/Harvard Medical School team including otolaryngology resident **Elliana Kirsh DeVore, MD**, **Matthew R. Naunheim, MD, MBA**, and **Mark A. Varvares, MD, FACS**, investigated the relationship between patient-reported and physiologic swallowing measures, including quality of life, after CRT for head and neck cancer.

The team reviewed adult patients who underwent CRT and presented for videofluoroscopic swallow studies. They showed that swallow function objectively worsened after CRT, but it did not correlate with patient-reported quality of life measures. The authors suggest that reduced patient awareness of swallow dysfunction years after completion of CRT has implications for management of dysphagia in the face of physiologic decline.

"This study demonstrates an important mismatch between patient-reported experience and objective data," states Dr. Naunheim. "It indicates that we have to pay close attention to survivors of head and neck cancer. Furthermore, it validates the notion that patient-reported outcome measures provide a complementary and useful set of information that does not always correlate with objective testing."

Kirsh E, Naunheim MR, Holman A, Kammer R, Varvares MA, Goldsmith T. Patient-reported versus physiologic swallowing outcomes in patients with head and neck cancer after chemoradiation. Laryngoscope. 2019 Sep;129(9):2059–2064.

Health utility values as an outcome measure in patients undergoing functional septorhinoplasty

Nasal obstruction is one of the most common presenting complaints of patients seen by otolaryngologists. Septorhinoplasties are one of the surgical options for these patients. By measuring health utility values (HUVs) after septorhinoplasty, the association of nasal congestion with overall health can be measured and the functional outcomes can be determined.

A team of surgeons from the Division of Facial Plastic and Reconstructive Surgery at Mass. Eye and Ear/Harvard Medical School, including **Robin W. Lindsay, MD**, and otolaryngology resident **Shekhar K. Gadkaree, MD**, reviewed 463 patients who underwent functional septorhinoplasty and completed the global quality of life survey, ED-5Q, before and after surgical correction of their nasal obstruction.[1] The global quality of life scores were

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converted to health utility values (HUVs) using population-based data for individuals with chronic diseases.

Through their analysis, the team demonstrated that nasal obstruction is associated with significant detriment to overall health, in line with other chronic conditions affecting the U.S. population. Overall mean preoperative HUV was 0.872 (0.01), compared to 1.00 for those with a perfect state of health. The lower HUV values for patients with a history of previous nasal surgery demonstrates the negative quality of life impact that failed nasal surgery has on patients and the importance of the correct diagnosis and treatment in primary septorhinoplasty.

Another team led by Dr. Lindsay and Dr. Gadkaree then analyzed data from 185 patients who had a history of previous nasal surgery and demonstrated that after functional septorhinoplasty, patients had an improvement in HUVs.[2] This suggests patients with a history of prior nasal surgery may represent a unique cohort when assessing health utility outcomes.

[1]Gadkaree SK, Fuller JC, Justicz NS, Weitzman RE, Derakhshan A, Mohan S, Lindsay RW. Health utility values as an outcome measure in patients undergoing functional septorhinoplasty. JAMA Facial Plast Surg. 2019 May 23.

[2]Gadkaree SK, Fuller JC, Justicz NS, Derakhshan A, Mohan S, Yu PK, Lindsay RW. A comparative health utility value analysis of outcomes for patients following septorhinoplasty with previous nasal surgery. JAMA Facial Plast Surg. 2019 Jun 13.

Pain may affect patient satisfaction after rhinoplasty

Cosmetic and functional rhinoplasties are outpatient surgical procedures that can lead to significant improvement in quality of life. In light of the current opioid epidemic, surgeons strive to balance successful surgical outcomes with responsible pain control after surgery. Facial plastic surgeons from Mass. Eye and Ear/Harvard Medical School, including **Linda N. Lee, MD, FACS**, **David A. Shaye, MD, MPH, FACS**, and otolaryngology resident **Shekhar K. Gadkaree, MD**, prospectively studied 104 rhinoplasty patients and examined how pain correlated with patient-reported cosmetic and functional outcomes.

Overall, this study showed that patients required minimal narcotics after rhinoplasty (an average of only five tablets). In purely functional rhinoplasty, the authors found a statistically significant inverse correlation between perception of pain and perception of functional outcome (P=.001). Patients who experienced less pain than expected self-reported an improved functional outcome. In contrast, patients who underwent rhinoplasty with simultaneous cosmetic changes had no correlation between pain and perception of cosmetic or functional success.

This study, published in *JAMA Facial Plastic Surgery*, is the first to evaluate the relationship between pain and patient satisfaction after rhinoplasty. It can be used to guide preoperative counseling to optimize patient outcomes after rhinoplasty.

Gadkaree SK, Shaye DA, Occhiogrosso J, Lee LN. Association between pain and patient satisfaction after rhinoplasty. JAMA Facial Plast Surg. 2019 Sept 19.

The proposed usage of intranasal steroids and antihistamines for otitis media with effusion

A recent invited article authored by **Rachel E. Roditi, MD**, **David S. Caradonna, MD**, and **Jennifer J. Shin, MD, SM**, of Harvard Medical School, reviewed the relationship between allergic rhinitis (AR) and otitis media with effusion (OME) and current treatment paradigms. An association between these disease states has been proposed and appears biologically feasible through a mechanism of eustachian tube dysfunction and allergic inflammation affecting the "unified airway." However, treatments typically offered for AR have not been effective in the treatment of OME in randomized controlled trials.

The authors reviewed the evidence for and against antihistamine and topical intranasal steroid use in the treatment of OME, and whether the treated OME occurred in isolation or concurrent with AR. Most of the literature does not support a benefit and adverse effects from therapy do exist. Therefore, current practice guidelines recommend against the use of antihistamines and topical intranasal steroid therapy for isolated OME. However, there is minimal data focusing specifically on the subgroup of patients with OME concurrent with intranasal problems such as congestion, allergy, or formally diagnosed adenoid hypertrophy.

From left to right: Drs. David Caradonna, Rachel Roditi, and Jennifer Shin.

The data suggest that further research into the specific subset of patients with OME and concomitant sinonasal symptoms would help us to more fully understand treatment effects and individualized recommendations for treating OME when it occurs concurrent with AR.

Roditi RE, Caradonna DS, Shin JJ. The proposed usage of intranasal steroids and antihistamines for otitis media with effusion. Curr Allergy Asthma Rep. 2019 Sep 5;19(10):47.

Gender disparities present in academic rank and leadership positions despite overall equivalence in research productivity

A team of investigators including **Gregory W. Randolph, MD, FACS, FACE**, of Mass. Eye and Ear/Harvard Medical School, examined potential disparities in scholarly performance based on gender, academic rank, leadership positions, and regional distribution of faculty in accredited head and neck surgery fellowships in the U.S.

The study looked at 37 accredited fellowships. A total of 732 faculty members were included in the study, 153 (21 percent) of which were female. Fifty-eight males (89.2 percent) held leadership positions, compared to only seven females (10.8 percent). There was no significant difference in overall productivity between male and female senior faculty. There were, however, regional differences in productivity by gender.

The authors concluded that females are underrepresented in senior faculty and within three common leadership positions. They also noted that scholarly productivity for male and female senior faculty and for those in leadership positions is similar.

Garstka ME, Randolph GW, Haddad AB, Nathan CO, Ibraheem K, Farag M, Deot N, Adib H, Hoof M, French K, Killackey MT, Kandil E. Gender disparities are present in academic rank and leadership positions despite overall equivalence in research productivity indices among senior members of American Head and Neck Society (AHNS) fellowship faculty. Head Neck. 2019 Nov;41(11):3818–3825.

Massachusetts Eye and Ear is top-ranked in the nation for otolaryngology care by *U.S. News & World Report.*

In a report released by *U.S. News & World Report* and the physician network Doximity, the Department of Otolaryngology–Head and Neck Surgery at Mass. Eye and Ear/ Massachusetts General Hospital was ranked #2 in the nation for otolaryngology care.

A note from our Alumni Association

We have undergone a reorganization and have big plans ahead. Keep an eye out for exciting alumni news online at: **oto.hms.harvard.edu/alumni**

Save the date! Join us Monday, September 14, at our alumni reception during the 2020 Academy Meeting. It will be held at the Liberty Hotel in Boston, MA. A formal invitation will be sent closer to the event.

HARVARD
Otolaryngology

News from the Harvard Medical School Department of Otolaryngology–Head and Neck Surgery
243 Charles Street, Boston, MA 02114

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Massachusetts Eye and Ear
Beth Israel Deaconess Medical Center
Boston Children's Hospital
Brigham and Women's Hospital
Massachusetts General Hospital