

NEWS FROM THE DEPARTMENT OF OTOLARYNGOLOGY AT HARVARD MEDICAL SCHOOL

HARVARD

Otolaryngology



3-D

Three-Dimensional Printing

How 3-D printing
is revolutionizing
the field of
otolaryngology

HARVARD Otolaryngology

News from the Department of Otolaryngology at Harvard Medical School

Spring 2016 ■ Vol. 13, No. 1
Published twice per year.

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Dear colleagues and friends,

Innovation plays a significant role in our field. Without it, advances in research, medicine, and patient care would not be possible. The passion we find in our physicians and researchers drives this continuous dialogue that is asking questions and finding answers to the unsolved problems in otolaryngology.

Over the years, we have seen significant advancements in technology. Cochlear implants and robotic surgery to name two. These advancements have shown us that achieving the once impossible becomes possible—then the possible a reality. As physicians, we have a promise to deliver expert and effective clinical care. By seeking to ask the right questions and focusing on the future of medicine and our patients, we are striving to fulfill that promise.

An example of innovation is three-dimensional (3-D) printing, which has become an exciting new tool in medicine, and especially in otolaryngology. Today, our physicians in the Harvard Medical School Department of Otolaryngology are using 3-D printing for cancer resections, creating implantable eardrums, training our residents, among other uses. In our cover story starting on page 10, we delve into some of the different applications of 3-D printing and the significant present and potential impact they are having on our residents, physicians, researchers, and patients.

In this issue, we're excited to share with you some of our recent technological advances and the role they are playing in improving patient care. As you read through the pages of our Spring issue, I hope you connect with the many ways that otolaryngology physicians and researchers at Harvard Medical School are contributing to our shared success through exceptional clinical care, research, and teaching advancements.

Thank you for your interest in and support of the Department's activities.

Sincerely,

D. Bradley Welling, M.D., Ph.D., FACS

*Walter Augustus LeCompte Professor and Chair
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*Chief of Otolaryngology
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Jeffrey R. Holt, Ph.D., and Dennis S. Poe, M.D., Ph.D.,

Promoted to Professors of Otolaryngology at Harvard Medical School



Middle photo: Drs. Gwenaelle Géléoc, Michael Cunningham, and Jeffrey Holt

Bottom photo: Dr. Jeffrey Holt with his wife and research collaborator, Dr. Gwenaelle Géléoc, his father, David Holt, and Drs. Brad Welling, Clifford Woolf, Michael Cunningham, and Scott Pomeroy



The Department recently celebrated the promotion of Jeffrey R. Holt, Ph.D., Director of Research in the Department of Otolaryngology and Communication Enhancement at Boston Children's Hospital, to Professor of Otolaryngology at Harvard Medical School.

A pioneering neuroscientist and researcher, Dr. Holt joined the faculty in the Harvard Medical School Department of Otolaryngology in 2011 and has been making substantial contributions in the area of gene therapy for hearing loss since.

Dr. Holt completed his undergraduate training in biology at Wofford College in 1986 prior to studying at the University of Rochester School of Medicine, where he received his master's degree in physiology in 1992 and doctorate degree in physiology in 1995, as a student with Ruth Anne Eatock, Ph.D. He completed a postdoctoral fellowship at the Howard Hughes Medical Institute at Harvard Medical School in 1999. There, he was mentored by David Corey, Ph.D., who sparked his interest in understanding how sensory cells of the ear convert a mechanical stimulus into an electrical signal.

Identifying genes and proteins necessary for normal inner ear function and determining why mutations in these genes cause hearing loss and vestibular disorders is what Dr. Holt has focused on throughout his career. Ultimately, he hopes to enhance the understanding of basic biology of the inner ear and to translate discoveries into clinical therapies designed to treat hearing and balance disorders.

Dr. Holt is one of two principal investigators for the Holt/Géléoc Lab, in the F.M. Kirby Neurobiology Center at Boston Children's Hospital, which focuses on the physiology and molecular substrates of inner ear function and dysfunction. Under the leadership of Dr. Holt and his long-term collaborator, Gwenaelle S. Géléoc, Ph.D., the lab identified TMC1 and TMC2—key molecules required for auditory processing—as components of the hair cell transduction channel. The lab has also successfully restored hearing in deaf mice using gene therapy techniques, which has the potential to lead to gene therapy for individuals with hearing loss caused by genetic mutations.

Teaching and mentoring students and postdoctoral trainees has also been a significant part of Dr. Holt's tenure. Aiming to instill enthusiasm and passion for science in his students, Dr. Holt has helped all of his trainees yield first author publications and has guided them into the flourishing careers they have today.

"Dr. Holt's contributions to hearing and balance function restoration have been highly significant to our field," said D. Bradley Welling, M.D., Ph.D., FACS, the Walter Augustus LeCompte Chair of Otolaryngology at Harvard Medical School. "Dr. Holt has made impressive advances in these areas that will change the way we treat our patients. I am certain that his work will lead to many novel treatments being made possible." ●



The Department recently celebrated the promotion of Dennis S. Poe, M.D., Ph.D., neurotologic surgeon in the Department of Otolaryngology and Communication Enhancement at Boston Children’s Hospital, to Professor of Otolaryngology at Harvard Medical School.

Dr. Poe first joined Harvard Medical School as a part-time Assistant Professor of Otolaryngology in 1996. He completed his undergraduate degree in bioengineering in 1978 from Syracuse University and earned his medical degree in 1982 from the State University of New York Upstate Medical Center. In 2011, Dr. Poe received his Ph.D. in pathophysiology and surgical treatment of the Eustachian tube from Tampere University of Technology in Finland. Having been trained in both bioengineering and medicine, Dr. Poe has married the two disciplines to create technological solutions to problems in otolaryngology throughout his career.

Dr. Poe was drawn to a career in medicine by the opportunity to not only treat patients, but to find permanent fixes to the problems they face. Dr. Poe has always been committed to spending time with his patients and doing the appropriate fieldwork to provide them with the best care possible.

Early on, Dr. Poe’s research contributions consisted of developing minimally invasive endoscopic surgery techniques, of which he was among one of the first to present the use of in 1992. This work was instrumental in learning more about diagnostic analysis, allowing physicians to identify what problems were in the middle ear.

More recently, he has worked on investigating the functional anatomy and pathophysiology of the Eustachian tube (ET) to help create new surgical procedures for treatment. As a result of his discoveries, Dr. Poe’s clinical practice has increasingly evolved into caring for patients with challenging chronic middle ear and mastoid disease in both children and adults.

As a leader in his field, Dr. Poe strives to ensure that the development of techniques and training in ET surgery continues to advance. In his efforts to accomplish this, Dr. Poe has left a lasting footprint around the globe. He has traveled nationally and internationally to share his expertise, teach his techniques, and work with field leaders to help shape the future of ET surgery. Additionally, Dr. Poe has organized an International ET Study Group and has hosted a number of international fellows.

“It is because of physicians like Dr. Poe that our field is able to make such great advancements, both nationally and internationally,” said D. Bradley Welling, M.D., Ph.D., FACS, the Walter Augustus LeCompte Chair of Otolaryngology at Harvard Medical School. “From his clinical skills to the innovative aspects of his research to his thoughtful teaching approaches, he has become the world leader in Eustachian tube dysfunction and we couldn’t be more proud of his work.” ●

Middle photo: Dr. Dennis Poe with Dr. Michael Cunningham

Right photo: Dr. Dennis Poe with Dr. Brad Welling

Boston Children's Hospital

Names Two Endowed Chairs

Dr. Margaret Kenna with her mother, Joan G. Kenna



Last fall, family and friends gathered to celebrate the accomplishments of two of Boston Children's Hospital's most treasured faculty as they were honored with newly established endowed chairs.

Margaret A. Kenna, M.D., MPH, FACS, FAAP

Margaret (Marly) A. Kenna, M.D., MPH, FACS, FAAP, Director of Clinical Research for the Department of Otolaryngology and Communication Enhancement at Boston Children's Hospital, is the inaugural recipient of the Sarah Fuller Chair for Hearing Loss and Hearing Restoration. This honor recognizes more than three decades of dedication and contributions to the field of pediatric otolaryngology. In 2008, Dr. Kenna was named the first female Professor of Otolaryngology at Harvard Medical School.

The Chair, which is funded by the generosity of the Sarah Fuller Foundation, also honors the legacy of Sarah Fuller, who was a pioneer in caring for children with hearing loss.

When Dr. Kenna first joined the department in 1995, she saw an unfilled need for expanded services for children who are deaf and hard of hearing, leading her to co-found and direct the Boston Children's Hospital Pediatric Cochlear Implant Program. This program gives children the tools they need to develop language and to learn to communicate effectively. Under Dr. Kenna's leadership, the program was initiated and has grown into one of the largest and most comprehensive pediatric programs of its kind in New England.

In 2003, Dr. Kenna assumed directorship of the Otolaryngology Clinical Research program at Boston Children's Hospital and has dedicated much of her time to her long-standing interest in genetic hearing loss research. Most recently, her work has demonstrated that the diagnosis of Usher syndrome, a deaf-blind-vestibular dysfunction syndrome, can be made in early infancy by using genetic testing and specific ophthalmologic measures.

One of Dr. Kenna's goals is to identify the cause of hearing loss in all of her patients. A definitive diagnosis provides both information about prognosis and management, as well as a bridge to potential therapeutic interventions. With the support from this Chair, Dr. Kenna hopes to establish a Center for Hearing Loss and Hearing Restoration at Boston Children's Hospital that would aim to achieve this goal.

"The Sarah Fuller Foundation was established to honor Sarah Fuller, stating that she was 'an advocate of integration and assimilation, treating the deaf children not as handicapped, but as those who communicated in a slightly different manner,'" said Michael J. Cunningham, M.D., FACS, Otolaryngologist-in-Chief and the Gerald B. Healy Chair in Pediatric Otolaryngology at Boston Children's Hospital. "Given this description, there is no one more appropriate than Dr. Kenna to be the inaugural recipient of this Chair as this has been the focus of Dr. Kenna's career." ●

Howard C. Shane, Ph.D.

Howard C. Shane, Ph.D., Director of the Center for Communication Enhancement at Boston Children's Hospital and Associate Professor of Otolaryngology at Harvard Medical School, has been named the inaugural recipient of the Center for Communication Enhancement Directorship Chair.

It was Dr. Shane's first job out of college that led him to discover his interest in speech and communication technology. He designed a communication device for children with cerebral palsy in 1969 and joined the Boston Children's Hospital Department of Otolaryngology and Communication Enhancement in 1977 to continue this line of work. Now, Dr. Shane is known internationally for his work in creating procedures and technologies for persons with complex communication disorders.

As Director of the Center for Communication Enhancement, Dr. Shane oversees the clinical and research operations of six programs housed within the center, which is dedicated to providing evaluation, consultative, and therapeutic services to patients who experience difficulties associated with communication. Under his leadership, Dr. Shane has been responsible for taking each of the six programs and turning them into multi-faceted, extensive services that are changing the lives of countless families. Additionally, under his direction, faculty from these programs are teaching the next generation of clinicians and frequently contributing to research literature.

As the Center continues to grow, Dr. Shane says that it is their obligation to stay current with state-of-the-art technologies and maintain the high standard of excellence they have accomplished. The Center's reach already goes beyond what happens within its physical location, and with this directorship, Dr. Shane is eager to see how far that reach can go.

This endowed Chair, funded by the Boston Children's Hospital Otolaryngologic Foundation, recognizes Dr. Shane's lifetime achievements at the hospital, honoring the work he has done and the work he will do for the organization in years to come. To further acknowledge his contributions, the Chair will be named for him in future years to help support his successors.

"When speaking of 'the integration and assimilation' of children into society, if we change the deficit from hearing to speech, it readily brings us to Dr. Shane," said Michael J. Cunningham, M.D., FACS, Otolaryngologist-in-Chief and the Gerald B. Healy Chair in Pediatric Otolaryngology at Boston Children's Hospital. "Whether it be wheelchair mounted computers, finger-touch computer screens, voice banking prior to a procedure that takes away a child's ability to speak, or computer software applications, Dr. Shane has enabled thousands of children to communicate with the world around them." ●



Top photo: Drs. Michael Cunningham, Margaret Kenna, and Howard Shane

Bottom photo: Dr. Howard Shane with his wife, Kathryn Shane



Inner Ear Drug Delivery Device

Researchers develop device that may improve preclinical testing of hearing restoration therapies

Affecting approximately 15 percent of adults in the United States, hearing loss has become one of the most common health problems in America. Auditory abilities have functional significance to our daily lives, so for many, a loss of hearing comes with a loss of quality of life—often leading to a higher chance of developing a psychological disorder and creating difficulties communicating, focusing, and making decisions.

While researchers are developing drugs capable of treating hearing loss, they often encounter difficulty demonstrating preclinical efficacy. Anatomical barriers within the inner ear, including the blood-cochlea barrier, make administration of drugs challenging and affect how efficiently these drugs reach their targets. This causes uncertainty regarding concentration of the medication at the intended delivery site and makes it hard to prove that the drug is responsible for any observed changes in hearing.

Researchers from Massachusetts Eye and Ear and Draper, a non-profit research and development company in Cambridge, Mass., are working to address these challenges. The collaborative efforts of the two institutions have led to the development of a device capable of delivering drugs directly to the cochlea—a structure that is difficult to reach with injections and systemic drug delivery.

“Unfortunately, drug delivery to the inner ear is not just as simple as popping a drug into the ear to get things to regenerate,” said Michael J. McKenna, M.D., Director of Otology and Neurotology at Mass. Eye and Ear and Professor of Otolaryngology at Harvard Medical School. “It requires a timed sequence of drugs, so we wanted to develop a device capable of getting drugs directly into the ear in a controlled manner.”

A new means of drug delivery to the inner ear

The inner ear is a small, protected space, which makes targeting the area difficult. As a result, drugs that treat hearing loss rely on indirect delivery methods to the inner ear and often require repeat administrations. Commonly used methods, such as oral delivery, may lead to undesirable, systemic side effects, and provide little control over the duration of drug delivery. Intratympanic injections, which are also regularly used, provide local access, but not all drugs can be delivered this way.

The intracochlear drug delivery device uses microfluidics technology to deliver the drugs directly into the cochlea. With direct delivery, the drug is able to bypass barriers and minimize systemic toxicity, which may eliminate many of the issues that can keep a patient from staying the course of their treatment. Overall, this technology is capable of increasing dosing precision, and can also be used to help determine drug concentration via its direct link to the cochlea.

“Ultimately, this device should be useful for delivering drugs where and when they are needed, in a concentration where they can be effective, and without unwanted systemic side effects,” said Sharon G. Kujawa, Ph.D., Director of Audiology Research at Mass. Eye and Ear and Associate Professor of Otolaryngology at Harvard Medical School.

The device will be surgically implanted behind the ear and will deliver precise quantities of one or more drugs in an automated, timed sequence directly into the fluid of the inner ear.

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— Dr. McKenna



| Inner Ear Drug Delivery Device | continued

Since the inner ear is sensitive to alterations in pressure and fluid volume, the device has been designed to keep the volume of the inner ear fluid constant while mixing in the drug. Its reciprocating delivery cycle ensures that there is no net gain of fluid to the ear and increases the treatment's safety and efficacy.

“One of the things that makes this device completely unique is the fact that it has what we call a zero-net volume delivery,” said Jeffrey T. Borenstein, Ph.D., the principal investigator for the intracochlear drug delivery device at Draper. “Over time, this process effectively distributes drugs through the inner ear in a manner that doesn't overpressurize the ear or cause any undue damage.”

This device can also be used to sample drug concentrations in the cochlea, a key step toward securing approval from the U.S. Food and Drug Administration (FDA).

“Hearing loss drugs hold the potential to restore the natural sense of hearing, but preclinical measurements of drug concentrations in the inner ear will be critical

in demonstrating that the drug is responsible for observed hearing changes prior to human trials,” said Dr. Borenstein.

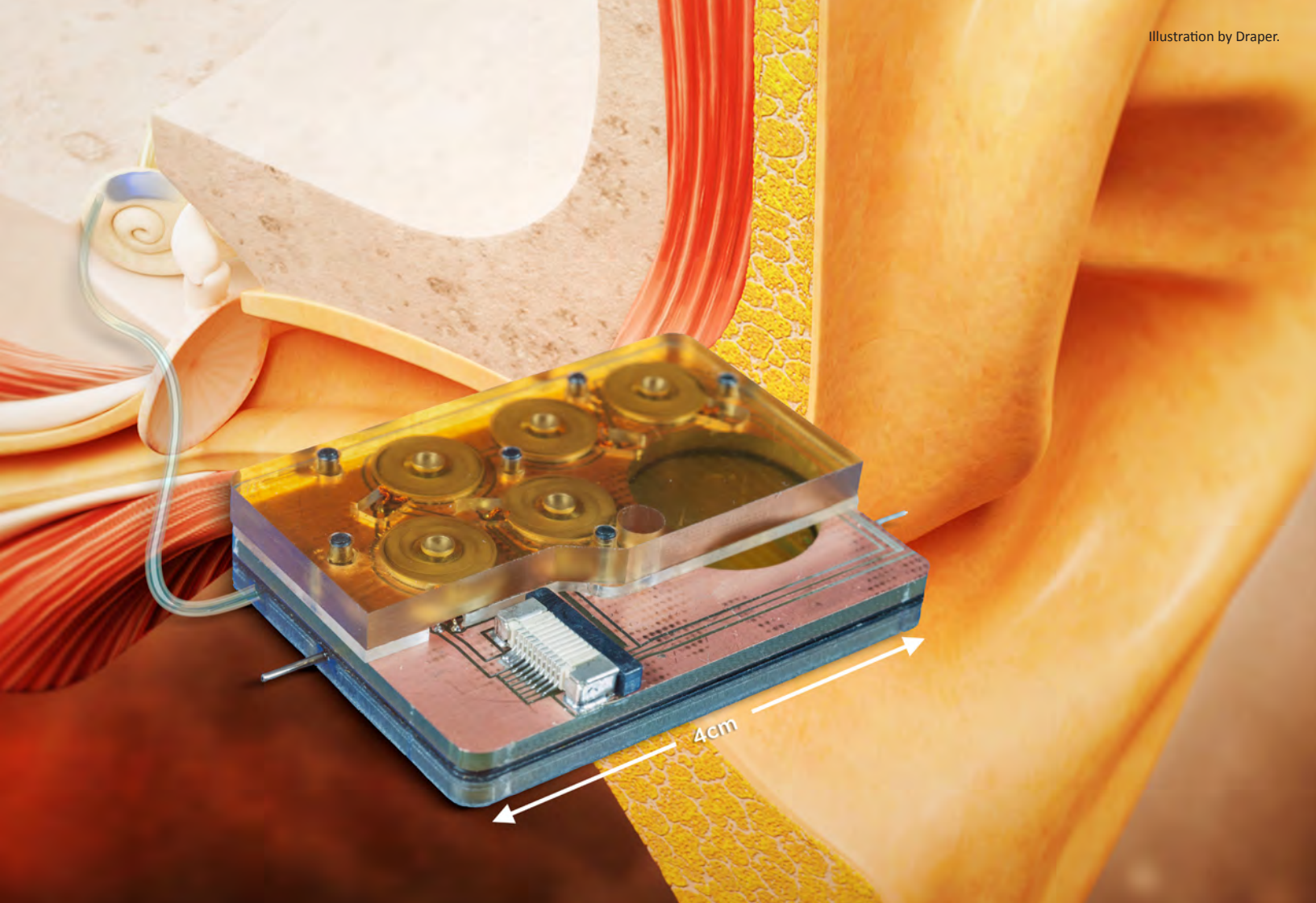
A promising future

William F. Sewell, Ph.D., another investigator from the Mass. Eye and Ear team and Professor of Otolaryngology at Harvard Medical School, has directed studies that successfully demonstrate the device's safety and efficacy in guinea pigs. During recent testing, Dr. Sewell and the research team addressed several microfluidic challenges, including maintaining controlled drug delivery at safe, low flow rates without increasing the volume of fluid in the cochlea. This work was recently published in the peer-reviewed journal *Lab on a Chip*.

Next steps for the project include improving confidence in results from preclinical trials, miniaturization of the device, and development of a version for human therapy.

Dr. Jeffrey Borenstein discussing the intracochlear drug delivery device with Drs. Michael McKenna and Erin Leary Pararas.





“With the local, intracochlear delivery provided by this device, it should be possible to take advantage of present and future breakthroughs in hearing loss treatment and prevention, with the potential to benefit our patients with hearing loss.”

— Dr. Kujawa



The goal for this device is to produce a long-term implantable and wearable delivery system that can help treat sensorineural hearing loss and degenerative inner ear disorders. In addition to long-term treatment of hearing loss, this system also has the potential for use in clinical and preclinical trials of drugs.

“With the local, intracochlear delivery provided by this device, it should be possible to take advantage of present and future breakthroughs in hearing loss treatment and prevention, with the potential to benefit our patients with hearing loss,” said Dr. Kujawa.

Eventually, researchers believe that this technology has the ability to become a platform that could open new

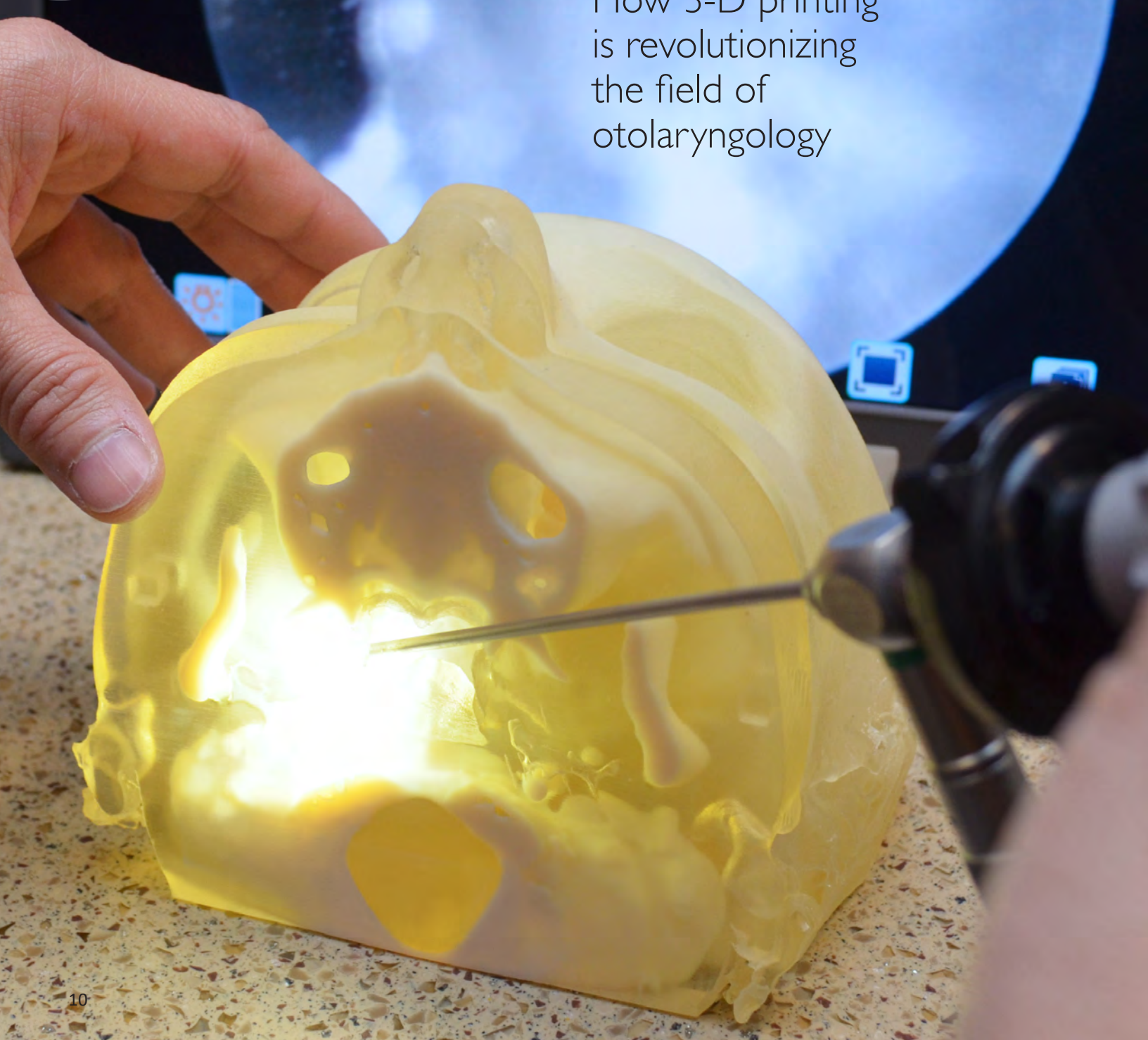
doors and solve a variety of problems in the future.

“What we ultimately would like to do with this device is to restore hearing in people who have lost hearing and to prevent hearing loss in people who are losing their hearing,” said Dr. McKenna. ●

The National Institutes of Health (NIH) is funding the project through a Bioengineering Research Partnership (BRP) grant to Draper from its National Institute on Deafness and Other Communication Disorders (NIDCD). The BRP funding mechanism is intended to bring together engineers and clinicians to solve important healthcare challenges, enabling Draper to form the collaboration with Mass. Eye and Ear to pursue these goals.

3-D Three-Dimensional Printing

How 3-D printing is revolutionizing the field of otolaryngology



It was the 1980s when Charles Hull created the first functional three-dimensional (3-D) printer, and, since then, industries of all kinds have been finding their own applications for it. For the medical industry, 3-D printing has become a means of life-saving and life-altering potential. Prior to 3-D printing, there were fewer options for training and preparation purposes. Now, physicians can take a CT scan or MRI and turn it into a complex, anatomically accurate model that looks and feels like the real thing in a matter of hours.

Throughout the Department of Otolaryngology at Harvard Medical School, 3-D printing is becoming integrated into daily practices—helping to train physicians, preparing surgeons for various procedures, and opening new doors for researchers. The emerging applications of 3-D printers in otolaryngology include surgical anatomic education, personalized preoperative planning for surgical procedures, and more recently, the design and manufacture of novel patient specific implantable devices.

“Three-dimensional printing is really important,” said Dennis S. Poe, M.D., Ph.D., Professor of Otolaryngology at Harvard Medical School and neurotologic surgeon in the Department of Otolaryngology and Communication Enhancement at Boston Children’s Hospital. “There are so many applications for 3-D printing in otolaryngology alone. It’s great because, no matter how you are using it, you get to learn a tremendous amount from it.”

3-D printing in surgical education

Using 3-D printing for educational purposes gives physicians and residents the opportunity to improve their skills before entering the operating room. They have a chance to learn about a patient’s anatomy and practice in an environment that allows for mistakes.

“Three-dimensional models are about making mistakes,” said Dr. Poe. “It is what they are designed to do. We put the trainees in situations that will challenge them and stress them. If they make an error, they can review it and learn from it. It’s something that will stick with them and it’s unlikely for that mistake to happen again.”

On a yearly basis, Dr. Poe teams up with Ralph B. Metson, M.D., Professor of Otolaryngology, part-time at Harvard Medical School, for a three-day endoscopic surgical training course, which uses 3-D models of the nasal sinuses and temporal bones.

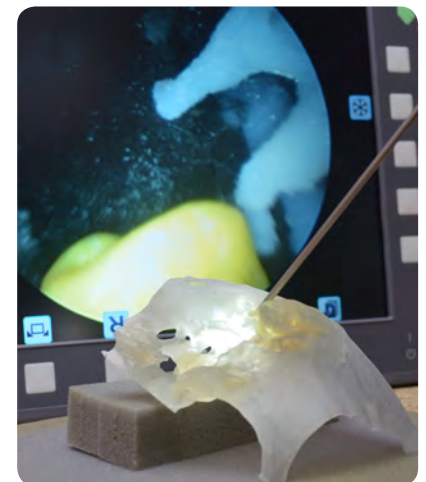
Practicing on these models gives trainees the opportunity to gain a better understanding of the framework of the nose, sinuses, and temporal bones while performing various procedures on them. Among these procedures, they focus on the treatment of Eustachian tube dysfunction, using the models to perform balloon dilations. They also introduce trainees to leading-edge technologies for endoscopic ear surgery and allow them to practice these techniques on the models.



“Three-dimensional models are about making mistakes. It is what they are designed to do.”

—Dr. Poe

Dr. Dennis Poe demonstrates how course participants can practice their endoscopic skills on nose and sinus simulation models. This model is a 3-D print of a patient with Eustachian tube dysfunction and gives participants the opportunity to practice accessing the sinuses and Eustachian tube as well as practice surgical techniques.



This is a temporal bone simulation model, which is a 3-D print of a patient with an abnormality of the inner ear, superior semicircular canal dehiscence, intended for participants to practice a challenging surgical approach through the mastoid.

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“With the 3-D prints, trainees can open them up and see how the sinuses relate to each other. We haven’t always been able to do this, so it’s a new level of learning for them.”

— Dr. Volk



“As the course progresses, trainees are put into harder and harder scenarios using these models,” said Dr. Poe. “From this, they really are practicing all of the same skills that they would in the operating room.”

Mark S. Volk, M.D., D.M.D., Assistant Professor of Otolaryngology at Harvard Medical School and Associate Surgeon in the Department of Otolaryngology and Communication Enhancement at Boston Children’s Hospital, also teaches a course on sinus surgery using 3-D models. This annual course has trainees perform a simulated decompression of a periorbital abscess on the 3-D prints.

Using the models and the appropriate instruments, they practice going through the small confines of the nose and sinuses. There is nothing else available that gives the type of detail and flexibility that these 3-D models can, so the trainees are given an accurate representation of the sinuses to learn from.

“Sinus anatomy is a little bit difficult in the beginning,” said Dr. Volk. “With the 3-D prints, trainees can

open them up and see how the sinuses relate to each other. We haven’t always been able to do this, so it’s a new level of learning for them.”

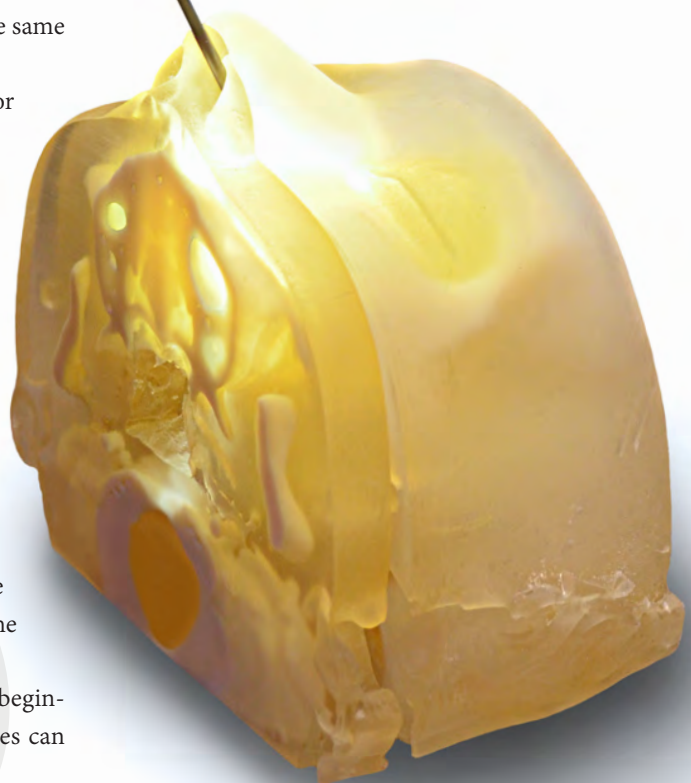
3-D printing in preoperative surgical planning

The level of personalized care achieved through 3-D printing has been influential in increasing accuracy and efficiency in procedures, cutting down operating room time, and improving surgical outcomes.

Working with patients who have cancer or radiation damage involving the mandible, Donald J. Annino, Jr., M.D., D.M.D., and Laura Ann Goguen, M.D., use 3-D models to help prepare for and implement their surgical resections and reconstructions at Brigham and Women’s Hospital.

“We use 3-D models for two reasons,” said Dr. Annino, Assistant Professor of Otolaryngology at Harvard Medical School. “We use it to help plan where we will make our bone cuts around the cancer and we also use it to help streamline and optimize the reconstruction.”

It starts with a CT scan that is turned into a 3-D image of the patient’s face. With this image, Dr. Annino and Dr. Goguen, Associate Professor of Otolaryngology at Harvard





Mass. Eye and Ear residents practicing sinus surgery on 3-D sinus models.

Medical School, determine where the bone cuts around the cancer will be and at what angles. Cutting guides, for intraoperative use, are then fashioned using 3-D printing.

Often times, there is a need to take part of the patient’s fibula to create a new jawbone and 3-D imaging is used to determine where fibula osteotomies will be. Additionally, it creates cutting guides for the fibula, which optimizes the bony contacts between the fibula and the native mandible.

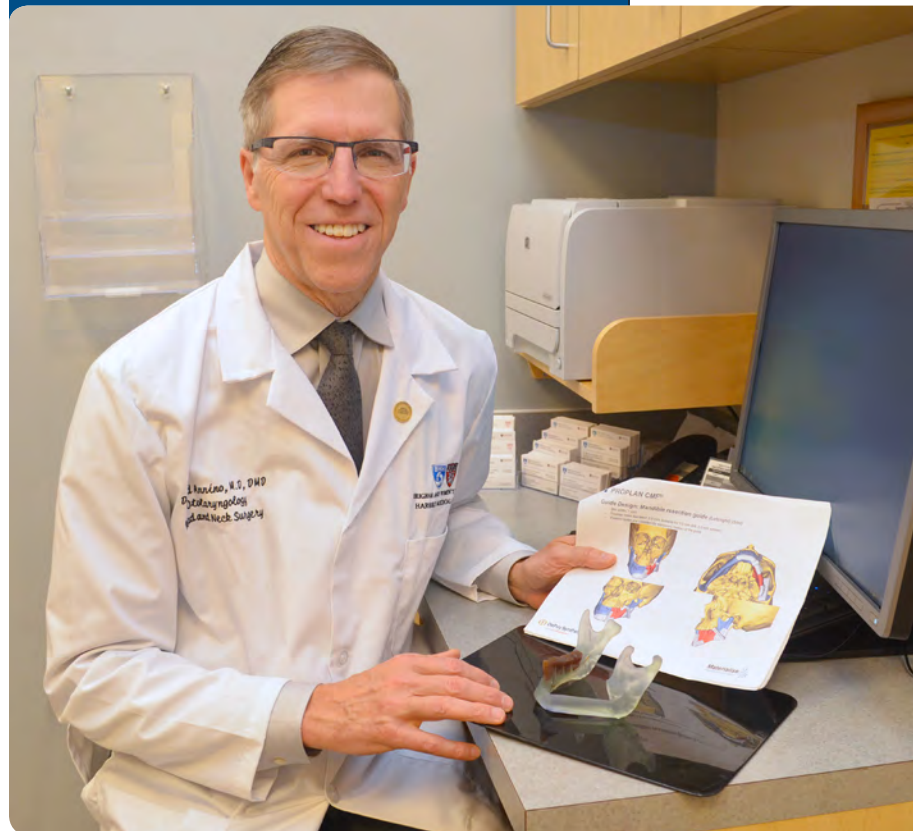
Once all of the cuts have been mapped out, the 3-D model is printed. These models are used to bend a titanium plate customized to the patient’s native mandible, which is implanted during surgery. In some instances, the models are also shared with patients to give them a better understanding of what the surgery will look like.

Improved cosmetic outcomes have been another advantage to 3-D printing. Patients who have mandibles that are excessively deformed are now able to achieve a result that is much more symmetric than before. Dr. Annino and Dr. Goguen use the 3-D images to take the opposite side of the mandible, invert it, and make it an exact mirror image of the other side of the jaw.

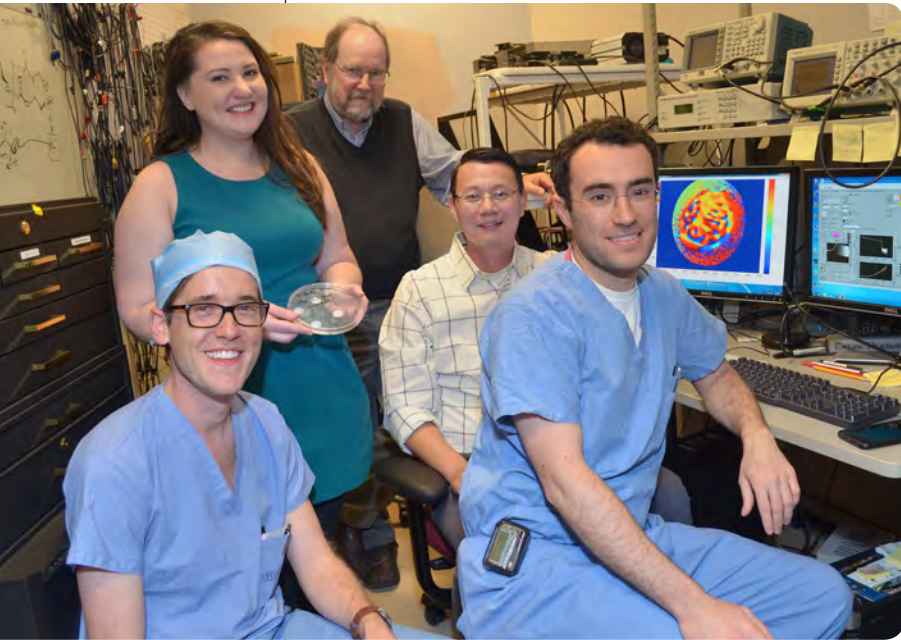
“For me, using 3-D models is the only way I will perform cancer resections and reconstructions of the mandible,” said Dr. Annino. “From a point-of-view of bone reconstruction anywhere in the head and neck region, using 3-D models is going to become the standard way to go.”

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“For me, using 3-D models is the only way I will perform cancer resections and reconstructions of the mandible.”
—Dr. Annino



Dr. Donald Annino with one of the 3-D printed mandibles



From left to right: Dr. Aaron Remenschneider, Nicole Black, Dr. John Rosowski, Dr. Jeffrey Tao Cheng, and Dr. Elliott Kozin

3-D printing for design and manufacture of implantable devices

Advances in 3-D printing now allow for the creation of biocompatible structures with impressive complexity. Knowing this, Massachusetts Eye and Ear/Harvard Medical School Otolaryngology/Neurotology Clinical Fellow Aaron K. Remenschneider, M.D., MPH, and Mass. Eye and Ear/Harvard Medical School Otolaryngology Resident Elliott D. Kozin, M.D., have begun exploring the feasibility of printing a multimaterial biomimetic tympanic membrane (TM) graft that could be implanted into a patient. Their goal is to overcome the

limitations of current graft materials to improve the outcomes following the surgical reconstruction of the eardrum, a procedure known as tympanoplasty.

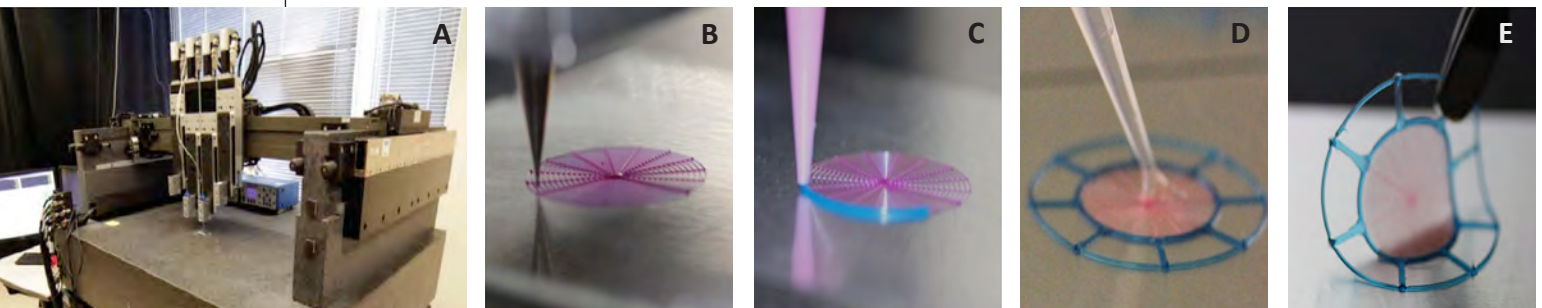
“Right now physicians must use imperfect materials for TM grafts,” said Dr. Remenschneider. “Unfortunately, these grafts fail in a subset of patients. Many individuals don’t obtain a good hearing result or are left with recurrent infections—so the surgery has to be repeated. If we could design a graft material from the ground up, and include optimized features, this would be a huge step forward. I think 3-D printing may now offer the means to produce such a graft.”

Currently, physicians use materials such as temporalis fascia, perichondrium, and cartilage for TM grafts. The problem with these materials is they do not possess similar structural features as the native TM, and this can leave the patient susceptible to chronic otitis media, a long-standing infection of the middle ear.

Working with Jennifer A. Lewis, Sc.D., and Nicole Black, MS, at the Wyss Institute for Biologically Inspired Engineering, Dr. Remenschneider and Dr. Kozin have also teamed up with experts in middle ear mechanics from Mass. Eye and Ear, including John J. Rosowski, Ph.D., and Jeffrey Tao Cheng, Ph.D. As a cross-disciplinary group, they have successfully demonstrated how 3-D printers can fabricate biomimetic TM grafts.

“Right now physicians must use imperfect materials for TM grafts. If we could design a graft material from the ground up, and include optimized features, this would be a huge step forward. I think 3-D printing may now offer the means to produce such a graft.”

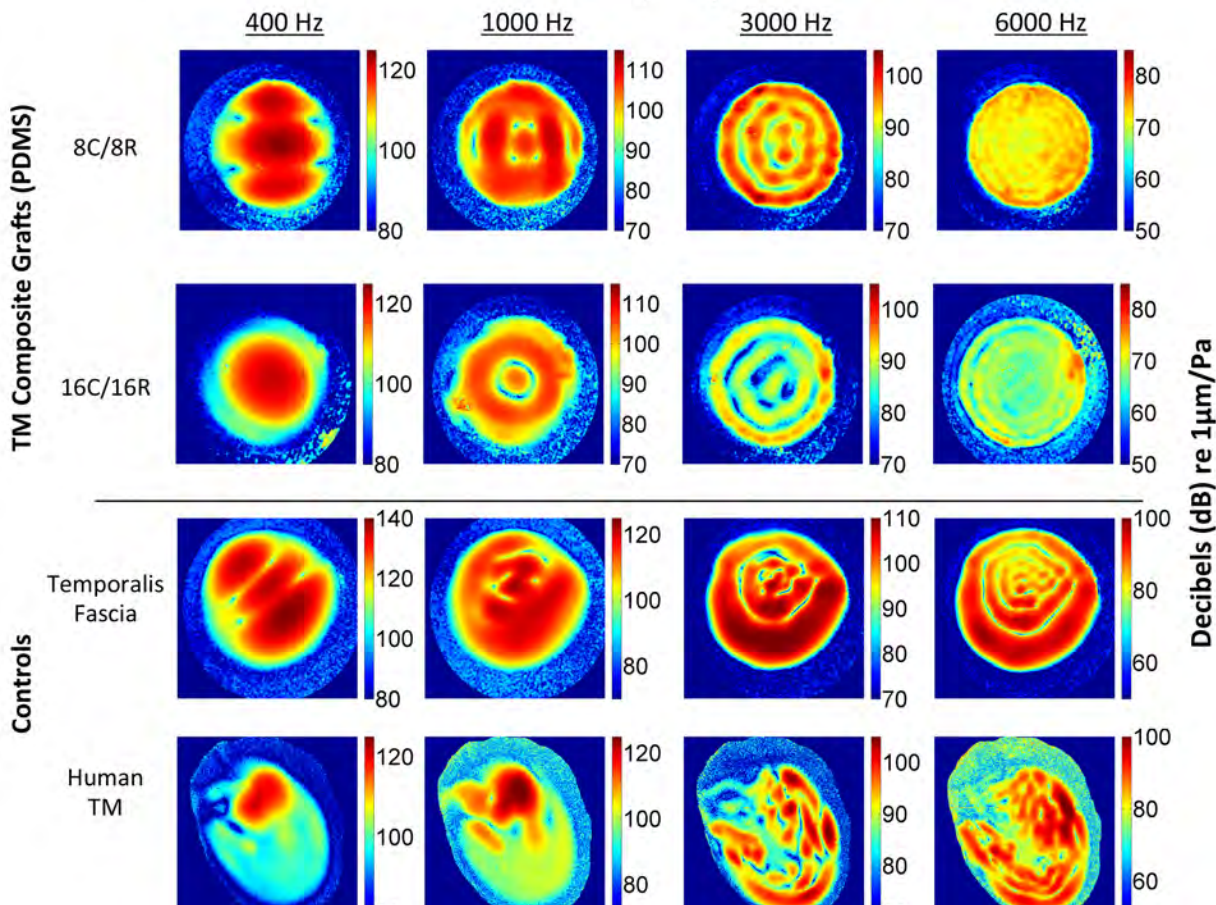
—Dr. Remenschneider



3-D printing of tympanic membrane composite grafts. (A) Multi-material 3-D printing apparatus. (B) Layered circumferential and radial filaments are printed first using a 100 μm nozzle. (C) The same material (with blue colorant) is then printed to create the outer border region. (D) The printed and cured scaffold is then infilled with 100 μL of fibrin/collagen hydrogel matrix. (E) Final composite graft with fibrin/collagen matrix.

Kozin ED, Black NL, Cheng JT, Cotler MJ, McKenna MJ, Lee DJ, Lewis JA, Rosowski JJ, Remenschneider AK. Design, fabrication and in vitro testing of novel three-dimensionally printed tympanic membrane grafts. *Hearing Research*. 2016 Mar 16.

Acoustically Driven Motion Patterns of 3-D Printed Tympanic Membrane Grafts



Digital opto-electronic holography (DOEH) fringe patterns of 3-D printed PDMS-based tympanic membrane composite grafts, human fascia, and tympanic membrane controls. Top row shows the displacement patterns of the visible 9 mm diameter section of an 8C/8R PDMS graft, the second row a 16C/16R PDMS graft, the third row a sheet of fresh human temporalis fascia, and the fourth row a human TM with intact middle ear. The four columns show displacement measurements at different frequencies. Similar to the human TM, TM grafts exhibit simple surface motion patterns at lower frequencies (400 Hz), with a limited number of displacement maxima. At higher frequencies (>1000 Hz), their displacement patterns are highly organized with multiple areas of maximal displacement separated by regions of minimal displacement. Small differences in displacement magnitude are measurable between grafts of varying fiber count. Temporalis fascia exhibited asymmetric and less regular holographic patterns.

Kozin ED, Black NL, Cheng JT, Cotler MJ, McKenna MJ, Lee DJ, Lewis JA, Rosowski JJ, Remenschneider AK. Design, fabrication and in vitro testing of novel three-dimensionally printed tympanic membrane grafts. *Hearing Research*. 2016 Mar 16.

Using non-absorbable materials, as well as biologics, such as collagen and fibrin, they have created tympanic membrane grafts with acoustic properties that can be tuned to reflect the sound induced motion patterns of the human TM. In addition, they found that 3-D printed grafts can be reliably produced and have structural features that are more consistent than temporalis fascia. Such grafts have promising implications for clinical applications. Their work was recently published in the journal *Hearing Research* and the team has presented their findings at several national and international meetings, including the Association for Research in Otolaryngology and Symposium on Middle Ear Mechanics in Research and Otology.

Recently, Dr. Remenschneider and Dr. Kozin began implanting the 3-D printed biomimetic TM grafts in an animal model. They hope to further understand how

effectively the grafts function in sound transmission and to determine whether the materials used have any harmful effects.

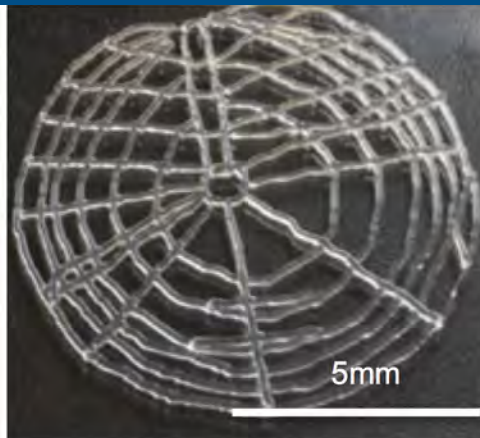
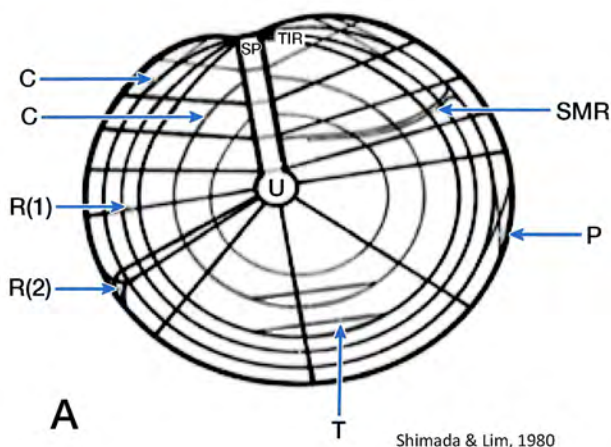
“In addition to creating a prosthetic TM for clinical use, 3-D printing offers a method to explore the structural significance of the tympanic membrane and middle ear. Important experiments that were not previously possible, can now be performed,” said Dr. Remenschneider. “Until now, we haven’t been able to modify specific structural elements within the TM in order to test prevailing theories on middle ear mechanics. With 3-D printing, we can rapidly create constructs with varying structural features and then answer these questions in a systematic way. This should help us generate a TM structure with the ideal features—a design that may one day be implanted into patients—and hopefully result in better outcomes.”

continued on page 16

Three-Dimensional Printing | continued

Kozin ED, Black NL, Walsh ML, Cheng JT, Cotler M, McKenna MJ, Lee DJ, Lewis JA, Rosowski JJ, Remenschneider AK. 3-Dimensionally printed biomimetic grafts for treatment of tympanic membrane perforations. Association for Research in Otolaryngology annual meeting. San Diego, CA. February 2016.

3-D Printing of TM Grafts



3-D printed biomimetic TM prototype: Schematic of fiber arrangement. (A) Arrangement of fibrous layer of the human TM as determined by electron microscopy (Shimada & Lim, 1980). (B) TM fibrous scaffold prototype without collagen filler printed with SE 1700 PDMS ink through a 200 μ m nozzle.

‘Prognosis’ of 3-D printing in surgery

“There is a healthy prognosis for 3-D printing in surgery as it plays into both the highly technical and creative aspects of our work,” says Dr. Remenschneider and Dr. Kozin.

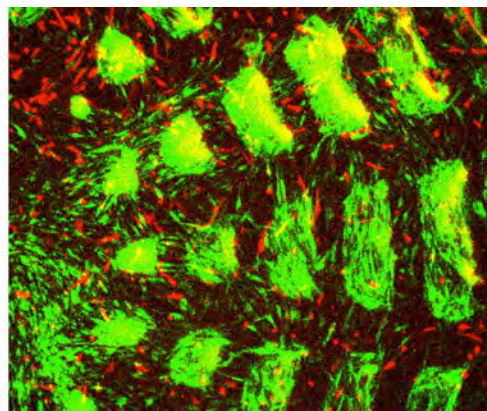
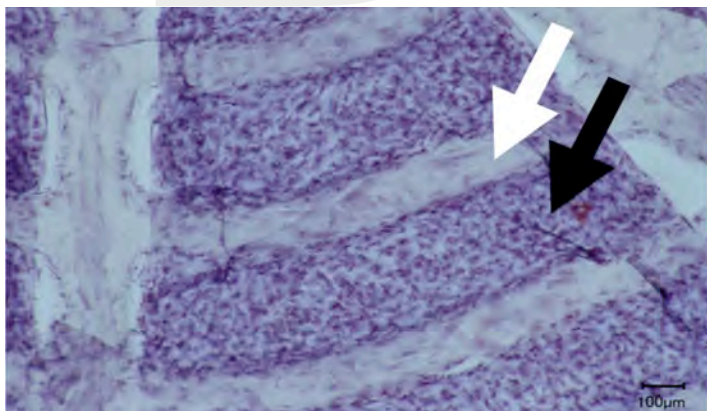
Three-dimensional printing is already directly affecting patient care, and it is easy to see how 3-D printers will play an important role in surgical planning and prosthetic design in the future. By being able to rapidly replicate anatomic scans or manipulate fine structural features of implanted devices, surgeons are now the ones in control of the production line.

“Three-dimensional printing is exciting as it provides surgeons the ability to rapidly study, design, and modify anatomic structures on a micron scale. Three-dimensional printing is democratizing the design and fabrication

process. Surgeons can now think and act outside the box in terms of what is possible,” said Dr. Kozin. “Whether it is being used to optimize operative techniques or to create new implantable constructs, 3-D printing is revolutionizing surgery and is here to stay.”

The applications of 3-D printing in the surgical field are going to continue to expand—discovering new medical questions to explore and finding more ways to improve procedures. Having the insights that are made possible with 3-D printing will also continue to lead to better surgical successes, solutions to unsolved problems, and enhanced patient care.

“The greatest thing about 3-D printing is that if you can imagine it, you can create it,” said Dr. Remenschneider. ●



Human fibroblasts incorporate and infiltrate 3-D printed grafts, depositing extracellular collagen matrix. (A) Masson's Trichrome stain of biomimetic 3-D printed TM composite graft. PDMS-based graft is infilled with fibrin hydrogel. Human fibroblasts are then introduced in vitro and show cellular growth and collagen deposition over graft infill (black arrow) and PDMS scaffold (white arrow). (B) Confocal z-stack image of 3-D printed TM seeded with human fibroblasts. Immunofluorescence stain for collagen I (green), fibroblasts (red), graft scaffold (black).

Black NL, Kozin ED, Cotler MJ, Walsh ML, Remenschneider AK, Lewis JA. Optimizing cell ingrowth into biomimetic 3-D printed tympanic membrane grafts. Association for Research in Otolaryngology annual meeting. San Diego, CA. February 2016.



The Alumni Giving Society of the Department of Otolaryngology at Harvard Medical School

The Department of Otolaryngology 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 helps drive continued achievement across all areas of education, research, and patient care. To date, we have 34 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, M.D., Ph.D., FACS

Walter Augustus LeCompte Professor and Chair of Otolaryngology
Harvard Medical School
Chief of Otolaryngology
Massachusetts Eye and Ear/
Massachusetts General Hospital

Michael B. Rho, M.D., FACS, '05

President of the Harvard
Otolaryngology Alumni Society
Medical Director, Otolaryngology,
Mass. Eye and Ear, Stoneham

Stacey T. Gray, M.D., '04, '05

Program Director, Residency in
Otolaryngology–Head and Neck Surgery
Harvard Medical School

Alumni Leaders

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



Current Alumni Giving Society members for fiscal year 2016 as of April 8, 2016

are listed below. With your gift of \$1,000 or more, you will be included in the 2016 Alumni Giving Society and listed along with your classmates and colleagues.

VISIONARY

Gifts of \$10,000 to \$24,999

John B. Lazor, M.D., MBA, FACS
Derrick T. Lin, M.D., FACS
Leila A. Mankariou, M.D.
Ralph B. Metson, M.D.
Michael M. Paparella, M.D.
Michael B. Rho, M.D., FACS
Herbert Silverstein, M.D., FACS

INNOVATOR

Gifts of \$5,000 to \$9,999

Anonymous
Richard E. Gliklich, M.D.
Paul M. Konowitz, M.D., FACS
Joseph B. Nadol, Jr., M.D.
D. Bradley Welling, M.D., Ph.D., FACS

PIONEER

Gifts of \$2,500 to \$4,999

Samir M. Bhatt, M.D.
Christopher J. Hartnick, M.D., MS
Jon B. Liland, M.D.
Cliff A. Megerian, M.D.
Steven D. Rauch, M.D.
Noah S. Siegel, M.D.
Phillip C. Song, M.D.
Eric H. Stein, M.D.
Oon Tian Tan, M.D., Ph.D.

FRIEND

Gifts of \$1,000 to \$2,499

Benjamin S. Bleier, M.D.
Nicolas Y. BuSaba, M.D., FACS
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Ronald K. de Venecia, M.D., Ph.D.
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Stacey T. Gray, M.D.
Eric H. Holbrook, M.D.
Matthew Jon Jackson, D.M.D.
William W. McClerkin, M.D.
John J. Rosowski, Ph.D.
Mark A. Varvares, M.D., FACS

Charles W. Cummings, M.D., HMS Otolaryngology Resident, Class of 1968

Adding New Twists in Every Turn



Charles W. Cummings, M.D., did not always see himself becoming an otolaryngologist, nor pursuing a career in academic medicine. It wasn't until his general surgery training that he found his interest in what would later become his career.

"When I did my surgical year at the University of Virginia Medical School, I spent a significant amount of time in otolaryngology and ended up falling in love with it. I fell in love with head and neck cancer work more than anything else. So that was the stimulus for me to go into otolaryngology," said Dr. Cummings, a Distinguished Service Professor in the Otolaryngology–Head and Neck Surgery Department of John Hopkins.

"People who have head and neck cancer wear their disease," he continued. "It can be seen and heard. You end up developing meaningful relationships with your patients."

Now a head and neck oncologist at John Hopkins and author of more than 140 scientific papers, Dr. Cummings has built his career wearing many hats and influencing institutions across the nation.

Originally from Boston, Dr. Cummings earned his undergraduate degree from Dartmouth College prior to attending medical school at the University of Virginia. He found his way back to New England in 1968 to complete his residency training at Massachusetts Eye and Ear/Harvard Medical School. He then joined the clinical staff at Mass. Eye and Ear and went into private practice with Boston Ear, Nose, and Throat Associates for a number of years after graduating.

He recognized that the time commitment of a full immersion into head and neck surgery was incompatible with a non-academic practice. So, in 1995, he accepted a faculty position at the State University of New York Upstate Medical Center in Syracuse, New York.

In 1998, the University of Washington offered him a chairmanship opportunity in Seattle, where he was able to remodel the department and lay a foundation that continues to influence the residents and staff today.

"I went in, recruited a fellow Mass. Eye and Ear graduate, Ernest A. Weymuller, Jr., M.D., along with some other folks, and we took on the task of growing the department into the premiere residency and research department you see today," said Dr. Cummings.

While there, Dr. Cummings was not only instrumental in the growth of a

department that is now known for its comprehensive teaching, training, and research programs, but he also became the founding senior editor of *Cummings Otolaryngology–Head and Neck Surgery*, now in its sixth edition.

After spending more than a decade in Seattle, he was recruited to join the John Hopkins faculty as Chairman of the Department of Otolaryngology–Head and Neck Surgery in 1990. He has been there ever since, sharing his perspective and expertise across the institution. In addition to his role as Chairman, he has been the Medical Director for John Hopkins International and the Interim Chair for both the Dermatology and Orthopedics Departments.

For Dr. Cummings, his greatest joy results from the successes and achievements of those who he has influenced during residency and fellowship training; 15 have gone on to chairmanship positions in academic institutions. Having the opportunity to practice in different locations, influence several residents and fellows, and add new twists to the menus of each place he has been is what has made his career so rewarding.

"As you move up the academic medicine ladder, you have opportunities to go to different locations. I think this was very important for my personal growth and perspective," said Dr. Cummings. "I have enjoyed everywhere that I've been. When I tell residents or fellows [who are looking for positions], I tell them the least important thing is the geographic location. Focus on the opportunities presented by the institution." ●

Sunil Puria, Ph.D., Eaton-Peabody Laboratories of Massachusetts Eye and Ear/Harvard Medical School, 1991–1997

Carrying Ideas from Research to Industry, Back to Research

Shortly after graduating college, Sunil Puria, Ph.D., realized that he wasn't ready to leave the classroom just yet.

"I never thought I was the kind of kid who was going to do a Ph.D.," said Dr. Puria, a biomechanics engineer and researcher who holds more than 25 U.S. and 10 international issued patents. "But my studies captured my imagination. I just wanted to continue learning about the applications of math to biology, especially their relation to speech and hearing."

A love for learning is what led Dr. Puria, a former post-doc who will rejoin the research staff of the Eaton-Peabody Laboratories (EPL) at Massachusetts Eye and Ear/Harvard Medical School this summer, to build a career that has balanced working on the biomechanics of hearing both in academia and industry.

A native of New York City, Dr. Puria earned his undergraduate degree in 1983 from the City College of New York prior to receiving his master's degree from Columbia University in 1985 and doctorate degree from City University of New York in 1991, all in electrical engineering. He conducted most of the research for his doctoral thesis at Bell Labs in Murray Hills, New Jersey. With the goal of learning how to perform physiology measurements, he then began his postdoctoral training at MIT and the Eaton-Peabody Laboratories at Mass. Eye and Ear/Harvard Medical School in 1991.

"As a post-doc, you want to go to the best place you can, and the EPL was certainly the best place I could think of," said Dr. Puria. "I always thought there were physiology measurement applications to the middle ear that could be applied to something, like making a better hearing aid. And at the EPL, I knew I would have the opportunity to learn about physiology."

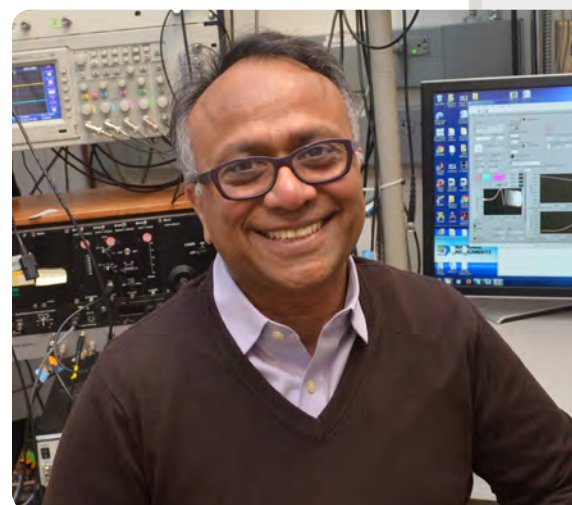
While at the EPL, he worked alongside John J. Rosowski, Ph.D., and William T. Peake, Sc.D., on developing techniques for characterizing the middle ear and on cochlear-pressure measurements, and with M. Charles Liberman, Ph.D., and John J. Guinan, Jr., Ph.D., on characterizing the efferent system. This work allowed him to develop techniques that he has carried throughout his career. Once he had completed his postdoctoral work, Dr. Puria was promoted to adjunct faculty in the Department of Otolaryngology at Harvard Medical School.

Dr. Puria moved to Stanford in 1997 to work as an Associate Professor in the Department of Mechanical Engineering. There, he developed a middle ear mechanics program and continued his research in modeling and measurements.

Dr. Puria began experimenting on forwards and backwards-reverse transmission measurements through the middle ear and realized that feedback pressure would be lower if you vibrate the middle ear directly through a device. This finding became the genesis of the company, EarLens Corporation, which is a new laser-driven hearing aid capable of broadband sound amplification, started by Dr. Puria and Rodney Perkins, M.D. The company recently received U.S. Food and Drug Administration (FDA) approval for the device.

"I think this is a really great model for going from academic research to industry," said Dr. Puria. "EarLens began with an idea partially formed through research, and I was able to find an application for that idea, which is something I always wanted to do."

After nearly 20 years in California, Dr. Puria recently made the decision to return to Boston this summer and once again work in the Eaton-Peabody Laboratories of



Mass. Eye and Ear/Harvard Medical School as an Amelia Peabody Scientist.

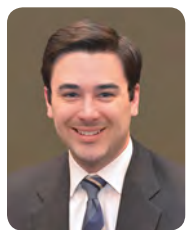
"When deciding whether or not to come back, I had to think about whether it was the best fit, and it really is," said Dr. Puria. "It is the same reason I did my post-doc training there. The lab is very different from anywhere else and even different from what it was before—it has grown quite a bit, is doing cutting-edge work, and it's exactly where I want to be. I am very fortunate and humbled by the opportunity."

In his new role, he will be working on middle ear mechanics, cochlea mechanics, and working with the Wellman Center for Photomedicine to develop an OCT-based measurement system for measuring organ of Corti vibrations without having to open the cochlea.

"If you ask me what one of my greatest accomplishments is, it's that I successfully carried over an idea from research and turned it into an application, which became the basis of a Silicon Valley company that now employs more than 100 people who are empowered to change the world of hearing," said Dr. Puria. ●

News from every corner of the Department of Otolaryngology at Harvard Medical School.

New Faculty



Blake Alkire, M.D., MPH, will join Mass. Eye and Ear Longwood in August. Dr. Alkire received his master's from the T.H. Chan Harvard School of Public Health and his medical degree at

Harvard Medical School prior to completing his otolaryngology residency training at Mass. Eye and Ear/Harvard Medical School. At Longwood, Dr. Alkire will practice general otolaryngology and, given his interests in global health initiatives, he will also work with the Office of Global Surgery and Health at Mass. Eye and Ear and the Program in Global Surgery at Harvard Medical School.



Caroline A. Banks, M.D., will join Mass. Eye and Ear Longwood this fall. Dr. Banks received her medical degree from Perelman School of Medicine at the University

of Pennsylvania prior to completing her otolaryngology residency at Medical University of South Carolina and fellowship in facial plastic and reconstructive surgery with Tessa A. Hadlock, M.D., at Mass. Eye and Ear/Harvard Medical School. Dr. Banks will devote much of her time to working in facial plastic and reconstructive surgery, conducting an acute facial paralysis clinic.



Gillian R. Diercks, M.D., will join Mass. Eye and Ear and the Newton-Wellesley practice as a Pediatric Otolaryngologist this fall. Dr. Diercks received her medical degree from Columbia University

College of Physicians and Surgeons prior to completing her otolaryngology residency at Mass. Eye and Ear/Harvard Medical School. Dr. Diercks also completed fellowship training in pediatric otolaryngology at Mass. Eye and Ear/Harvard Medical School under the mentorship of Christopher J. Hartnick, M.D., MS.



Amanda Griffin, Au.D., Ph.D., joined the Department of Otolaryngology and Communication Enhancement at Boston Children's Hospital this past January as the

Director of Hearing Research. She earned her clinical and research doctorates in audiology at the University of Massachusetts at Amherst. Dr. Griffin was recently appointed Instructor of Otolaryngology at Harvard Medical School.



Nathan Jowett, M.D., will join the Mass. Eye and Ear Division of Facial Plastic and Reconstructive Surgery in July. Dr. Jowett earned his medical degree from the University of

Toronto and completed residency training in otolaryngology at McGill University. He then did his fellowship training in head and neck surgery at the University Medical Center Hamburg-Eppendorf, with concurrent graduate work at the Max Planck Institute for the Structure and Dynamics of Matter, before completing additional training in facial nerve reanimation at Mass. Eye and Ear under the mentorship of Tessa A. Hadlock, M.D.



Sunil Puria, Ph.D., will join the Eaton-Peabody Laboratories (EPL) at Mass. Eye and Ear/Harvard Medical School as an Amelia Peabody Scientist in July. Dr. Puria received

his doctorate from City University of New York in electrical engineering prior to completing his postdoctoral fellowship at the EPL. Joining the laboratory from Stanford University, Puria returns to Boston to work on advances in middle ear and cochlea mechanics. (See page 19 for more on Dr. Puria.)

New Leadership



Michael S. Cohen, M.D., has been named Director of the Multidisciplinary Pediatric Hearing Loss Clinic at Mass. Eye and Ear.



Leila A. Mankarious, M.D., has been named Harvard Medical School Director of Hearing Registries at Mass. Eye and Ear.

Awards, Grants, and Honors

Neil Bhattacharyya, M.D., FACS, received the Distinguished Service Award from the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) for his service on committees in the scientific programs, exhibits, continuing education courses, and instructional courses of the society.

Jacob R. Brodsky, M.D., FAAP, and **Guang Wei Zhou, Sc.D., CCC-A,** hosted the 6th Annual Training Course for Healthcare Professionals on Vestibular and Balance Disorders in the Pediatric Population October 2-3, 2015. This course featured many internationally recognized experts in pediatric vestibular disorders.

M. Christian Brown, Ph.D., received an RO1 grant, which is funded for five years, for his project, "Descending systems to the cochlea and cochlear nucleus."

Zheng-Yi Chen, D.Phil., and **Mingqian Huang, Ph.D.,** have been awarded a grant through the Curing Kids Fund to support their project, "Novel protein delivery and genome editing to correct genetic deafness."

Michael J. Cunningham, M.D., FACS, was the James S. Reilly Guest Lecturer in Pediatric Otolaryngology at Thomas Jefferson University on March 2, 2016.

Albert Edge, Ph.D., received a new RO1 grant award from the National Institutes of Health (NIH) for his project titled, "Wnt signaling in hair cell generation from supporting cells."

Gerald B. Healy, M.D., was honored by The American College of Surgeons Foundation through its establishment of the Gerald B. Healy Traveling Mentorship Fund, which honors all that Dr. Healy has done for many young surgeons.

Jeffrey R. Holt, Ph.D., was a presidential symposium speaker at the Association for Research in Otolaryngology (ARO) annual meeting in San Diego, California, in February 2016.

M. Charles Liberman, Ph.D., was invited to give keynote addresses at the International Symposium on the Future of Hearing organized by the University of Hannover Medical School in Germany and at the Tinnitus Research Initiative Conference in Nottingham, England.

Dr. Liberman has also been appointed as Chair of Committee to write the 2017–2021 Strategic Plan for the National Institute on Deafness and Other Communication Disorders (NIDCD). This document lays out the research priorities for the Institute for the next five years.

Brian M. Lin, M.D., received a travel grant award from the American Academy of Otolaryngology–Head and Neck Surgery Foundation (AAO-HNSF) Humanitarian Efforts Committee for his humanitarian medical mission to Tamatave, Madagascar.

Derrick T. Lin, M.D., FACS, received a grant award from the Adenoid Cystic Cancer Research Foundation for his project, “Adenoid cystic carcinoma tumor biorepository.”

Daniel M. Merfeld, Ph.D., received an R21 grant award for his project titled, “Employing magnetic vestibular stimulation (MVS) during functional imaging.”

Joseph B. Nadol, Jr., M.D., received an R01 renewed grant award for his project titled, “Electron microscopy of the human inner ear.”

Matthew R. Nauenheim, M.D., MBA, was awarded first place for his presentation, “Acute and chronic laryngeal manifestations of rheumatoid arthritis,” at the December 2015 New England Ophthalmological Society (NEOS) meeting. **Phillip C. Song, M.D.**, is his faculty mentor.

Dennis S. Poe, M.D., Ph.D., and **Jennifer J. Shin, M.D., S.M.**, were two of the co-authors of the recently published AAO-HNS *Clinical Practice Guideline: Otitis Media with Effusion*.

Sidharth Venkata Puram, M.D., Ph.D., received the Research Grant Award from the New England Otolaryngological Society (NEOS).

Alicia M. Quesnel, M.D., has been named the recipient of the 2016 Eleanor and Miles Shore Fellowship Program Award for Scholars in Medicine.

Gregory Randolph, M.D., FACS, FACE, is the past treasurer and a current executive board member of the American Thyroid Association (ATA) and was one of the authors on the 2015 *American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer*.

Steven D. Rauch, M.D., received the 2015 Champion of Vestibular Medicine award from the Vestibular Disorders Association (VEDA).

Jo Shapiro, M.D., was recently appointed Chair of the Ethics and Professionalism Committee (EPCOM) of the American Board of Medical Specialties (ABMS) and is the Society of University Otolaryngologists’ Representative on the Board of Governors of the American College of Surgeons.

David A. Shaye, M.D., recently finished his second year serving in Rwanda as part of a seven-year grant, administered through CDC, Clinton Initiative, and Rwandan Ministry of Health, to augment medical education in the country. While there, he was named Associate Head of Department for Rwandan Otolaryngology and served as their primary faculty member.

Dr. Shaye also had a photo of his patient, whose cleft palate he repaired, featured on the cover of the December 19 issue of *The Lancet*. The photo was taken by Jessica Shaye and was submitted by Dr. Shaye.



Lavinia Sheets, Ph.D., has been awarded a grant through the Curing Kids Fund to support her project, “Bioactive molecule screen for drugs that modulate hair-cell nerve regeneration and synaptogenesis in zebrafish.”

HMS Promotions

Jeffrey R. Holt, Ph.D.,
Professor of Otolaryngology (See
page 2 for more on Dr. Holt’s promotion.)

Dennis S. Poe, M.D., Ph.D.,
Professor of Otolaryngology (See
page 3 for more on Dr. Poe’s promotion.)

Eelam A. Adil, M.D., MBA, FAAP,
Assistant Professor of Otolaryngology

Jacob R. Brodsky, M.D., FAAP,
Assistant Professor of Otolaryngology

David S. Caradonna, M.D.,
Assistant Professor of Otolaryngology

Jeffrey Tao Cheng, Ph.D.,
Assistant Professor of Otolaryngology

Pavan S. Mallur, M.D.,
Assistant Professor of Otolaryngology

Mark G. Shrime, M.D., MPH, Ph.D., FACS,
Assistant Professor of Otolaryngology
and Assistant Professor of Global Health
and Social Medicine

Guang Wei Zhou, Sc.D., CCC-A,
Assistant Professor of Otolaryngology

Yoojin Chung, Ph.D.,
Instructor in Otolaryngology
(promoted from training status)



HARVARD
MEDICAL SCHOOL
DEPARTMENT OF
Otolaryngology

Triological Society 2016 Combined Sections Meeting

Often, we see collaborations forming between alumni from the Department of Otolaryngology at Harvard Medical School and current Harvard Medical School faculty members, which proved to be significant at this year's 2016 Combined Sections Meeting held by the Triological Society. This January, three resident research awards were granted to research collaborations between Harvard Medical School faculty and alumni.

Awards

John J. Conley, MD Resident Research Award

*Quality Indicators for Head and Neck
Oncologic Surgery: Academic versus
Nonacademic Outcomes*

Neil Bhattacharyya, M.D., FACS, and
resident Sidharth Venkata Puram,
M.D., Ph.D.

Shirley Baron Resident Research Award

*Pediatric Otolaryngologic Conditions:
Racial and Socioeconomic Disparities
in the United States*

Neil Bhattacharyya, M.D., FACS,
alumna Nina L. Shapiro, M.D., and
Sophie G. Shay, M.D.

Vice President's Resident Research Award

*Functional Impact of Tinnitus on the
Prevalence of Anxiety and Depression*

Neil Bhattacharyya, M.D., FACS,
alumnus Harrison W. Lin, M.D., and
Jay M. Bhatt, M.D.



Dr. Trevor McGill Retiring After 40 Years

This fall, **Trevor McGill, M.D., FACS**, will retire as Senior Associate of Otolaryngology at Boston Children's Hospital and Professor of Otolaryngology at Harvard Medical School, leaving behind a legacy unmatched by any other.

Dr. McGill has played a pivotal role in establishing the reputation of the Department of Otolaryngology and Communication Enhancement at Boston Children's Hospital to its current status as one of the premier pediatric otolaryngology units in the nation. Following a two-year fellowship in otology at Massachusetts Eye and Ear, he took up a position as a Junior Attending at Boston Children's Hospital at the bequest of Harold F. Schuknecht, M.D., in 1976.

At Boston Children's Hospital, he initiated one of the first pediatric otolaryngology training programs, developing a template for programs alike throughout the world. Since then, he has been teaching and training residents and fellows, including many of today's leading experts in the field. From altering the understanding of congenital cholesteatoma of the middle ear based on histopathological studies, to his management of patients with complex vascular anomalies and head and neck tumors, Dr. McGill has been recognized, both nationally and internationally, for having transformed pediatric otolaryngology.

Throughout his career, Dr. McGill has published extensively, authoring 98 peer-reviewed publications and 48 book chapters, and has been the co-editor for three pediatric otolaryngology textbooks. Most notably, he has been invited to serve as a discussant at the weekly CPC at Massachusetts General Hospital on three separate occasions.

"Dr. McGill has made outstanding contributions to the field of pediatric otolaryngology in many respects, but perhaps most impressive is his clinical teaching and mentorship," said Michael J. Cunningham, M.D., FACS, Otolaryngologist-in-Chief and the Gerald B. Healy Chair in Pediatric Otolaryngology at Boston Children's Hospital. "I am certain this opinion is shared by the vast majority of residents, fellows, and junior faculty who have had the opportunity to work with Dr. McGill over the past four decades."

Following his retirement, Dr. McGill plans to write a book on the history of the Department of Otolaryngology at Boston Children's Hospital and visit extended family in Ireland and England. ●

Temporal Bone Dissection Course Held in Mbarara, Uganda

An inaugural Temporal Bone Dissection Course was held this past January at Mbarara University of Science and Technology (MUST) in Mbarara, Uganda.

Former Chairman of Otolaryngology at Massachusetts Eye and Ear/Harvard Medical School, **Joseph B. Nadol, Jr., M.D.**, donated four stations from the former Temporal Bone Lab to MUST as a demonstration of his belief in education as a catalyst for change.

For decades, the Temporal Bone Lab at Mass. Eye and Ear was an essential component of otolaryngology residency training. Now, the lab is back in service, providing a platform for critical learning for residents and clinicians throughout East Africa.

Attended by otolaryngology residents from MUST and Makerere University, the first course was coordinated by **Doreen Nakku, M.D.**, (MUST) and the faculty included **Ronald K. de Venecia, M.D., Ph.D.**,

(Mass. Eye and Ear) and **Brian Westerberg, M.D., MHS** (University of British Columbia).

Dr. de Venecia, Instructor in Otolaryngology at Harvard Medical School, took this as an exciting opportunity to transfer the curriculum taught in Boston to a new venue where it can reach residents and clinicians who would otherwise have limited access to otologic surgical skills training.

Throughout East Africa, the otologic burden of disease is high and often unmet. Future courses, which include rhinology, skull-base approaches, facial trauma, and ophthalmology, are being planned for both residents and attendees.

The vision of Mass. Eye and Ear is to have the lab serve as a regional center for surgical simulation training. ●



MUST otolaryngology faculty and Course Director Dr. Doreen Nakku



Course faculty Drs. Ronald de Venecia and Brian Westerberg with otolaryngology residents from MUST and Makerere University

Otolaryngology residents from Makerere University who traveled to MUST to take advantage of this pilot temporal bone course

The following are select research advances from the Department of Otolaryngology at Harvard Medical School.

Basic Science

Brain's 'amplifier' compensates for lost inner ear function



Researchers from Mass. Eye and Ear/Harvard Medical School, including **Daniel B. Polley, Ph.D.**, have described, for the first time, the adult brain's ability to compensate for a near-complete

loss of auditory nerve fibers that link the ear to the brain. The findings, published online in *Neuron*, suggest that the brain's natural plasticity can compensate for inner ear damage to bring sound detection abilities back within normal limits; however, it does not recover speech intelligibility. This imperfect hearing recovery may explain a common auditory complaint, in which some patients report difficulties understanding speech despite having normal hearing thresholds.

Using chemicals to wipe out nearly all of the nerve fibers charged with processing sound in the inner ears of mice, the researchers observed normal responses to sound and increased activity in the cortex—the highest stage of processing in the brain—and determined that the cortex is where the "amplifier" resides. But they also found that there were limits to what could be recovered by the brain's natural plasticity. The researchers found that the increased amplification at higher stages of brain processing could fully recover sensitivity to faint sounds, but that the ability to resolve differences in complex sounds, like speech, did not recover to the same degree.

Chambers AR, Resnik J, Yuan Y, Whitton JP, Edge AS, Liberman MC, Polley DB. Central gain restores auditory processing following near-complete cochlear denervation. Neuron. 2016 Feb;89(4):867–79.

Toxic secretions from intracranial tumor damage the inner ear

A team of researchers from Mass. Eye and Ear/Harvard Medical School, including **Konstantina M. Stankovic, M.D., Ph.D., FACS**, showed that in some cases of vestibular schwannoma, a sometimes-lethal tumor often associated with neurofibromatosis 2 (NF2), secretions from the tumor contain toxic molecules that damage the inner ear.



The findings, published online in *Scientific Reports*, explain why some vestibular schwannomas cause hearing loss even though they are not large enough to compress nearby

structures that control hearing and suggest that there may be a pharmacologic way to maintain hearing in some patients with vestibular schwannoma.

The researchers also identified TNF α , a toxic compound that has been implicated in other forms of hearing loss, as a causative toxic molecule in the secretions from human vestibular schwannomas. When they applied those secretions directly to a mouse cochlea, they found that the degree of cellular damage correlated to the severity of hearing loss in humans.

Dilwali S, Landegger LD, Soares VYR, Deschler DG, Stankovic KM. Secreted factors from human vestibular schwannomas can cause cochlear damage. Scientific Reports. 2015 Dec;5:18599.

Perinatal thiamine deficiency causes cochlear innervation abnormalities



A team from Mass. Eye and Ear/Harvard Medical School, including **Stéphane F. Maison, Ph.D., MS**, reported a link between inner hair cell loss and thiamine,

a water-soluble vitamin (B1) required for intermediary metabolism. Neonatal thiamine deficiency can cause auditory neuropathy in humans. To probe the underlying cochlear pathology, mice were maintained on a thiamine-free or low-thiamine diet during fetal development or early postnatal life. Researchers found no evidence for selective IHC loss; however, many thiamine-deprived animals showed dramatic abnormalities in the cochlear afferent and efferent innervation, and associated cochlear functional abnormalities consistent with the diagnosis of auditory neuropathy. It was concluded that the auditory neuropathy from thiamine deprivation was likely produced by loss of inner hair cell synapses.

Maison SF, Yin Y, Liberman LD, Liberman MC. Perinatal thiamine deficiency causes cochlear innervation abnormalities in mice. Hearing Research. 2016 Mar 2; 335:94–104.

Chronic conductive hearing loss causes cochlear neuropathy



A team of researchers from Mass. Eye and Ear/Harvard Medical School, including **M. Charles Liberman, Ph.D.**, showed that sound deprivation in adult mice irreversibly

damages the inner ear in ways similar to that seen in age-related and noise-induced hearing loss: i.e., it leads to loss of the synaptic connections between the sensory cells and the auditory nerve fibers that carry the information to the brain.

The findings, published in *PLOS ONE*, suggest that chronic conductive hearing loss, such as that caused by recurrent ear infection, leads to permanent hearing impairment if it remains untreated. At least 80% of children will experience one or more bouts of otitis media before they reach three years of age. These bouts can persist for many months in some cases and deficits in communication abilities can persist for years after the middle-ear pathology has resolved. Although

the mechanisms underlying this inner ear damage following sound-deprivation are not known, its effects need to be considered in the clinical management of chronic conductive hearing loss.

Liberman MC, Liberman LD, Maison SF. Chronic conductive hearing loss causes cochlear neuropathy. PLOS ONE. 2015;10(11):e0142341.

Round-window delivery of neurotrophin-3 regenerates cochlear synapses after acoustic overexposure in mice

Recent work from the Mass. Eye and Ear/Harvard Medical School labs of Sharon G. Kujawa, Ph.D., and **M. Charles Liberman, Ph.D.**, have shown that the synaptic connections between hair cells and the auditory nerve are the most vulnerable elements in the ear in both noise-induced and age-related hearing loss. This cochlear synaptopathy does not elevate audiometric thresholds—threshold elevation is caused by hair cell damage—but it must contribute to the difficulties hearing speech in noise that are so characteristic of many kinds of sensorineural hearing loss.

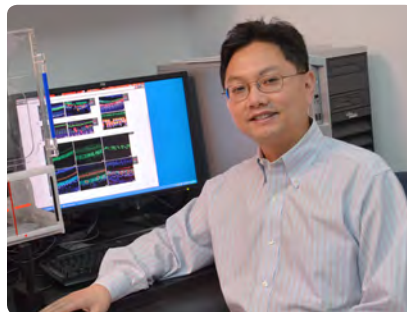


In this study, the Liberman lab showed that local delivery of a naturally occurring protein, neurotrophin-3, to the inner ear of noise-damaged mice, one-day post exposure, could regenerate the missing synapses and provide functional recovery of the degraded neural responses from the inner ear. The results point the way towards the development of regenerative therapies in hearing impaired humans with sensorineural hearing loss.

Suzuki J, Corfas G, Liberman MC. Round-window delivery of neurotrophin-3 regenerates cochlear synapses after acoustic overexposure. Scientific Reports. In Press.

Discovery and characterization of a peptide that enhances endosomal escape of delivered proteins *in vitro* and *in vivo*

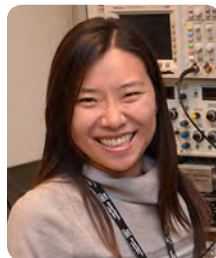
The inefficient delivery of proteins into mammalian cells remains a major barrier to realizing the therapeutic potential of many proteins. A team of researchers including, **Zheng-Yi Chen, D.Phil.**, showed that using



cationic-lipid reagents negatively charged proteins (supercharged) can be effectively delivered into mammalian inner ear with functions. Through delivery of protein Cas9 and guide RNA, the researchers achieved inner ear specific CRISPR/Cas9-mediated genome editing. They further demonstrated such methods could be used to target diverse inner ear cell types. This study opens a door to deliver proteins to the inner ear as therapeutic reagents for genome editing and for inner ear regeneration to treat different types of deafness.

*Li M, Tao Y, Shu Y, LaRochelle JR, Steinauer A, Thompson D, Schepartz A, Chen ZY, Liu DR. Discovery and characterization of a peptide that enhances endosomal escape of delivered proteins *in vitro* and *in vivo*. J Am Chem Soc. 2015 Nov 11;137(44):14084–93.*

Neural sensitivity to binaural cues with bilateral cochlear implants



Many profoundly deaf people wearing cochlear implants (CIs) still face challenges in everyday situations, such as understanding conversations in noise. Even with CIs in both ears, they have difficulty making full use of subtle differences in the sounds reaching the two ears (interaural time difference, [ITD]) to identify where the sound is coming from.

This problem is especially acute at the high stimulation rates used in clinical CI processors.

A team of researchers from Mass. Eye and Ear/Harvard Medical School, including **Yoojin Chung, Ph.D.**, studied how the neurons in the auditory midbrain encode binaural cues delivered by bilateral CIs in an animal model. They found that the majority of neurons in the auditory midbrain were sensitive to ITDs, however, their sensitivity degraded with increasing pulse rate. This degradation paralleled pulse-rate dependence of perceptual limits in human CI users.

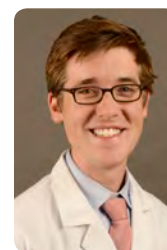
This study provides a better understanding of neural mechanisms underlying the limitation of current clinical bilateral CIs and suggests directions for improvement such as delivering ITD information in low-rate pulse trains.

Chung Y, Hancock KE, Delgutte B. Neural coding of ITD with bilateral cochlear implants in unanesthetized rabbits. The Journal of Neuroscience. In Press.

Clinical Practice

Patients with superior canal dehiscence syndrome experience significant boost in quality of life after surgical repair

Researchers from Mass. Eye and Ear/Harvard Medical School, including **Aaron K. Remenschneider, M.D., MPH, Daniel J. Lee, M.D., FACS**, and **David H. Jung, M.D., Ph.D.**, are the first to ask patients with superior canal dehiscence syndrome (SCDS) about their



general health-related quality of life before and after surgical repair. The team found that patients with SCDS have significant decreases in quality of life and that surgery helped restore their ability to work and participate in normal social activities. The research also provides important insight into the cost-effectiveness of surgery for SCDS.

Remenschneider AK, Owoc M, Kozin ED, McKenna MJ, Lee DJ, Jung DH. Health utility improves after surgery for superior canal dehiscence syndrome. Otol Neurotol. 2015 Dec;36(10):1695–701.

Office-based olfactory mucosa biopsies



A team of researchers including, **Eric H. Holbrook, M.D.**, from Mass. Eye and Ear/Harvard Medical School, have described a technique for obtaining olfactory

epithelium—containing the nerve cells responsible for detecting odors in the nose—from patients in the clinic for use in research and potentially for diagnostic and therapeutic purposes. Previous descriptions of these types of biopsies were poorly described and with limited success in obtaining proper tissue. In addition to providing a higher yield of olfactory tissue, this work also describes a method for evaluating the biopsy specimens to ensure that the tissue originated from the olfactory region, a practice that has not been routinely performed in prior published papers.

Holbrook EH, Rebeiz L, Schwob JE. Office-based olfactory mucosa biopsies. Int Forum Allergy Rhinol. 2016 Feb 2;doi:10.1002/alar.21711.

Risk factors for hearing loss in patients with cystic fibrosis



Researchers from Boston Children's Hospital/Harvard Medical School, including **Margaret A. Kenna, M.D., MPH, FACS, FAAP**, have been studying the risk factors for hearing loss in children with cystic

fibrosis (CF). In a pilot study of 50 patients with CF published in 2009, the researchers found a 14% rate of sensorineural hearing loss (SNHL) in a convenience sample of patients with sinopulmonary disease. The SNHL was most often bilateral and high frequency. Compared to CF patients with normal hearing, children with hearing loss were older, had received ≥ 10 courses of intravenous aminoglycosides, ≥ 5 courses of aminoglycoside nasal irrigations, and ≥ 5 courses of macrolides.

To verify these findings in a larger cohort, the researchers have completed a recent retrospective study of 178 CF patients, the largest published study to date looking at hearing loss in this population. A multivariable logistic regression model showed that older age and more frequent hospitalizations were associated with SNHL, with the odds of developing hearing loss increasing with every hospitalization in the year prior to the audiometric evaluation. The model also suggested that males and prior use of amikacin were also associated with SNHL, although neither reached statistical significance. When comparing the hearing loss in the CF population to National Health and Nutrition Examination Surveys (NHANES) data, the study population was much more likely to have bilateral hearing loss at any given age. All patients with SNHL included loss in the high frequencies. Two patients developed bilateral profound SNHL and underwent cochlear implantation. These two studies highlight the complexity of the etiologies of SNHL in the CF population, but also provide potential opportunities for interventions and possible prevention of the hearing loss.

Tarshish Y, Huang L, Jackson FI, Edwards J, Fligor B, Wilkins A, Uluer A, Sawicki G, Kenna MA. Risk factors for hearing loss in patients with cystic fibrosis. J Am Acad Audiol. 2016 Jan;27(1):6–12.

Cheng AG, Johnston PR, Luz J, Uluer A, Fligor B, Licameli GR, Kenna MA, Jones DT. Sensorineural hearing loss in patients with cystic fibrosis. Otolaryngol Head Neck Surg. 2009;141(1):86–90

Aeroallergen sensitivities and development of chronic rhinosinusitis in thirteen adults who initially had allergic rhinitis



A team of researchers from Beth Israel Deaconess Medical Center and Mass. Eye and Ear/Harvard Medical School, including **David S. Caradonna,**

M.D., D.M.D., studied what characteristics may make individuals with allergic rhinitis more prone to develop chronic rhinosinusitis. One of the natural questions that arise is whether the degree of atopy, as reflected

by the number of allergies (“aeroallergies”), may influence development of chronic rhinosinusitis in individuals with allergic rhinitis. In this study, the researchers found that the number of allergies that an individual with allergic rhinitis has is not associated with the subsequent development of chronic rhinosinusitis. These findings are consistent with what this group has also found in children with allergic rhinitis and provides valuable information in counseling and management of individuals with allergic rhinitis.

Sedaghat AR, Gray ST, Phillips KM, Caradonna DS. Aeroallergen sensitivities and development of chronic rhinosinusitis in thirteen adults who initially had allergic rhinitis. Clin Otolaryngol. 2016 Mar 4;doi:10.1111/coa.12644.

Successful intraoperative electrophysiologic monitoring of the recurrent laryngeal nerve

A multidisciplinary team of researchers from Mass. Eye and Ear/Harvard Medical School, including **Gregory Randolph, M.D., FACS, FACE**, developed a protocol for intraoperative nerve monitoring (IONM) of the recurrent laryngeal nerve (RLN) based on published evidence and their experience



with 3,000 patients over a 16-year period. The Departments of Otolaryngology, Anesthesiology, and Audiology at Mass. Eye and Ear worked together to present an up-to-date clinical algorithm, including setup and troubleshooting of an IONM system, endotracheal tube placement, and anesthetic parameters. The researchers reported that no complications related to monitoring or endotracheal tube placement were noted when the IONM protocol was implemented

at Mass. Eye and Ear. The IONM protocol has proven to be vital in standardizing care and in avoiding intraoperative errors. Their work, published in *Head & Neck*, is believed to be the first interdisciplinary collaborative protocol for monitored neck surgery based on their clinical and published experience.

Macias AA, Eappen S, Malikin I, Goldfarb J, Kujawa S, Konowitz PM, Kamani D, Randolph GW. Successful intraoperative electrophysiologic monitoring of the recurrent laryngeal nerve, a multidisciplinary approach: The Massachusetts Eye and Ear Infirmary monitoring collaborative protocol with experience in over 3000 cases. Head and Neck. 2016 Apr 9; doi:10.1002/hed.24468.

Usefulness of upper airway endoscopy in the evaluation of pediatric pulmonary aspiration



A team of researchers from Boston Children's Hospital/Harvard Medical School, including **Eelam A. Adil, M.D., MBA, FAAP**, analyzed the utility of direct laryngoscopy and bronchoscopy (DLB) in pediatric patients with unexplained chronic aspiration. Using a cohort of 532 patients, the group compared the yield of flexible laryngoscopy versus DLB in the

diagnosis of aspiration related airway lesions such as vocal fold immobility, laryngeal cleft, and H-type fistula. Older age (≥ 1 year of age), recurrent pneumonia, and history of intubation were significantly associated with the presence of an aspiration related airway lesion in the multivariate model. One hundred and ten patients eventually underwent surgical repair of an identified aspiration related airway lesion. The authors conclude that there is a high incidence of aspiration related airway lesions identified on DLB that are not seen on flexible laryngoscopy.

Adil E, Gergin O, Kawai K, Rahbar R, Watters K. Usefulness of upper airway endoscopy in the evaluation of pediatric pulmonary aspiration. JAMA Otolaryngol Head Neck Surg. 2016 Apr 1;142(4):339-43.



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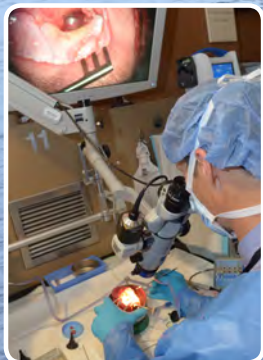
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#1

Mass. Eye and Ear ranked #1 in the nation for otolaryngology care by U.S. News and World Report.

In a report released by *U.S. News and World Report* and the physician network *Doximity*, the Department of Otolaryngology at Mass. Eye and Ear/Mass General was ranked #1 in the nation for otolaryngology care.



Upcoming Events

MassEyeAndEar.org/ENTCalendar

Please visit the online calendar for updated information about upcoming events in the Harvard Medical School Department of Otolaryngology.



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