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A Brush with Success: Toothpaste Delivers Immunotherapy for Allergic Rhinitis

Bright ideas can happen at any time – even while brushing your teeth. Just ask **William R. Reisacher, MD**, an otolaryngologist in the Department of Otolaryngology – Head and Neck Surgery at New York-Presbyterian/Weill Cornell Medical Center, who was doing just that while pondering a more effective and easier way to deliver allergenic extracts for people with allergic rhinitis.

“I was at home brushing my teeth,” he says. “I remember looking into the mirror and thinking, ‘All the foamy residue is covering the exact areas I want my extracts to go.’ That ignited an inferno inside my brain – it was my ‘aha!’ moment.”

While physicians have been using antigen-specific immunotherapy to desensitize people to airborne

allergens for a century, its efficacy in helping the estimated 50 million allergy sufferers in the U.S. has been limited because it is time-consuming, inconvenient, and people sometimes forget to use it, says Dr. Reisacher.

Compounding allows the physician to individualize treatment based on personal allergens, selecting specific extracts, with specific amounts, to be incorporated into the toothpaste.

Allergy extracts are usually delivered either via sublingual drops/tablets or subcutaneous injections. However, in order to achieve long-term benefit, people must continue these therapies consistently and uninterrupted for three to five years. Since

1996, sublingual immunotherapy (SLIT) has been recognized as a viable alternative to subcutaneous immunotherapy (SCIT) by the World Health Organization.

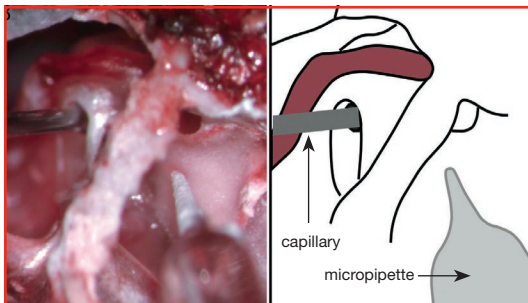
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Perfusion-Based Method for Cochlear Implant Electrode Insertion Holds Promise

Cochlear implants restore partial hearing to profoundly deaf individuals who do not benefit from conventional hearing aids. However, anatomical constraints of the human temporal bone and the facial recess approach used for cochlear implant (CI) surgeries and the variability in electrode array designs

can make the manual electrode insertion challenging and can destroy any residual hearing if the insertion damages the cochlea. Surgeons rely on tactile feedback from the implant to determine when to stop the insertion, but this manual method results in a large degree of inconsistency in surgical outcomes and possibly intra-cochlear trauma. Therefore, only those persons with profound or severe hearing loss are currently candidates for cochlear implantation.

Seeking to find a reliable, non-traumatic technique for deep CI electrode insertion, **Elizabeth S. Olson, PhD**, Director, Fowler Memorial Laboratory, and Associate Professor, Departments of Otolaryngology – Head and Neck Surgery and Biomedical Engineering at Columbia University Medical Center, and her colleagues



Set-up for electrode insertion showing micropipette sealed to the scala vestibuli hole and capillary holding the mock implant in the round window above the scala tympani

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A Brush with Success: Toothpaste Delivers Immunotherapy for Allergic Rhinitis (continued from page 1)

In fact, in Europe, the sublingual approach represents the majority of new immunotherapy prescriptions, and its use has been steadily increasing in the United States.

Yet studies have shown that this home therapy has poor long-term adherence, which decreases its effectiveness and also delivers extract to only a small portion of the oral cavity mucosa. There had to be a better way and, in fact, the 2013 position paper of the World Allergy Organization recognized the potential of the mucosal tissues in the oral vestibule and gingiva to induce an enhanced level of immune tolerance with decreased mast cell activation. They called for more work in this area – and Dr. Reisacher responded.

Scouring the literature, he discovered a paper that showed that the immune cells most responsible for desensitization were in the highest density in the gums. Working with a toothpaste formulation expert and a compounding pharmacy, Dr. Reisacher developed

a commercial-grade fluoride toothpaste – Allerdent – which could incorporate and stabilize the liquid extracts of common airborne allergens, among them, trees, grass, dust, mold, cats, dogs, cockroaches, and feathers. Successful desensitization is closely tied to

therapy adherence, and by integrating this treatment into a universally performed daily activity, Dr. Reisacher expects adherence will be optimized.

“A toothpaste formulation would also be advantageous during times of extended travel, such as military deployment,” says Dr. Reisacher. With a grant from the Empire State Development’s Division of Science, Technology and



Dr. William R. Reisacher

Innovation, Dr. Reisacher is currently testing the response of oral mucosal immunotherapy (OMIT), using Allerdent versus sublingual immunotherapy in clinical trials of people 18 years and older over the course of a year. If all goes well, Dr. Reisacher hopes to expand access to Allerdent beyond the 49 states (all except Nebraska), where the personalized toothpaste is currently available by prescription, and eventually seek approval from the U.S. Food and Drug Administration. In the future, Dr. Reisacher plans to investigate whether Allerdent could be used to help people with food allergies, which he notes, “is a much tougher nut to crack.”

Dr. Reisacher has been committed to finding better ways to help people suffering with allergies since starting his practice 14 years ago. Most recently he developed a mucosal brush biopsy as a simple, more effective way of testing for locally present immunoglobulin E (IgE) by collecting mucus and epithelial cells from the nasal mucosa. The first study in 2012 was a landmark proof of concept paper that demonstrated for the first time that antigen-specific antibodies inside the nose could be measured using the mucosal brush biopsy – today referred to as the LAMB (Local Antibody Mucosal Brush) test. [See *Advances in Ear, Nose, and Throat*, January 2014, at nyp.org/pro.]

“The allergy patient is the professional sufferer,” adds Dr. Reisacher. “Unfortunately, many people believe there is nothing they can do about allergies and that’s why they don’t even go to the doctor. There really isn’t a need for suffering. That’s what I want to change.”

A Case in Point

Following is a case report on an individual receiving Allerdent – an oral mucosal immunotherapy for seasonal allergic rhinitis – published in the July/August 2014 issue of the *International Journal of Pharmaceutical Compounding*:

C.R. is a 42-year-old female with a 25-year history of allergic rhinitis with sneezing, nasal itching, and rhinorrhea in the spring, along with perennial itching in the mouth when eating apples or raw vegetables. She has used oral antihistamines in the past, which have only partially controlled her symptoms. She underwent skin-prick testing (SPT) for tree pollens (Grade 0 to 4 based on the diameter of the wheal at 15 minutes), with positive reactions to oak (Grade 4), elm (Grade 3), cottonwood (Grade 3), birch (Grade 4), maple (Grade 3), and ash (Grade 4). She began oral mucosal immunotherapy toothpaste in February 2012 by brushing once daily for two minutes with 1 mL of a toothpaste delivery vehicle compounded with 0.02 mL of oak and 0.02 mL of birch extract (Antigen Laboratories, Liberty, Missouri), delivering approximately 25 micrograms per day of each major antigen.

In the first three days of treatment, she experienced a tingling sensation in the mouth without swelling, but experienced no adverse reactions for the remainder of the treatment, which continued until the end of May 2012. Allergy Outcome Survey was completed at baseline (February), mid-season (April), and at the end of the season (June). She did not require any medications during the treatment period for symptom control, only reporting morning congestion and skin itching intermittently in May. She reported that she was able to peel carrots and potatoes without sneezing, which she had not been able to do before, and that her seasonal allergies were “alleviated by about 95 percent overall.” Repeat SPT in June 2012 demonstrated an absence of skin reactivity to oak (Grade 0), while skin reactivity to birch and the other tree pollens remained unchanged.

Reference Article

William R. Reisacher, MD, FACS, FAOA, Shari Rudner, RPH, FIACP, FACA, Victoriya Kotik. Oral mucosal immunotherapy using a toothpaste delivery system for the treatment of allergic rhinitis. *International Journal of Pharmaceutical Compounding*. Vol. 18, No. 4. July/August 2014.

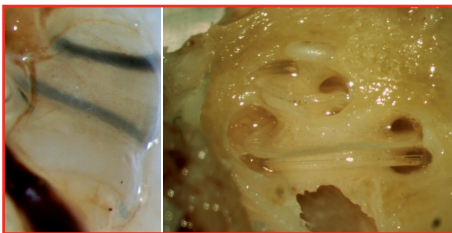
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Perfusion-Based Method for Cochlear Implant Electrode Insertion Holds Promise (continued from page 2)

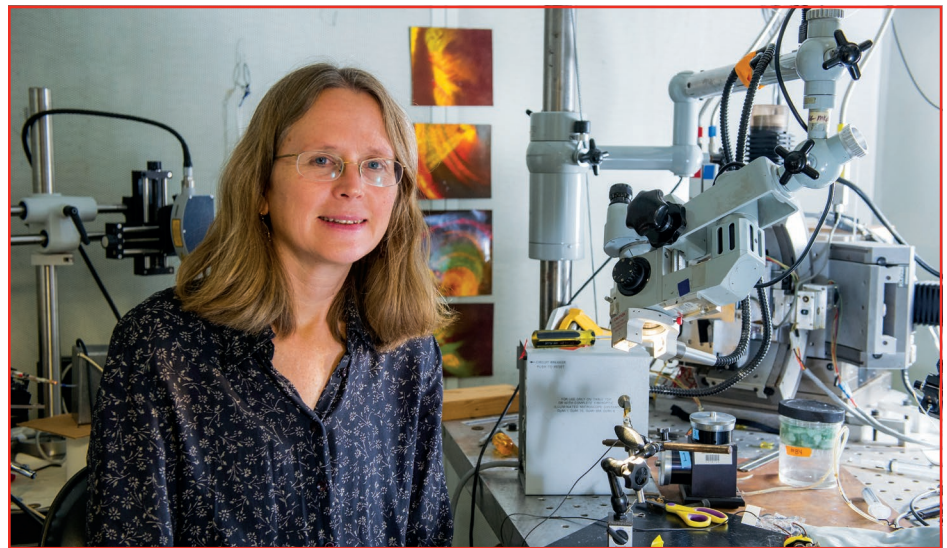
developed a flow-assisted method in which a viscous fluid “carries” the implant into the cochlea.

Their goal was to create an automated and standardized insertion technique across patients with more apical insertion than is possible by contemporary methods, while minimizing insertion trauma. “What we want to do is develop a less damaging way to do a cochlear implantation so that it can be made available to a larger group of very hearing impaired people,” explains Dr. Olson, whose work in this area is funded by the National Institute of Health’s National Institute on Deafness and Other Communication Disorders and the Emil Capital Foundation. “A big push now is to implant people who have decent low frequency hearing, but their high frequency hearing is very impaired. The low frequency hearing is the most apical – the most distal. It would be nice if the implant didn’t have to pass through a coiled structure, but since it does we came up with a way to thread in the electrodes by perfusing the cochlea very gently with a slightly viscous fluid. We could then put a very flexible implant into that fluid, which would allow it to ‘flow’ into the cochlea.”



Left: A gerbil with cochlear implant shown spiraling all the way to the apex of the cochlea. Right: Human cochlea with the implant seen spiraling within.

In their study, the Columbia researchers used their technique to insert silicone implants through to the cochlear apex in rats and gerbils. In light-microscopic



Dr. Elizabeth S. Olson

histology, the implantation occurred without cochlear trauma. “What we wanted to achieve with the flow was to make it naturally go down the channel, avoiding the cochlear partition,” notes Dr. Olson.

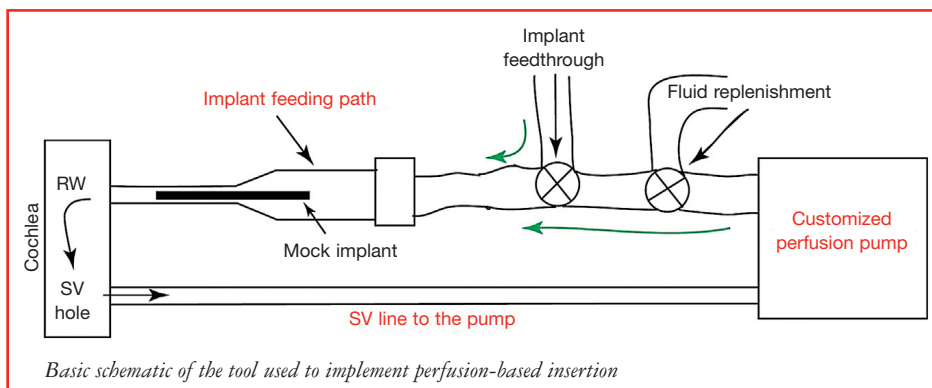
Electrode Insertion Methods

Initially mock electrodes were injected into the cochlea with the help of a syringe filled with a diluted sodium hyaluronate solution. The syringe tip holding the mock electrode was sealed to the round window using cyanoacrylate glue or dental cement and a small opening in the scala vestibule adjacent to the stapes served as an outlet. The round window and the neighboring area were filled with the hyaluronate solution to prevent air bubbles from entering the cochlea.

“Although with this method we could insert the mock electrodes deeply into the cochlea, the method was discarded, as the round window sealing step was difficult and traumatic to the cochlea in some cases,” says Dr. Olson. “In the next stage of development we tried pulling the mock electrodes

into the cochlea using a ‘reverse perfusion’ technique. In this method, the perilymph was removed from the cochlea via the scala vestibuli hole using a perfusion pump while being continuously replaced with the solution via the round window. Mock electrodes were introduced in the flow using a syringe after visually confirming the inflow of the solution into the round window.” Dr. Olson and her research team presented proof of concept results in the August 2014 issue of *Hearing Research*.

Although Dr. Olson and her colleagues have reported a successful method for deep insertion without overt tissue damage, what is still unknown is what modifications are needed to make the method truly non-damaging. To further assess the ototoxicity of the hyaluronate perfusion, the investigators measured compound action potential thresholds (CAP) following the perfusion of the hyaluronic acid, and found that the CAP thresholds were substantially elevated. “While we believe the method is still promising, a number of challenges remain and the technique will require further research and development before we know if it is clinically viable,” says Dr. Olson.



Reference Article

Kale S, Cervantes VM, Wu MR, Pisano DV, Sheth N, Olson ES. A novel perfusion-based method for cochlear implant electrode insertion. *Hearing Research*. 2014 Aug;314:33-41.

For More Information

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