

## AAO-HNS International Tinnitus Mini-Seminar 9/12/11: implants attempting tinnitus relief

The AAO-HNSF, Martha Entenmann Tinnitus Research Center, Inc., (METRC), Abraham Shulman, M.D., and Barbara Goldstein, PhD, International Tinnitus Mini-Seminar, the first named Mini-Seminar of the AAO-HNSF, presented in this second year of a five-year endowed series of Mini-Seminars for tinnitus a panel of national and international experts to present recent advances in the treatment of implantable devices attempting tinnitus relief. The series is supported by a generous gift from the Martha Entenmann Tinnitus Research Center, Inc.

The 2<sup>nd</sup> ITL TINNITUS MINI-SEMINAR SEMINAR (ITM) was well attended, as it was the first in excess of 400 attendees. The feedback has been that the ITM achieved its stated goals - primarily to assert the continued commitment and leadership of the specialty of otolaryngology for clinical and research efforts for tinnitus diagnosis and treatment for the ultimate benefit of the tinnitus patient; and to provide state-of-the-art information for tinnitus professionals.

John House M.D. introduced the audience to the meeting by acknowledgment and expression of appreciation of the AAO-HNSF for the support of the Entenmann family for tinnitus research and tinnitus education. He shared his reflections of past original efforts of cochlear implantation of William House, M.D., Howard House, M.D., and the House Ear Institute and their projections to the future. The cochlear implant for attempting tinnitus relief is consistent with the advance of this technology.

The program chairman and moderator of the **International Tinnitus Mini-Seminar** Michael E. Hoffer, M.D. welcomed the audience and introduced the panel. The panel included: Jay T. Rubinstein MD PhD; Michael D. Seidman MD; Paul Van de Heyning MD, PhD; and Abraham Shulman, M.D.

The Mini-Seminar program - "The Use of Implants in the Management of Tinnitus, Monday, 9-12-11, 10:30-11:50AM, San Francisco, CA -, included reports by three acknowledged leaders in the field of implants for tinnitus, a panel discussion, an abstract of the meeting and a case report of cochlear implantation in a patient with unilateral tinnitus followed by questions and answers. All presentations reflected an ongoing basic science and clinical research effort directed to understanding the influence of electrical stimulation for the tinnitus complaint and its translation for tinnitus treatment. The results reported are a reflection of completed and ongoing research efforts awaiting final results for clinical application.

### **Jay T Rubinstein MD, PhD, University Washington: Electrical stimulation and tinnitus.**

The long history of electrical stimulation and attempting tinnitus relief was briefly presented highlighting

the efforts of CJC Grapengiesser, a physician from Berlin, who in 1801 reported treating tinnitus with Volta's column of silver and zinc plates. Ongoing research efforts targeting electrical tinnitus suppression (ES) since 2002 with publications in 2002-2004 were reviewed. Highlights include response of the auditory nerve to sinusoidal electrical stimulation, the effects of high-rate pulse trains, and the effects of dose dependent ES. Clinically three cases of cochlear implantation (CI) and tinnitus were reviewed with reported positive and negative results. Conclusions and observations in these cases included for tinnitus suppression: 1) thresholds of high frequency sensorineural hearing loss; 2) specific stimulation paradigms which can suppress tinnitus; and 3) that "some forms" of tinnitus are treatable with the CI. The processing of sensory stimuli with a neural prosthesis attempting tinnitus suppression with single/multi channel stimulation and multichannel recording is suggested from past experience to involve the development of a specialized neurostructural device. All clinical results with ES need to respect the issue of the placebo effect when evaluating the efficacy of the CI attempting tinnitus relief.

**REF:** Rubinstein JT, Tyler RS, Wolaver A and Brown CJ. Electrical suppression of tinnitus with high-rate pulse trains. *Otology & Neurotology*, 24: 478-485, 2003

**REF:** Runge-Samuels CL, Abbas PJ, Rubinstein JT, Miller CA, Robinson BK. Response of the auditory nerve to sinusoidal electrical stimulation: effects of high-rate pulse trains. *Hearing Research* 194(1-2):1-13, 2004.

### **Paul Van Heyning, M.D., PhD. University Antwerp: Incapacitating unilateral tinnitus in single-sided deafness treated by cochlear implantation.**

Patient selection and results of cochlear implantation (CI), short and long term in excess of 4 years in 22 patients with single sided deafness and incapacitating tinnitus were presented.

Exclusion criteria were highlighted by clinical history of depression, and pulsatile tinnitus.

Twenty-one subjects who complained of severe intractable tinnitus that was unresponsive to treatment were selected for CI. Tinnitus loudness was measured with a Visual Analog Scale; loudness percepts were recorded with the device activated and deactivated. Tinnitus distress was measured with the Tinnitus Questionnaire before and after implantation.

The results reported in 2008 with electrical stimulation via a CI included a significant reduction in tinnitus loudness (mean +/- SD; 1 year after implantation, 2.4 +/- 1.8; 2 years after implantation, 2.5 +/- 1.9; before implantation, 8.5 +/- 1.3). With the device deactivated, tinnitus loudness was still reduced to between 6.1 and

7.0 over 24 months. The Tinnitus Questionnaire revealed a significant positive effect of CI stimulation. The results reported in 2008 for 2 years were updated at this time to 4 years. Similar results of a double blind study with ES at the round window were reported. Conclusion was that unilateral tinnitus resulting from single-sided deafness can be treated with electrical stimulation via a CI. The outcomes of the pilot study reported in 2008 and updated at this time demonstrate a new method for treatment of tinnitus in select subjects. Clinically, single-sided deafness and incapacitating tinnitus was presented to be an important new indication for cochlear implantation. The question and answer period included discussion of the short electrode as proposed in the past by William House.

**REF:** Van de Heyning P, Vermeire K, Diebl M, Nopp P, Anderson I, De Ridder D. 2008 Incapacitating unilateral tinnitus in single-sided deafness treated by cochlear implantation. Department of Otorhinolaryngology-Head and Neck Surgery, University Hospital Antwerp. *Ann Otol Rhinol Laryngol.* 2008 Sep;117(9):645-52.

#### **Michael D. Seidman, M.D., Henry Ford Health System**

The results of direct electrical stimulation of the auditory cortex to relieve symptoms of severe tinnitus, successfully demonstrated in two patients in the past were updated. At this time brain stimulation was reported for a total of 6 patients. Significant improvement was reported for N= 4/ 6 patients. Negative results were reported for N=2/6 patients. Past results continue as reported in 2006 of two patients, a male patient reported the tinnitus to be near eliminated; a female patient noted a 30% to 35% improvement. All patients reported a debilitating tinnitus refractory to conventional therapies. The evaluation included validated questionnaires, psychoacoustic measures, magnetoencephalography (MEG), and functional magnetic resonance imaging (fMRI). This initial experience is ongoing for transcortical surgical approaches for brain implants attempting tinnitus relief, not limited to single neuroanatomic sites, e.g. primary auditory cortex, but for the future possible multiple site(s) for brain implantation are being considered e.g. primary auditory cortex, amygdala, hippocampus, dorsolateral prefrontal cortex; anterior cingulate, medial temporal lobe, insula. The technique of magnetoencephalography (MEG) for achieving objective data of electrical activity in brain i.e. coherent imaging was described.

Neurostimulation techniques also to be considered should include the promontory of the middle ear and middle ear implants for hearing. Non-published results of middle ear implants ongoing since 2002 for attempting tinnitus relief were reported of "30-40%". Significant are occasional reports of increased tinnitus. For the future, the concept of middle ear implants for hearing improvement to be considered alone and/or in combination with transcortical approaches for achieving tinnitus relief was presented.

#### **Abraham Shulman, M.D., SUNY/Downstate/ LICH. Cochlear Implant Soft Failure and Tinnitus: Quantitative Electroencephalography (QEEG) Pet brain-A Case Report**

This was the first time, to the best of our knowledge, that objective electrophysiologic and metabolic data of brain activity in a cochlear implant (CI) patient with unilateral tinnitus has been recorded. The case report was of a soft failure of a cochlear implant, recommended for hearing improvement, and its effect on preexistent single sided tinnitus, to illustrate, with brain PET and QEEG, significant issues of brain structure and function which are to be considered in the patient selection, diagnosis and treatment of tinnitus patients pre/post CI.

The audience was asked to consider in the evaluation of the CI attempt to achieve tinnitus relief three issues:

- 1) identification of the clinical type of tinnitus and conditions in the ear and brain which can influence the CI results for tinnitus relief;
- 2) the global effect of CI on brain with the elicitation of multiple brain functions not only targeting hearing function/perception and tinnitus perception; and
- 3) a patient selection process to include an evaluation of brain pre/post CI for objective identification of efficacy.

The highlights and conclusions of the case report included the following:

1. The clinical course of the tinnitus in this patient 12/07-6/09 was a soft sign of CI failure.

2. The cochlear implant influences electrical brain activity over a wide frequency spectrum of response in multiple neuroanatomic substrates reflecting multiple brain functions), i.e. a final common pathway for tinnitus, (FCP tinnitus): fronto-temporal-thalamo-parietal-cerebellum.

3. The Pet brain images support: 1) central role of the thalamus in the FCP hypothesized/reported in 1995; and 2) the significance of the thalamo-cortical oscillation for brain function reported in the past by many, and recently proposed as a mechanism for tinnitus by Llinas 1999.

4. The CI influence on tinnitus is individual for each tinnitus patient. Tinnitus response to the ES of the CI is suggested in this patient to have been a reflection of the underlying brain structure/ function reflecting auditory reafferentation and brain plasticity.

5. QEEG is recommended as a clinical and research tool for tinnitus diagnosis, treatment and monitor for efficacy of treatment at this time. QEEG co registered with nuclear medicine Pet brain imaging in this patient.

6. It is suggested clinically that the PET/QEEG data in this patient reflects multiple brain functions in the presence of the tinnitus signal, predetermined by brain structure-NOT- specifically the tinnitus signal.

A question and answer period for the panel followed and included discussion of the single channel im-

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plant; paradigms for electrical stimulation, double blind study single sided deafness and incapacitating tinnitus; brain implants.

Concluding remarks by Drs. Hoffer and Shulman included take home messages of the 2<sup>nd</sup> International Tinnitus Mini-Seminar:

1) to alert the membership of the AAO-HNSF, the otolaryngology community and all tinnitus professionals to the expanding nature of our specialty, i.e. the translation of what is known of brain function for structure and function to the clinical application for the diagnosis and treatment not only for tinnitus, but for all sensations; and

2) the implants are but one of a number of new treatment modalities that are providing some relief for some tinnitus patients. The state-of-the-art of the new discipline, Tinnitology, is providing the tinnitus patient with evidence of future modalities for tinnitus relief.

All are invited to attend the Third International Tinnitus Mini-Seminar, Boston, MA - date and time to follow.

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Dr. Shulman said Dr. Seidman is to be congratulated for his effort and that the procedure was a significant step forward, but it is premature at this time to think of this as a treatment for tinnitus. The procedure is an ongoing research project. Its significance for tinnitus relief will be determined by the long-term clinical course of the tinnitus, as reported by patients following the procedure.

He also indicated that for success of the procedure in achieving tinnitus relief, patient selection will be critical and the reported tinnitus relief will most likely be individual and variable.

In addition, he noted that the auditory cortex may not be the only site for electrical stimulation.

You may be able to target areas other than the auditory cortex that aren't even in the auditory system, he commented. The obvious ones are the cochlea, the cochlear nerve, the inferior cochlear nucleus, the superior cochlear nucleus, the dorsal and ventral cochlear nuclei, and the medial geniculate body. There are different areas in the auditory pathway that you can target and have an effect. But beyond that, you can affect the places that mediate a response to a severely annoying symptom. For example, the amygdala and the hippocampus.

Currently, he is using short cochlear insert electrodes that may suppress tinnitus while causing no damage to the inner ear.

While it is too soon to tell if any of these approaches will offer an effective management tool for tinnitus, the experts agree that electrical stimulation offers exciting possibilities for treating persistent, debilitating cases.

"The cochlear implant is a wonderful piece of technology that results in varying degrees of success.

Although the surgery is an integral part of the process, in my mind it is far from the most important aspect. The fundamental challenge really belongs to the person getting the CI, and it is through that person's motivation and determination (with the help of someone like Dr. Ruckel) that a great outcome is possible.

The CI is not for everyone with a profound hearing loss. And there are known risks which I tell to all my patients. The risks include: bleeding (<1%), infection (1.3%), extrusion of the implant with the need to remove the implant (<1%), change or loss of taste (1.30%), dizziness, numbness near the surgical site on the scalp and ear (which seems to resolve in days to months, and worsening of tinnitus (<2%)."

#### ITD CONCLUSION SUMMARY REMARKS:

The research involves severe disabling tinnitus patients who seek relief and have volunteered to learn more of how the tinnitus brain responds to direct or indirect stimulation with implants.

The program will, in the context of implants attempting tinnitus treatment, provide information on what is known of neuroanatomic substrates and physiology of all sensation, with translation for tinnitus, an aberrant auditory conscious percept.

"We have learned that in brain the physiologic response to the presence of the tinnitus signal is manifested by multiple brain functions, highlighted for tinnitus by that of perception, consciousness, communication, affect-emotion, behavior, memory, reward, attention (to name but a few) all of which are not yet completely understood. The clinical heterogeneity and complexity of tinnitus is reflected in multiple brain functions. We need to think of tinnitus in the context of overall brain function. This is an ongoing education for the tinnitus patient and tinnitus professional in order to translate advances in the neuroscience of sensation to that of tinnitus, an aberrant auditory conscious percept," explained Abraham Shulman, M.D., Emeritus Clinical Professor Otolaryngology, State of New York/ Downstate Medical Center, Brooklyn, New York, and cofounder together with his coworker Barbara Goldstein, PhD, Audiology, Assistant Clinical Professor Otolaryngology, of the METRC.