

Royal Victorian Eye and Ear Hospital opens Australia's first Temporal Bone Bank

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The Royal Victorian Eye and Ear Hospital and the Department of Otolaryngology at the University of Melbourne have joined forces to establish Australia's first temporal bone bank. Building upon Melbourne's long research and clinical interests in cochlear implantation, the temporal bone bank will also focus upon neuro-otological histopathology.

Current initiatives in cochlear implant otopathology and vestibulopathology are underway.

Cochlear Implant Otopathology

In recent years, our primary research interest in Melbourne has been otoprotection in the context of cochlear implantation (1) (2) (3). This has prompted a reappraisal of the cochlear histopathology of inner ear surgery. Some interesting questions that now need to be addressed include an elucidation of the causes of hearing loss after electrode insertion, mechanisms of delayed hearing loss, and the effects of protective agents such as steroids on hearing and the tissue response to implantation.

Using micro-CT imaging techniques adapted from Wong and colleagues (4), we are gaining new insights into the nature of the fibrosis that accompanies electrode insertion. Guinea pig temporal bones have been fixed in osmium tetroxide and imaged

to reveal in detail both the electrode track and the fibrosis that accompanies electrode insertion. Osmication increases the radiodensity of the soft tissues within the inner ear so that these can be seen more easily on the CT-scanned images, including the organ of Corti and Reissner's membrane (Fig. 1a). Note that the auditory neurons and lateral wall are particularly well stained. It is apparent from Fig. 1b that the fibrosis is very broadly based, extending in this cochlea from the lateral scalar walls towards the implant, a perspective not so well appreciated from histological sections. Micro-CT makes quantification of the electrode tract, and the shape and extent of the tissue response easier. In keeping with previous studies in human and feline temporal bones, we have shown using conventional histology that a more extensive tissue response is associated with poorer local survival of hair cells and spiral ganglion cell neurons (5). Interestingly, a greater extent of tissue response is also associated with poorer auditory brainstem response thresholds in cochlear regions apical to the position of the electrode (5). It is not yet clear whether the fibrosis disrupts this hearing by disturbing cochlear mechanics, or whether both the fibrosis and the hearing loss reflect the degree of cochlear inflammation experienced in the postoperative period.

Delayed hearing loss after cochlear implantation has proven to be a major impediment for electroacoustic hearing. This is

continued on page 6

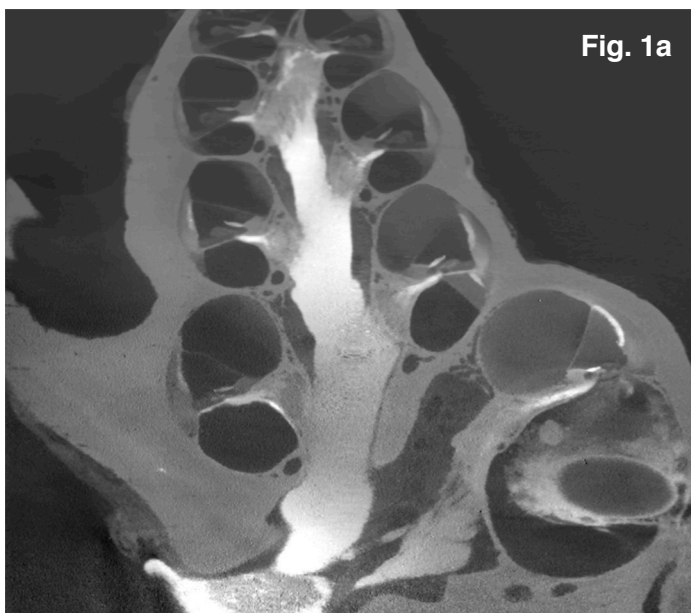


Fig. 1a

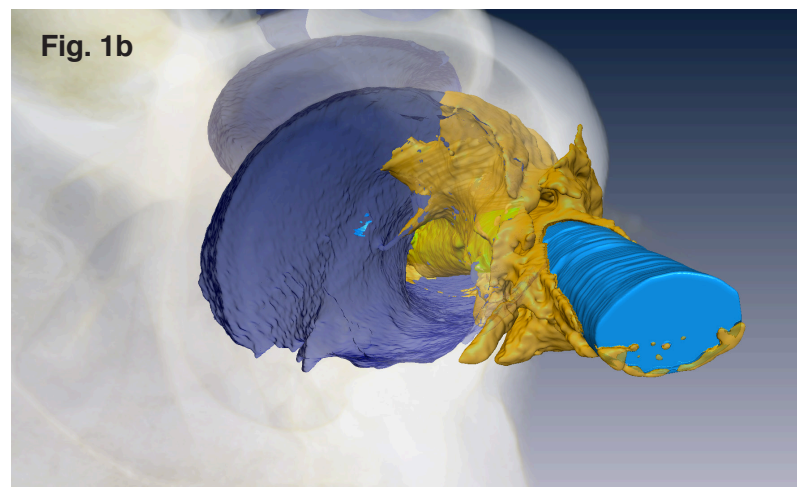


Fig. 1b

typified by deterioration in acoustic thresholds in the first few months after cochlear implantation, often rendering the residual hearing unaidable. Delayed hearing loss occurs in up to a third of patients who have undergone otherwise successful hearing-preservation cochlear implantation. A similar phenomenon can be observed in guinea pigs after cochlear implantation, so we have explored whether the extent of the tissue response to the cochlear electrode is associated with delayed hearing loss. We find that delayed hearing loss is seen only when the tissue response is extensive. Auditory brainstem response thresholds may actually improve over time when there is minimal fibrosis (5). We infer from these findings that more extensive inner ear injury is one potential mechanism for delayed hearing loss.

In view of the considerations above, it may be advantageous to seek to reduce the extent of fibrosis in the implanted cochlea. Glucocorticosteroids have been shown to protect hearing in several experimental models of cochlear implantation, so it is of interest to know whether these agents also modify the tissue response. Recently, we have compared the extent of fibrosis

surrounding the implant after the administration of either local or systemic steroids prior to electrode insertion. It was found that systemic, but not locally applied steroids reduced the amount of fibrosis within scala tympani (6). It seems, therefore, that steroids may not only improve hearing, but also modify the tissue response to surgery (although, the latter is influenced by the route of administration).

The Australian Temporal Bone Bank builds upon a small collection of human temporal bones within the Department of Otolaryngology, most of which were donated by cochlear implant recipients. We are looking forward to contributing further to cochlear otopathology through this new venture.

Vestibulopathology

We are also particularly interested in developing expertise in vestibular histopathology. A recent collaboration between our neurologist/neuro-otologist, Dr. David Szmulewicz and the Otopathology Laboratory at the Massachusetts Eye and Ear Infirmary demonstrates the potential benefits of the temporal

bone bank for improving an understanding of vestibular disease. Several years ago, a group of patients were identified with cerebellar ataxia and an abnormal visually enhanced vestibular ocular reflex (VVOR), which is a compound impairment of the three key corrective oculomotor reflexes, namely smooth pursuit, the vestibulo-ocular reflex (VOR) and the opticokinetic reflex (OKR). A peripheral neuropathy was found also to be integral to this syndrome that has subsequently been called Cerebellar Ataxia Neuropathy bilateral Vestibular Areflexia Syndrome (CANVAS) (7). It was not until the temporal bone and lower cranial nerves were examined that the histopathology was found to be a neuronopathy (ganglionopathy) of the vestibular, facial and trigeminal nerves (8). This is seen in Figure 2, where the vestibular nerve is seen to be atrophied, and there is a reduced neuronal density in Scarpa's ganglion. This condition can now be diagnosed at the bedside through the advent of fast video goggles that allow for diagnosis of an impaired VVOR (9), and more than 60 patients, including nine kindreds, have been identified. Identification of the causative gene is now well underway.

We would like to thank MEEI, and in particular the late Saamil Merchant, whose enthusiasm and generosity encouraged us to proceed with plans to establish a temporal bone bank. We would also like to thank the NIH for allowing us to adapt the Temporal Bone Registry's donor materials for use in Australia, to promote consistency in the patient information collected on each side of the Pacific. ■

< Fig. 2

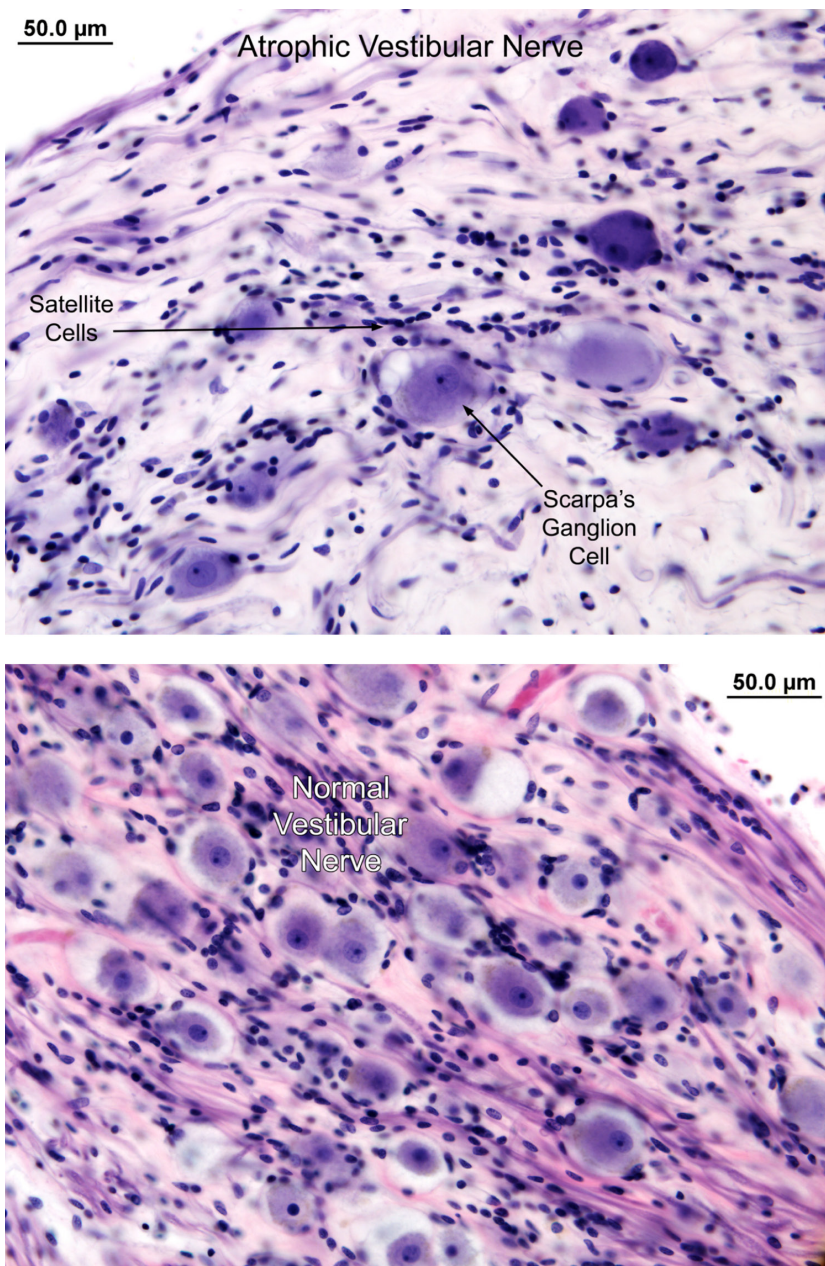


FIGURE LEGENDS

Figure 1a. Micro-CT of a cochlear turn in the guinea pig following fixation in osmium tetroxide. Note the cochlear dummy electrode present within scala tympani in the lower basal turn.

Figure 1b. The tissue response to cochlear implantation, rendered from a micro-CT volume. The basal turn on the left cochlea is viewed from the round window looking apically, with the wall of scalar tympani in purple (medial side to the left). The electrode (blue) was inserted via a cochleostomy and is tracking along the lateral cochlear wall. The tissue response (yellow) is broadly based, extending over a wide front from the lateral wall and spreading towards the electrode. These images are the work of Dr. Phillip Sale, from the Department of Otolaryngology, University of Melbourne.

Figure 2. The histopathology of the vestibular nerve in a case of CANVAS. The vestibular nerve is seen to be much more atrophic than normal, and the neuronal density in Scarpa's ganglion is significantly reduced. This work was a collaboration between MEEI, Dr. Szmulewicz and colleagues in Australia. The sections were processed in the Otopathology Laboratory at the Massachusetts Eye and Ear Infirmary.

REFERENCES

1. James DP, Eastwood H, Richardson RT, O'Leary SJ. Effects of round window dexamethasone on residual hearing in a Guinea pig model of cochlear implantation. *Audiol Neurotol*. [6136834]. 2008;13(2):86-96.
2. Chang A, Eastwood H, Sly D, James D, Richardson R, O'Leary S. Factors influencing the efficacy of round window dexamethasone protection of residual hearing post-cochlear implant surgery. *Hear Res*. [6136831]. 2009 Sep;255(1-2):67-72.
3. Connolly TM, Eastwood H, Kel G, Lisnichuk H, Richardson R, O'Leary S. Pre-Operative Intravenous Dexamethasone Prevents Auditory Threshold Shift in a Guinea Pig Model of Cochlear Implantation. *Audiol Neurotol*. [10268389]. 2010 Jul 29;16(3):137-44.
4. Wong CC, Curthoys IS, O'Leary SJ, Jones AS. Heavy metal staining, a comparative assessment of gadolinium chloride and osmium tetroxide for inner ear labyrinthine contrast enhancement using X-ray microtomography. *Acta Otolaryngol*. 2013 Sep 19;133(1):22-7.
5. O'Leary SJ, Monksfield P, Kel G, Connolly T, Souter MA, Chang A, et al. Relations between cochlear histopathology and hearing loss in experimental cochlear implantation. *Hear Res*. [Research Support, Non-U.S. Gov't]. 2013 Apr;298:27-35.
6. Lee JH, Ismail H, Kel G, O'Leary JS, Hampson A, Eastwood H, et al. Effect of both local and systemically administered dexamethasone on long-term hearing and tissue response in a guinea pig model of cochlear implantation. *Audiol Neurotol*. 2013;accepted 7 June 2013.
7. Szmulewicz DJ, Waterston JA, Halmagyi GM, Mossman S, Chancellor AM, McLean CA, et al. Sensory neuropathy as part of the cerebellar ataxia neuropathy vestibular areflexia syndrome. *Neurology*. 2011 May 31;76(22):1903-10.
8. Szmulewicz DJ, Merchant SN, Halmagyi GM. Cerebellar ataxia with neuropathy and bilateral vestibular areflexia syndrome: a histopathologic case report. *Otol Neurotol*. [Case Reports]. 2011 Oct;32(8):e63-5.
9. Szmulewicz, D. J., Waterston, J. A., MacDougall, H. G., Mossman, S., Chancellor, A. M., McLean, C. A., et al. Cerebellar ataxia, neuropathy, vestibular areflexia syndrome (CANVAS): a review of the clinical features and video-oculographic diagnosis. *Ann. N.Y. Acad.* (2011). Sci. 1233(1), 139–147.

Otopathology Mini-Travel Fellowship Program

The NIDCD National Temporal Bone Registry is pleased to announce the availability of mini-travel fellowships. The fellowships provide travel funds for research technicians and young investigators to visit a temporal bone laboratory for a brief educational visit, lasting approximately one week. The emphasis is on the training of research assistants, technicians and junior faculty.

These fellowships are available to:

- U.S. hospital departments who aspire to start a new temporal bone laboratory.
- Inactive U.S. temporal bone laboratories that wish to reactivate their collections.
- Active U.S. temporal bone laboratories that wish to learn new research techniques.

Up to two fellowship awards will be made each year (\$1,000 per fellowship). The funds may be used to defray travel and lodging expenses. Applications will be decided on merit.

Interested applicants should submit the following:

- An outline of the educational or training aspect of the proposed fellowship (1-2 pages).
- Applicant's curriculum vitae.
- Letter of support from temporal bone laboratory director or department chairman.
- Letter from the host temporal bone laboratory, indicating willingness to receive the traveling fellow.

Applications should be submitted to:

Michael J. McKenna, M.D.
NIDCD Temporal Bone Registry
Massachusetts Eye and Ear Infirmary
243 Charles Street
Boston, MA 02114
michael_mckenna@meei.harvard.edu