Establishing a mouse model to investigate the biological response to cochlear implantation

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Introduction

Despite the huge success of cochlear implants (CIs), some individuals experience less favourable outcomes than are desirable. A significant proportion of which are not due to hardware or surgical failures but are due to the biological response at the electrode-tissue interface. Therefore, despite the continuing improvement in electrode design, signal processing and surgical technique, there is still significant performance variability and underperformance which needs to be addressed. As availability of human tissue to investigate the inflammatory response to cochlear implantation is limited, there is great need for effective *in vivo* models. At Southampton, we are establishing a mouse model to investigate the inflammatory response at the electrode-tissue interface, to arrays designed and coated with sophisticated materials with the aim to improve implant design and reduce poor performance outcomes.

The clinical challenge

In our lab, the biological response at the electrode-tissue interface in a human explant case has been investigated.

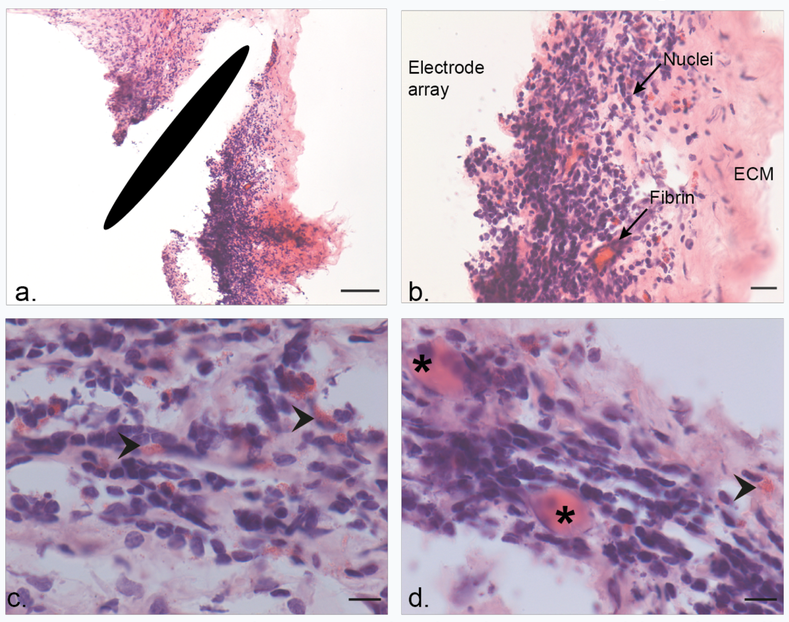


Figure 1: Human explant tissue that has been stained histologically which revealed information about the overall tissue composition and cellular arrangement. The tissue at the electrode-tissue interface showed signs of active inflammation and developing fibrosis.

Aims

To establish a reliable mouse model to enable the investigation of the active biological response at the electrode-tissue interface and throughout the auditory system.

Initial aims:

- Optimise implant design
- Optimise surgical technique
- Establish tissue processing methodology

Electrode arrays provided by Oticon Medical will be coated with varying materials.

Does changing the material that coats the electrode array have an affect on:

- Impedance
- Level of inflammation
- Tissue response

Overall aim:

To characterise the cellular phenotype at the electrode-tissue interface to gain a better understanding of the overall inflammatory response to different materials.

Results

Optimise implant design

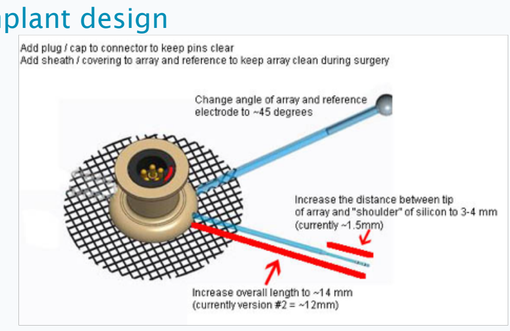


Figure 4: Diagram showing the implant designed by Oticon Medical, with information regarding the latest optimisations.

Optimise surgical technique

To allow:

- Easiest surgical implantation, with minimal physical damage to the cochlea and surrounding tissue
- Successful recovery of the mouse with the implant in
- Precision and repeatability in additional mice

Technique: Insertion of electrode array through bullotomy into the round window. Ground electrode tucked into neck muscles. Implant connector plug inserted through the skin at the back of the neck.

Methods

Surgical implantation: Surgically place electrode arrays into a mouse cochlea through the round window.

μCT:
- Provide 3D structural information about the cochlea pre-implantation.
- To validate surgical technique post-implantation.

Immunohistochemistry (IHC): To characterise cellular distribution and phenotype at the electrode-tissue interface, in the cochlea and central auditory pathway following cochlear implantation.

RNAscope: To characterise the gene expression to understand detail of the inflammatory response with high specificity and sensitivity.

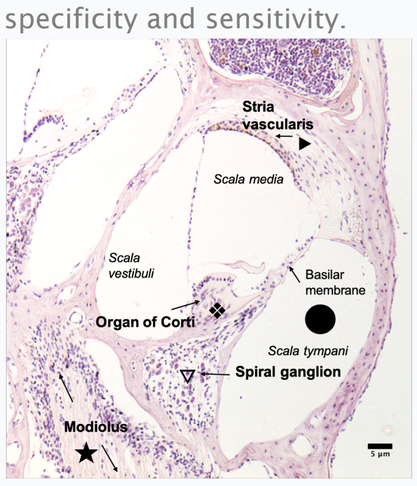


Figure 2: Cochlea histology highlighting key regions of interest in the cochlea including organ of Corti, stria vascularis, spiral ganglion and modiolus. Symbols used to highlight key regions in figure 2 and 3. The black circle indicates where the electrode array would be.

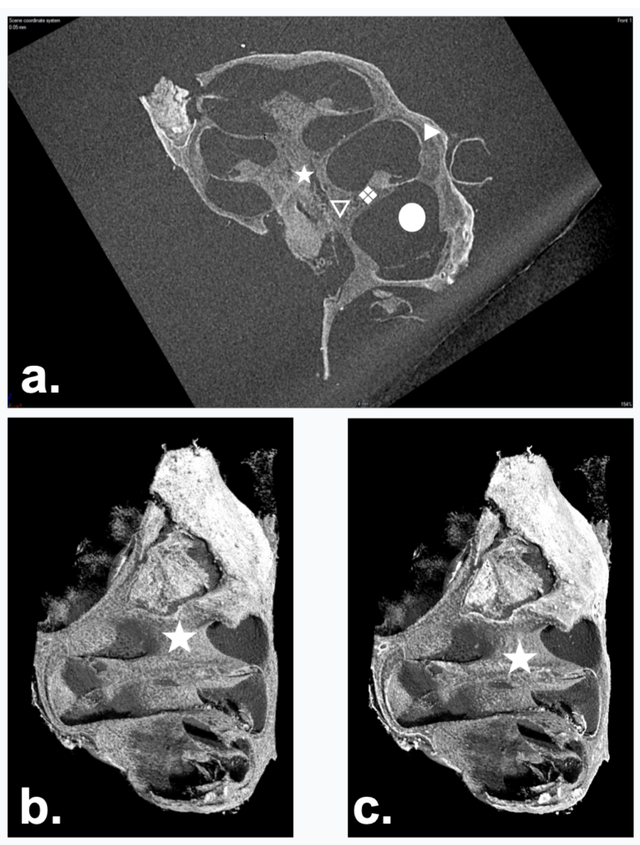
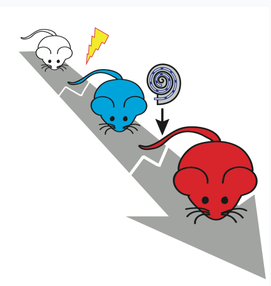


Figure 3: Pilot μCT data of a cochlea from a young mouse.
a. A single digital mid-modiolar section of the cochlea at one orientation showing regions of interest, highlighted with symbols as in figure 2.
b,c. Overall 3D images of the cochlea at high resolution with the modiolus indicated with a star.

Findings and Future work

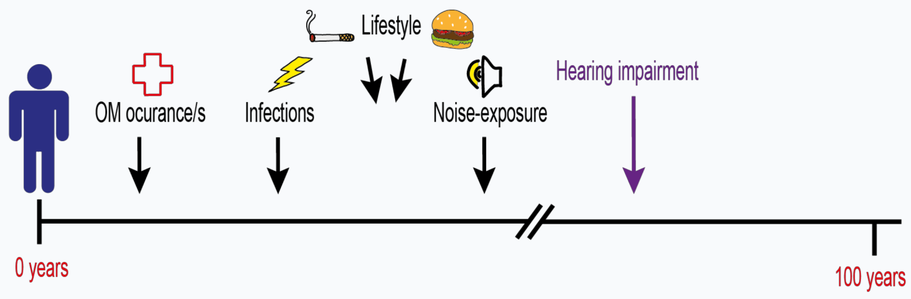
This work will provide a better understanding of the overall inflammatory response at the electrode-tissue interface to different materials, which will improve electrode design and cochlear implant outcomes.



Future work:

Mice that have been pre-exposed to an inflammatory insult such as noise exposure will be implanted to investigate the effects of lifestyle-history on auditory health and CI performance.

We hypothesise that lifestyle factors that affect our overall inflammatory status will influence how well individuals do with their implant.



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