The cellular response to cochlear implants, a study in a person undergoing implant replacement

K. Hough[1], A. Sanderson[1], M. L. Grasmeder[2], T. Mitchell[2], C. A. Verschuur[2], T. A. Newman[3]

Faculty of Engineering and Physical Sciences, University of Southampton, UK[1], Auditory Implant Service, University of Southampton, UK[2], Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, UK[3]

The clinical need

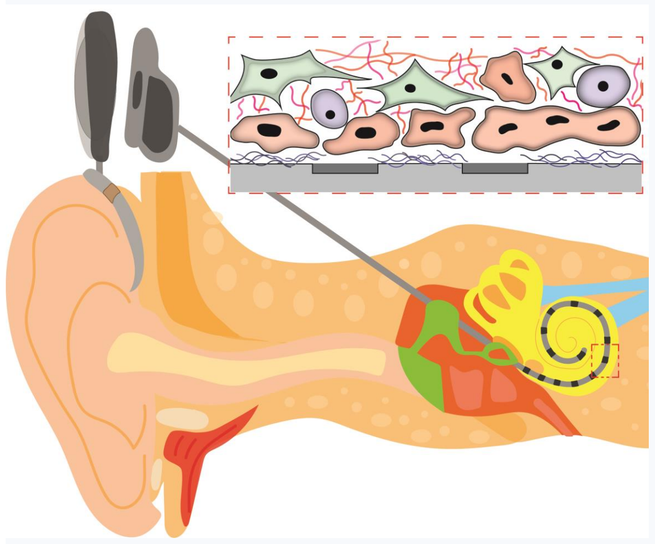
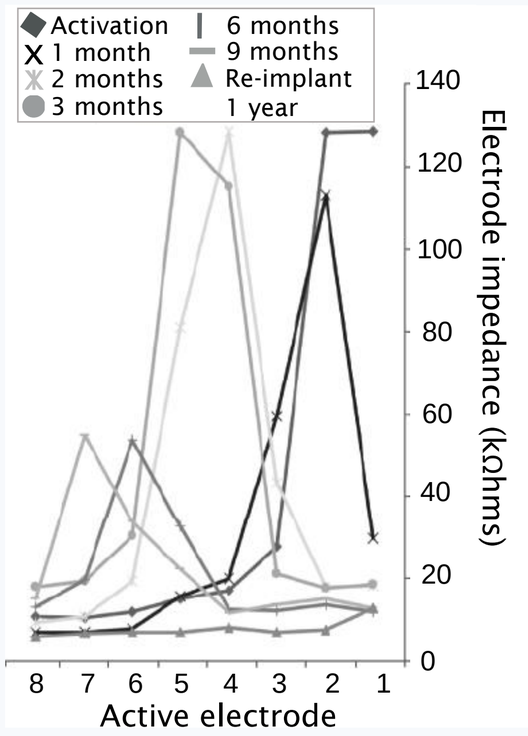


Figure 1. **The components of an ear with a cochlear implant.** When the array is implanted, a cellular environment (red box – insert) forms around the array as a result of the wound healing response. This consists of inflammation, repair and remodeling. This response should resolve, however in some cases there is increased inflammation and fibrosis leading to poor performance.

Soft failures are adverse events that are not caused by hardware or surgical factors and are therefore likely due to individual characteristics including an interaction between the body and the implant (cellular response). Soft failures are a persistent problem and lead to replacement of the implant. Understanding the causes and characteristics of soft failures may enable strategies to mitigate the risk of this type of failure.

We are hypothesising that the cellular response around the implant affects hearing outcomes and that different factors can influence the type of tissue response. Previous studies investigated the response in human post-mortem tissue (Li et al., 2007; Seyyedi and Nadol, 2014). The aim of the current approach is the development of a method that links hearing and implant measures to the tissue response, enabling associations between the tissue response and decline in hearing performance.

Clinical indicators of soft failure



Over the period of 10 months since implantation the person experienced non-auditory sensations, a decline in hearing performance, fluctuations in impedance, successive basal electrode deactivations and partial migration of the array out of the cochlea. The case was identified as a soft failure. The clinical decision was made for the person to undergo replacement surgery.

Figure 2. **Impedance telemetry in common ground mode from activation until shortly before re-implantation in the 8 most basal electrodes.** There was a shift in impedance across the period of implantation with an initial peak in electrodes 1 and 2. As electrodes were deactivated, the impedance peak shifts across electrodes 3-8 over the time of implantation. After 1 year of use with the new device, impedance measures were in the normal range.

Decision to characterise the tissue response

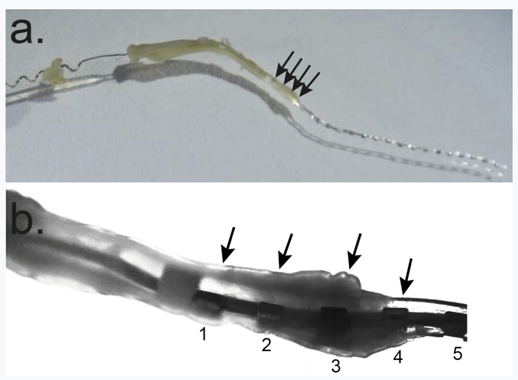


Figure 3. **Photograph of the array following removal, with fibrosis attached.**
a. Full length of the electrode array with the tissue that formed around it.
b. Higher magnification view of the array with the tissue covering at least four electrode contacts (black arrows).

On removal of the implant during replacement surgery, the implant was collected and immersed in fixative. The tissue associated with the implant was removed and processed, taking care to preserve tissue orientation.

The tissue response to the implant was characterised using histo- and immuno-histochemical labelling.

The gross structure and cellular organisation of the tissue was characterised using the stain, Haematoxylin and Eosin.

Finding: Evidence of unresolved, active inflammation and ongoing repair

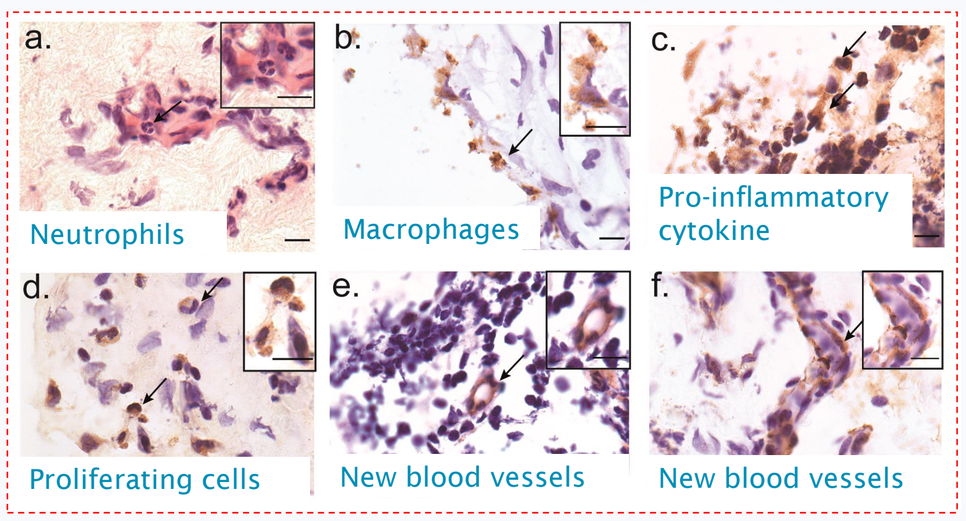


Figure 4. **Cellular evidence of ongoing inflammation and tissue repair.** Evidence of neutrophils (a), pro-inflammatory macrophages (CD68) (b), pro-inflammatory cytokine (IL-1B), proliferating cells (Ki-67) (c), the formation of new blood vessels (VEGFR2) (e) and myofibroblasts (α-sma) (f). Arrows indicate positively labelled cells. Scale bar = 10 μm.

As with post-mortem tissue analysed from human temporal bone studies (Li et al., 2007; Seyyedi and Nadol, 2014), we found evidence of immune cells such as neutrophils, macrophages and T cells suggesting active inflammation. We also found evidence of ongoing tissue repair and blood vessel formation across the tissue.

What we found

This response was unusual to see this long after surgery. We are hypothesising that there was an **unresolved wound healing response** with chronic inflammation and repair at the same time across the tissue, whereby the response didn't reach the remodeling phase. Increased inflammation and fibrosis has been shown to cause increased impedance and decreased hearing outcomes. The tissue response in this soft failure likely contributed to the deterioration in hearing performance.

Novel work compared to human temporal bone studies:

- Captures the tissue response close to the time of underperformance.
- Enables the **correlation** of the clinical measures and health data with the biological findings for the individual. This may inform of **factors** that **influence** the tissue response and subsequent **hearing performance**.

Potential outcomes:

- Identify **biomarkers** and **hallmarks** of performance decline.
- Inform ways to **improve outcomes** with earlier identification of the problem and subsequent intervention.

(Hough et al., 2021)
Scan QR Code

Ongoing work

Objective: Investigate the variability of the tissue response to cochlear implantation and the consequences for hearing quality.

Aim: Characterise the tissue response in people who are undergoing cochlear implant replacement surgery. We are in the process of applying for ethics and establishing an active patient and public involvement (PPI) group to work closely with.

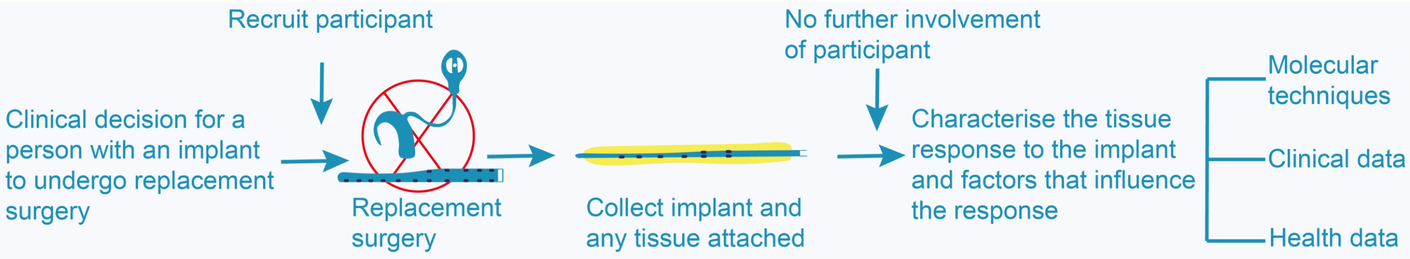


Figure 5. **Research project design.** If a person with a cochlear implant requires replacement surgery, they will be invited to participate in the study. During replacement surgery, the implant and any tissue attached will be collected. The tissue will be removed from the implant, processed and analysed using molecular techniques. Clinical and health data will be collected and analysed to identify any relevant factors that may influence the tissue response and hearing performance.

EPSRC
Engineering and Physical Sciences Research Council

Kate Hough
k.l.hough@soton.ac.uk

References:
Li, P. M. M. C., Somdas, M. A., Eddington, D. K., & Nadol, J. B. (2007). Analysis of intracochlear new bone and fibrous tissue formation in human subjects with cochlear implants. *Annals of Otology, Rhinology & Laryngology*, *116*(10), 731–738.
Seyyedi, M., & Nadol, J. B. (2014). Intracochlear inflammatory response to cochlear implant electrodes in humans. *Otology and Neurotology*, *35*(9), 1545–1551.
Hough, K., Sanderson, A., Grasmeder, M., Mitchell, T., Verschuur, C. A., & Newman, T. A. (2021). Inflammation at the tissue-electrode interface in a case of rapid deterioration in hearing performance leading to explant after cochlear implantation. *Otology & Neurotology*, *42*(4), e445–e450.

AUDITORY IMPLANT SERVICE
US/AIS
MAKING CONNECTIONS