Evaluation of Failure Mechanisms of Utah Electrode Arrays in Rat Cortex

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Statement of Purpose: Microelectrodes offer the potential to record from and stimulate nervous system tissue for the control of neuroprosthetic devices. However, these devices currently suffer from long-term performance stability. While the histological response to these types of devices has been studied for over half a century, researchers have only recently begun to describe overall failure mechanisms, including mechanical failure of such devices. Further, no group has successfully correlated the histological response around these devices to their performance in order to identify specific cellular mechanisms that may negatively influence device performance. Here we evaluate the failure mechanisms associated with the implantation of 4x4 Utah Electrode Arrays (UEAs) into rat cortex, and offer evidence that blood-brain-barrier (BBB) disruption may be a contributing factor to performance failure.

Methods: 4x4 UEAs connected to an Omnetics connector (Omnetics Connector Corporation, Minneapolis, MN) were obtained from Blackrock Microsystems (Salt Lake City, UT). Following ETO sterilization, UEAs were implanted into the cortex of young male Sprague-Dawley rats. One week after implantation, and at weekly intervals thereafter, electrophysiological recordings were obtained from each animal using a Cerebus recording system (Blackrock Microsystems). Animals were sacrificed by transcardial perfusion following failure of the device (mechanical) or performance failure (no recordings for two weeks). Failure mode was determined by gross examination of the implant at sacrifice. For histological analysis, brain tissue sections were collected at 30µm, stained for a battery of immunomarkers against neuronal cells and processes and inflammatory markers, and confocally imaged. Quantitative measurement of these markers was performed by subtracting tissue-negative area from the image (such as electrode tracks and areas outside of brain tissue) and calculating the average pixel intensity for each stain in the area around the implant. Intensity values were normalized to values obtained from contralateral images from each animal.

Results: The majority of animals in our study failed by three weeks post-implantation, with no animal being implanted for longer than six weeks (Figure 1). The majority of animals failed due to headstage failure, primarily due to loosening of the bone screws used to hold the headstage in place (Figure 2). We also observed lead wire breakage in several earlier animals due to animal manipulation, which was resolved through the implementation of Elizabethan collars on the animals. Correlating histological findings to device performance, we observed that animals whose devices maintain recording ability demonstrated a lower concentration of IgG around the implant compared with animals whose devices did not maintain recording ability. No other marker tested suggested a correlation to device

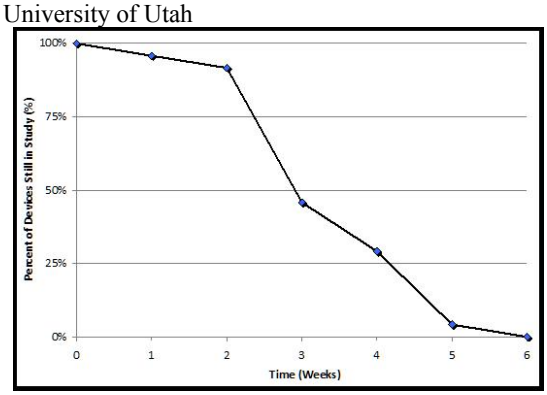

Figure 1: Failure timeline of devices shows that a majority of devices failed within three weeks of implantation.

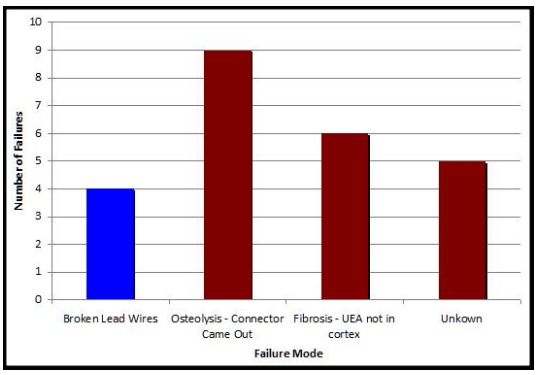

Figure 2: Failure modes demonstrate that headstage failure was the predominate failure mechanism. Devices placed in the unknown category are believed to have failed due to the biological response to the implants.

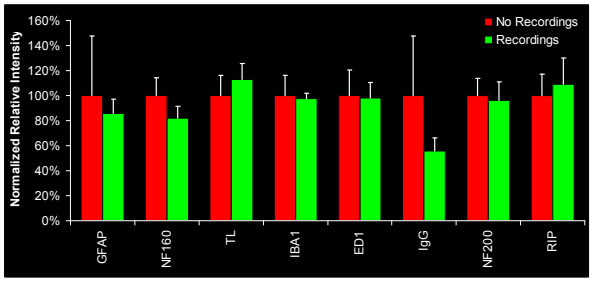

Figure 3: Correlative histology suggests a relationship between IgG concentration and device functionality, while no other markers tested suggest correlation.

Conclusions: This study shows that mechanical failure may be a major failure mode for microelectrode devices and should be further addressed in research to produce more reliable chronic implants. Further, this study suggests a possible relationship between IgG concentration and device functionality. This may be due to changes in the ionic milieu resulting from BBB disruption and should be the subject of future research.