Microelectrodes with Reduced Surface Area Show a Reduced Foreign Body Response

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Introduction: Long-term recording performance of implanted microelectrode arrays is believed to be adversely affected by the tissue response. Irrespective of the type of implanted electrode, researchers have observed persistent inflammation, reactive gliosis and neuron loss in the tissue surrounding the implanted array.[1] It remains unclear whether, and how, device architecture modulates the foreign body response.[2,3] Since macrophage secreted factors shape the tissue reaction, implant architectures that reduce macrophage activation may be used to improve biocompatibility and long-term recording performance. Toward this end, using biomarkers of the tissue response, we studied the chronic brain tissue reaction to silicon, planar microelectrode arrays of varying exposed surface area implanted in rat brain.

Materials and Methods: 300µm-wide planar solid and 300µm-wide planar, lattice arrays were supplied by the Center for Wireless Integrated Microsystems both at the University of Michigan. Microelectrode arrays (n = 6) were implanted stereotactically to a depth of 3 mm from the top of the cortex at -3.2 mm of bregma, and 2.0 mm lateral to bregma. Electrodes were then fixed to the skull with a custom-fabricated polyurethane grommet using a UV curable, medical-grade adhesive. At 8 and 12 weeks post-implantation, animals were transcardially perfused with 4% paraformaldehyde. Serial sections were taken in the coronal and horizontal planes and processed using indirect immunohistochemistry for ED-1 to assess activated microglia/macrophages, GFAP for astrocytes, NeuN for neuronal nuclei and counterstained with DAPI. Analysis was performed as previously described.[4]

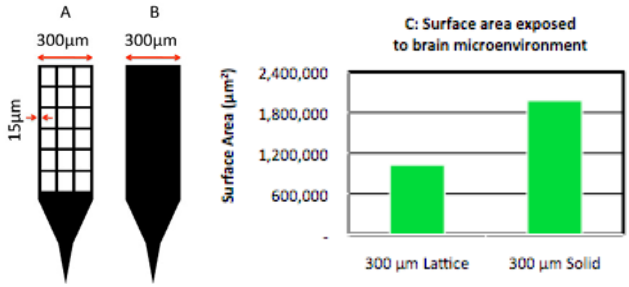

Figure 1: Solid work models showing the first millimeter of A) 300µm lattice and B) 300µm solid arrays. C) Calculated surface area exposed to brain microenvironment.

Results: Activated macrophages/microglia, identified with antisera against CD68 (ED-1), were observed at the electrode interface for both solid and lattice architectures (Figure 2). The ED-1 response surrounding the 300µm solid, planar arrays was similar to that which our group has described previously around other solid, planar arrays.[4] Compared to 300µm solid arrays we observed a reduction in the amount of ED-1 immunoreactivity near 300µm lattice arrays. Excitingly we also observed a significant reduction in neuronal loss surrounding the 300µm lattice arrays compared to the 300µm solid arrays.

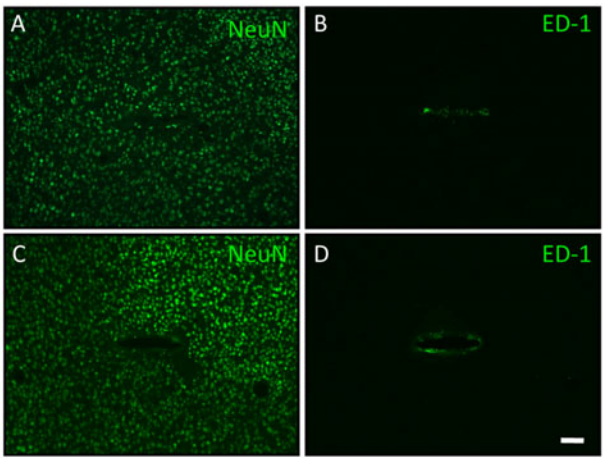

Figure 2: Chronic brain tissue response to implanted silicon microelectrode arrays. (A & C) Representative horizontal sections through the implantation tract of a 300µm lattice (A) and a 300µm solid array (C) showing the distribution of NeuN. (B & D) Representative horizontal sections showing ED-1 immunoreactivity adjacent to (B) 300µm lattice and (D) 300µm solid arrays. Silicon microelectrode arrays with reduced surface area showed reduced macrophage activation and neuronal loss.

Conclusions: In this study we found that planar silicon microelectrodes with less surface area elicited reduced microglial/macrophage activation, reduced reactive gliosis and reduced neuronal loss at the device/tissue interface. These findings support the notion that it is possible to modulate the tissue response by changing an implant's architecture. However, these exciting findings were also tempered by the fact that upon retrieval, unlike solid electrodes, retrieved lattice arrays had a significant amount of brain tissue associated with them. From an application perspective this may present a problem, especially with larger multi-shank devices, if the devices need to be explanted due to infection or other adverse clinical event. To prevent tissue in-growth through microelectrode architectures that contain openings, we are currently examining techniques to covalently tether hydrogels with various chemistries and physical properties within the lattice windows. Using this method, we are investigating how such treatments affect the chronic foreign body response in rat brain.

References:

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