Biodegradable Polymers for Stealth Neural Probes

Dan Lewitus[1] Karen L. Smith[2] William Shain[2], Joachim Kohn[1]

[1]New Jersey Center for Biomaterials, Rutgers University, Piscataway, New Jersey, USA

[2]Wadsworth Center, New York State Department of Health, Albany, NY, USA

Statement of Purpose Our aim is to investigate the use of novel degradable polymers as means to prolong the work life of cortical neural probes via a stealth approach. Neural probes are metal/silicon based prosthetic devices inserted into the brain for recording signals directly from neurons[1]. Gliosis, the foreign body response in the central nervous system, occurs as consequence to the insertion and presence of the probes in the tissue, and diminishes their recording performance with time.[2] Our polymer enables the use of micro-sized probes[3] by providing a short-lived, support structure with sufficient mechanical strength for insertion of the probe. After insertion, the support structure is rapidly resolved, thereby reducing the tendency of the surrounding brain tissue to develop a chronic tissue response around the micro-sized probe.[4] resulting in ameliorated gliosis and electrophysiological dysfunction.

Material and Methods A fast degrading polymer was identified among the library of tyrosine-derived polycarbonates.[5] In vitro degradation profile and dry/wet tensile properties were measured. Microwire probes, were dip coated in polymer solution, and used for the in vivo evaluation of brain tissue response to the polymer. Resorption of the coating was verified visually both in-vitro and in-vivo. Impedance of microwire probes was tested in buffer and monitored as the coating resorbed over time. In-vivo tissue response was evaluated by insertion of probes in rat brain, 3mm anterior to lambda, 3mm lateral from the sagittal suture. After dura removal, a plastic pedestal was placed over the exposed tissue to support the inserted probe. A ground screw was placed 2mm anterior to bregma. Histological tissue response was evaluated one and four weeks post insertion. Tissue was immunohistochemically labeled for 3 cell types, neurons (nissl/NeuN), astrocytes (GFAP) and microglia (Iba-1), and imaged using a confocal microscope. During the in-vivo evaluation period, recording of neural signals was performed using a Tucker Davis Technologies® system followed by spike sorting (Plexon®).

Results and Discussion Polymer dissolved completely in buffer after 2 hours, and lost significant strength 25 minutes after wetting. Modulus and stress at yield decreased to 80% of their dry value but strain at yield and maximum strain where retained. These findings indicate that the polymer is behaving as required, having initial high strength for insertion, followed by rapid loss of strength while degrading. The degrading polymer retained plasticity as indicated by the retention of strain properties. This property reduced the tendency to form fractured particulates during degradation. Time lapse imaging visually displays the process of the polymer dissolution/erosion, and correlates with decreasing impedance of coated probes. In-vivo, the resorption of the coating was verified after a 4 hour implantation period. After probes were recovered from fixed brain tissue, it was clear that the polymer coatings had completely resorbed (figure 1A). Imaging of fluorescent marker embedded in the polymer (5-dodecanoylaminofluorescein, DAF) allowed us to follow the diffusion of the polymer in vivo, though it seems that a 1% agarose model has slightly larger diffusivity than actual brain tissue (figure 1B.)

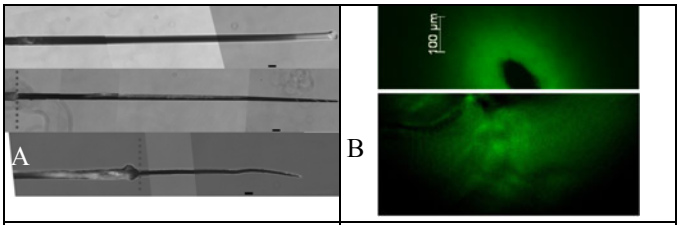

Fig 1: A. Top to bottom, polymer coated probe. Probe after erosion in agarose. Coated probe after in-vivo erosion in brain. (4 hours) grey dots denote depth of probe insertion.

B. Erosion of DAF loaded polymer coating after 4 hours. Top, brain tissue Bottom, agarose gel. scale bars - 100µm

Action potentials recorded from coated and non-coated implanted probes demonstrated the latent recording of neuronal signals. Initially weak signals are recorded, possibly associated with polymer impedance and insertion-related injury. Within a week, and for at least one month, action potentials with good signal-to-noise ratios were observed (figure 2), indicating polymer coating resorption and tissue recovery without significant damage to local neurons. Immunohistochemical evaluation of brain tissue reveals that after 1 week, an acute response is apparent, as evidenced by massive activation of microglia cells throughout a large area surrounding the probe. One month after insertion, the tissue response to the remaining probe diminishes and is similar to that of control, non-coated probes, with apparent tissue recovery.

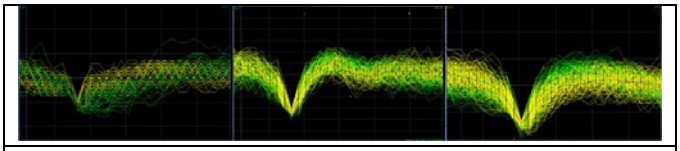

Fig 2: in-vivo electrophysiology. Recording from rat implanted with a polymer coated probe. Left, 11 minutes post insertion. Center, after 1 week. Right, after 4 weeks. 2 distinguished channels (yellow, green) are visible.

Conclusions we have identified a strong yet fast degrading polymer among the tyrosine-derived polycarbonates. The polymer physical properties, along with the lack of a prolonged adverse tissue effect to its presence in vivo, indicate its promising potential in the development of stealth neural probes.

References 1. Kipke D. R. Conf Proc IEEE Eng Med Biol Soc 2004, 7, 5344-7. **2**. Polikov V. S. J Neurosci Methods 2005, 148, (1), 1-18. **3**. Seymour J. P. Biomaterials 2007, 28, (25), 3594-607. **4**. Biran R. Exp Neurol 2005, 195, (1), 115-26. **5**. Kohn J. Biomaterials 2007, 28, (29), 4171-4177.