Gel-based Mimics for Tissue-Electrode Interfaces in the Brain Under Chronic Conditions

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THE brain tissue surrounding neural implants undergo dynamic changes in material properties under long-term conditions. Previous work done by our lab suggests that chronic implantation leads to a monotonic increase in the elastic modulus of brain tissue in the interface from 5-7 kPa on day 1 to 30-40 kPa after 4 weeks of implantation. [1] To facilitate reliability testing of chronic implants and development of novel bioactive coatings for microelectrode arrays, we have developed benchtop mimics of the brain tissue-electrode interface under chronic conditions. In this study, we compared various compositions of agarose-based hydrogels and silane-derived gels to the mechanical properties of the tissue-electrode interface in the brain under chronic conditions.

II. METHODS

A spherical indentation methodology was used to characterize the material properties of gels. To find the elastic modulus, gels were placed under a load cell powered by a motorized drive. Using a stainless-steel, spherical indenter (3 mm diameter), gels were indented for 200 µm at 13 µm/sec. Strain-rate dependency was also examined after stoppage of movement. All data were collected in Logger Pro V3.1. To calculate the elastic modulus, the spherical indentation model [2] was used:

$$\frac{P}{\pi a^2} = \frac{4}{3\pi} E^* \left(\frac{a}{R}\right)$$

where P is force, a is contact radius, E^* is the system composite modulus, and R is the radius of the indenter. The contact radius, a, is calculated based a previously established relationship between indentation depth and radius of the indenter. Poisson ratio of the brain tissue was assumed to be 0.5.

III.RESULTS

0.25%-3% agarose gel compositions were found to vary from 1.25 ± 0.156 kPa to 103 ± 12.6 kPa in elastic modulus (n=3). Stepped indentation and relaxation characterization for viscoelastic property determination showed hydrogels to be linearly elastic. Soft silane-based gels showed nearly identical force curves to brain tissue composition on day 1 of implantation with viscoelastic relaxation characteristics comparable to properties of the brain tissue. The long-term stability of hydrogels was however variable, displaying fluctuations in elastic moduli within one day. In comparison, silane-based gels retained their characteristic material properties after 8 weeks in artificial cerebrospinal fluid (aCSF) at 37°C *in vitro*. Currently *in vivo* tests are being conducted to test whether alleviation of the mechanical mismatch using soft gels leads to better long-term neural interfaces.

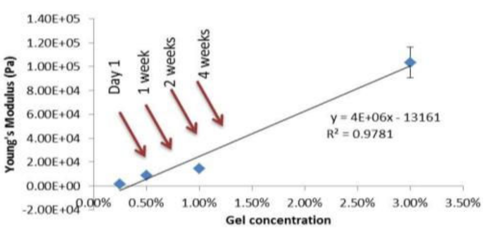

Figure 1. Elastic moduli of agarose gel compositions (0.25%-3%) (n=3). The arrows indicate points along the linear relationship between elastic modulus and gel concentration that correspond to brain tissue properties at various points under chronically implanted conditions.

IV.CONCLUSIONS

In this study we showed that mechanical properties of two different materials could be tunably changed to emulate the material properties of the brain tissue at the interface. By understanding the mechanical properties of classic materials in the context of the dynamic changes at the brain tissue electrode interface, we can potentially correct the mechanical mismatch at the brain-implant interface with novel, composite materials and perhaps avert the dynamic changes in material properties of the interface caused by mechanical remodeling. Novel interfacial bioactive coatings that capitalize on the advantages of both classes of materials can be developed to enable long-term success of implanted devices. Hydrogels represent one class that can be rendered chemically compatible to brain, while silane based gels represent mechanical compatibility of brain tissue.

REFERENCES

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