Biophysical attributes of an in vitro spinal cord surrogate for use in developing an intradural neuromodulation system

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(Received 25 June 2011; accepted 17 August 2011; published online 4 October 2011)

We have developed a spinal cord surrogate for use in testing a pial-surface spinal cord stimulator. Our surrogate is of a commercially available silicone mix, has an oval cross-sectional area that matches that of actual human spinal cord at the lower thoracic level, and has measured values of durometer A = (10.96 ± 1.68), durometer O = (14.76 ± 1.48), and durometer OO = (50.24 ± 2.65). These correspond to model-inferred elastic moduli of 0.41 to 0.44 MPa, which match well with the existing low-strain rate measurements of ex vivo human spinal cord. Upcoming applications for this surrogate in developmental studies of the new stimulator system are discussed. © 2011 American Institute of Physics. [doi:10.1063/1.3642976]

I. INTRODUCTION

Our laboratories are introducing a new approach to the neuromodulation-based treatment of intractable pain via electrical stimulation of the spinal cord. In this approach,1 as suggested in Fig. 1, a membrane containing a thin-film electronic receiver-and-stimulator circuit is positioned directly on the surface of the patient’s spinal cord. The electrodes on the underside of this membrane (which is termed the Iowa-Patch™ or “I-Patch”) are thus in direct contact with the pial surface, enabling the delivery of electrical stimuli without shunting of the energy by the relatively high conductivity cerebrospinal fluid, as otherwise happens with standard epidural spinal cord stimulation systems. The pulse sequences originate in a separate subcutaneous transmitter unit. A wireless link between that transmitter unit and the I-Patch conveys a frequency-modulated signal in which the pulse sequences are encoded, with subsequent demodulation, decoding, and distribution of the pulses to the selected electrodes done by the electronics on the I-Patch.

Because of the invasive nature of the surgical procedure needed for implantation of the I-Patch, this method of spinal cord stimulation will initially be proposed only for those patients who have failed all other therapeutic regimens. Extensive in vivo testing in a suitable large-animal model will clearly be needed in order to demonstrate the safety and potential efficacy of this method as part of the necessary regulatory approval process prior to commencing any use in human pilot studies. Although they are an important part of the overall development strategy, such in vivo investigations are expensive and time consuming; therefore, suitable in vitro models are often sought for use in early stage feasibility and engineering studies in such situations. In our case, a non-biological in vitro surrogate with good fidelity to the mechanical properties of actual spinal cord tissues would be quite useful in establishing the material and structural design parameters of the I-Patch device, testing methods for the fixation of the device on the spinal cord, and evaluating the performance of the wireless coupling mechanism on a long term basis, all without concern for degradation of the spinal cord model to which the I-Patch is affixed.

Our laboratories, in conjunction with several other colleagues, have a long history of developing in vitro gelatin models of central nervous system (CNS) structures for the purpose of testing different types of neurosurgical devices and systems.2–8 These models are faithful mimics of several important aspects of in vivo CNS tissues, but, as is true with the inevitable degradation that occurs in ex vivo tissue samples, they are not mechanically stable over time.

Therefore, we decided to investigate the possibility of designing a suitable spinal cord surrogate from a more durable soft material, such as a version of the silicone rubber used as the pericardium and diaphragm in a simulator for epicardial procedures that was also built in our laboratories.9,10 In what follows, we describe the materials and method used to make the spinal cord surrogate, present the results of our measurements of its mechanical properties, relate those data to the biomechanical measurements made by others on samples of human spinal cord, and discuss the role that this surrogate is playing in our I-Patch design effort.

II. EXPERIMENTAL ARRANGEMENT

A. Anatomical considerations

The cross-sectional shape of the human spinal cord is roughly oval, with semi-major and semi-minor axis diameters

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that generally decrease in the superior-to-inferior direction. For optimum neuromodulative performance in a clinical setting with chronic back and leg pain, the I-Patch device would be implanted in the thoracic region, where values for the transverse (semi-major) and sagittal (semi-minor) diameters have been measured and reported by many workers, e.g., Ko et al.\textsuperscript{11} As there is some variability (about \pm 2 mm) among individuals in the cord’s dimensions, we chose 10 mm and 6 mm, respectively, as the approximate initial values of the transverse and sagittal diameters for the surrogate. The I-Patch will be either circumferentially affixed directly on the spinal cord or anchored to the dentate ligaments.\textsuperscript{12} The present version of the surrogate has a simple axial structure free of lateral extensions that mimic those ligaments. Lastly, as the length of the I-Patch device \textit{in situ} is expected to be \approx 15 mm, we opted to make the length of our surrogates 60 mm in order to provide sufficient room on either end to attach any auxiliary devices, sensors, etc. that might be needed during our studies.

**B. Materials**

As is discussed in further detail later in the paper, Bilston and Thibault\textsuperscript{13} measured the response of \textit{ex vivo} samples of human spinal cord to loading and found that the elastic moduli as determined over a substantial range of strain rates “are similar in magnitude to those of a reasonably soft rubber.” As that would be on the order of 1 MPa, our standard 0.6\% agarose gel model of the spinal cord and other CNS tissues,\textsuperscript{5,8} which is useful in models of the infusion-based delivery of therapeutic agents, would be far too soft, because the moduli of such gels are two to three orders of magnitude smaller.\textsuperscript{14,15} Therefore, we investigated a silicone elastomer model similar to that of Kroeker \textit{et al.}\textsuperscript{16} but optimized for static rather than dynamic testing protocols, i.e., for the evaluation of long-term constant loading of the type produced by implantation of the I-Patch, as opposed to high-strain rate flexion-extension loading as needed in impact-type spinal cord injury studies.

The material chosen for use in our surrogate was Dragon Skin\textsuperscript{19}, which is a two-part, platinum-cure, liquid silicone rubber mix (Smooth-On, Inc., Easton, PA) that sets in approximately 5 h.\textsuperscript{17} Our experience with this material included its previous use as a diaphragm and pericardium surrogate in subxiphoid access tests done in the University of Virginia’s epicardial simulator,\textsuperscript{10} in which the low-strain rate insertion of the access needle had to feel the same to the clinician as insertion into the actual tissues (as done in epicardial electrophysiology procedures).\textsuperscript{18,19}

To make spinal cord surrogates of the geometry described above, we formulated a simple SolidWorks\textsuperscript{20} model of a hemi-cylinder. Pairs of them were rapid prototyped on a 3D printer and then clamped together to form a mold having an internal oval cross section with 10 mm x 6 mm semi-major and semi-minor axis diameters and a length of 60 mm. The silicone compound’s components were mixed per the manufacturer’s instructions, and the liquid mix was then poured into the mold and allowed to set. No release agent was needed to remove the surrogate spinal cord from the mold; the two hemi-cylinders were simply pulled apart, thereby releasing it. The surrogates were then trimmed of any flashing left at either end or along the sides (due to any residual gaps at the hemi-cylinder joints), and they were then ready for use. Figure 2 shows an example of one of the

**FIG. 1.** (Color online) Artist’s rendition of the I-Patch device as placed on the surface of the spinal cord. Power and stimulus control signals are transmitted to the I-Patch via a wireless coupling with the epidurally positioned component of the system. The blue dots represent some of the electrodes that generate the stimulus currents in the ascending and descending fiber pathways.
resulting surrogates, with Nitinol® scaffolds in place during preliminary tests of I-Patch mounting techniques.

C. Measurement methods

In order to confirm that the biomechanical characteristics of interest in the spinal cord surrogate were a satisfactory match to those of the actual tissues, we carried out a series of measurements aimed at exploring the parameters critical to the long-term performance of the I-Patch in situ. Whereas observations of the material response to dynamic loading and the subsequent extraction of the elastic moduli constitute the most widely used approach for evaluating the performance of materials, the static nature of the electrode impingement on the spinal cord calls for a somewhat different method here. In the I-Patch design, the electrodes that deliver the stimulus to the spinal cord are nominally 1 mm in diameter and are held gently in place, resulting in an inward dimpling of the pial surface of about 150 μm at each electrode site, as suggested in Fig. 3. The only ac component of motion that is present is the very low amplitude pulsation of the spinal cord that occurs at the heart rate of the patient (≈1 Hz) and which, in principle, is compensated for by the compliance of the structure of the device and the mechanics of the individual electrode mounting hubs. Thus, an evaluation of the performance of the surrogate material calls for the equivalent of static indentation testing that simulates dimpling and displacement of the pial surface by the electrodes (as opposed to high-strain rate dynamic loading, which instead is more suitable for testing impact injury mechanics).

In order to accomplish this, we chose to make a series of durometer measurements on samples of the silicone material of which the surrogates were composed, and then we interpreted the results in terms of equivalent values of the measured elastic moduli of actual spinal cord tissues. The material’s vendor specified that the cured silicone had a durometer value of 10 A. Therefore, we used an A-scale durometer gauge (Shore Instrument & Manufacturing Co., Jamaica, NY, Model Shore A-2) for one series of measurements. However, the softness of the material meant that the measurements were necessarily made at the low end of the instrument’s scale. Therefore, we also made independent measurements using higher sensitivity Shore-0 and Shore-OO devices (Rex Gauge Company, Inc., Buffalo Grove, IL, model 1600-O and 1600-OO gauges, respectively). Because there is some overlap in the A, O, and OO scales, it was possible to see whether the results of each independent series of measurements made with any one gauge yielded data that at least approximately confirmed those of the others.

The measurement procedures followed the guidelines of ASTM Standard D2240; in particular, all three durometers were either calibrated prior to use or had existing calibrations traceable to NIST documentation. All data were acquired manually at room temperature. The tip of each durometer gauge was lowered vertically downward onto layers of the silicone that were approximately 1 cm thick, and when the base of the gauge was flush with the silicone surface, the resulting gauge indication was recorded. In addition to the primary indentation observations, the durometer gauge was held in place for up to 1 min to check for the presence of creep relaxation in the silicone. The data sets consisted of 25 individual measurements, and the means and standard deviations of each series were calculated after the observations were recorded. In the next section, we present and discuss the results.

III. RESULTS AND DISCUSSION

A. Durometer findings

The means and standard deviations of the measurements were as follows: Durometer A = (10.96 ± 1.68), Durometer O = (14.76 ± 1.48), and Durometer OO = (50.24 ± 2.65). The vendor had specified that the cured Dragon Skin silicone was 10 A, and our data confirmed this. The fractional uncertainties (standard deviation divided by the mean) in each of the three cases were approximately 15%, 10%, and 5%, respectively, which reflects the fact that the relative error in a measurement is less for a more nearly full-scale reading than it is at the lower end of the scale. No measureable creep relaxation was noted in any of the observations.

The spring strengths and indenter-tip geometries are different for each class of durometer gauge (A, O, OO, and all of the others); thus, as mentioned above, there is only approximate correspondence between the scales of the various devices, and as a result there are no general conversion tables. However, the various durometer gauge and elastomer material manufacturers do provide reference charts for the semi-quantitative comparison of readings on different instruments, and the suggested agreement occurs at values of 10(A), 14 (O), and 55 (OO). We note that there is overlap within experimental error in our durometer A and O results, and that our OO result comes within 4% of the value for suggested agreement, with the difference most likely being due to the semi-quantitative nature of the comparison.

B. Estimation of elastic modulus

Gen and Qi et al. have derived engineering expressions that relate the Shore hardness S to the elastic modulus
\( E \) (in MPa) in elastomeric materials via analysis of the mechanics of the indentation process. The formula derived by Gent is

\[
E = \frac{0.0981(56 + 7.66S)}{0.137505(254 - 2.545)}, \quad (1)
\]

and that of Qi et al. is

\[
\log 10\left(\frac{E}{\text{MPa}}\right) = 0.0235S - 0.6403. \quad (2)
\]

Both expressions are very useful approximations, but they lose accuracy as \( S \) decreases. When applied to our durometer A mean value (\( S = 10.96 \)), we find close agreement between them: for Eq. (1), \( E \approx 0.44 \) MPa, and for Eq. (2), \( E \approx 0.41 \) MPa. Both of these results lie within the range of the low-strain rate values of the elastic modulus measured for human spinal cord by Bilston and Thibault,\(^{13}\) who found \( E = (1.02 \pm 0.75) \) MPa. We also note that the values of \( E \) inferred here for our surrogate spinal cord material are similar to those measured for the injury-mechanics spinal cord surrogate of Kroeker et al.\(^{16}\) (within \( \approx 2\times \)), which was of commercial QM Skin 30 silicone; their values ranged from 0.185 to 0.245 MPa, depending on the component mixing ratio.

**C. Potential improvements of the model**

There are two broad classes of additional work that we are pursuing. The first is aimed at improving our knowledge of the material properties of the surrogate spinal cord, and the second seeks to improve its functionality within the context of its use as a testing tool for evaluating I-Patch designs. Regarding the former, we will seek to make auxiliary loading-curve measurements of the elastic modulus in order to supplement the values inferred from our durometer indentation studies and to provide an independent check on the results approximated from Eqs. (1) and (2). We will also extend the time scale of the creep measurements in order to evaluate the long term static mechanical stability of the surrogate.

Regarding the latter, an important functionality that we will seek to add to the surrogate is pulsatile expansion and contraction, i.e., a low-amplitude volumetric “breathing mode” that mimics the cyclic physiological pulsations of the spinal cord.\(^{20}\) We expect to accomplish this by inserting a long thin balloon (e.g., an angioplasty balloon) into the mold and then filling the rest of the space in the mold with the liquid silicone mix. After the silicone is cured, the subsequent pressure cycling of the balloon will provide a means for testing the low-frequency dynamic response of the I-Patch device, e.g., allowing us to investigate the potential skidding of the I-Patch electrodes on the surface of the spinal cord.

Additional uses of the surrogate will include testing the I-Patch installer tool and evaluating the fixation stability of the I-Patch as the spinal cord’s position shifts with bending and other movements of the patient. The installer tool is a surgical device that allows the clinician to hold the arms of the I-Patch open, lower it onto the pial surface through a laminectomy gap, and then position and release it safely. The dimensions and surface softness of the surrogate make it an ideal test bed for practicing and mastering the implantation procedure prior to the start-up of in vivo testing. Moreover, by placing the surrogate inside of a thin tube that is otherwise filled with mock cerebrospinal fluid, one can simulate the morphology and environment of the interior of the spinal canal and explore the fixation stability of the I-Patch as the patient’s bending and twisting motions cause the cord to move relative to the inside wall of the artificial spinal canal.

**IV. CONCLUSIONS**

We have designed and synthesized a surrogate version of human spinal cord that will be useful in developing and testing a new device for the neuromodulation-based treatment of intractable pain. Our silicone surrogate has several biophysical attributes that are similar to those of actual spinal cord, including appropriate cross-sectional shape, dimensions, elastic modulus, and mechanical softness. We have employed redundant durometer testing of the silicone material used to fabricate it in order to arrive at values of the elastic modulus and compare them with that of actual human spinal cord (obtained by others) in a preliminary validation of this in vitro model. Applications of it in extensive testing of the new neuromodulation device are foreseen and discussed.
ACKNOWLEDGMENTS

We thank our colleagues D.J. O’Connell (Neuroventures LLC), R.S. Nelson, S. Scott, R. Shurig (Evergreen Medical Technologies LLC), and S. Sheehan (University of Iowa) for several useful technical discussions. This work was funded in part by the University of Iowa GIVF Seed Funds program, the University of Virginia Biomedical Innovation Fund, and the Kopf Family Foundation, Inc.