INNOVATION

Pulsatile spinal cord surrogate for intradural neuromodulation studies

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We have designed, built and tested a novel spinal cord surrogate that mimics the low-amplitude cardiac-driven pulsations of the human spinal cord, for use in developing intradural implants to be used in a novel form of neuromodulation for the treatment of intractable pain and motor system dysfunction. The silicone surrogate has an oval cross section, 10 mm major axis × 6 mm minor axis, and incorporates a 3 mm diameter × 3 cm long angioplasty balloon that serves as the pulsation actuator. When pneumatically driven at 1 Hz and 1.5 atmospheres (= 1140 mm Hg), the surrogate's diametric pulsation is ≈ 100 μm, which corresponds well to in vivo observations. The applications for this surrogate are presented and discussed.

Keywords: Spinal cord, Neuromodulation, Tissue surrogates, Pial surface, Intradural devices

1. Introduction and background

We are developing a fundamentally new approach to spinal cord stimulation for the treatment of intractable pain, as well as variety of motor system disorders, in which the neuromodulation device is placed directly on the pial surface of the spinal cord [1], for the purpose of optimizing the current density distributions in the targeted fibre pathways. A schematic representation of how the implant, referred to as the Iowa-Patch™ or I-Patch, is positioned to accomplish this is shown in figure 1. An extra-dural transmitter wirelessly couples the power and control signals onto the I-Patch receiver, which decodes the incoming signals and activates the selected electrodes accordingly. The intrinsic advantages of this method include stability of electrode position relative to the spinal cord (the spinal cord moves within the CSF-filled spinal canal during patient movement, resulting in a variable distance separating the spinal cord and conventional extradural electrodes) avoidance of CSF current-shunting (the stimulating electric field is largely within the spinal cord itself), and larger windows of therapeutic action (a potentially larger stimulation intensity range between the onsets of paresthesia and discomfort).

To aid in the development phase of this device, we have synthesized a silicone surrogate that mimics the anatomical and biomechanical characteristics of actual human spinal cord tissue [2]. The resulting moulded spinal cord models are made of platinum-cure polyorganosiloxane, are oval in cross section (10 mm major axis × 6 mm minor axis), soft and lifelike to the touch (Durometer A = 10, elastic modulus between 0.41 and 0.44 MPa), and can be made in any length needed for a particular test. Our standard segments are 5 to 6 cm long. These spinal cord dimensions were obtained from MRI based measurements of the thoracic spinal cord (T8) of a normal subject. These surrogates are very useful for evaluating methods of applying candidate I-Patch structures on the spinal cord and assessing their quality of fit, thus helping us to optimize the implant’s overall mechanical design using an inexpensive and robust in vitro model prior to any in vivo testing and human pilot studies.

In an effort to add a measure of physiological fidelity to this model, we have recently conceived and implemented a means for replicating in the surrogate the very low-amplitude, cardiac-driven pulsations that are present in the spinal cord (see, for example, Mügge et al. [3]). Quantitative measurements of the amplitude of these pulsations have been made by Matsuzaki et al. [4], who found that in canines the cyclical change in mean radius of the spinal cord, Δr, is on the order of 100 μm. This would imply a fractional change in radius of Δr/r ≈ 1% in the spinal cord of humans, occurring at the heart rate of the patient. There was a two-fold motivation for making this improvement to the surrogate. First, we wanted to have the ability to search for possible failure modes in the

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I-Patch structure that might arise from physiologically accurate levels of cyclical stress, in much the same way that intraarterial stents are tested for cyclical stress-induced failures driven by arterial pulsations. Second, the stimulus electrodes must all reside on the underside of the I-Patch in order for them to be in direct contact with the pial surface. Hence, there could be motion of the electrodes over the surface during the pulsation cycle. This is because the I-Patch cannot simultaneously be arbitrarily compliant both radially and circumferentially and still maintain a snug but non-constrictive fit to the spinal cord, and we sought a means that would allow us to investigate such effects.

In what follows, we present the design and construction details for an improved spinal cord surrogate that can mimic the low-amplitude pulsations found in vivo. We then provide preliminary data on its performance at normal cardiac heart rates, and we go on to outline the upcoming studies in which the improved surrogate described here will be used to investigate a number of I-Patch design issues, including those mentioned above.

2. Materials and methods

2.1. Design elements

Our own clinical experience during routine neurosurgical cases requiring spinal cord exposure (e.g. resection of spinal cord tumour or treatment of spinal cord syrinx) has allowed us to see, via the high resolution video microscopy needed for these procedures, that the amplitude of the cord’s cardiac-driven breathing-mode pulsations is indeed small; on the order of 100 μm. Therefore, the design challenge in creating a pulsatile spinal cord surrogate is one of developing a reliable means for generating a change in volume of about 2% in the 10 mm (major axis) × 6 mm (minor axis) × 6 cm (length) surrogate at the nominal heart rate of, say, 1 Hz, i.e. a cyclic expansion and contraction of ≈ 300 mm³ s⁻¹. Because the silicone material is very soft (elastic modulus of approximately 0.4 MPa), pulsatile inflation of the surrogate presented itself as a reasonable technique for achieving this rate of volumetric expansion and contraction. While the incorporation of a simple air-pumped cavity inside of the surrogate seemed the most straightforward approach, the creation of a suitable inlet seal on the surface of the silicone proved to be difficult. However, the problem was solved by using an angioplasty balloon catheter instead.

Like the spinal cord surrogate, an angioplasty balloon has a long and thin profile. Moreover, they are made to withstand very large internal pressures (approximately 20 times atmospheric pressure), and are thus very reliable. They have Luer lock fittings at the proximal end for ease of coupling to pressurization devices and gauges. Most importantly from our perspective, the typical rate of diametric expansion with pressure is very small and can be precisely controlled in these devices, as they are designed to remodel plaque inside arteries without expanding so much that they cause dissections of the arterial wall. Our surrogate design incorporating one such balloon is described below.

2.2. Prototype device

The specific balloon used for this purpose was integral to a NC Quantum Apex™ Monorail™ PTCA dilatation catheter (Boston Scientific, Maple Grove, MN, USA). It had a nominal inflation diameter and length of 3.0 mm and 30 mm respectively. The manufacturer rated the balloon's diameter sensitivity to pressure change for pressures as high as 20 atmospheres (2027 kPa). Over that entire range, the average diametric sensitivity was 32 μm per atmosphere. However, at the low end of that range it was given as approximately 80 μm per atmosphere (i.e. 0.8 μm kPa⁻¹ or 0.1 μm mm Hg⁻¹) reflecting the balloon's larger available mechanical compliance at that point.

To make a silicone surrogate with an internal balloon, we started with our existing mould (of oval cross-section) and two-part silicone mix, as described in detail elsewhere [i]. The silicone mix was poured into the upright mould, and the angioplasty balloon was then lowered straight downward into it along the centre-line via a vertically oriented, micrometer-driven translation stage. The catheter's distal-end stylet was kept in place inside the balloon during insertion so that the balloon's axis remained collinear with the centre-line of the mould. The balloons were initially in their (as-shipped) collapsed state prior to use. Therefore, immediately before insertion into the mould, the balloon was inflated and then allowed to relax to its atmospheric pressure, and are thus very reliable.

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at that point the surrogate was ready for use. Figure 2 shows a photograph of a representative device made in this way. Also shown there are a pair of the hemi-cylindrical shells which, when joined together, form the oval cross-sectioned mould in which the silicone is poured.

3. Results

The diametric response of the surrogate to pressure change was tested using a Basix25 inflation syringe with integral pressure gauge (Merit Medical Systems, Inc., South Jordan, UT, USA). The Luer fitting on the output end of this device mated directly with that on the proximal end of the angioplasty catheter, and the union was checked for leakage before use. A 10× digital video microscopy system (Edmund Scientific, Barrington, NJ, USA, model NT59–697) was used to monitor the surrogate’s expansion and contraction cycles in relation to a background scale in mm, as the balloon was manually pressurized and depressurized via the inflation syringe. Over $10^3$ such cycles pumped at a rate of 1 Hz, the surrogate’s diameter routinely reached a differential expansion of $\approx 100 \, \mu m$ at inflation pressures of about 1.5 atmospheres ($\approx 1100 \, mm \, Hg$). From the manufacturer’s distension specifications, the increase in the balloon’s diameter itself for that level of pressure change would have been about 160 μm. The somewhat smaller expansion observed for the surrogate is to be expected because of the compliance in the silicone layer surrounding the balloon. Figure 3 shows representative video microscopy images of the start and stop points of an inflation/deflation cycle relative to the background scale, revealing the associated change in surrogate diameter.

4. Discussion and conclusions

Our goal in this work was to develop a means for obtaining small, controllable and reversible distension of a soft-material spinal cord surrogate, in order to mimic the cardiac-driven pulsations observed in vivo. The assembly that was conceived, built and tested here meets that objective and provides an experimental platform for evaluation of the mechanical characteristics of candidate designs of the Iowa-Patch™ device. To maximize its utility in that role, a peristaltic pump, either pneumatic or hydraulic, will be incorporated to replace the manual inflation system described above. (The hydraulic pump option might enable higher-precision control over the balloon volume changes.) This will help enable automated measurements during stress-cycle searches for failure modes in the candidate devices, and studies of any pial-surface skidding motions that might be associated with particular electrode geometries and suspension techniques.

Figure 2. Photograph of the spinal cord surrogate with integral angioplasty balloon used to modulate the surrogate’s diameter. The catheter with internal channel for inflating the balloon is shown extending out of the left end of the surrogate. The blue plastic hemi-cylindrical shells above and below the surrogate join together to form the oval cross-sectioned mould in which the silicone is poured to form the surrogate. The small divisions in the upper scale are in mm.

Figure 3. (a) Surrogate with balloon deflated. (b) Surrogate with the balloon inflated at a pressure of approximately 1.5 atmospheres. The small divisions of the scale are in mm. The width of each small division line is estimated to be about 0.2 mm. Note the small white arrows pointing to the location of the edge of the surrogate at the 8.7 mm mark in both photos. In (a), part of that particular small division line is visible. However, after the balloon is inflated, the surrogate has expanded by about 100 μm, which is enough to cover all of that line as shown in (b).
Beyond that, the pulsatile surrogate will also be used to mimic the in vivo situation in tests of how the inductively coupled power transfer between the implant and the extradural transmitter coil in the I-Patch varies with displacements of the spinal cord that are associated with the patient’s movement. A preliminary experimental arrangement now being readied for that purpose is shown in figure 4. The I-Patch coil to be characterized will be mounted directly on the pulsatile surrogate, which as shown in the figure is positioned inside of a segment of clear flexible tubing that represents the spinal canal and dura. The distal end of a needle is inserted into the top end of the surrogate and its proximal end is attached to the platform of a custom-built motor-driven translation stage that we have previously described here should reduce the number of in vivo trials needed during the I-Patch development process, and thus help minimize the overall costs of the work. Several improvements to the device and its method of use are now being made.

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Declaration of interest: Authors Howard, Brennan, Dalm, Utz and Gillies may receive patent royalties from any commercial licensing of the Iowa-Patch™ intellectual properties that might be negotiated by their respective institutions.

References