Optimization of Intradural Spinal Cord Stimulator Designs via Analysis of Thoracic Spine Imaging Data

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Abstract

Axial magnetic resonance images of the thoracic spinal cord of 50 patients are analyzed in order to measure the length of the dorsal arc span between the dorsal root entry zones for the purpose of optimizing the mechanical design dimensions of the Human Spinal Cord Modulation System (HSCMS), which delivers electrical stimuli directly to the spinal cord. Two mathematical approaches are used to assess the data, with validation of the results conducted via a direct physical measurement using a magnified image. Results show that the nominal value of the arc length is 6.7 ± 1.0 mm (1 σ), with high and low values of 8.8 and 5.1 mm, respectively. The mean radius of the spinal cord was found to be 3.6 ± 0.5 mm. Taking into account previously reported measurements, it is suggested that values at the high end of this range be used for further morphometric studies of the cord in the thoracic region. The implications of these findings on the design of the HSCMS are discussed.

Keywords: Spinal cord stimulator, Intradural implants, Magnetic resonance imaging (MRI)

1. Introduction

Spinal cord stimulation (SCS) has become an accepted method of treatment for many patients who suffer from neuropathic back and leg pain as a consequence of failed back surgery syndrome and other chronic pain disorders [1]. In the standard approach, a lead is placed in the thoracic epidural space and a percutaneous pulse generator is programmed to deliver a sequence of waveforms to the electrodes on the lead which, in turn, emit the therapeutic stimuli. A variety of these systems are now in routine clinical use, with lead designs that range from simple cylindrical catheters with axially spaced electrodes to more complex paddle-shaped implants that incorporate multipolar electrode arrays [2]. Other features include programmable electrode activation [3], protocols for employing either constant-voltage or constant-current pulse trains [4], and the ability to minimize stimulus energy requirements [5]. In parallel with these technical advances have been a long series of improvements in the finite element modeling of the epidural stimulation process. In particular, Holsheimer and colleagues used this approach to investigate how the electrical current density patterns are distributed throughout the structures inside the spinal canal as a function of the tissue conductivity, electrode configuration, and stimulus signal parameters [6-8]. Several reviews have carefully documented the growth in use of the technique, the results of large-scale clinical trials, the reimbursement trends associated with it, and the general economic impact of SCS therapies both within the U.S. and abroad [9-13].

Even with all of this progress, epidural stimulators are nevertheless subject to migration of the lead [14], shunting of the stimulus currents by the cerebrospinal fluid (CSF) [15], and various other issues [16] that can diminish clinical efficacy. The result is often a failure to deliver adequate levels of current density to the targeted locations in the dorsal columns without the painful activation of the nearby dorsal-root entry zones (DREZ) and other non-targeted structures, producing limited to no improvement of pain symptoms in many patients [17].

To overcome these limitations, we are developing the Human Spinal Cord Modulation System (HSCMS) [18,19]. In it, the electrode-bearing implant is placed directly on the dorsal pial surface of the spinal cord, thus minimizing the propensity for either lead migration or the shunting and dissipation of stimulus currents by the CSF. The essential features of the implanted device are shown in Fig. 1(a), which provides a perspective view as seen from the dorsal surface of the spinal cord. The electrodes and their leads are positioned within a soft,
thin silicone membrane that loops back on itself underneath a polymeric attachment arm which is fitted just inside the dura mater. The durotomy is closed with a dural patch that allows a cable containing the leads to exit via a water-tight seal. A close-up cross-sectional view of this arrangement in place inside the spinal canal is shown in Fig. 1(b). The primary advantage of the intradural approach offered by the HSCMS as compared to the standard epidural approach of existing devices is its ability to selectively activate the targeted neural structures within the spinal cord, while avoiding undesired activation of non-targeted structures such as the DREZ [20]. With the HSCMS electrodes placed directly on the pial surface of the spinal cord, the stimulus signals are able to achieve a much deeper and focused penetration within the dorsal columns than is possible with epidural stimulation [21], which can typically activate the fibers in a layer no more than ~ 250 µm thick [15] and inadvertently stimulate the DREZ.

One of the key dimensional parameters for the HSCMS is the arc length that it subtends over the dorsal surface of the spinal cord. There are conflicting design goals related to this spinal cord anatomical feature. One is to make that span as long as possible, in order to maximize the number of electrodes and hence the stimulus-pattern coverage of the underlying dorsal columns. However, another is to ensure that the membrane does not make mechanical contact with the dorsal rootlets. To resolve these goals and arrive at an optimal design for the device, the present study investigates the relevant structural dimensions of the spinal cord at the level of the 4th through 10th thoracic vertebrae (i.e., the general region in which the HSCMS would be placed when treating patients with back and leg pain), and the DREZ-to-DREZ dorsal arc length in particular. The methodology employed in the measurements, the results, and the interpretation of their impact on the HSCMS design parameters are described.

2. Materials and methods

2.1 Imaging database

Although several measurements of the spinal cord mean diameter and CSF layer thickness have been reported, e.g., [22-24], there is little information in the literature regarding the DREZ-to-DREZ dorsal arc length. While its value can obviously be measured directly from anatomical specimens, there are concerns associated with that approach. First, any post-mortem specimens of the spinal cord will typically be fixed-tissue samples and it is well known that there are variable degrees of tissue shrinkage associated with the fixation process, e.g., see Silverman et al. [25], thus introducing a large source of systematic uncertainty into the results. Direct intraoperative measurements on living patients undergoing a spinal cord procedure might seem like a possible alternative, but such procedures are typically to correct a spinal cord abnormality (tumor, syrinx, etc.), leaving the associated data open to interpretation. Moreover, given the a priori expectation of large variations in spinal cord dimensions across patient populations as observed previously by others [22-24], it would likely be difficult to gather enough meaningful data from either approach to reach statistical significance in a DREZ-to-DREZ arc length study.

Therefore, we elected to carry out an informatic assessment of the magnetic resonance (MR) images of the thoracic spine for a large number (n = 50) of patients seen at the University of Iowa Hospitals and Clinics. In this institutionally approved study, one axial and sagittal slice from each patient was selected for analysis. The available images covered the range T4 through T10 from high-resolution MR scans of both male (n = 34, ages 17 to 77 years) and female (n = 16, ages 20 to 84 years) patients. The imaging studies had been ordered by clinicians to rule out pathological processes affecting the spine, and in all cases studied no pathological abnormalities were noted. All of the subjects were imaged in the supine position in a straight posture without any bending or flexing of the legs, hips, or spine. Of the selected slices, 70%
(n = 35) were at either T7 or T8 which will be the preferred location for HSCMS implantation in most patients. The remaining images were distributed above and below that zone to help ensure a representative assessment. With reference to Fig. 2, the bi-lateral locations of the dorsal root entry zones, P1 and P3, were identified by neurosurgeons on each of the 50 axial slices, and the linear separation, A, between them was measured relative to the calibration scale bar on each image. The distance, B, between the center of that line and the dorsal-most point of the spinal cord, P2, was also measured, as were the maximum sagittal and coronal diameters of the spinal cord (i.e., the minor and major axis diameters, respectively). The resulting data were then archived for subsequent analysis, with the primary goal being to determine the peripheral arc length, S, connecting the points P1, P2, and P3, and θ is the angular separation between those lines. In this case, because the actual arc S would lie just below the circumscribing path of SR, we would have a slight overestimate.

This means that the true physical value of S will be in the range SH < S < SR. Measurements to confirm this and establish the most likely value of S within that range can then be made directly on a magnified view of an axial image, using a flexible rule and the appropriate scaling factor to determine the distance along the span.

The resulting value of S, as determined across the entire patient population, can then be used as a design guide for the membrane length of the HSCMS. Moreover, the value of r in Eq. (2), as determined from the measured major and minor axis diameters, can then be used to establish the radius of curvature for the HSCMS membrane.

3. Results

3.1 Arc length from Pythagorean approximation

The results of the measurements of the lengths A and B are shown in Table 1. The relative uncertainties (standard deviation ± mean) in the values of A and B across all patients are approximately 14% and 27%, respectively. The value of A across all male patients was approximately 2% larger than the mean for all patients, and that for the female patients was approximately 5% smaller. Using these values of A and B in Eq. (1), we arrive at the values of SH shown in Table 2. In particular, across all patients, SH = 6.5 ± 1.2 mm, which, as noted above, will be slight underestimates. It is interesting to note that the difference between the largest mean value of SH (8.8 mm) and the smallest (5.1 mm) was 3.7 mm, which is approximately three times the size of the standard deviation (1.2 mm), indicating that this is a dimension of the neuroanatomy in which significant outliers will occur.

3.2 Arc length from angular separation approximation

As per Fig. 3, the variables of interest in determining SR are the distances, r, between the geometric center of the spinal cord and the points P1 and P3, and the angular separation, θ, between those lines. Note that each line approximately bisects

![Figure 2. Cross-sectional schematic diagram of the spinal cord and the measurement geometry used in the Pythagorean approximation of the dorsal arc length connecting points P1, P2, and P3. The line A connects the opposing dorsal root entry zones, and the line B connects the midpoint of line A to the dorsal apex.](image-url)
the sagittal-coronal quadrant in which it lies, hence \( r \) can be taken as a measure of the mean radius of the spinal cord, given by the average of the sagittal and coronal radii. As mentioned above, we measured the sagittal and coronal diameters of the spinal cord in each of the 50 axial images, finding values of \( 6.2 \pm 0.6 \text{ mm} \) and \( 8.3 \pm 0.8 \text{ mm} \), respectively, across all the patients. Therefore, from our data, the mean radius and quadratured-sum uncertainty of the spinal cord is \( r = 3.6 \pm 0.5 \text{ mm} \). However, while our measurement of inter-DREZ linear distance (i.e., the quantity \( A \) in Table 1) appears to be unique in the literature, there are several other independent measurements of spinal cord diameter and radius which have been reported, cf., [22-24]. After surveying the available results, and allowing for the possibility of dimensional shrinkage [25] in measurements made on fixed tissues [23], it seemed most conservative to take \( r = 4.1 \text{ mm} \) (at the high end of our allowed range) to be the working value of the mean radius, thus bringing consistency to the broadest determinations of \( r \). With that result in hand, and measuring \( \theta \approx 95^\circ \) for the example shown in Fig. 3, we find in that case \( S_8 \approx 6.8 \pm 1.0 \text{ mm} \), where the uncertainty is given by the quadratured sum of those measured for \( r \) and estimated for \( \theta \). Recall that this will be a slight overestimate of the actual value.

Figure 3. Axial image showing the geometry used for determination of the dorsal arc length via the angular separation approximation.

3.3 Final result

Lastly, these values of \( S_H \) and \( S_R \) were compared against physical measurements made with a flexible rule laid carefully along the dorsal arc pathway identified in a magnified (3x) version of Fig. 3. After accounting for the magnification factor, the result for the length of the dorsal arc span between the rootlet entry zones was estimated to be \( S = 6.7 \pm 1.0 \text{ mm} \). While as expected the means of the results from the three different approaches obey the expression \( S_H < S < S_R \), we note that they all overlap each other within the respective ranges of uncertainty that are assigned to them, thus providing a reassuring agreement between the three independent means of determining the arc length of interest.

4. Discussion

4.1 Implications for HSCMS design

The purpose of the present study was to help clarify some of the mechanical design requirements of the HSCMS implant. In particular, it was our intention to establish the nominal size of the dorsal arc span between the rootlet entry zones. The goal was to see whether there was an optimal width for the HSCMS which would maximize the stimulus coverage pattern over the dorsal columns below the pial surface, while minimizing the risk of having the electrode-bearing membrane make contact with the rootlets. We established that the nominal arc length of interest was \( 6.7 \pm 1.0 \text{ mm} \), suggesting that if the width of the HSCMS were \( 6.7 - 1.0 = 5.7 \text{ mm} \), then it would be a good fit to the spinal cords of at least 68% (1 \( \sigma \)) of the patients receiving the implant. The problem would come with the outliers at the high and low ends of the distribution of arc lengths. For those at the high end, the stimulus pattern coverage would be inadequate, while for those at the low end, a 5.7-mm-wide HSCMS would be too large. It thus appears that three sizes of device might be needed to adequately cover the full range of patient spinal cord anatomies: widths of 4, 6, and 8 mm. The form and function of the largest-size device would be complicated by the presence of additional electrode contacts and leads, while the smallest device might suffer from just the opposite problem: a reduced number of electrodes with a concomitantly smaller range of stimulus options. Alternatively, custom HSCMS devices could be fabricated for individual patients using patient-specific arc length measurements.

A second parameter of interest is the radius of curvature of the HSCMS membrane. The data from our study imply that the mean radius of the spinal cord across all patients is \( r = 3.6 \pm 0.5 \text{ mm} \), but when taking into account the measurements of others (and the possible presence of certain systematic effects), it is likely that a nominal mean value of \( r = 4.1 \text{ mm} \) should be chosen. This is within our range of allowable values and, by opting for a slightly larger radius of curvature, reduces the risk of spinal cord compression that might arise from too small a sizing.

4.2 Limitations of the study and suggestions for future work

While care was taken in the selection of the axial slices used in the analysis, we noted that the image planes in some of them were not precisely normal to the anatomical axis of the spinal cord. The resulting trigonometric offset in the measured lengths will introduce a small but non-negligible systematic component into the error budget for the overall uncertainty level of the measurements. Another such effect, and perhaps the ultimate limitation within the data set, arises from the natural pulsations of the (highly vascularized) spinal cord at the patient’s heart rate. These are known to be approximately 0.1 mm in amplitude, which adds a further component of systematic uncertainty to the error budget. While the former might be corrected by reorienting the direction of the slice in software, it is not clear how the blurring associated with the latter could be compensated without capturing images between heartbeats, which would call for sequences that are not typically available at the scanning resolutions needed for this type of work.

There are a number of other improvements that could be made to future studies of this type. The first and most obvious would be to increase the number of patients and the number of
axial slices per patient included in the analysis, with the benefit being improved statistical confidence in the results. Also, it would be beneficial to replace the present qualitative visual methods for identification of the key anatomical features (e.g., the DREZ sites, the sagittal and coronal diameters, etc.) with quantitative threshold-detection algorithms to enable faster, higher-sensitivity, and more standardized feature discovery. A similar algorithmic approach could also be used to replace the physical measurement of dorsal arc length used to confirm the computed results presented above.

Lastly, our study focused on thoracic levels T4-T10, as this is the most typical region for SCS device implantation [9]. Of course, implantations also occur at levels above and below this, depending on the particular pain syndrome or other problem to be treated. Therefore, it would be helpful to eventually make additional series of measurements elsewhere in the spine to gain a more complete understanding of how the inter-DREZ distance varies over the full length of the spinal cord. Although outside the scope of the present study, obtaining such data in future efforts would be very helpful in optimizing the design of the HSCMS for applications such as the treatment of angina pectoris.

5. Conclusion

Quantitative measurements of the spacing between the dorsal root entry zones on the spinal cord were made to establish the optimal sizing of the HSCMS, which is an intradural implant that will be used for direct electrical stimulation of the pial surface for the treatment of intractable pain. Results show that the DREZ-to-DREZ dorsal arc length over the surface of the spinal cord has a nominal value of 6.7 ± 1.0 mm, but with a very large difference between the smallest and largest measurements on individual patients, approximately 5.1 and 8.8 mm, respectively. Moreover, across all 50 patients in our study, the nominal radius of curvature of the spinal cord was 3.6 ± 0.5 mm, but the largest allowable value in that range, 4.1 mm, was taken as the best nominal value after comparison with the results of others. Possible implications for the mechanical design of the HSCMS were discussed.

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References


