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Computational Modeling Towards Focused Ultrasound Therapy for Spinal Cord Injury: Visualization of Beam Propagation through Patient-Specific Anatomy

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ABSTRACT

Ultrasound holds promise for use in spinal cord injury cases for both diagnostic and therapeutic purposes. Focused ultrasound applications demand an added threshold of study to ensure the safety and efficacy of the therapy. For optimal treatment outcomes, it is crucial to understand whether relevant structures are being targeted with sufficient energy without damaging neighboring tissue and vasculature. However, it is difficult to predict the expected displacement and pressure profile of the ultrasound wavefront due to challenges with visualizing an acoustic beam in real-time and complex patient-specific anatomy. This challenge is particularly prominent in anatomies with varying medium acoustic properties that cause reflection and distortion of the signal, which is inherent to the composition of the spinal cord and is exacerbated by the formations of injury-induced hematomas. Incorrect placement of focused ultrasound transducers can be detrimental to patient health, specifically if therapeutic ultrasound is used at higher intensities, as the beam propagation can target healthy tissue and important structures that could lead to tissue damage and death. We study how computational tools can be leveraged to aid placement of the transducer using an ultrasound simulation software, Wave 3000 Plus, that allows for the visualization of ultrasound propagation through anatomical structures. By simulating the propagation of ultrasound beams through patient-specific Digital Imaging and Communications in Medicine (DICOM) images, we study computational approaches to determine the optimal placement of devices. In this study, we use *in vivo* porcine spinal cord images following spinal cord injury (as an example medical use case) to determine if the injury site is being targeted appropriately and to visualize the distribution of pressure throughout the simulation. We demonstrate that Wave 3000 Plus is a viable approach for visualizing ultrasound propagation through patient-specific anatomies.

Keywords: ultrasound propagation, patient-specific therapy optimization, spinal cord injury, simulation

1. INTRODUCTION

Ultrasound is used in medicine for diagnostic (typically > 2 MHz) and therapeutic (typically < 3 MHz) purposes [1]. Due to its ability to characterize tissue and blood flow remotely (e.g., non-invasively) without ionizing radiation, ultrasound is a desirable option for detecting tissue and vascular abnormalities and modeling biological systems [2]. In spinal cord injury (SCI) cases, it is crucial for clinicians to monitor and control blood flow to the site of injury to promote proper healing. Without sufficient blood flow at the injury site, the damage can cascade, forming what is referred to as a secondary injury [3,4]. Low-intensity focused ultrasound therapy is hypothesized to achieve blood flow in the spinal cord after the routine decompressive laminectomy is performed, as the removal of the bone provides an acoustic window for ultrasound treatment [5,6]. For patient safety purposes, it is imperative to determine the ideal location for the placement of the transducer so that the anatomically relevant structures of the spinal cord (e.g., site of injury) are being targeted by the ultrasound signals.

Understanding where ultrasound waves focus and how they propagate through the anatomy of the spine is critical due to the damage that inaccurate focusing of therapeutic ultrasound can cause to healthy tissue. The complex geometry of the spinal cord anatomy poses unknown parameters to clinicians placing the ultrasound probe. An investigation of how the placement of the ultrasound probe can affect therapy outcomes is crucial for treating spinal cord injury. From this, we aim to find a range of optimal placements for the transducer that minimizes risk of healthy tissue damage. To facilitate the visualization of the propagation of ultrasound signals through the various biological structures and media, an ultrasound simulation software, Wave 3000 Plus (CyberLogic, Inc., New York, NY), is used to analyze probe placement outcomes on ultrasound images of the spine [7]. This software uses a finite-difference time-domain algorithm to solve the 3-dimensional (3-D) viscoelastic wave equation. The overall goal of this work is to study how ultrasound propagates in patient-specific anatomies to determine acceptable placement of focused ultrasound transducers. This goal is achieved by studying the ratio of pressure levels and time of flight of ultrasound waves as they propagate through the spinal cord and the surrounding tissue and measuring the localized pressure of the signal at physiologically relevant regions of interest.

2. METHODS

To simulate the effects of focusing and propagation of therapeutic ultrasound on spinal cord injury, ultrasound images of the spinal cord of a female Yorkshire pig subjects after inducing spinal cord injury were used. B-mode (grayscale) ultrasound images were collected using an IACUC-approved protocol (SW20M221) where a Canon Aplio i800 ultrasound system (Canon Medical Systems, Tustin, CA) connected to an i22LH8 transducer was placed above the spinal cord following a spinal cord injury. The computational aspects of this project are performed in the Wave 3000 Plus simulation software using Digital Imaging and Communications in Medicine (DICOM) ultrasound images of the porcine spinal cord.

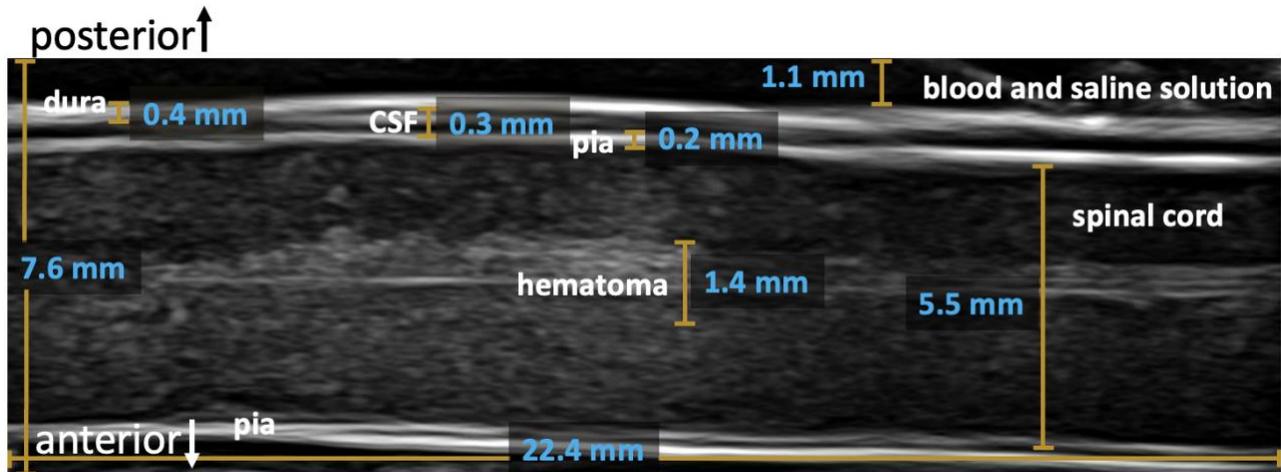


Figure 1: Ultrasound DICOM image (sample representation of typical images) shows sagittal view of a pig thoracic spinal cord (T5 level) after spinal cord injury. An acoustic window was provided via a laminectomy procedure to remove the posterior bony structures. The top of the figure is the posterior side of the cord where the ultrasound probe would be placed. The hematoma indicates the site of injury, which is filled with blood.

Figure 1 shows the B-mode image of a porcine spinal cord after performing a fourth through sixth thoracic (T4-T6) level laminectomy and inducing an injury with a 23-gram weight drop at T5. There are five main anatomical structures labeled in Figure 1 that were included in the simulations: the dura, the cerebrospinal fluid (CSF), the pia, the spinal cord, and the hematoma, which denotes site of injury. To effectively simulate ultrasound wave propagation, the ultrasound DICOM images were pre-processed into a format that is compatible with the Wave 3000 software [7]. Using MATLAB, the DICOM images were converted to 8-bit grayscale PCX images, with a different gray level corresponding to a specific region in the spinal cord anatomy. This step allows the software to distinguish among the various media (blood, dura, CSF, pia, spinal cord, and hematoma) and assign the appropriate medium parameters to each structure. Due to the similar echogenicity of the dura and the pia in the ultrasound image, they are assumed to have the same acoustic parameters.

To understand which acoustic properties of the medium are necessary to effectively model ultrasound wave propagation, we focused on the 3-D viscoelastic wave equation that Wave 3000 solves at each time step (Eq. 1) [7].

$$\rho \frac{d^2 \mathbf{w}}{dt^2} = \left[\mu + \eta \frac{d}{dt} \right] \nabla^2 \mathbf{w} + \left[\lambda + \mu + \phi \frac{d}{dt} + \frac{\eta}{3} \frac{d}{dt} \right] \nabla (\nabla \cdot \mathbf{w}), \quad (1)$$

where ρ is material density (kg/m^3), λ is the first Lamé constant (MPa), μ is the second Lamé constant (MPa), η is shear viscosity (N-s/m^2), ϕ is bulk viscosity (N-s/m^2), t is the time (s), and $w(x,y,z)$ is the displacement of the medium at location (x,y,z) .

Wave 3000 solves Eq. 1 within each voxel of the model and computes the longitudinal and shear displacement vectors at each grid element and at each time step of the simulation. Using the displacement, the pressure of the ultrasound signal can also be calculated at each receiver. For this equation, the density, first and second Lamé constants, and the bulk and shear viscosity need to be provided to the software for each of the five media in the spinal cord model. These parameters were obtained through a literature search for physiological accuracy (Table 1). The hematoma parameters were assumed to be the average values of spinal cord and blood because the injury in the spinal cord is filled with blood. We also assume that the dura, spinal cord, and hematoma are not associated with viscous damping, so the bulk and shear viscosity parameters are set to 0 within the simulation software.

Table 1: Acoustic properties of the materials used in the simulations.

Material	Density (kg/m^3)	First Lamé constant (λ) (MPa)	Second Lamé constant (μ) (MPa)	Bulk Viscosity (N-s/m^2)	Shear Viscosity (N-s/m^2)
Dura	1174 [8]	97.8 [9]	10.90 [9]	0	0
CSF	1007 [8]	2496.7 [10]	5.00 [10]	0.0007 [7]	0.01000 [7]
Spinal Cord	1075 [8]	0.9 [11]	0.10 [11]	0	0
Hematoma	1065	1317.0	0.05	0	0
Blood	1055 [7]	2634.0 [7]	0 [7]	0.1000 [7]	0.00001 [7]

After parameter selection, we used typical focused ultrasound transducer configurations to design the source within Wave 3000 (e.g., NeuroFUS Pro uTX-1000, BrainBox, UK) (Table 2). A source array with 5 elements was developed and placed above the dura, in the blood and saline solution, to represent a therapeutic ultrasound probe. Then, five receivers were added to the simulation to measure the strength of the ultrasound signal after it passes through the dura, the CSF, in the cord, and as it passes through the hematoma. For these simulations, infinite boundary conditions were assumed, meaning that the edges of the model continue infinitely to prevent signal distortion. The mesh was 224 by 76 by 1 voxel, with a 10 voxel/mm resolution. The simulation setup is shown in Figure 2.

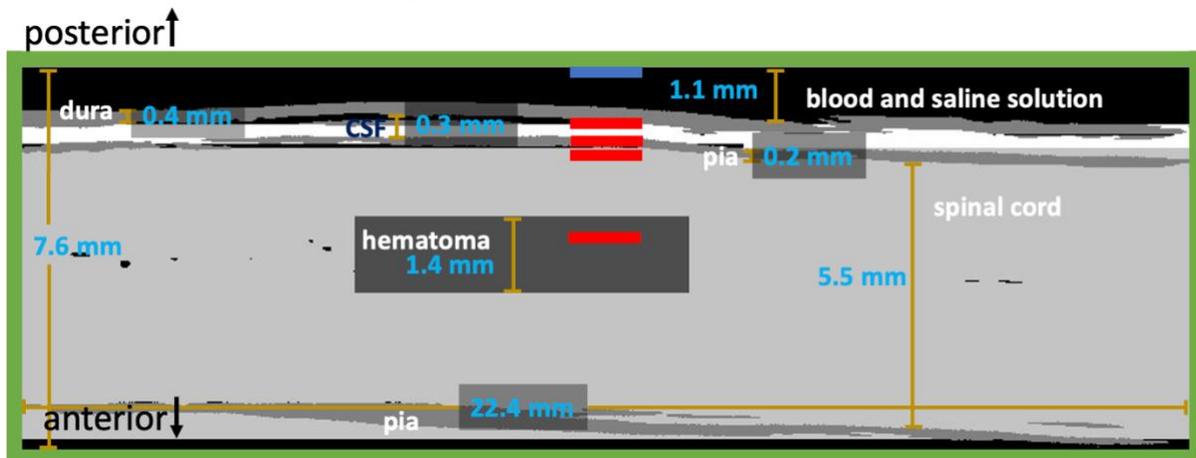


Figure 2: Spinal cord model in Wave 3000. Each gray level corresponds to an anatomical structure with distinct acoustic properties. The blue line corresponds to the focused ultrasound source and each of the red lines corresponds to a sensor that records the normalized pressure at that location (end of the dura, CSF, and in the cord and hematoma) for the duration of the simulations. The green border represents the infinite boundary condition to minimize reflection artifacts as the ultrasound signal propagates to the edge of the computational grid.

Once the model was successfully created within the software environment, there were various signal transmission parameters that were determined for the most accurate representation of ultrasound therapeutic transducers (Table 2). After importing the pre-processed ultrasound image into Wave 3000, the effects of the spinal cord geometry on ultrasound propagation were simulated. From these simulation results, the spatial and temporal distribution of the energy was measured to understand the possible impacts of the placement of the source.

Table 2: Parameters for therapeutic simulations.

Parameters	Therapeutic Simulation
Source Duration	2 μ s
Source Frequency	1 MHz
Source Shape	Continuous Sine Wave
Normalized Source Amplitude	10
Source Radius	1 mm
Source Focal Length	3.2 mm
Apodization	Uniform
Simulation Duration	100 μ s

3. RESULTS

Figure 3 shows four time points of the simulated ultrasound beam propagation, showing the acoustic particle displacement and pressure of the ultrasound wavefront as it propagates through the spinal cord anatomy. At individual time points, we can observe the behavior of the ultrasound wave over 100 μ s to determine how the specific placement of the source and the various media affects beam propagation and pressure distribution. We display the full simulation video in Video 1.

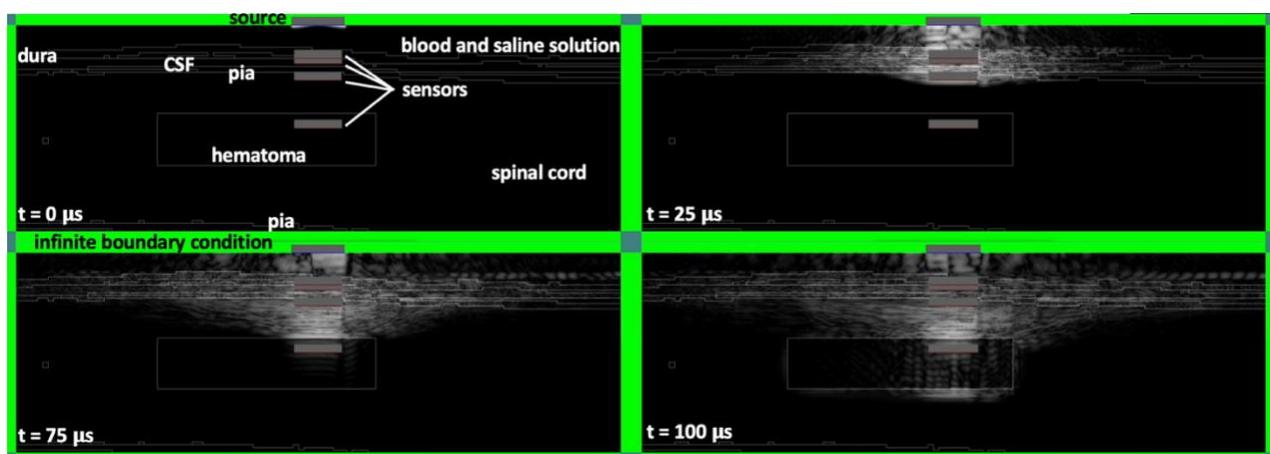
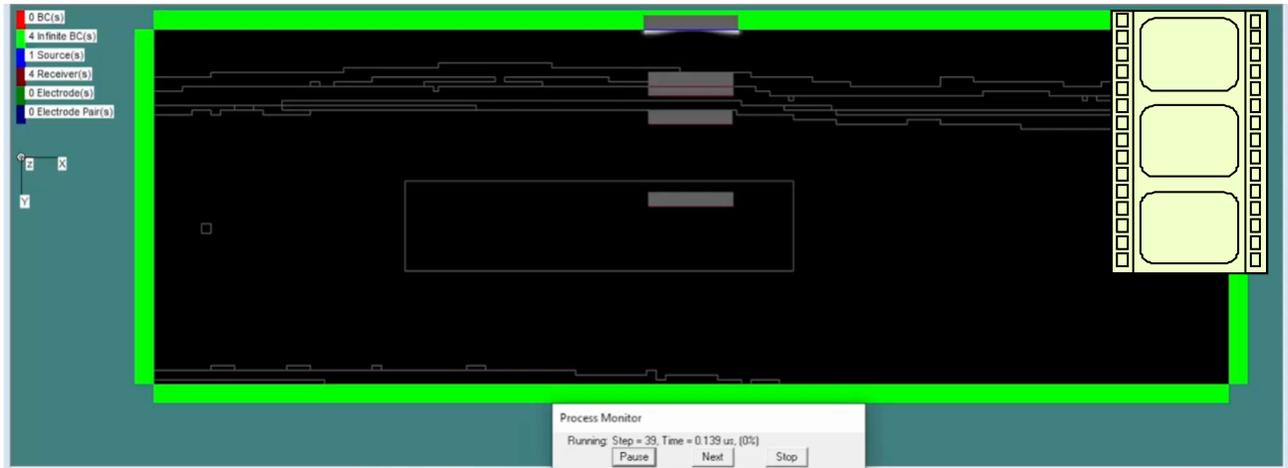


Figure 3: Distribution of the ultrasound wave at various timestamps ($t = 0, 25, 75, 100 \mu$ s), showing the distribution of the ultrasound wave as it propagates through the spinal cord. The brightness of the ultrasound wave is proportional to local pressure amplitude.



Video 1: The displacement and local pressure amplitude (indicated by the brightness of the signal) of the ultrasound wave as it propagates through the spinal cord for 100 μ s. <http://dx.doi.org/10.1117/12.2654357.1>

We observe that while the ultrasound beam profile includes the hematoma, the pressure at the site of injury is drastically less than the pressure in the dura and the CSF (Figure 4). The normalized pressure amplitude (arbitrary units) measured at each of the receivers corroborates this observation, showing that the maximum pressure in the hematoma is on the scale of 10^{-2} , while it is roughly half the source amplitude (10) in the dura (approximately 3.5) and in the CSF (approximately 5). The maximum amplitude of the pressure waveform at the sensor placed in the hematoma (approximately 0.12) is about 6 times larger than the pressure in the cord (approximately 0.02). The loss of signal amplitude at the dura and CSF can be attributed to signal attenuation as the source waveform propagates through different anatomical boundaries due to absorption, scattering, and reflection, as well as power loss from wave displacement [13]. As expected, the hematoma has higher pressure than the cord even though the sensor is placed farther away from the source due to the properties of focused ultrasound [1]. A higher intensity, and therefore higher pressure, is expected at the focal point (3.2 mm) compared to surrounding regions, which is around where the hematoma is in the computational model. We are also able to observe from the sensor plots the amount of time for the ultrasound wavefront to propagate to the sensors placed within the anatomy, which corresponds to the time in which the pressure amplitude is detected at the sensor. The complex geometry of the spinal cord structures results in the wave distortion present in the sensor plots, where we can observe the significant change in wave shape from the initial sine pulse that is emitted into the spinal cord. Future work can include more realistic signals (e.g., gaussian modulated sines). The total runtime for the simulation to complete was 53 minutes.

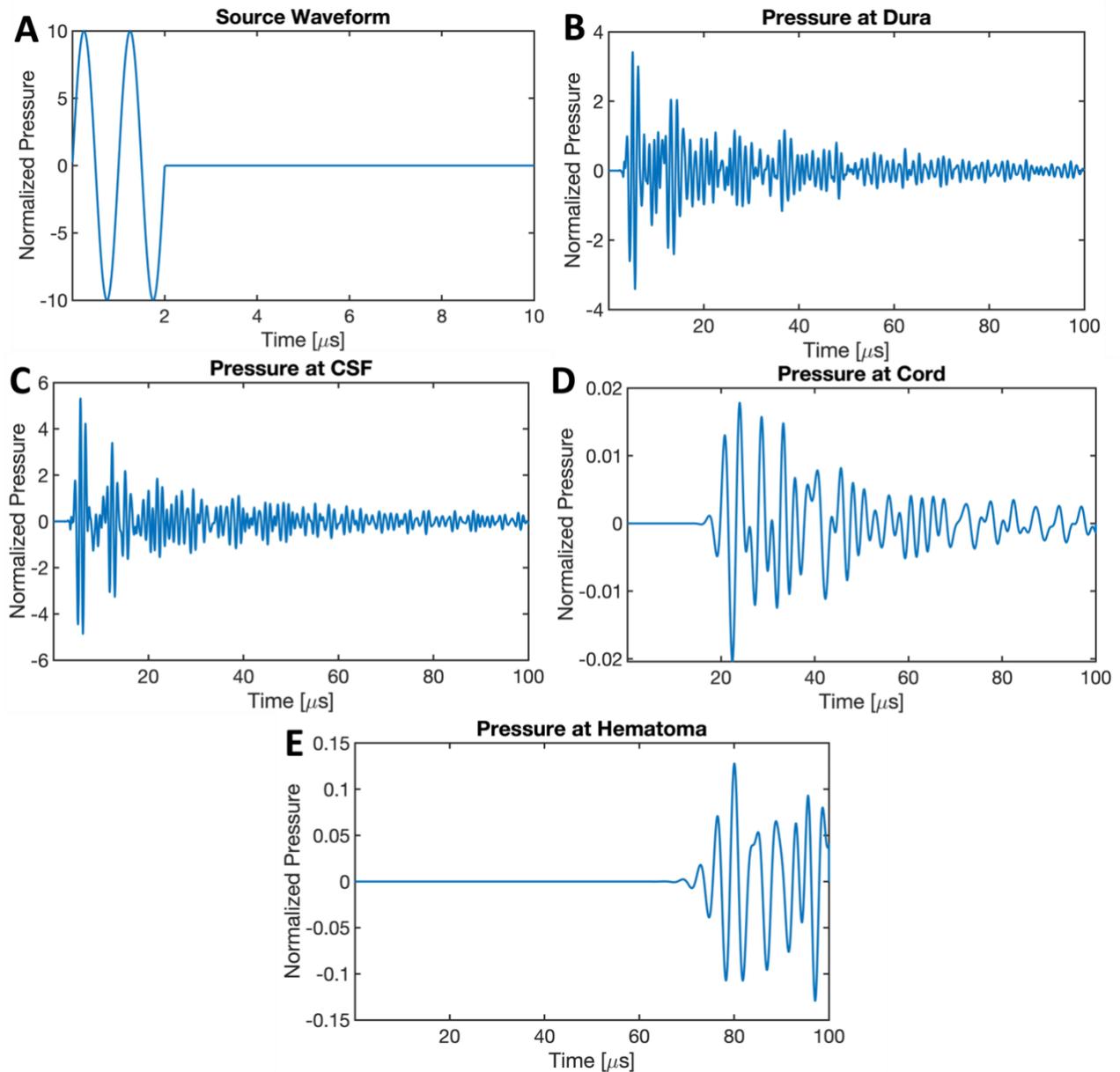


Figure 4: Sensor data recorded at different locations in the anatomy given the source waveform (A). The normalized pressure, measured at each time step for the duration of the simulation (100 μs), is shown for the sensors placed in the dura (B), CSF (C), cord (D), and hematoma (E).

4. CONCLUSION

In this study, we investigated how computational approaches, such as using simulation packages including Wave 3000 Plus, can simulate patient-specific data in realistic anatomical geometries. The software enables clinicians to visualize where the ultrasound beam is focusing and whether the beam profile includes the site of injury. As such, it is a highly effective tool for studying the propagation of ultrasound waves through 3-dimensional media, providing a promising avenue to investigate placement of therapeutic ultrasound probes. As we progress to simulating in a human model, we expect minimal differences in our computational results since pig spinal cord anatomy is similar to humans [13]. The visualizations and sensor data from these simulations provide a quantitative avenue for clinicians to pre-plan ultrasound therapy.

There are limitations to the current study which we aim to address in our future works. To obtain higher spatial and temporal resolution data of the wave propagation and quantify the pressure at each point throughout the spinal cord geometry, the simulation model will also be studied using a MATLAB toolbox k-Wave, which allows for time-domain acoustic simulations using partial differential equations derived from a generalized Westervelt equation to estimate changes in acoustic field [14]. This approach will enable the investigation of the pressure distribution throughout the entire spinal cord anatomy as we can simulate acoustic sensors covering the whole surface area of the model. This toolbox will also allow for the visualization of the maximum pressure at each location and can indicate when the pressure exceeds certain thresholds which can represent tissue damage [15]. Additionally, the DICOM images of the axial plane of the spinal cord will also be imported into the model to determine if the additional view provides consistent results. This study paves the path for human translation and optimization of ultrasound therapy.

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