Measuring Spinal Cord Swelling in a Porcine Model using Fiber Optic Pressure Sensors

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ABSTRACT

Spinal cord swelling is an indication of severe spinal cord injury (SCI) and may have negative effects on neurological outcome. Spinal cord swelling has been observed clinically and in animal models but is still not well understood and has never been mechanically quantified in terms of stress, strain or pressure. The purpose of this study was to evaluate the feasibility of using fiber optic pressure sensors to quantify swelling as a function of pressure in the spinal cord in our established in vivo porcine model of SCI. Fiber optic pressure sensors are suitable for in vivo measurements because they are electrically stable, can operate at body temperature, are highly biocompatible, small in size, and resistive to harsh chemical environments. These sensors are designed to measure pressure in gas and liquid however, the spinal cord is comprised of both fluid and structural elements, such as cerebrospinal fluid and nerve fibers respectively, and is characterized as a soft biological material. Therefore, we hypothesize that when we use these sensors in the spinal cord they may not be measuring fluid pressure but they may be measuring a quantity proportional to bulk stress in the cord instead. To evaluate the feasibility of using these sensors in the spinal cord, fiber optic pressure sensors were inserted directly into the spinal cord of recently euthanized pigs and the spinal cord pressure was measured while a stepwise increasing posterior to anterior force was applied onto the spinal cord. Results show that fiber optic pressure sensors are able to repeatably measure load-related changes in pressure in the spinal cord and most trials showed a strong linear trend between load and pressure. There was large variation in slope between trials however and future work will aim to make these measurements more predictable and to quantitatively relate the measured pressure in the spinal cord to a known applied stress or hydrostatic pressure.

INTRODUCTION

Post-traumatic swelling of the spinal cord is an indication of severe spinal cord injury (SCI) (Koyanagi, 1989 and Jones, 2012). Swelling may have negative effects on neurological outcome by inhibiting the flow of cerebrospinal fluid (CSF) and causing a decrease in blood flow within the spinal cord (Perkins, 1988). Swelling may also contribute to spreading of the spinal cord lesion, perhaps by ischemic or other mechanisms, causing additional damage above and below the injury site (so called ascending lesion) days or weeks after the primary injury (Aito, 1999). Spinal cord swelling has been observed following SCI clinically and in animal models. In surgery, spinal cord swelling is observed as a tense and non-pulsatile dura (Koyanagi, 1989 and

Perkins, 1988). The shape of the spinal cord itself can be observed on post injury and experimental medical imaging techniques such as CT-myelography and ultrasound. On these images, an increase in anterior-posterior spinal cord diameter or disappearance of the sub-arachnoid space indicates spinal cord swelling (Koyanagi, 1989 and Jones 2012). Despite all these observations, spinal cord swelling is not well understood and has never been mechanically quantified in terms of stress, strain or pressure.

Fiber optic pressure sensors are suitable for *in vivo* measurements and preliminary work in our laboratory leads us to believe they could be a promising tool to experimentally quantify spinal cord swelling after simulated SCI. Fiber optic sensors are electrically stable, can operate at body temperature, are highly biocompatible, small in size, and are resistive to harsh chemical environments. Fiber optic pressure sensors (Samba Preclin 420, Harvard Apparatus Canada, QC) have been previously used in our lab to measure pressure in the CSF in our established SCI pig model (Jones, 2012 and Lee, 2013). Following this study, an *in vivo* pilot study was conducted to measure pressure in a pig spinal cord prior to, during and after simulated SCI by inserting the sensors directly into the parenchyma of the thoracic spinal cord. We used a previously-developed weight-drop device which drops 50 gram from a height of 50 cm to produce the SCI followed by a 600 gram sustained compression (Lee, 2013). These preliminary results showed that the pressure steadily increased by approximately 10 mmHg as the cord swelled within several hours after injury, even after decompression surgery was simulated by removing the sustained compression. These sensors are designed to measure pressure in gas and liquid however, the spinal cord is comprised of both fluid and structural elements, such as cerebrospinal fluid and nerve fibers respectively, and is characterized as a soft biological material. Therefore, in order to properly interpret the results from our *in vivo* pilot study, we need to identify what quantity is being measured by these sensors in the spinal cord. We hypothesize that the sensors may not be measuring fluid pressure but measuring a quantity proportional to bulk stress in the cord instead. The purpose of this study was to evaluate the feasibility of using fiber optic pressure sensors to directly quantify swelling as a function of pressure in the spinal cord in our established *in vivo* porcine model of SCI (Lee, 2013).

METHODS

To evaluate the feasibility of using these sensors, we wanted to show that the sensors consistently reacted to a change in stress in the spinal cord and that we could obtain repeatable and predictable pressure measurements in the spinal cord as it was subjected to mechanical stress. As a first step to achieve these objectives, we have conducted *ex vivo* tests in which two fiber optic pressure sensors (Samba Preclin 420, Harvard Apparatus Canada, QC) were inserted into the spinal cords of ten pigs (Figure 1). The sensors were inserted using a 22 Gage 1.00 inch catheter and part of a 1mL syringe. In order to control the insertion depth of the catheter into the spinal cord, 2mm of a 200microL pipette tip was cut and slid onto the 22G catheter a distance of 4mm to act as a plug on the dura. The 1mL syringe was cut to the 0.3mL mark. The rubber stopper was removed and an 18 Gage catheter was used to feed the pressure sensor through it. The pressure sensor, with the attached rubber stopper, was then placed into the syringe. Prior to inserting the sensor into the animal, the 22G catheter (needle removed temporarily) was placed on the syringe tip containing the pressure sensor. The rubber stopper served to control the length

of the sensor protruding from the catheter guide tip and it was adjusted so that approximately 2.0 mm of the sensor tip was exposed. The catheter guide was then removed while the syringe, rubber stopper and sensor were left undisturbed with the predetermined position. Once the cord was exposed, the sensor insertion location was identified so that the sensor tip, which was 6.0 mm away from the plug on the catheter guide, would be at the desired distance away from the center of the load site. The 22G catheter was then inserted at a 30 degree angle into the spinal cord. The catheter needle was removed leaving only the guide in the spinal cord and the pressure sensor was fed into the catheter guide at which point the syringe was tightened onto the catheter guide. This leaves the pressure sensor tip inserted into the spinal cord at the desired distance away from the load site. Tape was used to further secure the sensor location. This process was repeated for both pressure sensors being inserted into the spinal cord for each trial. One sensor was inserted caudal and one rostral to the loading site. During these tests, after measuring baseline pressure for 5 minutes, a transverse compression was applied to the posterior aspect of the spinal cord by placing the 9.0 mm diameter cylindrical impactor with rounded edges (1.0 mm radius) from our custom weight drop apparatus onto the spinal cord (Lee, 2013). The impactor (14 grams) was carefully placed on the spinal cord. The load was then increased every 5 minutes by adding weights onto the impactor in 20 gram increments. In the first 10 trials, the distance between the sensor and the load site was varied from 0 – 10mm in order to identify an appropriate placement of the sensor such that pressure increases could be detected. In the 10 subsequent trials the "best case" distance identified from the previous animals was used. The trials were included in this study if the sensor was successfully placed at the appropriate distance from the load site, the sensor was not observed to migrate during the trial and the sensor picked up pressure increases in the spinal cord. Migration of the sensor was identified when the plug on the catheter guide was no longer in the dura at the end of the trial. Of the ten trials performed, seven trials were successful. The spinal cord deteriorates rapidly after death, causing an increase in stiffness with increasing time after death (Oakland, 2006). Therefore, these tests were carried out as quickly as possible after death and were completed within four hours of euthanasia.

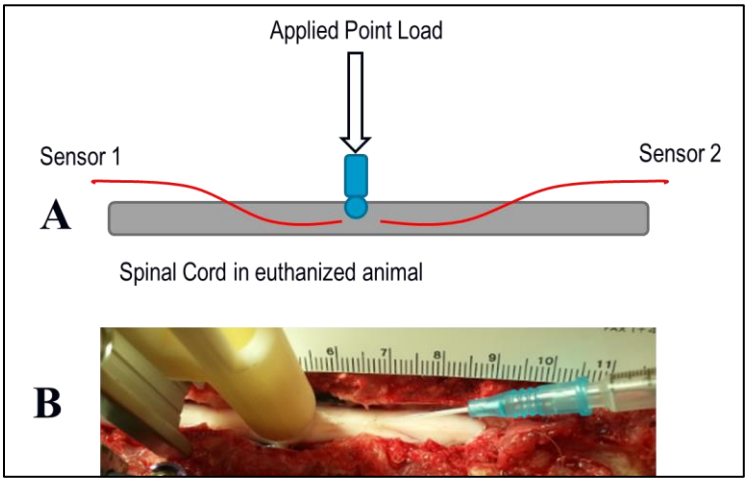

Figure 1**:** *Ex vivo* test set-up to measure pressure while applying a point load. A. Schematic of Components and B. Picture of set-up.

RESULTS

We found that the measured pressure increased with increasing mass and returned near the baseline pressure once all mass was removed (A, Figure 2 and 3). The distance from the sensor tip to the load site affected the magnitude and sensitivity of the pressure measurements (Figure 2). It was found that a distance from the sensor tip to the center of the load site of approximately 2 mm was appropriate for our purposes. This distance allows pressure changes to be visible in the sensor readings. This distance also prevents migration of the sensor during the trial which occurs when the sensor insertion is within close proximity to the impactor edge. At this sensor position the pressure readings followed a similar trend across the different trials (Figure 3).

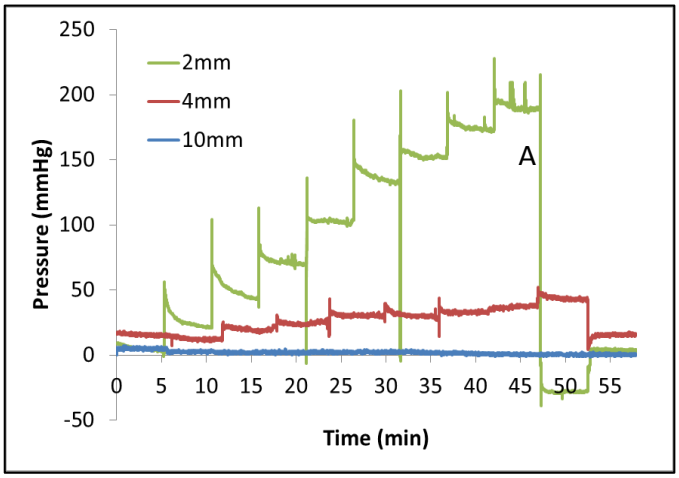

Figure 2: The effect of distance of the sensor tip from the center of the load site while measuring pressure. A. Weight was removed.

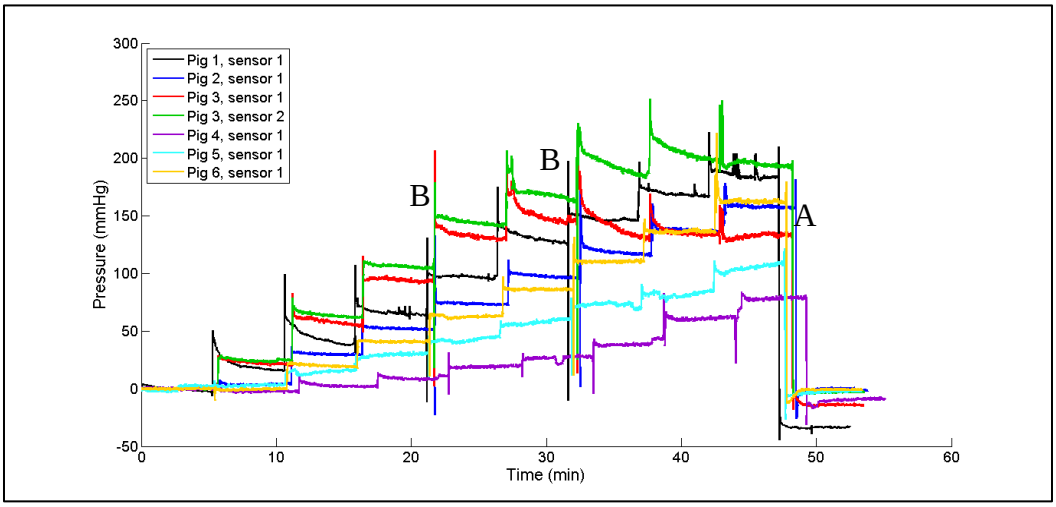

Figure 3: Pressure readings with sensor tip placed approximately 2 mm from the center of the load site. A. Weight was removed and B. Pressure spikes caused by changing the weight.

The trials shown in Figure 3 were post processed by subtracting the average baseline pressure from the entire pressure traces. The pressures were then averaged over 90% of each five minute time step in order to obtain a single pressure value for each weight addition to the spinal cord (Figure 4). A best fit line for the all the data was compared to the calculated average applied stress. This average applied stress is an approximation of the pressure we can expect to see in the spinal cord based on the force being applied onto the cord divided by the nominal area of the load site. This pressure is an approximation since the pressures seen in the cord will also be affected by stress concentrations at the edge of the impactor and contact stresses (Greaves, 2008).

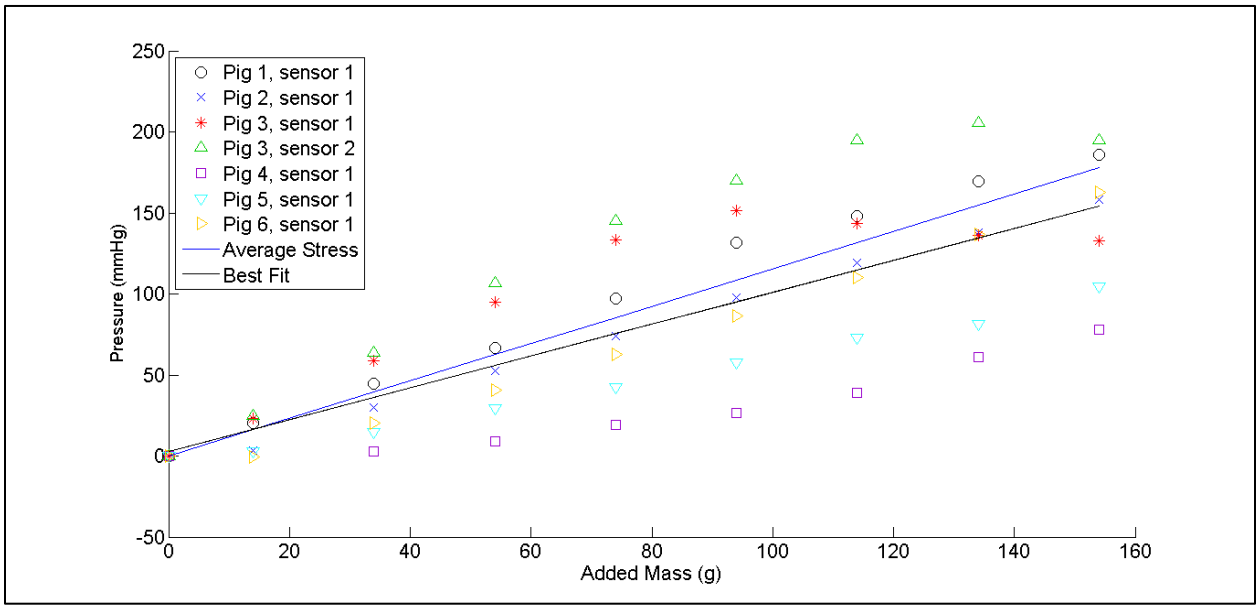

Figure 4: Best fit line for overall pressure data compared to average stress applied to spinal cord

It was found that the trials followed three different trends. The most common trend (N = 4) was a linear trend where the pressure measured in the spinal cord increased with added weight (Figure 5). Some trials (N = 2) followed a linear trend until a certain point where they reached a maximum pressure and a plateau was observed (Figure 6). Finally, one of the trials was observed to have a polynomial trend (Figure 7).

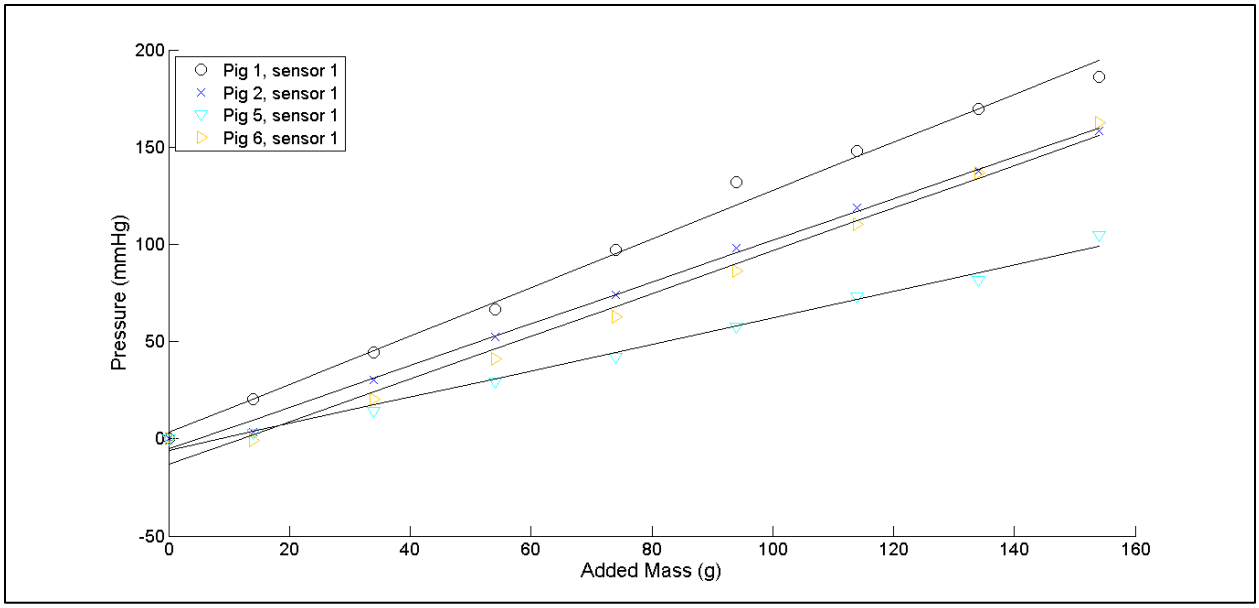

Figure 5: Pressure readings with linear trend (N = 4)

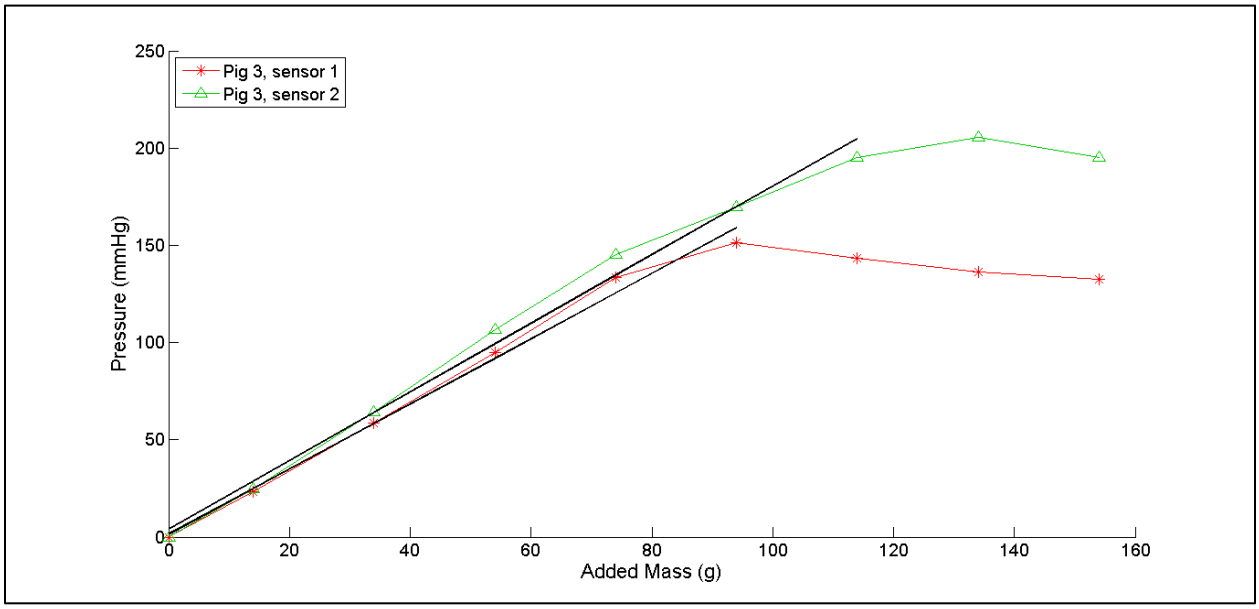

Figure 6: Pressure readings with linear and plateau trend (N = 2)

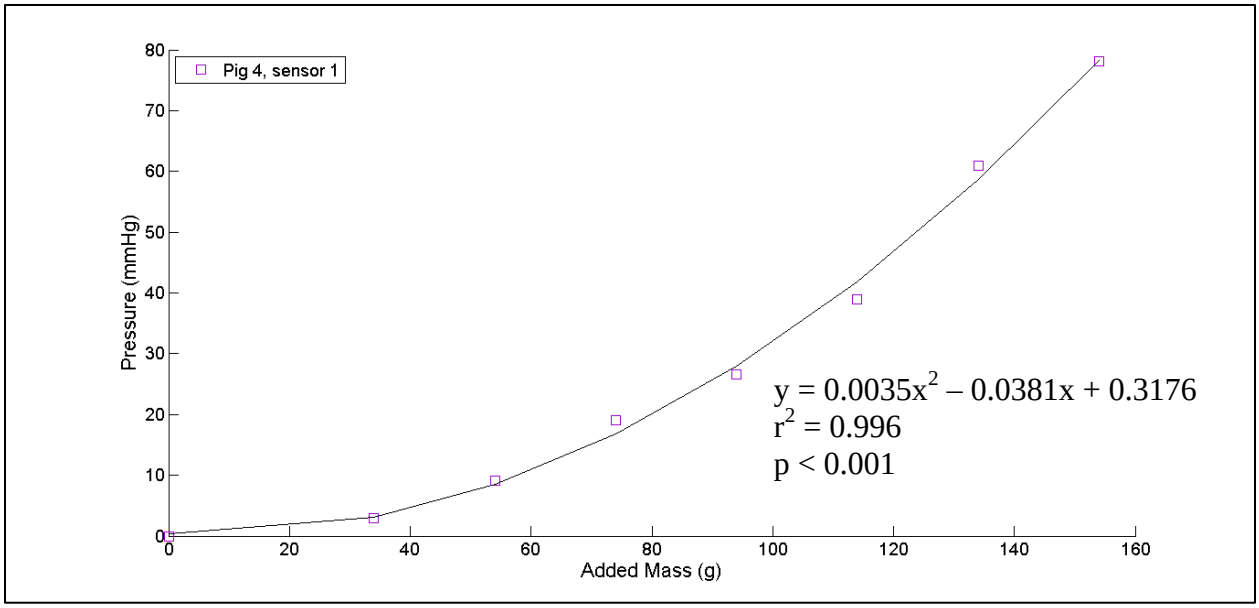

Figure 7: Pressure readings with polynomial trend (N = 1)

The results show that most trials are either linear or have a linear section prior to a plateau. We hypothesis that this plateau could be caused by reaching a maximum stress due to fluid in that area of the spinal cord being flushed out by the added stress and the change in fluid volume is affecting the sensor readings. It is also possible that a certain maximum displacement of the spinal cord was reached due to space constraints or material properties. In Table 1, linear trends of the individual trials show a strong association between measured pressures in the spinal cord and applied mass. However, when you combine all the trials and analyze the overall pressure data, the association becomes much weaker due to the differences in the slopes of the individual trials. This variation between trials makes it difficult to predict the outcomes of future trials however, it is clear that there is a relationship consistently present.

Table 1: Linear Trends of Trials and Overall Pressure Data

Linear Trends ($p < 0.001$)		
Trial Id.	**Slope**	**Coefficient of Determination (r^2)**
Pig 1, Sensor 1	1.24	0.993
Pig 2, Sensor 1	1.07	0.997
Pig 3, Sensor 1	1.68	0.993
Pig 3, Sensor 2	1.76	0.991
Pig 5, Sensor 1	0.682	0.991
Pig 6, Sensor 1	1.10	0.988
Overall	0.982	0.648

DISCUSSION

This study is a first step to evaluating the feasibility of using fiber optic pressure sensors to quantify swelling as a function of pressure in the spinal cord. In this study, we focused on the measurements taken in the spinal cord in a controlled environment. We have shown that fiber optic pressure sensors are able to pick up a change in transverse compression on the spinal cord as long as the sensors are placed approximately 2 mm away from the load site. The sensors can be inserted with an accuracy of ±1.0 mm. Sensor placement has been shown to have an effect (Figure 2) on the magnitude of the pressure readings and might account for some of the differences in magnitude and therefore slope between trials. We hypothesize that in an *in vivo* experimental SCI, the readings will have a larger magnitude and be most sensitive closer to the injury site. However, if injury is simulated using a drop weight device, care must be taken that the sensor insertion site far enough away from the impact site to avoid migration of the sensors.

In most trials, the pressure in the spinal cord was seen to decrease over the 5 minute intervals in Figure 3, even though the stress on the cord was held constant. This behavior is similar to the fluid phase pressure observed in creep tests of biphasic materials such as cartilage (Soltz, 1998). We think the spinal cord can be interpreted as a biphasic material since it is composed of solid elements, such as nerve fibers, and also contains cerebrospinal fluid. This comparison leads us to hypothesize that we may be measuring the fluid phase pressure in the spinal cord. However, future work needs to be done in order to be sure the solid elements are not affecting these pressure readings.

FUTURE WORK

A hydrostatic pressure on the spinal cord would be more representative of the *in vivo* situation where the cord swells against the dura circumferentially than a posteriorly-directed transverse load would be; therefore, in the future we will conduct another *ex vivo* test where we will apply a hydrostatic pressure to spinal cord segments using a fluid pressure tank. We will measure the pressure in the spinal cord as well as in the fluid tank, as shown in Figure 8.

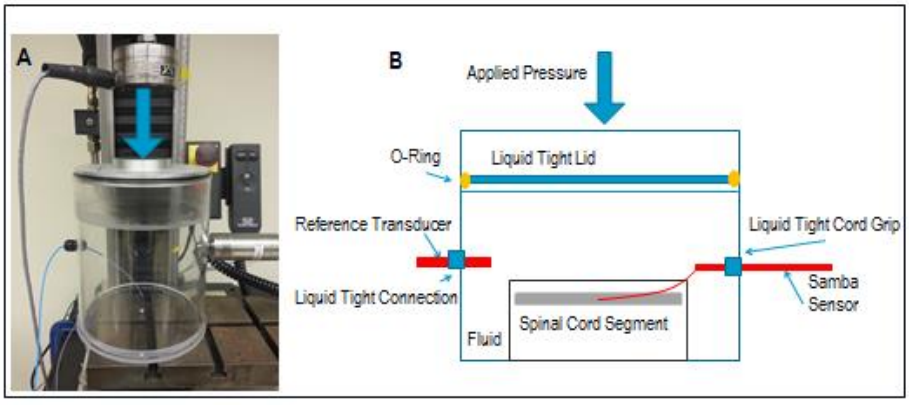

Figure 8: Pressure tank set-up for applying hydrostatic pressure to cord segment. A. Picture of set-up and B. Schematic of components

These experiments will allow us to explore both the repeatability as well as the predictability of the measurements further by comparing them to a known applied hydrostatic pressure. We expect to find a relationship between applied and measured pressures which will allow us to use fiber optic pressure sensors in the spinal cord to measure swelling pressure *in vivo*. By quantifying swelling, we hope to contribute to the understanding of spinal cord swelling and its effects on spinal cord injury outcomes.

CONCLUSIONS

We recorded increases in pressure in the spinal cord under increases in posteriorly applied transverse compression. It was found that sensor location with respect to the load site has an effect on the magnitude and sensitivity of the pressure measurements. It is beneficial to place the sensor tip as close as possible to the load site while avoiding migration of the sensor which can occur when the sensor insertion site is in close proximity to the impactor edge. We observed three distinct trends in the pressure traces: linear, linear with a plateau and polynomial. The linear trends or sections show a strong association however, the slopes of these lines vary between trials. Future work will be conducted to investigate the different observed behaviors in order to make the measurements more predictable.

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