Shape Memory Nitinol Based Minimally Invasive Spinal Cord Stimulation Lead Concept for Pain Relief

By
Shailen G. Sampath
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This thesis by Shailen G. Sampath is accepted in its present form by the Center of Biomedical Engineering as satisfying the thesis requirements of the degree of Master of Science.

Date: _____

_____
Vikas Srivastava Ph.D, Advisor

Recommended to the Graduate Council

Date: _____

_____
Albert E. Telfeian M.D Ph.D, Reader

Date: _____

_____
Edith Mathiowitz Ph.D, Reader

Date: _____

_____
David Borton Ph.D, Reader

Recommended to the Graduate Council

Date: _____

_____
Andrew G. Campbell Dean of the graduate school

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Abstract

Spinal Cord Stimulation (SCS) is a procedure that masks neuropathic pain for people with failed back surgery syndrome, postherpetic neuralgia and a host of other indications [1]. Insertion of a SCS can be achieved either percutaneously with a cylindrical lead or a surgically inserted paddle that is placed over the posterior spinal cord dura. A paddle electrode generally provides better coverage and relief of pain over cylindrical leads, since these broader electrodes provide more contact area with the dura, unidirectional stimulation, contain more electrodes, and diminish the possibility of lead migration [3]. However, paddle leads are more expensive to insert, less accessible, and require more invasive surgery that can lead to a host of postoperative complications [2]. In this thesis the design of a novel cylindrical lead that uses the shape memory alloy nitinol is presented as a potential improvement to current methods of SCS. The lead constructed of a nitinol interior can be inserted percutaneously, without the need of a laminectomy, and morph into a paddle-like geometry with greater dura contact area once it is inserted into the body. This design aims to reduce costs of SCS, increase accessibility, improve patient outcomes, reduce lead migration, and minimize post-operative complications. Proof of concept for the design will be discussed along with analogous devices using nitinol for vascular use. In addition, both thermal and mechanical methods to control the rate of shape recovery of the nitinol lead from a cylindrical to paddle like shape once inserted into the body will be discussed. Challenges with insertion and potential risk of this novel method for SCS will also be touched upon. In the future a cadaver test will be conducted to test how the device works in vitro and further improvements in prototyping and insertion methods will be made.

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1. Introduction and Background

1.1. Spinal Cord Stimulation

1.1.1. Purpose of Spinal Cord Stimulation

Chronic pain is prevalent across the world and is one of the most common reasons why a patient seeks medical help. According to the World Health organization 22% of the world's primary care patients experience chronic pain that is debilitating at some point. Chronic pain can be divided into two main categories: pain that is nociceptive, which is experienced from a stimulus being detected by a nociceptor around the body, or neuropathic, which is caused by damage or disease effecting the somatosensory or autonomic nervous system.[4] Spinal cord stimulation (SCS) therapy is a procedure that can effectively mask, or "block" pain signals before they can reach the brain and has been shown to be more efficacious and cost effective compared to pharmaceutical treatment for pain.[11] In SCS a device similar to a pacemaker delivers electrical pulses through an electrical lead surgically placed in the epidural space to stimulate the dorsal columns of the spinal cord. SCS is most commonly used in patients with neuropathic pain syndromes and works less effectively in patients with nociceptive pain. Hence it is rarely used in cancer and burn patients. Neuropathic pain from failed back surgery syndrome, spinal cord lesions with well circumscribed segmental pain, peripheral nerve injuries, phantom limb pain from amputation, postherpetic neuralgia, and complex regional pain syndrome are the most common afflictions where SCS is considered. In addition, other indications of SCS include treatment of pain associated with ischemia from peripheral vascular disease and intractable angina pectoris. Today over 50,000 SCS procedures are conducted a year worldwide. [3]

1.1.2. Spinal Cord Stimulation Mechanism

The exact mechanism of action of SCS remains controversial. SCS was first proposed on the basis of Melzak and Wall's gate theory of pain over 50 years ago. The gate theory of pain describes the masking of nociceptive input from the periphery by stimulation of induced antidromic activation of collaterals of large dorsal column fibers in the spine. [5, 3] This purports that pain signals are modulated in the spinal cord prior to being "perceived" in the brain. Today we know that SCS is preferentially better at treating neuropathic pain and there is not much research supporting its benefits against nociceptive forms of pain. This contradicts what would originally have been predicted if the gate theory, as it was originally proposed, stood true. The exact mechanism of how SCS actually works is still an active area of research, but from what researchers have found so far, we can at least conclude that the treatment of neuropathic pain works by affecting the pathological activity of the spinal neuronal circuitry that creates the pain sensation. [6] Therefore, by stimulating the dorsal column, which contains the neuronal circuitry for receiving pain sensation, we can create paresthesia coverage of pain.

1.1.3. Spinal Cord Stimulation Insertion and Placement

There are two main techniques that are used for the placement of SCS leads into the epidural space: Percutaneous insertion and insertion of the lead by Laminectomy. Percutaneous insertion of a lead entails placement of the lead through the percutaneous tissue into the epidural space, without any surgical removal of the vertebrae. In a percutaneous procedure the stimulation lead is inserted through a needle alongside local intradermal and subcutaneous anesthesia. The insertion needle (Tuohy) is angled steeply to get as close to horizontal as possible to allow for easy insertion of the lead parallel to the spinal cord. Optimal entry of most SCS leads, for percutaneously insertion, is conducted 1 to 3 spinal levels cephalad to the desired location of stimulation in the lumbar spine, as to reduce accidental damage to the spinal cord which ends at the start of the lumbar

spine. Once the electrode is inserted, it is gently advanced through the epidural space using fluoroscopy to check if the lead is going along the dorsal epidural midline. The lead can then be anchored either subcutaneously or at the site of the insertion needle. In a laminectomy a similar procedure is conducted but with a segment of the vertebrae surgically removed by a surgical specialist.

The exact placement of the lead is determined by the location and distribution of the patient's pain. For example, to alleviate shoulder pain leads are placed slightly off the midline between C2 and C4. When the entire upper extremity is targeted then leads are placed between C3 and C4 slightly off the midline. To stimulate the lower torso a lead can be placed on the midline between T8 and T9. lower extremity stimulation can be conducted by placement between T9 and T11 and distil lower extremity stimulation by placement as low as T12 and L1 with displacement of 1-4 mm of the midline. [7] Once the leads are placed in the appropriate site in the epidural space the proximal wires are then attached to a stimulation battery with a pulse generator.

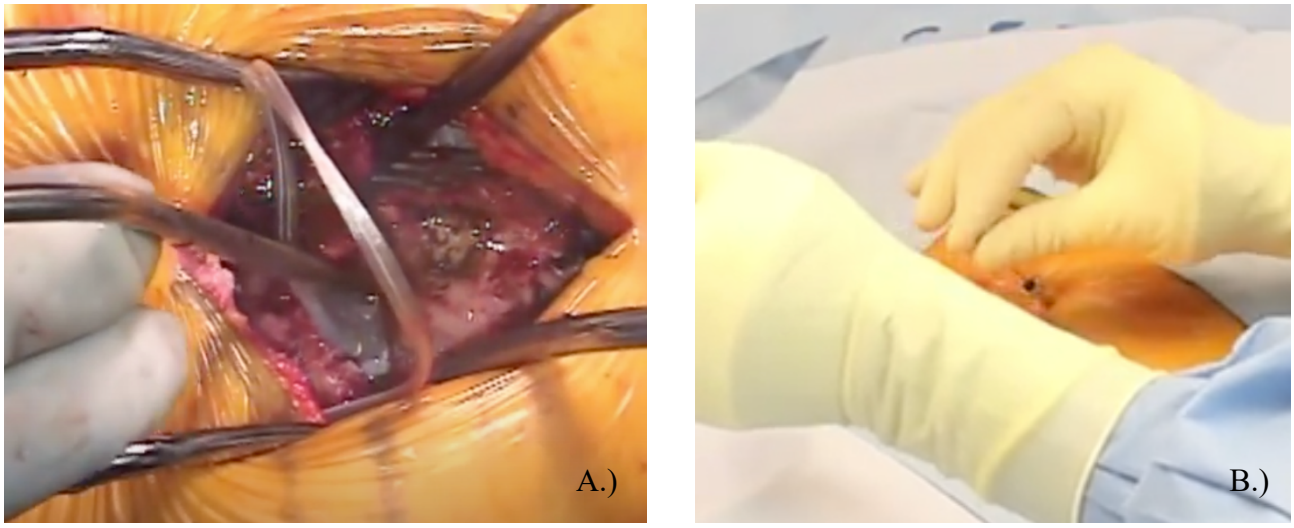


Figure 1. *This figure illustrates the difference in the invasiveness between the placement of a paddle leads via laminectomy, and a cylindrical lead via a Tuohy needle* **A.)** *Laminectomy procedure for insertion of paddle lead [21]* **B.)** *Insertion of Touhy needle for insertion of cylindrical lead [20].*

In addition to the technique used in inserting the leads, SCS can be categorized by the type of lead that is used. Today there are a wide range of electrode leads used in SCS. These electrodes can be classified into two broad categories: cylindrical leads and paddle leads. Paddle leads can only be placed surgically through a small laminectomy, while cylindrical are more commonly placed percutaneously. Cylindrical leads are smaller in diameter and are traditionally either quadripolar or octopolar. On the other hand, the simplest paddle electrodes are quadripolar but can have up to 8 to 26 contact points to stimulate multiple targets and have a face constructed out of flexible silicon. Since a higher number of electrodes allows for more optimization in choosing where to place cathodes and anodes on the lead, high density electrode arrays are considered more favorable and are commonly used. High density paddle arrays can have 16 to 32 electrodes across five columns and cylindrical leads can have 8 to 16 electrodes. [3] Both leads often use silver as a conductor within the lead and platinum iridium or platinum for their contacts, to allow for non-faradaic stimulation. The conductive wires in these leads are housed within an insulating layer, commonly polyurethane or silicone.

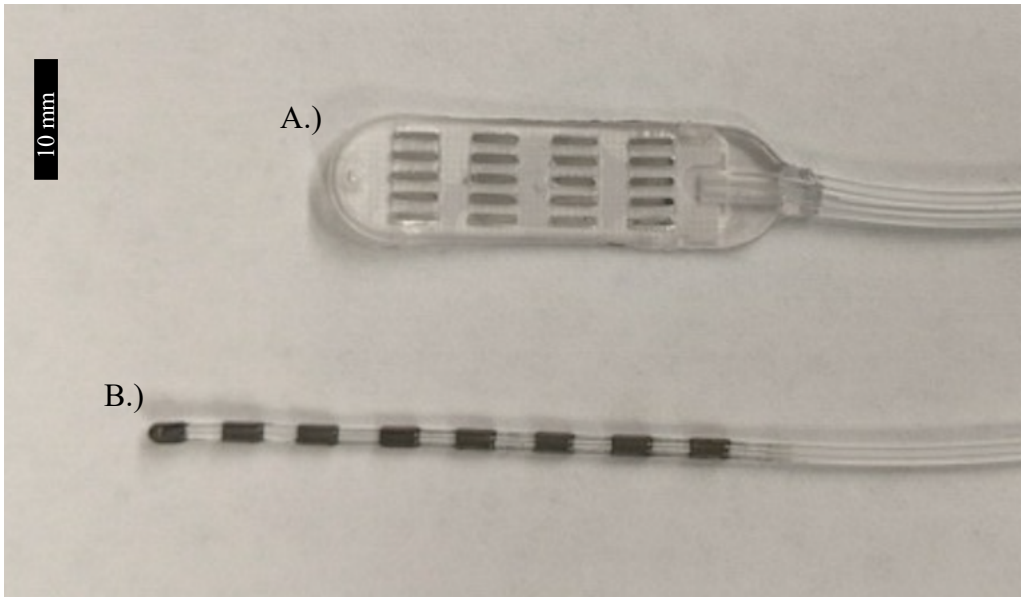


Figure 2. *This figure displays a paddle and cylindrical lead provided by Abbott Laboratories* **A.)** *20 electrode contact paddle lead* **B.)** *Octopolar cylindrical lead*

1.2. Clinical Need

While SCS proves efficacious for thousands of individuals [8] each year and modern advancements in waveforms have allowed for improved paresthesia coverage for both paddle and cylindrical leads, there still exist complications and tradeoffs when deciding between what kind of stimulator to have implanted. While percutaneously inserted cylindrical leads are more minimally invasive, cheaper, require local as opposed to general anesthesia, and more accessible to inert (due to not having to be inserted by a surgical procedure or mandating a surgical specialist), paddle leads have been shown to reduce complications of SCS in the future, such as lead migration, and they are shown to generally improve overall paresthesia coverage. [3, 2, 9, 10] Paddle leads provide better coverage due to their ability to insulate and conform to the dorsal surface better, more densely packed SCS electrode contacts, and unidirectionality in electrical impulse delivery. By having more electrodes along the width of the spinal cord better mediolateral resolution can be provided which allows for better coverage of targeted dermatomes. [3, 17] Unfortunately, paddle leads invasive method of insertion remains unfavorable with a higher risk for postoperative complications. [2] Thus, there exists a need for a stimulation lead which can simultaneously be inserted in a minimally invasive fashion, reducing post-operative complications; can cover optimal area of the dura, increasing efficacy of the procedure; can reduce lead migration, diminishing the call for future realignment procedures; and be more accessible, without the need of a surgical specialist.

2. Lead Design

2.1. Minimally Invasive Novel Design

To address the need for a device that can simultaneously possess the advantages of both a cylindrical and paddle stimulator several ideas have been proposed and tested in the past, including changes in the type of waveform used [3], insertion techniques [12], and geometry of the stimulation lead. Several of these advancements, particularly in the area of waveforms have resulted in substantial improvements for cylindrical leads, making cylindrical stimulation almost comparable to paddle lead stimulation. [3] Thin line paddle leads that have comparable number of contact electrodes as cylindrical leads (such as St. Jude Medical's S-series), are able to be inserted percutaneously through a special larger needle and have been shown to reduce lead migration. [13] However, all of these solutions have still fallen short of providing a stimulator which is able to best exhibit the advantages of both lead stimulator types.

Here I will propose a novel stimulation lead design which utilizes the unique properties of the shape memory alloy nitinol, to provide a lead that can be inserted in a minimally invasive fashion, can cover optimal area of the dura with electrodes, can reduce lead migration, and be more accessible simultaneously. There are two geometries proposed for this novel design. The stimulation leads in their final conformation are shown in Figure 3 below.

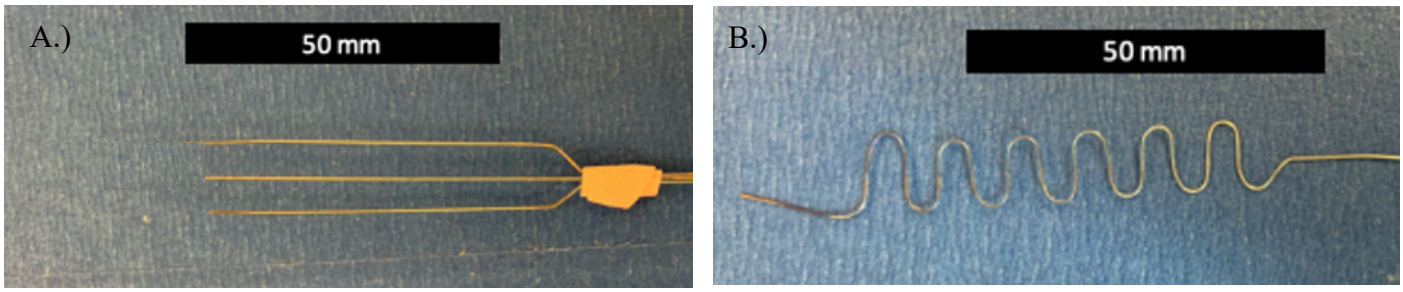


Figure 3. *This figure displays the two geometries proposed that will be inserted while in a linear shape and expand into the geometries displayed once a lubricated sheath is removed in the epidural space at body temperature* **A.)** *Trident geometry* **B.)** S-shaped *Zig zag geometry*

Our design consists of a cylindrical lead, or a series of three cylindrical leads as can be shown in the case of the trident geometry in Figure 3. These leads will have silver conductor running through them and platinum contacts, just as current stimulators have, but will have an internal nitinol component, in place of a polymeric shaft that is there to provide rigidity. At room temperature outside of the environment of the body the nitinol will be configured and held in a linear fashion. Due to nitinols material properties, the stimulation lead will be able to undergo temporary “deformation” and be held in this linear state. The novel lead will then be slid into a lubricated catheter sheath and will be inserted through a Tuohy needle, standardly used in percutaneous insertion. Once the lead is in the body, the nitinol will want to expand into a paddle like conformation. The sheath will provide mechanical resistance against this tendency and cold saline will also be potentially deployed along with the catheter to keep the nitinol in a linear shape. Once the physician has determined that the lead has been optimally placed by fluoroscopy, the cold saline will be stopped and the sheath will be removed, and the lead will expand into the geometries shown in Figure 3 within the epidural space. The 13 mm width of the lead will be comparable to paddle leads allowing for better mediolateral resolution and preventing lead migration. Further, the minimally invasive insertion technique will reduce the risk associated with a more invasive procedure and allow for the procedure to be conducted without the need of a surgical specialist. These steps are illustrated in Figure 4 for the S-shaped zig zag geometry.

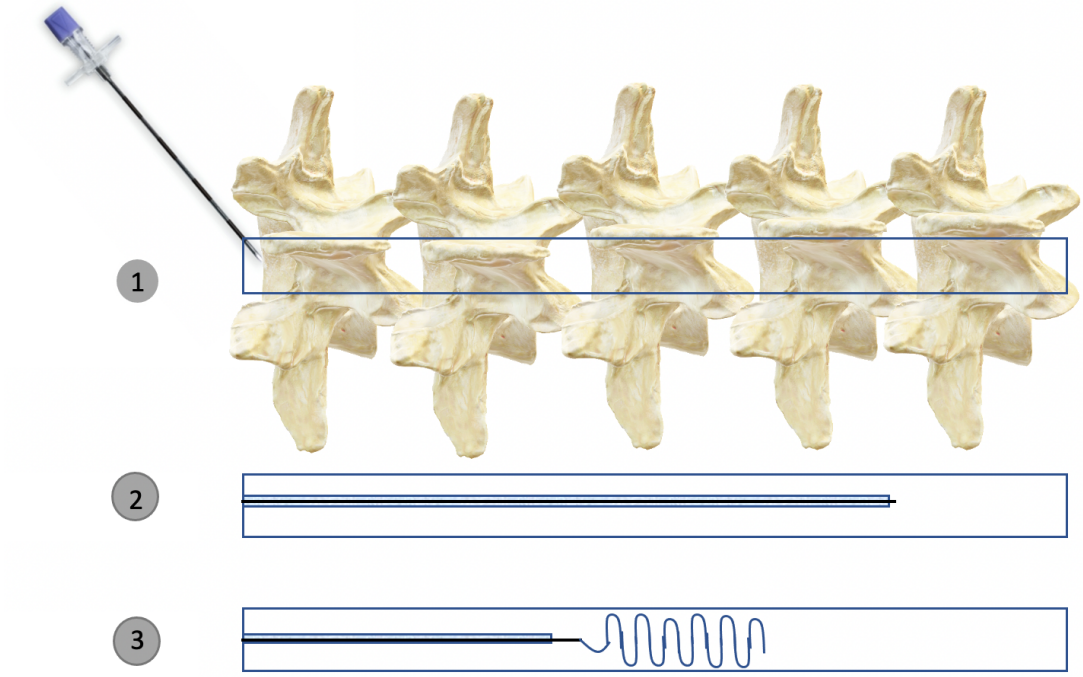


Figure 4. *This figure displays the deployment of a novel nitinol based spinal cord stimulation lead.* ***1****: Displays the vertebral bodies and the Touhy needle used for minimally invasive deployment of the nitinol lead into the epidural space. The rectangle drawn above the vertebrae represents the epidural space.* ***2****: Once the Touhy needle is inserted, the nitinol-based lead with a saline cooled catheter sheath over it will be guided to the appropriate location within the epidural space.* ***3****: Once the appropriate location has been determined via fluoroscopy, the sheath will be removed, and body temperature will induce the nitinol to take the advantageous S-shaped zig zag geometry.*

2.2. Shape Memory Alloy: Nitinol

2.2.1. Nitinol physical properties

Nitinol (Nickle Titanium Naval Ordnance Laboratory) is an alloy of nickel and titanium (NiTi) and was discovered in the Naval Ordnance Laboratory in the 1960s. Perhaps one of the materials most marketable aspects is its shape memory ability, which results from two temperature dependent crystalline structures. At lower temperatures nitinol can be found in a martensite phase. Martensitic nitinol has an elastic modulus of 28-41 GPa and is found in a twinned structure with "floppy" bonds that are free to move around, making the material seems as if it is easier to deform. At warmer temperatures nitinol can be found in an austenitic phase, with an elastic modulus of

around 81 GPa. Austenitic nitinol has a body centered cubic structure and is very stiff. In fact, austenitic nitinol is so stiff and springy that the material is termed super elastic. Since the material can be easily "deformed" in its martensitic phase while still maintaining its chemical bonds, when nitinol is heated into its austenitic phase it will revert back to its original trained shape. This effect is known as the shape memory effect. The trained shape is the shape the nitinol will take in its austenitic phase and can be changed by heat processing that will be described in further detail in section 3.2. The temperature range over which nitinol transforms from martensite to austinite has several critical temperatures that are important to take note of. The austinite start temperature is the temperature at which the martensite will start to convert to austinite, and the austinite finish is the temperature at which all the material will have converted to a body centered cubic rigid austinite structure. [14] Figure 5 below illustrates the shape memory ability of nitinol for our proposed application.

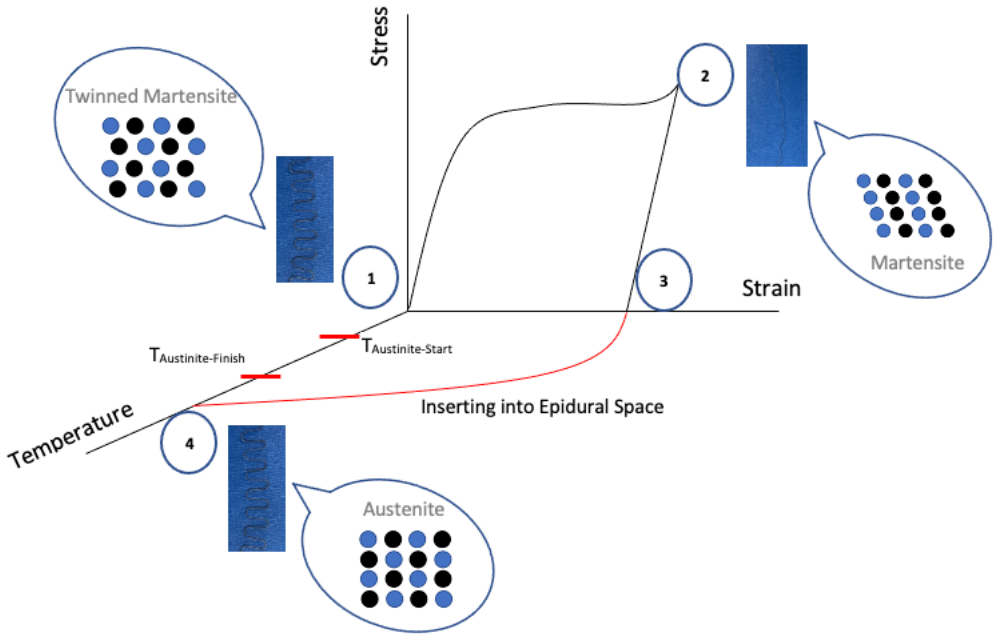


Figure 5. *This figure displays the transition of nitinol in our application from martensite to austinite. 1: Below the austinite start temperature ($T_{Ausitnite-Start}$) nitinol exists in a martensite phase, where the bonds are floppy, and "deformation" is easily introduced to the material. 2: In this floppy bond martensite state, the trained geometry will be "deformed" into a linear shape. 3: After the stress to change the shape of the martensitic nitinol is removed, the nitinol will remain in this temporary "deformed" linear shape. 4" once nitinol is heated above $T_{Ausitnite-Start}$ and $T_{Ausitnite-Finish}$ it will revert back to its original trained shape.*

Nitinol exists in an almost 50-50% equi-atomic composition. Deviation from this composition results in large deviations of the transition range. For example, a 1% chance in the amount of nickel or titanium can result in a 100℃ change in the transformation range. In general, a higher nickel concentration and impurities results in a lower transformation range, while more titanium increases the transformation range. [18] Thus, it is critical to have consistent quality of nitinol when manufacturing medical devices.

Nitinol also proves very useful in medical devices due to its magnetic resonance imaging compatibility. Nitinol is non ferromagnetic and has a smaller magnetic susceptibility than stainless steel. This means that it presents less artifacts under MRI and is more similar to titanium under an MRI. [15] For spinal cord stimulation, MRI compatibility is critical since the pathology of many of the candidates for SCS will often require additional screening and imaging of the spine.

2.2.2. Previous biological application with Nitinol

Many medical fields use the properties of nitinol to their advantage, from endovascular intervention to orthodontic use. Here we will pay particular focus to the use of nitinol in stent deployment, since our proposed device exhibits many parallels with the use of these self-expanding nitinol stents. Stents are structures that provide support for circulatory vessels. A stent must be able to handle large amounts of mechanical stress from daily motion and from the external environment. Nitinol is able to manage these external forces and also allows for efficient elastic deployment. Nitinol stents are loaded into catheter sheaths below their transition range. The catheter sheath is then navigated to the appropriate location with cold saline holding the temperature of the stent below its transition range. After the catheter sheath is removed the nitinol stents will expand 3 to 8 times the diameter of the catheter it was deployed in. [15] In a similar fashion, our device will deploy a nitinol stimulation lead within a catheter. When the lead has been properly placed the sheath will be removed allowing the lead to expand into a more optimal paddle like geometry. The

extensive use of nitinol in similar prior applications bodes well for potential regulatory feasibility of the idea proposed here for future trials.

3. Design and Development of Minimally Invasive Nitinol SCS Lead

In this section the proof of concept for the design proposed will be discussed in detail. The section will provide a description of how the geometry for the novel stimulation lead was determined, the method in which a new trained austinite shape was created, and the mechanical and thermal considerations that were taken in deploying the device. Finally, we will mention our plans to prove this concept through a cadaver test.

3.1. Geometry Design

Current cylindrical spinal cord stimulation leads have several conducting wires often made of silver that are wrapped in polyurethane or silicon insulation. Cylindrical leads typically have a total diameter of 1.3 mm. The conductive wires can be found at the periphery of the insulation in spaces called orbital lumens. There are as many orbital lumens as there are individually controlled contacts. These lumens have diameters ranging from .1 mm to .6 mm depending on the size of the conductive wires. At the center of the insulation is a central lumen with a diameter of .1 mm to .6 mm. [16] Within this central lumen a navigating wire, often made of a biocompatible polymer, is placed so that the stimulation lead can have enough stiffness to be navigated easily through the epidural space. In our design we hope to replace this interior component with nitinol. Due to the insulation between the conductive wires and the inner shaft and the higher resistivity of nitinol compared with silver, the addition of nitinol will not substantively interfere with the delivery of current through the conductive wires. For our design we chose to use a nitinol wire with a diameter of .4 mm, ordered from Kellogg Research Labs, for proof-of-concept purposes. However, as

discussed later in this thesis, a smaller diameter nitinol component may suffice in being able to bend the lead within the epidural space.

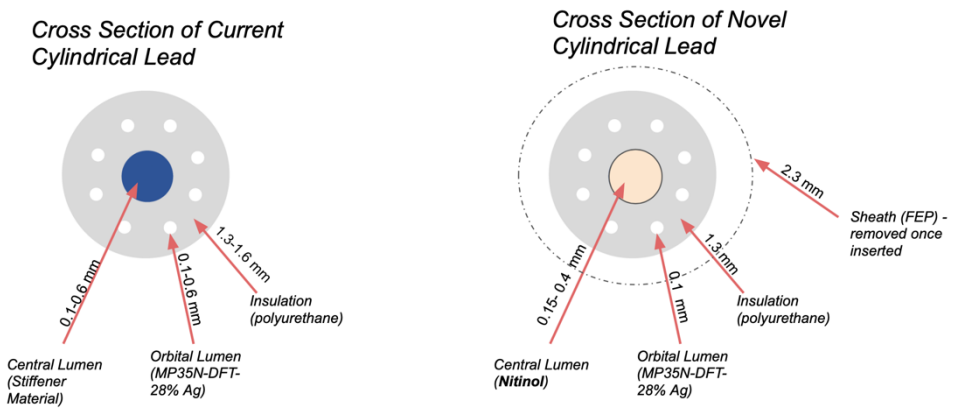


Figure 6. *This figure displays the cross section of current cylindrical leads and cross section if novel design. The grey exterior represents the insulation (often polyurethane), the white circles represent the orbital lumens that conductive wires go through, and the blue and gold circles represents the central lumen. For the design proposed in this thesis the central lumen will have nitinol alloy running through it rather than a polymer that provides stiffness to the lead.*

Once the dimensions of the nitinol were chosen, the geometry was optimized with two main considerations in mind: does the stimulation lead span enough lateral area in the epidural space to reduce lead migration and are there enough added electrode contacts available to allow for better theoretical stimulation. Since activation strength of the electric field falls by inverse cube root of the distance between the contacts and the nerves trying to be stimulated, our design aimed to fill the most electrodes within the given space, as to allow for the most customizability in the stimulation provided. [17] By designing a lead which has a larger fixed width, we were able to address both of these considerations, since more area would reduce lead migration and would also provide more area to introduce contacts. The first geometry we propose is a S-shaped zig zag shape, and the second geometry is a trident shape. To optimize, both of the geometries had a with width of between 10-13 mm, so that they would take up the entire width of the epidural space and mimic the width of current paddle leads.

For the zig sag geometry, to increase the number of contacts that fit within a given length, the radius of curvature of each of the bends had to be minimized. It is known that martensitic nitinol can only take up to 10%-11% strain before it is permanently deformed and will no longer exhibit shape memory characteristics. [15] Using the flexure formula for bending and a 10% strain rate the minimum radius was calculated as follows:

Equation 1.

$$Turning\ Radius\ =\ \rho =\ \frac{c}{\varepsilon} = \frac{Radius\ of\ Nitinol}{Max\ Strain} = \frac{.4\ mm}{.1} \approx 4\ mm$$

For the trident geometry, additional spokes offset from the center portion of the lead will allow for more contact coverage of the dura. Since we chose a .4 mm diameter wire for demonstration purposes this would allow three spokes to fit through the 13-gauge (1.8 mm inner diameter) or 14-gauge (1.6 mm inner diameter) Touhy needle commonly used for SCS procedures with enough space given for a sheath.

Therefore, assuming a 4 mm center to center distance between the 3 mm long electrode contacts, shown to provide optimal dorsal column fiber stimulation [17], the S-shaped zig zag and trident geometry we propose will be able to have 50% and 200% more electrode contacts when compared to a standard 16 electrode 64 mm long cylindrical stimulation lead.

It is important to note that this design as it is presented is not intended to prove that these geometries offers more advantageous stimulation in practice, rather we hope to propose the use of nitinol for spinal cord stimulation lead so that there can be more customizability in the way electrodes are configured. Further research would need to be conducted to determine which geometries could allow for stimulation that is optimal or comparable to the way stimulation is conducted now, since stimulation is not only dependent upon how much contact there is with the dura. Due to the versatility of nitinol the geometry of a nitinol lead could easily be modified to accommodate the most optimal stimulation electrode configuration.

3.2. Nitinol Material and Shape Programming

Once geometries were determined, that would provide the most contact area with the dura and reduce lead migration, a protype was developed that was configured in the correct trained austinite shape. As mentioned earlier nitinol exhibits super elastic characteristics when heated above its transition range from martensite to austinite. When nitinol is heated well above this range it goes into an annealing phase where the internal strain is diminishes and the atoms will reorient themselves into a body centered cubic structure creating a new trained austinite shape. Nitinol can be set into this new trained shape when it is heated at temperatures of 500-550 $°C$ while constrained in its desired shape within a fixture or mold. Longer heat treatment times of nitinol will result in more annealing of the material, forming a more exact shape, and will also result in lower tensile strength and spring-back of the material. If the nitinol is heat treated for shorter periods of time at lower temperatures the material will exhibit more strength and spring back. [18]

To shape set our geometries two specific molds were designed made from steel plates and steel screws. For the trident geometry two fasteners were placed on either end of the plate 64 mm meters apart and 2 screws were placed 10 mm apart 2.5 mm from the base fastener. For the S-shaped zig zag geometry, two steel fasteners were also placed 64 mm apart and size 8 screws were used for the mold, approximating the turn radius from the section above. 0.4 mm of space was left available between the drilled holes for the S-shaped zig zag geometry mold so that the nitinol wire could fit between screws and fixed appropriately. Nitinol was ordered from Kellogg Research Laboratory and was positioned in the mold appropriately. Once the screws were tightened the mold was placed in a furnace held at 500 $°C$, which was verified with an external thermocouple. After 60 minutes the mold was removed from the furnace and quickly quenched in water. The mold was subsequently dried, and the nitinol was removed from the mold in its new trained shape. By placing the mold at 500 $°C$ for 60 minutes the spring back of the nitinol was reduced, preventing possible damage to the epidural space once the sheath is removed, and a more exact shape was formed.

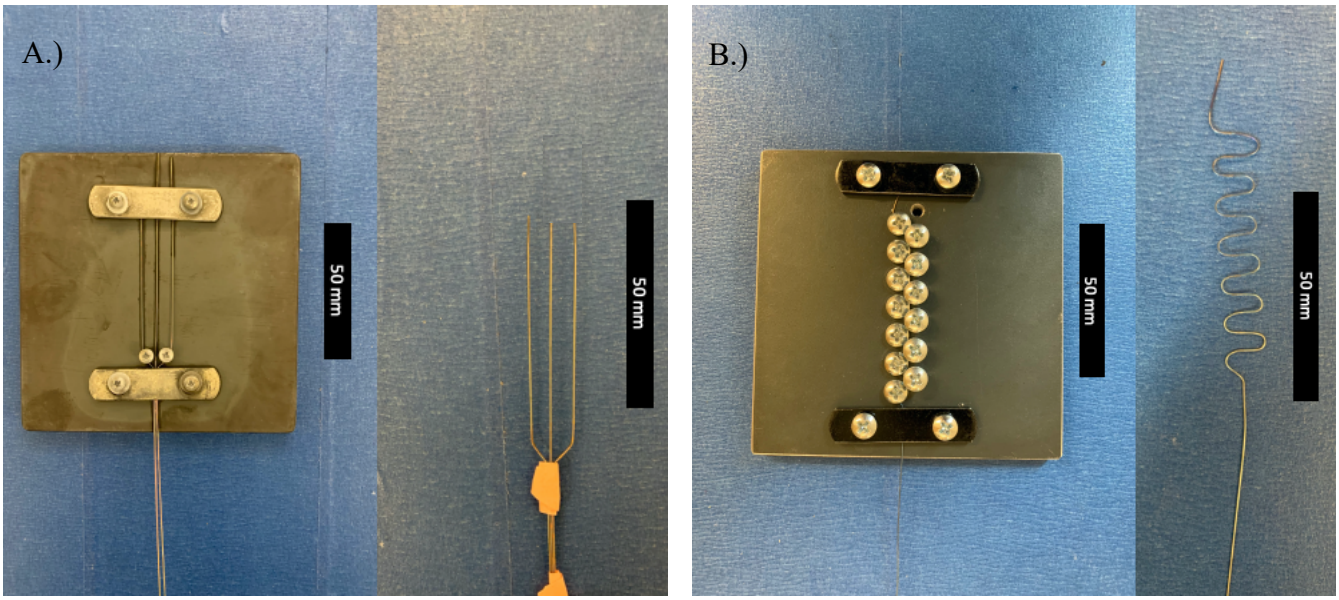


Figure 7. *This figure displays the molds that were used to train the austinite shape of the nitinol stimulation leads. Both of the molds shown were placed in an oven and heated at 500℃ for 60 minutes A.) The mold for the trident shape geometry, beside the nitinol after it had been removed from the mold. B.) The mold for the S-shaped zig zag geometry, beside the nitinol after removal*

Figure 8. *The furnace under the Prince Laboratory at Brown University. The molds displayed in figure 7 were heated in this furnace at 500℃ for 60 minutes and quenched in water in the steel tub displayed.*

3.3. Controlling Shape Recovery of Nitinol lead

As mentioned earlier the insertion of a cylindrical lead most often takes place at lumbar spine, caudal to the end of the spinal cord, and must be navigated several levels, to T9 or T8, where stimulation will take place for targeting lower limb pain. For the design proposed it is crucial that the lead can be placed at the appropriate location before the thermally induced expansion takes place. A paddle geometry, such as a lead with a width of 10 mm, is not able to be slide up the epidural space as a cylindrical lead would. Premature expansion of the nitinol-based lead would result in not being able to get the stimulator to the appropriate location. Several minutes must be allotted to allow the physician to place the stimulation lead appropriately within the epidural space. Since the nitinol will expand immediately upon reaching its austinite finish, a nitinol lead with an austinite finish at body temperature cannot simply be used alone without mechanical of thermal constraints. To control recovery mechanically, a sheath can be placed around the device and then removed once it is appropriately placed. To control recovery thermally, the austinite finish of the nitinol can be selected so that it is either body temperature or higher than body temperature. If the austinite finish is higher than the body temperature, then a heat pad can be used to control for when the shape recovery will occur. If the austinite finish of the nitinol is at body temperature then, insulation or a cooling mechanism must be provided to prevent recovery too early. Thermal and mechanical control can also be used in conjunction. In the next sections I will present methods that were used to try and test how best to control the shape recovery of the nitinol lead from a strait martensite to an austinite S-shaped zig zag or trident shape. Several proposed hypothetical solutions can be seen in the Figure 9 below.

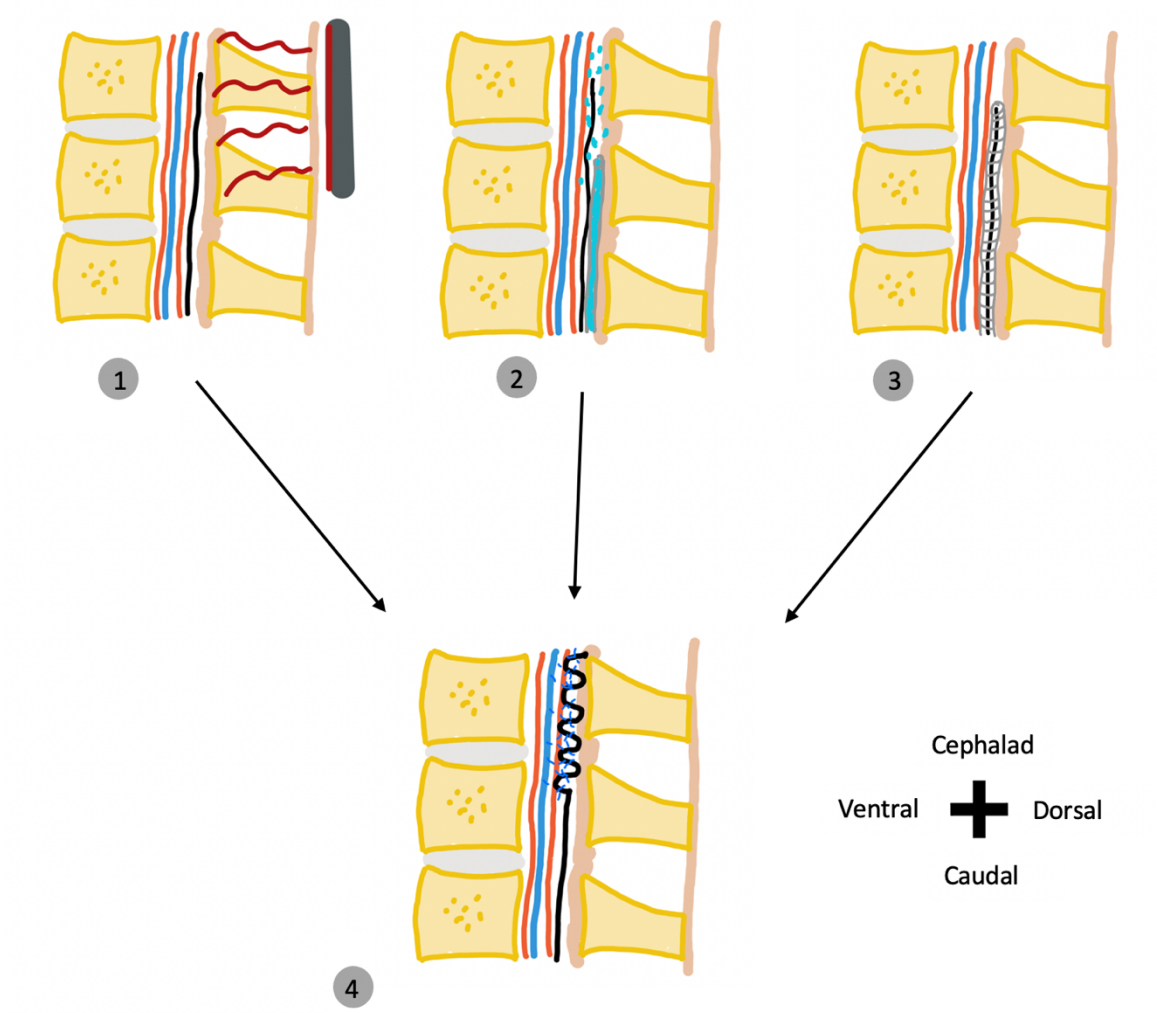


Figure 9. *This figure displays different methods in which to control premature shape recovery in the epidural space of the novel nitinol based spinal cord stimulator lead.* ***1****: By having a nitinol with an austinite finish well above body temperature, recovery would not occur until an external heat source is applied* ***2****: A stream of cold saline water could be used to thermally control a nitinol lead with an austinite finish at body temperature* ***3****: A sheath could be used that mechanically prevents recovery until appropriate placement in epidural space* ***4****: Final S-shaped zig zag geometry after mechanical or thermal method to postpone recovery has been used*

3.3.1 Thermal Restraint of Shape Recovery of Nitinol Lead

The first method that was tested in controlling the recovery of the nitinol stimulation lead was to try and thermally insulate the nitinol core of the lead. As mentioned earlier, in our design we plan on replacing a polymeric central lumen with a nitinol central lumen. SCS leads require insulation so that the conductive wires are not exposed. Thus, it would be an ideal solution if it

were possible to utilize the insulation already in place to control shape recovery. To test if an insulation can be used to stop recovery from starting for a period of at least five minutes theoretical calculations were conducted first, followed by an experimental test of recovery with varying thickness of insulation.

To determine how effective insulation would be in controlling how quickly the nitinol heats up the heat equation was used:

Equation 2.

$$\frac{\partial T}{\partial t} = \alpha \nabla^2 T$$

Where T is temperature, t is time and α is the thermal diffusivity, a material constant dependent on the thermal conductivity, specific heat capacity and density of a material. Plugging in different insulation materials (Teflon, TPUR, and Silicone) with varying thickness up to .55 mm it was found that recovery could not be delayed for more than a couple of seconds for our design. This can be seen in figure 10 and 11 below:

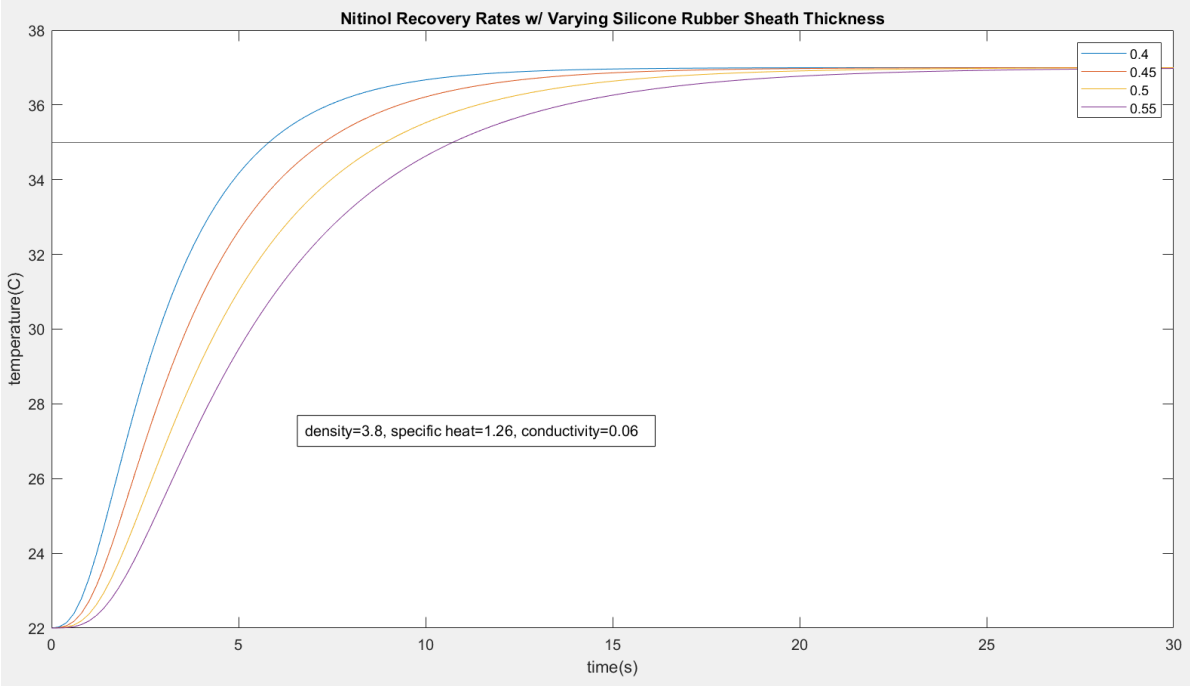


Figure 10. *This figure displays how long the center of a 0.4 mm nitinol wire would take to heat up to body temperature given varying thickness of an insulative silicone layer with varying thickness in mm.*

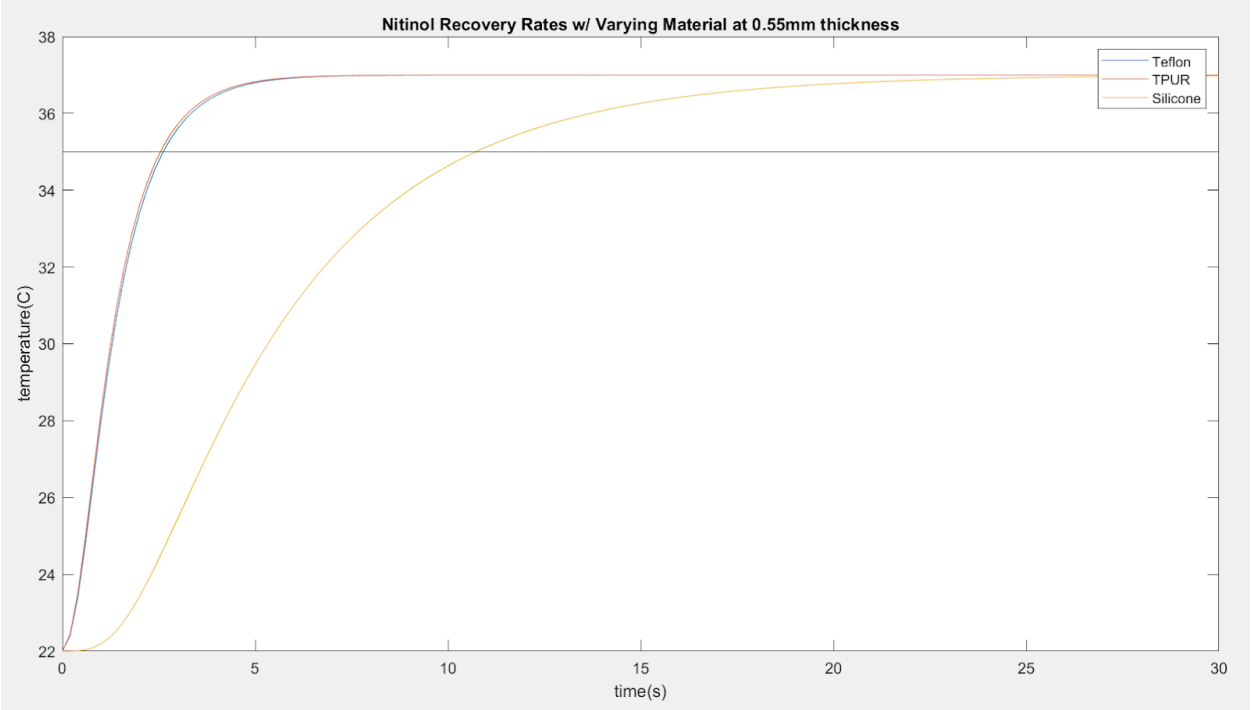
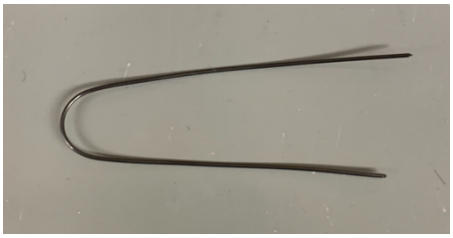


Figure 11. *This figure displays how long it would take for a 0.4 mm nitinol wire to heat up to body temperature with 0.55mm thick insulation of Teflon, TPUR and Silicone.*

From these theoretical calculations it was already clear that insulation would not be enough to prevent shape recovery of the lead in the time frame that was needed to conduct the procedure. However, this was also confirmed experimentally by putting a polymeric insulation around the nitinol, similar to the insulation that would be used in a real lead with conductive wire. The coating that was used for this experimental purpose was polyvinyl alcohol (PVA), which exhibits a low thermal diffusivity like other polymers. PVA was dissolved in 10 ml of dichloromethane for one day, after which the solution was used as dip coat for a cut out singular bend of the nitinol S-shaped zig zag geometry nitinol.

A.)



B.)

Figure 12. *This figure displays the 0.4 mm nitinol wire with a turn radius of 4 mm and PVA dissolving in dichloromethane. A.) 0.4 mm nitinol in bent trained austinite shape used to test shape recovery time B.) PVA pellets dissolving in dichloromethane used to dip coat.*

The data collected can be seen in Table 1 below:

Number of dips	Total Diameter of Lead (mm)	Shape recovery time (sec)
0	.400	< 1
1	.502	< 1
2	.622	3
3	.690	5

Table 1. *Displays the shape recovery time from linear to the bent trained austinite shape for different thicknesses of PVA from dip coating.*

As was predicted by the theoretical calculations the dip coating further proved that insulation alone will not be able to prevent recovery from occurring. The experiment also served additional value, since it provided a method to coat the nitinol and conductive wire if a more functional prototype were to be developed in the future.

Another option that could be used in thermally controlling the recovery could include using a nitinol with an austinite finish above body temperature, and then inducing shape recovery with an applied heat source. However, given that the transition range typically spans 10 $°C$ form austinite start to austinite finish, the nitinol selected would have to have an austinite finish over ten degrees above body temperature which may pose a danger to introduce to the patient. Alternatively, a cold

saline water injection or catheter could accompany the insertion of the nitinol lead with an austinite finish at body temperature. Cooler temperatures would certainly be much safer to the body as well. The use of cool saline has also been proven in prior nitinol deployment of stents.

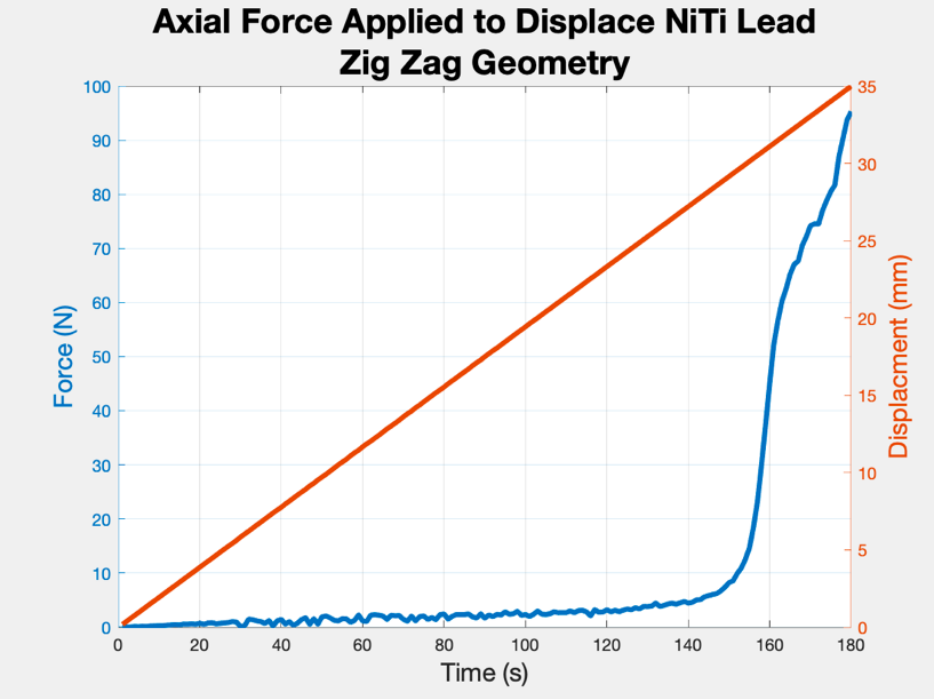
3.3.2 Mechanical Restraint of Shape Recovery of Nitinol Lead

Alternatively, a mechanical solution could be used to prevent the nitinol lead from deforming prematurely once in the epidural space. In current endovascular nitinol applications, a catheter is often used that mechanically prevents premature expansion of the austinite to its trained shape. Similarly, premature expansion of the lead could be prevented by a catheter that would be removed once the stimulation lead is appropriately placed. A catheter that serves this purpose would have to meet four criteria. First, the catheter would have to be stiff enough to be able to hold the lead straight enough so that it can be guided up the epidural space without kinking. Second, the catheter must be flexible enough that it can be inserted through a Touhy needle at a 30-degree angle at least, and ideally be able to be inserted at a 45-degree angle. Third, the catheter sheath must have a small enough kinetic and static friction coefficient that the stimulation lead within the catheter can be removed from the catheter sheath once the lead has been appropriately positions. Finally, the catheter must be able to have a large enough inner diameter to hold a stimulation lead and a small enough outer diameter to fit through a 1.8 mm inner diameter 13-gauge needle.

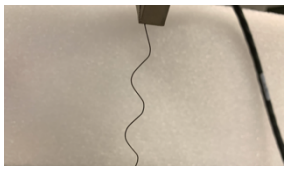
To test these criteria of mechanically holding the geometries proposed within a lead, the first step was to determine how much force the geometries proposed would exert as they recovered to their trained austinite shape. To determine the amount of force that would be required to hold fixed the nitinol, with an austinite finish at body temperature, and also determine how much force the nitinol would exert as it expands, a tension test was conducted using the MTS Bionix® Servohydraulic Test System. The geometries proposed where loaded into the machine, with 150 newton load cell attached, and gripped by both ends while in their original trained austinite shape and were then stretched at a constant rate under applied heat. To heat the nitinol above its

transition range so that it was in its austinite form a heat gun was used as the metal was pulled in tension. An infrared thermometer was used to show that the nitinol was heated above body temperature all the way to 45 $°C$ while being heated. We assume here that the force that is required to pull the nitinol to a certain level of deformation would be the force that the nitinol would exert outwards when transitioning in the body. 3 nitinol S-shaped zig zag geometry samples were created, using the methods described in section 3.2. One bent spoke of the trident geometry made out of .4 mm nitinol was tested and one shorter zig zag geometry, with approximately 4 bends, was tested, made out of .4 mm diameter nitinol. The results of this test can be shown in the figure below.

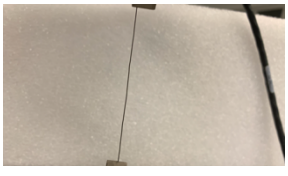
A.)



T = 0 s

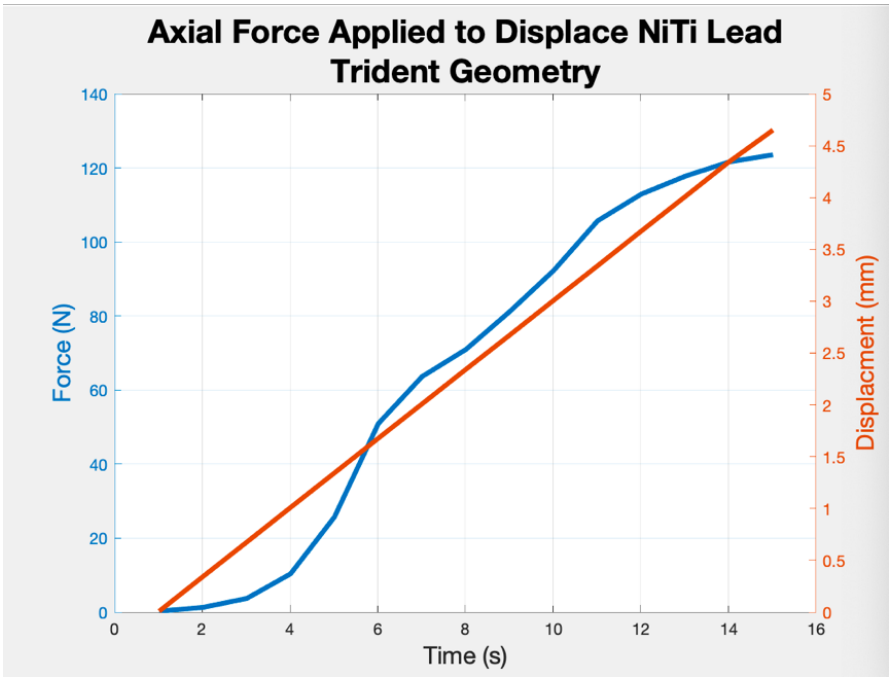


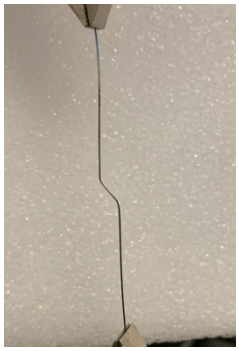
T = 90 s



T = 180 s

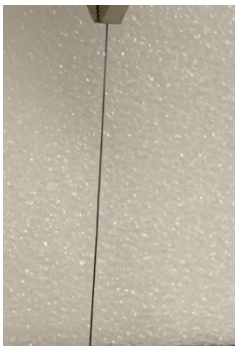
B.)





T = 0 s

T = 8 s



T = 16 s

Figure 13. This figure displays the amount force that is required to stretch our geometry into a linear shape while it is in austinite form at a temperature above 35 ℃. Below each figure is the image of the geometry loaded into the MTS machine. **A.)** The S-shaped zig zag geometry is loaded stretched out over a period of 180 seconds, from its trained S-shaped zig zag shape to a linear shape. **B.)** One spoke of the rident geometry is loaded and stretched out over a period of 16 second, from a trained bent shape to a linear shape. Heat is applied to both shapes in the MTS machine by a heat gun.

As can be seen from the figures above as the geometry was pulled from its trained austinite shape, the force experienced by the load cell increased, as the material wanted to spring back to its original shape. For the bend in the trident geometry this force increased relatively linearly. For the S-shaped zig zag geometry however, there was a sharp increase in the amount of force that was needed to undergo the final stages of deformation from bent to linear. From this data we can find

how much force must be exerted to hold our geometries in a certain conformation at body temperature. For the trident geometry, where there are two spokes with bends in them, we can simply multiply the force from the graph above by two. For the zig zag geometry, the force exerted outward by each bend can be determined by dividing the force shown in the figure above by 4. We divide by 4 since there were 4 bends that were present in the sample for the trail, this number can then be multiplyed by however many bends we plan to introduce in the zig zag geometry.

Once the force that nitinol will exert at different parts of recovery had been tested using the MTS machine several materials including FEP, PTFE and TPU, with varying inner diameters were preliminarily tested as catheter sheath materials around the .4 mm nitinol. It was found that as the catheter hugged the nitinol more tightly, with an inner diameter approaching .4 mm, kinks would be introduced within the catheter sheath, and shape recovery would partially take place within the sheath. However, as more space was given for the nitinol within the catheter sheath, the less kinks could be seen in the sheath. This is expected with what we saw from the force profiles above, since as the nitinol is forced to be more linear in the S-shaped zig zag geometry, there will be an almost exponential increase in the amount of force that the nitinol will exert against the walls.

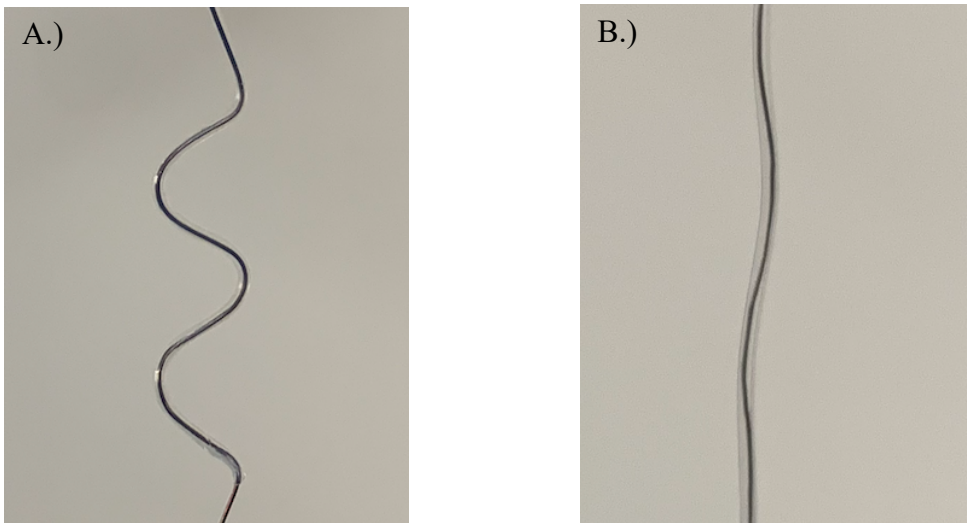


Figure 14. This figure displays nitinol austinite in a trained S-shaped zig zag geometry at 35 ℃ inside **A.)** a PTFE catheter sheath with an inner diameter of .508 mm and **B.)** FEP with an inner diameter of .81mm and. Notice how the smaller diameter tube is more kinked due to the higher force exerted by the nitinol in trying to keep it exactly strait.

To test the frictional force that would have to be overcome when pulling the catheter sheath off the lead to allow for shape recovery, another test was conducted using the MTS Bionix® Servohydraulic Test System. In this test 0.4 mm diameter nitinol in a zig zag geometry was slid into three catheter sheaths in a cold-water bath, so that the material was in its martensitic phase. The zig zag geometry was made to have 4 turns, just as it was made when conducting the tension tests. One of the sheaths was made out of 304 stainless steel metal with an inner diameter of 1.55 mm, another sheath was made out of fluorinated ethylene propylene (FEP) with an inner diameter of .81 mm, and the last sheath was made out of polytetrafluorethylene (PTFE) with an inner diameter of .508 mm. In the test one end of the nitinol geometry was exposed outside of the sheath and grasped in the MTS machine, while the other end had free hanging catheter sheath which was grasped in the top part of the machine. The catheter was moved upward at a constant displacement rate while a heat gun was pointed at the set up and the force on the 150 N load cell was measured.

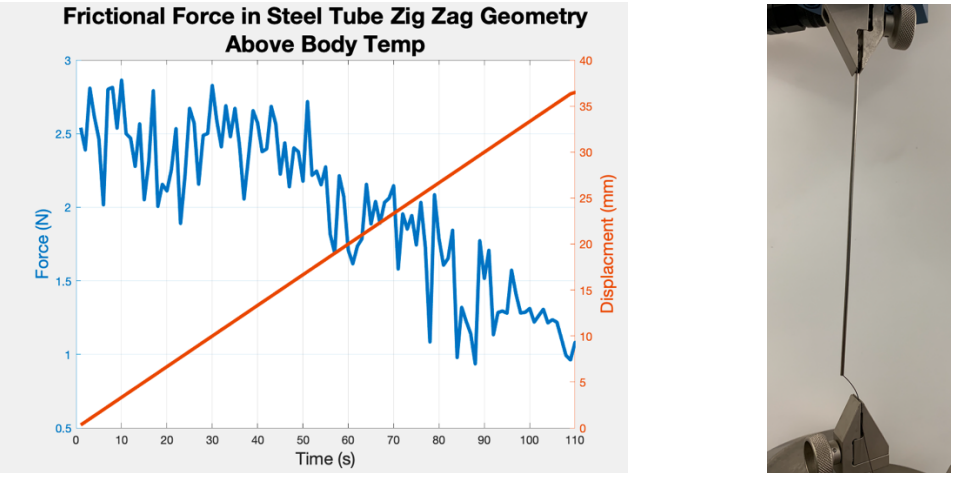


Figure 15. This figure displays the friction test that was conducted on the MTS machine for 0.4 mm nitinol austinite in a trained S-shaped zig zag geometry under 35 ℃ heat within a steel sheath. The maximum force recorded can be assumed to approximate how much force would be required to remove the sheath from the nitinol when in the body. This test was also conducted for a FEP and PTFE sheath.

The maximum force was detected for these tests by analyzing the data as shown in Figure 15 for each test run. From this we were given a general sense of how much force would be required to pull the nitinol out of each of the respective sheaths. 1.8 N for the PTFE, 2 N for the FEP, and 2.8 N for the steel were the maximum forces we obtained, by dividing these numbers by 4, we can find the friction generated by each bend in contact with the sheath. However, there are many confounding factors that interfere with providing appropriate information on how much frictional force is actually exerted within the sheath in this test. For starters, the force applied in lifting the catheter off the nitinol did not always result in sliding, at times the nitinol within the sheath would be straightened as the sheath was lifted. Due to the lack of sliding in some of the tests, especially the PTFE test, where the sheath was kinked, there were different lengths of sheath removed from the nitinol. In addition, in this procedure there was no way of making sure that heat was evenly distributed around the nitinol and sheath. As a result, this test only serves as an approximation for the amount of force that would be required to move the sheath.

In addition, the stainless steel and the PTFE were tested for demonstration purposes and would not be practical as a sheath for this application since the steel would not be able to be inserted at the angle needed between the needle and the epidural space, and the PTFE had too small of an inner diameter that would cause kinks within the sheath. This test also has limitations since in reality the end of the lead would not be fixed, as a physician tries to slide off the catheter with their hand.

To allow for easier removal of the catheter sheath, Surgilube Lubricating Jelly was used to reduce the friction. This test will be conducted once more for the 0.4 mm nitinol in the zig zag geometry in the FEP catheter sheath, with and without Surgilube. The results of this test are not shown in this thesis as of yet, since the test with the lubricated sheath is still on going.

To reduce the friction further, in the future this frictional test should be repeated with the nitinol having been dip coated in PVA since in reality the stimulation lead will be coated with an

insulative layer. This test would better approximate how much force we should expect in trying to remove the catheter sheath in practice.

3.6. In Vitro Testing

In the past two sections, thermal and mechanical mechanism to control shape recovery have been proposed. The most promising way to control the nitinol thermally would be to use saline solution while the nitinol is being deployed. Mechanically constraining the nitinol before it reaches its appropriate location catheter also seemed promising as a delivery mechanism. To test how delivery of this novel lead design would take place within the body using the different ideas proposed, a hot water bath approximating the epidural space was assembled. A steel tray was filled with water and heated to 36 ℃. An Omega thermocouple recorded the temperature of the water bath and a hot plate was used to heat the tray. A clear polycarbonate tubing piece was cut to roughly mimic the epidural space and taped to the bottom of the tray with Duck-Tape. A 13-gauge needle was provided by Dr. Telfeian, and a 2.5 mm hole at an angle of 45 degrees was drilled into the polycarbonate tubing. The cut polycarbonate tube has a width 30mm, so polystyrene foam was taped to the sides of the tubing so that the tube would have width of 13 mm. For the initial tests foam was not used so that lateral movement of the nitinol stimulation lead after it is inserted could be easily observed. An image of the setup is shown below in Figure 16 without the inner polystyrene foam along with table 2, which displays the tests that have already been and plan on being conducted.

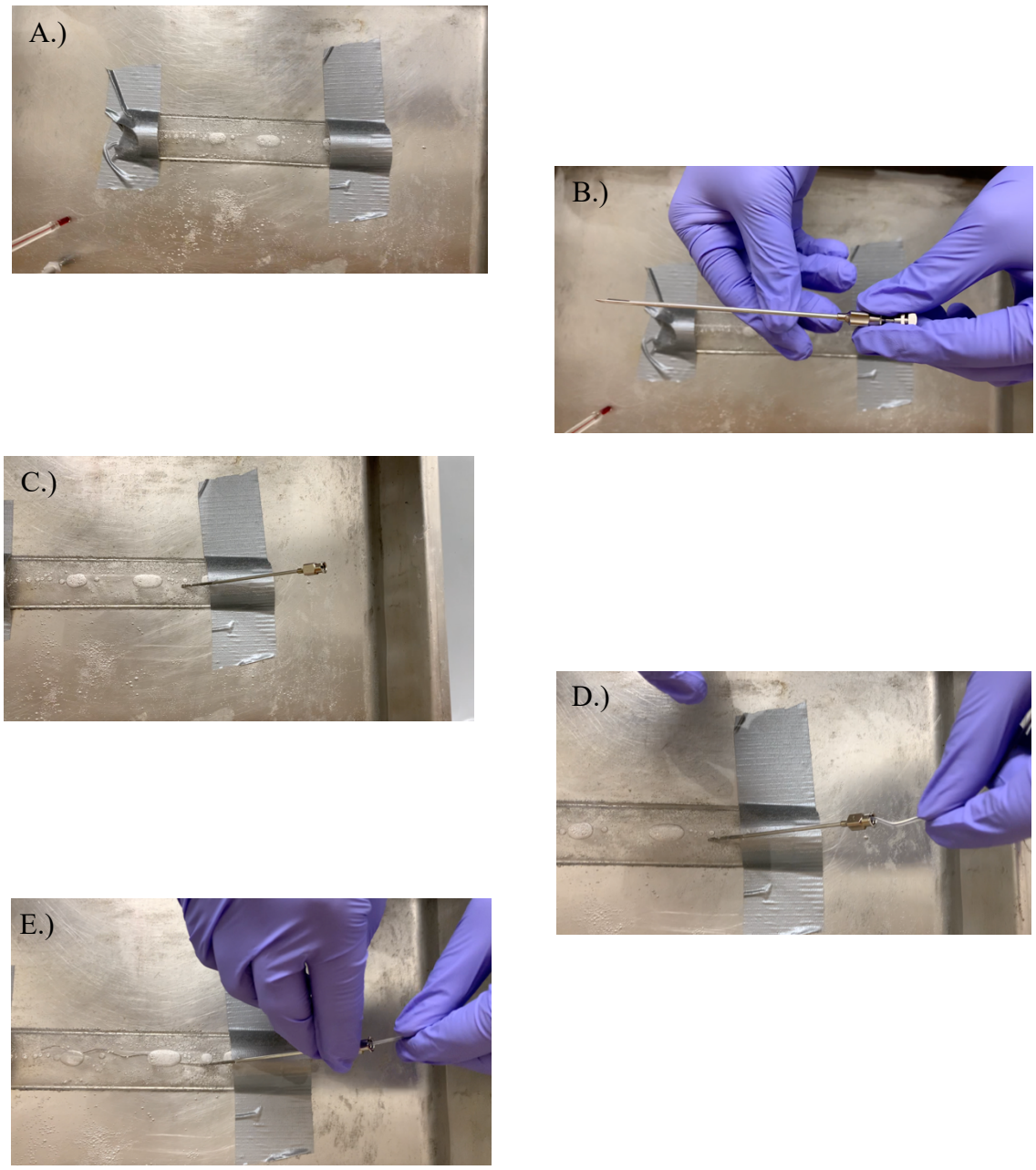


Figure 16. This figure displays the in vitro set up used for .4 mm nitinol, with a trained austinite zig zag geometry, deployed in a FEP sheath. **A.)** Polycarbonate tubing with Duck-Tape. **B.)** 13-gauge Touhy needle. **C.)** Needle inserted at 45-degree angle into tubing. **D.)** Nitinol in FEP sheath inserted through needle. **E.)** Sheath guided through tube and catheter sheath removed.

Geometry	Deployment Method	Nitinol Diameter	Austinite finish	45 degree turn between needle and in vitro epidural space	Shape Recovery
Zig Zag	No mechanical or thermal mechanism used	0.4 mm	$T_{AF} = 36$ °C	Difficulty in inserting lead into epidural space	Recovery began in needle making it difficult to slide device into epidural space
Zig Zag	Nitinol kept in freezer	0.4 mm	$T_{AF} = 36$ °C	No difficulties	Immediate upon entry into epidural space
Zig Zag	No mechanical or thermal mechanism used	0.4 mm	$T_{AF} = 45$ °C	No difficulties	Recovery begins upon entry
Trident	No mechanical or thermal mechanism used	0.4 mm	$T_{AF} = 36$ °C	No difficulties	Immediate upon entry into epidural space
Zig Zag	PTFE sheath used .508 mm inner diameter	0.4 mm	$T_{AF} = 36$ °C	No difficulties	Kinks visible as soon as device enters epidural space
Zig Zag	FEP sheath used .81 mm inner diameter	0.4 mm	$T_{AF} = 36$ °C	No difficulties	Linear within sheath, unable to remove sheath with hand to allow for recovery
Zig Zag	FEP sheath used .81 mm inner diameter, with constant cold-water saline	0.4 mm	$T_{AF} = 36$ °C	TBD	TBD
Zig Zag	FEP sheath used .81 mm inner diameter, lubricated	0.4 mm	$T_{AF} = 36$ °C	No difficulties	Was able to be removed from the sheath and expanded
Zig Zag	FEP sheath used .81 mm inner diameter, lubricated, nitinol dip coated in PVA	0.4 mm	$T_{AF} = 36$ °C	TBD	TBD
Trident	Larger diameter sheath used	0.4 mm	$T_{AF} = 36$ °C	TBD	TBD

Table 2. This table displays the in vitro tests that have been attempted and tests that still remain to be attempted.

3.7. Cadaver Test

Now that we have been able to delay recovery for long enough for insertion to take place appropriately, using a catheter sheath with lubricant, a cadaver test will be conducted for proof of concept of our deployment method. A cadaver facility has been identified at the Rhode Island Orthopedic Foundation (RIOF) and we are prepared to run our test. Dr. Albert Telfeian M.D Ph.D, will perform the procedure with a 13 gauge Touhy needle on a large male cadaver. X ray images will be taken during the procedure just as they would in a typical SCS insertion. The X-ray will be provided by the RIOF.

4. Discussion and Conclusion

The propose of this thesis was to prove that the use of nitinol in spinal cord stimulation is advantageous by proposing a design, which utilizes the unique properties of the shape memory alloy nitinol, that can be inserted in a minimally invasive fashion, can cover optimal area of the dura with electrodes, can reduce lead migration, and be more accessible simultaneously. So far, we have made several advancements towards this goal. We have been able to identify appropriate geometries that would be able to cover more area of the dura and allow for more customizability of electrode placement, increasing the number of electrodes that can fit in a given area up to 200% compared to current cylindrical leads. We have developed a methodology to create the geometries we have proposed, which allow for further testing, and we have proposed and tested several methods that can allow for effective insertion of this spinal cord stimulator. We will confirm that our insertion method is possible through the cadaver test.

While these are great first steps, there are still numerous issues and questions which still need addressing and require further investigation to prove that the use of the shape memory alloy nitinol within a spinal cord stimulation lead would be advantageous. In this section I will discuss

future work that must be conducted in optimizing the geometry of the lead, removal of the lead once it has been inserted, potential risk of injury to the patient, shorting of the conductive wires used, and other future directions to consider.

In this thesis for proof-of-concept purposes a nitinol diameter of .4 mm was used to place into the central lumen of current cylindrical design of spinal cord stimulators in place of a polymeric stiffener. However, a smaller nitinol wire diameter could potentially be used that would allow for enough spring back force of the material for similar shape recovery ability, but less friction between the lead and the sheath allowing for easier removal of the catheter sheath. A tension test was conducted on .15 mm nitinol, as was done on .4 mm nitinol in section 3.3.2 on the MTS machine. The results can be seen in the Figure 17 below.

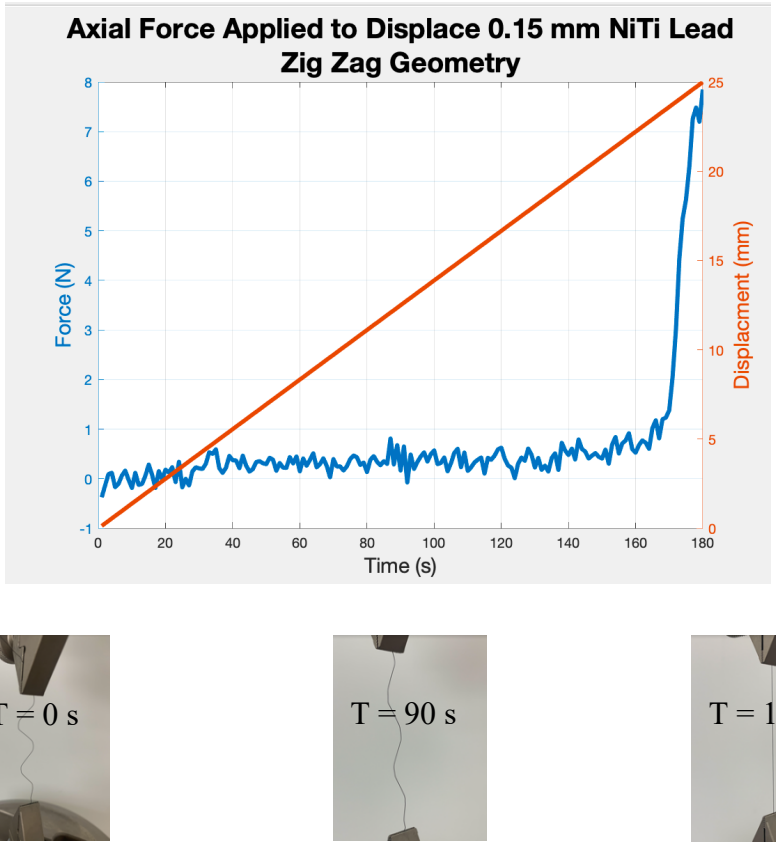


Figure 17. This figure displays the amount force that is required to stretch the 0.15 nitinol zig zag geometry into a linear shape while it is in austinite form at a temperature above 35 °C over a period of 180 seconds. Below the figure is the image of the geometry loaded into the MTS machine.

As can be seen when comparing the data from Figure 17 to Figure 13 in section 3.3.2 there is over 9 times less force necessary to stretch the austinite strait from its trained zig zag shape. Around 2 newtons of force per bend in the S-shaped zig zag shape compared to approximately 23 newtons of force per bend in the zig zag shape for the .4 mm diameter wire would certainly reduce the amount of friction that would have to be overcome when removing a catheter sheath. In addition, it would also reduce the chance of injury in the epidural space and prevent the nitinol from over expanding. Further testing would need to be conducted to confirm that smaller diameter nitinol would be able to exert enough force to move all the insulation and conductive wires into its final shape.

The trident and zig zag geometries would also have to be further investigated in the future. While the geometries proposed in this thesis are able to provide more space for contacts to fit within the epidural space, this does not necessarily mean that stimulation and pain coverage will be improved. Optimal stimulation is based on several factors including electrode coverage, electrode placement, and waveform used. [3] Due to the customizability of nitinol, luckily it would not be a difficult challenge to optimize geometry as necessary.

The removal of the nitinol based lead could also serve as a potential challenge that would need to be addressed in the future. Merely pulling the lead out with force may cause damage to the spinal cord or CSF leakage. Further investigation would need to be conducted on the safety of removing such a device if it were to be placed in the epidural space.

Potential damage may also be caused by the shape recovery of nitinol if it exerts to much force against the vertebral canal the dura, leading to potential CSF leak and spinal cord damage. The amount of strain deformation that the dura can take before it is damaged ranges from 14 to 8 percent. [19] Future work would need to ensure that this range is not exceeded. Potential damage could also be reduced by using a lower spring back strength smaller diameter nitinol wire as mentioned earlier.

The shape recovery of the nitinol may also cause shorting of the conductive wires that provide stimulation. An appropriate coiling of conductors to prevent shorting would have to be determined in the future for this design, just as is done in deep brain stimulation electrodes. A figure of coiled copper wire conductors around the nitinol body of our design can be seen in Figure 18.

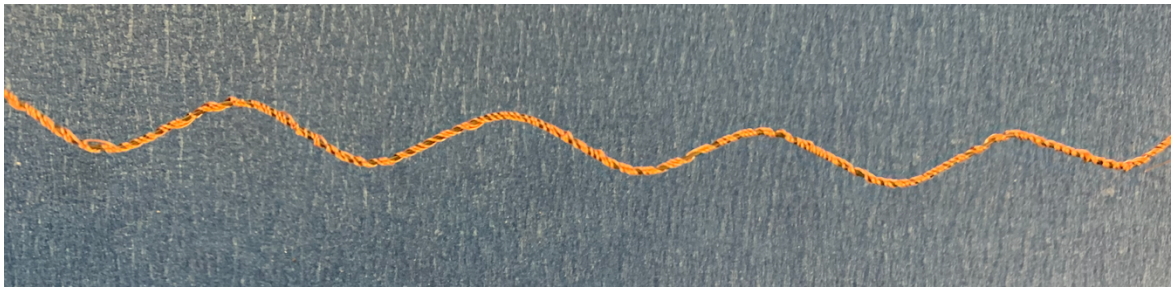


Figure 18. This figure displays 0.2 mm conductive copper wire coiled around .4 mm nitinol martensite below body temperature.

In conclusion, the use of the shape memory alloy nitinol seems to be promising in the design of future spinal cord stimulation leads that will potentially be able to be inserted in a minimally invasive fashion, cover optimal area of the dura with electrodes, reduce lead migration, and be more accessible.

6. Citations

[1] Dones, Ivano, and Vincenzo Levi. “Spinal Cord Stimulation for Neuropathic Pain: Current Trends and Future Applications.” *Brain Sciences*, vol. 8, no. 8, 2018, p. 138., doi:10.3390/brainsci8080138.

[2] Babu, Ranjith, et al. “Outcomes of Percutaneous and Paddle Lead Implantation for Spinal Cord Stimulation: A Comparative Analysis of Complications, Reoperation Rates, and Health-Care Costs.” *Neuromodulation: Technology at the Neural Interface*, vol. 16, no. 5, 2013, pp. 418–427., doi:10.1111/ner.12065.

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