Experimental Study

Shape Memory Nitinol Based Minimally Invasive Spinal Cord Stimulation Device Concept for Improved Pain Management

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Background: Spinal cord stimulation (SCS) is a common treatment for neuropathic pain. There are 2 main categories of SCS leads: paddle leads and cylindrical leads. Paddle leads have reduced long-term complications and provide better coverage of target dermatomes when compared to cylindrical leads. However, insertion of a paddle lead requires invasive surgery that comes with significantly higher costs and more short-term complications, such as postoperative pain and infection. In contrast, cylindrical leads can be inserted minimally invasively using percutaneous techniques but provide less coverage of targeted dermatomes and have a higher tendency to migrate from intended neuronal targets.

Objectives: Our objective is to develop a novel improved cylindrical spinal cord stimulation device that can convert into an optimal geometry once exposed to the body's environment after minimally invasive surgery. Such a device would be able to reduce long-term complications, lead migration, and better cover targeted dermatomes.

Study Design: Biomaterial selection, medical intervention device design with an in-vitro lab-scale test, and cadaveric experimental study.

Methods: A shape memory alloy nitinol-based cylindrical lead was designed, and its nitinol core material was processed and geometrically programmed for percutaneous insertion into the epidural space and morphing into an optimal geometry once exposed to the body's environment. Deployment of the nitinol component of the design was tested in the lab and human cadaveric models of the epidural space.

Results: Deployment of the nitinol component of the proposed cylindrical lead was successfully demonstrated in both a lab model of the epidural space and in the epidural space of a human cadaver in a minimally invasive fashion, indicating that a similar component could be used clinically in a full SCS electrode manufactured in a custom final geometry.

Limitations: The focus of this study was to test the deployment of a novel minimally invasive lead that provides optimal coverage of intended dermatomes using in-vitro methods. Our study does not include in vivo trials. We do not test the electrical components of the design proposed since our design does not make changes to the electrical components of current commercially used cylindrical leads.

Conclusion: The unique shape memory property of nitinol shows promise in allowing cylindrical spinal cord stimulation leads to expand into a more optimal geometry within the epidural space. By having a body temperature-dependent geometry change, nitinol-based cylindrical leads could reduce lead migration, increase dermatomal coverage, and increase electrode density while maintaining the advantages of minimally invasive insertion.

Key words: Spinal cord stimulation, pain management, shape memory alloy, nitinol, minimally invasive surgery, percutaneous insertion

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An estimated 1 in every 10 adults over the age of 30 suffer from some form of chronic neuropathic pain, including chronic back pain, failed back surgery syndrome, complex regional pain syndrome, and postherpetic neuralgia (1,2). Spinal cord stimulation (SCS) is a common treatment of neuropathic pain for patients (3) and is shown to reduce costs and improve outcomes compared to conventional pain treatments (4-6). In addition, SCS is shown to reduce the use of opioids for the management of pain (7,8). SCS is delivered through an electrode lead that is inserted into the epidural space attached to a pulse generator surgically implanted subcutaneously. The SCS electrode lead modulates pain in the epidural space by delivering electrical stimulation over the spinal cord dorsal columns to target specific dermatomes (9,10).

Current Issues With Spinal Cord Stimulation Devices

SCS electrode leads can be divided into 2 main categories: paddle leads that have a width of ~10 mm and are placed through an open laminectomy or hemilaminectomy procedure under general anesthesia and cylindrical leads that have a width of ~1.3 mm that are typically placed percutaneously through a needle (3) using local anesthesia. Each lead type has characteristics that pose advantages over the other. Paddle leads are shown to have significantly lower long-term reoperation rates and significantly better coverage of targeted dermatomes when compared to cylindrical leads (11-14). Paddle leads provide this better coverage due to their ability to insulate and conform to the dorsal spinal cord surface, more densely packed electrode contacts, and unidirectionality in electrical impulse delivery. In addition, the increased number of electrodes along the width of the spinal cord in a paddle lead allows for a more robust mediolateral resolution (13).

Cylindrical leads, due to their small diameter, may not have the ability to closely target as many neuronal components but come with the benefit of having an insertion procedure that is minimally invasive and does not require a spine surgeon or the need for general anesthesia (15). Paddle lead insertion requires a partial laminectomy (16), is an inpatient procedure, and requires an incision of ~80 mm. Conversely, cylindrical lead insertion is an outpatient procedure conducted under local anesthesia through a small needle and only requires an incision of ~ 2.5 mm (17). This small incision results in significantly lower short-term complications (11) and operation costs for cylindrical leads (15).

Overall, there are more cylindrical leads inserted a year than paddle leads (18). Therefore, from a patient perspective, a potentially less mechanistically effective treatment option is more commonly being chosen due to the increased complexity of the insertion, lower accessibility, and higher cost for a paddle lead. Therefore, there exists a need to combine the advantages of minimally invasive, lower cost, cylindrical lead insertion with better spinal cord coverage and reduced lead migration of paddle leads.

Several attempts have been made in the past to address the need for a device that can simultaneously possess the advantages of both a cylindrical and paddle stimulator. These attempts include changes in the type of waveform used (12,19-22), insertion techniques (23), and geometry of the stimulation lead (24). 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 (12). Thin line paddle leads that have a 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 (25). However, all of these solutions have still fallen short of providing a stimulator that is able to best exhibit the advantages of both paddle and cylindrical leads (12).

Proposed Solution

To address the significant drawbacks within current SCS lead types, we develop, design, and test a solution that utilizes the shape memory effects of the biocompatible nickel-titanium alloy (nitinol) (26-28). Shape memory materials have been studied and discussed for biomedical applications extensively in the past (29,30). In our proposed solution, nitinol will replace a polymeric stiffener commonly found in the central lumen of cylindrical leads (31), as is shown in Fig. 1. The method of delivering electrical stimulation will remain unchanged. Nitinol's material properties will allow the cylindrical lead to stay in a linear shape at room temperature (~22°), allowing for standard minimally invasive cylindrical lead insertion. Once introduced to the higher temperature of the body (~37°), the nitinol-based cylindrical lead will be able to undergo a temperature-dependent transformation into a customizable optimal geometry (32). An introducer sheath will be used to prevent premature recovery of the shape memory nitinol into this optimal geometry,

allowing sufficient time for the lead to be positioned appropriately. The insertion technique that we propose and test is illustrated in Fig. 2.

The shape memory ability of nitinol facilitates this insertion process and results from 2 temperature-dependent crystalline structures. At lower temperatures, nitinol can be found in a martensite phase. Martensitic nitinol has an elastic modulus of ~40 GPa and has a twinned monoclinic structure when it is stress-free. When this martensite is deformed, the twinned structure easily transforms into a de-twinned structure without any dislocation movement or the development of slip bands. At warmer temperatures, nitinol is in an austenitic phase with an elastic modulus of ~80 GPa (33). The geometry that the nitinol takes in its austenitic phase is known as the nitinol's "trained shape"

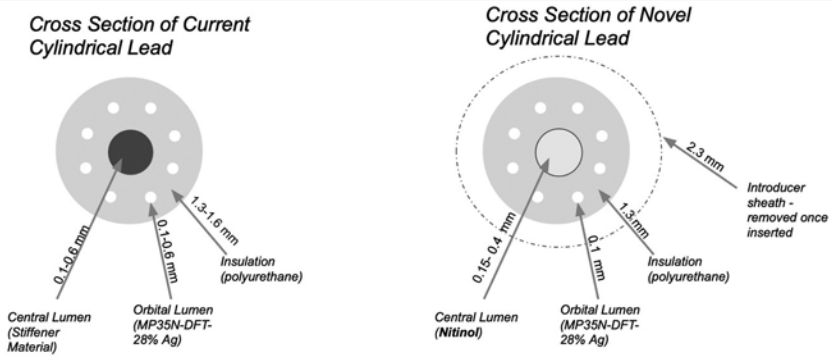

Fig. 1. *Drawings of cross-sections of current market cylindrical leads (left) and proposed shape memory nitinol cylindrical leads (right).*

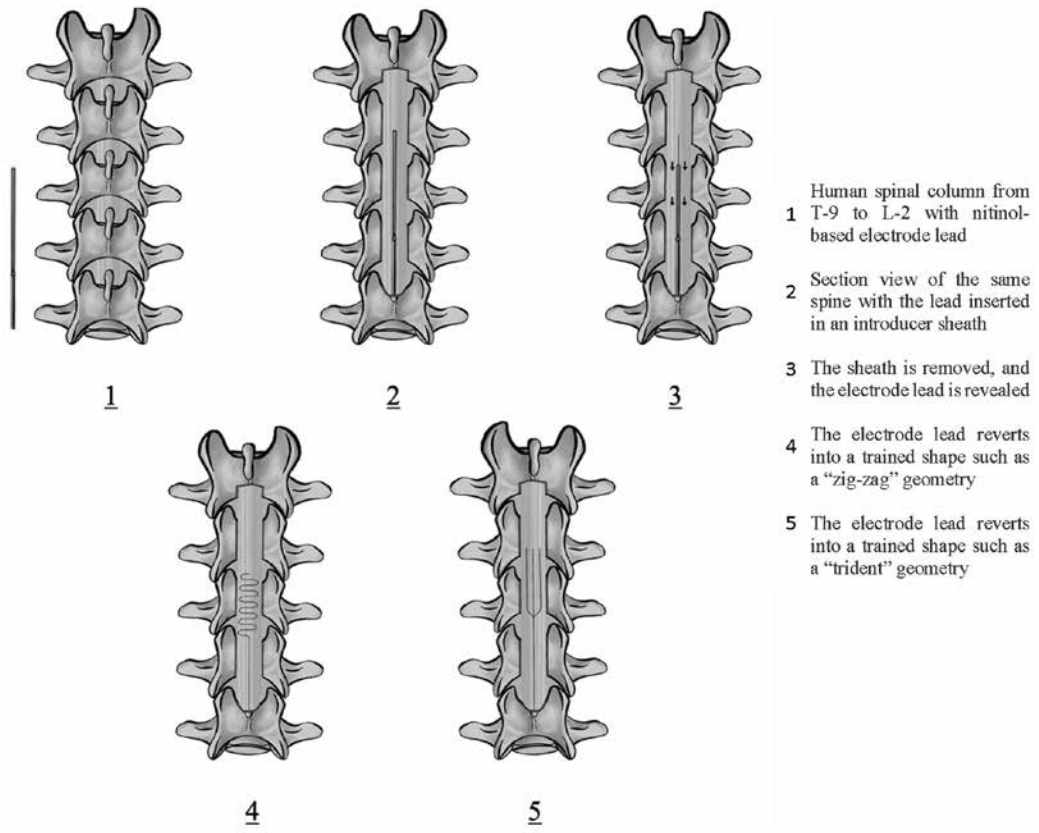

Fig. 2. *Steps in the insertion and deployment of the shape memory alloy-based lead system.*

or "programmed shape." The trained austenite shape can be set by heat processing. Austenitic nitinol has a body-centered cubic structure and is very stiff. In fact, austenitic nitinol is termed super elastic and will spring back into its trained shape if it is put under strain.

When the material is cooled into its martensitic phase from its austenitic phase, nitinol can be easily "deformed" and hold the position it was distorted into while still maintaining its original chemical bonds up to 10% strain. When the nitinol is heated back up into its austenitic phase, it will revert to its original trained shape that the material remembers by its chemical bonds. This effect is known as the shape memory effect. The temperature range over which nitinol transforms from martensite to austenite can be customized by material composition (34). For the SCS concept designed and tested here, the nitinol will have a trained austenite shape that optimally covers dermatomes in the epidural space. It will be in its martensitic phase at room temperature, where it can be maintained in a straight configuration, and an austenite phase at body temperature, as is shown in Fig. 3.

Methods

To test the use of shape memory nitinol as a component in a cylindrical spinal cord stimulation lead, 0.4 mm diameter nitinol was identified and ordered from Kellogg Research Laboratory (Salem, NH). The nitinol was heat-treated into an optimal austenite trained shape that could allow for more contact electrodes to fit into the epidural space, and the insertion method was tested with an in-vitro laboratory setup and human cadaveric model.

When nitinol is heated well above its transition temperature range, it goes into an annealing phase where the internal strain diminishes, and the atoms will reorient themselves into a body-centered cubic structure, creating a new austenite trained shape (35). Therefore, to set the nitinol into a new optimal geometry, the originally procured wire was heated to a temperature of 500°C while it was constrained in its desired shape within a mold designed using steel plates and steel screws, as shown in Fig. 4 (36). Two steel fasteners were placed 64 mm apart, and size 8 screws were used for the mold. The screw size, which determines the turn radius of the nitinol, was selected to allow for the maximum turn 0.4 mm nitinol could make while still retaining its shape memory ability. Once the screws were tightened over the nitinol, 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 a large container of 20°C water. The mold was subsequently dried, and the nitinol was removed from the mold in its new trained shape.

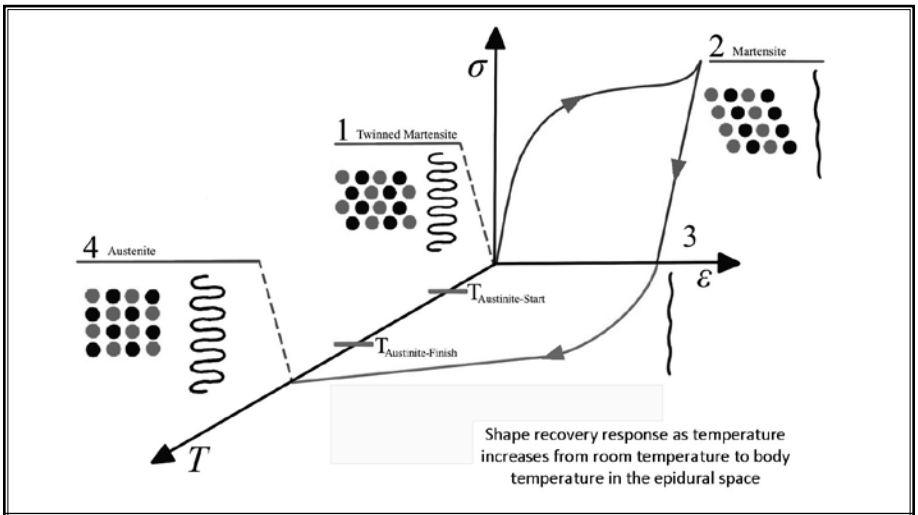

Fig. 3. *Stress-strain behavior of nitinol core of proposed SCS lead in different microscopic states with respect to temperature. 1) Below the austenite start temperature ($T_{Austenite-Start}$) nitinol exists in a martensite phase. 2) In this martensite state, nitinol is deformed from its trained permanent shape into a linear shape. 3) After the stress is removed, the nitinol will remain in a temporary linear shape. 4) once it is heated above austenite finish temperature. ($T_{Austenite-Start}$) it will revert to its permanent shape.*

After setting a new austenite trained shape, the nitinol component of the cylindrical lead was tested in an epidural space model and cadaveric specimen. For both tests, the nitinol was straightened at room temperature and placed into a Fluorinated Ethylene Propylene (FEP) introducer sheath. The sheathed nitinol was then introduced through a 14-gauge Tuohy needle. This is the same needle configuration used clinically for SCS surgery. Our in-vitro epidural space model was 13 mm in width and made of polycarbonate tubing with polyurethane foam on

the inside representing the tissue (37). The cadaveric sample was an excised spine of 6 vertebral levels from T-9 to L-2. A fluoroscopic video was taken while insertion of the nitinol component of our lead took place in the cadaver.

Results

The nitinol component of the minimally invasive cylindrical lead design was able to be successfully deployed repeatedly, 5 times in both the epidural space model and the cadaveric specimen. As can be seen in Fig. 5, the nitinol component of the lead was successfully inserted at a 45-degree angle into the 13 mm wide space of the in-vitro epidural space model. The nitinol was successfully navigated with minimal resistance to a desired location 45 mm from the insertion of the needle with the help of an FEP introducer sheath over a period of 1 minute. Once the positioning was confirmed, the sheath was removed, and the nitinol immediately began to revert into its optimal set geometry over the course of a couple of seconds.

Similarly, during the cadaveric test, the nitinol component of the lead was successfully inserted through a needle placed at a 15-degree angle into the collapsed epidural space of the cadaver shown in Fig. 6. The x-ray fluoroscopic images of successful insertion are shown in Fig. 7. The cadaver was heated to body temperature in a water bath prior to insertion of the nitinol, and the temperature was checked periodically while insertion was taking place. To remove the nitinol between trials in both the cadaveric and epidural space model test, the nitinol was pulled back into its sheath and then removed via the same route of insertion.

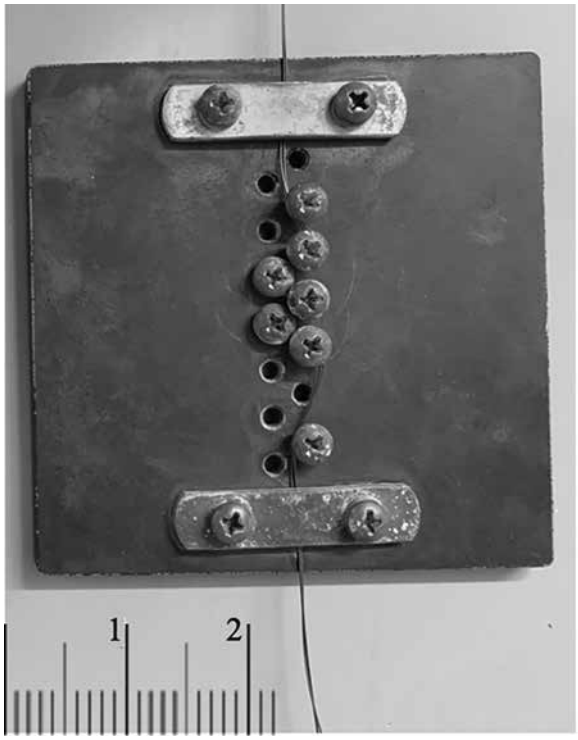

Fig. 4. *Example of a mold made on a 4"x 4" steel plate with steel screws to hold the nitinol in its desired shape while being heated to set a new austenite geometry.*

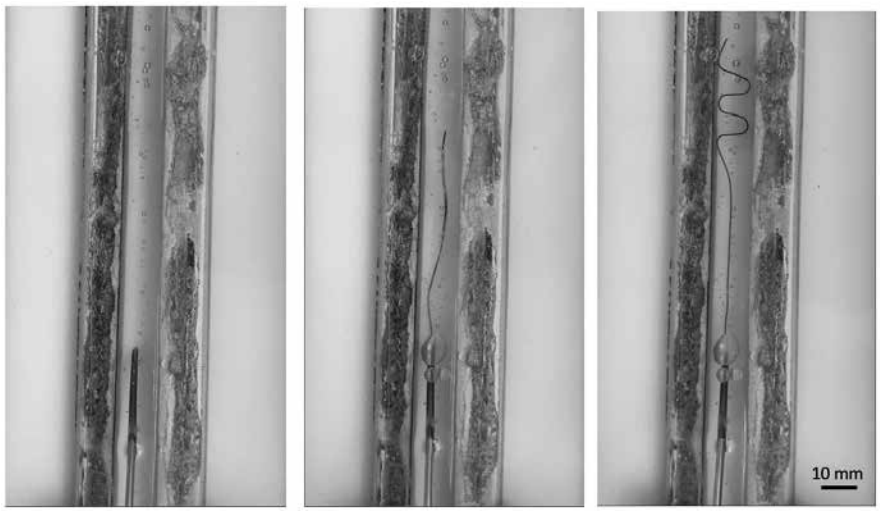

Fig. 5. *Successful deployment of proposed design into a model epidural space. 1) Insertion of sheathed nitinol; 2) removal of sheath from nitinol; 3) recovery of nitinol into trained shape.*

Discussion

The objective of this study was to design and test a lead that can exhibit combined advantages of both cylindrical and paddle leads, thereby allowing for more optimally placed electrode contacts, reduced lead migration, increased acces-

sibility, and reduced postoperative complications. The potential advantages of using a shape memory alloy such as nitinol for SCS are numerous: for one, nitinol allows for a higher density of contacts to be placed in the epidural space compared to current cylindrical leads on the market. As of now, the cylindrical leads available on the market have up to 16 contacts (38). A shape memory-based lead could drastically increase the contacts that fit within the same amount of length. Secondly, nitinol allows for a highly customizable design (39) of SCS contact placement. Due to the ability to create a new austenite trained shape via heat and quench treatment as was done in our study, many geometries and sizes can be manufactured with the use of a versatile mold. This can be useful as the size of the epidural space varies dramatically between individuals, and neuronal targets can vary based on the indication (40). Recent studies have also shown the benefits of different orientations of cathode and anode configuration in SCS. For example, a study by Canna et al discusses the potential benefits of orientation-selective stimulation, where contacts are placed off the plane of traditional placement of contacts (41). A shape memory nitinol-based electrode such as the one demonstrated here could allow for the reorientation of these contacts while maintaining minimally invasive insertion methods. As the mechanism of action of SCS is better understood, and the specific anatomical structures are better associated with more effective stimulation, our design could have significant potential in allowing the most optimal placement of electrode contacts. In addition, a shape memory-based lead could be advantageous in having the ability to selectively place electrode contacts in a minimally invasive fashion not only for spinal cord stimulation but for dorsal root ganglion stimulation, peripheral nerve stimulation, brain stimulation, and neural recording.

Fig. 6. *Cadaveric sample of spine excised from T-9 to L.*

Nitinol has already been used extensively in clinical use for vascular stenting procedures and orthodontics and has good biocompatibility and favorable toxicity and wear debris profiles (42-46). The extensive use of nitinol in vascular applications also is promising to overcome the regulatory pathways that would need to be crossed to approve a nitinol-based SCS lead. Nitinol would also not dampen or affect the electrical conduction properties of SCS by introducing any impedance due to the polymeric insulation around nitinol in the

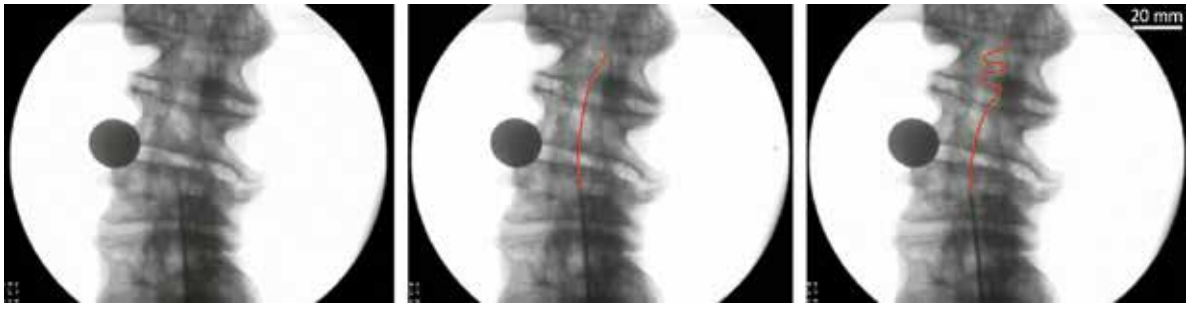

Fig. 7. *X-ray fluoroscopy images of the same procedure from Fig.6 and a quarter for reference with the nitinol highlighted over in Red. 1) insertion of sheathed nitinol, 2) removal of sheath from nitinol, 3) recovery of nitinol into trained shape.*

proposed SCS design and the larger resistivity of the material (47,48) compared to the conductors used to deliver stimulation in SCS. In addition, Nitinol is MRI compatible (49), which is critical as many patients who receive SCS tend to have imaging done later in their lives.

The nitinol cylindrical SCS lead insertion method proposed and tested here could also be expanded to other insertion techniques that could possibly be more favorable. For example, cold saline could be deployed along with the nitinol-based lead to prevent premature recovery of the lead into its optimal geometry with or without the use of a sheath. A stylet placed within a hollowed-out tube of nitinol within the central lumen of the cylindrical lead could be used to navigate the lead as well, as has been done in the past in non-nitinol based SCS leads (50). The stylet could prevent premature recovery of the nitinol mechanically and be removed from inside the central lumen once the lead has been appropriately positioned.

One concern of a shape memory polymer such as nitinol in the epidural space would be potential spinal cord compression as the nitinol morphs into its intended configuration. This can be minimized by changing the diameter and composition of nitinol in the lead such that if it met critically high resistance, its expansion would immediately stop. This would ensure that the novel SCS would be deployed in the epidural space over the dorsal columns of the spinal cord as opposed to acting as a space-occupying device with compression. Since the elastic moduli and strength of the meninges vary across the various level of the spine (51), to further ensure that there is no risk, a safe size and strength of the nitinol component would need to be selected based on adequate preoperative imaging, planning, and the utilization of mathematical models of the shape recovery transformation behavior (52,53) and tissue response (54).

Another concern in using a self-expanding nitinol-based SCS lead is the removal of the device once it has been deployed. Simply removing the lead by force back into the sheath, as was done in the experiments here could suffice or in some instances, it may not suffice when dealing with real tissue and may result in an unintended epidural or subdural hematoma or compression. Removal by invasive surgical procedures would also be suboptimal and counter the reason for using a nitinol-based lead in the first place. One solution to help with removal could be the use of cold saline. Cold saline has been used widely for the removal of nitinol stents (55,56) and could similarly be used when removing a nitinol-based SCS lead.

When using shape memory-based leads, the anatomical target of where to place the contacts would need to be predetermined to achieve optimum pain management efficacy. Several studies have shown that anatomical placement of contacts is as effective as paresthesia mapping, particularly for novel paradigms of stimulation, such as burst stimulation (57-59). Burst stimulation in the past decade has been shown to be more effective than traditional tonic SCS at 30 to 70 Hz (60) and is delivered at sub-sensory amplitudes producing analgesia without paresthesia. As a result, the use of a nitinol-based SCS would be well suited for this modern paradigm since intended anatomical regions could be identified prior to insertion (57-59). However, despite the ability to effectively place contacts solely off anatomical considerations, setting the lead shape prior to insertion could still pose a potential challenge if reorientation of the lead is needed.

As the population ages and more people suffer from neuropathic pain, it is likely that SCS placement will increase significantly. Moreover, it has been demonstrated that SCS usage diminishes opioid use and dependence (61), an important component of any future neuropathic pain treatment strategy. As our understanding behind the mechanism of SCS also continues to advance alongside new waveforms, the use of a nitinol-based lead that can best position the electrode in a cheaper, non-invasive fashion could significantly expand the number of candidate patients for SCS placement in the future.

Further research will need to be conducted to prove the clinical efficacy of a nitinol-based cylindrical SCS lead in the future. Specifically, the potential damage to surrounding live tissue during insertion and removal of the device will need to be tested alongside the design's ability to give optimal stimulation with the electrical components added. These tests will need to be conducted in animal models if shape memory alloys are ever to be used clinically for SCS.

Conclusion

We show proof of concept using a nitinol shape memory alloy as a component in cylindrical leads that can be actuated by body temperature to take an optimum expanded shape after minimally invasive SCS insertion. We demonstrate the promise of the device design to allow for minimally invasive insertion while

simultaneously providing better proximity of electrode contacts to their desired neural targets, reduced lead migration, and increased access to SCS procedures. As SCS is shown to stabilize or decrease opioid usage (61,62), a nitinol-based SCS lead could help combat the opioid epidemic in the United States and improve the management of pain overall. Further research will need to be conducted to ensure the safety of such a device and its success in both animal models and a clinical setting.

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