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Acute Implantation of a Bioresorbable Polymer Scaffold in Patients With Complete Thoracic Spinal Cord Injury: 24-Month Follow-up From the INSPIRE Study

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BACKGROUND: Based on 6-month data from the InVivo Study of Probable Benefit of the Neuro-Spinal Scaffold for Safety and Neurological Recovery in Patients with Complete Thoracic Spinal Cord Injury (INSPIRE) study (NCT02138110), acute implantation of an investigational bioresorbable polymer device (Neuro-Spinal Scaffold [NSS]) appeared to be safe in patients with complete thoracic spinal cord injury (SCI) and was associated with an ASIA Impairment Scale (AIS) conversion rate that exceeded historical controls.

OBJECTIVE: To evaluate outcomes through 24 months postimplantation.

METHODS: INSPIRE was a prospective, open-label, multicenter, single-arm study. Eligible patients had traumatic nonpenetrating SCI with a visible contusion on MRI, AIS A classification, neurological level of injury at T2-T12, and requirement for open spine surgery ≤96 hours postinjury.

RESULTS: Nineteen patients underwent NSS implantation. Three patients had early death determined by investigators to be unrelated to the NSS or its implantation procedure. Seven of 16 evaluable patients (44%) had improvement of ≥1 AIS grade at 6 months (primary end point) to AIS B (n = 5) or AIS C (n = 2). Three patients with AIS B at 6 months had further neurological improvement to AIS C by 12 (n = 2) and 24 (n = 1) months, respectively; none have deteriorated per latest available follow-up. No unanticipated or serious adverse device effects were reported.

CONCLUSION: In this small group of patients with complete thoracic SCI, acute NSS implantation within the spinal cord appeared to be safe with no long-term neurological issues identified during the 24-month follow-up. Patients remain stable, with additional AIS conversions observed in some patients at 12 months and beyond. These data further support the safety and probable benefit of NSS implantation in this patient population.

KEY WORDS: Absorbable implants, Biopolymers, Clinical trial, Spinal cord contusion, Spinal cord injuries, Spinal cord regeneration, Tissue scaffolding

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Traumatic spinal cord injury (SCI) is a devastating and debilitating condition associated with significant morbidity, individual and societal burden, and long-term costs.[1-3] In the United States (US), there are ~294 000 people living with SCI and ~17 800 new cases annually.[3] Despite advances in the field, SCI remains a significant problem, and no new effective treatment strategies have been identified for many years.[1,4]

The Neuro-Spinal Scaffold ([NSS]; InVivo Therapeutics Corporation) is an investigational device that is surgically implanted within the spinal

ABBREVIATIONS: ADE, adverse device effect; **AE,** adverse event; **FDA,** Food and Drug Administration; **HD,** hospital discharge; **INSPIRE,** InVivo Study of Probable Benefit of the Neuro-Spinal Scaffold for Safety and Neurological Recovery in Patients with Complete Thoracic Spinal Cord Injury; **ISNCSCI,** International Standards for Neurological Classification of Spinal Cord Injury; **MedDRA,** medical dictionary for regulatory activities; **NLI,** neurological level of injury; **NSS,** Neuro-Spinal Scaffold.

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cord contusion cavity with the goal of providing structural support to spared tissue, minimizing expansion of necrosis, and facilitating spinal cord repair, as observed in animal studies.[5,6] This highly porous bioresorbable polymer comprises poly(lactic-co-glycolic acid)-b-poly-(L-lysine) (PLGA-PLL),[7] a material widely used in US Food and Drug Administration (FDA)-approved devices.

The NSS has been designated as a Humanitarian Use Device by the US FDA. The Humanitarian Device Exemption regulatory pathway requires demonstration of safety and probable benefit rather than effectiveness. Primary (6-month) results from the InVivo Study of Probable Benefit of the Neuro-Spinal Scaffold for Safety and Neurological Recovery in Patients with Complete Thoracic SCI (INSPIRE; ClinicalTrials.gov identifier, NCT02138110) were reported previously.[8] This follow-up analysis evaluates outcomes through 24 months postimplantation.

METHODS

Study Design

INSPIRE was a prospective, open-label, single-arm, multicenter trial in patients with complete thoracic SCI. Patients were enrolled at 12 study sites in North America between October 13, 2014, and June 23, 2017. Detailed methodology was reported previously.[8] "This study was conducted in accordance with the ethical principles of the Declaration of Helsinki, International Conference on Harmonization guidelines for Good Clinical Practice, and applicable regulatory requirements. All patients provided signed written informed consent before enrollment in the study or undergoing any study procedure. The protocol and all relevant study forms were approved by the respective institutional review board/research ethics board of each institution. An independent Data and Safety Monitoring Board provided recommendations."[8]

Patients

"Key enrollment criteria implemented at the study sites included the following: age ≥16 years to ≤70 years, traumatic nonpenetrating SCI (contusion injury) no less than 4 mm in diameter on MRI, ASIA [American Spinal Injury Association] Impairment Scale (AIS) grade A classification, neurological level of injury (NLI) at T2-12, and requirement for open spine surgery ≤96 hours of SCI (as part of standard treatment) allowing access to the dura overlying the injured spinal cord for NSS implantation. Key exclusion criteria were complete transection of the spinal cord or more than 1 discrete SCI on MRI, significant traumatic brain injury or coma, terminal illness, and clinically significant preexisting neurological or respiratory comorbidities."[8]

Surgical Procedure and NSS Implantation

"Open spine surgery was performed (bony decompression, reduction, and/or stabilization). On visualization of the dura, intraoperative ultrasonography was performed to localize the area of maximal damage as initially assessed by preoperative MRI. Durotomy and myelotomy, if needed, were performed to expose the intramedullary contusion site. The contusion cavity was then irrigated with isotonic saline solution to wash away any superficial hemorrhagic material and devitalized tissue. The NSS was soaked in isotonic saline solution and, if necessary, trimmed at one end to the size needed to fit the postirrigation contusion cavity without causing any undue tension on the surrounding spinal cord. The NSS was then gently implanted lengthwise into the epicenter of the intraspinal contusion cavity, followed by dural closure."[8] An intraoperative video demonstrating myelotomy and NSS implantation was published previously.[8] Based on preclinical testing (InVivo Therapeutics Corporation, unpublished data on file), the NSS is expected to be essentially resorbed (mass loss of ≥85%) from the implantation site within 4 to 8 weeks. All patients were treated according to standard of care at a qualified trauma center and participated in a comprehensive rehabilitation program after hospital discharge.

Study Assessments and Outcomes

The details of preplanned study assessments through 24 months postimplantation and long-term follow-up are provided in Table 1.[9-11] The primary efficacy end point was the proportion of patients who had an improvement of ≥1 AIS grade at the 6-month follow-up visit. Secondary outcomes were changes in NLI, sensory pin prick and light touch scores, motor scores, and spinal cord anatomy, as determined by MRI.

Statistical Analysis

This analysis evaluates 24-month follow-up data (data cutoff June 20, 2019). The efficacy analysis set includes all patients who underwent NSS implantation with no major protocol deviations and had completed the 6-month follow-up visit. The preimplantation International Standards for Neurological Classification of SCI (ISNCSCI), screening MRI, and 1-month postimplantation bowel and bladder awareness assessments were used as the baseline for identifying changes at subsequent time points. Responders are defined as patients who met the primary end point (≥1 AIS grade improvement at 6 months). A post hoc analysis assessed bowel and bladder awareness by response. The safety analysis set includes all treated patients. Data were analyzed using SAS for Windows version 9.3. SAS Inc.

RESULTS

Patients

Baseline demographics and injury characteristics of patients who underwent NSS implantation (n = 19) are provided in Table 2. The mean (range) time from injury to the start of surgery was 41 hours (7-81) with most patients (84%) undergoing surgery within 72 hours postinjury. There were 3 withdrawals within 2 weeks postsurgery because of death determined by investigators to be unrelated to the NSS or its implantation (cerebrovascular accident,

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TABLE 1. Summary of Preplanned Study Assessments

Assessment	Details	Timing

Neurological status	• Assessed by the investigator or a designated trained medical professional according to the ISNCSCI[9] and ASIA 2015 worksheet
	• ISNCSCI examinations determined bilateral sensory and motor levels, NLI, and sensory and motor scores
	• The 5-grade AIS was used to determine the completeness of the patient's injury as follows:
	  • AIS A (complete: no motor or sensory function in the lowest sacral segments S4-S5)
	  • AIS B (sensory incomplete: sensory but not motor function is preserved below the level of injury and includes sacral segments S4-S5)
	  • AIS C (motor incomplete: motor function is preserved below the level of injury and voluntary anal contraction or sparing of motor function 3 levels below injury)
	  • AIS D (motor incomplete: similar to AIS C, but with ≥50% of key muscles below injury functioning against gravity)
	  • AIS E (normal function)
	• NLI refers to the lowest spinal cord level that shows normal bilateral sensory and motor function
	• Sensory pin prick and light touch scores range from 0 to 112 each; minimum scores indicate absent function and maximum scores indicate intact function
	• Total motor scores comprising upper and lower extremity scores range from 0 to 100; minimum scores indicate absent function and maximum scores indicate intact function
		• Screening
		• Preimplantation (<8 h before open spine surgery to confirm a reliable ISNCSCI examination and AIS A classification)
		• Postimplantation (at hospital discharge and 1, 2, 3, 6, 12, and 24 mo)

Spinal cord anatomy	• MRI studies without contrast • The follow-up MRIs were used to assess the presence or absence of cyst formation, where a cyst is defined as a well-defined, fluid-filled area of tissue loss within the spinal cord that is isointense with CSF on all MRI sequences	• Screening • Postimplantation (at 72 h and 3, 6, 12, and 24 mo)

Bowel and bladder function	• Patients were interviewed regarding their awareness of the need to:
	  • Defecate within the past 4 wk (normal [direct], indirect, none, or unknown)[10]
	  • Empty the bladder (no, yes, not applicable, or not known)[11]
		• Postimplantation (at 1, 2, 3, 6, and 12 mo)

Safety event monitoring	• MedDRA version 17.0 (March 2014) was used to classify all safety events throughout the 24-month postimplantation follow-up period
	• Safety event definitions:
	  • An AE is a safety event not related to the investigational device or the procedure to implant the investigational device
	  • An ADE is a safety event related to the use of an investigational medical device
	• Safety event monitoring included a check for deterioration from preimplantation in NLI of >2 levels[a] on 2 successive examinations ≥8 h apart which would trigger a study stopping rule
		• Surgery
		• Postimplantation (at 24, 48, and 72 h; 1 wk; hospital discharge; and 1, 2, 3, 6, 12, and 24 mo)[a]

Long-term general health	• Conducted through telephone to collect general health information, including any serious safety events	• Annually from 3 to 10 y postimplantation

ADE, adverse device effect; AE, adverse event; AIS, ASIA Impairment Scale; ASIA, American Spinal Injury Association; CSF, cerebrospinal fluid; ISNCSCI, International Standards for Neurological Classification of Spinal Cord Injury; MedDRA, Medical Dictionary for Regulatory Activities; NLI, neurological level of injury.
[a]Safety event monitoring for the NLI-based stopping rule was assessed using the ISNCSCI examination at hospital discharge and at 1, 2, 3, 6, 12, and 24 months postimplantation.

pulmonary embolism, and sepsis, respectively). Sixteen patients (84%) completed the 6-month postimplantation assessment. Of these, 3 were lost to follow-up by 12 (n = 1) or 24 (n = 2) months.

Efficacy

Seven of 16 evaluable patients (44%) were responders (ie, had improvement of ≥1 AIS grade at 6 months postimplantation). Changes in AIS grade for each responder are provided in the Figure. The 2 responders who had converted to AIS C by 1 month[8] remained AIS C through 24 months (except for an AIS B grade reported at 3 months in 1 patient[8]). Three responders who had initial conversion to AIS B (by 1, 2, and 3 months, respectively)[8] had further improvement in neurological function to AIS C by 12 (n = 2) or 24 (n = 1) months. In addition, 2 responders who had converted to AIS B (by 2 and 6 months, respectively)[8] were subsequently lost to follow-up (by 24 and 12 months, respectively). An additional patient had converted to AIS B by 1 month[8] but was AIS A at all following assessments and was, therefore, classified as a nonresponder. No other AIS grade changes were reported among nonresponders.

TABLE 2. Baseline Demographics and Injury Status Characteristics

Characteristic	Neuro-Spinal Scaffold (n = 19)
Mean age (range), years	37 (18-69)
Sex, n (%)	
Female	4 (21)
Male	15 (79)
Race, n (%)	
American Indian or Alaskan Native	1 (5)
Black or African American	1 (5)
White	16 (84)
Other	1 (5)
Ethnicity, n (%)	
Hispanic or Latino	4 (21)
Non-Hispanic or Latino	15 (79)
Mean height (range), cm	172 (147-185)
Mean weight (range), kg	83 (58-127)
Mean BMI (range), kg/m^2	28 (20-38)
Cause of injury, n (%)	
Fall	5 (26)
Others—all terrain vehicle	1 (5)
Vehicular	13 (68)
Preimplantation NLI, n (%)	
T2-T5	8 (42)[a]
T6-T9	6 (32)
T10-T12	5 (26)

BMI, body mass index; NLI, neurological level of injury.
[a]Includes one patient who did not have a preimplantation assessment (<8 h before surgery) but was assessed as T3 at screening.

Changes in NLI and sensory scores are provided in Table 3. Four patients (25%) demonstrated improvement in motor score. One patient had improvement in total motor score at the 1-, 3-, 6-, 12-, and 24-month assessments (2, 8, 10, 18, and 18 points, respectively), 1 had improvement at 12 and 24 months (both 4 points), and another had improvement at 24 months (1 point). An additional patient with improvement in lower extremity motor scores was not fully testable according to the ISNCSCI because of lower extremity fractures at screening and preimplantation. However, motor scores reported at 2, 3, 6, 12, and 24 months (59, 59, 61, 62, and 68 points, respectively) indicate a minimal improvement of 9 to 18 points across these time points. The remaining 12 patients had no change in total motor score indicating no change in motor function and no lower extremity motor function present.

Cysts were present on MRI in 8 of 12 patients with evaluable images at the 24-month postimplantation visit. These were first observed at 3 (n = 3), 6 (n = 1), and 12 months (n = 4), respectively. An additional patient had evidence of cyst formation at 6 and 12 months (the 24-month assessment was not performed). Seven of 9 patients with cysts were nonresponders and remained AIS A per latest follow-up. Of these, 3 also had documented spinal cord adhesion at 24 months (first observed at 6 months in 1 patient) and another had a documented syrinx at 3 months with a decrease in size noted at 6 months. None of these events required surgical intervention.

In a post hoc analysis, normal or indirect awareness of the need to defecate within the past 4 weeks was reported in 4 of 7 responders (57%) and 1 of 7 nonresponders (14%) with available data at 1 month, and awareness of the need to empty the bladder was reported in 4 of 7 responders (57%) and 1 of 8 nonresponders (13%). At 12 months, all 6 responders (100%; with the remaining responder lost to follow-up at this time point) and 2 of 9 nonresponders (22%) each had awareness of bowel and bladder, respectively.

Safety

The most common adverse events (AEs) not related to the NSS were urinary tract infection (74%), muscle spasms (58%), and neuralgia (53%) (**Supplemental Digital Content**, http://links.lww.com/NEU/D23 for further details). There were 2 AEs of interest in a single patient (moderate thoracic cerebrospinal fluid leak and moderate deep wound infection), both occurred within the first 6 months and were resolved. Three serious AEs leading to death were reported (cerebrovascular accident, pulmonary embolism, and sepsis); none were deemed by investigators to be related to the NSS or its implantation procedure. No other safety events led to study discontinuation.

Adverse device effects (ADEs) in patients who underwent NSS implantation are presented in Table 4; no serious or unanticipated ADEs were reported.

Deterioration in NLI of >2 dermatome levels was reported in 2 patients. However, the Data and Safety Monitoring Board did not recommend stopping the study after careful and thorough review of these cases. Both patients remained on study through 24 months postimplantation at which time their injuries were classified as AIS A and AIS C, respectively.

DISCUSSION

Generalizability

Approximately 20% of US-based patients with SCI have complete paraplegia.[3] Those with complete thoracic SCI represent a particularly challenging population for clinical study. They typically sustain high-impact injuries, present with multiple comorbidities, and despite enormous efforts continue to have poor prognosis for functional neurological recovery.[1,4,12]

The current study provides proof-of-concept that this high-risk population can safely undergo acute spinal stabilization surgery with additional surgical intervention aimed at the SCI itself without added morbidity. Furthermore, it provides evidence that treatment aimed at providing an architectural framework at the site of neural insult offers the potential for improving neurological recovery. This approach represents a novel paradigm shift in the surgical treatment of SCI and may have important implications for future research eg, for cervical SCI, where relatively small improvements in neurological function can result in important

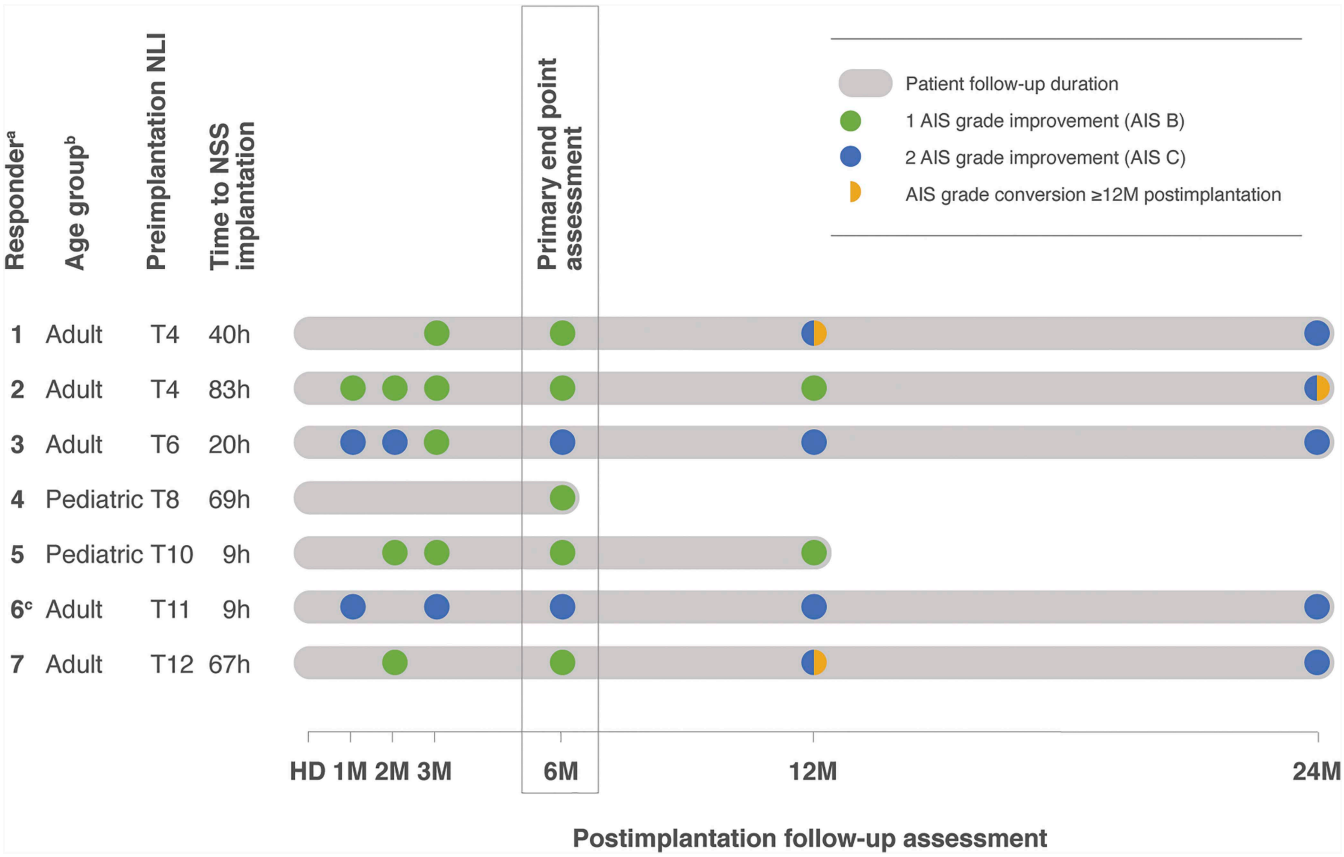

FIGURE. *Changes in AIS grade from preimplantation in patients with complete (AIS A) thoracic spinal cord injury who responded to NSS implantation. [a]Responders are defined as patients who met the primary end point (improvement of ≥1 AIS grade at the 6-month postimplantation follow-up visit), [b]Pediatric is defined as age ≤21 years per the US Food and Drug Administration definition for medical devices. [c]2-month postimplantation visit for this patient was not required per protocol approved at the time. AIS, American Spinal Injury Association (ASIA) Impairment Scale; HD, hospital discharge; M, month; NLI, neurological level of injury; NSS, Neuro-Spinal Scaffold.*

functional ramifications or as a foundation for combination with other synergistic modalities.

Key Results and Interpretation

As reported previously, the 6-month AIS conversion rate in patients who underwent NSS implantation (44%; 7/16 evaluable patients) exceeded historical benchmarks for patients with complete thoracic SCI (~14%-21%).[8,13-16] This includes comparison with a recent analysis of data from the North American Clinical Trials Network (NATCN), European Multicenter Study about Spinal Cord Injury (EMSCI), and SCI Model Systems registries (CONTEMPO Registry Study, sponsored by InVivo Therapeutics Corporation), which used more stringent patient eligibility criteria closely matching those of the INSPIRE study.[15]

In the current follow-up analysis, 3 of 7 responders (43%) had further improvement in neurological function to motor incomplete injury (AIS C) by 12 (n = 2) or 24 (n = 1) months postimplantation, and none have deteriorated per latest follow-up. These later conversions did not appear to be age-related (patients were aged 40, 67, and 83 years, respectively). There are limited data in the literature regarding the timing of spontaneous AIS conversions in patients with complete thoracic SCI. However, based on studies with mixed SCI populations most conversions are expected to occur within the first 3 to 6 months postinjury and late conversions are rare.[12,17,18]

Overall, 31% of INSPIRE patients (5 of 16 evaluable patients) had conversion to motor incomplete injury (AIS C), which seems to be higher than natural history rates (≤17%).[13-15] In any case, it has been reported that patients with incomplete injuries (even sensory incomplete [AIS B] injuries) have a lower likelihood of rehospitalization, lower lifetime costs, and a reduced risk of complications (eg, pressure ulcers).[19-21]

In the current study, fluctuations in NLI mostly occurred within the first 3 months and generally remained stable at later time points.[8] Most patients (14 of 16) had changes within 2 levels in either direction and both patients who had a >2 level deterioration remained on study through 24 months postimplantation. The median changes in sensory scores were positive, and 4

TABLE 3. Changes From Preimplantation in Neurological Level of Injury and Sensory Scores in Patients Who Underwent Neuro-Spinal Scaffold Implantation

	Postimplantation follow-up assessment		
	6 mo (n = 16)	12 mo (n = 15)[b]	24 mo (n = 11)[c]
Change in NLI,[a] n (%)			
2	2 (13)	1 (7)	1 (9)
1	3 (19)	5 (33)	2 (18)
0	3 (19)	3 (20)	5 (45)
−1	4 (25)	4 (27)	1 (9)
−2	3 (19)	1 (7)	1 (9)
<−2	1 (6)	1 (7)	1 (9)
Median change in sensory pin prick scores (min, max)	2 (−12, 10)	2 (−10, 14)	2 (−11, 28)
Change in sensory pin prick score direction, n (%)			
Improved	10 (63)	10 (67)	7 (64)
No change	0	0	0
Worsened	6 (38)	5 (33)	4 (36)
Median change in sensory light touch scores (min, max)	2.5 (−8, 13)	4 (−10, 20)	2 (−7, 26)
Change in sensory light touch score direction, n (%)			
Improved	10 (63)	11 (73)	8 (73)
No change	2 (13)	1 (7)	0
Worsened	4 (25)	3 (20)	3 (27)

ISNCSCI, International Standards for Neurological Classification of Spinal Cord Injury; NLI, neurological level of injury.
[a]A positive change indicates caudal improvement, whereas a negative change indicates rostral deterioration.
[b]Of the 16 patients who completed the 6-mo primary end point visit, 1 patient was lost to follow-up before the 12-mo visit.
[c]Of the 16 patients who completed the 6-mo primary end point visit, 3 patients were lost to follow-up before the 24-mo visit, and protocol-mandated ISNCSCI examination was not completed in 2 others because of a lapse in assessor training at this time point.

patients (25%) had an improvement in motor score of 1 to 18 points by 24 months. Changes in NLI and sensory and motor scores appeared to be aligned with natural history data for this patient population.[13-15]

One potential benefit of the NSS is to reduce cyst progression after SCI. In a rat contusion model, untreated animals developed large cavities with minimal spared tissue, whereas NSS implantation largely prevented cystic cavitation and was associated with increased tissue sparing and new tissue formation rich in neuropermissive extracellular matrix.[5] In the current study, 7 of 9 patients with cysts were nonresponders. However, it should be noted that greater cord tissue width at 1 month postinjury has been shown to be predictive of better outcomes at 1 year.[22,23] Patients with no or smaller cysts will have wider

TABLE 4. Adverse Device Effects in Patients Who Underwent Neuro-Spinal Scaffold Implantation

	Postimplantation follow-up period		
	0-6 mo (n = 19)	6-24 mo (n = 16)[a]	Overall (n = 19)
All ADEs, n (%)	5 (26)	1 (6)	6 (32)
Mild myelomalacia[b]	1 (5)	1 (6)	2 (11)
Mild neuralgia[b]	1 (5)	0	1 (5)
Mild postoperative respiratory failure[c]	1 (5)	0	1 (5)
Moderate incision site pain[c]	1 (5)	0	1 (5)
Moderate neurological decompensation[c]	1 (5)	0	1 (5)
Severe increase in generalized pain[c]	1 (5)	0	1 (5)
Serious ADEs, n (%)	0	0	0
Unanticipated ADEs, n (%)	0	0	0

ADEs, adverse device effects; NSS, Neuro-Spinal Scaffold.
[a]Of the 19 patients who underwent NSS implantation, there were 3 early withdrawals because of death (cerebrovascular accident, pulmonary embolism, and sepsis, respectively) within 2 wk of surgery; all were determined by investigators to be unrelated to the NSS or its implantation procedure.
[b]Considered to be related to the NSS and its implantation procedure.
[c]Considered to be related to the implantation procedure but not to the NSS.

tissue bridges; therefore, it is logical to assume that those with cysts will have less endogenous sprouting and a lower likelihood of AIS conversion.

Bowel and bladder function are important factors contributing to quality of life in patients with SCI.[24] Awareness of the need to defecate or empty the bladder may lead to improved quality of life as well as having other important implications for patients such as reducing the likelihood of complications (eg, autonomic dysreflexia, a potentially dangerous medical problem, or urinary tract deterioration[25]). Furthermore, this information may provide insight into whether afferent sensory tracts are intact or restored.[26] In a post hoc analysis of the INSPIRE study data, all 6 responders with available data at 12 months postimplantation had awareness of the need to defecate or empty the bladder compared with 2 of 9 nonresponders. Baseline values were recorded at 1 month at which time 4 responders and 1 nonresponder each noted bowel and bladder awareness making it difficult to assess improvement. However, deep anal pressure sensation and voluntary anal contraction were absent during preimplantation rectal examinations.

AEs reported during the study were concordant with those seen during the routine care of patients with SCI.[27] The majority were reported within the first 6 months, and no new safety signals were identified during subsequent follow-up. One ADE (mild myelomalacia) was reported beyond 6 months; however, this event is not uncommon as a sequalae of SCI and is part of the natural history of imaging in these patients. Importantly, there were no serious or unanticipated ADEs related to the NSS or its implantation at any time during the 24-month follow-up period.

Limitations

Study limitations include the small sample size, a common issue across SCI clinical trials because of the low number of eligible patients presenting at study sites,[28,29] and open-label study design. Furthermore, the lack of a control group makes it difficult to account for the effect of early surgery and myelotomy on neurological recovery in this patient population; therefore, it is unclear from the current clinical study how much the potential beneficial effects are due to the NSS vs cyst debris clearance with irrigation. When looking at animal data, myelotomy plus irrigation alone was associated with significantly reduced cavity volume and increased white matter width vs controls.[5] However, when NSS implantation was added to the treatment procedure, further benefits were observed (eg, new tissue formation, almost no cystic cavitation, and an extensive region of Schwann cell (SC)-derived P0-positive myelin in the spared tissue).[5]

Future Directions

Based on the INSPIRE data, a randomized, controlled, single-blind, multicenter study evaluating the safety and probable benefit of NSS implantation vs standard-of-care open spine stabilization has been initiated and is currently recruiting patients (INSPIRE 2.0; ClinicalTrials.gov number, NCT03762655).

CONCLUSION

In this small group of patients with complete (AIS A) thoracic SCI requiring open spine surgery, acute implantation of the NSS within the spinal cord seemed to be safe through 24 months follow-up with no long-term neurological issues identified. After a promising 6-month AIS conversion rate, patients remain stable per latest follow-up with additional AIS conversions observed at 12 months and beyond. This analysis further supports the safety and probable benefit of NSS implantation in this patient population and encourages additional clinical investigation.

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Disclosures

Dr Kim has received research funding from Empiric Spine, Fziomed, InVivo Therapeutics Corporation, Medtronic, Orthofix, Seikagaku, Vertex, and Zimmer Biomet Spine; received compensation for serving as a member of an Advisory Board (INSPIRE study steering committee) for InVivo Therapeutics Corporation; been a consultant for Integra, Globus, Medtronic and Zimmer Biomet; received royalties from Precision Spine and Zimmer Biomet Spine; and serves on the Board of Directors and holds stock options at Molecular Matrix. Dr Lee has served as a member of an Advisory Board (INSPIRE study steering committee) for InVivo Therapeutics Corporation. Dr Coric has received research funding from InVivo Therapeutics Corporation to execute IDE study; been a consultant for Medtronic, Premia Spine, Spinal Kinetics, Spine Wave, and Stryker; received royalties from RTI Surgical and Spine Wave; is a stockholder with Spinal Kinetics, Spine Wave, and Premia Spine; and has served as an advisory board member for United Health Care. Dr Harrop has been a consultant for Depuy Synthes and Ethicon and served as an advisor for Abbvie and AlaMab Therapeutics. Dr Theodore has been a consultant for Globus Medical and received royalties from Depuy Synthes and Globus Medical. Dr Toselli serves as Chief Medical Officer/Chief Executive Officer and holds stock options at InVivo Therapeutics Corporation.

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Supplemental Digital Content. Table. Adverse events not related to the NSS or its implantation procedure.

COMMENT

This is a very interesting article where the authors describe the 24-month follow-up of the patients from the INSPIRE Study. Key messages I distill from the paper is that the procedure is safe in this subgroup of patients, their rate of ASIA conversion is higher than expected (44%) compared to historical benchmarks, and that those patients who converted in the first 6 months exhibit the potential to improve further up to the 24-month follow-up (43% of responders improved beyond the first 6 months evaluation).

However, as recently reported,[1] comparing to historical benchmarks in this field poses the risk of overestimating the real effect of any new therapy, since the outcomes of the spinal cord injured patients have been slowly but steadily improving for the last 30 years. Also, the surgical technique could be technically demanding, prolonging the surgery, and complicating the management of the antithrombotic prophylaxis in the postoperative period.

With those concerns in mind, we should eagerly expect the results of the prospective randomized trial that will surely address these issues (INSPIRE 2.0; ClinicalTrials.gov number, NCT03762655). Any improvement in the management of the spinal cord injured patients should be assessed cautiously and thoroughly to avoid unnecessary disappointment, but with hope and an open mind.

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