

Pain relief and multidimensional outcomes of fast-acting subperception spinal cord stimulation therapy for chronic pain: the FAST prospective, multicenter study

Magdalena Anitescu ¹, Eric Loudermilk ², James North ³, Sayed Wahezi ⁴, Ajay Antony ⁵, Tim Leier ⁶, Drew Trainor ⁷, John Noles ⁸, Gregory Moore ⁹, Jennifer Lee ¹⁰, Julio Paez ¹¹, Derron Wilson ¹², Virginie Van Belleghem ¹³, and Edward Goldberg ¹³

1. University of Chicago Medical Center, Anesthesia and Critical Care Medicine, Chicago, IL USA
2. Piedmont Comprehensive Pain Management Group, PCPMG Clinical Research Unit LLC, Greenville, SC USA
3. Carolinas Pain Institute and Center for Clinical Research, Winston-Salem, North Carolina, USA
4. Multidisciplinary Pain Program, Montefiore Medical Center, Bronx, NY USA
5. The Orthopaedic Institute, Gainesville, Florida, USA
6. Vitamed Research, Palm Desert, California, USA
7. The Denver Spine and Pain Institute, Denver, CO USA
8. Spine and Pain Specialists, Shreveport, LA USA
9. Pacific Sports and Spine, Eugene, Oregon, USA
10. Department of Sports & Spine, Evergreen Health Medical Group, Kirkland, WA USA
11. South Lake Pain Institute, Clermont, Florida, USA
12. Goodman Campbell Brain & Spine; Ascension St. Vincent's; Carmel, IN, USA
13. Boston Scientific Neuromodulation, Valencia, CA, USA

Corresponding author: Magdalena Anitescu (manitescu@bsd.uchicago.edu)

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Abbreviations

6MWT, 6 Minute Walk Test	IRB, institutional review board
AE, adverse event	VNRS, verbal numerical rating scale
BDI, Beck Depression Index	ODI, Oswestry Disability Index
EC, ethics committee	PCS, Pain Catastrophizing Scale
EQ-5D-5L, EuroQol 5 Dimension 5 Level	P-GIC, Patient Global Impression of Change
FAST, Fast-Acting Sub-Perception Therapy	PPR, percent pain relief
IC, informed consent	PSQI, Pittsburg Sleep Quality Inventory
ICF, informed consent form	SCS, spinal cord stimulation
IFU, instructions for use	TUG, Timed Up-and-Go Test

Table S1. Ethical approvals

Principal investigator	IRB Name	Initial IRB Approval Date	Current IRB Approval Date	IRB reference number/ID
Magdalena Anitescu	University of Chicago IRB	31-Aug-2021	25-Sep-2025	IRB20-1900-AM001
Eric Loudermilk	WCG IRB	15-Jan-2021	23-Mar-2025	20203916
James North	Sterling IRB	02-Jul-21	6-Aug-2025	8431-JMNorth
Sayed Wahezi	BRANY IRB	18-Aug-2021	11-Jun-2025	BRANY IRB File # 21-02-221-01
Ajay Antony	Sterling IRB	10-Dec-2020	6-Aug-2025	8431-ABAntony
Tim Leier	Sterling IRB	02-Jul-21	6-Aug-2025	8431-TULeier
Drew Trainor	Sterling IRB	25-Mar-21	6-Aug-2025	8431-DMTrainor
John Noles	Sterling IRB	16-Nov-20	6-Aug-2025	8431-JGNoles
Gregory Moore	Sterling IRB	20-Nov-20	6-Aug-2025	8431-GMPhillips
Jennifer Lee	Sterling IRB	12-Jul-2021	5-Sep-2023 (site has closed)	8431-JLee
Julio Paez	Sterling IRB	14-Sep-23	6-Aug-2025	8431-JCPaez
Derron Wilson	Ascension IRB	29-Apr-2021	26-Mar-2025	R20210031

Table S2. Full inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
1. Chronic pain (predominantly neuropathic) of the trunk and/or limbs for at least 6 months with back pain greater or equal to leg pain. 2. Chronic, intractable pain of the trunk and/or limbs which has been refractory to conservative therapy (e.g., pain medications, physical therapy, facet joint/medial branch nerve blocks). 3. No back surgery within 6 months prior to Screening. 4. Average targeted pain intensity (leg and/or low back pain) of 6 or greater on a 0-10 numerical rating scale at Baseline Visit, based on 7-day recall. 5. If taking prescription opioids for primary chronic pain complaint (low back and/or leg pain), must have been on a stable prescription (same drug(s) and dose(s)) 30 days prior to Screening. 6. Achieved 80-100% pain paresthesia overlap during intraoperative testing performed during permanent placement of percutaneous leads. 7. Received bilateral, tight-spaced, 8-, 16-, or 32-contact leads, placed midline and secured using Klik-X anchor to ensure appropriate placement during implant (permanent). 8. Consumed an average total daily morphine equivalent ≤ 200 mg during the 30 days prior to Screening. 9. Willing and able to comply with all protocol-required procedures and assessments/evaluations. 10. Baseline Oswestry Disability Index score ≥ 30 and ≤ 80. 11. 22 years of age or older when written informed consent was obtained. 12. Eligible candidate for SCS from a psychological and psychiatric standpoint, as determined within 180 days prior to Baseline Visit, per site's routine screening process. 13. Able to independently read and complete all questionnaires and assessments provided in English. 14. If female of childbearing potential: not pregnant, as evidenced by a negative pregnancy test at Screening.	1. Average leg pain intensity was greater than average low back pain intensity, as reported during Baseline Period. 2. Patient exhibited catastrophization based on physician evaluation (e.g., average targeted daily pain intensity of 10 on a 0-10 numerical rating scale, every day during the 7 days prior to Screening, based on patient recall). 3. Radiographic evidence of spinal instability requiring fusion. 4. Primary pain complaint of vascular origin (e.g., peripheral vascular disease) or mechanical pain. 5. Spinal pain secondary to neoplasm, infection, autoimmune disorder with spinal involvement, or a spinal metabolic disorder. 6. Visceral pain referred to the low back and/or legs. 7. Any pain-related diagnosis or medical/psychological condition or external factors that, in the clinician's best judgment, might have confounded reporting of study outcomes (e.g., pelvic pain, anginal pain, chronic migraine, brain or spinal cord tumor, involved in litigation, workmen's compensation). 8. Required implantation of lead(s) in the cervical epidural space. 9. At Screening, systemic infection, or local infection in close proximity to anticipated surgical field. 10. High surgical risk. 11. Body mass index ≥ 45 at Screening. 12. Terminal illness with anticipated survival < 12 months. 13. Current condition associated with risk of immunocompromise that might have increased risk of infection during study duration. 14. On any anticoagulant medications that could not be discontinued during perioperative period. 15. Significant cognitive impairment at Screening that, in the opinion of the Investigator, would reasonably be expected to impair the patient's ability to participate in the study. 16. Participating (or intended to participate) in another drug or device clinical trial that may

15. Patient signed a valid, IRB-approved ICF provided in English.	have influenced the data being collected for this study. 17. Previous SCS trial or was already implanted with an active implantable device(s) (e.g. pacemaker, drug pump, implantable pulse generator). 18. A female who was breastfeeding. 19. A female of childbearing potential planning to get pregnant during the course of the study or not using adequate contraception. 20. Planning to receive any massage or manipulation directly over the leads or by the anticipated location of the IPG or treatments that involved sudden jerking motions of the torso at any time during the course of the study. 21. A condition currently requiring or likely to require the use of diathermy and/or MRI not approved per applicable device IFU. 22. Any injury or medical/psychological condition that might be significantly exacerbated by the implant surgery or the presence of an implantable stimulator or otherwise compromise subject safety. 23. Unable to operate the study device, or mobile app for reporting and/or did not have a smartphone to support use of the mobile app.
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Table S3. Data collection

	Screening	Opioid medication lock visit	Baseline period	Baseline visit	Implant procedures (trial and permanent)		Activation visit	Program-ming lock visit	3-month visit	6-month visit	9-month visit	12-month visit	Unscheduled visit
		Up to 35 days from IC	14 days post-opioid medication lock	0-7 days post baseline period	Up to 90 days post-baseline visit		Day 0	7-70 days post-activation	90 + 14 days post-activation	180 ± 30 days post-activation	270 ± 30 days post-activation	365±30 days post-activation	
ICF	X					Healing period (14-28 days)							
Inclusion/exclusion criteria evaluation													
Demography and medical history				X									
BDI-II				X					X			X	
ODI v2.1a				X					X	X	X	X	
EQ-5D-5L				X					X	X	X	X	
Pain intensity (NRS)				X					X	X	X	X	
PCS				X					X	X	X	X	
PSQI				X					X	X	X	X	
Procedure information					X ^a								X ^b
End of SCS trial Assessment					X								
Programming parameters ^c					X		X	X	X	X	X	X	X
Self-defined functional objectives				X					X	X	X	X	
6MWT				X					X	X	X	X	
TUG				X					X	X	X	X	
Activation questionnaire							X						
PGIC									X	X	X	X	
PPR									X	X	X	X	
TSQM-9m									X	X	X	X	
Video recording (optional)							X						
Concomitant medications (opioid medications)		X		X	X		X	X	X	X	X	X	X
AEs ^d	X	X	X	X	X		X	X	X	X	X	X	X

Opioid medications locked

^a The device remained off after permanent implantation until the activation visit; ^b for unscheduled visits where procedures were performed; ^c only when device programming was performed; ^d rates of occurrence of all device hardware, device stimulation, and procedure-related non-serious adverse events, all serious adverse events, and unanticipated adverse events through the end of the study.

Table S4. Clinical assessments

Assessment	Details
VNRS (Verbal Numerical Rating Scale)	The numeric rating scale (NRS) is a numerical scale with numbers from 0 to 10 evenly spaced across the page, where 0 is “no pain” and 10 is “worst pain imaginable”. Patients are instructed to circle the number that represents the amount of pain that they are experiencing at the time of the evaluation. A variation of this scale is the verbal numeric scale (VNRS), in which patients are asked to verbally state a number between 0 and 10 that corresponds to their present pain intensity [1].
PPR (Percent Pain Relief)	The patient-reported pain percentage reduction, generated by asking patients to rate their perceived improvement of pain as a percentage, scored from 0–100%. The percentage of pain reduction considered to be significant has been placed at 50% [2].
ODI (Oswestry Disability Index)	A patient-completed questionnaire evaluating the level of disability for different activities of daily living. A total score of 0% indicates no disability and 100% indicates the highest level of disability [3].
6MWT (6-Minute Walk Test)	A sub-maximal exercise test used to assess aerobic capacity and endurance. The distance covered over a time of 6 minutes is used as the outcome by which to compare changes in performance capacity [4].
TUG (Time Up-and-Go test)	A simple tool that helps assess functional mobility. It consists of timing a person as they stand up from a chair with armrests, walk a distance of three meters, turn around, walk back to the chair, and sit down again [5].
EQ-5D-5L (EuroQol 5 Dimension 5 Level questionnaire)	Designed to capture health status in five key dimensions—mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It includes five questions, each targeting a specific dimension, plus a Visual Analogue Scale (VAS) for self-rated health [6].
PSQI (Pittsburgh Sleep Quality Inventory)	A self-report questionnaire that assesses sleep quality over a one-month time interval by capturing multiple dimensions of sleep, including subjective experiences and objective parameters. 19 individual items are grouped into seven component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction; the sum of these seven scores yields a single global score [7].
BDI (Beck Depression Inventory)	A 21-item, self-report rating inventory that measures characteristic attitudes and symptoms of depression [8].
PCS (Pain Catastrophizing Scale)	A self-assessment questionnaire to examine catastrophizing in clinical and non-clinical populations. Catastrophizing is commonly described as an exaggerated negative orientation toward noxious stimuli and plays an important role in experiencing and coping with pain. A total score of >30 represents a clinically significant level of pain catastrophizing [9].
P-GIC (Patient Global Impression of Change)	Consists of a single, self-administered question asking individuals to rate how their condition has changed following treatment using a 7-point verbal scale. This protocol was validated in individuals aged 18 years and older who were being treated for chronic pain [10].

Table S5. Minimal clinically important differences for functional and psychosocial outcomes

Scale	MCID	Reference
Oswestry Disability Index	10 points 15 points	[11,12] [3]
6-Minute Walk Test	60-75 meters	[13]
Timed Up-and-Go test	0.9-6.0 seconds (mean 3.4 seconds)	[14]
EuroQol 5 Dimension 5 Level questionnaire	0.037-0.069 (0.069)	[15]
Pittsburgh Sleep Quality Index	3 points	[16]
Pain Catastrophizing Scale	6.8 points	[17-19]
Beck Depression Index	5 points	[20,21]

Table S6. Parameters for the sample size calculation

The primary endpoint was the proportion of subjects with 50% or greater reduction (responder rate) from the Baseline Visit in average targeted pain intensity at 3 months post-activation, with no increase in baseline average daily opioid medications used to treat pain.

The primary statistical hypothesis was that the proportion of subjects with 50% or greater reduction from Baseline Visit in average daily targeted pain intensity at 3 months post-activation was non inferior, compared to an Objective Performance Criteria (OPC) of 40%.

$$H_0: \pi_{opc} - \pi_t \geq 0.20$$

$$H_1: \pi_{opc} - \pi_t < 0.20$$

Where π_t is the proportion of subjects with 50% or greater reduction from Baseline in average daily targeted pain intensity at 3 months post-activation with no increase in baseline average daily opioid pain medications, π_{opc} is the responder rate of an OPC based on Kumar et al. 2008 [22]. The study's non-inferiority margin was 0.20. The required sample size for this study was calculated based on the following assumptions:

Test significance level (α)	0.025
1- or 2-sided test	1
Difference in Response (ϵ)	0.00
Non-inferiority margin (δ)	0.20
Objective Performance Criteria	0.40 (Kumar et al. [22])
Power ($1 - \beta$)	0.85
N	59 with two interim looks
Attrition (%)	10
N	66

The 95% confidence interval of $\pi_{opc} - \pi_t$ was computed. The study was considered a success if, using the Intent-To-Treat (ITT) analysis, the upper bound of the two-sided 95% confidence interval for the difference was less than 0.20. For the primary endpoint, statistical testing was performed to determine if the targeted pain responder rate was non inferior to the OPC of this study with a margin of 0.2. The statistical test was a Fisher's Exact test for a single proportion.

This study had a total of three looks, with two interim analyses at 20 activated subjects at 3-Month Visit (futility and effectiveness stopping) and at 45 activated subjects at 3-Month Visit (futility and effectiveness stopping).

Table S7. Serious adverse effects (Medical Dictionary for Regulatory Activities classification) reported at up to 12-month in all consented patients (N=177)

System organ class	Preferred term	Number of events	Related to device / procedure? (Y/N)
Musculoskeletal and connective tissue disorder	Rotator cuff syndrome	2	N
	Arthritis	1	N
	Musculoskeletal pain	1	N
	Pain in extremity	1	Y (device)
Nervous system disorders	Cerebrovascular accident	4	N
	Dizziness	1	N
	Idiopathic intracranial hypertension	1	N
	Peripheral neuropathy	1	N
Injury, poisoning, and procedural complications	Ankle fracture	1	N
	Fall	1	N
	Spinal fracture	1	N
	Tibia fracture	1	N
	Upper limb fracture	1	N
Infections and infestations	Pneumonia	3	N
	Sepsis	3	N
	Covid-19	2	N
	Bateraemia	1	N
	Cellulitis	1	N
	Extradural abscess	1	N
	Influenza	1	N
Renal and urinary disorders	Hydronephrosis	1	N
	Ureterolithiasis	1	N
Cardiac disorders	Atrial fibrillation	1	N
Surgical and medical procedures	Hip surgery	1	N
Not coded	—	1	N
	Total	34	

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