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Long-term performance and user satisfaction with implanted neuroprostheses for upright mobility after paraplegia: Two to 14-year follow-up

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Abstract

Objective—To quantify the long-term (LT) (>2 years) effects of lower extremity (LE) neuroprostheses (NPs) for standing, transfers, stepping and seated stability after spinal cord injury.

Design—Single-subject design case series with participants acting as their own concurrent controls, including retrospective data review.

Setting—Hospital-based clinical biomechanics laboratory with experienced (>20 years in the field) research biomedical engineers, physical therapist and medical monitoring review.

Participants—Twenty-two (19 male, 3 female) LT (6.2 ± 2.7 years) at-home users of implanted NPs for trunk and LE function with chronic (14.4 ± 7.1 years) spinal cord injury resulting in full or partial paralysis.

Interventions—Technical and clinical performance measurements, along with user satisfaction surveys.

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Suppliers' list

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- b. Advanced Mechanical Technology, Inc. 176 Waltham Street, Watertown, MA 02472

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Main Outcome Measures—Knee extension moment, maximum standing time, body weight supported by lower extremities, three functional standing tasks, two satisfaction surveys, NP usage, and stability of implanted components.

Results—Stimulated knee extension strength and functional capabilities were maintained with 94% of implant recipients reporting being “very” or “moderately” satisfied with their system. Greater than half (60%) of the participants were still using their implanted NPs for exercise and function for more than 10 minutes per day on nearly half or more of the days monitored, although maximum standing times and percentage body weight through LEs decreased slightly over the follow-up interval. Stimulus thresholds were uniformly stable. Six-year survival rates for the first-generation implanted pulse generator (IPG) and epimysial electrodes were close to 90%, while those for the second-generation IPG along with the intramuscular and nerve cuff electrodes were greater than 98%.

Conclusions—Objective and subjective measures of the technical and clinical performances of implanted LE NPs generally remained consistent for 22 participants after an average of 6 years of unsupervised use at home. These findings suggest that implanted LE NPs can provide lasting benefits that recipients value.

Keywords

electrical stimulation; lower extremity; neural prosthesis; satisfaction; spinal cord injury

Passive standing in braces, a standing frame or standing wheelchair after spinal cord injury (SCI) can positively impact physical health in a variety of important ways, including circulation, skin integrity, reflex activity, bowel and bladder function, digestion, and sleep [1,2]. Standing has also been shown to significantly improve perceived quality-of-life, further suggesting that such assistive technologies could be beneficial psychologically as well as physically [2, 3]. Active standing achieved by contracting the otherwise paralyzed muscles with neuroprostheses (NPs) utilizing electrical stimulation (ES) should have similar or enhanced physiological effects [4]. In addition to the health benefits and improved quality-of-life offered by standing with conventional interventions, standing with stimulation also exercises the large lower extremity (LE) muscles and offers the potential to negotiate architectural barriers and access objects or physical locations not normally available to wheelchair or standing frame users [5].

NPs for standing after SCI have been under investigation since the 1970s, and numerous systems employing surface or implanted electrodes have been reported [6-9], and a variety of electrode types and implant locations have been deployed to achieve functional LE movements [10,11]. Recently, four participants with motor-complete SCI achieved full weight-bearing standing after 80 training sessions with epidural lumbosacral spinal cord stimulation delivered by commercially available implanted technology [12]. In another study, four non-functional ambulators with incomplete SCI received an implanted NP consisting of femoral nerve electrodes for locomotor training as part of a NP to control bladder dysfunction via stimulation of the pelvic/sacral/pudendal nerves [13]. All participants could perform voluntary weight-bearing and walk at least 10m using the implanted NP and a walker after 17 months of treatment. Activating the quadriceps and

biceps femoris with surface stimulation was also shown to reduce arm forces during sit-to-stand transfers for six individuals with chronic SCI [14]. Similarly, stimulation-assisted treadmill walking therapy using 8-channels of surface stimulation was shown to be equally effective as an aerobic and resistance training program at improving the spinal cord independence measure (SCIM) mobility sub-score at 12-month follow-up [15].

In spite of their potential to impact health and daily function after SCI, the long-term (LT) effects of LE NPs have yet to be fully quantified, and most reports describe only acute effects of stimulation after a prescribed intervention period. Our group previously published a longitudinal study of the performance of an implanted NP for standing after SCI in 15 participants approximately one-year post-discharge to home-use with the system [16]. This article extends that study to report what is potentially the largest cohort (22) and longest follow-up interval (averaging > 6 years) of implanted LE NPs, encompassing both first-generation 8-channel systems employing epimysial electrodes [17-19] and second-generation 16-channel systems utilizing intramuscular and nerve cuff electrodes [20-24] (Figure 1).

We hypothesized that a) quantifiable measures of clinical performance (knee extension strength, maximum standing time and body weight supported by LEs) and functional abilities with the system would remain unchanged from discharge, b) users would express satisfaction with the neurotechnology at LT follow-up, c) patterns of NP usage would be consistent with original measures, and d) implanted components would be reliable and stimulus thresholds would remain stable over time.

Methods

Participants

Nineteen male and three female subjects with SCI (levels C5-T11, AIS A-D) resulting in full or partial paralysis participated in the study (Table 1). Participants were LT recipients of implanted NPs for exercise and standing (19) [16,25-28], walking (2) [29-31], or seated stability (1) [32]. After Institution Review Board approval at the Louis Stokes Cleveland Veterans Affairs Medical Center, 26 eligible implant recipients (3 declined participation and 1 was lost to follow-up) from a variety of previous protocols were invited to participate in a 1-4-day data collection session. Informed consent was obtained, including allowing identifiable photos and linked medical diagnoses to be used in scientific publications, before starting study activities. Due to variations in implanted components and capabilities based on prior study enrollment, not all participants completed all tests (Table 2). The group was 14.4 ± 7.1 years post-injury and 6.2 ± 2.7 years post-rehabilitation and discharge to home-use with the system at evaluation, with minimum and maximum follow-up ranging from 2 to almost 14 years.

Outcome Measures

Knee Extension Strength—Stimulated knee extension moment was measured with a Biodex Pro System 3 dynamometer (Shirley NY) for 16 participants (32 legs). Stimulus pulse duration and current amplitude for typical exercise, standing or walking with the

implanted systems were applied to the quadriceps at a frequency of 30Hz to fully extend the knee from approximately 90° of flexion at 30°/s. The peak moments from five repetitions separated by 15s rest were averaged to calculate knee extension strength for each participant.

Maximum Standing Time—Thirteen participants stood for as long as possible with implanted stimulation to the knee, hip, and trunk extensors, with instructions to use their upper extremities (UEs) only as needed for balance. Maximum standing times and stated reasons for ending the test were recorded. Tests were usually terminated by the participant, but could be ended by the research physical therapist for participant safety (i.e. knee buckling) or upon reaching an upper limit of 60 minutes of elapsed standing.

Body Weight Supported by Lower Extremities—The same 13 participants stood quietly one foot on each force plate (AMTI, Waltham MA) in a standard walker, which did not interfere with the force plate recordings, while using the UEs as needed for balance to measure mean weight supported by the LEs over the initial 30s of steady-state standing. Percentage of body weight (%BW) supported by the LEs was calculated by dividing the weight on the force plates by the participant's total weight.

Functional Tasks—Three functional tasks were tested: standing, standing to retrieve an object from an overhead shelf, and performing a standing pivot transfer (Figure 2). Fifteen participants attempted all or some of these maneuvers and the tasks were marked as completed if performed independently or with stand-by-assistance.

Satisfaction—Seventeen participants completed the Quebec User Evaluation of Satisfaction with assistive Technology (QUEST) [33], which rates both device characteristics and service delivery on a scale from 1 (not satisfied at all) to 5 (very satisfied). Participants additionally listed their 3 most important satisfaction items. Four of the remaining six participants did not complete the questionnaire because it was not a part of their prior study protocol.

A custom, standardized, User Questionnaire [34] was administered to determine how 18 implant recipients perceived their experiences with the NP, including subjective assessments of impact on health, via a scale from -3 (much worse or very dissatisfied) to +3 (much better or very satisfied). If a participant did not answer a portion of the questionnaire appropriately, the affected questions were not included in the group summary. Four of the remaining five participants did not complete the questionnaire because it was not a part of their prior study protocol.

Usage—External control units of the NPs automatically recorded (to internal memory) the type and duration of usage by the participants. Usage logs were downloaded during follow-up visits for 19 of the participating participants, and analyzed over the 90-day period that preceded the visit by 90 days. Participants had been informed that usage was being monitored, but they were unaware of the period being examined. Number of days the NP was used was tallied, as well as number of hours spent performing strength- or endurance-building exercise and doing functional tasks like standing, walking, wheelchair propulsion,

and transferring with the NP. For the remaining 3 participants, usage data was not retrievable for this specific monitoring period.

Stability of Implanted Components—For all 22 participants, the lowest stimulus intensity, or threshold, that elicited a twitch response was recorded at study intervals for all electrodes. Following Triolo et al 2012 [16], stable electrodes were defined as those exhibiting small changes in threshold over time (<4% of the maximum charge deliverable by the NP), while moderate (4-20%) and large (>20%) increases indicated less stability, although they were still intact and functional. In cases when an electrode was surgically replaced between the study intervals due to mechanical failure or poor functional response, the discharge date for just that electrode was adjusted based on the revision surgery date.

For all 22 participants, the number of implanted pulse generators (IPGs) and electrodes that were operational at discharge to home-use and still operational at the most recent follow-up visit were used to calculate survival rate. When available due to other study visits with the participants, component survival was recorded even more recently than the official LT visit in order to capture the most current information.

Statistics—To address the previously stated hypotheses, parametric data (knee extension strength, maximum standing time, body weight supported by LEs) were checked for normal distribution with Q-Q plots and 2-tailed paired samples t-tests ($\alpha=0.05$, $\beta=0.20$) were run to compare performance at discharge to home-use to that observed at the LT visit. Wilcoxon signed-rank tests were applied for non-parametric data (User Questionnaire) to determine if they were significantly different than zero (no change). The Kaplan-Meier method was used to determine the probability of survival of the implanted components.

Results

Knee Extension Strength

Knee extension strength was 0.54 ± 0.31 Nm/kg for the group of 16 participants (32 legs) at LT follow-up. For the 11 participants (22 legs) with data at discharge to home use (0.53 ± 0.26 Nm/kg), knee extension strength was maintained without change ($p=0.761$) at the LT visit (0.51 ± 0.36 Nm/kg).

Maximum Standing Time

The group of 13 participants exhibited an average maximum standing time of 10.8 ± 17.6 minutes at LT follow-up. Nine participants (69%) stood 1-5 minutes while four participants (31%) stood 10-60 minutes. Although maximum standing times decreased ($p=0.013$) from discharge (28.1 ± 24.7 minutes), all participants could still stand for greater than one minute, which is sufficient time to perform a standing pivot transfer.

Body Weight Supported by Lower Extremities

An average of 78.4 ± 16.9 %BW was supported by the LEs during standing for the group of 13 participants. For the six participants with paired data from discharge (89.3 ± 10.2 %BW), a decrease ($p=0.043$) was observed at the LT visit (75.9 ± 21.4 %BW).

Functional Tasks

For a subset of 15 participants, 14 could stand, 5 of 6 could stand to retrieve an object from overhead, and 9 of 12 could perform a standing pivot transfer independently or with stand-by assistance at LT, using a walker for UE balance. Twenty-eight of the 32 tasks (87.5%) tested at discharge were maintained at LT.

Satisfaction

The group of 17 participants who completed the QUEST were “quite satisfied” (score of 4) with the device as evidenced by a mean rating of 3.88 ± 0.77 (median = 3.88), and “very satisfied” (score of 5) with the service received as indicated by a mean rating of 4.54 ± 0.67 (median = 5.00). Overall, implant recipients appeared to be “quite satisfied” with the total experience (4.08 ± 0.65 , median = 4.17). The 3 most important satisfaction items (and number of subjects listing them) were: “easy to use” (11), “effectiveness” (8), and “professional service” (5).

In the User Questionnaire, 18 participants rated their overall health and frequency (decrease) of spasms as “somewhat better” (score of +2, $p = 0.003$) because of using the NP, while the severity of spasms, frequency of urinary tract infections, and number of pressure sores were unchanged (score of 0).

Fourteen of 18 (78%) said the NP lived up to their expectations, 15 of 18 (83%) said they would go through the same process again for the same result, and 17 of 18 (94%) said they would recommend the experience to others. These feelings led to 15 of 16 (94%) being either “very satisfied” (score = +3, 10 participants) or “moderately satisfied” (score = +2, 5 participants) with the NP ($p < 0.001$). Of 16 respondents, 8 (50%) said they would most like to use their NP for standing or walking, although 14 (88%) reported using it most often for exercise.

Usage

As shown in Table 3, 19 participants used their implanted systems during 43 ± 31 (median = 44) days of the 90-day monitoring period (48% of the days surveyed). On average, it was used twice as much for exercise as for functional tasks. Specifically, one-fifth of the participants (4/19) used the system for less than 10% of the days, one-fifth (4/19) used it for ~20-30% of the days and three-fifths (11/19) used it for ~50% or more of the days. On average, more than three-fifths of the participants (12/19) used the system for more than 10 minutes per day and the median daily usage across the group was 17 minutes. Of the 18 participants with non-zero usage, 13 (72%) spent the majority (80%) of their time exercising and three (17%) spent almost their entire time (98%) performing functional tasks. Only 2 (11%) divided their time more equally between exercising and functional tasks (in a 2-to-1 ratio).

Stability of Implanted Components

For the group of 22 participants, the majority of electrodes were stable over the six years with 81.4% exhibiting low changes in threshold, and only 18.1% exhibiting moderate changes, between discharge to home-use and LT visit (Figure 3). For all 22 participants, at

least 80% of all devices survived through 7.9 ± 3.4 (median = 7.4) years of unsupervised home and community use (Table 4). Furthermore, the predicted probability of device survival after six years was 87.1% for first-generation 8-channel IPG, 89.8% for epimysial electrodes, and 98.6% for intramuscular electrodes. No failures occurred during the study interval for the second-generation 16-channel IPG or nerve cuff electrodes.

Discussion

The NP produced sufficient knee, hip and trunk extension moment for independent standing. Average knee extension strength (0.54 ± 0.31 Nm/kg) far exceeded the 0.14 Nm/kg per leg required for standing as defined in prior analyses [35]. Additionally, the majority of body weight (78.4 ± 16.9 %BW) was transmitted through the legs, which was comparable to the 76 ± 7 %BW measured when 11 participants used a standing frame with their arms on the tray [36].

Although maximum standing times varied (1/3 of participants could stand for >10 minutes while 2/3 could stand for <5 minutes), 14 of 15 participants could stand independently or with stand-by assistance for at least one minute. This was sufficient to allow participants to perform functional tasks like retrieving an object from overhead (ex: extract an item from a kitchen cabinet) and performing a standing pivot transfer (ex: transfer to a restaurant booth or car) with their implanted systems. These results supported Hypothesis A that measures of clinical performance would be comparable from discharge to LT.

Implanted components were stable with the large majority exhibiting low changes in thresholds and high survivability across the six-year period of home-use, supporting Hypothesis D. This is consistent with previous reports of the stability of all eight electrodes in one participant with an UE NP utilizing the same technology after nine years [37]. Although survivability of 238 electrodes in 28 UE NPs users (98.3% over 7.1-year follow-up) [38] was slightly higher than our results (93.4% at 6 7.9 years), the observed differences may be due to the additional stresses and shear forces applied to electrodes and surrounding tissues while sitting or performing sliding transfers in LE NP recipients.

These survivability results compare favorably to similarly constructed electrodes and IPGs utilized for deep brain stimulation (DBS), spinal cord stimulation (SCS), and implantable defibrillators. Technical malfunctions (short circuits, disconnections, or loose contacts) were found in 3.2% of electrodes implanted in 591 patients with DBS systems, which generally occurred immediately after implant or revision [39]. A similar study of 153 patients (298 electrodes) with 64 ± 36 month follow-up reported two malfunctions of the IPG (1.4%) and no lead fractures [39]. Of 527 recipients of implanted SCS systems with an average follow-up of 3.4 years, connector failures and lead breakage occurred in 9.5% and 6%, respectively [41]. In a recent review of SCS safety, the incidence of electrode failure was 3-9%, while lead and IPG failures were less frequent (2-5%) [42]. Finally, a large retrospective study reviewing 4078 defibrillator leads from three different manufactures implanted in 3802 patients identified only 3.5% known lead failures during the 15.6 year implant period [43]. While our first generation 8-channel IPG with epimysial electrodes had higher failure rates (20.0% and 14.7%) than those reported for similar components in these commercial devices,

later systems utilizing intramuscular electrodes, our second-generation 16-channel IPG and nerve cuff electrodes performed much better (<2%). This level of survivability is encouraging given the additional loads placed on leads of LE motor system NPs due to the large muscle forces and angular motions of the hip, knee and ankle joints during sit-to-stand or stand-to-sit.

Satisfaction and appropriateness have been correlated to continued use of mobility devices [44]. Both the QUEST and User Questionnaire ratings demonstrated that NP recipients were satisfied with the devices they received, supporting Hypothesis B. Recorded usage logs supported the system satisfaction findings with 58% of participants using their NP nearly half or more of the days monitored, which was comparable to prior work [16] where 42% of participants (5/12) used their NP on at least 12 days of the 28-day monitoring period (43%), confirming Hypothesis C. These patterns of usage were comparable to a group of 65 first-generation UE NP recipients [45], in which 37 (56%) reported “regular use” of their UE NP at 8-13 years post-implant. Because this study utilized similar components, continued usage of the LE NPs demonstrates that this type of implanted technology may be a viable clinical option. Although a majority of the training and testing with the NPs pre-discharge focused on functional tasks like standing and walking, usage patterns shifted toward more exercise during the intervening years of unsupervised home-use. This continued use demonstrated the value participants placed on both the exercise and function the NPs provided.

These LT results confirm and extend those previously presented for one-year follow-up of 15 implanted NP recipients for standing [16], but over a longer time of home-use and in a more heterogeneous population including NP systems designed for trunk control or walking and participants with motor-incomplete SCI. Many of the outcome measures are the same between manuscripts, providing continuity. The same implanted technologies have also shown to have significant therapeutic effects when incorporated into programs of overground gait training for persons with partial paralysis due to multiple sclerosis [46], incomplete SCI [47] and chronic hemiplegia [48]. Similarly, stimulation from implanted systems appears to be an effective means of exercise and can result in improved muscle strength, decreased muscle atrophy, and assist with spasm management [49].

Study Limitations

One limitation of this study is lack of complete data sets from all 22 participants. Data collection was not uniform because certain measures may not have been required by original study protocols or were inappropriate for a participant's level of impairment or ability to complete testing. For each of the measures, however, at least 59% of the group completed the assessment at LT follow-up. Furthermore, component survivability and stability data were available for all participants and usage data were recorded for 19 participants, demonstrating continued operation and value for an average of 6 years home-use. Injury level (C5-T11), time post-injury (6-29 years), and time at home with the NP (2-14 years) also varied for the cohort, along with the frequency of NP use (0-100% days). Effects of these factors on the results were not formally quantified, but no obvious trends were evident. With 32% of the participants utilizing the NP an average of 30+ minutes per day during the monitoring period, there is a limited ability to compare using this NP to the health effects of

standing 30 minutes per day in a passive device like a standing frame [2]. The external control unit is not capable of recording the context for each system usage, so it is not possible to know why the subject chose to use the NP at that time. Additionally, the effects of stimulation on bone density, muscle atrophy, bowel and bladder function, quality-of-life and societal participation were not measured, which would be important information for physicians treating SCI and should be the focus of future studies.

Future Work

Continuous technology advancements will contribute to additional NP function and reduce reliance on UEs, while translation of technologies to other etiologies (i.e., stroke, AVM, MS) will strengthen the field of LE NPs. We hypothesize the incorporation of more engaging exercise modalities, such as overground biking or utilization of commercial exercise equipment, will help maintain LT NP use. In addition to the physical and psycho-social benefits of LE NP usage, we will continue to enhance the technology and explore how NPs can be incorporated into more aspects of daily life. We would like to add to our bank of LT users and increase the follow-up duration.

Conclusions

Objective and subjective measures of the technical and clinical performance of implanted LE NPs generally remained consistent for 22 participants after an average of six years of unsupervised use at home. Stimulated knee extension strength and functional capabilities were maintained, and 94% of implant recipients reported being “very” or “moderately” satisfied, would repeat the experience and recommend it to a friend, and felt it improved overall health. Over three-fifths of the participants were still using their implanted NPs for exercise and function more than 10 minutes per day on nearly half or more of the days monitored, although maximum standing times and percentage body weight through Les decreased slightly over the average 6-year follow-up interval. Stimulus thresholds were uniformly stable, and 7.9-year survival rates for first-generation IPG and epimysial electrodes were close to 90% while those for second-generation IPG, intramuscular and nerve cuff electrodes were greater than 98%. These findings suggest that implanted LE NPs can provide lasting benefits that recipients value.

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References

1. Eng JJ, Levins SM, Townson AF, Mah-Jones D, Bremner J, Huston G. Use of prolonged standing for individuals with spinal cord injuries. *Phys Ther.* 2001; 81(8):1392–9. [PubMed: 11509069]
2. Walter JS, Sola PG, Sacks J, Lucero Y, Langbein E, Weaver F. Indications for a home standing program for individuals with spinal cord injury. *J Spinal Cord Med.* 1999; 22(3):152–8. [PubMed: 10685379]

3. Gallien P, Brissot R, Eyssette M, Tell L, Barat M, Wiart L, Petit H. Restoration of gait by functional electrical stimulation for spinal cord injured patients. *Paraplegia*. 1995; 33(11):660–4. [PubMed: 8584301]
4. Nightingale EJ, Raymond J, Middleton JW, Crosbie J, Davis GM. Benefits of FES gait in a spinal cord injured population. *Spinal Cord*. 2007; 45(10):646–57. [PubMed: 17646840]
5. Ragnarsson KT. Functional electrical stimulation after spinal cord injury: current use, therapeutic effects and future directions. *Spinal Cord*. 2008; 46(4):255–74. [PubMed: 17846639]
6. Creasey GH, Ho CH, Triolo RJ, Gater DR, DiMarco AF, Bogie KM, Keith MW. Clinical applications of electrical stimulation after spinal cord injury. *J Spinal Cord Med*. 2004; 27(4):365–75. [PubMed: 15484667]
7. Peckham PH, Creasey GH. Neural prostheses: clinical applications of functional electrical stimulation in spinal cord injury. *Paraplegia*. 1992; 30(2):96–101. [PubMed: 1589297]
8. Kralj A, Bajd T, Turk R. Electrical stimulation providing functional use of paraplegic patient muscles. *Med Prog Technol*. 1980; 7(1):3–9. [PubMed: 6966735]
9. Kralj A, Vodovnik L. Functional electrical stimulation of the extremities: part 1. *J Med Eng Technol*. 1977; 1(1):12–15. [PubMed: 300109]
10. Ho CH, Triolo RJ, Elias AL, Kilgore KL, DiMarco AF, Bogie K, Vette AH, Audu ML, Kobetic R, Chang SR, Chan KM, Dukelow S, Bourbeau DJ, Brose SW, Gustafson KJ, Kiss ZH, Mushahwar VK. Functional electrical stimulation and spinal cord injury. *Phys Med Rehabil Clin N Am*. 2014; 25(3):631–54. [PubMed: 25064792]
11. Sheffler LR, Chae J. Neuromuscular electrical stimulation in neurorehabilitation. *Muscle Nerve*. 2007; 35(5):562–90. [PubMed: 17299744]
12. Rejc E, Angeli C, Harkema S. Effects of lumbosacral spinal cord epidural stimulation for standing after chronic complete paralysis in humans. *PLoS ONE*. 2015; 10(7):e0133998. [PubMed: 26207623]
13. Possover M. Recovery of sensory and supraspinal control of leg movement in people with chronic paraplegia: a case series. *Arch Phys Med Rehabil*. 2014; 95(4):610–4. [PubMed: 24269993]
14. Jovic J, Azevedo Coste C, Fraisse P, Henkous S, Fattal C. Coordinating Upper and Lower Body During FES-Assisted Transfers in Persons With Spinal Cord Injury in Order to Reduce Arm Support. *Neuromodulation*. 2015; 18(8):736–43. [PubMed: 25917248]
15. Kapadia N, Masani K, Catharine Craven B, Giangregorio LM, Hitzig SL, Richards K, Popovic MR. A randomized trial of functional electrical stimulation for walking in incomplete spinal cord injury: Effects on walking competency. *J Spinal Cord Med*. 2014; 37(5):511–24. [PubMed: 25229735]
16. Triolo RJ, Bailey SN, Miller ME, Rohde LM, Anderson JS, Davis JA Jr, Abbas JJ, DiPonio LA, Forrest GP, Gater DR Jr, Yang LJ. Longitudinal performance of a surgically implanted neuroprosthesis for lower-extremity exercise, standing, and transfers after spinal cord injury. *Arch Phys Med Rehabil*. 2012; 93(5):896–904. [PubMed: 22541312]
17. Uhlir JP, Triolo RJ, Davis JA, Bieri C. Performance of epimysial stimulating electrodes in the lower extremities of individuals with spinal cord injury. *IEEE Trans Rehabil Eng*. 2004; 12:279–87.
18. Davis JA, Triolo RJ, Uhlir JP, et al. Surgical technique for installing an 8-channel neuroprosthesis for standing. *Clin Orthop Rel Res*. 2001; (385):237–52.
19. Smith B, Peckham PH, Keith MW, Roscoe DD. An externally powered, multichannel, implantable stimulator for versatile control of paralyzed muscle. *IEEE Trans Biomed Eng*. 1987; 34(7):499–508. [PubMed: 3610200]
20. Hart RL, Bhadra N, Montague FW, Kilgore KL, Peckham PH. Design and testing of an advanced implantable neuroprosthesis with myoelectric control. *IEEE Trans Neural Syst Rehabil Eng*. 2011; 19(1):45–53. [PubMed: 20876029]
21. Fisher LE, Tyler DJ, Anderson JS, Triolo RJ. Chronic stability and selectivity of four contact spiral nerve-cuff electrodes in stimulating the human femoral nerve. *J Neural Eng*. 2009; 6(4):046010. [PubMed: 19602729]

22. Fisher LE, Miller ME, Bailey SN, Davis JA Jr, Anderson JS, Rhode L, Tyler DJ, Triolo RJ. Standing after spinal cord injury with four-contact nerve-cuff electrodes for quadriceps stimulation. *IEEE Trans Neural Syst Rehabil Eng*. 2008; 16(5):473–8. [PubMed: 18990650]
23. Smith B, Tang Z, Johnson MW, Pourmehdi S, Gazdik MM, Buckett JR, Peckham PH. An externally powered, multichannel, implantable stimulator-telemeter for control of paralyzed muscle. *IEEE Trans Biomed Eng*. 1998; 45(4):463–75. [PubMed: 9556963]
24. Memberg WD, Peckham PH, Keith MW. A surgically-implanted intramuscular electrode for an implantable neuromuscular stimulation system. *IEEE Trans Biomed Eng*. 1994; 2:80–91.
25. Fisher LE, Tyler DJ, Triolo RJ. Optimization of selective stimulation parameters for multi-contact electrodes. *J Neuroeng Rehabil*. 2013; 10:25. [PubMed: 23442372]
26. Nataraj R, Audu ML, Triolo RJ. Comparing joint kinematics and center of mass acceleration as feedback for control of standing balance by functional neuromuscular stimulation. *J Neuroeng Rehabil*. 2012; 9:25. [PubMed: 22559852]
27. Mushahwar VK, Jacobs PL, Normann RA, Triolo RJ, Kleitman N. New functional electrical stimulation approaches to standing and walking. *J Neural Eng*. 2007; 4(3):S181–97. [PubMed: 17873417]
28. Davis JA Jr, Triolo RJ, Uhler J, Bieri C, Rohde L, Lissy D, Kukke S. Preliminary performance of a surgically implanted neuroprosthesis for standing and transfers--where do we stand? *J Rehabil Res Dev*. 2001; 38(6):609–17. [PubMed: 11767968]
29. Foglyano KM, Schnellenger JR, Kobetic R. Development of a self-contained accelerometry based system for control of functional electrical stimulation in hemiplegia. *Conf Proc IEEE Eng Med Biol Soc*. 2011; 2011:5448–51. [PubMed: 22255570]
30. Dutta A, Kobetic R, Triolo RJ. Gait initiation with electromyographically triggered electrical stimulation in people with partial paralysis. *J Biomech Eng*. 2009; 131(8):081002. [PubMed: 19604014]
31. Hardin E, Kobetic R, Murray L, Corado-Ahmed M, Pinault G, Sakai J, Bailey SN, Ho C, Triolo RJ. Walking after incomplete spinal cord injury using an implanted FES system: a case report. *J Rehabil Res Dev*. 2007; 44(3):333–46. [PubMed: 18247230]
32. Triolo RJ, Boggs L, Miller ME, Nemunaitis G, Nagy J, Bailey SN. Implanted electrical stimulation of the trunk for seated postural stability and function after cervical spinal cord injury: a single case study. *Arch Phys Med Rehabil*. 2009; 90(2):340–7. [PubMed: 19236990]
33. Demers L, Weiss-Lambrou R, Ska B. Item analysis of the Quebec User Evaluation of Satisfaction with Assistive Technology (QUEST). *Assist Technol*. 2000; 12(2):96–105. [PubMed: 11508406]
34. Agarwal S, Triolo RJ, Kobetic R, Miller M, Bieri C, Kukke S, Rohde L, Davis JA Jr. Long-term user perceptions of an implanted neuroprosthesis for exercise, standing, and transfers after spinal cord injury. *J Rehabil Res Dev*. 2003; 40(3):241–52. [PubMed: 14582528]
35. Kagaya H, Sharma M, Kobetic R, Marsolais EB. Ankle, knee, and hip moments during standing with and without joint contractures: simulation study for functional electrical stimulation. *Am J Phys Med Rehabil*. 1998; 77:49–54. [PubMed: 9482379]
36. Bernhardt KA, Beck LA, Lamb JL, Kaufman KR, Amin S, Wuermser LA. Weight bearing through lower limbs in a standing frame with and without arm support and low-magnitude whole body vibration in men and women with complete motor paraplegia. *Am J Phys Med Rehabil*. 2012; 91(4):300–8. [PubMed: 22407161]
37. Kilgore KL, Peckham PH, Keith MW, Thrope GB, Wuolle KS, Bryden AM, Hart RL. An implanted upper-extremity neuroprosthesis. Follow-up of five patients. *J Bone Joint Surg Am*. 1997; 79(4):533–41. [PubMed: 9111397]
38. Kilgore KL, Peckham PH, Keith MW, Montague FW, Hart RL, Gazdik MM, Bryden AM, Snyder SA, Stage TG. Durability of implanted electrodes and leads in an upper-limb neuroprosthesis. *J Rehabil Res Dev*. 2003; 40(6):457–68. [PubMed: 15077658]
39. Allert N, Markou M, Miskiewicz AA, Nolden L, Karbe H. Electrode dysfunctions in patients with deep brain stimulation: a clinical retrospective study. *Acta Neurochir*. 2011; 153(12):2343–9. [PubMed: 21989778]
40. Doshi PK. Long-term surgical and hardware-related complications of deep brain stimulation. *Stereotact Funct Neurosurg*. 2011; 89(2):89–95. [PubMed: 21293168]

41. Mekhail NA, Mathews M, Nageeb F, Guirguis M, Mekhail MN, Cheng J. Retrospective review of 707 cases of spinal cord stimulation: indications and complications. *Pain Pract.* 2011; 11(2):148–53. [PubMed: 21371254]
42. Bendersky D, Yampolsky C. Is spinal cord stimulation safe? A review of its complications. *World Neurosurg.* 2014; 82(6):1359–68. [PubMed: 23851231]
43. Cohen TJ, Asheld WJ, Germano J, Islam S, Patel D. A Comparative Study of Defibrillator Leads at a Large-Volume Implanting Hospital: Results from the Pacemaker and Implantable Defibrillator Leads Survival Study (“PAIDLESS”). *J Invasive Cardiol.* 2015; 27(6):292–300. [PubMed: 26028656]
44. Samuelsson K, Wressle E. User satisfaction with mobility assistive devices: an important element in the rehabilitation process. *Disabil Rehabil.* 2008; 30(7):551–8. [PubMed: 17852301]
45. Kilgore KL, Peckham P, Keith MW. Twenty-year experience with implanted neuroprostheses. *Conf Proc IEEE Eng Med Biol Soc.* 2009; 2009:7212–5. [PubMed: 19965280]
46. Selkirk SM, Kobetic R, Lombardo LM, Pinault G, Triolo RJ. Feasibility of Restoring Walking in Multiple Sclerosis with Multichannel Implanted Electrical Stimulation. *Am J Phys Med Rehabil.* 2017 Epub ahead of print.
47. Bailey SN, Hardin EC, Kobetic R, Boggs LM, Pinault G, Triolo RJ. Neurotherapeutic and neuroprosthetic effects of implanted functional electrical stimulation for ambulation after incomplete spinal cord injury. *J Rehabil Res Dev.* 2010; 47(1):7–16. [PubMed: 20437323]
48. Makowski NS, Kobetic R, Lombardo LM, Foglyano KM, Pinault G, Selkirk SM, Triolo RJ. Improving walking with an implanted neuroprosthesis for hip, knee, and ankle control after stroke. *Am J Phys Med Rehabil.* 2016; 95(12):880–888. [PubMed: 27231842]
49. Hamid S, Hayek R. Role of electrical stimulation for rehabilitation and regeneration after spinal cord injury: an overview. *Eur Spine J.* 2008; 17(9):1256–69. [PubMed: 18677518]

Abbreviations

DBS	deep brain stimulation
ES	electrical stimulation
IPG	implanted pulse generator
LT	long-term
LE	lower extremity
NP	neuroprosthesis
%BW	percent body weight
QUEST	Quebec User Evaluation of Satisfaction with assistive Technology
SCI	spinal cord injury
SCS	spinal cord stimulation
UE	upper extremity

Figure 1. NP system components. (Note that panels are not to the same scale.) (a) External control unit, fingerswitch, and transmitting coil.* (b) Implanted pulse generator. (c) Intramuscular, nerve cuff, and epimysial electrodes. * Photo credit: Nathaniel Welch.

Figure 2.

Three functional tasks were tested: standing (a), standing to retrieving an object from an overhead shelf (b), and performing a standing pivot transfer (c). Additionally, 3 participants with incomplete SCI could walk using their NP (d).

Figure 3.
Stability of electrodes from 22 participants in terms of increases of muscle activation threshold at LT follow-up.

Table 1

Demographics table for the 22 study subjects.

Original Study Purpose	Study ID	Gender	Level	AIS	Injury to follow-up (years)	Home usage (years)
Trunk Control	S01	Male	C5	A	29.33	6.71
	S02	Male	C5-6	C	18.15	5.74
Standing	S03	Male	C6	A	8.03	5.24
	S04	Male	C6	C	15.75	7.93
	S05	Male	C7	B	11.95	8.83
	S06	Female	C7	C	16.03	2.52
	S07	Female	C7	C	8.32	6.25
	S08	Male	T4	A	22.78	5.31
	S09	Male	T4	A	13.50	5.56
	S10	Male	T4	A	12.09	7.37
	S11	Male	T5	A	20.09	4.81
	S12	Male	T5	B	26.56	8.63
	S13	Male	T5/6	A	27.07	10.06
	S14	Female	T5/6	B	9.89	4.99
	S15	Male	T6	A	15.23	7.07
	S16	Male	T6	A	5.61	2.37
	S17	Male	T6	B	7.85	3.44
	S18	Male	T8	A	15.78	13.89
	S19	Male	T8	A	9.16	5.86
	S20	Male	T11	B	6.34	2.04
Walking	S21	Male	C6	C	9.30	7.19
	S22	Male	C6	D	8.20	3.87
Mean					14.41	6.17
SD					7.05	2.74

AIS = American Spinal Injury Association Impairment Scale

Table 2

Completed tests for all 22 subjects.

Study Type	Subject ID	Knee Strength		Max Stand Time		BW Distribution		Functional Tasks		QUEST	User Q	Usage Data	Stability	Survivability
		DC	LT	DC	LT	DC	LT	DC	LT					
Trunk Control	S01									✓	LT	✓	✓	✓
	S02		✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
	S03		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	S04									✓	✓		✓	✓
	S05	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓	✓
	S06		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	S07	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓
	S08	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓
	S09		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	S10									✓	✓	✓	✓	✓
	S11												✓	✓
	S12	✓	✓	✓		✓		✓	✓	✓	✓	✓	✓	✓
	S13	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	S14	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	S15	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	S16	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	S17												✓	✓
	S18	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	S19	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓
	S20	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	S21		✓							✓	✓	✓	✓	✓
	S22											✓	✓	✓
# of subjects	22	11	16	15	13	12	13	15	15	17	18	19	22	22

DC = discharge to home-use with the system, LT = long-term, BW = body weight, Q = questionnaire

✓ = data collected, blank = not collected, gray = test not part of prior protocol

(Due to variations in implanted components and capabilities based on prior study enrollment, not all subjects completed all tests.)

Table 3

Summary of usage data as recorded by the NP for 19 subjects during the 90-day period that preceded the follow-up visit by 90 days.

ID	Days used (out of 90)	Functional Task (hours)	Exercise (hours)
S01	2	1.2	0.0
S02	23	0.0	13.0
S03	44	2.6	49.6
S05	71	175.8	0.4
S06	88	47.4	94.1
S07	90	38.0	170.7
S08	8	0.0	4.0
S09	59	0.0	12.1
S10	0	0.0	0.0
S12	47	2.2	15.6
S13	42	0.0	24.9
S14	84	10.2	118.2
S15	28	0.0	26.3
S16	49	0.5	67.2
S18	4	0.0	1.3
S19	18	0.7	1.1
S20	76	29.5	0.5
S21	15	0.0	17.7
S22	76	6.9	31.8
Mean	43	17	34
SD	31	41	47
Median	44	1	16

Table 4

Survival of NP components for all subjects at the most recent follow-up.

<i>Numbers of devices</i>	Implanted Pulse Generators		Electrodes		
	16-channel	8-channel	NC	IM	EP
Operational at discharge	7	15	10	105	68
Still operational at most recent follow-up	7 (100.0%)	12 (80.0%)	10 (100.0%)	103 (98.1%)	58 (85.3%)

NC = nerve cuff electrode, IM = intramuscular electrode, EP = epinysial electrode