Original Article

Implantable FES system for upright mobility and bladder and bowel function for individuals with spinal cord injury

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Study design: Postintervention.

Objectives: To determine the effectiveness of the Praxis multifunctional implantable functional electrical stimulation (FES) system (Neopraxis Pty. Ltd, Lane Cove, NSW, Australia) to provide standing and stepping ability and bladder and bowel management for individuals with motor complete thoracic level spinal cord injuries (SCI).

Setting: Pediatric orthopedic hospital specializing in SCI.

Subjects: Three males, ages 17 and 21 years, with motor-complete thoracic level SCI and intact lower motor neurons to the muscles targeted for stimulation.

Methods: Each subject was successfully implanted with the Praxis FES system. All three subjects received electrodes for upright mobility and the first two subjects received additional electrodes for stimulated bladder and bowel management. Following training, subjects were evaluated in their ability to use FES for nine mobility activities. Acute and chronic experiments of the effect of stimulation on bowel and bladder function were also performed.

Results: All three subjects could independently stand up from the wheelchair and could walk at least 6 m using a swing through gait pattern. Two subjects were able to independently perform swing through gait for 6 min and one subject was able to independently ascend and descend stairs. Suppression of reflex bladder contractions by neuromodulation (subject 1) and stimulated contractions of the rectum (subject 2) were observed in acute experiments. When stimulation was applied over the course of several weeks, a positive effect on bowel function was measured. Stimulated bladder contractions were not achieved.

Conclusion: The feasibility of using the Praxis FES system for upright mobility and aiding aspects of bladder and bowel function was demonstrated with three subjects with thoracic level SCI.

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Introduction

For the population with spinal cord injury (SCI), functional electrical stimulation (FES) has been shown to be effective for several clinical applications such as upper or lower limb motions, bladder function, and respiratory pacing. An FES device capable of providing multiple functions may decrease the amount of implanted material, reduce surgical time and the number of

surgical procedures, and allow for easy coordination between stimulated functions.

The Praxis system (Cochlear Ltd, Lane Cove, NSW, Australia) was developed to provide standing and stepping function as well as enhanced bladder and bowel management for individuals with thoracic level SCI. Initial development of the device included only mobility functions. In 1991, the initial device, the Nucleus FES-22, was implanted in a 21-year-old male with paraplegia. In the laboratory, this subject was able

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to stand continuously for up to 60 min using Andrew's floor reaction orthoses and knee joint angle feedback to economize the level of stimulation.¹ A later version of the device, the FES 24-A, included channels for stimulated bladder and bowel function. It was implanted in a 35-year-old male with paraplegia in 1998. The subject was able to perform one handed reaching tasks while standing with closed loop stimulation. Pulsatile stimulation to the S3 and S4 nerve roots produced bladder contractions and voiding.¹ Further technical modifications were made to the device leading to the development of the current Praxis system.²

The main aim of this study was to determine the effectiveness of the Praxis multifunctional implantable FES system to provide standing and stepping ability and bladder and bowel management for individuals with motor complete thoracic level SCI.

Methods

Subjects

Three males between the ages of 17 and 21 years with motor-complete thoracic level SCI (T3–T8) of 1–1.5 years duration participated in the study. All three subjects had intact peripheral nerves associated with the targeted lower extremity muscles. The two subjects who received electrodes for bowel and bladder function (subjects 1 and 2) exhibited hyper-reflexic bladders confirmed by cystometrography and used intermittent catheterization for bladder emptying. Subject 1 took anticholinergic medication to prevent urinary incontinence. All subjects and the parent of subject 1 received education about the study and signed the informed consent form approved by the governing Institutional Review Board.

Praxis stimulation system

The Praxis system² consists of a 22-channel implant stimulator, extension leads and epineural electrodes (Figure 1). The leads emanating from the stimulator are configured in three tresses: two tresses of nine leads each for stimulation of lower extremity muscles (Table 1) and one tress of four leads for stimulation for bladder and bowel function. A body-worn controller transcutaneously powers and controls the implanted stimulator via a magnetically held radio frequency transmit coil.

Current pulses produced by the implanted stimulator are transmitted to the appropriate electrodes via stretchable, insulated leads. The available stimulation parameters are 0.2–8 mA amplitude, 25–600 μ s pulse duration, and 2–500 Hz pulse frequency per channel. Subjects initiated stimulation for standing and walking through the use of push buttons on the walker. Up to five two-degree-of-freedom sensors can be hardwired to the controller to provide sagittal and coronal plane feedback concerning joint position, velocity, or acceleration. These sensors were not employed during this initial evaluation.

Figure 1 Illustration of the location of the implanted 22-channel stimulator, electrodes and leadwire pathways of the Praxis FES system

Table 1 Muscles implanted per channel of stimulation

Muscle(s)
Posterior adductor magnus
Biceps femoris – long head ^a or short head ^b
Gluteus maximus
Gluteus medius, minimus, and tensor fascia lata
Vastus lateralis and vastus intermedius
Vastus medialis and vastus lateralis
Tibialis anterior and extensor digitorum longus
Gastrocnemius, soleus, and flexor hallucis longus
Iliopsoas ^c

^aSubjects 1 and 2

^bSubject 3

^cSubjects 2 and 3

Surgical implantation procedure

Implantation of the electrodes and stimulator was accomplished in multiple surgical procedures (Figure 1). Placement of each electrode was determined intraoperatively after dissection to localize the branch of the nerve innervating the desired muscle(s). The identification of the appropriate nerve branch was confirmed by directly stimulating the nerve and observing the muscle response. The response was monitored in the desired muscles as well as muscles innervated by the same nerve trunk to attempt to avoid or minimize stimulation to distal muscles. Once the appropriate response was obtained, the electrode was secured to the tissue surrounding the nerve branch.

During the first procedure, the subject was positioned supine on the operating table. The stimulator was placed into the subcutaneous fascia of the left chest just superior to the costal margin and slightly lateral to the vertical nipple line. The extension leads (that connect the stimulator and electrode leads) were then passed subcutaneously from the stimulator to one of three connection points: two points, one for each leg, just above the iliac crest, for connections to the lower extremity electrodes and a third just below the costal margin and lateral to the placement of the stimulator for connections to the electrodes for bladder and bowel function. To facilitate the passing of the leads for the right leg iliac pocket (side opposite the stimulator), an intermediate incision was made in an area of the right upper abdomen. Epineural electrodes were then placed in proximity to branches of the femoral nerve to stimulate the vastus medialis, intermedius and lateralis. Electrode attachment to surrounding tissue was by suture and staple. For each leg, two stimulation channels were dedicated to recruiting the quadriceps muscles. In some instances, a channel was bifurcated such that the current was split between two electrodes in an effort to balance recruitment of the quadriceps muscles.

In subsequent procedures the subject was in a prone position. Electrodes were usually positioned in a proximal to distal order. Generally, the electrodes for gluteal muscle (gluteus maximus and medius) stimulation were placed followed by sciatic nerve (biceps femoris, adductor magnus), then the peroneal (tibialis anterior) and tibial nerves (gastrocnemius). For the latter two nerves, the electrodes were placed within the sciatic sheath proximal to the knee. Subjects 2 and 3 had electrodes placed for stimulation of the iliopsoas for hip flexion. For this procedure, the subject was placed in a lateral decubitus position and an approximately 8 cm incision was made on the lateral flank at the level of the intercostal space between ribs 11 and 12. Fluoroscopy was used to visualize the L2–L3 vertebrae and help guide electrode placement. Using blunt dissection, the iliopsoas muscle was identified and split, and the nerve branch between the vertebral bodies of L2 and L3 that innervates the muscle was identified and tested with stimulation to determine optimal electrode placement.

For subjects 1 and 2, linear paraspinal (LPR) electrodes for bladder and bowel stimulation were placed extradurally on the S2, S3 and S4 mixed nerve roots. For subject 1, electrodes were inserted bilaterally through the S2, S3 and S4 respective sacral foramina with the final position determined by the stimulated response and guidance from fluoroscopy. One stimulation channel was connected to the two electrodes at each sacral level via a bifurcated lead. For subject 2, a laminotomy was performed at S3 and S4 to visualize the sacral nerves for electrode placement. Electrodes were placed bilaterally at S3 and on the left side at S4. In this case, three stimulation channels were used, one to each electrode.

Stimulation and training for upright mobility

Upright mobility was achieved through either continuous stimulation to the lower extremities for standing and swing through gait or through alternating extension and flexion for reciprocal walking. Transitions between sitting and standing were achieved by ramping stimulation up or down. Swing through gait was achieved by continuous stimulation of the quadriceps muscles, gluteal muscles, adductor magnus, and biceps femoris. Subjects initiated standing and sitting with the use of push button switches attached to the assistive device or by touching the screen on the body worn controller. For reciprocal gait, swing of the leg was achieved through stimulation of one or two of the following muscles or nerves: the iliopsoas, the short head of the biceps femoris, and the peroneal nerve. Stimulation to the peroneal nerve can create a flexor withdrawal response in which a reflexive contraction of the hip and knee flexors and the ankle dorsiflexors occurs. This response can be used to create a step to initiate the swing phase of gait. Subjects initiated steps through the push button switches. Bilateral ankle foot orthoses were worn for all upright mobility activities.

At 4 weeks after surgical implantation of the lower extremity electrodes, each electrode was tested to determine its stimulation threshold (minimum) and saturation (maximum) levels. The saturation was determined for each muscle by increasing stimulation parameters until there was no further increase in isometric muscle force. Maximum isometric force was assessed for the quadriceps and hamstring muscles using an isokinetic dynamometer with the knee positioned in 20° of flexion to determine optimal stimulation levels and to allow determination of a strengthening effect after training. The remaining muscles were tested using manual muscle testing (MMT).

Prior to standing with FES, each subject participated in 20 sessions of stimulated lower extremity conditioning. Four strategies were performed (Table 2) 5 days per week for 4 weeks. The kicking strategy was performed with weights strapped around the ankle. The total amount of weight was increased in increments of 1 lb when the leg could move fully against gravity for all five sets with the current weight. After 2 weeks of conditioning, each subject began standing with FES in a supportive stander in addition to the exercise program to develop tolerance for standing with FES in preparation for the upright mobility phase of training. Following the conditioning phase, maximum isometric force was again assessed for the quadriceps and hamstring muscles.

Upright mobility training began after the completion of the exercise phase. Training during this period included programming of the upright mobility strategies and training on their functional use. Goals included achievement of transitions between sitting and standing, swing through and/or reciprocal gait with a walker or crutches, and prolonged standing. Additional training goals include advanced activities, such as ascending and descending stairs and achievement of subject specific goals (Figure 2).

Table 2 Exercises performed prior to initiating standing

Strategy	Muscles stimulated	Position	On time	Off time	Repetitions
Kicking	Quadriceps	Supine with knees in 30° flexion	9 s ^a	8 s	5 sets of 10 repetitions (2 min rest between sets)
Bridging	Gluteus medius & maximus, adductor magnus, biceps femoris	Supine with knees in 30° flexion	9 s ^a	8 s	5 sets of 10 repetitions (2 min rest between sets)
Dorsiflexion & Plantarflexion	Anterior tibialis, gastrocnemius (alternating)	Supine	6 s ^b	6 s	50 repetitions
Endurance	All implanted muscles	Supine	5 s ^b	3 s	675 (90 min total)

^aIncludes 2 s ramp up and 2 s ramp down times^bIncludes 1.5 s ramp up and 1.5 s ramp down times **Figure 2** A subject stands with the Praxis system to perform a functional activity

After completion of at least 13 weeks of training, data were collected for nine upright mobility activities (Table 3). The completion times and levels of independence, based upon the functional independence measure (FIM), were recorded. Three trials were collected for each activity. All activities were tested using continuous stimulation and each subject chose to perform the walking tests using a swing through gait pattern.

Measures of stimulation on bladder function

In tests to develop stimulated bladder contractions, approximately 250 ml of normal saline were infused into the bladder prior to the onset of stimulation. Instrumented catheters measured vesical, external urethral sphincter, rectal, and anal sphincter pressures. Detrusor pressure was calculated as the difference between vesical and rectal pressures. Efficacy was based on an ability to maximize detrusor pressure as stimulation parameters were varied. The effect of low- (20 Hz) and high- (500 Hz) frequency stimulation waveforms on external urethral sphincter pressure was also recorded.

To test acutely the effect of neuromodulation, the bladder was filled at a rate of 30 ml/min. Instrumented catheters in the bladder and rectum measured vesical and rectal pressures, respectively. Electrical stimulation was initiated at the onset of reflex bladder contractions and reductions in bladder pressure were noted. Different combinations of sacral nerve stimulation channels and various stimulation parameters were used to optimize the response. Neuromodulation was only conducted with subject 1 as subject 2 demonstrated a large bladder capacity (800–1200 ml) without the use of anticholinergic medication; therefore, neuromodulation to allow the bladder to fill to greater capacities would be unsafe for this subject.

The positive results of the acute modulation tests in subject 1 provided the basis for a multiweek study to assess the effect of chronic stimulation on bladder continence. Four conditions were considered:

- (1) On medication – This was the typical, preimplant bladder regiment: using anticholinergic medication (oxybutynin chloride 5 mg t.i.d.), no electrical stimulation, data collected for 7 days.
- (2) Off medication – Assess bladder management without the use of either medication or stimulation, evaluation initiated 4 days after medication discontinued, data collected for 7 days.
- (3) On ‘continuous’ neuromodulation – Stimulate whenever possible, approximately 18 h/day, data collected for 5 days.
- (4) On ‘night’ neuromodulation – Stimulate only overnight, approximately 7 h, data collected for 9 days.

The patient catheterized as needed and recorded the time of day, the volume obtained, and any occurrences of incontinence. Efficacy for each of the four conditions was based on maximizing the average time between successive catheterizations and minimizing the frequency of incontinence as well as dysreflexive responses in which the subject reported feeling hot with a subsequent rise in blood pressure.

Measures of stimulation on bowel function

For bowel management, we studied the ability of stimulation to improve bowel motility by causing smooth muscle contractions in the distal colon. Acute studies with subject 2 were first conducted to assess the effect of stimulation on the rectal and anal sphincters. Two tandem, balloon catheters placed in the rectum and in the anal sphincter measured local pressures. Stimulation parameters that maximized bowel contractions and minimized anal sphincter resistance in acute tests became part of a multiweek protocol to assess the impact of two stimulation strategies on bowel management. The first approach (Strategy 1) called for use of only low-frequency stimulation applied for 30 s, then removed for 30 s. This on-off strategy was continued for 5–10 min in an attempt to facilitate bowel motility. As required, subject 2 would then digitally stimulate the rectum to evacuate fecal material. If necessary, this procedure would then be repeated. A second approach (Strategy 2) followed 5–10 min of low-frequency stimulation with 5 min of low/high frequency combination stimulation. The goal was to reduce anal sphincter

resistance with high-frequency stimulation and facilitate defecation. Efficacy of the stimulation protocols was based on a diary kept by the patient wherein he described the quantity of stool passed during each daily session, the time spent, and a numerical 'satisfaction' rating from 1 (least satisfied) to 10 (most satisfied).

Results

Upright mobility

All subjects completed the conditioning phase, upright mobility training, and post-training data collection. After strengthening, all subjects showed improvements in maximum isometric torque of the quadriceps muscles (Table 4). Two subjects showed further increases following the training period.

For each subject, the average time to complete the activities is shown in Table 5. Subjects 1 and 3 each used a walker with wheels to perform the mobility activities and subject 2 used forearm crutches. None of the subjects required physical assistance to complete the activities. Subjects 1 and 3 required supervision (FIM score 5) for all tested activities, and subject 2 was independent (FIM score 6) for all activities except stairs where he required supervision (FIM score 5). Data for ascending and descending stairs were not collected with subject 1 as the activity was felt to be unsafe for him. Several activities could not be performed by subject 3 secondary to complaints of shoulder pain related to poor scapular muscle control.

Table 3 Mobility activities

Activity	Description
Sit to stand	Stand up from a standard chair with a seat height of 46 cm and no armrests
Stand to sit	Sit down to standard chair with a seat height of 46 cm and no armrests
6 m walk	Walk along an 8 m walkway. The middle 6 m are timed
Access of unmodified toilet	Walk into the bathroom stall and sit on the toilet
Timed up and go	Stand up from a standard chair without armrests, walk 3 m, turn and walk back to chair and sit down
Ascend stairs	Ascend 3 stairs using one crutch and one rail
Descend stairs	Descend 3 stairs using one crutch and one rail
6 min walk	Walk back and forth along a 30 m walkway for 6 min. Distance traveled is recorded
Functional standing test ²⁴	Stand for up to 60 min and move containers of different weights between a table and shelves at different heights every 10 min. Maximum standing time is recorded
Donning mobility equipment	Don all mobility equipment from a seated position

Table 4 Isometric quadriceps torque in Newton meters

Subject	Baseline		Postexercise		Post-training	
	Left	Right	Left	Right	Left	Right
1	29.2 ± 1.7	34.3 ± 0.8	38.0 ± 2.3	40.1 ± 5.8	46.8 ± 1.0	53.3 ± 1.8
2	14.9 ± 0.5	21.5 ± 0.8	30.2 ± 0.5	34.4 ± 0.7	46.5 ± 0.3	49.2 ± 0.4
3	22.8 ± 1.0	28.1 ± 1.8	51.3 ± 1.2	66.6 ± 2.3	39.9 ± 1.4	52.8 ± 2.1

Table 5 Time in seconds (distance for 6-min walk) to complete mobility activities

Activity	Subject 1	Subject 2	Subject 3
Sit to stand (standard chair)	12.9 ± 0.3	13.5 ± 2.7	20.87 ± 1.41 ^a
Stand to sit (standard chair)	11.8 ± 1.2	15.0 ± 1.7	17.28 ± 1.27 ^a
6 m walk (velocity)	32.4 ± 3.5 (0.2 m/s)	9.1 ± 0.8 (0.7 m/s)	58.32 ± 2.36 ^a (0.1 m/s)
Bathroom transfer	42.0 ± 0.4	34.7 ± 2.4	NT
Timed up and go (standard chair)	114.7 ± 11.2	48.7 ± 4.1	NT
Upstairs	NT	13.2 ± 1.4	NT
Downstairs	NT	15.9 ± 1.5	NT
6-min walk	39.3 ± 5.7 m (0.1 m/s)	215.1 ± 39.3 m (0.6 m/s)	NT
Functional Standing Test ²¹	968.3 ± 390.4 (16.1 ± 6.5 min)	2048.7 ± 374.4 (34.1 ± 6.2 min)	122.0 ^b (2.03 min)
Donning mobility equipment	282.31 ^b	124.7 ± 8.1	337.82 ± 23.17

NT = not tested

^aPerformed from subject's wheelchair due to shoulder strain from the standard chair, which has a lower seat to floor height^bOne trial only

In addition to a swing through gait pattern, all subjects were trained in the use of a reciprocal gait pattern. Subject 1 accomplished stepping through a flexor withdrawal response created by stimulating the peroneal nerve electrode, as he did not have the iliopsoas muscles implanted. Subject 2 used a combination of the iliopsoas muscle and a flexor withdrawal response, and subject 3 used a combination of the iliopsoas and the short head of the biceps femoris. Using these patterns, subjects 1 and 3 could ambulate up to 20 feet and subject 2 up to 75 feet. All subjects reported preferring a swing through pattern for walking as they felt it was faster. However, subject 2 was able to ascend stairs using a reciprocal pattern in which the iliopsoas and the tibialis anterior of his left leg would be stimulated to negotiate the step. Once the foot cleared the step and landed, the left knee extensors would be stimulated to straighten the leg and simultaneously lift the right leg to the same step. This sequence was then repeated for each step. The subject reported preferring this pattern to the alternative of lifting his entire body weight up onto the next step. He reported less upper extremity demand and overall less effort was needed to ascend reciprocally.

Subject 2 did experience a complication during the training period. During his 12th training session, increased spasticity was present in his left lower extremity while standing and walking. Examination of the extremity revealed that the medial side of dorsum of the left foot was swollen. Palpation along the first metatarsal created a flexor withdrawal response of the left lower extremity. Radiographs and a bone scan were obtained, which revealed a stress fracture of the proximal first metatarsal. The subject reported that he believed the fracture happened with one step in which his left leg experienced greater impact at initial contact due to his poor control of swing for that step. The subject was immobilized for 6 weeks in a brace, which resulted in a mild plantarflexion contracture. This contracture was easily reduced through standing and stretching, and he was able to return to training without further problems.

Three of the 52 electrodes placed for lower extremity stimulation experienced changes in the responses of the muscles. Subject 2 had a significantly decreased response from the left biceps femoris 8 months postoperatively. It was not replaced, as he was able to use the system as he desired without that electrode. In addition, his right psoas electrode ceased functioning several weeks postoperatively. During a subsequent revision surgery, it was noted that the electrode lead had become disconnected at the connector site from the implant lead. This was reconnected without further problems. A similar problem was suspected for the right tibial nerve electrode in subject 3, which stopped functioning 8 months postoperatively. Testing of this electrode revealed a high impedance, suggesting a disconnect along the electrode path. It was decided to not address this disconnection and to program this electrode out of the stimulation patterns.

Bladder and bowel management

Neuromodulation Multiple neuromodulation studies with subject 1 demonstrated the ability of stimulation to suppress reflex bladder contractions acutely, and thereby reduce vesical pressure (Figure 3). During these studies, stimulation with parameters 2.5 mA amplitude, 350 μs pulse width, and 14 or 50 Hz frequency was applied bilaterally to S3. These parameters corresponded to stimulation levels just below that required for motor response in the lower extremities. When initiated following the onset of reflex bladder contractions, stimulation caused vesical pressure to drop immediately. The subject did experience symptoms of mild dysreflexia when reflex bladder contractions occurred; however, these symptoms subsided with initiation of stimulation.

The results seen in the acute neuromodulation tests provided the basis for a subsequent study with subject 1 that compared the effectiveness of chronic neuromodulation with alternative bladder management strategies. Four strategies – on anticholinergic medication, no medication, 'continuous' stimulation, 'night' stimulation

Figure 3 Acute neuromodulation: the bladder was filled at a rate of 30 ml/min. Stimulation was applied immediately after a reflex contraction of the bladder occurred as shown by an increase in bladder pressure. Stimulation caused the bladder pressure to decrease following each reflex contraction until the fill volume reached approximately 350 ml at which time the bladder was emptied, as contractions could not be suppressed

– were considered. Stimulation parameters for both continuous and night neuromodulation were the same – S3 bilaterally, 2.5 mA, 350 μ s, 14 Hz. Figure 4 demonstrates that the catheterization schedule with chronic stimulation was comparable to that seen with the use of anticholinergic medication. No episodes of incontinence/mild dysreflexia occurred while subject 1 followed his medication protocol, five episodes occurred during the ‘no meds’ period, one episode during ‘continuous’ neuromodulation, and two episodes during ‘night’ neuromodulation. Voiding volumes remained unchanged across these strategies.

Bladder and sphincter contractions None of the stimulation studies with subject 1 or subject 2 demonstrated an ability to generate significant increases in detrusor pressure. Therefore, stimulation-induced voiding was not achieved in these initial studies.

In several tests, a high-frequency stimulation signal (500 Hz, 350 μ s, 8 mA) superimposed onto a low-frequency stimulation signal (20 Hz, 350 μ s pulse width, 8 mA amplitude) appeared to produce less sphincter pressure as compared to that caused by low-frequency stimulation alone. There was an approximately 40% reduction in sphincter pressure during simultaneous application of low/high frequency stimulation as compared to low-frequency stimulation alone. This phenomenon was repeatable on three of four different test days.

Stimulated bowel function Acute testing demonstrated that low-frequency electrical stimulation (20 Hz, 350 μ s, 8 mA) of S3 bilaterally in subject 2 caused a significant increase in both rectal pressure and anal sphincter

Figure 4 These graphs represent the times between catheterizations and bladder volumes obtained under each of the tested conditions: initial assessment while taking anticholinergic medication (Meds), after stopping the medication for 4 days (no Meds), with continuous neuromodulation (18 h/day), and with neuromodulation over night only (7 h/day)

pressure. High-frequency stimulation alone (500 Hz, 350 μ s, 8 mA) appeared to have no effect on rectal pressure and produced a reduced pressure in the anal sphincter as compared to low-frequency stimulation alone. A combination of low- and high-frequency (500 Hz, 350 μ s, 8 mA) stimulation appeared to increase rectal and anal sphincter pressures, but to a level less than that caused by low-frequency stimulation alone.

The daily use of electrical stimulation appeared to cause a reduction in the time to complete defecation by 40% with the first stimulation strategy and by 60% with the second strategy (Table 6). As compared to bowel management without stimulation, with stimulation there was also a reduction in the proportion of days the subject failed to defecate and greater satisfaction with bowel management overall.

Discussion

The results of this study demonstrated the feasibility of the Praxis FES system for multifunctional use. All three

Table 6 Effectiveness of stimulation strategies on bowel management

	<i>Days evaluated</i>	<i>Days failed to defecate</i>	<i>Days digital stimulation not used</i>	<i>Average daily time spent (min)</i>	<i>Satisfaction (1–10)</i>
Preimplant strategy	7	5	0	52	5
Stimulation strategy 1	17	2	3	32	6.6
Stimulation strategy 2	29	4	2	23	6.7

Satisfaction was rated on a numerical 'satisfaction' rating from 1 (least satisfied) to 10 (most satisfied)

subjects demonstrated the ability to stand, walk, and perform functional upright mobility activities and the two subjects with sacral nerve electrodes were able to realize benefits from stimulation for bladder and bowel function. Stimulation for both functional purposes was controlled by one external control unit (a pocket personal computer) with power and data delivered via radio frequency to one central implanted stimulator.

Upright mobility

Most critical to achieving and maintaining an upright posture with FES is the stimulated strength of the quadriceps. In our study, two channels were dedicated to quadriceps muscles, providing the ability to stimulate the vastus lateralis, vastus medialis, and vastus intermedius. For all three subjects, stimulated muscle strength of the quadriceps increased following the muscle conditioning phase and strength was sufficient for reaching and maintaining a standing position and for stepping. Subjects 1 and 2 continued to gain strength through the upright mobility training phase, even though they performed minimal lower extremity exercises during this time period, suggesting that further strength increases occurred from standing and walking with FES.

Of note, after exercise with electrical stimulation, the maximum knee extension torque for all three subjects (30.2–66.6 Nm) exceeded the theoretical minimum values that have been reported as necessary for standing with FES. Kagaya *et al*³ reported empirical formulas to determine minimum knee extension torque required for both the sit to stand transition and quiet standing with FES in adults with SCI using the upper extremities for assistance. Using these formulas with our subjects' data, subject 1 would require 35.8 Nm and subjects 2 and 3 would require 24.3 Nm in order to perform sit to stand. For quiet standing, subject 1 would require 21.9 Nm and subjects 2 and 3 would require 14.9 Nm. Kobetic *et al*⁴ reported that subjects were required to generate a minimum of 30 Nm of quadriceps torque before initiating standing. In our subjects, stimulation levels for the quadriceps muscles during standing were titrated to a minimum value that would provide functional standing while minimizing muscle fatigue. For each channel, these values ranged from 26 to 80% of the muscle's saturation level (mean $58.5 \pm 19.1\%$). This corresponds to torque values of approximately 10.6–41.6 Nm per channel of stimulation as determined

through recruitment curves. To transition from sitting to standing, these values ranged from 45 to 100% of the muscle's saturation level (mean $86.7 \pm 20.4\%$) and torque values from 19.1 to 44.6 Nm.

Previous research in our laboratory has compared the use of an 8-channel implanted FES system (NeuroControl Corporation, Valley View, OH, USA) to the use of long leg braces for short duration upright mobility activities in children and adolescents with SCI.⁵ In that study, the FES system provided upright mobility through continuous stimulation to the implanted muscles to allow a swing through gait pattern using an assistive device. In that study, subjects of similar ages and injury levels as the subjects in this Praxis study achieved comparable levels of function in activities tested as part of each study (6 m walk, stairs, access of unmodified toilet, and transitions between standing and sitting). Despite attaining similar levels of function, the Praxis system possesses the potential for further advancement, such as ambulation without AFO, a goal of all three subjects. While not formally tested, two subjects were able to stand and walk short distances without AFO using stimulation to the ankle dorsiflexors and plantarflexors, muscles that are not stimulated in our study with the 8-channel system. Two of the Praxis subjects also used stimulation to the dorsiflexors as a way to stretch the plantarflexors as opposed to traditional stretching methods. This in particular was useful after subject 2 developed plantarflexor tightness following the stress fracture. Another advantage of the Praxis system over the 8-channel system was the ability to implant two channels of stimulation to the quadriceps muscles. Several subjects with the 8-channel system experienced a flexor withdrawal pattern when stimulation to the quadriceps was increased to a certain level; therefore, limiting the ability to maximize force output. Two of the subjects with the Praxis system also experienced flexor withdrawal responses with quadriceps stimulation and the ability to alter stimulation levels across two channels was useful in minimizing the withdrawal response while maximizing force.

The first 2 subjects in our study received electrodes to stimulate the long head of the biceps femoris, which was beneficial for obtaining upright stance by providing hip extension. However, as this muscle is biarticular, it interfered with the ability to create stimulated hip flexion to assist with swing initiation during reciprocal gait, as the hip extension component competed with the hip flexion needed for limb clearance. The hip flexion

created by the iliopsoas and/or the flexor withdrawal reflex was unable to overcome the extension force. Due to this, subject 3 received an electrode to the short head of the biceps femoris, which successfully assisted with swing initiation. This electrode was necessary for this subject to perform reciprocal walking as the flexor withdrawal response was unable to be obtained as it was in subjects 1 and 2. Similar to our findings, Kobetic *et al*⁴ reported using the semitendinosus, semimembranosus, and long of the biceps femoris primarily as hip extensors during stance and using the short head of the biceps as the primary knee flexor during swing along with secondary knee flexion created by the sartorius and gracilis muscles. Our findings as well as those of Kobetic *et al*⁴ suggest the importance of considering the goals of the subject when selecting muscles for implantation when limited by the number of channels available for stimulation.

In our study, subject 2 was able to achieve reciprocal stair climbing, obtaining sufficient hip flexion for clearance of the step. To achieve this, a combination of stimulation to the iliopsoas and the peroneal nerve for the flexor withdrawal response was used. Using percutaneous electrodes to the iliopsoas, Nandurkar *et al*⁶ reported that subjects with SCI, traumatic brain injury, or stroke could obtain 45° of hip flexion during walking, which they report is barely sufficient for ascending stairs. In their study, three different approaches were used to implant the iliopsoas, one of which is somewhat similar to our technique in that the L2 and L3 nerve roots were implanted, but with a more posterior implantation technique with the electrode first entering the skin 8 cm lateral to the paraspinal muscles. With this technique, greater hip flexion was obtained as compared to approaches through the groin and the lateral abdomen. However, pure hip flexion could only be obtained at low levels of stimulation. With higher levels, the hip adductors were recruited as well as the quadratus lumborum and later the quadriceps, preventing increasing the stimulation to obtain stronger hip flexion. Our approach likewise produced a combination of hip flexion and adduction that increased with increasing stimulation levels, but without creating knee extension. In addition, the adduction could be minimized with stimulation to the gluteus medius. In subject 2, the iliopsoas alone was unable to provide adequate hip flexion for step clearance despite being able to flex to 90° from a supine position. Stimulation to the peroneal nerve for the flexor withdrawal response also was insufficient to provide step clearance. However, a combination approach was successful. In an attempt to selectively activate the iliopsoas, Nandurkar *et al*⁶ reported that an intramuscular technique through the abdomen was being investigated. However, it is unknown if this alone would provide sufficient hip flexion for stair climbing.

Our subjects all reported preferring a swing through gait pattern for ambulation as they felt it was faster, even though walking speeds ranged from 0.1 to 0.7 m/s during a 6 m walk. They were willing to accept the

increased demand on the upper extremities in exchange for the ability to move more quickly. Our subjects were all young men in overall good health who were very active prior to their SCI. It is possible that an older or less fit population with SCI might prefer a reciprocal walking pattern for short distance ambulation. Despite preferring a swing through pattern for ambulation, subject 2 reported preferring a reciprocal pattern for ascending stairs due to the decreased demand on the upper extremities for lifting the body up onto an 8-in step, a greater demand than what is required for ambulation. Of note, we did not focus on a reciprocal gait pattern during all programming and training sessions due to the subjects' preferences. Perhaps more training time devoted to this would have led to results comparable to those obtained with a swing through pattern. Kobetic *et al*⁴ reported that a well-conditioned subject with 32 channels of stimulation per leg could walk reciprocally at a speed of 0.5 m/s over a distance of 300 m, which is fairly comparable to what was achieved with our most conditioned subject (subject 2) when using a swing through gait pattern.

As stated earlier, subject 2 did experience a stress fracture during training. Individuals with SCI have been shown to have decreased bone density,^{7–10} and fractures are known as a risk for individuals with SCI who choose upright mobility. It is unlikely that the use of the FES itself contributed to the stress fracture sustained by subject 2 due to his report of greater impact on that leg prior to developing spasticity. Previous studies have examined the effects of the use of FES for upright mobility on the musculoskeletal system. Betz *et al*¹¹ reported no evidence of joint destruction after 1 year of percutaneous FES use in adolescents and Agarwal *et al*¹² reported no adverse musculoskeletal effects after 17 years of percutaneous FES use in two adults.

The responses of three lower extremity electrodes did change during the study. One was known to result from a disconnected lead and another was suspected to have the same cause. The cause of the decreased response from the other electrode is unknown and was not investigated. Johnston *et al*⁵ reported stable responses in 83% of implanted lower extremity electrodes during the training period for subjects with an 8-channel implanted system. A combination of intramuscular and epimysial electrodes were used in that study. Following successful revision surgeries, the electrodes functioned without difficulty for the remainder of the training period. Uhler *et al*¹³ reported that 95% of the epimysial electrodes implanted into the lower extremities were functional one to 3 years postoperatively. Failures were shown to be isolated to those implanted posteriorly in the buttock and thigh. They estimated that the probability of survival after 2 years is 93%, with a plateau occurring at 90% after 4 years.

Stimulation for bladder and bowel management

With respect to stimulation for bladder and bowel function, the goal of the Praxis FES system is to reduce

detrusor hyperreflexia by neuromodulation (with selective of activation of large afferent fibers using low-amplitude stimuli), and to provide active bladder voiding and enhanced bowel function with high-amplitude low-frequency stimulation of efferent nerve fibers. With the two subjects for which sacral electrodes were implanted, we were able to examine the effects of sacral nerve stimulation on several aspects of bladder and bowel management – suppression of bladder hyper-reflexia, urine voiding, and facilitation of fecal evacuation.

Acute urodynamic tests in subject 1 suggested that low amplitude stimulation of the S3 root bilaterally inhibited reflex bladder contractions and facilitated filling. These results are similar to those reported previously in the spinal cord injured population using the implanted Finetech–Brindley electrodes to the mixed sacral nerve roots¹⁴ and by surface electrical stimulation of the pudendal nerve.^{15,16} With chronic neuromodulation studied over a period of several weeks, subject 1 was able to maintain the same catheterization schedule (about every 6h) with neuromodulation as he did on his anticholinergic medication. When not using either medication or neuromodulation, the subject needed to catheterize on average every 4h. However, because the estimated voiding volumes were essentially not different across the strategies one cannot rule out a difference in fluid intake between the neuromodulation and control periods or other factors such as the subject's estimates of voiding volume, to account for the change in catheterization time.

Kirkham *et al*¹⁴ reported on one subject who intermittently used neuromodulation (via implanted electrodes applied to the sacral nerve roots) at home. Volumes obtained during catheterization while undergoing neuromodulation were compared to those generated both on anticholinergic medication and without any intervention (control). The volume obtained during self-catheterization was significantly smaller during the control period as compared to the periods of neuromodulation or medication use and there was no difference between volumes obtained at the neuromodulation and medication periods, suggesting that bladder capacity was increased effectively with neuromodulation.¹⁴

None of the stimulation studies with subject 1 or subject 2 demonstrated an ability to generate significant increases in detrusor pressure. It is likely for both subjects that the electrodes were not sufficiently close to the sacral nerves to excite the smaller efferent fibers although in subject 1 the electrodes at S3 were in sufficient proximity to the nerves to excite the larger afferent fibers for a neuromodulation effect. Due to the inability to generate sufficient detrusor pressure in subjects 1 and 2, the decision was made not to place the electrodes for bowel and bladder management in subject 3.

The impetus to explore the effects of high-frequency electrical stimulation comes from the results reported by Boyer *et al*.¹⁷ Using a canine model, it was shown that a high frequency–low amplitude signal (to selectively

fatigue the external urethral sphincter muscle) superimposed on a low frequency–high amplitude signal (to contract the bladder) generated a pressure gradient sufficient for urine voiding. In our study, the superposition of the high-frequency stimulation appeared to reduce the increase in urethral sphincter pressure associated with stimulated bladder contractions as compared to a low-frequency stimulation signal alone. However, due to an inability to generate bladder pressures, we could not assess whether the drop in sphincter pressure would allow or enhance voiding.

This or other techniques¹⁸ to decrease urethral sphincter resistance may be important to overcome detrusor-sphincter dysnergia (DSD) especially if neuromodulation is used in place of the dorsal rhizotomy procedure. The primary role of the rhizotomy procedure is to increase bladder capacity and thereby provide urinary continence. However, the posterior rhizotomy may, at least for patients with severe DSD, also allow or enhance voiding using the intermittent stimulation technique. Kirkham *et al*¹⁴ found in three of four patients that had sacral electrodes placed (for neuromodulation and stimulation for voiding) and did not undergo a dorsal rhizotomy, that bladder emptying with stimulation was less than 50% and that dyssynergic external urethral sphincter contractions were present between the stimulation pulses.

For subject 2, electrical stimulation at S3 increased anal sphincter and rectal pressure and over a 2-month period appeared to provide a significant improvement in bowel management, causing an increased frequency of defecation, a decrease in time required for bowel evacuation, and improved satisfaction over his non-stimulation evacuation methods. Anecdotally, the subject related that his satisfaction with using stimulation correlated not with the decreased time required to defecate, but with the greater quantity of fecal material he felt he passed. With the Finetech–Brindley implanted stimulator, it has been reported that sacral nerve stimulation provided both an improvement in the frequency of defecation¹⁹ and a decreased time for bowel evacuation.²⁰ In our study, the high–low-frequency stimulation paradigm appeared to provide added benefit over a low-frequency only pattern in that the average defecation time was further reduced by 20%. However, there was not a wash out period before the transition to the high- to low-frequency pattern so that possible carryover effects of the low-frequency pattern were not accounted for.

Conclusion

The feasibility of using the Praxis FES system for upright mobility and aiding specific aspects of bladder and bowel function was demonstrated with three young men with thoracic level SCI. All three were able to stand and walk to varying degrees using assistive devices. Neuromodulation to inhibit reflex bladder contractions was demonstrated in one subject while another subject successfully used the Praxis system to assist with bowel

emptying. Further research is needed to further understand and compare the benefits of swing through *versus* reciprocal ambulation and on techniques to successfully create stimulated bladder contractions and voiding with the Praxis FES system.

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