First Clinical Experience with BION Implants for Therapeutic Electrical Stimulation

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■ ABSTRACT

The objective of this study was to assess the usability and safety of BION injectable neuromuscular microstimulators for therapeutic electrical stimulation (TES) to treat two conditions involving disuse atrophy: poststroke shoulder subluxation in hemiplegic subjects and knee osteoarthritis. Clinicians were provided with PC-based software to track implants and to design the exercise programs. Subjects self-administered TES (3 sessions/day, 10–30 min/session) for 6 or 12 weeks. Outcome measures included subluxation for the shoulder study and knee function and pain for the osteoarthritis study. All subjects were comfortable with the BION equipment and therapy; eight of 10 experimental subjects elected to continue treatment after the study period. Shoulder subluxation was reduced by 55% ± 54%; knee function was enhanced by 65% ± 24%; and knee pain decreased by 78% ± 18%. The devices did not migrate and did not cause inflammation or pain. Thresholds were stable over time. We conclude that the use of BION implants to exercise atrophic muscles was well-accepted and provided effective rehabilitation in these two clinical conditions. ■

KEY WORDS: electrical stimulation, hemiplegia, implantable microstimulators, knee osteoarthritis, shoulder subluxation.

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INTRODUCTION

Muscle weakness is secondary to many types of pathologies that fall broadly into three categories: (1) Lesions or diseases of the peripheral neuromuscular system produce profound muscle atrophy when both electrical activity and neural trophic effects are interrupted. (2) Lesions or diseases of the central nervous system can produce modest to marked weakness with varying degrees of spasticity and atrophy when voluntary control of the muscle is impaired. (3) Disorders of skeletal

and connective tissues cause weakness when pain, immobility, or both limit normal muscle use. Electrical stimulation is able to improve muscle strength, especially in situations in which peripheral nerves and muscles are intact but underused (1–4).

Numerous types of neuromuscular electrical stimulators have been developed to rehabilitate weakened muscles in clinical settings. Such treatments are not commonly used, at least in part because of shortcomings of the various electrical interfaces to the body. Transcutaneous electrodes can be awkward to affix and can produce unpleasant cutaneous sensations because high currents must be passed through the skin to stimulate the underlying muscles. Percutaneously inserted wire electrodes are cosmetically unappealing, serve as a potential conduit for infection, and are prone to breakage. Fully implanted systems with lengthy leads are expensive and invasive to implant (5).

As an alternative to these methods, Loeb and colleagues (6) have developed small, injectable microstimulators called BIONs that avoid some of the problems associated with previous generations of electrical stimulators. Each BION is a small (16 mm length × 2 mm diameter), single channel stimulator encased in a glass package with an electrode at each end. The tantalum and iridium electrodes provide a biocompatible interface with minimal foreign-body reaction when implanted passively or actively in animals (7,8). They deliver current pulses whose power and command signals are supplied by inductive coupling through an external coil worn near the implanted devices (6,9).

In this report, we describe our clinical experience to date with BIONs in two clinical applications in which articular function has been compromised. Some of these data have been reported previously in preliminary form (10). In the first application, devices were injected close to the motor points of the deltoid and supraspinatus muscles of subacute stroke subjects in order to reduce shoulder subluxation and pain, which in turn may improve shoulder and arm function. In the other, knee extensor muscles were stimulated by BIONs inserted close to the femoral nerve to improve the strength of the quadriceps muscle, improve the functionality of the knee, and reduce pain in subjects with chronic, progressive osteoarthritis. Definitive demonstration of efficacy awaits completion of these trials, but there is now sufficient experience to discuss issues of safety, stability, and clinical usability for this revolutionary new technology.

MATERIALS AND METHODS

The BION System

BION devices used in this study were glass-enclosed, single channel devices fabricated by the Alfred E. Mann Institute for Biomedical Engineering at the University of Southern California (Los Angeles, CA; Fig. 1). A detailed description of the specifications and performance of these devices is available

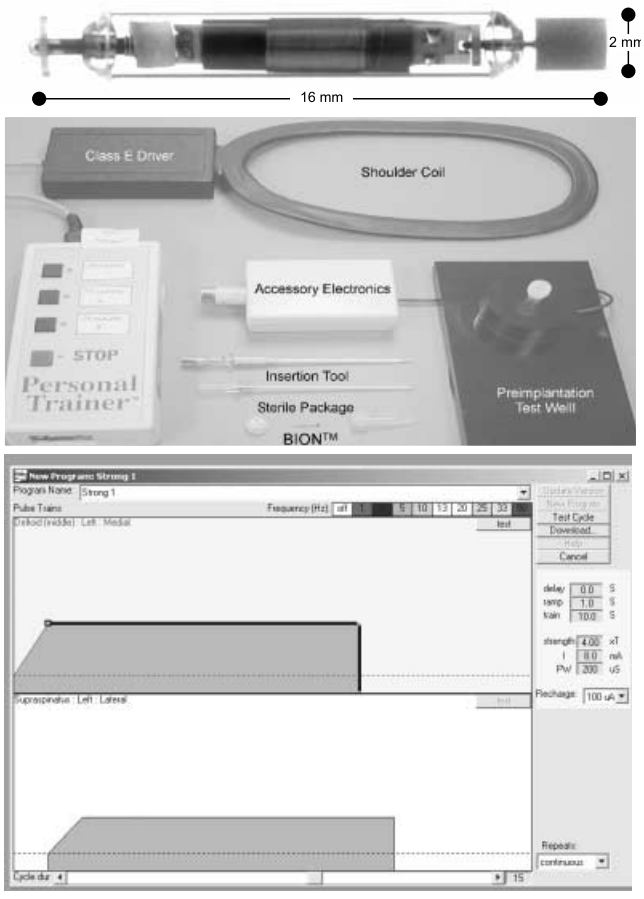

Fig. 1. BION System. Top: BION implant (with dimensions). Middle: coil, Personal Trainer, and other peripheral accessories. Bottom: ClinFit Stimulation Program window. The stimulation channel that is being set (upper trace) has click-and-drag handles to adjust parameters graphically, with numerical values shown in the box at right. Stimulus strength is shown relative to threshold (dashed horizontal line) and ramp up and hold time are shown relative to cycle duration (adjustable via scroll bar at bottom). Stimulus frequency is indicated by color from palette shown at top.

elsewhere (6,9). Briefly, each BION can be individually commanded to generate pulses with durations of up to 512 μs (range 2–512 μs, in steps of 2 μs) and amplitudes of up to 30 mA (two ranges: 0–3 mA in 0.2 mA steps and 0–30 mA in 2 mA steps), at pulse rates of up to 50 pps.

BIONs are autoclaved and shipped in sterile packages. Prior to implantation, the functional status and address of each BION is assessed while in its sterile package, which is placed into a test well to detect capacitively its electrical response to a valid command. The BION implant is injected through the plastic lumen of a 12-gauge Angiocath (Becton Dickinson Vascular Access, Sandy, Utah) whose metal trochar has been modified to connect to a clinical nerve stimulator.

Power and data are transmitted to the implanted devices by a transmitter coil worn over the shoulder or thigh, in the vicinity of the implants. For present applications in which more than one device was typically activated, we used an ovoid flexible coil shaped to the dimensions of the shoulder or thigh with sufficient range to address multiple devices simultaneously (Fig. 1). The oscillator and power circuitry that drive the coil are housed within the coil device itself to avoid having to transmit high voltages in the flexible cable from the control unit.

The commands issued by the coil are personalized for the subject using a graphical software package called ClinFit (developed in-house) installed on a personal computer. ClinFit is used to identify and track stimulation thresholds, and to define or change the frequency, intensity, pulse-train duration, and shaping of the stimulation sequences, as shown in the stimulation program window in Fig. 1. The graphical user interface allows the physician to adjust the intensity and temporal patterning of stimulation in up to eight implanted BIONs to create exercise programs. Up to three programs can be loaded into the memory of the Personal Trainer (built by Aztech Associates, Kingston, Ontario, Canada), a microprocessor-based controller that the subject takes home to self-administer the treatment. The subject initiates a treatment session by pressing the start button associated with a particular program, as indicated on a label that the clinician slips into a clear pocket on the top panel of the Personal Trainer. The Personal Trainer records the time and duration of each exercise session and transfers this information to ClinFit when the subject returns for follow-up visits.

One feature of ClinFit is the use of graphical interfaces whereby the clinician sets the stimulus parameters without having to enter numerical values (9). The stimulation parameters of current and pulse width are combined into a single stimulus "strength" value based on their product (which is in units of charge). An algorithm selects the appropriate current and pulse width to achieve the desired exercise strength as a multiple of threshold (which is depicted graphically, as shown in Fig. 1, bottom). If the threshold changes, the software can automatically scale the stimulus parameters to maintain the same intensity relative to threshold.

BIONs are now being produced in small quantities in a laboratory setting, making it difficult to estimate their ultimate cost. Their components are relatively inexpensive; their actual cost will depend on the volumes in which they are eventually manufactured.

Experimental Design

Shoulder Subluxation

Experimental procedures for this randomized, crossover trial were reviewed by the investigational review boards of Queen's University and St. Mary's of the Lake Hospital in Kingston, Ontario and the Therapeutic Products Branch of Health Canada. The first patient signed his consent form on November 17, 1999. To date, 10 subjects have been recruited within 12 weeks of an acute stroke. Subjects are considered to be eligible for the trial if the stroke results in significant hemiparesis with either present or likely future shoulder subluxation due to the flaccidity of the shoulder muscles. After obtaining informed consent, subjects are randomized into two groups by having the study coordinator draw a number from an envelope for each newly recruited subject; subjects with odd numbers receive BION TES therapy and those with even numbers are control subjects. Control subjects are treated by conventional occupational and physical therapy regimens similar to those recommended for all poststroke subjects with hemiplegia and subluxation. Subjects in the TES group are implanted with a single BION in each of the middle deltoid and supraspinatus muscles in an office procedure. They receive the conventional therapy,

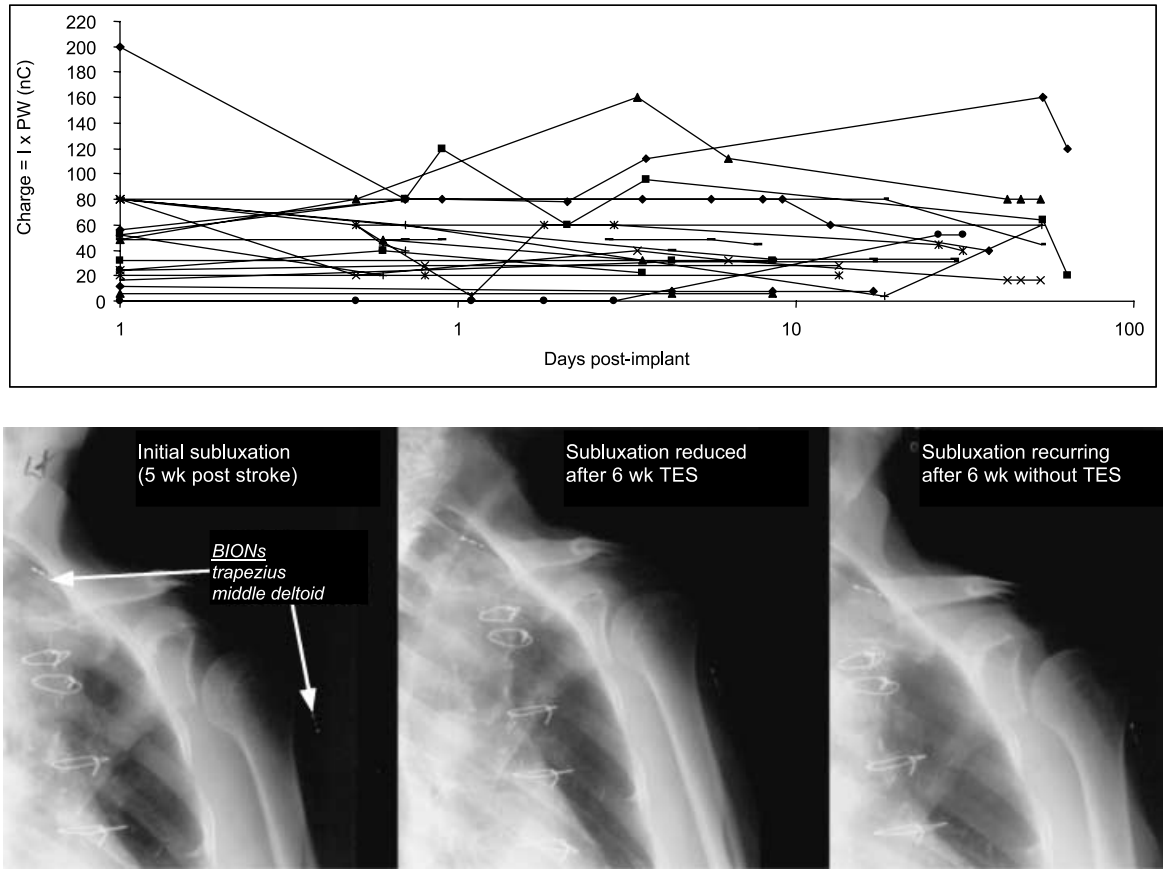

Fig. 2. Stability of BIONs over time. Top: Threshold of 22 implanted BIONs over time in units of charge (nC = mA × μs). Bottom: X-ray of Subject 1's shoulder in the subluxation study. Left: a few days after implantation of BIONs, before stimulation therapy was started. Middle: subluxation is reduced after six weeks of therapy; BIONs are off. Right: subluxation recurring after six weeks off therapy.

but additionally are treated with daily electrical stimulation using BIONs for six weeks. This is followed by a "nonstimulation" period of six weeks, designed to study whether the effects of stimulation (if any) have some permanence.

At study commencement, the shoulders of each subject are imaged radiologically (45° anterior–posterior approach; Fig. 2). The thickness of the middle deltoid and supraspinatus muscles is measured using ultrasonography (Sonoline Elegra 4000 ultrasound system with a linear 5 MHz probe; Siemens Medical Systems, Issaquah, WA). During the trial, all subjects are assessed every three weeks for clinical subluxation (measured manually), upper-extremity strength, range of motion, stimulation thresholds (current and pulse width), and every six weeks for subluxation by radiography, upper-extremity function, and shoulder pain (Visual Analog Score) (Table 1). Student *T*-tests were performed and a *p*-value of 0.05 was used to determine if improvement was significant. All tests were performed with the BION devices turned OFF.

Subjects with BIONs begin stimulation sessions three times per day at four to seven days after implantation of the devices. During the first few sessions, stimulation periods are kept short, about 10 min per session. These periods are extended gradually to 30 min as muscles become more fatigue-resistant. Pulses are typically delivered in 10-s trains of 5 pps, spaced by 5-s relaxation periods. Stimulation strength is also increased in subsequent sessions to recruit as much of the muscle as possible.

Control subjects are followed in an identical way through the first six weeks. They are then offered treatment with BIONs if glenohumeral subluxation is present. Four of five control subjects had symptomatic shoulder subluxation after the six weeks of observation. Three of these four subjects chose to have the implants. If the subject chose to receive implants, the effects of therapy

Table 1. Summary of the BION Shoulder Subluxation and Knee Osteoarthritis Studies.

	Subacute Shoulder Subluxation	Knee Osteoarthritis
Location	Kingston, Canada	Milan, Italy
Design	Randomized, cross-over	Longitudinal, repeated measures
Baseline	No	Yes, 12 weeks
Stimulation period	6 weeks	12 weeks
Off-stim. period	6 weeks	No
Stimulation frequency	5 Hz	2 Hz
Assessment	Subluxation, active/passive ROM, strength, arm function, VAS pain, muscle thickness (ultrasound).	WOMAC, Knee Function, VAS pain, muscle cross-sectional area (MRI).
# subjects (July 2002)	10 (5 TES; 5 control initially)	5
# control subjects crossed-over to TES	3 (out of 5, above)	N/A
# total TES	8 (5 initial; 3 cross-over from control)	5
# noncompliant TES	3 (out of 8, above)	0
Final subject distribution	5 compliant TES; 3 noncompliant TES; 5 control	N/A
# BIONs implanted (July 2002)	17 (8 TES subjects—one has two BIONs in the supraspinatus because of technical failure)	8 (subjects 1–3 have 2 BIONs each; subjects 4–5 have one BION each)

are assessed similarly to the TES subjects in the first six weeks of the trial; however, not all tests were performed in control subjects being implanted when this study started. As a result, some tests were not performed on all implanted subjects. After the study is completed, all subjects with implants are allowed to continue BION TES if they desire it.

For the implantation procedure, the skin site is cleaned and a local anesthetic is injected. The insertion tool is advanced into the muscle of interest through a 2-mm skin incision. Electrical pulses from a conventional clinical nerve stimulator are delivered through the trochar to assure that the tip of the needle is near the muscle's motor point, judged by the ability to elicit muscle contractions at low stimulus strengths, typically between 1 and 4 mA at 200 μs. The trochar is removed and the BION is advanced using a push-rod, through the lumen of the needle sheath and into the muscle tissue. The site of the injection is covered with an adhesive strip. Small tattoo marks are placed on the skin overlying the middle deltoid and supraspinatus to aid the repeated imaging of muscle thicknesses at these sites.

The first subject in this trial died two years following BION implantation from pneumonia associated with a disseminated carcinoma recognized more than one year after device implantation. During most of this time, he had elected to continue TES treatment on a reduced schedule (15 min once a day). Permission was given to explant the devices at autopsy (Fig. 3). Tissues surrounding the devices were fixed in formalin, stained with hematoxylin and eosin, and cut for microscopic slides.

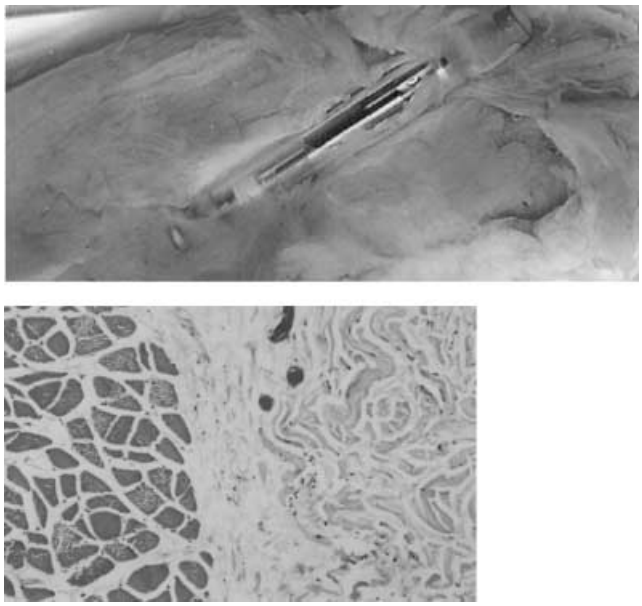

Fig. 3. Top: BION being removed from Subject 1 in the shoulder subluxation study (trapezius). Bottom: histologic section of excised muscle (left: muscle cells; right: scar tissue around device).

Knee Osteoarthritis

Five subjects have been recruited from an outpatient population at the Istituto Ortopedico Gaetano Pini

in Milan Italy. The repeated measures design was reviewed and approved by the Pini Comitato Etico (Institutional Ethics Committee). Subjects eligible for inclusion are diagnosed with stable or progressive, unilateral knee osteoarthritis and associated quadriceps muscle hypotrophy. During an initial 12-week baseline period, a series of assessments are carried out to determine the muscle cross-sectional areas using MRI, the functionality of the knee using the Western Ontario-McMaster (WOMAC) knee-function scale, and Knee Society Function tests, and pain by Visual Analog Scale (VAS). Student *T*-tests were performed and a *p*-value of 0.05 was used to determine if improvement was significant. Using a procedure similar to that described above, a single device is implanted adjacent to the femoral nerve in the groin (in the first three subjects, a second device was placed close to the motor-point of the vastus medialis muscle). Stimulation of the femoral nerve results in a distributed contraction of the quadriceps muscle heads, whereas stimulation of the vastus medialis results in a relatively localized muscle contraction as might be expected for a muscle that appears to be divided into multiple neuromuscular compartments.

Four to seven days after the implantation procedure, a stimulation regimen was individualized for the subject by using the Personal Trainer and the subject's reports of fatigue or discomfort. As in the shoulder subluxation trial, stimulation periods are initially short, but are lengthened gradually until the subject is receiving stimulation for about 30 min, three times a day. Stimulus regimens were typically delivered at 2 pps in trains of 10 s with rest periods of 5 s.

Human Factors Analysis

The clinicians participated in initial planning meetings to consider the approach to the muscles and the operation of the insertion tool and stimulus control equipment and software. An experienced observer attended their initial implantations and fitting sessions to answer questions and to collect feedback on the performance of the equipment and software. Subsequent implantations were usually performed with their usual clinical assistant to handle the sterile instruments.

The engineering team responsible for the various components of the hardware and software system interacted closely with clinicians and subjects to refine the design and performance of various elements in response to clinical experience. A questionnaire was developed to provide a more structured way of capturing physician experiences and insights on the perceived problems of use and efficacy of BION therapy.

RESULTS

Safety and Biocompatibility of Devices

In both subject populations, the injection of BIONs was associated with no significant swelling, pain, or inflammation. Physicians reported no difficulty implanting the BIONs in these two areas. Patients reported negligible pain during and after the procedure. In the first subject of the shoulder study, the BION destined for the supraspinatus muscle fell short of its target and was implanted into the trapezius; subluxation was nevertheless reduced after six weeks of BION TES in this subject. For all subjects, the site of injection healed within a few days of implantation and there was no visible evidence of the BION or its implantation. Over the course of the trials, no evidence of migration was apparent when visualized in repeated X-rays (Fig. 2), and the devices maintained relatively stable electrical thresholds (Fig. 2).

Subjects with BIONs reported no painful sensations that might reflect the recruitment of cutaneous or muscular nociceptors by the relatively low intensity pulses used in this study. However, two subjects in whom devices were placed beside the femoral nerve near the crease of the groin found after several weeks that the presence of the device could be felt when sitting with the hip flexed. One subject reported a mildly unpleasant stretching or pulling sensation under the skin; another reported an intermittent change in sensory feeling over a small region of the thigh. The former subject elected to have this device removed after it had been in place and used for several months, but volunteered that she would be willing to receive another implant if it were relocated more distally (she still has a BION in the vastus medialis muscle). The femoral BION was removed through a skin incision in a procedure lasting approximately 30 min. After discussion with the surgeon, it was concluded that the BION had been

oriented in a manner that might result in pressure on the adjacent tissues when the hip was flexed. Most subjects did not have any sense that the device was present, and seemed to regard the muscle contractions as if they were self-generated, rather than produced by an implanted device. The muscle contractions were reported to be pleasant and easily tolerated in both the shoulder and thigh.

In the single autopsied subject, muscle tissues appeared healthy (Fig. 3). Devices were surrounded by a thin layer of opalescent connective tissue (capsule) that appeared contiguous with the perimysium of the muscle. Histologic evaluation showed scar but no evidence of necrosis or other inflammatory reactions. The two removed devices were tested for electrical function in saline and found to be operating without change from their preimplantation performance (which is characterized in detail for each serially numbered BION as it completes manufacture).

Subject Compliance

Subject compliance was generally good. The subjects with osteoarthritis were cognitively intact and had no difficulty self-administering the therapy at home. A few poststroke subjects had cognitive changes, including memory loss. In one subject, memory lapses and depression increased progressively after the stroke, resulting in withdrawal from the trial. Other poststroke subjects managed the therapy either alone or with help from a caregiver after a few (three to five) in-hospital supervised sessions. Four of four spouses of TES subjects interviewed reported that the use of the devices seemed to improve the mood and self-image of the subjects.

In the shoulder subluxation study, three of five compliant TES subjects chose to continue BION therapy for at least four weeks, and up to a year after the trial, usually on a reduced schedule. As well, three of five control subjects asked for and received BIONs; they then started TES with the same schedule as the TES subjects, with the same series of tests and assessments. In the knee study, all five subjects opted to continue the BION therapy after the trial (although we have not re-implanted the subject whose BION was removed). They use it at their discretion and report that it maintains better function in their leg.

In general, subjects reported that the therapy was pleasant. In most cases, subjects set up the equipment rapidly (with help from a spouse if needed) and used it during normal sitting activities. The subjects expressed satisfaction that they could receive treatment without needing a therapist or a nurse. They described the stimulation as a "tingly feeling", or simply the "muscles contracting". All subjects who answered the questionnaire would recommend this therapy to others with the same condition as themselves, and credited BION therapy for improvement in their joint function.

Equipment Failures

The external hardware and software functioned adequately from the beginning, but several changes were made to correct minor problems. The accessory test well used to check BION function preimplantation could not be used with certain portable PCs because of electrical noise generated on their serial ports. The Personal Trainers were modified to be sturdier because subjects would accidentally drop them and disrupt the enclosed circuitry. Some subjects found the on/off toggle switch to be difficult to operate, so it was replaced with an auto-power-off function. The original DIN connectors to the coil-driver and accessory test well were replaced with lighter, easier to operate RJ-style telephone jacks. In all cases malfunctioning Personal Trainers were replaced and reprogrammed within a day, so therapy was minimally interrupted.

A few minor ClinFit functions were found to be confusing or contained small faults, but this did not affect the clinical function of the system. The clinicians' comments were noted and changes were made to correct the problems and add some features. A new version of the software has been released to the clinicians; it is provided on a CD-ROM, which self-installs ClinFit and the required MS-Access database in one step.

Communication between the transmitting coil and the implanted BIONs was generally reliable. In two implanted BION subjects in the shoulder study (one from the original TES and one from the control group), however, it was difficult to align the transmitting coil to activate both BIONs with the coil in a single position. Because the two subjects could not administer their therapy effectively, their data were pooled with that of the noncompliant

subject. This problem was traced to variability in the electrical function of the custom integrated circuit chip in the implants. It has been corrected as a result of more extensive electrical function testing during manufacture.

No changes in the response of the BIONs after magnetic resonance imaging (MRI) were seen; BIONs were functional after MRI procedures. Subjects did not complain of discomfort related to BIONs during MRI procedures.

Subluxation Reversal

Data are available from five control subjects, five stimulated subjects (both control and the original TES), and three implanted but noncompliant subjects (both control and the original TES). Subluxation of the hemiplegic shoulder is the primary outcome measure. For both manual and radiologic measurements, significant decrease was found comparing subluxation levels before and after six weeks of BION therapy ($p < 0.05$); VDM (vertical displacement measurement) radiologic measurements improved by 55% ± 54% over the six weeks of treatment. If no BION therapy was administered, no significant difference was found between original measurements (at the beginning of the trial) and six weeks later (Fig. 4). Other outcome measures are listed in Table 2, but have not demonstrated significant effects with the presently available sample.

Knee Function

In the knee osteoarthritis trial, five subjects have completed the study. Function improved over the 12 weeks of BION therapy, as indicated by the WOMAC score (improvement of 65% ± 24%; significant difference: $p < 0.01$) and the Knee Society Function score (improvement of 8.3% ± 7.8%; significant difference: $p < 0.05$) (Fig. 5). Pain decreased significantly over the 12 weeks of therapy, as measured by the Visual Analog Scale measurement of pain (improvement of 78% ± 18%; significant difference: $p < 0.002$) and the Knee Society Pain-Free index (improvement of 60% ± 82%; significant difference: $p < 0.05$). MRI data have not been analyzed yet. One subject cancelled scheduled knee replacement surgery, although she may need to consider this option again as her cartilage degenerates further. She still uses BION therapy once a day.

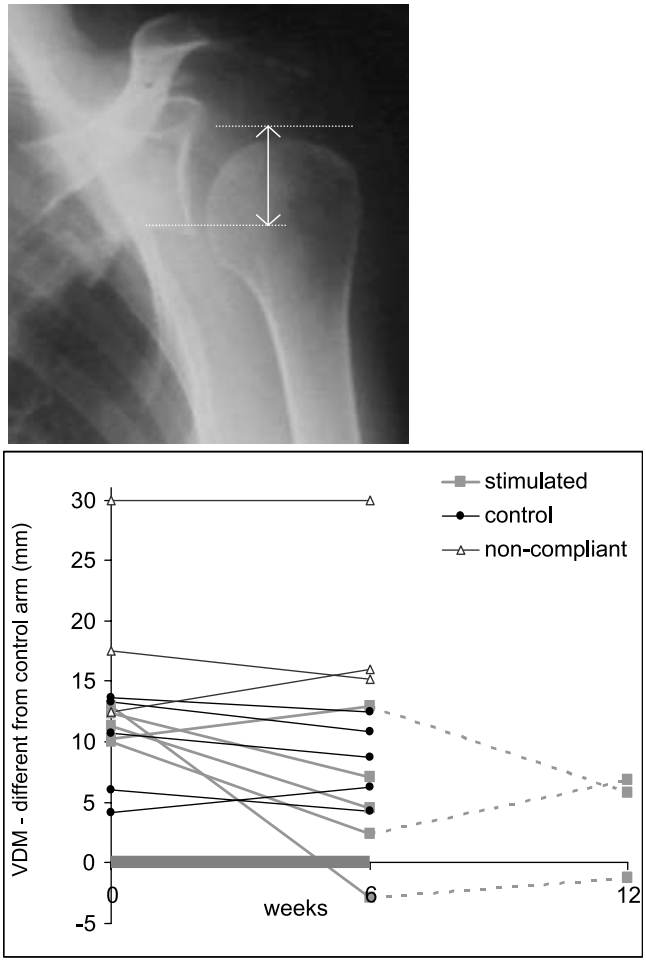

Fig. 4. VDM subluxation index. Top: VDM = The vertical distance separating the apex of the humeral head and the inferior margin of the glenoid fossa. Bottom: Subluxation VDM measurement. Significant difference between zero and six weeks for stimulated subjects ($p < 0.05$); no significant difference for control or noncompliant subjects.

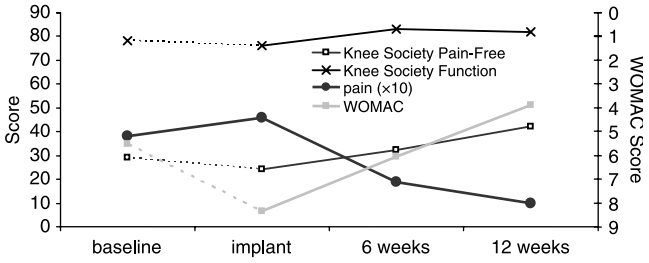

Fig. 5. Knee study results. $N = 5$. WOMAC: Significant difference between implant time and 12 weeks ($p < 0.01$) (right hand-side ordinate). Pain: Significant difference between implant time and 12 weeks ($p < 0.002$). Knee Society Pain-free: Significant difference between implant time and 12 weeks ($p < 0.05$). Knee Society Function: Significant difference between implant time and 12 weeks ($p < 0.05$).

Table 2. Summary of Results for Shoulder Subluxation Study.

	Change: 6 week TES (mean ± SD)	Student *t* -test: before and after 6 weeks of TES	N for statistical analysis
Subluxation X-ray DLT	55 ± 54%	$p < 0.05$	5
Subluxation X-ray Dv	57 ± 49%	$p < 0.03$	5
Subluxation manual	55 ± 18%	$p < 0.02$	3
Active ROM—shoulder	9° ± 18° Shoulder Abductors	$p = 0.2$ Abductors	3
	3° ± 6° Shoulder External Rotators	$p = 0.2$ Rotators	
Passive ROM—shoulder	−17° ± 11° Shoulder Abductors	$p =$ NS Abductors	3
	−19° ± 24° Shoulder External Rotators	$p =$ NS Rotators	
Strength	−0.4 ± 3.2 N Shoulder Abductors	$p =$ NS Abductors	3
	−1.1 ± 1.9 N Shoulder External Rotators	$p =$ NS Rotators	
Arm function	No changes—all identical scores		3
Pain (VAS)	1 subject had pain disappear; the other did not have any change in pain, which was nonexistent to start.		2
Muscle thickness	3% ± 14% deltoid	$p =$ NS deltoid	5 subjects; each 2 sites/muscle
	8% ± 20% supraspinatus	$p =$ NS supraspinatus	

NS = Non-Significant (≥ 0.05)
N < 5 for some tests when control subjects were implanted after the study.

DISCUSSION

Safety and Biocompatibility of Devices

Clinicians reported no difficulty in implanting BIONs in these two areas. The subjects reported that the implantation caused little pain either during or after the procedure. The implantation time (including searching for a low threshold site) is approximately 20 min per device. We believe this can be reduced further with improvements in the design of the insertion tool that are now underway. In our first subject, a BION was implanted in the trapezius muscle instead of in the supraspinatus, but this problem was subsequently avoided by revising the approach. Additional BIONs can be injected at any time; unneeded BIONs do not have to be removed.

We found that BIONs are well tolerated by the subjects, except for one subject who requested removal of the BION implanted in the groin. BIONs do not migrate once implanted in muscle as confirmed by both radiologic studies of the shoulder and stimulus threshold tracking. The shape of the BION appears to encourage connective tissue to "anchor" the implant at the necks of the electrodes (6). In the one instance when tissue around the BIONs could be examined, there was evidence of a thin connective tissue capsule anchoring the BIONs in the muscles, but no evidence of a progressive reaction, confirming that the BIONs are stable and well-tolerated, as least in these sites.

Subluxation Reversal

Shoulder subluxation was diminished significantly by 55% ± 54% ($p < 0.05$) in stimulated subjects, despite the small number of subjects having received the therapy as designed (five subjects). This is very encouraging because we are using lower-frequency stimulation than has been typical in studies using transcutaneous stimulation (11–13). The resulting unfused contractions produce lower contractile forces in the stimulated muscle units. We do not know whether intramuscular BION stimulation is recruiting more or less of the muscle than is typically achieved with transcutaneous stimulation.

Knee Function

Knee function was significantly improved as reported above and pain decreased in subjects with osteoarthritis. This resulted in the delay of knee surgery for at least one subject. Postponing surgery provides an immediate health care cost

savings and reduces the longevity required of the prosthesis. When arthroplasty becomes necessary, the BIONs already in place could be used to facilitate postoperative rehabilitation.

CONCLUSION

Although these are preliminary results of two clinical trials with few subjects, significant improvement has been seen already in the primary outcome measure of each study. We were encouraged by the generally high level of compliance of the subjects, who reported the therapy to be pleasant and easily integrated into daily activities. BIONs are inherently relatively inexpensive to manufacture and to implant, and patients find it easy to deliver regular therapy without professional supervision. Thus, we believe that BIONs could eventually be integrated into clinical practice to treat many types of paralysis and disuse atrophy. We are currently developing some of these other applications for future clinical trials.

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