Functional Electrical Stimulation and Spinal Cord Injury

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KEYWORDS

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KEY POINTS

- Functional electrical stimulation (FES) of the peripheral and central nervous system may be used for rehabilitation and management of complications after spinal cord injury (SCI).
- FES may improve the functional status and quality of life of many persons with spinal cord injuries.
- Many of the FES strategies are already commercially available, whereas others are being tested in human and laboratory studies.
- FES should be routinely considered as part of the rehabilitation and medical management of eligible persons with spinal cord injuries.

An injury to the spinal cord can disrupt communications between the brain and body, leading to a loss of control over otherwise intact neuromuscular systems. By taking advantage of these intact neuromuscular systems, several neuroprostheses have been developed to restore functions through functional electrical stimulation (FES) of the central and peripheral nervous system. Neuroprostheses using FES to control the paralyzed muscles may prevent many secondary medical complications and improve functional independence by providing a means to exercise and negotiate physical barriers. Improvements in multiple body systems and functions have been reported through the use of FES, and they are discussed in this article. These devices range in complexity and include components such as power supplies (which may be completely external to the body or implanted and recharged with radio frequency waves), a control circuit (ie, the brains of the device), lead wires, connectors, external braces, and sensors. This article describes the basic properties of the electrodes, the current FES system being developed in research and in clinical practice, and the future of these devices.

THE BASIC PROPERTIES OF ELECTRODES FOR NERVE STIMULATION

In neuroprostheses, electrodes are the interface between the external circuitry and the tissue, delivering a charge that stimulates the nerves connected to the muscles of interest. This charge perturbs the resting potential of the neuron (typically around −65 mV); if this value is raised beyond a threshold, membrane depolarization occurs. This depolarization results in an influx of Na^+ ions, initiating an action potential that can travel spatially down the length of an axon. A coordinated group of action potentials can lead to a muscle contraction.[1] By targeting nerves rather than the muscle fibers themselves (which can also be stimulated electrically), substantially smaller charge densities may be used, consuming less power and avoiding tissue damage.[2]

Provided that the neuromuscular system is intact, stimulation may be achieved at a variety of locations (from the origin of the neuron in the spinal cord to the peripheral nerve and to the skin above the muscle) using various types of electrodes. The simplest configuration uses large (of the order of square centimeters) electrodes placed on the surface of the skin. The electrodes are easily replaced; however, achieving accurate and precise positioning is challenging, and charge is distributed over a large area. A more invasive approach is to implant needlelike electrodes percutaneously into the muscle of interest. This method is considered a precursor to fully implanted systems, although subcutaneous electrodes themselves can remain functional for years.[3] When electrodes are fully implanted in close proximity to the nerve,

even more precise targeting can be achieved using even smaller current densities, which are less likely to damage the tissue.

Electrodes have been designed to wrap around individual nerves, with a range of geometries, including spiral,[4] helical,[5] and rectangular.[6] To selectively address smaller groups of axons within a nerve and to reach areas that are not readily accessible from the surface, intrafascicular electrodes may be inserted into the nerve itself.[7] Pools of neurons may also be stimulated directly in the spinal cord in intraspinal microstimulation (ISMS).[8] Although implanted devices offer superior targeting, the obvious drawback is the invasiveness of the insertion process and the potential risk of infection, although this has not been reported as a significant issue.[9]

In FES, the electrode typically acts as a conductor, delivering electrical charge from a power supply to the tissue. Charge transfer occurs when voltage applied between the active electrode and a second electrode (called the reference electrode) generates an electric field, which in turn forces electrical charge to flow. In systems in which multiple stimulation channels are used, a single reference electrode may be used. When a voltage is applied, the energy can drive several unwanted chemical reactions. To avoid generating H_2 gas from water, the voltage generated between the electrodes must not exceed the amount required to electrolyze water (-0.6 V to -0.8 V depending on electrode type[10]). The amount of charge that can be delivered within these limits depends on the impedance of the material, which should be low to maximize the current delivered. To balance the charge injected to stimulate the neurons and prevent the electrochemical decomposition of tissue, a secondary pulse of opposite polarity should be included in the stimulation profile (ie, a biphasic pulse should be applied). The electrodes themselves must be selected to be resistant to corrosion under physiologic conditions, even under an applied voltage. Common electrode materials for implanted devices include corrosion-resistant stainless steel and noble metals such as PtIr or Pt (which have highly stable atomic configurations and therefore are resistant to chemical processes such as corrosion or oxidation). Other metals (including silver, iron, and copper) are known to elicit dramatic inflammatory response in vivo and should be avoided.[11]

The time-dependent failure of neural interfaces in vivo is an impediment to long-term use, particularly for recording electrodes and stimulating electrodes, which inject small currents into small target areas. The principal cause of failure of these devices is the encapsulation, which occurs as a part of the foreign body response, insulating the electrodes from their surroundings.[12] To avoid scar formation initiated by mechanical mismatch between stiff electrodes and soft tissues, there is an increasing interest in fabricating electrodes and arrays from soft (low modulus) materials such as silicone elastomer.[13] Beyond this, several strategies have been undertaken to modify the surface properties of electrodes to improve the interactions that take place with surrounding tissue and reduce glial scar formation.[14] When developing new electrodes, arrays, and coatings, in vitro testing may be used initially to screen the cellular response, but they must be tested in vivo following the standard ISO 10993.

UPPER EXTREMITY FUNCTIONAL RESTORATION WITH FES

For persons with cervical-level SCI, restoration of hand function is their top priority.[15] Neuroprostheses using FES provide the most promising method for significant gain in hand and arm function for this population. Muscle contractions can be orchestrated to produce coordinated grasp opening and closing; thumb opening, closing, and positioning; wrist extension and flexion; forearm pronation; and elbow extension for persons with C5-C6–level SCI. Neuroprostheses can be coupled with tendon

transfers to maximize function.[16] The objectives of these neuroprostheses are to reduce the need to rely on assistance from others; the need for adaptive equipment, braces, or other orthotic devices; and the time it takes to perform tasks. Neuroprostheses make use of the patient's own paralyzed musculature to provide the power for grasp and the patient's voluntary musculature to control the grasp. Typically, persons with SCI use the neuroprosthesis for eating, personal hygiene, writing, and office tasks.

Neuroprostheses have been clinically implemented and investigated using systems based on surface electrodes, percutaneous electrodes, and implanted devices. Surface and percutaneous systems have potential application in muscle conditioning and in short-term research or clinical applications.[17] Implanted systems are generally used for long-term functional enhancement.

All existing upper extremity neuroprosthetic systems consist of (1) a stimulator that activates the muscles of the forearm and hand and (2) an input transducer and control unit. The control signal for grasp is derived from an action that the user has retained voluntary control over, which can include joint movement, muscle activity, respiration, or voice control.[18] A coordinated stimulation pattern is developed so that the muscles are activated in a sequence that produces a functional grasp pattern as the user typically has control over grasp opening and closing but does not have direct control over the activation of each muscle.

Surface stimulation of the forearm and hand can be used to exercise and to produce functional movements. Nathan[19] developed a splint that incorporates surface electrodes for grasp. This system is commercially available (NESS H200, Bioness, Valencia, CA, USA) and is primarily intended for therapeutic applications after stroke or SCI, such as building muscle strength, preventing joint contractures, and improving tissue viability. Popovic and colleagues[20] have developed a surface stimulation system called the ETHZ-ParaCare neuroprosthesis. This system is capable of 4 channels of stimulation and can be interfaced with a variety of control inputs. Early functional results indicate that subjects can use the system to perform a variety of activities of daily living (ADL) in the home.[21]

Implanted FES systems have been used for long-term functional enhancement for persons with cervical SCI. The largest clinical trial of an upper extremity neuroprosthesis was the Freehand trial, initiated by the Cleveland Functional Electrical Stimulation Center in 1992.[22] The Freehand neuroprosthesis used an implanted 8-channel receiver-stimulator, and control of grasp opening and closing was achieved through graded elevation of the user's contralateral shoulder. Using the neuroprosthesis, 100% of the participants (n = 28) improved in independence in at least 1 task, and 78% were less dependent in at least 3 tasks. More than 90% were satisfied with the neuroprosthesis.[23] The Freehand system was transferred to industry (NeuroControl Corp, Elyria, OH, USA) and was implemented successfully in more than 200 patients with SCI using neuroprostheses.[24] Despite the clinical success, the company exited the SCI market in 2001 and no longer markets the Freehand System.

A second-generation implanted neuroprosthesis has been developed, improving on the features of the Freehand System.[25] This system, called the Implanted Stimulator Telemeter Twelve-channel System (IST-12), has 12 stimulation channels and 2 channels of myoelectric signal recording acquisition.[26] To date, 12 subjects with SCI have been implanted with the IST-12 system, including 3 subjects with systems for restoring movement in both hands. Subjects successfully use the processed myoelectric signal from a wrist extensor for proportional control of grasp opening and closing. Every subject has demonstrated improvement in at least 2 activities and as many as 11 activities. Most commonly, improvement was demonstrated in eating with a fork

and writing with a pen. Other tasks in which subjects showed improvement included office tasks, using a cell phone, getting money out of a wallet, and embroidery,[25] as illustrated in Fig. 1.

Availability

At present, commercially available FES systems for grasp function in cervical SCI are limited to surface stimulation systems. Specifically, the NESS H200 is available by prescription at multiple sites throughout the world (www.bioness.com). Other systems, such as the Compex system, are primarily targeted for exercise training rather than function benefit. Efforts are underway to increase the availability of implanted neuroprostheses to persons with SCI (http://casemed.case.edu/ifr/).

Future Directions

Future directions for FES hand systems include the development of fully implanted systems that eliminate the need to don and doff components[27] and the expanded use of myoelectric control algorithms to control multiple functions at the same time.[28] The use of signals derived directly from the brain (brain-computer interface), either externally or through implanted electrodes, is expected to result in more natural hand system control.[29] In addition, systems are being developed to provide whole-arm function for those with C4 or higher SCI.[30]

LOWER EXTREMITY FUNCTIONAL RESTORATION WITH FES

In persons with SCI, the inability to stand or step significantly limits the performance of many ADL such as washing dishes at a counter or reaching items on high shelves. For persons with thoracic-level complete SCI, stimulated contractions of the lower extremity muscles can enable standing and stepping, increase personal mobility, and improve general health and quality of life.[31] In persons with incomplete injuries, walking performance can be improved.[32]

Eight channels of continuous stimulation to the knee, hip, and trunk extensors can power the sit-to-stand transition and support the body vertically against collapse (Fig. 2).[33] Stimulation to the hip ab/adductors and ankle plantar/dorsiflexors has been included in experimental systems for sensor-based control of standing balance in the coronal and sagittal planes.[34] Existing neuroprostheses for lower extremity function use maximal levels of constant stimulation at the hips and knees.[35] Recipients of a neuroprosthesis with epimysial and intramuscular electrodes that continuously activated the vasti, gluteals, hamstrings, and lumbar erector spinae exhibited mean and median standing times of 10 and 3 minutes, respectively.[33] This time is sufficient for facilitating transfers to high surfaces, performing swing-to gait for short distances in wheelchair-inaccessible environments, and participating in other social, work, and personal activities. Some implant recipients in a phase II clinical trial of the system were able to stand for more than 20 minutes, and all were able to release 1 hand from a walker or assistive device to reach objects overhead (Fig. 3). On average, 90% of body weight was placed on the legs, reducing requirements on the arms to only light touch to maintain balance. System performance and patterns of usage were maintained after discharge for at least 1 year of follow-up. Although there were no discernible interactions between injury level, degree of preserved sensation, or time postinjury and system performance, outcomes seem to be inversely proportional to height and weight, implying that body mass index may be an important clinical factor for determining expectations.[35] Long-term use of neuroprostheses for standing was safe and effective and had no adverse physiologic effects.

Fig. 1. Functional activities performed using the IST-12 myoelectrically controlled neuroprosthesis. From left to right: eating with a fork, holding a pen to write, holding a cup, needle embroidery, holding a tennis racquet.

Fig. 2. Implant recipient (C7 AIS C) standing with FES to the knee, hip, and trunk extensors, and hip/trunk ab/adductors. Multicontact cuff electrodes on the femoral nerves selectively activate the uniarticular heads of the quadriceps (vastus lateralis, intermedius, and medialis).

Fig. 3. Eight-channel implant recipient (T9 AIS A) releases one hand for overhead reaching activities while standing with the neuroprosthesis.

Stepping of up to 100 m has also been achieved after paralysis with simple preprogrammed patterns of open-loop stimulation delivered from the surface or via 8- and 16-channel implanted pulse generators.[36] Once initiated by the user, stepping motions can cycle continuously while the appropriate adjustments are made with the upper body until the pattern is stopped. Alternatively, the stimulation for sequential steps can be triggered from successive depressions of ring- or walker-mounted switches or automatically from body-mounted sensors, such as inclinometers, accelerometers, gyroscopes, or foot or heel switches.[37] The largest potential impact of stimulation may be for people with motor incomplete injuries (**Fig. 4**) who require activation of a small number of muscles during the gait cycle to become household or community ambulators.[38] In such cases, gait training with stimulation can have a therapeutic effect in terms of improved voluntary strength, walking speed, stride length, and cadence even after completion of aggressive conventional therapies.[39] Interactive use of stimulation to assist gait resulted consistently in an additional 20% improvement in walking speed and 6-minute distance, as well as a more than 3-fold increase in maximum walking distance, illustrating a significant neuroprosthetic effect. Walking with stimulation was also more dynamic as evidenced by decreased time spent in the double support phases of gait. The electromyographic activity of muscles under volitional control has also been exploited as a command source to control stimulation in persons with incomplete injuries, which has the potential to coordinate stimulated contractions with voluntary motor function, and in so doing reinforce voluntary movement patterns and provide a mechanism to continuously modulate walking speed and cadence.[40]

Surface FES to the lower extremity muscles with intact innervation has allowed cycling movement that simulates exercise training, leading to increase in oxygen consumption during exercise,[41] muscle mass and strength, and quality of life in persons with chronic SCI.[42]

Fig. 4. Subject with incomplete SCI (C5 AIS D) walking with an 8-channel implanted receiver stimulator for activation of hip flexors and ankle dorsiflexors.

Availability

Although implanted standing and walking systems clearly provide significant functional and clinical benefits, such systems are only available on a research basis. Limited lower extremity function is possible with commercially available surface stimulators with reduced channel counts.[43]

FES cycling devices are available through Restorative Therapies, Inc. (www.restorative-therapies.com) and Therapeutic Alliances, Inc. (www.musclepower.com) in the United States.

Future Directions

Standing performance with implanted neuroprostheses can be improved significantly by using nerve-based electrodes, which more fully recruit the target muscles. Continuous stimulation of the femoral nerve with a multicontact cuff electrode below the branches to the rectus femoris and sartorius was shown to extend standing time and accelerate progress through reconditioning rehabilitation and balance training with the system.[44] The potential to delay the effects of fatigue by alternating activation of independent motor unit pools within a muscle via multicontact nerve cuffs or multiple independent nerve- or muscle-based electrodes is also being investigated.[45] At present, neuroprostheses are generally unresponsive to environmental disturbances, necessitating use of the arms for balance on an assistive device. Additional research is also focusing on automatically modulating stimulation in response to perturbations to reduce reliance on the upper extremities, allow users to alter their postures in advance of anticipated disturbances, and minimize the risk of falls while standing or using advanced biomechanical modeling techniques to optimize stimulus patterns during walking or while assuming various task-dependent standing postures.[46] Another promising development involves the combination of FES with exoskeletal bracing that can lock, unlock, or couple the joints as necessary to avoid fatigue and smoothly shape limb trajectories or that can inject small amounts of assistive power when the stimulated responses are too weak or fatigued to complete a motion.[47] With such an approach, users would be able to walk under their own power and therefore accrue the physiologic benefits of exercising the paralyzed muscles in addition to those of standing, weight bearing, and mobilization.

TRUNK CONTROL AND POSTURE WITH FES

After SCI, trunk muscles can oftentimes not provide the necessary forces to adequately control trunk posture because of a lack of innervation[48] and/or muscle atrophy,[49] significantly limiting their performance during ADL[50] and even leading to secondary health complications such as reduced respiratory capacity.[51] To compensate for insufficient muscle control during sitting, persons with SCI usually tilt their pelvis further backward to increase stability in the anterior direction.[52] When reaching, they oftentimes use one arm thrown over the back of their chair to provide the external forces necessary to keep the trunk from bending forward uncontrollably. Compensational sitting arrangements can, however, lead to kyphosis[52] and pressure ulcers (PUs) that arise from asymmetric trunk orientation and infrequent weight redistribution. It is therefore not surprising that persons with SCI have prioritized the recovery of trunk control over the recovery of walking function and other essential functional abilities.[15]

Bracing devices such as corsets are perhaps the most common items for stabilizing the trunk after SCI. To improve reaching and wheelchair propulsion, some persons with SCI use chest straps.[53] In the general case of reaching from a wheelchair during ADL, chest straps or other restraints are highly undesirable as they hinder free and

spontaneous movement, decrease available trunk range of motion, and draw undue attention to themselves. Other studies have shown that the large forces exerted on the abdomen by a fabric corset might cause abnormal increases in the intra-abdominal pressure, potentially leading to disturbance of the viscera.[54]

Stiffening the paralyzed trunk and hip extensors with continuous FES has a multitude of benefits: it can correct kyphotic seated postures, normalize lateral vertebral alignment, improve ventilation and respiratory volumes, and alter interface pressures.[55] It can also expand bimanual workspace,[48] statically stabilize the torso (**Fig. 5**), increase the forces that can be exerted on objects with the upper extremities, return users to erect sitting from a fully forward-flexed posture, and improve manual wheelchair propulsion efficiency at comfortable speeds.[56] Independent bed turning and wheelchair transfers can also be facilitated by more rigidly coupling the pelvis to the shoulders when the paralyzed core trunk muscles are continuously activated with stimulation to stiffen the torso.[57] In addition, activating the quadratus lumborum with surface or implanted electrodes has been shown to enhance mediolateral stability and assist with attaining side leaning postures, whereas coactivation with the abdominal muscles can further stiffen the trunk while seated or assist in attaining forward leaning postures. Some of the required muscles to achieve these clinical outcomes can be accessed via surface stimulation; however, strong and isolated contractions are robustly and repeatably achieved by exciting the T12-L2 spinal nerves associated with the lumbar erector spinae and other muscles (**Fig. 6**) using intramuscular electrodes and surgically implanted pulse generators.[58] The strategy of continuously activating the core trunk and hip muscles only substitutes one statically stable posture for another. Upper extremity effort is still required to stabilize the body during transitions between nonstimulated and stimulated postures and to maintain balance or restore erect sitting when exposed to internal or external perturbations.

Fig. 5. Effect of FES on seated posture. By stimulating the trunk and hip muscles, consistent significant changes in posterior pelvic tilt and shoulder height were recorded.

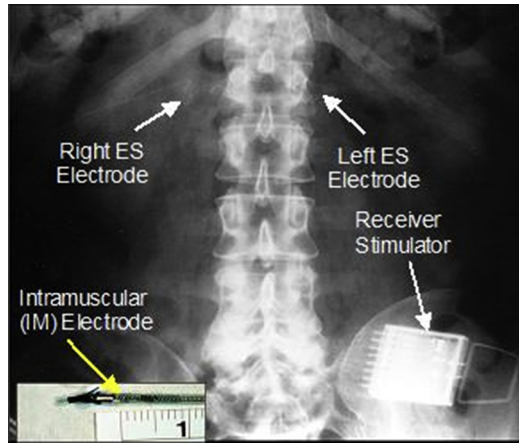

Fig. 6. Radiograph of an implanted trunk system showing intramuscular electrodes (*inset*) inserted into T12-L1 to activate the lumbar erector spinae muscles.

Extensive studies have been carried out to assess the strategy used by the intact central nervous system to mediate trunk balance in neurologically intact persons. Such studies mainly involve biomechanical simulations and experimental observations of the static and dynamic behaviors of trunk posture in a seated pose.[59] These studies confirmed the initial feasibility of using continuous stimulation to increase trunk stiffness, vary trunk posture, and resist static perturbations. Moreover, they resulted in tools for evaluating more sophisticated control systems that might allow users to set their own task-dependent postures and maintain balance during internal or external perturbations. Studies have established the feasibility of a self-righting control system that works on the dynamic movement of the trunk to automatically return to an erect posture from forward-flexed positions by monitoring trunk tilt and modulating stimulation to the trunk and hip extensors appropriately (**Fig. 7**).[60] In this study, 5 persons with SCI volunteered to test a simple threshold-based set-point controller. The controller worked consistently across all subjects despite considerable intersubject variability in terms of SCI level and motor and sensory impairment.

Availability

At present, neuroprostheses for controlling the paralyzed torso and enhancing seated function can be obtained only through research and development studies, whereas attempts to commercialize such systems are ongoing.

Future Directions

Advanced systems to control seated posture and trunk balance have the potential to prevent falls from the wheelchair while performing ADL, during sudden collisions and unexpected stops, and while negotiating bumpy or uneven terrain, thus eliminating the need for chest straps or other constraints that would hinder function. New systems that can sense trunk and wheelchair positions, velocity, or acceleration, as well as communicate the user's intent to closed-loop controllers need to be developed. Important requirements of such systems are that they are portable, appear natural, and can be easily integrated with any residual motor and/or sensory function. Such systems also need to be translated into routine clinical use and disseminated widely

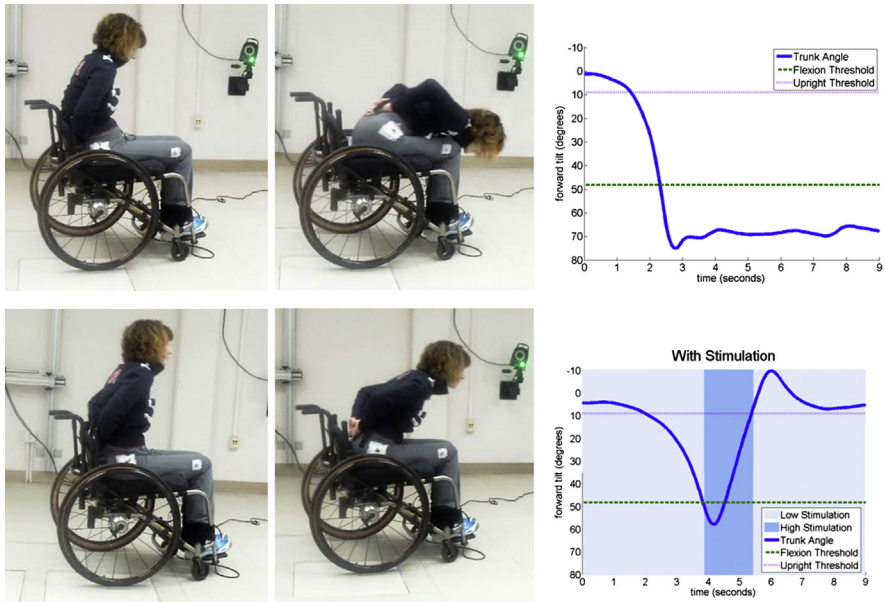

Fig. 7. Simple threshold-based control of seated balance based on trunk tilt in a subject with C8 tetraplegia. Without stimulation (*top*) of the hip and trunk extensors, the subject cannot return to erect sitting from a fully forward-flexed position without use of the arms. With the controller active (*bottom*), forward trunk tilt is arrested before a forward fall, and upright posture is automatically restored.

in home and community environments. Future directions also include the timing of the stimulation to coincide with different phases of the manual wheelchair propulsion cycle to improve efficiency during ramp ascent or varying speeds, utilization during rowing exercise, and early introduction of trunk control systems soon after injury to prevent the development of spinal deformities and help vary posture to augment pressure relief maneuvers.

FES TECHNIQUES TO RESTORE RESPIRATORY MUSCLE FUNCTION

The use of FES to improve respiratory muscle function is discussed in depth in the article by Dalal and DiMarco elsewhere in this issue.

PREVENTION OF PRESSURE ULCERS THROUGH FUNCTIONAL ELECTRICAL STIMULATION

PUs are a common complication after SCI. They cause psychological distress, have a detrimental effect on quality of life, and place a significant burden on health care systems, with costs estimated at $6 to $15 billion per year in the United States.[61] Preventing PUs from developing in the first place reduces patient suffering, improves patient outcomes and quality of life, and reduces the large health care costs associated with treating them. Indeed, it has been estimated that prevention of PUs is approximately 2.5 times more economical than treating them.[62]

PUs can develop in one of 2 ways. They can originate at the surface of the skin and progress inward if unattended. Skin inspections are often effective in detecting these ulcers at an early stage of development. If unattended, these ulcers can progressively

affect deeper tissue layers ending at the bone. PUs can also originate at deep muscle-bone interfaces and progress outward. These ulcers have only recently been acknowledged clinically and are now referred to as deep tissue injury (DTI). Sustained pressure leads to unrelieved mechanical deformation, tissue ischemia, and ischemia-reperfusion injury. Muscle is more susceptible to breakdown because of mechanical deformation and ischemia-reperfusion injury than skin; thus, damage originates within muscle tissue around bony prominences much sooner than in the skin. Skin inspections are ineffective in detecting DTI at their earliest stages of development, and there are no clinically viable methods for the early detection of DTI. Therefore, these ulcers often develop unbeknownst to the affected individual or their caregiver. Once DTIs exhibit obvious skin signs, for example, purple discoloration, extensive damage in the underlying soft tissue had already occurred. Prevention strategies such as pressure redistributing surfaces (mattresses and seating cushions) and periodical weight shifts have not decreased the incidence of PU; in fact, with the improved awareness of DTI, the prevalence of PU is on the rise.[63] Other approaches to prevent PU are necessary. FES through surface stimulation and implanted electrodes are two novel ways to prevent PU, each having their own specific advantages and disadvantages. Both systems require intact innervation to the gluteal muscles.

Intermittent Electrical Stimulation for the Prevention of DTI

Intermittent electrical stimulation[64] (IES) was developed for the prevention of DTI. This method applies brief electrical stimulation through surface electrodes to muscles around bony prominences that are loaded during sitting or lying down (eg, the gluteus maximus muscles) every few minutes causing them to contract. These periodical contractions mimic the subconscious postural adjustments conducted by able-bodied persons in response to discomfort while sitting or lying down. Ten seconds of IES causing fused muscle contractions in the gluteus muscles every 10 minutes while sitting redistribute surface pressure away from the ischial tuberosities and increase tissue oxygenation in study participants independently of gluteal muscle mass.[65,66] Moreover, IES-induced contractions significantly redistribute internal pressure away from the bony prominences[67] and reduce tissue deformation in the muscles between the ischial tuberosity and skin even when loading levels as high as 75% of body weight in adult pigs with SCI were applied.[67] IES is effective in significantly reducing or completely eliminating the formation of DTI in adult rats and pigs,[68] thus establishing a strong scientific support for the utility of IES as a means for preventing DTI in clinical settings.

Implanted Neuromuscular Stimulation for Tissue Health and Pressure Ulcer Prevention

Another approach of FES for PU prevention is through stimulation of the inferior gluteal nerve, which innervates the gluteus maximus muscle and lies deep to the buttock surface and close to the sciatic nerve. Surface electrode placement for preferential recruitment of the inferior gluteal nerve can be difficult for users to achieve. Moreover, repeatable electrode placement in the upper buttock region may be hard to accomplish for either independent users or their carers. Implanted neuromuscular electrical stimulation (NMES) systems for long-term therapeutic use have dual advantages. The stimulating tip of the electrode can be located close to the motor point of the nerve of interest; this reduces the charge required to elicit a contractile response and ensures that the response is repeatable and predicable. The user does not have to replace the stimulating electrode every day, so the system is both reliable and simple to use.

The gluteal stimulation v1 (GSTIM I) system using implanted electrodes with percutaneous leads provides both concurrent bilateral and alternating gluteal stimulation to deliver muscle conditioning and regular weight shifting to the user. GSTIM I has been shown to have a positive impact on multiple aspects of tissue health. Subjects who received GSTIM I have shown statistically significant changes between baseline and postintervention ischial region interface pressure (Fig. 8). Maximum gluteal muscle thickness significantly increased and was maintained with regular use of gluteal NMES.[69] Tissue oxygen levels also improved with regular use of dynamic stimulation but decreased on withdrawal.

In addition to the long-term changes in muscle characteristics, weight shifting induced by gluteal NMES dynamically alters conditions at the seating support interface facilitated by stimulated muscular contractions. This dynamic effect increases over time as the paralyzed muscles become stronger with regular use of implanted gluteal NMES. Chronic application of gluteal stimulation is thus uniquely able to affect the intrinsic properties of paralyzed muscle through contractile responses to repeated stimulation, increasing muscle thickness and blood flow together with reducing regional interface pressures.[70,71] Use of GSTIM I also increased sitting tolerance and minimized the impact of minor incidents such as skin tears due to poor transfers, which were reported to be resolved in days rather than in weeks.

Therapeutic implanted NMES provides a unique intrinsic approach to reducing the risk of PU development for persons with SCI. Daily use of NMES is indicated to

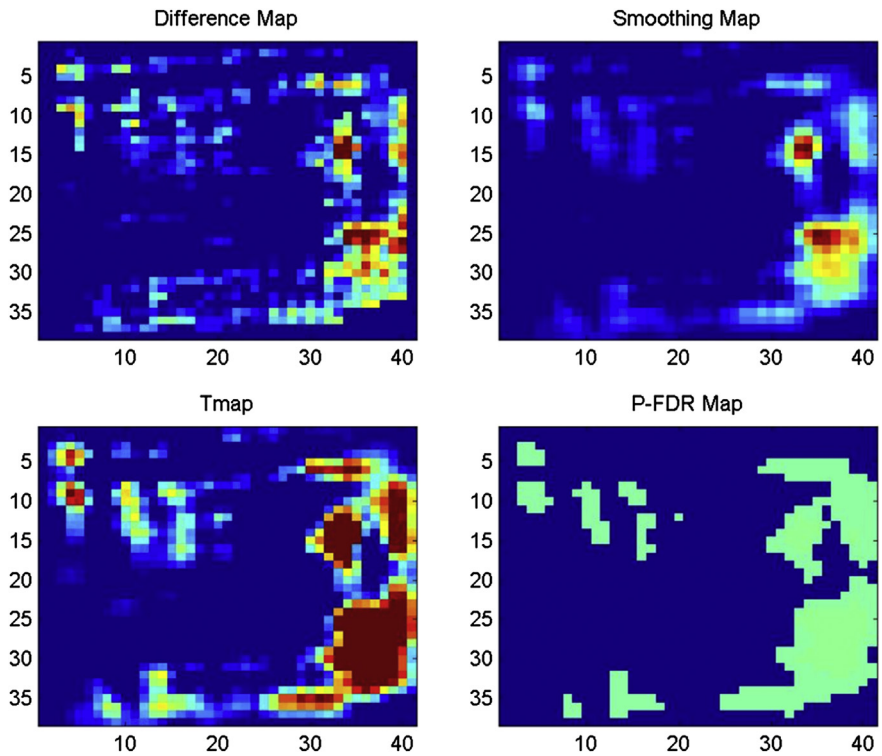

Fig. 8. Multistage longitudinal analysis and self-registration analysis maps showing areas of significant change in seated interface pressures over time (output adjusted for simultaneous testing at multiple locations).

maintain hypertrophy of paralyzed muscles. Long-term use of gluteal NMES using implanted systems may provide an adjunctive method to ensure a regular pressure-relief regimen in high-risk persons, which can reduce the risk of PU development and allow users to participate more fully in ADL.

Availability

Both the IES system and the fully implanted NMES for the prevention of PUs are under research protocol use only.

Future Directions

Further research is underway to examine the efficacy and effectiveness of the approach for PU prevention with both the surface stimulation and implanted systems. A system for clinical use to deliver IES to the gluteal region, known as Smart-e-Pants[72] (Smart-electronic-Pants) (**Fig. 9**), was developed. It is composed of a garment, surface electrodes, and a small battery-operated stimulator. The electrodes are placed on mesh panels in the garment. Safety, feasibility, and acceptability of Smart-e-Pants have been tested in a wide range of health care settings, including 50 volunteers in an acute rehabilitation unit, tertiary rehabilitation hospital, a long-term care facility, and home care. Study participants used the system for at least 4 weeks, 12 hours per day. The system proved to be safe and feasible in all 4 clinical settings. No PU was observed in any of the participants. Donning and doffing of the Smart-e-Pants system took between 7 and 18 minutes. Patients and caregivers did not find the application of Smart-e-Pants or IES to be disruptive and indicated that the stimulation was acceptable as part of their daily routine in more than 97% of the time. These preliminary clinical studies on IES as a preventative treatment strategy are promising. Studies are currently underway to test the effectiveness of the IES approach in preventing pressure ulcers, and demonstrate the improvements in health and cost outcomes that it may provide.

Future development of the fully implanted NMES system will use a small, rechargeable stimulator customized to provide 2 synchronized channels of stimulation to

Fig. 9. Smart-e-pants system showing garment, mesh panel for surface electrodes, and stimulator. (*Courtesy of* Project Sensory Motor Adaptive Rehabilitation Technology (SMART), Edmonton, Alberta, Canada; with permission.)

automatically produce the regular weight-shift maneuvers recommended for periodic pressure relief when seated in the wheelchair.

FES FOR RESTORING BLADDER CONTROL

The lower urinary tract (LUT) functions in the storage and emptying of urine. After SCI with an upper motor neuron injury to the sacral nerve roots, volitional control of these functions is frequently lost and the LUT becomes hyperreflexive. Incontinence can occur when the detrusor produces large, uninhibited reflex contractions at low volumes of stored urine. Simultaneously with detrusor contractions, the external urethral sphincter (EUS) may reflexively contract as pressure builds in the urethra during voiding, producing detrusor-sphincter dyssynergia (DSD). This uncoordinated reflex and the subsequent high bladder pressures can result in inefficient voiding, incontinence, and ureteric reflux, causing renal injury. In addition, DSD can also cause autonomic dysreflexia (AD), which can be life-threatening if not resolved. Finally, loss of bladder control has a severe impact on quality of life and self-image. Persons with SCI list bladder function restoration among the highest priority for restoration, more than standing and ambulation.[15]

Persons with SCI frequently report ineffectiveness with existing bladder management, medication side effects, challenges associated with bladder catheterization strategies, and complications associated with surgical solutions. Similar to many other complications of SCI discussed earlier, there remains a critically unmet need to restore bladder function lost to SCI and the use of FES may offer an effective solution.

FES offers a means to restore LUT function by activating the bladder and inhibiting the urethral sphincter to produce voiding or by inhibiting the bladder to provide urinary continence and reduce triggers for AD and restore LUT function.[73] The Brindley approach was the first widely clinically available FES system for bladder function.[74] This approach produces bladder contractions by stimulating bladder motor efferents in the sacral roots. To avoid cocontraction of the EUS and detrusor preventing fluid flow, stimulation is delivered in repeated bursts. After each burst, the striated EUS muscle relaxes, but the smooth-muscle bladder relaxes more slowly, maintaining bladder pressure and creating a pressure gradient that causes poststimulus urine flow. This system has been implanted in thousands of persons with SCI and is both medically effective and cost-effective.[75] However, this approach requires transection of the dorsal spinal roots (dorsal rhizotomy) to eliminate unwanted bladder and urethral reflexes due to sensory feedback. This rhizotomy also eliminates desirable reflexes that affect sexual and bowel functions and removes the opportunity for future clinical therapies, markedly reducing acceptance of this approach by persons with SCI.[76]

Stimulation of peripheral sensory pathways can access and influence the spinal neural circuits that control pelvic reflexes and function. Afferent-mediated neural prostheses take advantage of natural nervous system processes and are potentially less invasive than spinal-root-based approaches such as the Brindley system. This approach has the potential to provide more natural function than motor-driven approaches, although it is more dependent on stimulation patterns and other inputs to the spinal circuits. One such approach uses genital nerve stimulation to achieve direct spinal level bladder inhibition. This approach has primarily been applied for immediate use, but it has also shown to improve urinary continence and bladder capacity in persons with SCI during short-duration use.[77,78] If longer-term use is effective, then this approach may provide both a noninvasive and implanted option. Bladder inhibition via implanted electrodes on the pudendal nerve[79] and sacral roots[80] can also provide bladder inhibition in persons with SCI.

Availability

There are several neural prostheses in development to restore pelvic functions for persons with SCI to activate or inhibit the bladder and urethral sphincter and provide a rhizotomy-free Brindley system. They are not commercially available yet.

Future Directions

Some approaches have been shown to be effective in animal models and may be promising for human studies. Bladder activation and voiding via pudendal urethral afferent stimulation has been demonstrated in animal models, and human studies suggest that bladder excitation can be achieved.[81] This approach may provide a peripheral-based alternative to sacral-root-based bladder activation.

Urethral sphincter inhibition and bladder voiding can be obtained with patterned afferent stimulation of sacral dermatomes.[82] This approach has achieved clinical daily voiding of awake animals with chronic SCI. It may potentially provide a less-invasive alternative in humans. Finally, high-frequency (kilohertz) stimulation can provide temporary, reversible, and complete conduction block of the pudendal nerve, and thus stop reflexive EUS contractions, allowing bladder voiding equivalent to nerve transection.[83] Bilateral pudendal nerve block can provide clinical daily voiding of awake animals with chronic SCI. If this approach is effective in humans, it could be combined with pudendal bladder inhibition to restore bladder function with a single implant.

INTRASPINAL MICROSTIMULATION FOR GAIT RESTORATION

Apart from the aforementioned systems that are either commercially available or closer to clinical availability, one novel experimental approach is worth noting. A significant limitation of the surface stimulation system to restore walking is that many of the key muscles required for walking lie deep in the leg and are not accessible with surface electrodes. Even with the percutaneous implantation system, many channels are required to stimulate these different muscles. Mushahwar and colleagues [84–87] have pioneered the use of implanted electrodes in the spinal cord to overcome these problems. This approach, known as intraspinal microstimulation (ISMS), has shown promising results in pre-clinical animal studies. Intraspinal microstimulation entails the implantation of a few fine, hair-like wires in the ventral horns of the small lumbosacral enlargement of the spinal cord (~5 cm long in humans). This region contains the cell bodies of the motoneurons innervating all the muscles of the lower extremity, as well as large proportions of the neural networks involved in locomotion. Tapping into this region allows access to the standing and stepping control centre in the spinal cord. Stimulation through a single ISMS microwire can produce selective movements around one joint.[85,86,89] A single ISMS microwire can also activate synergistic muscle groups that produce coordinated multi-joint movements such as downward full limb extension, upward flexion, forward reaching, and backward propulsion,[87] which eliminates the need for routing electrodes widely through the body to each member of a muscle group producing these movements. The levels of stimulation with ISMS (<0.1 mA) are orders of magnitude less than those required for stimulation through the skin or percutaneous electrodes. Moreover, the levels required for generating functional limb movements generate no signs of discomfort or pain in conscious experimental animals implanted with ISMS microwires. By activating the underlying locomotor-related networks in the lumbosacral enlargement, ISMS activates the motoneurons trans-synaptically. This in turn recruits the motor units in a near normal physiological order which produces graded recruitment of force and large improvements in fatigue-resistance relative to FES systems targeting the muscles or

peripheral nerves.[84,90] In chronically implanted animals, ISMS microwires remained stable throughout the duration of implantation and produced negligible damage in the spinal cord.[88,91] In adult cats, ISMS was effective in producing long durations of standing that, on average, were 5 times longer than durations produced by peripheral FES.[92] Moreover, ISMS produced long durations of in-place stepping in animals with chronic SCI and atrophied muscles.[93] In deeply anesthetized animals, ISMS was capable of producing long distances (>1 km) of weight-bearing and propulsive over-ground walking[94]; these distances were 10 times longer than walking distances produced by peripheral FES.[95] The produced walking was adaptable on-the fly using intelligent control strategies that adjusted the stimulation pattern based on miniature force and position sensors mounted on the legs.[95,96] The intelligent control strategies allowed for automatic adaptations to perturbations as well as muscle fatigue. Interestingly, both standing and walking with ISMS were produced with as few as 4 microwires in each side of the spinal cord.

Given the promising results obtained by ISMS, a proof-of-principle human study is currently planned, and a number of considerations are under discussion. These include patient selection, instrumentation, level of spinal cord injury, and fusion of spinal vertebra around the implant region. The most common sites of traumatic SCI are the cervical and thoracolumbar junction, while mid-thoracic injuries constitute 35% of all injuries. The appropriate volunteers for the study would be drawn from the mid-thoracic pool. While younger patients are generally better candidates for any experimental therapy, a temporary implant or an intra-operative mapping procedure to determine the ability of ISMS to produce functional leg movements may preclude these persons from undergoing permanent implantation in the future. Multiple penetrations of the spinal cord may result in gliosis, and opening the dura mater may produce a scar in the pia mater and arachnoid layers, making surgical re-exploration more difficult. Other surgical considerations include the ease of implanting very fine wires <100 μm in diameter into the spinal cord. Specialized instrumentation has been designed to inject stem cells successfully into the anterior horn of lumbar spinal segments[97,98] and could be adapted to insert electrodes as well. As with stem cell injection, anticipated complications include cerebrospinal fluid leakage. Minimally invasive insertion methods may be considered and fusion may be undertaken as part of the procedure to secure wires ema.

SUMMARY

Functional electrical stimulation has been well-studied and can be used in many ways to improve the well-being and functionality of persons with SCI. The scope of applications for FES in SCI continues to grow. Many options are commercially available both for institutional and home use, while others are still in research phase. When appropriate, SCI clinicians are encouraged to consider the use of FES as part of their standard regimen for rehabilitation or medical management of persons with SCI.

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