Neuroprostheses

Milos R. Popovic
University of Toronto, Toronto, Ontario, Canada

T. Adam Thrasher
Toronto Rehabilitation Institute, Toronto, Ontario, Canada

INTRODUCTION

A neuroprosthesis, sometimes called a neural prosthesis, is a device that provides short bursts of electrical impulses to the central or peripheral nervous system to produce sensory and/or motor functions. Over the past four decades, neuroprostheses have been developed for a wide variety of applications. Some have achieved great success, such as the cochlear implants and bladder management stimulators that are produced in large volume worldwide. Other neuroprostheses, such as those for walking and grasping, have not yet matured to a level that creates a significant consumer demand. There are far too many neuroprostheses on the market and in development to list comprehensively, so this review involves the general features, principles, and functions of some of the most notable devices past and present.

PHYSIOLOGICAL OVERVIEW

In nerve cells, information is coded and transmitted as a series of electrical impulses called action potentials, which represent a brief change in cell electric potential of approximately 80 mV. Nerve signals are frequency modulated; that is, the number of action potentials that occur in a unit of time is proportional to the intensity of the transmitted signal. Typical action potential frequency is between 4 and 12 Hz. An action potential can be elicited artificially by changing the electric potential of a nerve cell or a nerve axon by inducing electrical charge into the cell (Fig. 1). This process, when used to produce action potentials in motor neurons to generate body function, is termed functional electrical stimulation (FES).

Where sufficient electrical charge is provided to a nerve cell, a localized depolarization of the cell wall occurs, resulting in an action potential that propagates toward the end of the axon (orthodromic propagation). Concurrently, an action potential will propagate backward towards the cell body (antidromic propagation). Typically, FES is concerned with orthodromic impulses, using them to generate muscle contractions by stimulating motor nerve axons that can produce desirable body functions. Until recently, antidromic impulses were considered a useless side effect of FES, but there is new interest in the potential role of antidromic impulses in neural rehabilitation.[1]

Since generation of action potentials and their propagation occur in the axons, the motor nerves of the stimulated muscles must be intact. If peripheral axons are missing (if they have been cut or have degenerated, for example), the muscle becomes denervated and therefore highly resistant to electrical stimulation. However, contractions can be elicited from denervated muscles by applying extremely intense electrical fields across the muscle fibers, as demonstrated by researchers at the University of Vienna.[2]

Nerves can be stimulated using monophasic or biphasic current or voltage pulses. The monophasic pulses are seldom used because they lead to unbalanced charge delivery to the tissues, potentially causing damage due to galvanic processes. Most modern FES systems implement biphasic current or voltage pulses, or so-called monophasic compensated pulse shapes.

Another way to activate muscles is to stimulate ascending axons of sensory neurons that trigger reflex arcs. The case where electrical stimulation is used to stimulate sensory neurons and thus alter reflexes or central nervous system functions is commonly described by the term neuromodulation.

TECHNOLOGY

Neuroprostheses come in many different shapes and sizes and serve many different purposes. The common components in all neuroprostheses are: 1) a power source; 2) a stimulus generator; 3) a user-control interface; and 4) electrodes. Most modern neuroprostheses are batteries, disposable or rechargeable, as a power source. Some still use external AC power. Stimulus generators have been miniaturized dramatically over the years. Nowadays, commercial and laboratory-class stimulators tend to be lightweight (less than 1 kg) and handheld. User-control

DOI: 10.1081/E-EBBE 120013941

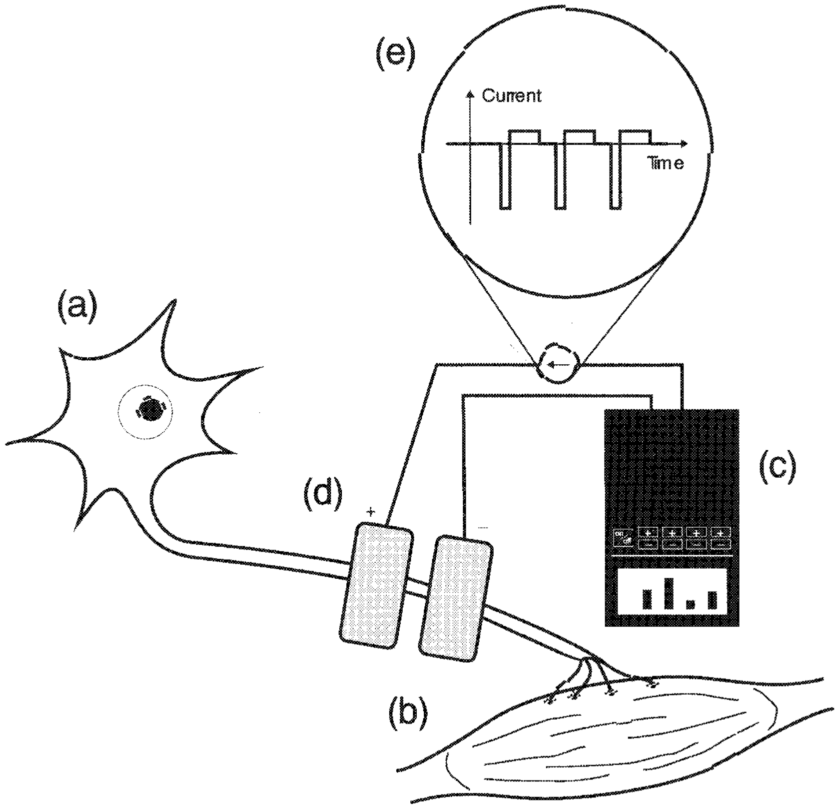


Fig. 1 Illustration of direct stimulation of a motor neuron. The cell body (a) is responsible for synthesizing input from dendrites and deciding whether or not to generate signals, which are transmitted to the corresponding muscle fibers (b). Following a stroke or spinal cord injury, muscles are impaired because motor neurons no longer receive sufficient input from the central nervous system. A neuroprosthesis (c) injects electrical current into the cell axon (d). A train of negative pulses (e) produces a series of action potentials. Depolarization occurs where negative current enters the axon at the active electrode indicated.

interfaces usually consist of a simple control panel with standard manual controls such as switches, buttons, dials, and sliders, plus some kind of visual output such as light emitting diodes or, on more sophisticated models, a liquid crystal display. In addition, input devices are often mounted on the user's assistive devices, such as a pushbutton attached to a cane or walker. In some cases, input devices are attached to the user's clothing or body, such as an inclinometer on the shank of the leg or pressure sensors in the insole of a shoe. The most sophisticated neuroprostheses use real-time feedback control, which requires sensors such as goniometers, accelerometers, or gyroscopes to provide continuous-state feedback.

Nerves can be stimulated using either surface (transcutaneous), percutaneous, or implanted electrodes. Surface electrodes contact the skin (Fig. 2). They are noninvasive, easy to apply, and generally inexpensive. However, due to the impedance of the skin and the dispersion of current, much higher-intensity signals are required than with subcutaneous electrodes. Current amplitude typically ranges from 10–150 mA in surface stimulation. A major limitation is that some nerves, for example those innervating the hip flexors, are too profound to be stimulated by surface electrodes. Percutaneous electrodes consist of thin wires that are inserted through the skin and into muscular tissue, remaining in place for a temporary period of time. In percutaneous

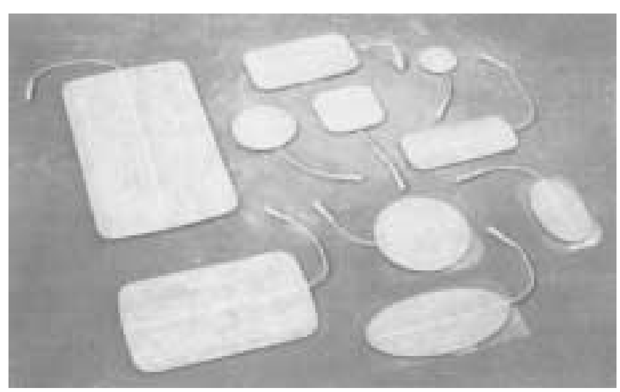


Fig. 2 Reusable, self-adhesive electrodes for surface stimulation come in a variety of shapes and sizes.

stimulation, current amplitude is rarely higher than 25 mA. The third class of electrodes is implanted electrodes, which are permanently implanted. Compared to surface electrodes, implanted and percutaneous electrodes potentially have higher stimulation selectivity with much less electrical charge applied, both of which are desired characteristics of FES systems. The drawbacks are that implants require a lengthy, invasive surgical process to install and that percutaneous electrodes can be used only temporarily and may cause infection at the penetration site.

There is a brand of miniature electrode, the BION™, that can be implanted via hypodermic needle.[3] They are cylindrical in shape, with a diameter of 2 mm and a length of 15 mm. Once implanted, they are powered and controlled via radio waves from an external controller that can be worn by the patient.

HISTORICAL NOTES

In 46 A.D., Scribonius Largus described what may be considered the first neuroprosthesis: the torpedo ray, which is capable of generating an electric potential of 25 to 30 V.[4] For centuries, torpedoes were prescribed for all sorts of ailments, including headaches, hemorrhoids, and even mental illness.

Following the invention of the electrostatic generator in the late 17th century, electrical discharges were found to excite animal preparations. Stronger discharges, and hence stronger biological responses, were made possible when the first capacitor was invented 1745. Physicians began treating a wide range of diseases by applying electrical discharges to their patients. Benjamin Franklin pioneered some of these techniques.

In 1791, Luigi Galvani published his discovery that dissected frog legs could be stimulated by touching a bimetallic rod to nerve and muscle. Michael Faraday built the first electric generator in 1831. It introduced the possibility of applying a series of high-frequency electrical pulses to nerves, which is the basis for all modern electrical stimulation. G. B. Duchenne utilized Faradism extensively in the latter part of the nineteenth century to treat various neurological disorders. Duchenne developed electrodes for localizing currents, and he produced a set of maps of the body indicating locations called motor points, where electrodes can be positioned to excite specific muscles.

NEUROPROSTHESES FOR WALKING

There are many neuroprostheses that address lower-extremity movement. As early as 1960, Kantrowitz demonstrated paraplegic standing by applying continuous surface FES to the quadriceps and gluteus maximus muscles of a patient with complete spinal cord injury.[5] Around the same time, Liberson and colleagues developed a simple neuroprosthesis to correct drop foot. This common symptom in hemiplegia is characterized by a lack of dorsiflexion during the swing phase of gait, resulting in short, shuffling strides.[6] Liberson's device, which has the distinction of being the first neuroprosthesis to receive a patent, consisted of a power supply worn on a belt, two surface electrodes positioned for stimulation of the common peroneal nerve, and a heel switch. The stimulation was activated whenever the heel lost contact with the ground, and was deactivated when the heel regained contact with the ground.

Stimulation of the common peroneal nerve causes contraction of the muscles responsible for dorsiflexion (i.e., tibialis anterior and extensor hallucis longus among others.). It can also trigger the flexor withdrawal reflex, which may not be desirable. The flexor withdrawal reflex occurs naturally when a sudden, painful sensation is applied to the sole of the foot. It results in flexion of the hip, knee, and ankle of the affected leg and extension of the contralateral leg in order to get the foot away from the painful stimulus as quickly as possible. To prevent this from happening during FES-assisted ambulation, Vodovnik proposed using a low-pass filter to slow the onset of stimulation current.[7]

Following Liberson's invention and Vodovnik's revisions, a number of drop foot stimulators were developed. Some were commercialized, for example the MikroFES (Josef Stefan Institute, Ljubljana, Slovenia) and the Odstock Dropped Foot Stimulator.[8] The latter was shown to significantly increase walking speed and efficiency, and a carryover effect was observed in stroke patients; that is, their walking speed and efficiency without the stimulator were improved.[9] Similar studies have reported no carryover effect.[10] Users of the Odstock device were generally satisfied with it, but almost all of them identified the surface electrodes as problematic, and two thirds would consider an implanted system instead.[11]

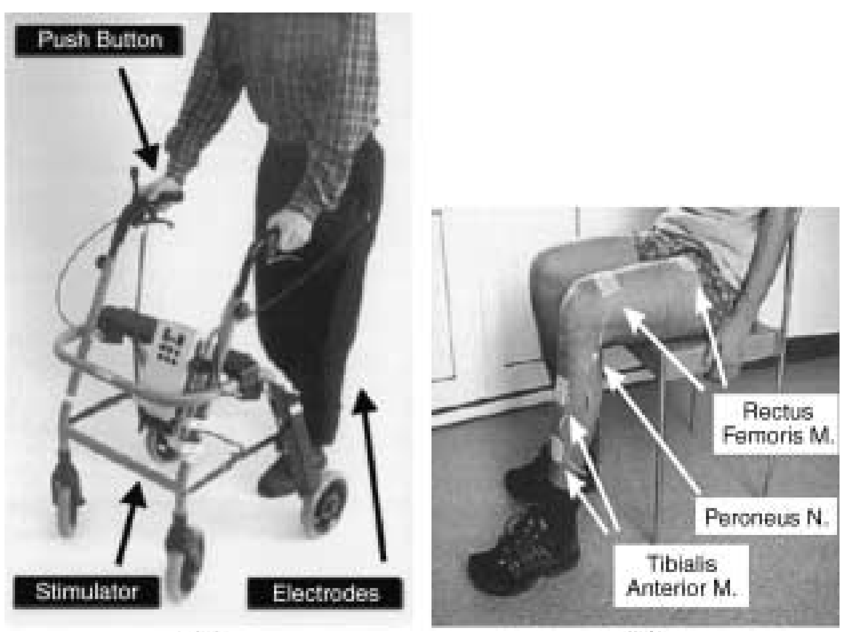
The first commercially available implanted drop foot stimulator was developed by Rancho Los Amigos Medical Centre and Medtronic Inc.[12] The surgically implanted compounds were a radio-frequency (RF) receiver, a pulse train generator, and one bipolar electrode implanted adjacent to the peroneal nerve. An external unit worn on the belt delivered power via the RF coil and received input commands from a wireless foot switch. Despite some problems with electrode migration and infection, the device was considered successful. Since then, more reliable and easier to implant systems such as the IPPO[13] and the Aalborg University implanted stimulator[14] have been devised, but they are not commercially available. The latter uses input from an implanted cuff electrode around the sural nerve, which is the nerve innervating the skin sensors on the sole of the foot. This system is unique in that it requires no external sensors.

Most modern drop foot stimulators continue to use a heel switch for active input. Burridge et al. tried using the foot switch on the nonaffected leg, but found it was not preferable unless the patient was unable to reliably achieve heel contact on the affected leg.[15] Vodovnik was one of the first to experiment with manual pushbuttons and EMG sensors.[7] Other alternatives to the heel switch include a heel/toe switch,[16] an array of four single-axis accelerometers positioned on the shank,[17] a tilt sensor positioned on the shank,[18] electroneurography,[14] a knee goniometer,[19] and the Gait Phase Detection System.[20]

The earliest neuroprostheses for paraplegic gait provided continuous stimulation to the quadriceps to produce a mode of gait similar to long leg-brace walking. Later systems used alternating bilateral quad/glut stimulation (during stance phase) out of phase with peroneal nerve stimulation (during swing phase). One such system was a six-channel stimulator developed at the University of Ljubljana in Slovenia.[16] Later at the same institution, Kralj and colleagues described a technique for paraplegic gait using surface stimulation, which remains the most popular method today.[21] According to Kralj's technique, four channels of stimulation are used. Electrodes are placed over the quadriceps muscles and peroneal nerves bilaterally. The user controls the neuroprosthesis with two pushbuttons attached to the left and right handles of a walking frame, or on canes or crutches (Fig. 3). F3/AQ9 When the neuroprosthesis is turned on, both quadriceps are stimulated. The left button initiates swing phase in the left leg by briefly stopping stimulation of the left quadriceps and stimulating the peroneal nerve. This stimulation is applied suddenly so as to trigger the flexor withdrawal reflex, resulting in simultaneous hip and knee flexion as well as dorsiflexion. After a fixed period of time, peroneal nerve stimulation is stopped and quadriceps stimulation is resumed. Similarly, the right button initiates swing phase in the right leg. Kralj and colleagues successfully applied this system to more than 50 subjects with spinal cord injury.

Many neuroprostheses for walking have employed the basic technique described in this section. As micropro- AQ10 cessor technology developed, neuroprostheses became more portable and flexible. The Parastep system uses Kralj's technique.[22,23] It is the only neuroprosthesis for walking to receive approval from the United States Food and Drug Administration (FDA) and the first neuropros- AQ11 thesis to receive FDA approval. It includes an ankle-foot orthosis to bolster ankle stiffness. The Parastep is commercially available, and more than 600 people have used it successfully.

A major limitation of neuroprostheses for walking that are based on surface stimulation is that the gait is slow, awkward, and unnatural looking. Perhaps a major reason for this is that the hip flexors cannot be stimulated



(a) (b)

Fig. 3 The ETHZ-ParaCare walking neuroprosthesis for hemiplegic subjects and subjects with unilateral paraplegia, developed in Zurich, Switzerland. (From Ref. [38].) (a) Stimulator and push button attached to walker; (b) surface electrodes attached to legs underneath clothing.

directly. Therefore, hip flexion during walking must come from voluntary effort, which is often absent in paraplegia, or from the flexor withdrawal reflex (initiated by peroneal nerve stimulation). Implanted systems have the advantage of being able to stimulate the hip flexors. They also provide better muscle selectivity and more natural gait patterns. Two such systems are the Praxis24 and the system proposed by Kobetic, which use 24 and 32 electrodes respectively.[24,25] The Praxis24 system also enables bladder voiding.

NEUROPROSTHESES FOR REACHING AND GRASPING

A number of neuroprostheses have been developed and used to assist stroke and spinal cord-injured subjects to improve their grasping function. The best-known grasping neuroprostheses are the Freehand system,[26] the Handmaster NMS-1,[27] the Bionic Glove,[28] the NEC AQ12 FESMate system,[29] the Compex Motion neuroprosthesis for grasping,[30,31] and the systems developed by Rebersek and Vodovnik[32] and Popovic et al.[33] With the exception of the Freehand and NEC FESMate systems, all use surface stimulation.

The key element for achieving the synergistic activity AQ13 of muscles that results with reaching and grasping is the appropriate sequencing of electrical pulses. The available neuroprostheses for grasping can restore the two most frequently used grasping styles: the palmar and the lateral grasp. The palmar grasp is used to hold bigger and heavier objects such as cans and bottles, and the lateral grasp is used to hold smaller and thinner objects such as keys, paper, and compact discs. The lateral grasp is generated by first flexing the fingers to provide opposition, which is followed by the thumb flexion. The palmar grasp is generated by first forming opposition between the thumb and the palm, which is followed by simultaneous flexion of both the thumb and the fingers.

The Freehand system, manufactured and distributed by NeuroControl Co., U.S.A.,[34] consists of eight implanted epimysial stimulation electrodes that stimulate flexion and extension of the fingers and the thumb in order to provide lateral and palmar grasp. Commands are given by an external position sensor that is placed on the shoulder of the subject's opposite arm. An additional external switch allows the user to choose between palmar and lateral grasp. This sequence is then sent via a radio frequency coil to the implanted unit, which generates the stimulation sequences for each channel.

The electrode leads are tunneled subcutaneously to the implanted stimulator located in the pectoral region. Surgical procedures to enhance both voluntary and stimulated hand functions are often performed in conjunction with the stimulator implantation. More than 200 quadriplegic subjects have received the Freehand neuroprosthesis at more than a dozen sites around the world. The subjects have demonstrated the ability to grasp and release objects and to perform activities of daily living more independently when using the neuroprosthesis. The Freehand system is the first neuroprosthesis for grasping approved by the FDA. The main advantage of the Freehand system is that it is implanted, and the time needed to don and doff the system is shorter compared to most of the surface FES systems.

In the 1980s, the group led by Handa at Sendai University, Japan, developed a microcomputer-controlled neuroprosthesis for grasping. Soon after that, Handa's team proposed a system with 16 percutaneous intramuscular stimulation electrodes that is both portable and programmable.[29] This system consists of a NEC PC-98LT personal computer and an external microcontroller-based stimulator. The stimulator applies trapezoidal stimulation patterns to generate muscle contractions. The stimulation patterns were ''cloned'' from the muscle activity recorded during voluntary grasping movements of able-bodied subjects. Stimulation sequences were triggered with a pushbutton or a pneumatic pressure sensor. This system demonstrated that spinal cord injured subjects with complete C4 to C6 spinal cord lesions could reach and grasp. In collaboration with NEC Inc., the Sendai team developed a fully implantable 16-channel electric stimulator called the NEC FESMate. Although 200 of these stimulators have been manufactured,[35] the NEC FESMate is not available outside of Japan.

The neuroprosthesis developed by Rebersek and Vodovnik was one of the first FES systems for grasping.[32] This neuroprosthesis has three stimulation channels, which are used to generate grasping by stimulating the finger flexors and extensors and the thumb flexors. Although this device was developed almost three decades ago, it is one of the rare systems that allows a subject to control the stimulator via different sensory interfaces such as an EMG sensor, a sliding resistor, or a pressure sensor. This option is important because it allows the neuroprosthesis to be tailored to the subject. The main disadvantages of this neuroprosthesis are that donning and doffing times are long and that selectivity of stimulation is quite limited. Mereltti et al. Modified this system and used it for stroke subjects.[36] They applied two channels to augment the elbow and fingers/wrist extension. They concluded that FES contributed greatly to recovery of hand and elbow movements in five stroke subjects, but in the remaining three the improvement was significant only at the elbow joint.

The Handmaster (Fig. 4) is a neuroprosthesis for F4/AQ14 grasping that is manufactured and distributed by NESS Ltd., located in Israel.[27] It consists of an orthosis that has

Fig. 4 The Handmaster system manufactured and distributed by NESS Ltd., Israel. (From Ref. [27].) The flexible, adjustable unit is worn over the forearm, wrist, and palm.

built-in flexibility to enhance and control freedom of movement within the forearm and hand, while supporting the wrist joint at a functional angle of extension. The Handmaster multiplexes a single channel of stimulation through a selected combination of surface electrodes on the inner surface of the orthosis, which effectively transforms the device into a six-channel neuroprosthesis. One stimulation channel is used to stimulate the extensor digitorum communis at the dorsal side of the forearm. The second channel stimulates the flexor digitorum superficialis. Electrodes are positioned over the muscles of the forearm and hand intrinsics during an initial setup session with a clinician. The setup position of the electrodes depends on the device user's specific needs. The Handmaster is controlled with an array of push buttons allowing the subject to select the operating mode and to trigger programmed movement sequences. Using the buttons, the subject can also control stimulation intensity and thumb posture, thereby adjusting the grasp to the size and the shape of the target object. Originally, the Handmaster was envisioned as a permanent orthotic system, but it is also used as an exercise and rehabilitation tool. One of the major advantages of the Handmaster is that it is easy to don and doff. It is exceptionally well designed and is one of the best neuroprostheses for grasping on the market. There are currently more than 2000 in use.

The Bionic Glove is a neuroprosthesis designed to enhance the tenodesis grasp in subjects who have good voluntary control over wrist flexion and extension.[28] By extending their wrist, users can cause passive finger flexion due to the limited length of the finger flexors. The Bionic Glove stimulates finger flexors and extensors during tenodesis grasp, significantly enhancing the strength of the grasp. Four self-adhesive surface stimulation electrodes provide stimulation, and the stimulator and a wrist position sensor are located on the forearm of the glove. An easy-to-use interface with three push buttons on the stimulator is used to set the stimulation parameters, and the optional audio feedback facilitates faster learning. Clinical evaluation of the Bionic Glove has indicated that it is generally beneficial to quadriplegic subjects, but only about 30% of potential users accepted it for long-term use.[37] It is available only for clinical evaluation from the University of Alberta, Canada, and it is presenly being modified into a new system called the Tetron that will provide several grasping patterns and strategies.

The Belgrade Grasping-Reaching System proposed by Popovic et al. is a neuroprosthesis for grasping that also provides reaching function.[33] It consists of four stimulation channels, three of which are used to generate grasping function. The fourth channel is used to stimulate the triceps brachii muscle augmenting elbow extension. Reaching is achieved by measuring the subject's shoulder velocity with a goniometer and by generating a synergistic elbow motion by stimulating the triceps brachii muscle. This neuroprosthesis, similar to the system proposed by Rebersek and Vodovnik, requires more time to don than the Handmaster and is not yet commercially available.

The Compex Motion neuroprosthesis is a very flexible device designed to improve grasping and walking functions in both spinal cord injury and stroke patients.[38] This multichannel surface stimulation system is programmable and can be interfaced with any sensor system. As a four-channel neuroprosthesis for grasping, it provides both palmar and lateral grasps. It can be controlled with proportional EMG, discrete EMG, pushbuttons, or sliding resistor control strategies. Thus far, more than 50 stroke and spinal cord-injured patients have used the neuroprosthesis in a clinical setting or at home in activities of daily living. One of the main disadvantages of this system is that it requires about eight-minutes to put on or take off.

NEUROPROSTHESES FOR BLADDER MANAGEMENT

Neuroprostheses have been very successful in treating lower urinary tract dysfunctions commonly associated with spinal cord injury, such as urge incontinence and urinary retention. The first attempts to electrically stimulate the bladder were made in the 1950s, when researchers sought ways to induce bladder emptying. At that time, a bladder wall stimulator was developed and implanted in three humans,[39] and animal studies of pelvic nerve stimulation were carried out.[40] Later, it was found that electrical stimulation of the sacral anterior roots produces excellent results, and this led to the development of the Finetech-Brindley stimulator, which is the most widely used neuroprosthesis for bladder management today.[41]

Attempts to manage incontinence using electrical stimulation began in the 1960s.[42] It was found that urethral resistance could be increased by stimulating the muscles of the pelvic floor, vagina, and rectum using external electrodes.[43] Eventually, fully implanted systems were developed to suppress the detrusor muscle, thus preventing reflex incontinence and increasing bladder volume.[44] Most spinal cord injuries result in reflex incontinence. Typically, detrusor-sphincter dyssynergia develops, in which the detrusor and urethral sphincter contract simultaneously rather than reciprocally. The detrusor also becomes hyper-reflexic, and the bladder becomes overactive. The standard treatments are anticholinergic medication, which blocks the neuromuscular junctions, and sensory rhizotomy (surgical transection of the posterior sacral roots). Neuroprostheses for bladder management serve as a practical alternative to these treatments. They can also augment sensory rhizotomy.

The Finetech-Brindley stimulator has been implanted in more than 2000 patients, usually those who have had a rhizotomy.[45] The electrodes are positioned on the second, third, and fourth sacral roots, bilaterally and extradurally. If a rhizotomy has not been performed, the electrodes must be implanted inside the dura to prevent crossover stimulation of the sensor neurons, which will trigger the detruser reflex. A portable external controller transmits power to the implant via radio frequency coil, and the user initiates bladder voiding by pushing buttons on the external unit. Micturition is usually achieved with residual volumes of less than 50 mL, contributing to a dramatic reduction in urinary tract infections.[46] The Finetech-Brindley stimulator has proven to be extremely robust, with only one failure expected every 80 implant-years.[47]

The Medtronic Interstim stimulator is a sacral root implant for incontinence, using neuromodulation to correct the inappropriate reflex behaviour.[48] It consists of fine wire electrodes inserted into the sacral foramina. When active, these electrodes inhibit the detrusor, but the mechanism of this inhibition is not yet properly understood. Thorough testing must be done using a temporary implant before permanent implantation is recommended. The stimulation parameters commonly used are a pulsewidth of 60–270 μs and a frequency of 10–15 Hz, with the stimulation on for 10 s, then off for 2 s. Current amplitude is twice the sensory threshold. The clinical success rate of this device is about 50%. Bladder emptying has to be achieved either voluntarily or by means of intermittent catheterization.

COCHLEAR IMPLANTS

Cochlear implants are neuroprostheses for the hearing impaired who have severe (70 to 90 dB) or profound (>90 dB) hearing loss. A long wire electrode is implanted directly into the cochlear duct, and electrical stimulation is applied to the residual spiral ganglion cells of the cochlear nerve. These devices were first developed in France in 1957. Since then, cochlear implants have been refined and miniaturized, and now they have received widespread acceptance, more so than any other class of neuroprostheses. More than 75,000 patients have received cochlear implants worldwide. Originally, few hearing-impaired people were eligible for cochlear implantation, but as the technology has improved, the selection criteria have expanded greatly to include a wide range of hearing impairments.[49]

Due to the success and popularity of cochlear implants, there are many different brands on the market. Most brands, however, are essentially similar. Differences between the currently available cochlear implants mainly involve the number of electrode channels (12 to 22), speech coding strategies, and the mode of electrode stimulation.[50] A recent study carried out at the University of Toronto, for example, concluded that the Clarion CI (Advanced Bionics, Symlar, CA) and the Nucleus 22 (Cochlear Corp., Syndey, Australia) cochlear implants were totally comparable in function or performance.[51] Both devices succeeded in reducing tinnitus, thereby increasing word and sentence recognition, but there was no significant reduction in vestibular function. Among the implantatees, 76% reported that they were satisfied with their implants, and 96% reported an overall positive impact on quality of life. Some other brands of cochlear implant are the COMBO 40+ system (MED-EL, Durham, NC), Digisonic (MXM, France), and the SOUNDTEC direct system (SOUNDTEC, Palo Alto, CA), most of which are FDA approved.

Cochlear implants generally consists of the following: 1) an external earpiece; 2) a speech processor; and 3) an internally implanted unit (Fig. 5). The earpiece, usually very small and lightweight, is worn comfortably behind the ear, much like a hearing aid. It contains an ear-level or in-ear microphone and a radio frequency coil to transmit signals to the implanted components. The speech processor, can be in the form of a small box worn somewhere on the body or, in some models, it is contained in the external unit worn behind the ear. The internally implanted unit consists of a receiver coil located

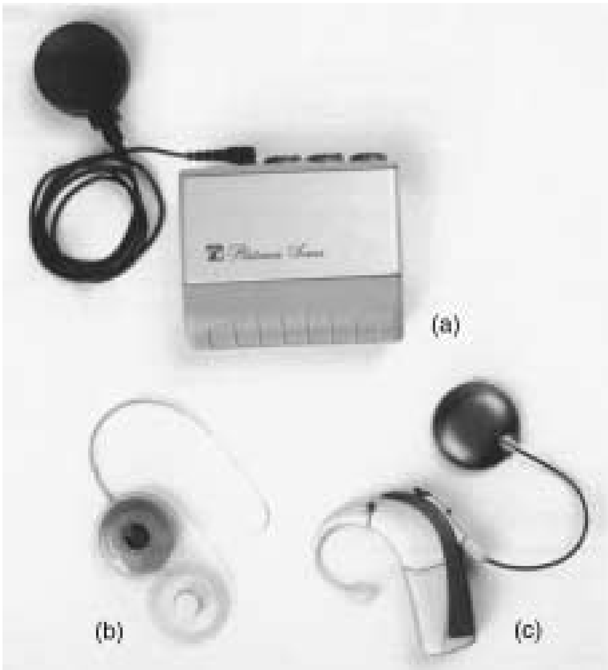


Fig. 5 The Clarion CII Bionic Ear system by Advanced Bionics (Symlar, California, USA). (a) Sound processing unit; (b) internal, implantable unit; (c) external earpiece.

underneath soft tissue in a cavity drilled in the temporal squama, and a 20–24 mm insulated wire ending in a multichannel electrode array, which is inserted into the cochlear duct. Sound waves are received by the external microphone and converted into electrical signals that are input to the external speech processor. There, the signals are digitally encoded and transmitted to the internal unit via radio frequency coil. The internal unit decodes the radio signals back into elementary electrical signals to stimulate each channel of the electrode array. Therefore, the multichannel device provides a complex sound analysis similar to the physiological analysis of sound in normal patients.

CONCLUSIONS

The first modern FES devices were developed over 40 years ago, and since then there has been a great deal of innovation resulting in scores of new neuroprostheses. The most successful of these technologies, in terms of consumer acceptance, are cochlear implants—more than AQ19 30,000 units have been implanted worldwide. Bladder management stimulators have also achieved wide acceptance, but not quite to the same degree.

Despite many advances and positive reports over the decades, neuroprostheses for walking and grasping have not achieved widespread approval. Most are used only for research purposes, and few have been used regularly by patients for activities of daily living. Some have been put to clinical use, and those are usually abandoned after a short period of time. The general perception among clinicians is that the neuroprostheses for grasping and walking are not fully matured and their application is often labor-intensive, whereas a favorable outcome cannot be guaranteed. Nevertheless, recent studies indicate that these tools have great potential in the rehabilitation of stroke and spinal cord-injured subjects.[30,31,52,53] In particular, these studies indicate that a significant number of patients who were trained with these systems recover voluntary reaching, grasping, and walking functions due to intensive and repetitive training with these systems. Current efforts are focused on understanding the mechanism of short- and long-term improvements and recoveries observed in these patients.

Neuroprostheses are a new and emerging technology that has significant potential. However, implementation of this technology to its full potential presents numerous challenges that have yet to be addressed. We believe that the 21st century will be the century when most of these technical and implementation issues are resolved and neuroprostheses are established as one of the important classes of rehabilitation systems available to patients with disabilities ranging from spinal cord injury to blindness.

ARTICLES OF FURTHER INTEREST

REFERENCES

1. Rushton, D.N. Functional electrical stimulation and rehabilitation—An hypothesis. Med. Eng. Phys. **2003**, *25* (1), 75–78.
2. Reichel, M.; Breyer, T.; Mayr, W.; Rattay, F. Simulation of the three-dimensional electrical field in the course of functional electrical stimulation. Artif. Organs **2002**, *26* (3), 252–255.
3. Loeb, G.E. Presentation highlights: Bionic neurons (BIONs^{TM}). J. Rehabil. Res. Dev. **2002**, *39* (Supplement 3), 5–6.
4. Schechter, D.S. Origins of electrotherapy. N. Y. State J. Med. **1971**, *71*, 997–1008.

5. Kantrowitz, A. A Report of the Maimonides Hospital. In *Electronic Physiologic Aids*; Brooklyn: New York, 1960.
6. Liberson, W.T.; et al. Functional electrotherapy: Stimulation of the peroneal nerve synchronized with the swing phase of the gait of hemiplegic patients. Arch. Phys. Med. Rehabil. **1961**, *42*, 101–105.
7. Vodovnik, L.; Long, C.; Reswick, J.B.; Lippay, A.; Starbuck, D. Myo-electric control of paralyzed muscles. IEEE Trans. Biomed. Eng. **1965**, *12* (3), 169–172.
8. Taylor, P.N.; Burridge, J.H.; Dunkerley, A.L.; Wood, D.E.; Norton, J.A.; Singleton, C.; Swain, I.D. Clinical use of the Odstock Dropped Foot Stimulator: Its effect on speed and effort of walking. Arch. Phys. Med. Rehabil. **1999**, *80* (12), 1577–1583.
9. Taylor, P.N.; Burridge, J.H.; Dunkerley, A.L.; Lamb, A.; Wood, D.E.; Norton, J.A.; Swain, I.D. Patients' perceptions of the Odstock Dropped Foot Stimulator. Clin. Rehabil. **1999**, *13* (5), 439–446.
10. Granat, M.H.; Maxwell, D.J.; Ferguson, A.C.; Lees, K.R.; Barbenel, J.C. Peroneal stimulator; evaluation for the correction of spastic drop foot in hemiplegia. Arch. Phys. Med. Rehabil. **1996**, *77* (1), 19–24.
11. Taylor, P.N.; Mann, G.; Wood, D.E.; Hobby, J. In *Pilot Study to Evaluate the Safety and Efficacy of an Implanted Dropped Foot Stimulator*, From Technology to Market: Bridging the Gap, Proceedings of the International Functional Electrical Stimulation Society, Maroochydore, Australia, July 1–5, 2003.
12. Waters, R.L.; McNeal, D.; Perry, J. Experimental correction of foot-drop by electrical stimulation of the peroneal nerve. J. Bone Jt. Surg., Am. **1975**, *57-A*, 1047–1054.
13. Strojnik, P.; Acimovic, R.; Vavken, E.; Simic, V.; Stanic, U. Treatment of drop foot using an implantable peroneal underknee stimulator. Scand. J. Rehab. Med. **1987**, *19*, 37–43.
14. Haugland, M.K.; Sinkjaar, T. Cutaneous whole nerve recordings used for correction for footdrop in hemiplegic man. IEEE Trans. Biomed. Eng. **1995**, *3*, 307–317.
15. Burridge, J.H.; Taylor, P.N.; Hagan, S.A.; Wood, D.E.; Swain, I.D. The effects of common peroneal stimulation on the effort and speed of walking: A randomized controlled trial with chronic hemiplegic patients. Clin. Rehabil. **1997**, *11* (3), 201–210.
16. Strojnik, P.; Kralj, A.; Ursic, I. Programmed six-channel electrical stimulator for complex stimulation of leg muscles during walking. IEEE Trans. Biomed. Eng. **1979**, *26*, 112–116.
17. Willemsen, A.T.M.; Bloemhof, F.; Boom, H.B.K. Automatic stance-swing phase detection from accelerometer data for peroneal nerve stimulation. IEEE Trans. Biomed. Eng. **1990**, *37*, 1201–1208.
18. Dai, R.; Stein, R.B.; Andrews, B.J.; James, K.B.; Wieler, M. Application of tilt sensors in functional electrical stimulation. IEEE Trans. Rehabil. Eng. **1996**, *4* (2), 63–72.
19. Sweeney, P.C.; Lyons, G.M. Fuzzy gait event detection in a finite state controlled FES drop foot correction system. J. Bone Jt. Surg., Br. **1999**, *81-B* (Suppl. I), 93.
20. Pappas, I.P.; Popovic, M.R.; Keller, T.; Dietz, V.; Morari, M. A reliable gait phase detection system. IEEE Trans. Neural Syst. Rehabil. Eng. **2001**, *9* (2), 113–125.
21. Kralj, A.; Bajd, T.; Turk, R. Enhancement of gait restoration in spinal injured patients by functional electrical stimulation. Clin. Orthop. Relat. Res. **1988**, *223*, 34–43.
22. Graupe, D.; Davis, R.; Kordylewski, H.; Kohn, K.H. Ambulation by traumatic T4-12 paraplegics using functional neuromuscular stimulation. Crit. Rev. Neurosurg. **1998**, *8*, 221–231.
23. Graupe, D.; Kohn, K.H. Functional neuromuscular stimulator for short-distance ambulation by certain thoracic-level spinal-cord-injured paraplegics. Surg. Neurol. **1998**, *50*, 202–207.
24. Davis, R.; Houdayer, T.; Andrews, B.J.; Barriskill, A. In *Paraplegia: Implanted Praxis24 ± FES System for Multi-Functional Restoration*, Proceedings of the International Functional Electrical Stimulation Society, Sendai, Japan, 1999.
25. Kobetic, R.; Triolo, R.; Morsolais, E. Muscle selection and walking performance of multichannel FES systems for ambulation in paraplegia. IEEE Trans. Rehabil. Eng. **1997**, *5*, 23–28.
26. Smith, B.; Peckham, P.H.; Keith, M.; Roscoe, D. An externally powered, multichannel, implantable stimulator for versatile control of paralyzed muscle. IEEE Trans. Biomech. Eng. **1987**, *34* (7), 499–508.
27. Ijzerman, M.; Stoffers, T.; 't Groen, F.; Klatte, M.; Snoek, G.; Vorsteveld, J.; Nathan, R.; Hermens, H. The NESS handmaster orthosis: Restoration of hand function in C5 and stroke patients by means of electrical stimulation. J. Rehabil. Sci. **1996**, *9* (3), 86–89.
28. Prochazka, A.; Gauthier, M.; Wieler, M.; Kenwell, Z. The Bionic Glove: An electrical stimulator garment that provides controlled grasp and hand opening in quadriplegia. Arch. Phys. Med. Rehabil. **1997**, *78*, 1–7.
29. Hoshimiya, N.; Handa, Y. A master-slave type multichannel functional electrical stimulation (FES) system for the control of the paralyzed upper extremities. Automedica **1989**, *11*, 209–220.
30. Popovic, M.R.; Hajek, V.; Takaki, J.; Bulsen, A.; Zivanovic, V. In *Restoration of Reaching and Grasping Functions in Hemiplegic Patients with Severe Arm Paralysis*, From Technology to Market: Bridging the Gap, Proceedings of the International Functional Electrical Stimulation Society, Maroochydore, Australia, July 1–5, 2003.
31. Adams, M.; Takes, V.; Popovic, M.R.; Bulsen, A.; Zivanovic, V. In *Restoration of Grasping Functions in Patients with Quadriplegia*, From Technology to Market: Bridging the Gap, Proceedings of the International Functional Electrical Stimulation Society, Maroochydore, Australia, July 1–5, 2003.
32. Rebersek, S.; Vodovnik, L. Proportionally controlled functional electrical stimulation of hand. Arch. Phys. Med. Rehabil. **1973**, *54*, 168–172.
33. Popovic, D.; Popovic, M.; Stojanovic, A.; Pjanovic, A.; Radosavljevic, S.; Vulovic, D. In *Clinical Evaluation of the Belgrade Grasping System*, Proceedings of the 6th

Vienna International Workshop of FES, Vienna, Austria, 1998.

34. Smith, B.; Peckham, P.; Keith, M.; Roscoe, D. An externally powered, multichannel, implantable stimulator for versatile control of paralyzed muscle. IEEE Trans. Biomech. Eng. **1987**, *34*, 499–508.
35. Takahashi, K.; Hoshimiya, N.; Matsuki, H.; Handa, Y. Externally powered implantable FES system. Jpn. J. Med. Electron. Biol. Eng. **1999**, *37*, 43–51.
36. Merletti, R.; Acimović, R.; Grobelnik, S.; Cvilak, G. Electrophysiological orthosis for the upper extremity in hemiplegia: Feasibility study. Arch. Phys. Med. Rehabil. **1975**, *56* (12), 507–513.
37. Popovic, D.; Stojanovic, A.; Pjanovic, A.; Radosavljevic, S.; Popovic, M.; Jovic, S.; Vulovic, D. Clinicl evaluation of the Bionic Glove. Arch. Phys. Med. Rehabil. **1999**, *80* (3), 299–304.
38. Popovic, M.R.; Keller, T.; Pappas, I.P.I.; Dietz, V.; Morari, M. Surface-stimulation technology for grasping and walking neuroprostheses. IEEE Trans. Eng. Med. Biol. Mag. **2001**, *20*, 82–93.
39. Boyce, W.H.; Lathem, J.E.; Hunt, L.D. Research related to the development of an artificial electrical stimulator for the paralyzed human bladder: A review. J. Urol. **1964**, *91*, 41–51.
40. Bors, E.; Comarr, E. *Neurological Urology: Physiology of Micturition, Its Neurological Disorders and Sequelae*; Karger Verlag, 1971.
41. Brindley, G.S.; Polkey, C.E.; Rushton, D.N.; Cardozo, L. Sacral anterior root stimulators for bladder control in paraplegia: The first 50 cases. J. Neurol. Neurosurg. Psychiatry **1986**, *49*, 1104–1114.
42. Caldwell, K.P.S. The electrical control of sphincter incontinence (preliminary communication). Lancet **1963**, *2*, 174–175.
43. Alexander, S. Research and clinical experience in the treatment of the neurogenic bladder by electronic implant and prosthesis. Paraplegia **1968**, *6* (3), 183–193.
44. Rijkhoff, N.J.M.; Wijkstra, H.; van Kerrebroeck, P.E.V.; Debruyne, F.M.J. Urinary bladder control by electrical stimulation: Review of electrical stimulation techniques in spinal cord injury. Neurourol. Urodyn. **1997**, *16*, 39–53.
45. Schurch, B.; Rodic, B.; Jeanmonod, D. Posterior sacral rhizotomy and intradural anterior sacral root stimulation for treatment of the spastic bladder in spinal cord injured patients. J. Urol. **1997**, *157*, 610–614.
46. Creasey, G.H. Restoration of bladder, bowel, and sexual function. Top Spinal Cord Inj., Rehabil. **1999**, *5* (1), 21–32.
47. Vastenholt, J.M.; Ijzerman, M.J.; Buschman, H.P.J.; Snoek, G.J.; van der Aa, H.E. In *Seven Year Follow-Up of Sacral Anterior Root Stimulation and Sacral Posterior Root Rhizotomy for Bladder Control in Patients with a Spinal Cord Injury, Complications and Quality of Life*, Proceedings of the International Functional Electrical Stimulation Society, Cleveland, Ohio, 2001.
48. Siegel, S.W. Management of voiding dysfunction with an implantable neuroprosthesis. Urol. Clin. North Am. **1992**, *19* (1), 163–170.
49. Lenarz, T. Cochlear implants, selection criteria and shifting borders. Acta-Rhino-Laryngol. Belg. **1998**, *52* (3), 183–199.
50. Gstoettner, W.; Adunka, O.; Hamzavi, J.; Baumgartner, W.D. Rehabilitation of hearing-impaired patients with cochlear implants, a review. Wien. Klin. Wochenschr. **2000**, *112* (11), 464–472.
51. Higgins, K.M.; Chen, J.M.; Nedzelski, J.M.; Shipp, D.B.; McIlmoyl, L.D. A matched-pair comparison of two cochlear implant systems. J. Otolaryngol. **2002**, *31* (2), 97–105.
52. Popovic, M.B.; Popovic, D.B.; Sinkjaer, T.; Stefanovic, A.; Schwirtlich, L. Restitution of reaching and grasping promoted by functional electrical therapy. Artif. Organs **2002**, *26* (3), 271–275.
53. Thrasher, T.A.; Popovic, M.R. In *FES-Assisted Walking for Rehabilitation of Incomplete Spinal Cord Injury*, From Technology to Market: Bridging the Gap, Proceedings of the International Functional Electrical Stimulation Society, Maroochydore, Australia, July 1–5, 2003.