The Role of Rechargeable Systems in Neuromodulation

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Abstract

Neuromodulation is an effective treatment for many types of neuropathic pain but a significant limitation of any neuromodulating system is that electrical power must be conveyed in a reliable and sterile way to an implanted electronic device and transmitted to its associated electrodes. In recent decades radio-frequency-coupled devices and internal pulse generators have been developed. These were significant advances but were limited either by the need for bulky external power sources or the need for surgery at intervals to replace the internal system battery. More recently, rechargeable neuromodulatory systems have become available. These considerably improve patient convenience and mobility. After surgical implantation, the system can be charged from an antenna placed at the skin surface, avoiding the need for repeated surgery, external equipment or wires penetrating the skin. Charging can be completed within a few hours and can last for up to one month, depending on use. Battery life is up to 25 years, depending on the manufacturer. Varied system programmability and availability of high power output make rechargeable systems applicable to a range of different neurological conditions and will make these systems a valuable approach to controlling chronic neuropathic pain.

Keywords

Neuromodulation, neurostimulation, spinal cord stimulation, deep brain stimulation, rechargeable systems, rechargeable batteries

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All neurostimulation needs a source of power – now universally a battery-powered system to power the implant and to allow patient mobility. As independence from a fixed power supply is essential, the generation, storage and supply of electricity has been one of the foremost limiting factors when it comes to developing new devices. Historically, electrical power was derived from an external induction coil, which was then largely overtaken by the use of an implanted non-rechargeable battery. More recently, the introduction of transcutaneously rechargeable systems has aroused considerable interest. To date, there is relatively little experience in the use of these systems, particularly in the long term, but on-going studies are accumulating evidence. This article, therefore, will consider neuromodulation from a historical perspective and discuss the opportunities and advantages offered by these new rechargeable systems.

Radio-frequency-coupled Devices

The first spinal cord stimulation (SCS) device was implanted in the 1960s and the initial patient was a cancer case whose pioneering neuromodulation therapy is attributed to Shealy.[1] *Table 1* shows a timeline for the major developments in neuromodulation devices. The internal device was externally powered by radio-frequency (RF)-coupled transmission; this used electromagnetic induction to power the device. When successful, these systems operated well, and some patients continue to use the devices after many years without the need for any medical intervention. However, RF devices were not without their problems. One study reported that significantly more electrode interventions were required with RF systems, compared with internal battery systems, for SCS devices (60 electrodes for 42 battery patients versus 67 electrodes for 27 RF patients, p=0.0018).[2] Often, those using RF systems had poor stimulation quality and could only obtain paraesthesias using higher amplitudes or by frequently changing their parameters.[2] As the transmitting coil required specific positioning over the subcutaneously implanted receiving coil, it had to be held in position by adhesive tape or discs, which resulted in a form of contact dermatitis or swelling in some patients. More complete comparisons of RF and neurostimulation devices with internal batteries however, will require that the effects of different electrode shapes, materials and connections are investigated as well as the effects of different pulse profiles and current charge densities produced by these systems. RF-coupled neurostimulation systems offer various advantages but clinical data on their use are as yet, limited.

RF-coupled devices, however, have fallen out of favour, due to the inconvenience of an external power source and transmitting coil, which restricted the activities of the individual while using the neurostimulator – for example, swimming or showering.[3] Furthermore, excessive

Table 1: A Timeline for Major Development of Cranial, Spinal and Peripheral Neuromodulation Devices

Year	Innovation in Neuromodulation Devices
1952	First report of deep brain stimulation (intracranial electrode placement) – possible value in psychotic patients
1967	First spinal electrodes
1968	First report of peripheral nerve electrode
1972	One-electrode radio-frequency system
1993	Two-array, four-contact (2 x 4) radio-frequency system
1994	Two-array, eight-contact (2 x 8) radio-frequency system; one-array implantable pulse generator
2004	Rechargeable two-array spinal IPG (FDA-approved)
2009	Rechargeable two-array cranial IPG (FDA-approved)

Here an array is a series of contacts on an electrode. These can be arranged in a linear formation or in multiple rows. For example, a four-contact electrode consisting of two contacts positioned side by side can be referred to as a 2 x 2 array. If arranged in a single row, it would be a 1 x 4 array. A 2 x 4-contact array could be two parallel arrays or could be a 1 x 8 contact array; a 16-contact array would be two parallel arrays of eight contacts, etc. FDA = Food and Drug Administration; IPG = internal pulse generator.
Sources: Coffey, 2008,[4] Barolat and Sharan, 2000,[37] Delgado et al., 1952,[38] North, 2008,[39] Schwalb and Hamani, 2008,[40] Waltz, 1997[41] and Law, 1992.[42]

perspiration resulting from exercise or physiotherapy may make proper contact of the antenna problematic.[3] The power supply for the transmission coil was held in a box that also contained the programming facility and used standard domestic batteries for convenience, but these needed frequent replacement. Furthermore, the effect of stimulation declined as the batteries discharged. Considerable expense was incurred by the patient in battery purchase, and anecdotal evidence suggests that domestically available rechargeable batteries were not as powerful or effective, as their charge decreased rapidly during use.

Internal Pulse Generators

In order to release the patient from the need to carry around the power pack and transmitting coil, devices were developed to contain their own internal pulse generators (IPGs), i.e. a lithium battery that used similar technology to that developed for cardiac pacemaker systems.[3] Although relatively small, IPG devices were larger than the previous generation of RF transmission devices. The lifespan of the battery varies depending on the parameters used, such as voltage, rate and pulse width (PW),[3] as well as the amount of use. The main drawback to these systems is that the non-rechargeable battery, once fully discharged, would require surgery to replace, and in the later devices increasing size did become a problem as manufacturers looked for greater longevity and the availability of more programs. The entire pulse generator, containing the integral battery, has to be replaced. Each battery change requires hospital admission, albeit only for a day-case procedure under local anaesthetic; additionally, each procedure is accompanied by the inevitable risk of infection and of damage to the leads, and also has cost implications. Most patients receiving SCS can expect a non-rechargeable battery to last 2.5–4.5 years.[3] In an attempt to lengthen battery life, and thus reduce the need for replacement surgery, these devices were developed with lower stimulation rate and PW compared with RF transmission devices.[4] Overall, patients preferred the extra freedom gained from the fully implanted systems and the previous RF-coupled systems became reserved for patients requiring frequent battery changes because of the need for a higher stimulation rate or voltage to manage their symptoms.

In addition to requiring frequent battery changes, a second issue with IPG devices is that some of the newer applications and the more complex electrode array systems require greater power levels from increasingly large non-rechargeable batteries. Examples of this include stimulators that help treat axial low back pain[5] and dual electrode systems used for deep brain stimulation (DBS).[6] Initially, DBS required the placement of two battery systems, one for each deep brain electrode. This led to the development of dual-channel systems such as the Medtronic Kinetra® for DBS that allows unipolar stimulation but this requires much larger non-rechargeable batteries than previous systems. In applications such as dystonia and several others, the use of higher frequencies, voltages and PWs means that even with larger non-rechargeable batteries, replacement intervals are unacceptably short. By developing lower impedence systems, some improvements were made but the advantages gained have been relatively small.

Rechargeable Systems

Rechargeable systems are now available, with an estimated battery lifespan of between nine and 25 years, depending on the battery chemistry and modelling of the recharging cycles.[3,7] These systems consist of a surgically implantable device that is positioned approximately 2.5 cm below the skin surface. The devices are mostly ovoid in shape, with a maximum length/diameter of approximately 5 cm (footprint 20–26 cm^2) and a thickness of approximately 1.1 cm.[8–10] The device houses programmable electronics that control the electrical stimulus output and a rechargeable battery (usually lithium). Electrical stimulus is conducted through leads connected to one or more electrodes positioned at appropriate points in the brain or other body site. The battery is charged by positioning an antenna unit on the skin over the site of implantation. This is connected to a hand-held RF control device and power supply. Recharging time ranges from a few minutes to 12 hours depending on the level of use of the system. A charge can last from only one or two days up to one month, depending on the number of stimulus program cycles operated per day and the power output required. During the development of these systems, two technical difficulties had to be overcome. The first was to develop a battery that would withstand several years of recharging cycles and the second was to ensure that the recharging process did not cause dangerous heating. In addition, recharging times were required to be as short as possible and intervals between charging also had to be as long as possible.

Since rechargeable systems are relatively new, there is a paucity of published literature regarding their use in patients, particularly long-term data, which are needed to establish duration of the battery life. In the authors' experience in clinical practice, occasionally patients have reported mild heating from the recharging (and charging post-operatively, with surgical clips in place, causes heating) or have found the light harness used to position the recharger less convenient than they would ideally like, but all have managed. There is one published study[11] which confirms this anecdotal view: patients achieved a similar success rate with the Restore™ (Medtronic, Inc.) rechargeable implantable neurostimulator as with non-rechargeable implants, and in all cases patients were able to successfully recharge the device. Furthermore, the majority of patients were satisfied recharging the device, with 78.5 % of patients reporting that one month after implantation the device was easy or somewhat easy to recharge and that 12 months after implantation 80.5 % of patients reported 50–100 % pain relief. The study was not designed to prove superiority in terms of efficacy of the devices, nor that they were

Table 2: Mean Annual Costs for Patients with Chronic Pain

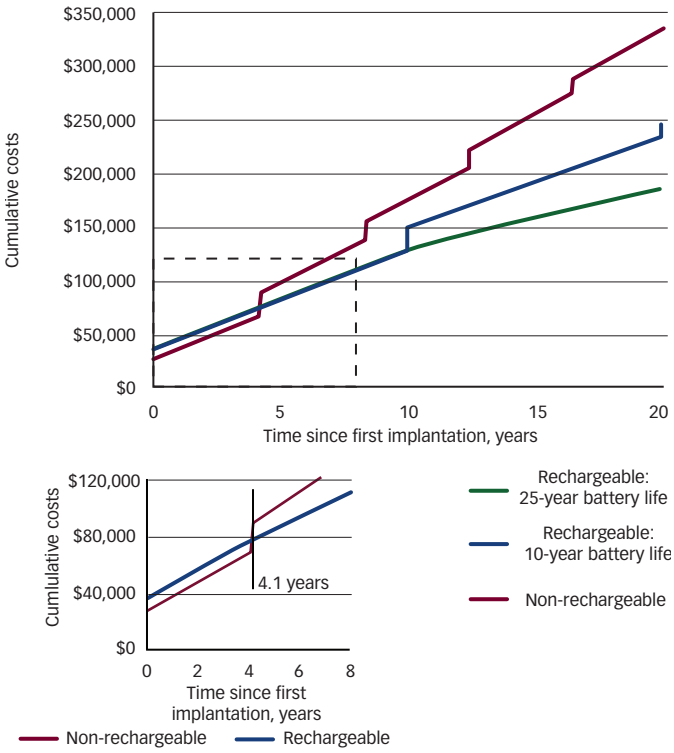
		With Spinal Cord Stimulation Implanted		After Spinal Cord Stimulation Removed	
Type of Service	Cost Per Unit of Service, US$	Number of Service Units	Total Cost, US$	Number of Service Units	Total Cost, US$
Doctor's office visit	51	9.1	462	24.3	1,239
Accident and emergency department visit	192	0.4	67	1.6	307
Medical hospitalisation	4,248	0.7	2,974	2.9	12,320
Nerve block injection	306	2.5	765	15.7	4,805
Surgery	8,689	0	0	1.3	11,296
Magnetic resonance imaging scan	472	0.1	47	1.7	779
Computed tomography scan	294	0.3	74	1	294
Medication			1,250		2,075
Rehabilitation			350		1,250
Total mean annual cost			5,989		34,365

Source: Hornberger, et al., 2008.[7]

better tolerated or preferred; however, rechargeable devices certainly performed as well as non-rechargeable systems. In addition, a case study reported that four patients were very satisfied with the quality of stimulation provided by the rechargeable Restore neurostimulation system and noted a significant improvement in quality of life.[12]

Another advantage of rechargeable devices is that more power can be delivered, since frequent recharging can replace the energy in the system. For example, PW programming ranges of rechargeable implantable pulse generators now match those of RF systems, with programmability up to 1,000 µs.[4] Furthermore, much more complex systems have been developed that have multiple channels (independent programming of individual contacts allowing for steerable electrical fields) and constant current systems as well as constant voltage.[3] These features can accommodate changing electrode–tissue impedance over time. In several small clinical trials, this contact impedance has been shown to be highly variable and can reduce the efficacy of neurostimulation but complex electrode systems were shown to be a means of mitigating the problem.[13–16] Some of these more complex applications can be delivered from non-rechargeable battery powered devices; however, the development of these technologies has resulted from a freedom to design systems that are not restricted in power output. An additional benefit of rechargeable systems is that they can be made much smaller than their non-rechargeable equivalents.

Figure 1: Cumulative Costs of Spinal Cord Stimulation System from Time of First Implantation, Rechargeable versus Non-rechargeable



Source: Hornberger, et al., 2008.[7]

Cost-effectiveness of Rechargeable versus Non-rechargeable Neuromodulation Devices

The rechargeable systems have a higher initial set-up cost compared with their non-rechargeable equivalents. However, one study that investigated the average difference in lifetime costs between rechargeable and non-rechargeable IPGs used in SCS for failed back surgery syndrome (FBSS) showed that a rechargeable SCS system is projected to require between 2.6 and 4.2 fewer pulse generator replacements for battery depletion than a non-rechargeable SCS system.[7] The study also showed that although rechargeable systems are currently more expensive than non-rechargeable systems, these costs can be offset 4.1 years after implantation (see *Figure 1*).[7] Furthermore, the total lifetime cost of a non-rechargeable system for an average 34.2 years, including implantation, complication, removal and follow-up costs was estimated to be US$404,666 (2006 prices) compared with US$254,369 for a rechargeable system, giving a saving of US$150,297.[7] These costs reflect estimations that patients with non-rechargeable systems will need 5.9 replacement procedures compared with 2.2 (range 1.7–3.3) for patients with rechargeable systems, that is, 3.7 fewer battery replacements over their lifetimes. The mean annual costs for patients with chronic pain for durations with implanted SCS devices and after removal are given in *Table 2*.

Recently, the National Institute for Health and Clinical Excellence (NICE), the advisory body in the UK, has published a health technology assessment for SCS which modelled the costs of treatment, including the need for battery replacement.[17] The report showed that SCS was effective in reducing the chronic neuropathic

Table 3: Comparison of Commercially Available Spinal Cord Stimulators

Feature	Boston Scientific Precision Plus™	Medtronic RestoreULTRA™	St Jude Eon Mini™
System type	Constant current at each contact (MICC)	Constant voltage (single source)	Constant current (single source)
Number of power sources	16	1	1
Move electrical field in 1 % increments	Yes	No	No
Tightly spaced contacts	Yes (1 mm)	Yes (1.5 mm)	No[a]
Joystick control	Yes	No	No
Auto impedance adjust at each contact	Yes	No	No
Multi-lumen lead construction	Yes	No	No
Ability to detect relative lead position	Yes (EGL Scan™ technology)	No	No
Max pulse width, µs	1,000[b]	1,000[c]	500[a]
Max voltage, V	15[b]	10.5[c]	12[a]
Max frequency, Hz	1,200[b]	1,200[c]	1,200[a]
Cordless charger	Yes[b]	No[d]	No[e]
Cordless remote within 60 cm wireless range	Yes[b]	No[f]	No[e]
Battery warranty voided by over-discharge	No[b]	Yes[g]	Yes[h]
Battery explant due to over-discharge	No[b]	Yes[i]	Yes[h]
End-of-life battery shut-off	No	Yes (9 years)[j]	No
IPG footprint, cm^2	20[k]	26[k]	21[k]
Volume, cm^3	22[b]	22[c]	18[a]
Maximum thickness, mm	11[b]	11[i]	11[a]

IPG = internal pulse generator; MICC = multiple independent constant current.
Sources:
[a]St Jude Eon Mini Neurostimulation System Clinician's Manual, 37-1004-01E, March 2008;96–107.
[b]Boston Scientific Physician Implant Manual, 9055521-003 Rev A.
[c]Medtronic System Eligibility Battery Longevity Specifications, MA00152A037, 2007;45–6.
[d]Medtronic Patient Programmer Manual, 37743, 2007–9;43.
[e]St Jude Eon Mini Neurostimulation System Clinician's Manual, 37-1004-01E, March 2008;17–8.
[f]Medtronic Patient Programmer Manual, 37743, 2007–9;56.
[g]Medtronic Limited Warranty, Special Notice.
[h]St Jude Eon Mini Neurostimulation System Clinician's Manual, 37-1004-01E, March 2008;79–80, 89–90.
[i]Medtronic RestoreULTRA Implant Manual, 37712, 2007–9;9.
[j]Medtronic System Eligibility Battery Longevity Specifications, MA00152A037, 2007;14.
[k]Boston Scientific calculations. Data on file.
[l]Medtronic RestoreULTRA Implant Manual, 37712, 2007–9;7.
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Eon Mini is a trademark of St Jude Medical, Inc.

pain caused by FBSS and complex regional pain syndrome (CRPS) type 1. The report concluded that a rechargeable system could be justified if the expected lifetime costs of the therapy made it more cost-effective, that is, if the costs of replacements could be avoided.

Competition

There are three currently available rechargeable neurostimulators for SCS. Technical data, features and specifications for each system are compared in *Table 3*. The authors will leave the readers to make their own comparisons.

Indications

The indications for stimulation-mediated neuromodulation vary from the accepted through to the speculative. The targets can be divided into peripheral, spinal cord and deep brain targets.

Peripheral Nervous System Stimulation

Peripheral nervous system stimulation can be used to treat a wide range of conditions, including resistant hypertension, via electrical stimulation of the carotid sinus baroreceptor,[18] and faecal incontinence and constipation and overactive bladder syndrome, by sacral nerve stimulation.[19,20] A major application of peripheral nervous system stimulation is in chronic pain in which specific areas of neuropathic pain are targeted.[21] In this method, electrodes are positioned along the length of peripheral nerves, or simply in the peripheral field, and a weak electrical current is applied that stimulates non-painful sensory pathways, diminishing pain conduction.[22,23] Treatment usually starts with the fitting of a temporary electrode with external controls and power which, if effective in reducing pain, is replaced by a permanent electrode with an integral battery. The method has an excellent safety record and has proven effective in the treatment of transformed migraine, occipital neuralgia, cervicogenic headache, neuropathic facial pain and multiple others.[22–25]

Spinal Cord Stimulation

Electrical SCS consists of rectangular impulses delivered to the epidural space through an implanted electrode; the target is probably the dorsal column. The NICE health technology assessment recently concluded that there is sufficient evidence to support the use of the technology for neuropathic pain (including FBSS and CRPS), but not for angina or peripheral vascular disease.[17] Controversies persist regarding the treatment of low back pain.[5] Currently, it is thought that more complex electrode arrays are required, with independent manipulation of positive and negative contacts. Furthermore, multiple programs allow patients to benefit from targeting different areas of the body, and the differences in stimulation amplitude allow patients to maintain symptom relief after changing position, for example, lying to sitting or standing.

Deep Brain Stimulation

Pain

Although this technology was originally explored in the 1950s for pain (and psychiatric disorders), applications have been limited and the evidence published is not conclusive. There are a variety of targets, including the sensory thalamus and the periaqueductal and periventricular grey areas of the brain.[26] There is also interest in the cingulate gyrus as a stimulation target for pain.[27] There is, however, no current Food and Drug Administration (FDA) or NICE support for these indications. The NICE guidelines state that DBS should only be used in patients with refractory chronic pain syndromes that other treatments have failed to control and that patients should be selected by specialist teams in pain management.[28]

Movement Disorders

DBS is now accepted practice in the treatment of movement disorders.[6] It is approved by NICE and the FDA for Parkinson's disease

that is levodopa-responsive, for dystonia and for tremors, either parkinsonian or essential tremor.

Epilepsy and Psychosurgery

Several small trials evaluating the use of DBS to treat intractable epilepsy have been completed and other trials are on-going. In one such trial, Stimulation of the anterior nuclei of thalamus for epilepsy (SANTE), the implantation of electrodes in 54 patients with refractory epilepsy markedly reduced seizures compared with 55 patients who received no such stimulation. This effect in stimulated patients persisted for two years.[29] In a cross-over study with eight patients with obsessive-compulsive disorder (OCD), subthalmic stimulation given over a three-month period significantly reduced OCD symptoms compared with sham stimulation ($p<0.01$) as determined using the Yale-Brown OCD Scale.[30] The treatment however, was associated with a substantial risk of adverse events such as intracerebral haemorrhage and infections. DBS has also shown some efficacy in the treatment of a variety of other neurological conditions including depression and Tourette's syndrome although, in each case, studies have, to date, been limited to small numbers of patients and larger trials are required to fully evaluate these indications.[31–33]

Other Indications

Recent and on-going trials include stimulation of the posterior hypothalamus for the treatment of cluster headache, and of the lateral hypothalamus for obesity.[6] Rechargeable systems are particularly pertinent for the treatment of dystonia and certain psychiatric conditions that require the application of high currents. Numerically, the indications for psychosurgery, in particular depression, are likely to greatly exceed the number of other indications if the therapy is shown to be successful.

Disadvantages of Rechargeable Neuromodulation Devices

Rechargeable systems depend on the ability of the patient to handle the recharger. For some indications they may require inconvenient frequent recharging. Furthermore, it can be critical that systems are not allowed to fully discharge, as this may result in an abrupt end to pain relief or the recurrence of dystonia, and even with a rebound or exacerbation. Some rechargeable systems have a complex procedure to reset the system when it has fully discharged and if this happens on repeated occasions then, in the case of one manufacturer, the system cannot be reset and has to be replaced.

Future Developments

The development of very small rechargeable batteries has enabled the fabrication of some extremely small devices for neurostimulation. This reduction in battery size, however, comes at the expense of shorter recharging intervals. The smallest is currently the investigational BION® (Boston Scientific Neuromodulation), in which the casing of the device forms the electrode and the entire device is 27.5 x 3.2 mm. It has been used for occipital nerve stimulation[34] and may be useful for peripheral neuromuscular stimulation.[35] Work is now under way to develop devices for different types of DBS that might be implanted into the skull, avoiding the present situation where the wires must be tunnelled to the infraclavicular fossa where quite a bulky device has to be implanted.[36]

Discussion

Non-rechargeable battery systems still represent the most commonly implanted type of neuromodulatory system worldwide, in part because non-rechargeable battery systems have lower initial set-up costs compared with rechargeable systems. Over the long term, however, rechargeable systems may prove to be more cost-effective, especially if surgical operations to replace batteries are no longer required. This helps patients to maintain a more independent life, with a lower risk of potential complications associated with surgery.

An anecdotal rule sometimes applied is that 80 % of customers or patients will use 20 % of the facilities of any given complex gadget. From this it follows that the majority of patients will be well treated with much simpler devices. This would mean that many patients may not have the opportunity to benefit from improvements in technology, including better electrode systems, lower profile leads and the smaller size of the rechargeable battery. However, in the authors' clinical experience, when there has been the need for an increased complexity of array, such as in the treatment of low back and leg pain in patients with FBSS, it has been found that the extra capability provided by the programming function of the electrode system is beneficial to patients. Automated programmable implanted SCS devices have also been shown to improve the management of pain compared with manual methods of adjustment.[36] Further technological advances are likely to occur in closed-loop electrode systems, and also in the programming of complex arrays of electrodes that becomes necessary once the number of independent electrode contacts rises above four. Some devices now sense different body positions e.g. sitting, lying and standing, and alter the amplitude accordingly. The early experience of one author (PE) of devices with such capability is positive.

In conclusion, rechargeable systems do everything non-rechargeable battery-powered systems can do; however, their capability is substantially greater, particularly due to their potential for miniaturisation and the removal of the limit on power output. Rechargeable systems have a number of clinical benefits, including extending therapeutic longevity, avoiding frequent replacement surgeries and any subsequent complications that may arise from repeated surgeries. Rechargeable systems also allow the high-power stimulation that is necessary for some complex indications and mitigate the clinical problem of managing battery life versus optimal patient care. These characteristics will make rechargeable systems more patient-friendly. The further development of rechargeable systems is likely to produce an exciting range of enhanced capabilities and applications in neuromodulation. ■

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