The History of the Development of the Implantable Spinal Cord Stimulator

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The first portable battery powered electrical stimulator commercially produced to be used as a treatment was the Electreat at the turn of the 20th century. It was patented in 1919 by C. W. Kent, a naturopath from Peoria, Illinois, and remained on the market through the 1940s, despite intense attack by the FDA and rejection by the medical profession, largely because of the outrageous claims made by the manufacturer of being able to cure a variety of maladies. The manufacturer called the Electreat the “artificial heart” in deference to its invigorating capabilities. The FDA was formed in 1938 and the Electreat became the first product prosecuted for fraudulent advertising, thereafter being forced to limit its curative claims to pain alone. Over 250,000 were sold and was used clinically up until the company was bought in 1993. The device operated on 2-D batteries and had a roller as one pole and a sponge pad as the other. However, the Electreat was used by physicians administering a variety of treatments to patients in the early 1900s to stimulate vitality, increase muscle mass, and to increase body temperature. It was especially used to treat neurasthenia, a diagnosis of the time that effectively meant women were overstressed, were fatigued, and had a variety of aches and pains, and needed to rest, and not trouble themselves with issues of the world, education, or books. Dr S. Weir Mitchell used the Electreat as part of his “Rest Cure” in addition to massage (which was the beginning of massage therapy in the US). Unfortunately, neurasthenia was simply a Victorian era belief of the inherent “weakness” of women (meaning emotionally weak) and served as a device to prevent women from physically straining themselves, moving forward in their station in life or becoming educated, effectively making them more subservient to the head of the house. Some
physicians including Shealy, the father of the spinal cord stimulator, maintained Electreat was not a simple DC device, but had output in the gigahertz range (Soul Medicine, Dawson Church and Norman Shealy), but this claim has not been independently substantiated. Shealy had acquired an Electreat for use in his patients.

Earl Bakken began Medronic with his brother in law in his garage in 1949. He was a graduate student at the time, trying to make extra money by repairing hospital equipment for Northwestern Hospital. He became so successful at this that he quit graduate school. Initially he was a representative for 3 equipment companies, and had many interactions with physicians who desired some custom engineering and invention work. He began to modify or make equipment requested by the physician to be used clinically. Bakken made more than 100 custom applications during the early years, none was FDA approved, and none were patented. He did run into difficulty with the FDA when they ultimately required approval for some of his custom products he was selling. Bakken worked to develop pacemakers and defibrillators in the 1950s onward. This gave him the expertise in miniaturization, external and internal battery supplies, and in lead construct that would ultimately be useful in spinal cord stimulation construction.

In 1954, Heath electrically stimulated a cancer patient’s septum pellucidum at intervals of 15 min daily to weekly and derived cancer pain alleviation.

Also in 1954 Texas Instruments first commercially produced silicon transistor that had been developed by Bell Lab scientists earlier in the same year. The commercial production made it increasingly possible to provide miniature circuitry.

Also in 1954, Pool used frontal lobe stimulation to treat psychiatric diseases.
The first integrated circuit was developed a few years later in 1958 and underwent rapid improvement.

**THE FIRST IMPLANTABLE PACEMAKER: SIEMANS 1958**

In 1958 the first pacemaker was developed by Siemens. The pacemaker was used as the model for the technology for the spinal cord stimulator. Pacemakers have the same parameters that may be adjusted as the spinal cord stimulator generators of two decades later.

The amplitude, frequency, and pulse width are adjustable. The major difference is that the power requirements are higher for spinal cord stimulation compared with cardiac pacing.

The first implanted pacemaker lasted 3 hours before it failed.

Also in 1958, Heath implanted septum pellucidum electrodes (in the brain) as a treatment for cancer pain. The patient had relief for their last 7 months of his life.
1963 Barostat was an electrical stimulator device manufactured by Medtronic and used to stimulate the carotid sinus (located in the neck) for the treatment of high blood pressure. In 1965 Angiostat was created by Medtronic to stimulate the carotid sinus for angina treatment.

1965 Gate theory Melzack-Wall was proposed. Pain perception involves a gate that can be opened or closed to allow pain sensation to pass through or to block it. If the activity of small pain fibers predominates, then the gate will open. On the other hand, large pain fibers that predominate (touch, position sense) will close the gate and not allow as much pain through to the brain. This created the idea that pain could be blocked by opening and closing these gates.

1966 J. Thomas Mortimer, at the time a graduate student in engineering at Case Western University (graduate student) was recruited by Norm Shealy to begin working on a spinal cord stimulator prototype. Shortly afterwards in 1967, Norm Shealy, the Chief of Neurosurgery at the Gunderson Clinic, Mortimer, and other collaborators, began to perform experiments on cats to prove the gate theory and stimulation of the dorsal columns as reported in the Journal Anesthesia & Analgesia May/June edition 1967. The following edition July/Aug 1967 was the report of the first patient use as outlined below.

1967 The gate theory was tested in 1967 by Wall and Sweet who stimulated their own infraorbital nerves under the eyes. Subsequently Sweet recruited Roger Avery, a colleague in engineering at MIT, to make an implantable stimulator. Sweet and Wepsic used the stimulator to provide peripheral nerve stimulation for pain management.

Also in 1967, Norm Shealy the neurosurgeon stimulated the large nerves of the spinal cord in the dorsal column in the lab and found it was possible to block sensation.
1967 The first human dorsal column stimulator (later termed spinal cord stimulator) was implanted in April 1967 by C. Norman Shealy, M.D. of the Gunderson Clinic in LaCross Wisconsin and designed by Mortimer after experimentation in a feline model. The first patient suffered thoracic chest wall and abdominal pain from wide spread metastatic cancer from a primary cancer of carcinoma of the lung. He had a single cathode electrode implanted "approximating the dorsal columns" by suturing the electrodes to the dura after laminectomy at T2-3 for exposure. The anode was intramuscular, both electrodes being made of Vitallium. The stimulator was external and connected to the implanted leads via hypodermic needles that were placed through the skin into the lead jacks. The stimulator was turned on only for an hour the first day, changing the frequency when the patient began to experience pain again. The second day the patient used the dorsal column stimulator for 10 out of 12 hours, again changing the frequency when he began to experience pain. The following day, the patient was too ill for stimulation and died that night. Later publications mistakenly purported the device was used for the last several months of the patient’s life, when in actuality was for only 11 hours over the last 3 days of the patient’s life. The autopsy demonstrated the patient suffered from endocarditis with cerebral embolism that resulted in paraparesis and death. The first spinal cord stimulator could not be measured as a success given the short amount of time used in stimulation and the unrelated death of the patient with cancer, but it spurred further interest since there was a reduction in pain during the stimulation. But having to plug in to jacks that were being accessed with needles placed through the skin was not an optimal way to deliver power to a stimulation system. Mortimer knew this, and set out to improve his system.
Mortimer subsequently contacted an engineer, Norm Hagfors of Medtronic, where he had interviewed two years before for a job. Mortimer surmised the Medtronic radiofrequency (external) powered cardiac generator could be used to power a spinal cord stimulator. The second stimulator powered by the Medtronic cardiac generator modified Barostat, provided pain relief for four years from chronic pain. The second electrode was designed by Mortimer to work with the Barostat radiofrequency technology. The leads on the second implant were platinum iridium of the same shape as the first stimulator with an external coil for the transmission of power. A portable control box with adjustable rate, amplitude, and the rate of frequency change was connected to the external coil. The rate and amplitude were generated in the controller then translated into radiofrequency waves picked up by the receiver, that re-assembled the RF signal into the final stimulation parameters. Parameters of amplitude and frequency were patient controlled. This second patient had adequate stimulation for pelvic carcinoma lasting 4 years. The leads were sealed in silastic. Shealy attempted to publish his outcomes, but the publication was rejected by the Journal of Neurosurgery and instead presented this at a neurosurgery meeting and published in the journal Anesthesia & Analgesia. He subsequently went on to implant dorsal column stimulators for 7 years before abandoning these due to complications, and instead switched his energies to development of TENS units.
1968 Myelostat was the first commercially available spinal cord stimulator, and was based on the implants of Shealy and the Barostat modified input-output characteristics. Shealy suggested this concept to Medtronic.

The Myelostat was a radiofrequency (RF) powered unit with an external generator worn in a pocket or on a belt, and a RF transmitter antenna ring was placed over the implanted receiver. The stimulation power all resided in batteries in the controller unit. The receiver was primarily an antenna/receiver only. This unit was a predecessor to several other RF units used in spinal cord stimulation, including Xtrel, Mattrix, and Renew systems developed much later.

Also in 1968, Roger Avery reported in the literature the implantation of peripheral nerve stimulators for pain. He was an engineer at MIT and a contemporary of Sweet, who had proved the gate theory via stimulation of facial nerves. He developed his own implantable peripheral nerve stimulator system in 1968. His system was also a RF system.

1969 Timm and the Regents of the University of Minnesota filed a patent application with the US Patent Office for “Implantable Electronic Stimulator Electrode and Method”. It described in vague detail a programmable stimulator, coupler, and electrodes for stimulation of “a mass of electrically excitable tissue without stimulating nearby tissue structures”. The patent 3,646,940 was approved in March, 1972. Also in 1969, Norm Shealy presented the results of spinal cord stimulation to the Harvey Cushing Society, a prestigious neurosurgical meeting, after having a paper rejected previously by the Journal of Neurosurgery on the subject.
1970- The Intradural pocket was created for placement of spinal cord stimulator plate leads (the only kind available) since subarachnoid placement (the most commonly used) was causing spinal cord trauma (direct injury to the spinal cord during placement or afterwards due to pressure exerted by the dorsal column paddle electrodes), bleeding, arachnoiditis (a chronic permanent inflammation of the spinal nerve roots resulting in clumping and sticking of nerves together and ultimately pain and motor dysfunction), and paraplegia (loss of motor function from the waist down) due to the thickness of the leads. The dura mater is the thick membrane surrounding the spinal cord. Creation of a split in this membrane to allow for placement of the stimulator lead inside the dura rather than under the dura protected the spine from some of the complications, but epidural (on top of the dura) was safest. However there was no way to secure the paddle lead so it did not migrate therefore the intradural route was a compromise, but was technically difficult to perform.
1971 Avery Labs developed the single lead RF system for spinal cord stimulation. An article published in Popular Mechanics July 1971 featured the spinal cord stimulation system. Unlike the Medtronic system that used subarachnoid or intradural leads, the Avery system used an epidural lead and was more flexible. Roger Avery started the company in his garage in 1968. The Popular Mechanics article was wildly popular and significantly increased sales for Avery Labs.

Avery’s radiofrequency spinal cord stimulator system was developed with the generator to be carried in the pocket (arrow) and the antenna lead connected to the transmitting antenna located directly over the implanted radiofrequency
receiver. The receiver was connected subcutaneously to the dorsal column electrodes, implanted in the thoracic spine. From the early 1970s through 1990, the receiver was primarily located in the anterior abdomen to allow the transmitter antenna to be easily placed. This became the basis for the location of the early implantable battery units that were placed in the anterior abdomen. There was really no other reason for this other than a single study by Medtronic demonstrating possibly less lead fracturing with an anterior implantation site.

In 1971 the only units on the market were Avery’s model 100A and the Myelostat by Medtronic. By July 1971 Neurosurgeons around the country had implanted over 200 dorsal column stimulators.

1972 Avery Laboratories, founded initially to develop phrenic nerve pacemakers as a treatment for diaphragmatic paralysis, began marketing heavily their spinal cord system in 1972. Avery marketed the DCS system to neurosurgeons beginning in that year.

1973 First deep brain stimulator for chronic pain by Hosobuchi who implanted a stimulator electrode in the somatosensory thalamus for treatment of denervation pain with anesthesia dolorosa

1974 The first patient worn TENS unit was created and patented. Shealy continued to use spinal cord stimulation for 7 years, then concluded the risks were too high for its use. However, he continued using the Electreat during that time on patients that were candidates for spinal cord stimulation, and subsequently approached Medtronic, who had made his initial dorsal column implantable device in 1967, but Medtronic at the time had no interest in transcutaneous uses of electricity, being the world leader in cardiac pacemaker implantable devices. Shealy then spoke with a Medtronic engineer who left the company in the early 1970s to form a new company Stim-Tech, that introduced the first solid-state modern skin stimulator, also called the Stim-Tech. The initial
stim-tech model was nearly a foot long and 4 inches thick, and used a square wave with an output of only 3mA (modern TENS units have up to 90mA output). Shealy, a proponent of the ancient Electreat system, believed the Stim-Tech was not as effective as the spike waves produced by the Electreat, and subsequently convinced Medtronic to begin manufacturing spike wave transcutaneous stimulators.

Pre-operative TENS seemed to reduce the perception of pain almost as well as the dorsal column implant (Hymes 1984). While the original goal of transcutaneous stimulation was screening of patients for spinal cord stimulators, it became apparent quickly that stimulation of the skin was often sufficient to provide pain control alone (Long 1991). Subsequently private industry had developed more than 200 TENS units and biofeedback devices by the 1980s. By 1991, there were over 600 published papers on TENS including basic science research. In 2013, TENS units were available without physician prescription, and the cost of these units dropped by up to 95%.

1976 Cordis (later acquired by Johnson and Johnson) introduced the first totally implantable spinal cord stimulator, made in epoxy and containing a mercury battery. It was a modified cardiac pacemaker. This device had externally changeable amplitude and rate.

1977 Medical devices were added to the umbrella of FDA regulatory power, requiring approval by the FDA before marketing.

1978 Medtronic introduced a percutaneously inserted electrode for permanent use.

1979 Neuromed Company was formed and introduced Multistem (a portmanteau for multiprogrammable spinal cord stimulator), an external quadrupole on a single lead (novel for the time) and RF receiver power/programming device.

1980 Cordis manufactured the 900X-MKI, the first spinal cord stimulator device to achieve FDA approval for pain relief. This was a unipolar device.

1980, Neuromed released the RF Quatrode system.

Also in 1980, Myelostat by Medtronic dorsal column stimulator was approved by the FDA K801384. It had been on the market for many years by this point but was released before the FDA was required to approve implantable medical devices.

1981 Medtronic released a four electrode percutaneous lead, the Pisces (acronym for percutaneously inserted spinal cord electrical stimulation).

1981 Avery retired, their sales and marketing of dorsal column stimulation ceased, and the company continued their concentration in diaphragmatic and phrenic nerve stimulation.
Also in 1981, Cordis released the model 904 MK-II unipolar and bipolar implantable programmable generator (IPG). It had a lithium battery and was patient controlled via an external magnet with up to 8.5mA current, fixed pulse width, and variable frequency of up to 115 hz with a titanium housing.

1984 Medtronic received approval from the FDA to market Itrel, a primary cell (non-rechargeable) totally implantable spinal cord stimulation system. This was Medtronic’s first implantable system with internally contained battery (IPG). The Itrel was a 4 electrode system on a single lead. Several modifications were made to the Itrel over time with several generations of this primary cell on the market for decades. The platform for all subsequent Medtronic products was built on the constant voltage system adopted by Medtronic.
1986 Neuromed manufactured an 8 electrode lead for their single lead RF system (Octrode).

1988 Medtronic released the Xtrele RF system. 4 total contacts, model 3470. This was a dual lead system with 2 contacts on each lead. It was the successor to the Myelostat system. It has since been discontinued from production. It featured an improved implanted module with an enhanced antenna and improved lead throughs (where the leads insert into the unit).
1991 Medtronic released Itrel II IPG with 4 total electrodes and improved battery life from this primary cell unit. The Itrel continued to use a total of only 4 electrodes, making programmability very limited, albeit improved over the Itrel I. The Itrel II became increasingly popular. A lithium battery was used.

1991 Neuromed introduced into clinical trials the TIME (acronym for totally implantable multistim electronics) implantable spinal cord stimulator in both the US and Europe. However, by 1993 the device was pulled from the market by the FDA after the agency cancelled the investigational device exemption (IDE) and rescinded the export authority for Neuromed after alleged violations by the former management of the company. The allegations included violation of applicable rules and regulations including good manufacturing practices. The clinical trials were discontinued and the product was withdrawn from the market. (Source: SEC Filing Quest
1993 **Advanced Bionics** was formed by spinning off **MiniMed**, a leader in implantable diabetic microinfusion pumps. Advanced Bionics developed a very popular HiResolution cochlear implant and in the late 1990s elected to enter the spinal cord stimulator market. The company submitted an application to the FDA in 2000 for a radically new spinal cord stimulator system: a rechargeable system. The FDA waited several years to approve the device.

1994 Neuromed received FDA approval to market the dual octrode lead radiofrequency coupled spinal cord stimulator system. This small company had the only product on the market at the time to compete with Medtronic, and with double the number of electrodes.
1995 Quest Medical acquired Neuromed.

1995 Medtronic released the 8 electrode MatriX RF spinal cord stimulator system. The RF system was the successor to the Exrel system and a competitor of the Neuromed RF Coupled system. The MatriX was not heavily marketed by Medtronic since they had a primary cell that required replacement every 3 years and provided a steady recurring revenue source for Medtronic. The system was also not patient friendly compared to the primary cell systems. It was a radiofrequency coupled system in which the stimulation parameters were achieved in the generator that converted the signal into a radiofrequency signal in order to transmit both the power and programming parameters through the skin to the receiver. The receiver was a radioantenna with frequency converter that used the power being transmitted to drive the energy needed to power the electrodes but also convert the RF energy into specifically defined stimulation parameters. The system used an external battery that was initially NiCd (did not work well) and ultimately a NiMH rechargeable external battery. Patients did not like the system very well, could not use it in the shower or when swimming, it required precise placement (with adhesive) of the transmitting coil directly over the receiving coil. It finally fell into obscurity as ultimately did all the RF systems due to the inconvenience of use.
1995 Medtronic released Itrel 3, the next generation in the Itrel system. It was first implanted in Belgium in 1994 and was released in the US in 1995. The battery life was extended compared to the Itrel II, the only other primary cell on the market in 1995. It had 4 total electrodes splittable between 2 leads. However with only 2 electrodes per lead, any lead movement(121,424),(898,995) (common with the lead systems of the time) would lose stimulation. The 8 and 16 electrode systems had significant advantages due to this fact and because of lead anchors that frequently failed and allowed lead movement or were uncomfortable. The battery life was touted as up to 5 years but frequently lasted 2-3 years. The size of the titanium can was 22ml, it weighed 42g, was programmable at a frequency of 2-130Hz, pulse width of 60-210mS, and amplitude of 0-10.5V.

1998 Quest Medical changed their name to Advanced Neuromodulation Systems (ANS)

1999- ANS Renew System released. This was a successor to the Neuromed System. It also was a dual octrode (the first 16 total electrode) system. It was a radiofrequency coupled system. An improved programmer that was easy to use was the primary movement. The system was an economical "lifetime" system.
but ultimately the system did have its problems with leakage in the seals of the system (the throughputs) with shorting out and malfunction after years of use. The cumbersomeness of the RF power ring having to be exactly positioned over the receiver was an issue for patients. However the system was appealing since it had round and paddle leads available and if there were a slight movement of the lead, reprogramming rather than surgery recaptured the stimulation parameters for pain control.

1999 Synergy primary cell by Medtronic model 7427 was released. The system had dual quad electrodes, doubling the number of electrodes previously available in a primary cell. The battery size was therefore also increased to accommodate the increased number of electrodes. It had 8 electrodes, volume of 51cc, weight 83g, rate 3-130Hz, pulsewidth 90-450 microseconds, 0-10.5V amplitude. It used a combined silver vanadium oxide 3.2V battery.
2001 Advanced Neuromodulation Systems (ANS) brought to market their first primary cell non-rechargeable implantable programmable generator (IPG) amid much fanfare since it was the only product on the market to compete with the Medtronic primary cell (non-rechargeable) systems. When ANS released their rechargeable version of the cell several years later, Genesis was renamed Genesis Prime Cell. It was still being implanted in successor Genesis products as late as 2012. Its volume was 29ml, weight 53g, frequency 50-1200Hz, pulsewidth 50-500 mS, amplitude 0-25.5mA. The battery was 3.7 volt lithium thionyl chloride.

2002 ANS released an entire family of primary cell generators to compete with Medtronic. The Genesis XP model 3609, Genesis XP Dual model 3644, and Genesis G4 (effectively the original Genesis) model 3604. They had larger battery sizes with external dimension sizes that were huge. The XP had nearly double the volume and was very heavy compared to the Genesis. With larger battery sizes available, the longevity of these primary cells was longer than the Genesis or Medtronic however patient discomfort was becoming a real issue with the large IPGs (Implantable Programmable Generators).
2002 Medtronic released the Synergy Versitrel model 7427V with 4 or 8 contacts available (to compete with Genesis XP Dual). The volume was 40ml, weight 65g, frequency rate 3-130Hz, pulse width 60-450Hz, Amplitude 0-10.5V. Same battery as the Synergy. Primary difference is the size is slightly smaller and weighs less.

2004 Advanced Bionics received FDA PMA approval to market the first rechargeable (secondary cell) IPG generator (the Precision) and lead system. This was a much smaller system than the primary cell units on the market by ANS and Medtronic. The volume was 22ml, weight 33g, frequency 0-1200Hz, pulse width 0-1000 microseconds, power up to 20mA @15Volts, 16 programs, fractional charged electrodes, and 16 total electrodes (double those available with other units). The battery capacity was 200 mA-hrs. It was a
constant current product like the ANS primary cell systems.

This system quickly became a game-changer, forcing other companies to scramble to develop a rechargeable system. The engineering on this product was extraordinarily good for their first foray into the spinal cord stimulator market, and with only some tweaks since that time, the same principles used in the original units are still employed today.

2004 The ANS Genesis RC was the second rechargeable IPG released and was significantly larger than the Precision. It also had a plastic surface on one side that if accidentally was cut or incised during implantation, could disable the IPG. It was available later than the Advanced Bionics system, but did offer an alternative.
2005 St. Jude Medical purchased Advanced Neuromodulation Systems

2005 Eon Rechargeable secondary cell IPG released by St. Jude Medical (ANS). It was a dual octrode system, 42cc volume, constant current system. It also had a plastic coating over the face of the device that could not be incised or scratched without potentially damaging the device. The device has output of 0-25.5mA, 50-500microsecond pulse width, frequency 2-1200Hz, 24 programs, and capacity of 325mA-hr (more than 50% more than the Precision).

2005 St. Jude Medical (ANS) released the Genesis dual 4 channel primary cell IPG model 3643 FDA approved.

2005 Synergyplus+ model 7479 and Synergy compact+ primary cell IPGs were released by Medtronic. These represented expanded and contracted sizes of the Synergy. They were discontinued in a few years. The Synergy compact and versitrel batteries are about half the size of the synergy.
2005 Restore rechargeable spinal cord stimulator was released by Medtronic. This was their first secondary cell (rechargeable) IPG and was model number 37711. There was a class I recall on the stimulator issued November 2005. Implants continued until at least the end of 2011 but was superseded by other Restore models. The frequency range was 0-130Hz, pulse width 60-450 microseconds, amplitude 0-10.5V, capacity 300mA-hr.

2006 Boston Scientific acquired Advanced Bionics.

2006 RestorePRIME, a non-rechargeable Medtronic spinal cord stimulator system was released in 2006. It had 16 electrodes with 32 programs. Model number 37701. Its volume was 39ml, weight 67g, pulse width 3-130Hz, pulse width 60-450 microseconds. Amplitude 0-10.5V. The implant depth is <4cm.
Also released in 2006 was the Medtronic PrimeADVANCED. This was a primary cell IPG that had a longer life battery. The model was 37702. The volume is 39cc, 16 electrodes, rate 3-130Hz, pulse width 60-450 microseconds, amplitude 0-10.5V. It has 32 programs. It also has an implant depth of <4 cm.

There appears to be little difference comparing this IPG with the Restore Prime in size, weight, programs, and parameters. It appears Medtronic claims a longer battery life with the PrimeAdvanced battery.

2007 St. Jude received FDA approval for the model 3688 Eon-C, a primary cell non-rechargeable, with extended battery life, and 16 contacts. It adjusts power output automatically based on impedance changes. It had more and 40% more battery capacity than the Medtronic Restore and could control up to 8 pain areas independently. The volume was 49ml. Frequency range is 50-1200Hz, pulse width 50-500 microseconds. The amplitude is 25.5mA and there are 24 programs. The volume is 49cc compared to 42cc for the Eon. This is the first extended life primary cell released by St. Jude/ANS.
2008 Medtronic released Restore Ultra model number 37712 approved by the FDA with provisional head 1.5T MRI under certain conditions. It has 16 electrodes. Volume 22cc, weight 45g, rate 2-1200Hz, pulse width 60-1000 microseconds with 16 programs.

2008 St. Jude (ANS) received approval for the Eon-mini, a mineaturized 16 electrode secondary (rechargeable) cell that is smaller than other units on the market. Volume 18ml, weight 29g, 0-25.5 mA current at 12 Volts; 50-500 microsecond pulse width, 2-1200Hz frequency with 24 programs. For medium current use, the recharge interval is 22 days vs 56 for the Eon. The mini Eon is 40% of the volume occupied by the Eon.
2011 Medtronic received approval for the RestoreSensor, a rechargeable IPG with an accelerometer (electronic gyroscope) model 37714. The accelerometer is a means to change the output of the constant voltage system by changing the current depending on the position of the body. The accelerometer detects the position of the body and automatically changes this value. This has been a problem for the Medtronic constant voltage system platform for years whereas both St. Jude and Boston Scientific systems have some automatic adjustment of the output based on impedance. The Medtronic system is approved for provisional MRI 1.5T. The volume is 22cc, weight 45g, battery life 9+ years (rechargeable), 16 contact, 2-1200Hz stimulation frequency, 60-1000microsecond pulse width, 0-10.5V.

2012 Medtronic released the Itrel 4 models 37703 and 37704. It is a 4 electrode system usable as a primary cell system (non-rechargeable) used for single limb pain. It is provisionally approved for head MRI. The volume of the 37703 is 28ml and 44g weight. The frequency of stimulation is adjustable from 2 to 130Hz, pulse width 60-450 microseconds, amplitude 10.5v max.
2013 Medtronic received approval in March 2013 for Restore Sensor Surescan. The FDA many years of design changes as instituted by the FDA in order to have full body MRI capability. On May 10, 2005, the FDA sent out a public health notification that effectively banned physicians from performing MRIs on patients with spinal cord stimulators. There had not been any reported injuries from MRI performance in patients with spinal cord stimulators, however the FDA lacked the sophistication or medical knowledge to understand the differences between spinal cord stimulation and deep brain stimulation. Deep brain stimulators have the leads implanted directly into neural tissue of the brain whereas spinal cord stimulator leads are separated from both spinal fluid and the spinal cord by a thick membrane called the dura mater. Unfortunately due to ignorance, the FDA conflated the two uses and simply reacted to a couple of reports from deep brain stimulation injuries in MRI and effectively banned all MRIs for anyone with any implantable devices including pacemakers, sacral stimulators, vagus stimulators, etc. Years of subsequent research demonstrating pre and post ban safety were presented in scientific meetings and to the FDA to no avail. Medtronic had petitioned years before for approval of total body MRI for submitted systems but could not satisfy the FDA safety demonstration requirements. Suddenly the FDA approved the request after redesign of the leads by shielding them with coils placed around the active leads, and to shield the lead throughs (place the stimulator transmits energy to the leads). The company was not ready for the approval and did not have any product generally available for 5 months after the FDA announced the approval. The Surescan technology allows for scans of any part of the body with an implanted spinal cord stimulator system subject to certain limitations. The stimulation parameters are identical to that of the RestoreSensor IPG.

2013 in April Boston Scientific Launched Precision Spectra in the US. 32 electrodes independently programmable with positive, neutral, or negative full or fractional charges. The patient can have 4 x 8 electrode leads or 2 x 16 leads or a central 16 electrode lead flanked by an 8 electrode lead on either side or other combinations. The IPG rechargeable amplitude is up to 25.5mA while the stimulation rate is 2-1200Hz. The pulse width
range is 20-1000 micro seconds. There are 16 available programs.

2014 April Protege spinal cord stimulator by St. Jude was released. This IPG rechargeable is the smallest on the market (17.7ml) with a lithium ion battery rechargeable. It is the first software upgradable spinal cord stimulator programmer as software is approved by the FDA. Amplitude up to 25.5mA, pulse width tonic 50-500 microseconds, frequency 2-1200 Hz, Stimulation mode Tonic. It has the potential to upgrade to Burst stimulation via software upgrade when approved by the FDA. The battery life is 10 years on High Setting. Warranty is 7 years with a maximum out of pocket cost to the patient of $1250.

2015 St. Jude Prodigy model 3799 has received CE Mark in Europe and is awaiting FDA approval in the US. It is a secondary (rechargeable) Lithium ion cell with upgradable software and pulse burst technology. It is part of a system that includes a rapid programmer and charger modules. It also has a patient programmer. Specifications include volume of 18ml, weight 29g, amplitude 0-25.5mA, 50-500 microseconds pulse width, pulse width burst mode 50-1000 microseconds, frequency 2-1200 Hz, stimulation modes tonic or burst.
2015 Approved by the FDA: Nevro Senza high frequency spinal cord stimulation system. The Senza system has had excellent results in Europe and is now in trials in the US. Unlike other systems, the Senza is operating at up to 10,000 Hz (8 times faster than other systems approved by the FDA) that the patient does not feel the stimulation, but achieves pain relief.
2016 Boston Scientific was approved by the FDA to release the Precision Montage spinal cord stimulator (MRI Compatible) with thermally shielded leads, making Boston Scientific only the second company to have a fully MRI compatible system for 1.5T MRI scanners (the most common type).

SPINAL CORD STIMULATION COMES OF AGE
After the initial experiment in 1967 on the lung cancer patient with widely disseminated metastasis (would be a very poor candidate for spinal cord stimulation today), Shealy continued implantation of dorsal column plates and electrodes that were very large, required a laminectomy, and were connected to an external device. By 1970, six patients had undergone this treatment. By 1972, series of patients having these dorsal column implants (that were quite primitive having only one bipolar (2 electrodes) contact set on one lead, were described in the literature with a 30 patient series showing the most success in burning pain from nervous system injury. In 1972, dorsal column stimulators were initially marketed to neurosurgeons in the US, and the devices were later named spinal cord stimulators. In 1974, case reports of serious complications were published including delayed intraspinal hemorrhage and spinal cord transection, both ostensibly due to the extremely large electrodes being used at the time. By 1976, cardiac pacemaker technology battery and programmer advances led to the development of the first completely implantable neurostimulator (Medtronic). Slow advances were made in the 1970s and 1980s due to constraints in the battery size and continued development in lead design. The number of electrodes was very limited during this time, and the devices were expensive and frequently required revision. With only 2 electrodes, programming was extremely limited and there was frequently motor stimulation of the legs given the units of the time. There were ultimately several
advances in technologies that began in the 1990s and continues to accelerate, in part due to extreme competition between the three manufacturers of spinal cord stimulation, and now deep brain stimulation systems. The advances have come about partially due to patient convenience and acceptance of the product but some have come through basic research design changes to make a better product with fewer failures. These advances can be categorized into several areas:

1. Battery life. Using more contacts on leads brought about greater programmability and enhanced pain control but also the implantable programmable stimulators (IPG) expanded programming parameters tended to chew up the early stimulator implanted batteries quickly. The use of higher stimulation frequencies, increased pulse widths, and more active contacts caused higher drain on the battery life of these units. The Itrel would sometimes only last a few months before battery depletion. The Itrel III with better programming capacity and a larger battery may last only 1-2 years before replacement was necessary. Because of this limitation, both Medtronic and ANS began developing ever larger batteries until the patients began complaining of the physical size of the generator being a limiting factor. IPGs that were twice the size may only last 50% longer than the smaller IPGs and the cost continued to escalate with each generation of larger batteries but also with the cost of not infrequent replacement of the IPG. The batteries are sealed inside the implanted generator and therefore when depleted, require replacement of the entire IPG. Therefore something had to be done about the increasing size of the batteries and the increasing power requirements due to enhanced programming sophistication. The external power supplied units (RF) attempted to solve the problem by using a power pack hung on the patient’s belt and a RF transmitter ring was secured to the skin directly over the very small implanted RF receiver. Much greater power was available using this system, and the receiver theoretically would not have to be changed. However these units proved to be cumbersome to many patients, not being able to wear them in the shower or when swimming, and the RF transmitter ring would often dislodge from the skin, causing an interruption in power to the receiver and an increase in pain. The rechargeable batteries of the time were Nickel Cadmium batteries, that held a charge for often less than a day. The frequent recharging of batteries and the finicky nature of the device finally drove some people away from the systems. Other reasons people moved away from the RF system was a tendency to form leaky seals in the receiver, causing the unit to short out and be non-functional. The rechargeable RF systems were coming onto the market for other applications, and it became readily apparent this design would permit battery and IPG miniaturization for patient comfort, but retain the programmability and power needed for complex programming uses with chronic pain. The Precision rechargeable was the first rechargeable IPG on the market in 2004, followed by the Genesis RC (ANS) and Restore (Medtronic). The manufacturers have continued to use improved lithium ion battery technology and have created extremely small spinal cord stimulators that weigh just over an ounce.

2. Lead design. The spinal cord stimulator leads have advanced from the purely surgically implantable leads in the 1960s to round percutaneous leads in the 1990s to complex surgical lead designs with 16 and soon 32 electrodes, and use of combinations of 2 or 3 round leads to give better coverage. The leads continue to
become smaller and thinner with radically differing lead designs used by the three manufacturers. However, some of the manufacturers have conversions systems to permit an already indwelling lead to be connected to their IPG. The leads are typically multistranded straight wires with each of the 4 to 8 bundles enclosed in a flexible plastic sheath. The wires extend internally from one end to the other, connecting to the platinum-iridium electrodes at the end of the lead. The spacing of the lead contacts is now selectable by the physician based on the anticipated needs and area of coverage. The old coiled leads are not used as often now. Because of the improvements in leads, the breakage factor is much less than in the past, and the ultralow impedances preserve the battery life. The lead configuration has also been shown to help with certain types of pain. For instance, low back pain may be best treated with a tripole (3 leads side by side) as treatment for low back pain.

3. IPG Programmability. From the origins of spinal cord stimulation when effectively a given waveform was available and the amplitude of voltage was the only adjustable parameter, we now have a plethora of choices in programming. Each contact can be positive, negative, or neutral. One system permits independent fractional charge for each of 32 electrodes. The pulse width, frequency, service time on, and scanning across leads are all programmable using an external programmer. The multiple programs available (4-32) dependent on the manufacturer, permit selection of the most soothing program for different activities. The latest advance will use a position sensor to change the stimulation pattern when the patient changes from sitting to standing or lying down to standing positions, thereby reducing the shock potential when changing positions. There are now millions of programming combinations available for each stimulator.

Some of the most exciting advances include the use of high frequency stimulation and the use of burst stimulation (small bursts of frequency with nothing inbetween) both of which are helping reduce the acclimation of the spine and brain to the stimulator, resulting in better pain control.

4. Anchor design. The leads containing the contact electrodes must be secured permanently to some structure. Typically selected are the thick fascial planes outside the spinal back muscles or to the ligaments between the spinal bones. A series of anchoring devices have been developed and continue in rapidly advancement to permit secure placement of leads so that the traditional 15% lead migration rate (movement away from the optimal placement for stimulation) is eradicated. Newer anchors included the Titan by Medtronic and later anchors and Synch anchor by St Jude. There is a new twist lock anchor by St Jude that makes movement of the lead virtually impossible outside of major trauma to the back. Boston has developed a screw system anchor that is also excellent. The anchor designs have reduced the number of surgical revisions of the leads and therefore has cut the overall expense significantly.

5. External programmer function. Both the patient programmers and the industry representative programmers have advanced features that drastically reduce the amount of time required to program optimally the spinal cord stimulator system.
Boston Scientific has a very impressive system for this, and the other manufacturers have dramatically improved their programming capabilities.

6. Company support. In the old days of the 70s-90s, it was not always easy to find the company representative to support the product and have them readily available in case a revision or trouble shooting was required. This is no longer the case, as each company has multiple tiers of representatives making them virtually always available by phone to patients or physicians.

7. MRI Compatibility. The ultimate goal of spinal cord stimulation systems is to be as patient friendly as possible. The chances of a patient needing an MRI at some point in their lifetime is very high. Stimulator systems were used for years without issue with MRI and there were hundreds of thousands of MRI scans in patients with spinal cord stimulator systems without complications or injury. The FDA in what was a clear over regulation without evidence of injury but based on the theoretical possibility of injury nearly overnight stopped MRI scans of patients with spinal cord stimulation systems in 2005 with their unwarranted warning letter. Many patients were injured because of continuing pain and tissue injury due to inability to MRI image, had delayed surgeries, had ersatz imaging by CT resulting in sometimes wrong surgical procedures, or had the spinal cord stimulator system explanted due to the need for a MRI then reimplemented later. The FDA reluctantly agreed to allow some stimulators with leads implanted in the thoracic spine to be eligible for head MRI under certain conditions. However full MRI compatibility was for whole body MRI was first granted to Medtronic in 2013 then to Boston Scientific in 2016. As of 2016, neither Nevro or St. Jude have full MRI compatibility. With two companies on the market as of 2016 with full 1.5T MRI compatibility and given the extremely high chance of needing an MRI somewhere in the body other than the head, it is illogical to continue to implant non-MRI compatible units in patients. For many years, pain physicians in particular were insouciant to the potential future needs of their patients, and willy nilly implanted non-MRI compatible units based on their own preference for a stimulator rather than what was best for the patients.

COMPLICATIONS OF SPINAL CORD STIMULATION
No implanted device, whether it be a pacemaker or deep brain stimulator or insulin pump or artificial hip are without complications. Certain factors increase risks such as being a diabetic increases the infection risk by up to 10 times that of a non-diabetic patient. Most risks are related to the surgery and not to the devices. In a Medtronic registry of complications reported to Medtronic in 2009 from all of their previously implanted spinal cord stimulators, the following were noted: 5 events related to the neurostimulator malfunction, 157 events related to lead dysfunction (half of these were due to lead migration before the new anchors were introduced), 11 events due to lead extension breakage and issues. There were also 60 complications surrounding the IPG pocket (mainly infection and pain at the site), 14 lead tract issues, 109 patient related complications (2/3 of these were for failure to meet patient expectations and loss of effect), and 140 spinal cord stim units were replaced due to expected battery depletion. These same ratios would be expected for other manufacturers products, and are only a small fraction of the hundreds of
thousands of spinal cord stimulators that have been implanted thus far. Statistics in the scientific literature collected even 3 years ago are now obsolete compared to those with new IPG and leads and lead anchor implants, therefore the complication rate continues to improve. There can always be neurological disasters from placement of spinal cord stimulators, but these are exceedingly rare.

HISTORY OF SPINAL CORD STIMULATOR COMPANIES

HISTORY OF MEDTRONIC SPINAL CORD STIMULATION

Medtronic was the original of the spinal cord stimulator companies and was present at the very beginning of development in 1967, making the devices implanted by Shealy. The Itrel implantable programmable generator (IPG) was a neurostimulator (4 total electrodes) approved by the FDA in 1984. This unit was to be used for spinal cord stimulation in which a series of electrodes on a single lead were placed into the epidural space over the dorsal column of the spinal cord, thus the moniker “dorsal column stimulator”. The Itrel II was a drastically improved version of the Itrel with FDA approval being achieved in 1992 (8 electrodes), and the Itrel III was approved in 1995. Synergy was the next generation of IPG by Medtronic, receiving FDA approval in November 1999. This unit had twice the battery capacity as the Itrel III but the size was also much larger. The Restore rechargeable system was approved by the FDA in 2005 and a miniature version, the Restore Ultra was FDA approved in 2008. The Restore system continued to advance with FDA approval of their RestoreSensor system with built in position detection accelerometer in 2011 and the addition of SureScan (Total Body MRI Compatible) in 2013. The Mattrix system, was not an IPG, but was a radiofrequency powered unit approved by the FDA in 1992. It was a device that used an external power source that was placed on a belt loop outside the body, with a RF antenna used to transmit energy through the skin and to the implanted small receiver unit.

HISTORY OF ADVANCED NEUROMODULATION SYSTEMS (ANS)-ST JUDE

The precursor to Advanced Neuromodulation Systems (ANS) was incorporated in May 1979 as Medicor, Inc. by veterans of the medical device field, including its president, Thomas C. Thompson, who had earlier founded a company that made intravenous catheters. After the intravenous catheter company was sold to Baxter Travenol, Thompson joined forces with seasoned executives who had worked at Johnson & Johnson, Eli Lilly’s IVAC unit, and IMDE, a Warner-Lambert subsidiary. The partners got into business in October 1979 through acquisition, picking up a four-year-old Dallas company called Med-Pro Ltd., which made its money selling surgical tape but harbored a great deal of potential in the intravenous (IV) tubes and electronic IV devices it had under development. A few months later, in January 1980, Medicor changed its name to Quest Medical, Inc. A small company, Neuromed, in 1991 developed a radiofrequency powered spinal cord stimulation system that used a small implantable receiver and an external power unit to control the spinal cord stimulator. Ultimately Neuromed was acquired by Quest in 1995 for $15 million plus stocks, who divested their company of other non-profitable products
over several years, then changed their name to Advanced Neuromodulation Systems (ANS) in 1998 as spinal cord stimulation became the most profitable element in the company. Led by Chris Chavez, a former Johnson and Johnson executive and a Harvard Business School Graduate, the company began to leap forward introducing the Renew RF system in 1999 (16 total electrodes) and capturing 50% of the RF market that year. Subsequently, through a series of partnerships and acquisitions, ANS developed their first implantable programmable generator (Genesis) in 2002 in the US and late in 2002, the Genesis XP with a larger battery size. In 2005, the Genesis RC (rechargeable battery) was introduced in the US, followed by the Eon rechargeable and in 2008 the mini-Eon, a very small rechargeable 16 electrode generator. The company was acquired by St Jude Medical in 2005.

HISTORY OF ADVANCED BIONICS-BOSTON SCIENTIFIC
Advanced Bionics received PMA for its Precision spinal cord stimulator as an aid in management of chronic, intractable trunk and limb pain in 2004. All are fully implanted devices. The company had approval for cochlear implantation stimulators in 1998. Advanced Bionics had the first rechargeable generator and the first independent current controlled contacts on their leads. Their Precision spinal cord stimulator has been implanted throughout the world into chronic pain patients. The company was ultimately acquired by Boston Scientific.

NEVRO is the latest company to enter the market in 2015 with their high frequency stimulator system with head only MRI compatibility. The downside of their unit is its size and the fact that very frequent recharges of the unit are necessary.

OTHER STIMULATOR HISTORY
The Cordis 900A programmable neurostimulator from Cordis, Corp. was approved in 1981. Cordis was ultimately acquired by Johnson and Johnson and stopped manufacturing spinal cord stimulators. Cordis had the first implantable self contained stimulator on the market in 1976.

Avery Labs was established in 1968 in a garage. The company marketed RF system spinal cord stimulator systems beginning in 1971. By 1981, their chairman retired, and Avery stopped making spinal cord stimulators.

Medtronic was also started in a garage in 1949. Apparently garages are excellent locations to develop great ideas and to actually make them into something.