

US Neurostimulation Market

An Industry Commentary by Scientia Advisors, LLC.

The market for neurostimulation devices, which employ implanted electrodes to help treat certain nerve-related disorders, is likely to continue growing at an average rate of 16 percent through 2012--along with increasing proof of efficacy, physician acceptance, an aging population, and the need for treatments that are quicker, safer and less expensive than drug-based therapies. Neurostimulation devices likely to show the greatest growth are those targeting the deep brain, the spinal cord and the sacral area. While current products are relatively straightforward, opportunities and unmet needs include smaller devices that are easier to use, longer battery life and better feedback mechanisms. Advances in remote patient monitoring, wireless technology, and microprocessor hardware may add complexity and utility, thus adding indications. Scientia recommends that device companies consider developing or purchasing technologies in this growing field.

Background & Major Players

Currently, there are three types of neurostimulation devices on the market: those that target the spinal cord, those that target the sacral nerve, and those that target deep in the brain. The first two are indicated for chronic pain, while the latter is used for a growing number of problems, from essential tremors and Parkinson's to cognitive disorders. Medtronic is the clear leader in this space, manufacturing all three types of devices and having the only product on the market for sacral nerve stimulation and deep brain stimulation. Boston Scientific and St. Jude are two other major players with spinal cord stimulation products. Additionally, new companies are also coming forth with innovative neurostimulation devices that target other areas of the body and brain.

Spinal Cord Stimulation

Spinal cord stimulation (SCS) is a mode of exciting the spinal cord with electrical impulses to disrupt the relay of pain signals to the brain, replacing it with a tingling sensation, termed paresthesia. SCS devices are composed of one to two leads placed in the space between the spinal cord and the vertebrae, called the epidural space of the spine, with multiple electrodes per lead, attached to an implanted electric pulse generator and battery system. It is used for alleviating chronic pain, complex regional pain syndrome, and painful neuropathy.

Medtronic has the dominant market share in spinal cord stimulation, though technology advances by competitors, such as Boston Scientific's small battery and improved lead design, keep the market competitive. St. Jude also has a SCS product and is developing the therapy for a new indication: chronic angina. The market size, estimated at just under a billion, is expected to double in growth in five years as patients and physicians become more educated on and comfortable with its application.

Currently, only 4% of the 3 million people with treatable chronic pain are receiving spinal cord stimulation therapy. Physician acceptance will improve with the release of positive study data. A recent study illustrated that SCS with conventional drug therapy decreased pain by 50%, while conventional therapy alone decreased pain by only 9%. Additionally, SCS has demonstrated good safety and low side effects in comparison to the current drug treatment therapy.

Sacral Nerve Stimulation

Sacral nerve stimulation (SNS) works by delivering electrical signals to the sacral nerve, the nerve that innervates the muscle systems lining the bladder sphincter and the pelvic floor. The current device is similar to the spinal cord stimulator, with a subcutaneously implanted pulse generator and battery connected to a 4-electrode lead that attaches to the sacral nerve root. Presently, sacral nerve stimulation is used primarily for urinary incontinence, but is also indicated for fecal incontinence.

Medtronic controls the entire SNS market, which is a little less than \$200MM and projected to triple in the next five years. Medtronic is cementing its leadership position in the SNS market by acquiring emerging companies, such as NDI Medical, which is developing alternative products for urinary incontinence. The only other product likely to compete with Medtronic in the near future is Boston Scientific's BION® system, which has CE certification in Europe.

While urinary incontinence affects nearly 5% of the US population, only a small subset require sacral nerve stimulation treatment. SNS is the treatment of last resort for urinary incontinence, only used after patients fail to respond to the primary treatments of oral pharmaceuticals, injections, and minor surgeries. Opportunity for SNS lies in the increasing aging population, as 10% of people over 65 suffer from serious urinary incontinence. Additionally, as with SCS treatment, SNS may move up the treatment formulary as positive study data is released. Recent research suggests that it may also be useful for the management of Painful Bladder Syndrome (PBS)/Interstitial Cystitis (IC).

SNS differs from SCS in that it is indicated for muscular disorders, while SCS treats pain. The success of this stimulation method is opening up new doors for muscular therapy, as emerging companies are developing stimulation devices that target other areas, such as Synapse Biomedical's NeuRx Diaphragm Pacing System.

Deep Brain Stimulation

The brain is the control center of the body, with areas responsible for very specific nerve relays encompassing all actions, from senses to movements to thoughts and feelings. Deep brain stimulation (DBS) targets these areas through the direct application of electrical impulses. Like both SCS and SNS, the DBS device is composed of one to two leads connected to an implanted pulse generator and power source. The leads are placed within different the regions of the brain depending on the desired

therapeutic effect. For example, stimulating the thalamus, the part of the brain that controls sensory and motor integration, reduces tremor. Currently, the use of DBS is limited to movement disorders, including Parkinson's disease, essential tremor, and dystonia. Because the brain is involved with a large variety of disorders, DBS represents a significant market opportunity with attractive near-term 'movement' indications, and attractive long-term 'cognitive' indications.

In the relatively new DBS market, Medtronic has the only device with FDA approval and looks to maintain a strong position, with the addition of epilepsy indication expected in the near future. St. Jude is working on Parkinson's, migraine, and major depressive disorder indications, expected to enter the market in 2011. Several smaller companies, including NeuroPace, Intelect Medical, and Northstar Neuroscience, are also developing DBS devices for more movement and cognitive conditions. The introduction of these devices for new indications will drive growth, almost doubling the DBS market from less than \$200MM to over \$300MM in the next 5 years.

As with the other neurostimulation devices, DBS has a large, underpenetrated, treatable patient population. An estimated 5 million people have treatable essential tremor, 0.25 million people have treatable dystonia, and 1 million people have treatable Parkinson's disease. Of all three of these, only 40 thousand, or 0.6%, of the potential populations is being treated with DBS. The poor rate of adoption is mostly due to poor physician acceptance and patient discomfort. Understandably, the prospect of receiving direct jolts to the brain from an implanted device is enough to make anyone pause. However, studies continue to show the efficacy of DBS, especially as compared to current drugs, in treating movement disorders. Patients using DBS show an immediate decrease in tremors and have fewer negative side effects, in comparison to pharmaceuticals, which have a delayed effect and many side effects. As physicians realize these benefits and become more confident in DBS technology, population penetration will improve. Additionally, indications for cognitive disorders such as depression have the potential of introducing large new patient populations.

Conclusion

All three subsegments of neurostimulation have underpenetrated, treatable populations, largely due to a lack of physician acceptance. As the technologies become more familiar to end-users and studies continue to confirm their safety and efficacy, they should see greater adoption and move up the patient care formulary.

Spinal Cord Stimulation is the most mature, largest sub-segment of neurostimulation and is the only segment with devices from multiple companies on the market. While relatively underpenetrated, its applicable indications are limited to alleviating pain.

Sacral Nerve Stimulation is another emerging category examined herein. While its main indications meet the criteria for clear clinical endpoints and unmet needs, SNS represents a limited, albeit growing, opportunity within neurostimulation

Deep Brain Stimulation is the least mature sub-segment of neurostimulation examined. Due to the complexity of the brain, a wide variety of indications remain untapped, representing significant opportunity. Medtronic is soon to be joined by new entrants, which will grow this nascent market and help establish safety records for DBS treatments.

The potential size and current growth of neurostimulation markets makes them attractive in both the near and long term. While current products are relatively straightforward, advancements in remote patient monitoring, wireless technology, and microprocessor hardware may add complexity and utility to neurostimulatory products, enabling their development for more advanced indications.