vizient®

Spine and neuromodulation technologies

Technology Watch | 2018 Volume 2

Table of contents

Disclaimer: Members of the Vizient orthopedic staff attend clinical sessions at important orthopedic meetings throughout the year. The staff meets with suppliers, reviews new technologies and monitors data from pertinent clinical trials. The information is consolidated into this overview of product and practice trends in the various orthopedic segments. This document is intended to educate nonclinical hospital staff by offering them insights into new and innovative technologies. Vizient staff members have no personal financial connections with the suppliers and no conflicts of interest in the development of this document. The products presented are for educational purposes. Vizient does not endorse any of the products described in this document.

Introduction

The Vizient® Spine and Neuromodulation Technology Watch is intended to educate and provide insights into new and innovative technologies that support delivery of the highest-quality care. This issue highlights the latest products and technologies available in the market, as well as those in clinical trials and in development. The Technology Watch also includes pricing trends, describes the impact of new technologies to the economic market and provides information on the reimbursement landscape.

Market watch

The spine and neuromodulation markets are influenced by different factors, yet both remain dynamic. The spine market is characterized by moderately increasing procedural numbers fueled by the aging population, as well as low barriers to competitive entry. Spine suppliers are investing to complete their respective product offerings, expand their 3D additive manufacturing capacity and advance their implant designs, all while building competitive barriers in an attempt to slow decreasing pricing. The neuromodulation market is characterized by rapid growth and an expanding number of different applications. Suppliers in many clinical markets have limited competition, enabling pricing to increase. This report highlights the devices being developed in each market; statistics are shown below.

Spine market

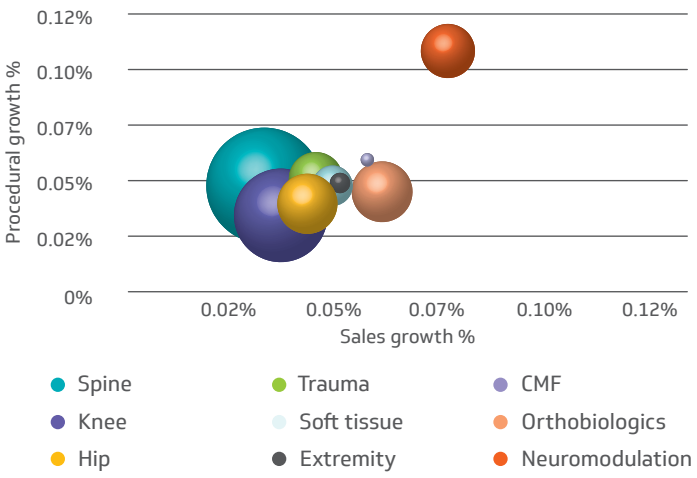
- Moderate 3 to 4% U.S. growth is forecast through the mid-2020s
- Outpatient surgery will reshape this market
- Key suppliers are expanding their product offerings to provide a full range of products
- Little innovative technology is forecasted, with narrowing product differentiation
- Hospitals are obtaining lower supply costs through supplier consolidation
- Robotic-assisted surgery is on the horizon
- 3D additive manufacturing is being widely adopted

Neuromodulation market

- U.S. market is growing at an estimated 8 to 9% annually
- Nine product indications, with limited supply choice in eight
- Magnetic resonance imaging (MRI)-conditional device options are emerging
- Price increases are occurring in all but pain management segments
- Nine new indications in development will accelerate hospital cost

Figure 1 shows the neuromodulation market outpacing various orthopedic and spine markets. Since companies invest research and development funds into growing markets, neuromodulation, extremity and small joint arthroplasty, and soft tissue products will see the greatest development in the next several years. The spine market will also see research and development funds invested in robotic-assisted surgery, 3D additive manufacturing and next-generation evolutionary devices. These strategies continue to enable suppliers to slow price erosion. Hospitals should continue to question higher prices on evolutionary devices for which there is no meaningful clinical evidence of improved patient benefit.

Figure 1. Neuromodulation market has surpassed orthopedic and spine markets



Source: Millennium Research, 2017.
Abbreviation: CMF = cranio-maxillofacial.

Economic watch

Price projections for lumbar and cervical spine products, as well as for neurostimulation generators, are shown in Table 1. The pricing trends reflect the change in price over the past 12 months comparing the average 2017 versus 2018 prices. Table 2 shows the current average market pricing by product segment. All prices listed include the average prices for that category of products, rather than sale prices for specific products. Individual hospital pricing may vary depending on considerations such as rebates, quality and volumes that are not included in these estimates.

Table 1. Changes in pricing trends over the last 12 months

Cervical spine products

Category	Change (%)
Pedicle screw system	↓ 1.8
Plating system	↓ 3.1
Minimally invasive surgery device	↓ 7.2
Artificial disc	↓ 0.2

Lumbar spine products

Category	Change (%)
Pedicle screw system	↓ 3.4
Plating system	↓ 1.9
Minimally invasive surgery device	↑ 6.4
Interspinous system	↑ 7.3
Artificial disc	↓ 6.6
Vertebral compression device	↓ 11.2

Neurostimulation generators

Category	Change (%)
Parkinson's disease	↑ 3.3
Chronic pain management	↓ 0.5
Epilepsy	↑ 10.3
Urologic	↑ 2.0

Source: Vizient Savings Actualyzer, 2018.

Table 2. Average prices for neuromodulation devices

Chronic pain management

Supplier	Average price
Abbott	$16,940
Boston Scientific	$17,930
Medtronic	$17,940
Nevro	$13,920
Nuvectra	$15,640

Epilepsy

Supplier	Average price
LivaNova	$25,420
NeuroPace	$25,970

Gastric stimulation

Supplier	Average price
Medtronic	$8,820

Parkinson's disease

Supplier	Average price
Abbott	$15,230
Medtronic	$13,770

Urologic

Supplier	Average price
Medtronic	$11,430

Source: Vizient Savings Actualyzer, 2018.

Economic impact of new technologies

The economic impact of new technologies remains complex, with variability based on the markets.

Spine market

The spine market will realize minimal significant cost increases, as no disruptive technology is forecast. One downside, however, is that robotic-assisted surgery systems can only be used with the supplier's implant(s); for example, the Stryker Mako robot can only be used with Stryker implants. This may result in reduced competition and increased implant prices. Other device enhancements will not have a significant cost impact. Any pricing changes can be managed through a hospital's established value analysis or new product review processes.

The increasing number of outpatient procedures is one economic variable affecting the spine market. As the number of procedures rapidly shifts from inpatient to outpatient, the economic impact will be felt by hospitals. Lower reimbursement rates will require hospitals to work more closely with their physicians to improve efficiencies. Although many hospitals are already well on their way to accomplishing this goal, others are struggling with this challenge.

Neuromodulation market

The economic impact of neurostimulation devices remains complex. Pressure arises because of tighter reimbursement — or a lack of reimbursement — for some indications. With a forecasted market growth in the double digits, the burden on hospitals and sustained margin pressures will increase. Most of the forecasted growth within the next several years will be due to device replacement procedures. While improved battery life and rechargeability will moderate the number of replacements in the longer term, hospitals must understand the financial impact of these procedures. Suppliers will continue to increase device prices in the movement disorders and deep brain segments, where minimal competition will strain hospital budgets. Split reimbursements between lead placement and generator placement exist in the chronic pain management segment, which causes additional complexity if procedures are being performed both inside and outside of the hospital. A single payment for both procedures may result in better control of provider margins and costs. Although device construction between neurostimulation and cardiac rhythm management devices is similar, neuromodulation generators are 67 percent more expensive according to Vizient Savings Actualyzer™ data from June 2017 to May 2018 ($13,500 versus $8,070 for neuromodulation and cardiac rhythm generators, respectively). Given the rapidly expanding indications and projected procedural growth, neuromodulation will continue to have an increasing economic impact on hospitals. Thus, hospitals must align with physicians to begin to control pricing.

Reimbursement landscape

Spine procedures

The 2019 inpatient and outpatient reimbursement rates for spine procedures are projected to increase modestly by 1.6 percent.[1] This increase depends on whether or not hospitals have met governmental reporting and outcomes measures. Other reimbursement changes are due to the shift to outpatient procedures and the potential bundled payment. The outpatient procedure reimbursement rate is much lower than that for inpatient procedures; reported differences between the two rates can be as high as 60 percent[2] if procedures shift to ambulatory surgery centers. The number of outpatient procedures is expected to grow as much as 20 percent[3] in 2019, which will cause hospitals to experience a real decrease in income. As the number of Centers for Medicare & Medicaid Services' (CMS) covered lives continues to grow and future spine reimbursement rates remain stagnant, the financial impact on hospitals will increase.

Bundled spine payments will also have an impact on reimbursement rates. While bundled payments for knee and hip joint arthroplasty have been delayed, data from other bundled procedures demonstrate that the concept works to both enhance patient outcomes and decrease procedural cost — a fact that has not gone unnoticed by the government. As health care costs continue to climb, the CMS will reintroduce bundled payments across a wide number of procedures, including orthopedic and spine.

Neuromodulation procedures

Current reimbursement rates for neurostimulation procedures vary by payer and therapy. For example, neurostimulation for chronic pain management is reimbursed, but neurostimulation for other indicated uses may not be. Strict "medically necessary" criteria require hospitals to coordinate patient care with the physician to ensure appropriate hospital reimbursement. For example, reimbursement exists for spinal cord stimulation, but the CMS concluded that coverage for treatment-resistant depression is not reasonable and necessary. In the longer term, the continued positive clinical data and changing health care environment point to expanding coverage at potentially lower reimbursement rates.

Neuromodulation implants are contraindicated for MRI scans, which many physicians do not consider when treating patients. In July 2018, the CMS approved the reimbursement of minimally invasive spine surgery (MIS) scans on patients with cardiac rhythm management implants. Although MRI scans on patients who have neuromodulation implants are not reimbursed, this approval opens the possibility of future reimbursement, especially since most major suppliers are now manufacturing MRI-safe devices.

Reimbursement rates for neuromodulation procedures are projected to remain relatively constant in 2019. Supply chain professionals should continue to be vigilant as the average neuromodulation generator costs remain well above 50 percent of the 2018 average Medicare reimbursement rate. The neuromodulation system type will dictate how much of a hospital's reimbursement will be used by the cost of the generator and lead. For example, based on reimbursement rates using diagnosis-related groups 029 and 040, Medicare Inpatient Prospective Payment System data and Savings Actualyzer cost information, spinal cord stimulating systems will compose 60.3 percent of inpatient reimbursement (68.5 percent of the total reimbursement), while Parkinson's and epilepsy systems will compose 111.0 percent of inpatient reimbursement. For some systems and indicated uses, reimbursement may not be available. Hospitals must be aware of these devices' growing impact on their overall margins.

Supplier watch

Mighty Oak Medical

Mighty Oak Medical is focused on developing and marketing spinal technologies. The company's mission is to improve surgical outcomes using a cost-effective, patient-centered approach. The company currently has one product: Firefly, a patient-specific, 3D-printed pedicle screw navigation guide system. Because the rate of misplaced screws reported in the literature may be as high as 15 percent,[4] and surgical robots are used in only about one in 20 spine procedures,[5] Mighty Oak is positioning its solution to lower misplaced screw implantation and bridge this gap.

Firefly technology

The Firefly pedicle screw navigation guide, which complements traditional pedicle screw surgical techniques, uses 3D printing to create guides for each vertebral level as well as a biocompatible bone model that replicates a patient's spine. The system features a suggested presurgical plan, as well as an autoclavable bone model, predetermined screw sizing, surgeon-approved preselected trajectories, an intraoperative digital plan, and 3D-printed patient-specific guides to mechanically constrain the drill and tap to follow the preselected trajectories. Knowing the screw size in advance enables physicians to select the appropriate screw without the need for probing and calculating screw size. Confirming the screw's fit on the autoclavable bone model prior to placement on a patient's anatomy helps surgeons gain tactile feedback on how the guide should feel when placed.

The single-use, scalable technology does not require an upfront capital expenditure. In addition, it does not require any fluoroscopy to place pedicle screws. A computed tomography (CT) scan can produce images with all the data needed to create patient-specific guides and exact

bone model replicas of a patient's spine, with the added benefit of a decreased radiation dose to the patient and none at all to the operating room staff and surgeon. The guides help surgeons drill, tap and place the pedicle screw in the correct trajectory and at the proper depth. Mighty Oak does not manufacture pedicle screws, which enables physicians to select any pedicle screw system. The company is collaborating with a strategic channel partner to explore pediatric applications.

In July 2018, the company received U.S. Food and Drug Administration (FDA) 510K clearance for the expanded indication of S2AI trajectory for sacral-iliac fixation in complex spinal reconstruction surgeries such as scoliosis. The precise mechanical guidance of patient-specific guides is ideal for the S2AI trajectory, since it is a challenging trajectory that crosses the sacral-iliac joint. Like many emerging technologies, Firefly is not separately reimbursed. The added cost must be considered when reviewing its use; however, its ability to reduce the high rate of misplaced screws will improve outcomes and potentially offset its cost.

Technology watch

Spine market

The U.S. spinal device market continues its slow, steady growth. *Becker's Spine Review* estimates its value at over $5 billion, with a projected value of $7 billion by the end of 2020.[6] Experts project the overall market compound annual growth rate will range from 3 to 4 percent through the mid-2020s.[7,8] More importantly, the shift from inpatient to outpatient spine procedures will dramatically impact this market.

The Sg2® 2017 Impact of Change® report estimates outpatient procedures overall will significantly increase. Over the past 10 years, increases in outpatient procedures have occurred in the orthopedic area (Table 3).

The outpatient procedure trend is anticipated to continue as the CMS opens reimbursement of an increasing number of outpatient procedures. Sg2 estimates the growth in outpatient spine procedures to be 6 percent through 2021, while inpatient procedures are projected to remain flat.[9] In addition, outpatient procedures will compose a third of total orthopedic and spine procedures by 2021. Future changes in reimbursement — including bundled payments — may drive an even faster shift to outpatient procedures.

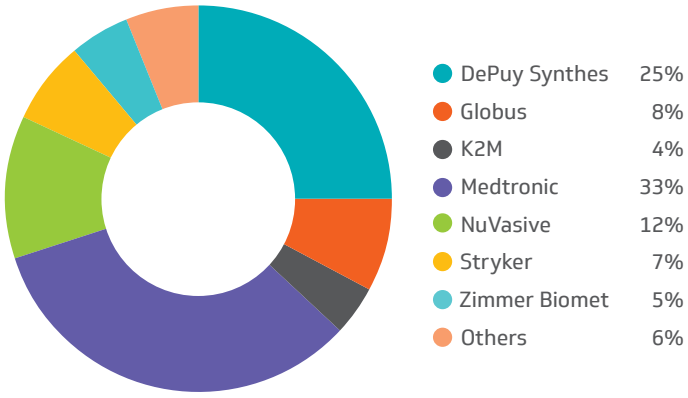
The ease of market entry, growing market size and device similarity continue to fuel over 200 suppliers within the spine market. However, recent Vizient Savings Actualyzer data indicate that five suppliers control an estimated 85 percent of the market (Figure 2).

Table 3. 10-year growth for outpatient orthopedic and spine procedures

Supplier	10-year change (%)	2017 volumes
Primary shoulder replacement	879	11,425
Primary knee replacement	797	73,063
Primary hip replacement	624	47,970
Lumbar/thoracic spinal fusion	225	31,575
Motion preservation procedures	189	12,158
Partial knee replacement	129	88,781
Cervical spinal fusion	111	98,222
Primary ankle replacement	98	1,962
Spinal decompression/ laminectomy	41	475,998
Revision spinal procedure	38	10,226

Sources: Sg2 Impact of Change forecast, 2017; OptumInsight report, 2015; CMS limited data sets: carrier, denominator, home health agency, hospice, outpatient and skilled nursing facility, 2015; Claritas Pop-Facts, 2017.

Figure 2. 2017 U.S. spine market share



Source: Vizient Savings Actualyzer, July 2018.

Procurement trends indicate that an increasing number of hospitals are standardizing the number of suppliers they contract with, resulting in reduced cost. Instead of waiting for the government to implement change, many hospitals are proactively developing spine bundled programs and outpatient ambulatory surgery center strategies. These new spine strategies and continued competition for market share will create additional pressure on device pricing.

Spine device development continues to evolve, although no revolutionary spine devices with the ability to significantly impact patient care are on the horizon. Basic device design will continue to evolve using various coatings, material combinations and manufacturing processes. These changes will provide some suppliers with a competitive advantage; however, with minimal clinical data demonstrating long-term patient benefit, pricing pressure will continue to influence device design. Currently, all the major spine suppliers are expanding their product portfolios to provide broad, complete offerings. Whether through acquisition or product development, the dominant spine suppliers are positioning themselves to compete in a spine market that aims to minimize suppliers. One trend that will have a long-term impact on the market is the increasing use of robotic-assisted surgery. The success larger suppliers have experienced in the total joints market will continue to influence the spine market. Other trends include using 3D additive manufacturing and the U.S. FDA's increased oversight of some biologic products.

Robotic-assisted surgery

The use of robotic-assisted surgery systems in spinal procedures is evolving, fueled by prospective, randomized trials that compared robot-assisted pedicle screw placement to conventional fluoroscopic guided placement; results of these trials indicated more accurate screw placement in the conventional group.[10-12] Even preliminary data from ongoing clinical trials continue to support the positive patient benefit of using robotic-assisted spine surgery. Market experts predict the use of robotic-assisted procedures will grow rapidly within the next several years. For example, based on Stryker's experience using robotic-assisted joint arthroplasty surgery to improve outcomes and protect market share, Medtronic and Zimmer Biomet have entered the market with acquisitions of robotic technologies.

Devices in market

Rosa spine system (Zimmer Biomet)

The Rosa spine system is designed for various neurological procedures. It is intended for the spatial positioning and orientation of instrument holders or tool guides, and can be used by neurosurgeons to guide standard neurosurgical instruments during spine surgery. Guidance is based on an intraoperative plan developed with 3D imaging software, provided that the required fiducial markers and rigid patient anatomy can be identified on 3D CT scans. The system, which is indicated for the placement of pedicle screws in lumbar vertebrae with a posterior approach, received U.S. FDA clearance for spine surgery in 2016. Zimmer Biomet anticipates a full launch of the system in late 2018.

ExcelsiusGPS robotic trajectory guidance and navigation (Globus Medical)

ExcelsiusGPS is a robotic system that combines surgical navigation and robotic guidance for spinal surgery. The technology supports minimally invasive and open orthopedic and neurosurgical procedures, with screw placement applications in spine and orthopedic surgery. The system seamlessly integrates the company's current implants and instruments, and is compatible with preoperative CT, intraoperative CT and fluoroscopic imaging modalities. The system — designed to minimize radiation exposure, streamline workflow and reproducibly assist in implant placement — received U.S. FDA clearance in August 2017.

Mazor X robotic guidance system (Medtronic plc)

Mazor Robotics was acquired by Medtronic to enter the spine robotic-assisted surgical market. Its surgical platforms are mounted directly to patients' bones and use 3D modeling to place surgical instruments that are then controlled by surgeons. The system's robotic elements improve accuracy and reduce the amount of radiation used to visualize the space when surgeons operate without the automated assistance. The Mazor X platform includes preoperative analytics to help surgeons plan their operation, intraoperative guidance with robotically placed tools, real-time 3D verification through proprietary fluoroscopy-based technology and connectivity features. The Mazor X system received U.S. FDA clearance in 2016.

Devices in clinical trials

MIS ReFRESH: Robotic vs. Freehand Minimally Invasive Spinal Surgeries (NCT02057744)

Study size: 2,000 patients

Observational, partially randomized, controlled, multicenter U.S. study

This study was designed to quantify potential short- and long-term benefits of robotic-assisted MIS for adult patients with lower back degeneration by comparing a matching group of control patients whose procedures were performed using a minimally invasive approach (i.e., freehand or with image guidance or navigation techniques). Preliminary six-month study data presented on 379 patients enrolled in the study (287 in the robotic-guided arm and 92 in the fluoroscopy-guided control arm) demonstrated the following:

- Relative risk for an adverse event or complication was 5.3 times higher in the fluoroscopy-guided control arm compared to the robotic-guided arm ($P < .001$).
- Relative risk for revision surgery was 7.1 times higher for a fluoroscopy-guided surgery compared to the robotic-guided cases ($P = .012$).
- A total of 78% less fluoroscopy was used in the fluoroscopy-guided control arm compared to the robotic-guided arm.

Devices in development

Mako robotic-arm assisted surgery (Stryker)

Stryker has focused its development and commercialization efforts toward the joint arthroplasty market. Its Mako total knee replacement system combines robotic technology with the company's total knee implant, solidifying Stryker's competitive barrier in this segment. The system's flexibility lends itself to spine applications. Market analysts believe an announcement on a spine system will be announced soon, which could help the company's spine market position. The device is not available commercially or for distribution or sale.

Orthotaxy robot-assisted orthopedic surgery (DePuy Synthes)

Johnson & Johnson purchased this French company, which develops robot-assisted orthopedic surgery solutions. Currently, its primary development efforts are focused on joint arthroplasty applications. Like other robot-assisted surgery systems, this system may be expanded for spine applications. The device is currently investigational and is not available commercially or for distribution.

DLR Miro robot-assisted system (Institute of Robotics and Mechatronics)

The DLR Miro is a second-generation robot arm for surgical applications, and features a low system weight and dimensions similar to those of a human arm. The system can help surgeons at the operating table, where space is scarce. The possible applications of this robot arm range from guiding a laser unit for precise cutting of bones in orthopedics to setting pedicle screws and performing minimally invasive surgery. The system is being developed for sale or license to a company that is looking to enter the robotic-assisted surgery market. The device is currently investigational and is not available commercially or for distribution or sale.

Phecda robotic system (Tinavi Medical Solutions)

Tinavi is a Chinese company that develops robotic-assisted surgery systems for orthopedics. The company is backed by China's Ministry of Science and Technology, the Beijing government and the Chinese Academy of Sciences. In 2010, it was the first Chinese company to be awarded the China Food and Drug Administration (CFDA) permit to manufacture its first-generation orthopedic robot. These orthopedic robots have been installed in more than 10 Chinese hospitals, and have been used to complete approximately 2,000 surgeries. Its newest medical robot, Phecda (designed for minimally invasive spinal surgeries) is still pending CFDA approval. The spine system is currently investigational and is not available commercially or for distribution or sale in the U.S.

3D additive manufacturing

3D additive manufacturing (3D printing) is innovative, and has advanced significantly from the first 3D-printed spine implant produced by 4Web Medical in 2011. 3D printing is a process that creates a three-dimensional object by building successive layers of raw material. Each new layer is attached to the previous one until the object is complete. This manufacturing technique creates structures that traditional manufacturing cannot produce. The process

works by combining the raw metal material in a powder form with high-energy welding. In the case of spinal devices, the devices are "grown" using multiple layers of material. Titanium powder is selectively applied to the growing device and high-energy laser beams weld each successive layer. The manufacturing technique produces porous implants and novel surface textures that encourage better tissue in-growth and improved patient outcomes. 3D printers are expensive, providing a competitive advantage to larger spine suppliers, but smaller companies are also investing in these printers. Stryker — the leader in the use of 3D additive manufacturing for orthopedic and spine product production — introduced its first spinal implant in 2016. Johnson & Johnson is also investing in the process, inking a partnership deal with GE to advance research, products and process. Smaller companies such as 4Web Medical are also embracing and developing innovative 3D-printed spinal implants.

The use of 3D printing not only improves manufacturing efficiency, it also offers expanded options to create customized implants that achieve more favorable clinical outcomes. Several manufactures have introduced customized spinal products, including Mighty Oak Medical, a finalist in the Vizient Innovative Technology competition in 2017. However, there are limitations to the increased use of customized spinal implants, including:

- Cost — The cost to manufacture a patient-specific implant is higher than one that is mass-produced.
- Improved outcomes — The nature of customized implants prevents them from being clinically proven to provide better patient and economic outcomes.
- Time — Consulting with patients about implant measurements, as well as designing, manufacturing and sterilizing customized implants, takes time. It will shorten as efficiencies are realized but will never match an off-the-shelf implant.
- Regulatory issues — The U.S.FDA has not established a process to manage and clear customized patient-specific spinal implants.
- Reimbursement — Payers have been reluctant to reimburse for expensive spine implants (e.g., artificial discs). The inability to demonstrate improved outcomes — as well as the potential for increased procedural costs — may delay payers approving these types of devices.

In spite of these limitations, the use of 3D printing to manufacture medical devices is being rapidly adopted in the orthopedic and spine markets. In particular, the customization of spine implants will continue to evolve and increasingly become an option.

Devices in market

Firefly S2AI pedicle screw navigation guide (Mighty Oak Medical)

The Firefly pedicle screw navigation guide is a patient-customized system that combines safe and accurate screw placement with reduced fluoroscopy use. The system features presurgical planning by trained engineers; an autoclavable bone model; predetermined screw sizing; surgeon-approved preselected trajectories; an intraoperative digital plan; and 3D-printed, patient-specific guides to mechanically constrain the drill and tap to follow the preselected trajectories. The system features an open platform and is compatible with all pedicle screw systems. The expanded indication — which includes S2AI trajectory for sacral-iliac fixation in complex spinal reconstruction surgeries such as scoliosis — received U.S. FDA clearance in June 2018.

Capri small 3D static corpectomy cage system (K2M Group)

The Capri is a 3D-printed expandable corpectomy cage with cervical indications. The spine implant provides a surgical solution for stabilizing the thoracolumbar spine (T1 to L5) in cases of vertebral body resections resulting from trauma or tumor. Its porous structure and rough surface are designed to allow bony integration throughout an implant. The system's lordotic options help support the anterior spinal column, which helps to achieve sagittal balance. It was the first-to-market, 3D-printed corpectomy cage to receive U.S. FDA clearance, which was granted in June 2017.

UNiD spinal cages (Medicrea Group)

The UNiD spinal cage is the first patient-specific cage approved in the U.S. The company specializes in patient-specific spine implant devices, and the new implant will be added to its existing breadth of patient-specific implants delivered just in time for surgery. It digitally designs 3D-printed titanium devices using its proprietary predictive analytics model to develop an implant that fits with a patient's natural anatomy. It was the first-to-market, 3D-printed patient-specific spinal cage to receive U.S. FDA clearance, which was granted in May 2018.

Fortilink-TS and -L IBF systems (RTI Surgical)

Fortilink-TS and –L are the newest additions to a growing series of interbody fusion devices. The implants are the company's first 3D-printed polymer-based interbody fusion devices to use a proprietary technology that incorporates a nano-rough surface that has demonstrated more notable trabecular bone ingrowth compared to polyether ether ketone (PEEK) and titanium-coated PEEK. The implants are

intended for use in lumbar interbody fusion procedures at one or two adjoining levels in patients with degenerative disc disease. They received U.S. FDA clearance in May 2018.

ARTiC-L spinal system (Medtronic)

The ARTiC-L implant is made of titanium, and is designed for use in transforaminal lumbar interbody fusion spine surgery. The implant's 3D-printed honeycomb design acts as an osteoconductive scaffold for bony growth into the implant, and the structure also provides improved mechanical load distribution. The implant is the first to be developed with the company's TiONIC technology, and is designed to facilitate sagittal alignment of the spine by offering various lordotic angles up to 20°. The device received U.S. FDA clearance in May 2018.

Zyston strut open titanium interbody spacer system (Zimmer Biomet)

The Zyston strut open titanium interbody spacer system is a series of lumbar cages that are designed to enhance the strength, graft capacity and visualization of the interbody spacer in spinal fusion cases. They are available in multiple sizes to account for the wide variation in human anatomy as well as in surgical approaches, and include surgical instruments for inserting, manipulating and removing implants. This system is the company's first titanium spinal implant manufactured via a 3D printing process; it received U.S. FDA clearance in May 2018.

Tritanium TL curved posterior lumbar cage (Stryker)

The Tritanium TL curved posterior lumbar cage has open central graft windows that help reduce stiffness, aid in visualization of fusion and enable bone graft containment. It's shaped for steerability, with teeth designed for multidirectional fixation so surgeons can steer and rotate the cage to their desired placement. The teeth are also designed to maximize surface area for endplate contact with the implant. The cage has a smooth, tapered leading edge for insertion into the intervertebral space and a central column that spans endplate to endplate for structural integrity. The implant is indicated for use with autograft and allogenic bone graft comprising cancellous or corticocancellous bone graft when used as an adjunct to fusion in patients with degenerative disc disease at one level or two contiguous levels from L2 to S1. It should be implanted via a posterior approach. The device received U.S. FDA clearance in March 2018.

EIT cellular titanium cervical cage (Emerging Implant Technologies GmbH)

EIT is focused on creating 3D-printed titanium implants for spinal applications. Its 3D-printed porous titanium cervical cage was designed with an ideal pore shape and size to optimize cell proliferation and bone ingrowth. The anatomical design of the EIT cervical cage addresses the surgical and biomechanical challenges of cervical multilevel fusion by providing maximized vertebral endplate contact and sagittal balance restoration. The implant is indicated for multiple contiguous cervical levels (C2 to T1), and is one of very few cervical cages approved for multilevel use. The device received U.S. FDA clearance in January 2018.

Devices in development

EIT cellular titanium PLIF cage (Emerging Implant Technologies GmbH)

The EIT PLIF cage is a 3D-printed fully adjustable interbody fusion cage. It is printed as one piece with no assembly needed during the production process. This reduces cost significantly compared to regular expandable cages that are manufactured with traditional machining processes. The adjustable cage allows for restoration of lordosis angles up to 18° and supports minimally invasive insertion techniques. The bone contact areas are composed of cellular titanium, a porous structure that enhances primary stability and bony integration. The goal is to reduce intraoperative trauma, optimize size adaptation and improve restoration of sagittal balance to improve fusion rates, and reduce subsidence and adjacent segment disease related to insufficient sagittal balance restoration. The cage is the first of its kind and received Conformité Européene mark approval in February 2018. The implant is currently investigational and is not available for distribution or sale in the U.S.

Other spine products

iFuse implant system (SI-BONE)

The minimally invasive iFuse implant system is designed to treat conditions such as sacroiliac joint dysfunction, which is a direct result of sacroiliac joint disruption and degenerative sacroiliitis. The system consists of cannulated triangular titanium (Ti-6Al4V-ELI) implants that have a porous surface and an instrument system. The implant surface and shape are designed to prevent rotation and motion of the sacroiliac joint. Although the system has been available since 2009, recently published data has resulted in payers such as Blue Cross Blue Shield Association raising its clinical evidence rating for the minimally invasive procedure. The company also launched a warranty program for iFuse to guarantee procedural success.

Long-Term Outcomes from INSITE/SIFI (NCT02270203)

Principle investigator: sponsored by SI-Bone

Study size: 57 patients

Prospective, randomized, open-label, controlled, multicenter U.S. study

The objective of this study was to report clinical and functional outcomes of sacroiliac joint fusion using triangular titanium implants in the treatment of chronic sacroiliac joint dysfunction due to degenerative sacroiliitis or sacroiliac joint disruption at three years postoperatively. Study results show that clinically significant improvements for patients were sustained at three years. There were no reported adverse events related to the study device or procedure in the extended follow-up period. Three-year follow-up was 93 percent. Mean preoperative sacroiliac joint pain was 81.5 (0 to 100 on the Visual Analogue Scale for pain), which decreased to 26.2 at three years, a 55-point improvement. The mean preoperative Oswestry Disability Index was 56.3, which decreased to 28.2 at three years, a 28.1-point improvement.

Spine precision partnership (Nuvasive and Siemens Healthineers)

Nuvasive and Siemens Healthineers have joined forces to advance their proprietary technologies and create solutions that improve operating room workflow efficiency and increase precision in the delivery of minimally disruptive spine surgery technologies. The partnership will work to integrate Nuvasive's Pulse surgical platform with Siemens' Cios Spin mobile 3D imaging system. The Siemens Cios Spin is pending 510(k) clearance, and is not yet commercially available in the U.S.

ReVeal anterior cervical plating system (ReVivo Medical)

The ReVeal anterior cervical plating system uses elastic micromotion to produce an elastically deformable plate that facilitates controlled continuous load-sharing with the interbody space. The deformable plate design is analogous to a serpentine spring, with double struts supporting each transverse member of the spring. The transverse members and struts stabilize the motion segment, which facilitates interbody fusion and promotes a favorable load-sharing environment with the interbody space through the entire range of physiological motion. The elastically deformable plates are fabricated from titanium alloy (Ti-6Al-4V) using traditional manufacturing methodology. The implant is investigational, and is not available for sale.

M6 artificial disc (Orthofix)

In March 2018, Orthofix acquired Spinal Kinetics and the M6 artificial disc replacement technology. The M6 discs are designed to mimic natural disc anatomy with an artificial viscoelastic nucleus and fibrous annulus. Discs are made from polycarbonate urethane, and have a woven fiber annulus made from polyethylene and titanium outer plates with kneels to anchor them to bone. M6 aims to give patients a more natural range of motion while providing long-term stability in the spine. The implant is investigational and is not available for sale in the U.S.

Simplify Disc (Simplify Medical)

The Simplify Disc is an artificial cervical disc indicated for one-level cervical implantation between C3 and C7. Composed of primarily nonmetal materials such as PEEK-on-ceramic, the disc design is considered MRI-conditional, and can be viewed on MRI with minimal artifacts. With minimal metal articulating components, it is designed for longer durability. A lower profile device design also improves implantation and expands the range of patients who can receive the device. The company completed its U.S. clinical trial for FDA premarket approval in February 2018. The implant is investigational and is not available for sale in the U.S.

DTRAX spinal system (Providence Medical Technology)

The DTRAX spinal system comprises several specialized single-use instruments, including a facet joint access instrument, lateral mass decortication trephine, mallet, cannula, decortication rasp, decortication burr and bone graft tamp. The system is indicated for use in posterior cervical fusion in patients with cervical degenerative disc disease. These instruments enable surgeons to access the posterior cervical spine by decorticating the bony surfaces of the posterior lateral mass and articular surfaces of the facet joints. The instruments can then be used to apply autograft or allograft bone. The largest instrument is less than 1 cm in diameter, enabling it to be used in a variety of minimally invasive procedures. The system received U.S. FDA clearance in May 2018.

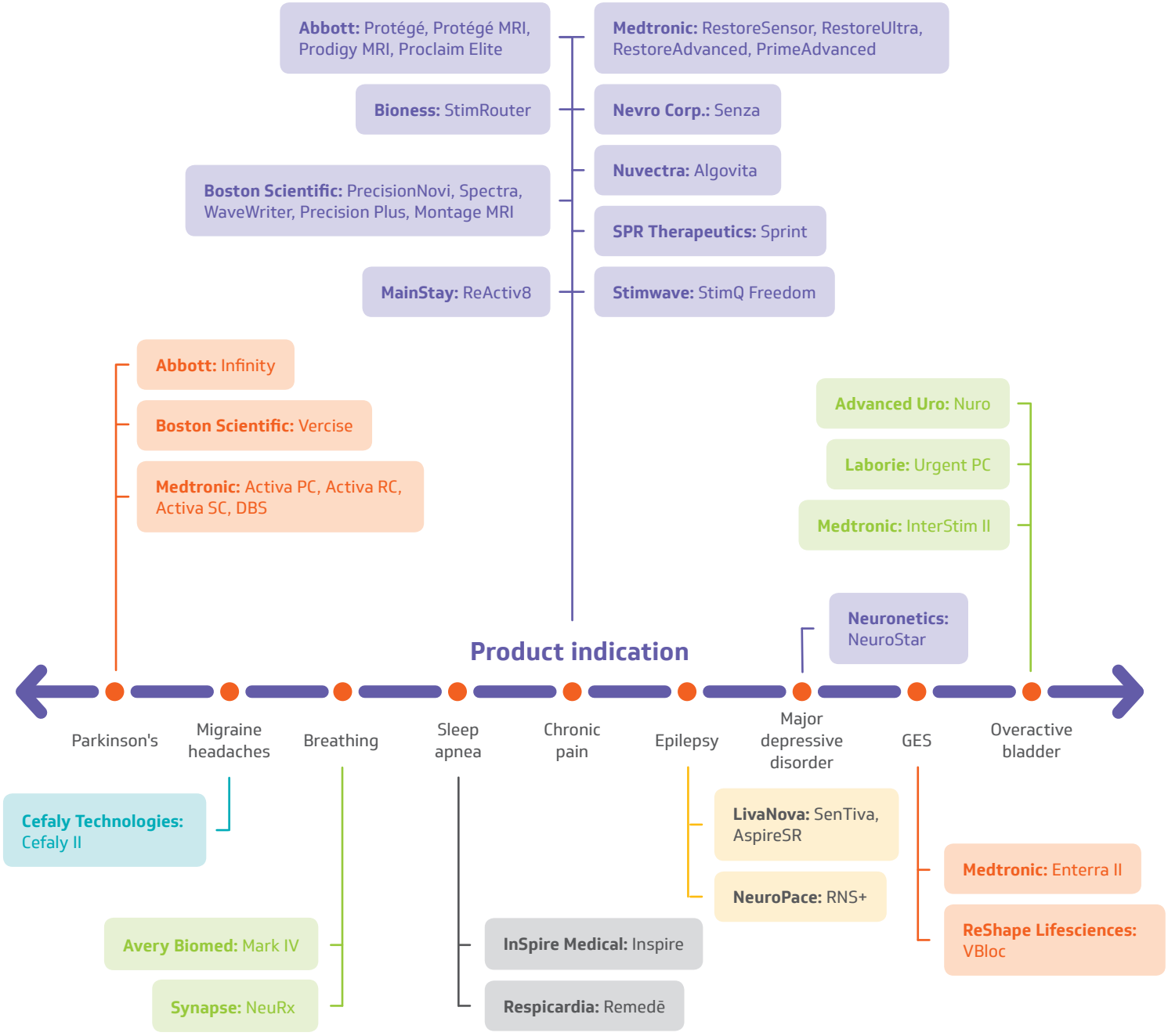
Magec X system (Nuvasive)

Magec X features updates across all rod diameters in the Magec portfolio, including 5.0-mm diameter rods for patients, delivering a 68 percent performance increase over the previous generation of titanium rod fatigue testing. The system can be paired with the Reline small stature system, a pediatric deformity fixation solution that integrates both 4.5-mm and 5.0-mm rods. The system enables the physician to upsize rods with low-profile screws, providing flexibility at the time of surgery without having to change the screws. The internal rod mechanism of the previous product generation has been redesigned with a robust actuator seal, a reinforced locking pin and anti-jam protection. The new design's aesthetic improvements provide visual indicators for cutting and implanting the rod. The system is being launched with the Embracing the Journey Together Program, which features a limited warranty on Magec X rods when used with cleared NuVasive procedural solutions. The system and program were launched in the U.S. in May 2018.

Neuromodulation market

The neuromodulation market continues its rapid growth and new indication expansion. Since our last report in 2016, the U.S. FDA has approved a number of new neuromodulation devices, primarily for pain reduction (Figure 3). In addition, a number of new indications — such as MRI use, battery rechargeablility and smaller generators — have been approved and are now available for conditions such as obesity, sleep apnea and heart failure. The number of suppliers has also increased.

Figure 3. Vendor products by FDA-approved indication



Source: Data were derived from supplier websites, investor reports, meeting information and news articles, 2017-2018.
Abbreviations: DBS = deep brain stimulation; FDA = U.S. Food and Drug Administration; MRI = magnetic resonance imaging; GES = gastric electrical stimulation.

Neuromodulation uses an implantable generator to apply low-level energy to the nervous system to block nerve signals. Neurostimulator systems typically consist of three implantable components (the extension, lead and power source) and two external components (the control magnet and a handheld programmer). The extension is used to connect the lead to the power source, and the lead is used to deliver the electrical stimulation to the targeted nerve(s).

Using electrical stimulation to produce specific nerve activity has led to the development of new therapies to treat human conditions. As each new indication proves itself, researchers look to use neurostimulation to treat even more. The FDA has approved the use of neurostimulation therapies to target various nerves and indications (Figure 4).

Figure 4. Indications that can be treated using neurostimulation

- **Deep brain stimulation:** Parkinson's, essential tremor, epilepsy, certain psychiatric disorders
- **Sacral nerve stimulation:** Overactive bladder, bowel control
- **Spinal cord stimulation:** Chronic pain management
- **Upper airway stimulation:** Sleep apnea
- **Vagal nerve stimulation:** Epilepsy, obesity

Source: Vizient internal data, 2016-2018.

In addition, ongoing product development and clinical trials are exploring the potential of the technology to treat more indications (Figure 5).

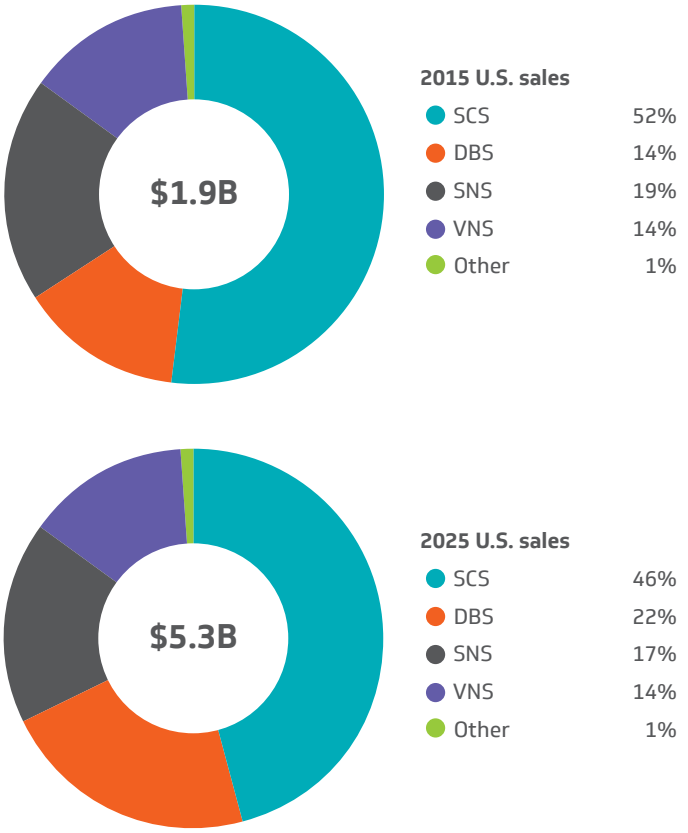
Figure 5. New indications that may be treated using neurostimulation

- **New indications:** Alzheimer's, heart failure, stroke recovery, diabetic neuropathy, migraine headaches, refractory angina relief, hypertension, chronic respiratory insufficiency, gastrointestinal disorders

Source: Vizient internal data, 2016-2018.

Neurostimulation is being used in a growing number of procedures. Recent market estimates from Millennium Research project that the compounded annual growth rate will hold at 10.3 percent through 2025.[6] The market is being fueled by increasing device implantation, replacement and pricing. In addition, earlier generation devices that used single-use batteries are now being replaced; thus, by the end of the forecast period, half of the devices being implanted will be replacements. Vizient data indicate the average selling pricing has been mixed, with an overall increase of 5.4 percent over the past two years.[13] This trend will continue driving the U.S. neuromodulation market toward $5.3 billion by 2025 (Figure 6).[14]

Figure 6. Neuromodulation market growth rate



Source: Vizient Savings Actualyzer, July 2018.
Abbreviations: DBS = deep brain stimulation; SCS = spinal cord stimulation; SNS = sacral nerve stimulation; VNS = vagus nerve stimulation.

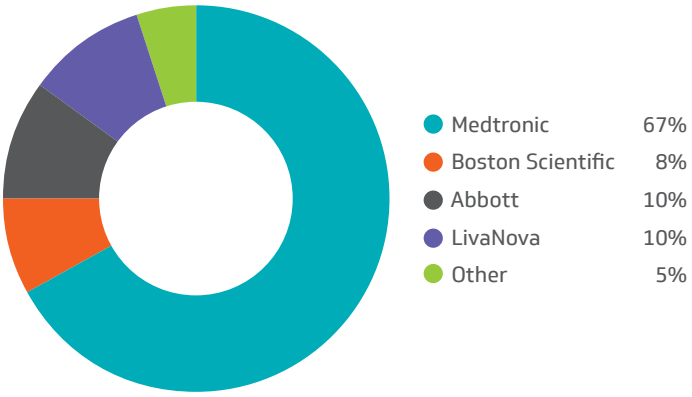
The market is being driven by an underserved patient population, expanded device indications and improved reimbursement. Over half of the U.S. population has conditions that make them ideal candidates for a neurostimulation device. The prevalence of these conditions is shown in Table 4.

Table 4. Number of individuals that are candidates for neurostimulation based on health conditions (U.S.)

Condition	U.S. incidence
Obesity	93 million[15]
Chronic pain	50 million[16]
Migraine headache	39 million[17]
Major depression	16.1 million[18]
Involuntary tremor	5 million[19]
Epilepsy	3.0 million[20]
Parkinson's	1.0 million[21]

The market remains supplier dominated, with their ability to control implant selection due to the lack of competition within the various subcategories (Figure 7). For years, only one company offered a device for a specific clinical indication, resulting in a lack of choice for the physician. The chronic pain management segment has experienced the largest growth in the number of suppliers, resulting in both limited market dominance by a single supplier and slower price escalation. In all segments of the neurostimulation market, sales representatives still exert influence regarding clinical decision-making and device selection.

Figure 7. Neurostimulation market by supplier



Source: Vizient Savings Actualyzer, July 2018.

While the neuromodulation market is divided by its various clinically approved uses, the chronic pain management segment dominates the others. It appears that the delay in being able to introduce new devices has resulted in both Boston Scientific and Abbott losing market share. Medtronic is the overall market leader due to its strong position in multiple segments.

During the past 18 months, one product feature has become available that may influence the use of neuromodulation: MRI-conditional designation. Up until recently, a patient with a neuromodulation device could not receive an MRI scan. Today, the MRI-conditional devices provide patients with increased options. All major suppliers have incorporated MRI-conditional capabilities into their devices, which may force smaller suppliers to develop next-generation systems or exit the market entirely.

Devices recently approved by the FDA

A number of new devices were approved in late 2016 and 2017. Although device approvals have slowed, suppliers continue to develop new devices and the pipeline is rich. The following new neurostimulation systems have been approved by the FDA.

Spectra WaveWriter spinal cord stimulator system (Boston Scientific Corporation)

The Spectra WaveWriter spinal cord stimulation system is the latest offering in Boston Scientific's family of chronic pain management devices. The system integrates multiple therapies into a single device so that treatment can be provided for both paresthesia-based and sub-perception therapy. Paresthesia-based therapy provides pain relief with a light tingling sensation, while sub-perception therapy works without that sensation. The device received FDA approval in January 2018.

Evaluation of Spinal Cord Stimulation Pulse Rate On Clinical Outcomes (PROCO) (NCT02549183)

Simon Thomson (U.K., Basildon University Hospitals [Orsett]), principle investigator

Study size: 22 patients

Prospective, randomized, multicenter, double-blinded, U.K. trial

The PROCO study was a multicenter, prospective, double-blind, randomized study in which patients acted as their own control. This study established that, in de novo patients, similar pain relief and improvement in quality of life measures can be achieved regardless of the type of frequency (from 1 kHz up to 10 kHz) used in sub-perception spinal cord stimulation therapy when the proper target and dose are identified.

Medtronic deep brain stimulation system (Medtronic plc)

The Medtronic deep brain stimulation (DBS) system has been approved in the U.S. since 1997. The new indication expands the device use to include bilateral anterior thalamic nucleus stimulation in patients with epilepsy. The system is indicated for use in patients who averaged six or more seizures per month over the three most recent months (with no more than 30 days between seizures). The FDA approved the expanded indication in March 2018.

Stimulation of the Anterior Nucleus of the Thalamus in Epilepsy (SANTE) (NCT00101933)

Robert Fisher (U.S., Stanford Medical Center [Palo Alto]), co-principle investigator (member)

Study size: 110 patients

Prospective, randomized, multicenter, double-blinded, U.S. trial

The seven-year follow-up of the SANTE trial provided the clinical data needed to expand the indication of the Medtronic device. The clinical trial was a prospective, randomized, double-blind pivotal study that evaluated the use of DBS therapy for patients with medically refractory epilepsy with partial-onset seizures — with or without secondary generalization — that were drug-resistant to three or more antiepileptic medications. Patients in the active group received neurostimulation and were monitored for a reduction in seizure rates compared to patients in the control group, who did not receive neurostimulation during the three-month double-blind phase. After the double-blind phase, all patients received neurostimulation. The study showed the median total seizure frequency reduction from baseline was 40.4 percent versus 14.5 percent for the placebo group at three months, and 75 percent at seven years. Seizure severity and quality of life scales both showed statistically significant improvements from baseline at year seven. No significant cognitive declines or worsening of depression scores were observed through the blinded phase or at year seven.

Vercise DBS system (Boston Scientific Corporation)

The Vercise DBS system is indicated for the treatment of tremor, including essential tremor, the most common form of this movement disorder. Tremor is characterized by involuntary and rhythmic shaking, and is usually associated with difficulty performing activities such as writing or holding and controlling items. The system uses a rechargeable 25-year battery and features independent stimulus control, which enables clinicians to direct stimulation precisely to a neural target to help minimize unwanted side effects. The device is investigational in the U.S. and is currently being evaluated in the DBS for the Treatment of Parkinson's Disease (INTREPID) study. The device received U.S. FDA approval in December 2017.

Remedē sleep apnea system (Respicardia, Inc.)

The Remedē transvenous implantable neurostimulation system stimulates the phrenic nerve, and engages the diaphragm to restore natural breathing during sleep in patients with central sleep apnea. The device worked in only about half of study subjects. Patients with obstructive sleep apnea, active infections or who need MRI scans cannot use the system. The system received U.S. FDA approval in October 2017.

Stimulation of the Anterior Nucleus of the Thalamus in Epilepsy (SANTE) (NCT01816776)

Maria Rosa Costanzo (U.S., Edward Hospital [Naperville, Illinois]), principle investigator

Study size: 151 patients

Prospective, 1:1 randomized, open-label, multicenter, worldwide trial

The Remedē system pivotal trial evaluated the safety and effectiveness of transvenous phrenic nerve stimulation in patients with moderate to severe central sleep apnea. The primary effectiveness outcome was a comparison of the proportion of patients in the treatment versus control groups achieving a reduction in apnea-hypopnea index (AHI) of 50 percent or greater from baseline to six months. The trial met its primary endpoint for efficacy. In the modified intention-to-treat population, significantly more patients in the treatment group achieved 50 percent or greater reduction in AHI from baseline to six months than those in the control group, with a clinically meaningful difference of 41 percent ($P < .0001$). Additionally, the "12-month freedom from serious adverse events related to the implant procedure, system or delivered therapy" was 91 percent.

SenTiva vagus nerve stimulation system (LivaNova plc)

The SenTiva is a next-generation vagus nerve stimulation (VNS) system for the treatment of patients with drug-resistant epilepsy. The device is smaller than the prior generation ASPIRA system, and an enhanced programming system features a wireless wand and new user interface on a small tablet. Together, the components offer patients with drug-resistant epilepsy a physician-directed customizable therapy with smart technology. The device received U.S. FDA approval in October 2017.

GammaCore vagus nerve stimulator (ElectroCore LLC)

The GammaCore is a noninvasive VNS therapy for the treatment of primary headaches (migraine and cluster). The device noninvasively stimulates the cervical branch of the vagus nerve. A sham-controlled pilot study on noninvasive VNS — published in *Neurology* in August 2016 — reported that the therapy can reduce the number of headache days per month for chronic migraine patients. The company, which is partially funded by Merck, guarantees the device with a full refund should the therapy not work. The device was U.S. FDA cleared in April 2017.

TrueTear intranasal tear neurostimulator (Allergan)

The TrueTear system stimulates the lacrimal gland to produce tears with a two-pronged probe inserted in the nostril. It provides a temporary increase in tear production during neurostimulation in adults. The device uses a reusable base unit, which produces electrical stimulation. Disposable tip inserts contain hydrogel, which provides the contact for conducting the stimulation current into the nasal cavity and to the target intranasal tissue. The tips should be replaced every 48 hours, and the base unit should be recharged every 48 hours. The system was granted U.S. FDA clearance in February 2017.

Products in development

The clinical evidence supporting the use of neurostimulation to treat multiple conditions and the rapid market growth is driving greater product investment and development. Many companies new to the neuromodulation market are investigating the use of the technology to treat a range of disorders, including obesity, depression, leg pain, treatment-resistant hypertension, sexual dysfunction, urinary tract disorders, heart failure and drug addiction.

Movement disorders

TNM caloric vestibular stimulation system (Scion Neurostim, LLC)

Scion Neurostim is developing a system to prevent episodic migraine headaches using caloric vestibular stimulation. The device alternately heats and cools the inside of the ear canal by delivering thermal currents that activate balance-related organs in the inner ear. The hypothesis is that these organs in turn affect activity in the brainstem, which is associated with the onset of migraines. This early-stage product successfully completed its first-in-human clinical trial, which found the system to be clinically efficacious and highly tolerable adjuvant therapy for the prevention of episodic migraine. An additional clinical study is underway. The device is investigational and is not available for use or sale.

directSTIM directional DBS system (Aleva Neurotherapeutics)

Aleva and Nuvectra are codeveloping this new device, which combines Aleva's innovative directional lead technology with Nuvectra's neurostimulation platform. The directSTIM is a complete directional DBS system designed for long-term therapy in patients with Parkinson's disease and essential tremor. It will be combined with another device, the spiderSTIM, to provide a full solution for intrasurgical placement of DBS electrodes. The device is investigational and is not available for use or sale.

Alzheimer's disease

BDS-f DBS system (Functional Neuromodulation Ltd.)

Functional Neuromodulation is developing a deep brain stimulator designed to treat Alzheimer's. The system targets the stimulation of the fornix, a large arch-like bundle of 1.2 million axons that connects the hippocampus to other parts of the limbic system, a group of interconnected structures in the brain that mediate emotions, learning and memory. The fornix is a major inflow and output pathway in the brain's memory circuit and is one of the first areas of the brain affected by Alzheimer's. Early clinical study data demonstrated the technology may produce improvement in glucose metabolism in brain areas associated with Alzheimer's, possibly indicating an increase in energy utilization and function of these areas. The device is investigational and is not available for use or sale.

Parkinson's disease

Temporally optimized patterned stimulation (Deep Brain Innovations, LLC)

Deep Brain Innovations is developing technology to improve neural stimulation in the brain. Its proprietary Temporally Optimized Patterned Stimulation (TOPS) technology is being developed to enable the highly efficient delivery of DBS systems for the treatment of Parkinson's disease. The technology is designed to decrease power consumption, maximize device longevity, minimize implant size and reduce replacement-related risks and costs. The device is still in the design phase and is not available for use or sale.

AlphaDBS system (Newronika s.r.l.)

The AlphaDBS is a closed-loop deep brain neuromodulation system. The system interprets bioelectrical neuronal activity in the brain areas where stimulation is delivered and accordingly continuously adapts stimulation to follow a patient's clinical condition. The sensing technology is able to record noise-free brain signals while electrical stimulation is delivered. The device is not available for use or sale in the U.S.

Epilepsy

Nemos transcutaneous VNS system (Cerbomed GmbH)

The Nemos is designed to treat drug-resistant epilepsy. The system uses transcutaneous VNS, which uses electrical impulses to stimulate a branch of the vagus nerve through the skin in areas of the outer ear. The system consists of a handheld generator and a dedicated ear electrode. The generator, which is approximately the size of a mobile phone, sends out the electrical impulses. It is connected with the ear electrode, which patients wear like an earphone. The therapy is delivered during sessions lasting at least an hour, in three or four sessions a day, for a total of four to five hours per day. The device is not available for use or sale in the U.S.

FitNeS VNS system (CerebralRx)

The FitNeS VNS system treats refractory epilepsy, and is designed for patients with partial onset seizures who cannot achieve full seizure control with available prescription drugs. The system consists of an implanted stimulator and stimulation lead. The company claims that the system is an improvement over existing VNS devices because it employs lower currents, minimizes nerve damage through a unique nerve electrode interface, reduces current leakage through improved cuff isolation, and enables safe and easy explant of the electrode if required. The device is not available for use or sale in the U.S.

Unknown (NeuroVista Corp)

NeuroVista is an early-stage medical device company pioneering new technologies that will revolutionize the management and treatment of epilepsy. The company is developing a DBS system, which is investigational and not available for use or sale.

Chronic pain management

Lightpulse 100 (NeurImpulse srl)

The Lightpulse 100 implantable, nonrechargeable neurostimulator is a quadripolar pulse generator indicated for the treatment of chronic pain by the stimulation of peripheral nerves. The neurostimulator is equipped with an inline connector with four electrodes and it accommodates one bipolar or tetrapolar lead. The device is investigational and is not available for use or sale in the U.S.

Altius system (Neuros Medical)

The Altius high-frequency nerve block system is designed to block chronic pain such as post-amputation pain, chronic postsurgical pain and chronic migraine. The components of the system are similar to those of spinal cord stimulators. For pain control for patients with below the knee amputation, electrodes are placed on the common peroneal and tibial nerves, and for above the knee patients, on the sciatic nerve. Early clinical trial results look positive. The device is investigational and is not available for use or sale.

Psychiatric disorders

tDCS-LTE system (Soterix Medical)

The tDCS-LTE therapy system works by delivering a low-intensity electrical current to the part of the brain found to be hypoactive in patients with major depression. It is a nonsurgical, nonsedation, seizure risk-free alternative to techniques such as VNS. The system optimizes the delivery of energy to the brain, which improves mood. To enhance tolerability, the system combines the use of proprietary technology to minimize overall power delivery. The device is investigational and is not available for use or sale.

Monarch eTNS system (NeuroSigma, Inc.)

The Monarch eTNS system is a noninvasive medical device that stimulates the V1 branch of the trigeminal nerve on the forehead via an external conductive patch. Trigeminal nerve stimulation (TNS) is the electrical stimulation of branches of the trigeminal nerve, including those located near the surface of the forehead. The trigeminal nerve projects, either directly or indirectly, to specific areas of the brain, such as the locus coeruleus, nucleus tractus solitarius, thalamus and the cerebral cortex, all of which are involved in attention deficit hyperactivity disorder, depression and other disorders. The device is investigational and is not available for use or sale in the U.S.

Migraine headaches

ThermoNeuroModulation device (Scion NeuroStim LLC)

The Scion NeuroStim ThermoNeuroModulation device is a noninvasive, thermal vestibular stimulator for migraine headaches. The device stimulates the vestibular system by applying tightly controlled thermal waveforms through earpieces placed in a patient's ear canal. It is indicated for the prophylactic treatment of episodic migraine in adolescent and adult patients 12 years or older. The device received U.S. FDA clearance in March 2018.

Pulsante sphenopalatine ganglion microstimulator system (Autonomic Technologies, Inc.)

The Pulsante sphenopalatine ganglion (SPG) microstimulator is a miniaturized wireless device designed for patient-controlled, on-demand therapy to relieve the acute pain of chronic cluster headaches or for patients with highly disabling migraine. The device targets the SPG, a group of nerve cells located deep in the face, behind the nose. The miniature implant is inserted above the upper jaw in an outpatient oral procedure that leaves no visible scar. The device is under an investigational device exemption study in the U.S. for the treatment of chronic cluster headache, and is not available for sale or use in the U.S.

Overactive bladder and bowel control

Axonics r-sacral neuromodulation system (Axonics Modulation)

The Axonics r-sacral neuromodulation (SNM) system is a rechargeable sacral nerve stimulator for the treatment of urinary and bowel dysfunction. The system includes a temporary disposable external trial system; an implantable, miniaturized rechargeable impulse generator, qualified to function for at least 15 years; a tined lead; a charging system; and a patient remote control. The company's U.S. pivotal clinical trial, Axonics SacRal NeuromodulaTIon System for UrinAry Urgency Incontinence TreatmeNt (ARTISAN-SNM) — a 120-patient, single-arm, prospective clinical study — completed patient enrollment in June 2018. The device is investigational and is not available for use or sale in the U.S.

Virtis SNM system (Nuvectra Corporation)

The Virtis SNM system treats chronic urinary retention and the symptoms of overactive bladder. The system will feature a new lead design that enables easier placement and the use of fins rather than tins to hold the lead in place. The battery will be the first rechargeable one in this segment. The device is investigational and is not available for use or sale anywhere.

Unknown (InCube Labs, LLC)

InCube Labs is developing an implant that could improve or restore bladder function in patients who have suffered spinal cord injuries. No further information is available.

OAB-1000 (BlueWind Medical)

The OAB-1000 device is a wireless, battery-less neurostimulator implanted in a minimally invasive procedure near the tibial nerve in the lower leg. The device stimulates the nerve to treat overactive bladder, and is 90 percent smaller than other neurostimulators. The device is powered wirelessly by an external control unit, which patients wear for only 30 minutes per day. The device is investigational and is not available for use or sale in the U.S.

Diabetes

Unknown (Metavention, Inc.)

Metavention is developing a novel transcatheter-based metabolic neuromodulation therapy for glucose control in patients with type 2 diabetes (T2D). Overactive sympathetic nervous system activity is associated with elevated blood glucose levels in T2D patients; the hypothesis is that modulation of the nerve activity will reduce glucose levels. The device is investigational and is not available for use or sale.

Sleep apnea

Nyxoah obstructive sleep apnea system (Nyxoah)

Nyxoah is developing neurostimulation-based therapy for obstructive sleep apnea. The system uses a small implant inserted at the back of the tongue that causes a slight motion, preventing obstruction of the airway during sleep. The implant, which is 20 mm in diameter with a 2.5-mm thickness, is energized using an adhesive battery patch that is placed on the chin over the implant site. The implant is estimated to last 12 years. The device is investigational and is not available for use or sale in the U.S.

aura6000 system (LivaNova plc)

The aura6000, based on proprietary technology, delivers neurostimulation to the hypoglossal nerve. It increases the muscle tone of multiple tongue muscles and prevents the tongue from collapsing into the upper airway during sleep. The technology is designed to address nighttime upper airway blockage, enabling obstructive sleep apnea patients to achieve normal, restful sleep. The system consists of two implantable components: a small rechargeable pulse generator placed under the skin near the collarbone, and a multielectrode lead placed in the upper neck. The device is investigational and is not available for use or sale in the U.S.

Heart failure

Equilia heart failure therapy system (LivaNova plc)

Cardiovascular disease has been shown to be associated with an imbalance in the autonomic nervous system, which controls cardiac activity. This imbalance overstresses the heart and contributes to the worsening of heart failure. The Equilia system's pulse generator acts like a cardiac pacemaker by stimulating the vagus nerve, and is expected to improve heart function. The device is being investigated in the VNS Safeguarding Heart Failure Patients (Vanguard) clinical study, which is designed to evaluate the device and therapy for heart failure patients. The device is investigational and is not available for use or sale in the U.S.

Barostim neo Legacy system (CVRx, Inc.)

The Barostim neo Legacy system is an implantable device used to stimulate the baroreceptors of the carotid sinus. The human body has mechanisms for sensing changes in blood pressure and flow. This natural system is largely located in the brain and the walls of the carotid arteries. Pressure sensors, called baroreceptors, are found on the carotid artery and in the carotid sinus. These sensors measure and report blood flow to the brain, which then compare it to the body's needs. Providing high-frequency, minute electrical impulses to the carotid sinus nerves and the receptors can provide positive feedback to the brain and reduce blood pressure. The device is investigational and is not available for use or sale in the U.S.

CardioFit vagus nerve stimulating system (BioControl Medical)

The CardioFit system is intended to treat severe heart failure patients who have failed to achieve symptomatic improvement through standard evidence-based management. The system works by stimulating the vagus nerve. A sensing lead in the right ventricle detects the patient's heart rate, while a second lead sends electrical stimulation to a cuff around the vagus nerve. The device is investigational and is not available for use or sale in the U.S, although it is available outside the U.S.

Stroke rehabilitation

Navigated brain therapy (Nexstim plc)

The navigated brain therapy (NBT) system uses navigated transcranial magnetic stimulation (nTMS) to aid in stroke rehabilitation. The NBT technology is capable of modeling the electric field in the brain. The e-field and electromyographic (EMG) response-based navigation offers more accuracy, repeatability and more precise dose control. This unique way of applying noninvasive magnetic stimulation pulses in combination with EMG measurement can be used to obtain an input-output curve and estimated motor threshold in one fast scan lasting 60 to 90 seconds. The device is investigational and is not available for use or sale in the U.S.

Vivistim paired VNS system (MicroTransponder, Inc.)

The Vivistim system stimulates the vagus nerve while a patient undergoes a rehabilitative movement, which tells the brain to "pay attention" to that movement. This simultaneous pairing strengthens motor circuits associated with the physical movement. The electric signal passes through the nucleus tractus solitarius to two distinct brain regions; when these regions receive the electric signal, they enhance brain activity. The device is investigational and is not available for use or sale in the U.S.

Gastric stimulation

Abiliti (IntraPace, Inc.)

The Abiliti system treats obesity by helping to control appetite, and automatically recording when a person eats, drinks and exercises. The Abiliti system has three main parts: an implantable gastric stimulator, an implantable lead and a food sensor. The gastric stimulator and lead are implanted in a minimally invasive procedure. The system delivers a series of low-energy electrical impulses to the stomach to create a feeling of fullness, and collects data to provide a detailed picture of food consumption and exercise trends. These data can be downloaded at the physician's office and may be used by patients and their health care providers to monitor their progress toward weight loss goals. The device is investigational and is not available for use or sale in the U.S.

Other

tPEMF TheraCap system (Endonovo — Rio Grande Neurosciences)

The tPEMF TheraCap system is a baseball cap-like device that uses a proprietary FDA-approved pulsed electromagnetic field technology to treat postsurgical neuroinflammation. The TheraCap is a noninvasive, portable treatment that inductively delivers a weak electrical therapeutic field to the brain; it is used to address pain and edema. The company is also studying the device to treat traumatic brain injury and other indications that involve neuroinflammation, including concussion and multiple sclerosis. The device is investigational and is not available for use or sale in the U.S.

Serenity system (MicroTransponder, Inc.)

The Serenity system uses VNS, which causes the release of neurochemicals in the brain, to improve tinnitus, a ringing in the ears in the absence of external sound. The system pairs VNS with listening to sounds using headphones, which helps decrease brain hyperactivity over time. The device is investigational and is not available for use or sale.

Unknown (Neurent Medical)

The Neurent device is in development for the treatment of rhinitis. Rhinitis, an inflammatory disease of the nose, is reported to affect up to 40 percent of the population and is the fifth most common chronic disease in the U.S. The device uses a minimally invasive handheld radiofrequency device in combination with a microelectrode array. The single-use device is introduced through the nostrils into the nasal cavity under direct endoscopic visualization. The electrode array delivers targeted energy to interrupt the autonomic function within the mucosal structures of nasal cavities, which is believed to reverse the inflammatory cascade. The device is investigational and is not available for use or sale.

Atrostim phrenic nerve stimulator V2 system (Atrotech Oy)

The Atrostim phrenic nerve stimulator (PNS) is a diaphragm pacing system for long-term artificial ventilation. The system consists of surgically implanted stimulators and electrodes, a portable controller unit and transmitter coils that are attached on the skin over the stimulators to power the implants. The controller unit is operated with two rechargeable batteries (one battery is in use while the other one is being charged). Patients who benefit from the use of PNS suffer from respiratory muscle paralysis or central alveolar hypoventilation. The system uses sequential multipole stimulation for the electrical impulse activation of the phrenic nerve, which results in diaphragm contraction and the inhalation of air. The use of PNS requires normal function of phrenic nerves and diaphragm muscle. The device is investigational and is not available for use or sale in the U.S.

EndoStim lower esophageal sphincter stimulation system (EndoStim Inc.)

EndoStim is a minimally invasive neurostimulation therapy for patients with gastroesophageal reflux disease (GERD). The system consists of a generator, implantable bipolar lead and wireless external programmer (used in clinic). The device battery is expected to last approximately seven years under recommended stimulation algorithms. Electrical stimulation of the lower esophageal sphincter using neuromodulation has been proven to be safe and effective for treating carefully selected patients with persistent GERD symptoms despite proton pump inhibitor therapy. The system delivers mild electrical signals to the sphincter automatically throughout the day. The valve stimulation is designed to allow it to function normally: it stays closed to prevent reflux, and opens to allow food and drink to pass into the stomach. The device is investigational and is not available for use or sale in the U.S.

Neuromodulation device for inflammatory disease (SetPoint Medical, Inc.)

SetPoint Medical is developing a neuromodulation device about the size of a penny that stimulates the vagus nerve. The doses of electricity activate the cholinergic anti-inflammatory reflex in patients with rheumatoid arthritis to produce a systemic immuno-restorative effect. The company has published positive results from a first-in-human proof-of-concept trial in rheumatoid arthritis in Proceedings of the National Academy of Sciences. The company is conducting U.S. clinical trials to advance its bioelectronic technology for chronic inflammatory conditions and Crohn's disease. The device is investigational and is not available for use or sale.

Spirit diaphragm pacing transmitter (Avery Biomedical)

The Spirit diaphragm pacing transmitter provides support for patients with chronic ventilatory insufficiency whose diaphragm, lungs and phrenic nerves have residual function. The system consists of electrodes, radio receivers, and an external transmitter control unit and antenna assembly that provides power to the system using AA batteries. The new system's left and right antennas send radiofrequency energy to each passive receiver. The antennas are placed on the skin over the implanted receiver. The radiofrequency waves are transmitted through the skin to the implanted receiver, which converts the waves into electrical pulses that are delivered to the phrenic nerve via the electrode. The device is not yet available for use or sale in the U.S.

References

1 Eisner W. Uncle Sam proposes raising ortho payments 1.8% in 2019. Orthopedics This Week website. https://ryortho.com/breaking/uncle-sam-proposes-raising-ortho-payments-1-8-in-2019/. Published May 15, 2018. Accessed June 22, 2018.

2 Molliqaj G, Schatlo B, Alaid A, et al. Accuracy of robot-guided versus freehand fluoroscopy-assisted pedicle screw insertion in thoracolumbar spinal surgery. *Neurosurg Focus*. 2017;42(5):E14.

3 Custer L, Allen S. Doing the deal: Understanding the key differences between ASC and hospital RCM. *Becker's ASC Review* website. https://www.beckersasc.com/asc-coding-billing-and-collections/doing-the-deal-understanding-the-key-differences-between-asc-and-hospital-rcm.html. Published May 13, 2016. Accessed August 14, 2018.

4 Intraoperative navigation: The options. Spinal News International website. https://spinalnewsinternational.com/intraoperative-navigation-the-options/. Published June 28, 2016. Accessed August 27, 2018.

5 Hartford J. Which spine robot will dominate? Medical Device and Diagnostic Industry website. https://www.mddionline.com/which-spine-robot-will-dominate. Published October 31, 2016. Accessed August 17, 2018.

6 Dyrda L. North American spine surgery market in 5 years: 8 things to know. *Becker's Spine Review* website. http://www.beckersspine.com/orthopedic-a-spine-device-a-implant-news/item/23595-north-american-spine-surgery-market-in-5-years-8-things-to-know.html. Published December 10, 2014. Accessed July 11, 2018.

7 Wood M. 50 things to know about the spine industry. *Becker's Spine Review* website. https://www.beckersspine.com/spine/item/35530-50-things-to-know-about-the-spine-industry-2017.html. Published February 27, 2017. Accessed August 14, 2018.

8 Spinal implants: market insights (United States). Decision Resources Group website. https://decisionresourcesgroup.com/report/567706-medtech-spinal-implants-medtech-360-market-insights/. Published December 2017. Accessed July 10, 2018.

9 Spine Service Line Snapshot 2018 report authored by Sg2 Health Care Intelligence, page 2.

10 Hartford J. Zimmer Biomet joins surgical robotics race. Medical Device and Diagnostic Industry website. https://www.mddionline.com/zimmer-biomet-joins-surgical-robotics-race. Published July 18, 2016. Accessed August 15, 2018.

11 Good C. Complications and revision rates in robotic-guided vs. fluoro-guided minimally invasive lumbar fusion surgery: The MIS ReFRESH study. Presented at: North American Spine Society (NASS), 35th Annual Scientific Meeting; October 26, 2017; Orlando, FL.

12 Solomiichuk V, Fleischhammer J, Molliqaj G, et al. Robotic versus fluoroscopy-guided pedicle screw insertion for metastatic spinal disease: a matched-cohort comparison. *Neurosurg Focus*. 2017;42(5):E13.

13 Vizient Savings Actualyzer, July 2018.

14 Neurostimulation devices market insights, U.S. Decision Resources Group website. https://decisionresourcesgroup.com/report/521401-medtech-neurostimulation-devices-medtech-360-market/. Published March 2017. Accessed August 16, 2018.

15 Adult obesity facts. Centers for Disease Control and Prevention website. https://www.cdc.gov/obesity/data/adult.html. Accessed July 22, 2018.

16 Nahin RL. Estimates of pain prevalence and severity in adults: United States, 2012. *J Pain*. 2015;16(8):769-780.

17 Migraine facts. Migraine Research Foundation website. https://migraineresearchfoundation.org/about-migraine/migraine-facts/. Accessed July 22, 2018.

18 Understand the facts: anxiety disorders and depression. Anxiety and Depression Association of America website. https://adaa.org/understanding-anxiety. Accessed July 22, 2018.

19 Essential tremor. Remedy's Health Communities website. http://www.healthcommunities.com/essential-tremor/essential-tremor-overview.shtml. Published January 1, 2000. Updated September 14, 2015. Accessed July 22, 2018.

20 Facts and figures. American Epilepsy Society website. https://www.aesnet.org/for_patients/facts_figures#Eight. Accessed July 22, 2018.

21 Parkinson's disease statistics. Parkinson's News Today website. https://parkinsonsnewstoday.com/parkinsons-disease-statistics/. Accessed July 22, 2018.

Notes

vizient®

290 E. John Carpenter Freeway
Irving, TX 75062
(972) 830-0000

www.vizientinc.com

For more information, contact us at (800) 842-5146
or vizientsupport@vizientinc.com.

As the nation's largest member-driven health care performance improvement company, Vizient provides network-powered insights in the critical areas of clinical, operational, and supply chain performance and empowers members to deliver exceptional, cost-effective care.

11/18 13922