Chapter 5 Worldwide Orthopedic and Spine Market

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OVERVIEW

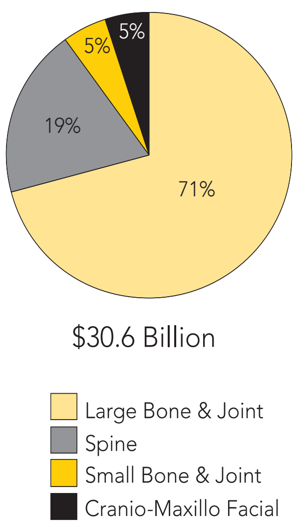
Over the past 15 years, internal fixation with spinal implants has been used at an accelerated rate in spinal fusion procedures. In the last two years, the advent of non-fusion technologies, including artificial discs, Nucleus Arthroplasty™ motion preservation technology and dynamic stabilization systems, have cannibalized revenues from traditional fixation and interbody fusion (IBF) markets. Based on historic data, the orthopedic sector is trending towards an industry that will be classified by anatomy. Currently, orthopedics can be divided into four major segments:

- *Large bone and joint* - Hip and knee replacements and ancillary technologies
- *Spine* - Fusion technologies and now evolving towards motion preserving technologies
- *Small bone and joint* - From the finger to the shoulder and from the toe to below the knee joint
- *Cranio* - Maxillo facial

IN THE LAST TWO YEARS, THE ADVENT OF NON-FUSION TECHNOLOGIES, INCLUDING ARTIFICIAL DISCS, NUCLEUS ARTHROPLASTY MOTION PRESERVATION TECHNOLOGY AND DYNAMIC STABILIZATION SYSTEMS, HAVE CANNIBALIZED REVENUES FROM TRADITIONAL FIXATION AND INTERBODY FUSION (IBF) MARKETS.

The chart below shows the 2006 estimated market size of the orthopedic sector by segment. The large bone & joint and spine sectors are expected to account for the lion's share of revenue with 90% of the market. It is anticipated that the orthopedic sector will have the single largest impact on the global healthcare industry over the next decade, generating over $100 billion in revenues worldwide. Future growth is highly dependent on both innovation and distribution. We can expect to see consolidation in this sector, which will create efficiencies in distribution and set the stage for

2006E Musculoskeletal Industry By Segment



Source: Viscogliosi Bros., LLC, 2006

large-scale multinational companies to focus on the entire musculoskeletal system. These companies will work to develop a multifaceted arsenal of pharmaceutical, biotech, and nanotech solutions. Ultimately, the orthopedic sector will grow through life-changing, surgeon-developed inventions, and the adoption, production, and global distribution of these devices to patients who demand not only pain relief, but also the restoration of motion.

The worldwide spine market is estimated to be a $5.8 billion industry in 2006 and is expected to grow an average 15% to 20% annually. While historically, this market segment has experienced a 15% annual growth rate, certain niche markets have been growing as fast as 40% to 100% per year. The spine market in 2006 is 58 times larger than it was in 1990 when revenues totaled a mere $100 million. Despite this dramatic increase, this market is poised for significantly greater growth in the near future due to a variety of reasons including:

- A philosophical revolution toward non-fusion technologies
- The availability of new technologies globally to treat expanding indications
- A trend in spine surgery toward less invasive procedures
- A demographic increase in the number of patients with back pain
- A continuation of intense scientific interest in the study of spine and back pain
- The increased awareness of successful treatment methods and technologies among spine surgeons
- The interest of surgeons and patients in long-term outcomes

In the last few years, the international spine market has seen the introduction of non-fusion technologies, including Nucleus Arthroplasty motion preservation system, artificial discs, and dynamic stabilization systems. The goal of these motion preservation technologies is to stabilize the spine yet allow for movement. Although spinal fusion is a highly documented and proven form of treatment for many patients, spine surgeons have expressed significant interest in pain relieving therapies designed to preserve the natural motion of a given spinal segment while restoring disc height and stability. Of particular interest are non-fusion therapies focused on the treatment of patients with mild or moderate disc conditions. These new motion preserving technologies can be divided into three broad product categories:

- Dynamic stabilization
- Nucleus Arthroplasty technology
- Total disc replacement (TDR)

It is our belief that these non-fusion technologies are starting to cannibalize revenues from the traditional fixation and interbody fusion markets.

U.S. LUMBAR SPINE TREATMENT CONTINUUM

For many years, neurosurgeons and orthopedic spine surgeons have recognized the limitations of fusion procedures for treating back pain and have been actively seeking alternatives. While today's spine market is focused on fusion, we believe this will change dramatically over the next several years as non-fusion devices are introduced and proven to be more effective and beneficial for patients. This will significantly affect the industry's reliance on fusion revenues and will force the current industry leaders to reevaluate their product portfolios in order to maintain their market share.

An estimated 30 million people in the U.S. report back pain annually. Of this population, approximately 4.5 million people continue to experience back pain after receiving conservative treatment such as physical therapy and/or medication. Only a small segment from this unresolved pain group, approximately 10%, will be prime candidates for more aggressive treatments such as TDR or spinal fusion. At this time, there is no well-defined treatment scenario for the remaining individuals with unresolved pain. The situation is frustrating for surgeons who do not have the therapeutic options to help the large number of patients suffering from low back pain.

The current U.S. spine care continuum is delineated as follows:

Conservative treatment - The first treatment is commonly conservative therapy consisting of bed rest, pain medication, and physiotherapy. If conservative therapy does not result in sufficient pain relief, surgical procedures are then considered.

Discectomy/laminectomy - This is the most common surgical treatment for ruptured or herniated discs. The procedure is considered to be less invasive than other treatment options. However, many surgeons believe discectomy is only a temporary solution in which the patient will require secondary surgery, particularly in the case of disc herniation resulting from degenerative disc disease (DDD). This type of surgical intervention may not be a definitive solution as, in many cases, a discectomy results in temporary pain relief, but unfortunately creates instability within the spinal column, thereby, usually accelerating the degenerative process.

Total Disc Replacement (TDR) - The rationale for the use of a total disc replacement device is to remove the entire disc, which some believe to be the pain generator. This procedure replaces the removed disc with a mechanical device that to varying degrees mimics the natural disc motions and biomechanics. TDRs are mainly used to treat patients with severe and advanced DDD. At this time, TDR manufacturers who have received or are seeking Food and Drug Administration (FDA) approval are utilizing designs that are mechanical in nature and composed of materials commonly found in orthopedic devices.

Fusion - Fusion was developed for the treatment of spinal instability or deformity. It has also been utilized for the surgical elimination of painful motion, such as the treatment of low back pain secondary to DDD. This particular indication has been controversial, although there is medically-based evidence of its effectiveness. Fusion is an invasive, traumatic, and expensive procedure requiring a lengthy recovery time. It is considered the treatment of last resort and is reserved for patients with significant intractable pain and/or neurological deficits. The procedure has seen many improvements throughout the years, however, fusion procedures have not always resulted in the best clinical outcomes leaving many patients unsatisfied. Although fusion may not be the "gold standard" in the future, it will continue to be used.

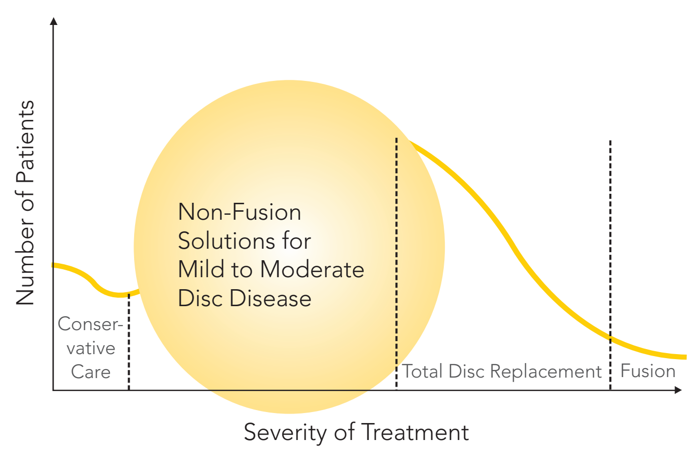
There are at least two gaps that can be identified in the current treatment continuum that motivate surgeons to seek alternative non-fusion treatment options. The treatment gaps are as follows:

Gap between conservative treatment and discectomy - If a patient fails conservative care and his/her condition does not warrant a discectomy or laminectomy, the patient is left without effective treatment options. The only option is to continue conservative care until the patient's condition worsens and surgical intervention is required.

Gap between discectomy and total disc replacement - If a patient is unable to achieve a successful outcome after discectomy, the patient may be a candidate for TDR. Current TDR solutions represent an endstage non-fusion approach as the technology requires sacrifice of the native disc and thus may pose significant challenges should the treatment prove to be ineffective.

As a result, it is expected that the spine treatment continuum of the future will shift as shown in the accompanying figure.

Future of Spine Surgery



Source: Viscogliosi Bros., LLC, 2006

New treatment options such as Nucleus Arthroplasty technology can offer several benefits to address unmet patient and surgeon needs with improved long-term clinical outcomes, less invasive surgical techniques, shorter recovery times, and the maintenance of movement. These advantages will become even more pronounced as spinal arthroplasty device technologies advance and become one of the principal methods of care for spinal segment degeneration.

FUTURE OF NUCLEUS ARTHROPLASTY MOTION PRESERVATION TECHNOLOGY

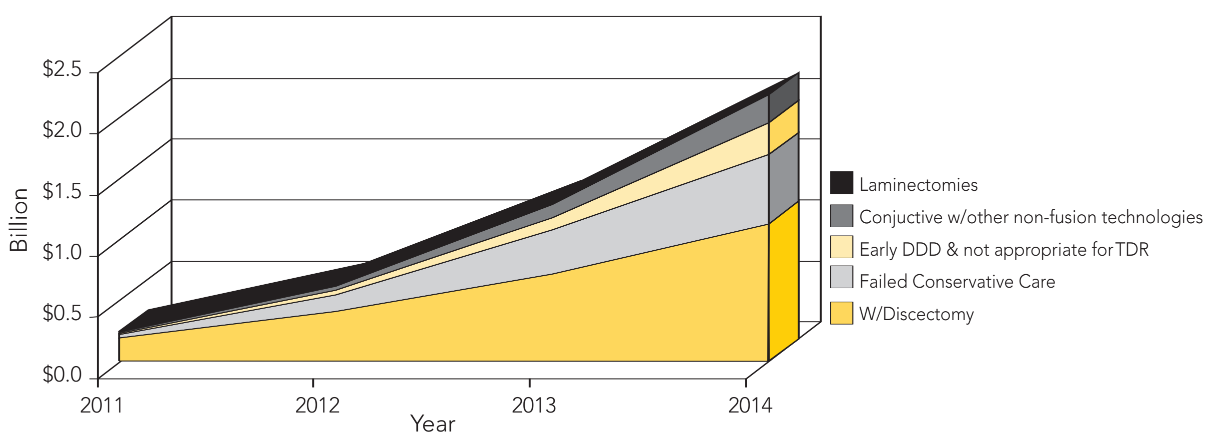
Growth in Nucleus Arthroplasty technology usage will likely be driven by demographic changes, increased use by spine specialty surgeons, and better defined inclusion/exclusion criteria. Given the treatment gaps and unmet medical needs, there is a greater necessity for non-fusion treatment options for surgeons. The following are some of the possible indications for Nucleus Arthroplasty systems:

- Mild or moderate DDD with low back pain
- Prophylactic at same level after discectomy or adjacent level for adjacent level disease
- Central herniation
- Hybrid (with posterior dynamic systems)

The indications for a nucleus replacement are much broader than that for a TDR, as the purpose of TDR is to remove the disc that is generating pain and replace it with a mechanical device meant to mimic a healthy spinal disc. Nucleus Arthroplasty motion preservation technology, on the other hand, is designed to repair the nucleus and alleviate the associated back pain with a less invasive process than TDR. While replacing the total disc may be a solution for some people, it is far too aggressive for others.

Nucleus Arthroplasty technology offers a treatment option for early stage DDD using less invasive surgical techniques and it is expected to supercede many other surgical options. The procedure results in minimal anatomical destruction with many surgical access options. Nucleus Arthroplasty technology can used be as a conjunctive treatment with other non-fusion or fusion therapies or as an adjunctive treatment above or below the treated level. When combined with other therapies including dynamic posterior stabilization, TDR, or fusion, Nucleus Arthroplasty technology can provide anterior and posterior column support and stabilize abnormal motion while maintaining segmental mobility. The Nucleus Arthroplasty motion preservation technology market is expected to grow to an estimated $2.2 billion by the year 2014.

2014 Nucleus Arthroplasty Motion Preservation Technology Market



~$2.2 Billion by 2014

Source: Viscogliosi Bros., LLC, 2006

IN THE NEXT DECADE, IT IS EXPECTED THAT SPINAL ARTHROPLASTY WILL BECOME THE PRINCIPAL MARKET FOR SPINAL CARE. IT IS A BROAD MARKET THAT IS GAINING INCREASING SURGEON ACCEPTANCE.

In the next decade, it is expected that spinal arthroplasty will become the principal market for spinal care. It is a broad market that is gaining increasing surgeon acceptance. A greater number of arthroplasty procedures are being performed each year. More instrumented spine surgeries have been performed during the past five years than in the preceding ten years. The increasing numbers will broaden the market for non-fusion technologies and create the opportunity for surgeons and patients alike to recognize the benefits of Nucleus Arthroplasty technology.

U.S. CLINICAL EXPERIENCE

The Hospital for Special Surgery (HSS), New York, New York, performed a retrospective review of contraindications to lumbar TDR in 2002 to better understand the indications of this technology and possible clinical impact on their practice. The study can be summarized as follows:

- Of 100 consecutive patients, 56 received fusions
  - 0/56 eligible for TDR (0%)
- 44 received decompressive, non-fusion treatments
  - 5/44 eligible for TDR under strict IDE criteria (11%)
- 40% of the total patient population could have received a disc nucleus replacement

As this study demonstrates, the patient population for Nucleus Arthroplasty technology could be larger than the patient population for TDR, because Nucleus Arthroplasty technology addresses a treatment gap. It broadens the indications by allowing for the treatment of a patient population that has been ignored by the current spine treatment continuum.

A subsequent study performed by HSS focusing on indications and contraindications for Nucleus Arthroplasty devices found the following:

- Of 85 consecutive patients (117 levels) treated surgically for symptomatic DDD after a minimum of six months of conservative treatment
  - 53 patients with 1 level disease
  - 32 patients with 2 level disease
- Contraindications included:
  - Schmorl's nodes
  - > 50% collapse of disc space
  - Irregular/convex endplates on the MRI
  - Large annular defects
  - BMI > 30
- Overall, 44/117 levels (37.6%) had no radiographic and clinical contraindications for nucleus replacement
  - 15/53 (28.3%) with 1 level disease were eligible
  - 11/32 (34.5%) with 2 level disease were eligible at both levels
  - 6/32 (18.8%) with 2 level disease were eligible at 1 level

The most recent study corroborates the results of the earlier study in that approximately 40% of patients surgically treated for DDD are eligible for Nucleus Arthroplasty procedures. The second study also demonstrates that Nucleus Arthroplasty technology can expand the patient population because multiple treatments can be performed on one patient.

THE MOST RECENT STUDY CORROBORATES THE RESULTS OF THE EARLIER STUDY IN THAT APPROXIMATELY 40% OF PATIENTS SURGICALLY TREATED FOR DDD ARE ELIGIBLE FOR NUCLEUS ARTHROPLASTY PROCEDURES.

IMPACT ON A SURGEON'S PRACTICE

The availability of a Nucleus Arthroplasty treatment option in the U.S. could greatly expand a surgeon's practice by providing the possibility to solve complex problems that were previously ignored. Nucleus Arthroplasty technology provides the possibility of higher clinical success for patients because the treatment is more appropriate to the level of degeneration. Higher clinical success rates in turn increase the number of referrals to the surgeon leading to growth in the practice itself.

Although artificial discs have garnered significant market attention, they are only one of a number of devices that will transform spine surgery over the next five to ten years. Nucleus replacement "could be a huge treatment expander," says Scott L. Blumenthal of the Texas Back Institute, "because you can intervene much, much earlier–when the patient first herniates or ruptures a disc–in order to obviate a more aggressive or invasive surgery later on." Stephen H. Hochschuler, MD, also of the Texas Back Institute, agrees. "I think there could be a much larger market for the nucleus than the total disc, because you can use the nucleus much earlier."[1]

Dr. Blumenthal doesn't believe that nucleus replacement will make disc replacement redundant, because you can't use artificial nuclei for later-stage degenerative problems. Rather, he says, "I think there will be a place for both."[1] Dr. Hochschuler says that spine surgeons can use a combination of new technologies. "You can put in a new nucleus or new disc and do dynamic stabilization. You can put in a total disc and also replace the facet joints. You can put in a new nucleus and repair the annulus at the same time. So we won't be choosing just one of these new technologies; there will be combination. That's what's so intriguing."[1]

SUMMARY

Although the specific indications for nucleus replacement technologies are still evolving, it can already be seen that they are much broader than that for TDR. Given that nucleus replacement technologies provide for treatment earlier in the cascade of disc degeneration, they will expand the patient population. The procedure is more surgeon and patient friendly, and the revision strategies are easier and safer.

REFERENCES

1. Cassak D. Texas Back Institute: Spine's Technology Laboratory. IN VIVO. The Business & Medicine Report. May 1, 2005. Windover Information, Inc