VOLUME 5, ISSUE 32 | OCTOBER 20, 2009

# Orthopedics This Week

## week in review


**05 AAOS: Choose Evidence Over Opinion** ♦ In one corner is a controlled, randomized study…in the other, Dr. X's opinion. Guess who loses. Evidence-based medicine, says AAOS, is the appropriate, ethical path toward treating patients…and it is the future.

**09 Stem Cell Nobel Prize and Other News** ♦ This year's Nobel Prize in Medicine went to cellular researchers, and it came the same week as a number of other interesting stem cell news items hit the wires—including the first 20-year follow-up data for stem cells. All in all, the industry continues to percolate.

**13 AAOS '08: Failure to Disclose** ♦ Ninety-five of 344 presentations made by physicians at AAOS' 2008 meeting failed to disclose industry ties. What caused this failure and what is the Academy doing to assure that their 2010 meeting is "disclosure compliant"? AAOS President Joseph Zuckerman, M.D., explains it all to *OTW* readers in a recent interview.

**17 Extremities Device Market—Still Undefined!** ♦ What does "extremities" really mean? Ask five different companies and you will likely hear five different answers. In order to truly compare companies' market shares, do we need a standard definition of extremities?

**21 New Device Idea? Seek Help** ♦ Developing new medical products often requires a strong partnership between physicians and industry. How can they see eye to eye? Sometimes it takes a little extra guidance from the experts.


## the picture of success


**48 Dr. John Bergfeld** ♦ Dr. John Bergfeld, an orthopedist at Cleveland Clinic, had a rocky start in life. Yet he grew up to be team doctor for the Cleveland Browns and helped grow the sports medicine field.


## breaking news


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**Biomet,** Off To Fast Start in 2010

**Platelet Rich Plasma:** Positive Early Results

**Bone Growth** Breakthroughs


**For all the news that is Ortho, read on.**

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2009 Orthopedics This Week Spine technology Awards

# Reserve your seats now for the gala banquet!

*November 9, 2009 • The Palace Hotel • San Francisco*

All of the spine technology submissions have been received, and seats for the Spine Technology Awards and Gala Banquet are going fast.

These awards are the first of their kind and are designed to honor the best spine products, engineering teams and inventors of 2009. Don't miss this unique and important night when 100 attending spine surgeons will vote on entries in eight categories:

- Device Technologies for Cervical Care
- Lumbar Care
- Motion Preservation of the Spine
- Minimally Invasive Care
- Biomaterials
- Diagnostics and Imaging
- Pain Management
- Regenerative Technologies

**Each company or individual that submits products for evaluation will be recognized by *Orthopedics This Week* at the podium during the awards ceremony.**

The 24 finalists and the first place, second place and third place **awards in each category will be determined by real-time surgeon votes at the November 9 event.** The engineers/inventors for the top three products in each of the eight categories will be invited to the podium to describe their invention. The top three products in each category will receive crystal awards at the ceremony.

## *Reserve your seats today—the number of spots remaining is extremely limited!*

***Click here*** to print a reservation form and obtain more information, or contact Tom Bishow at tom@ryortho.com or Lisa Carpenter at lisa@ryortho.com.

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VOLUME 5, ISSUE 32 | OCTOBER 20, 2009

# Orthopedic Power Rankings

## Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

**This Week:** Quick question: which major orthopedic company can best survive a price squeeze should that develop as a result of future Medicare cuts? Clue: check the operating margin. Zimmer's 29% beats just about every other firm except Medtronic. ZMH's remains #1 this week.

| Rank | Last Week | Company | TTM Op Margin | 30-Day Price Change | Comment |
|---|---|---|---|---|---|
| 1 | 1 | Zimmer | 29.31% | 1.29% | Paying 12.7x earnings for a company with 29% profit margins is a flat out bargain. |
| 2 | 4 | Stryker | 23.28 | (4.87) | In terms of Market Power in orthopedics, SYK is huge, but valuation is at historic lows. Up two spots this week. |
| 3 | 2 | Orthofix | 7.65 | 3.25 | Can't wait for the 3rd and 4th quarter reports. More good news on the cash flow front likely. |
| 4 | 3 | Smith & Nephew | 20.95 | (5.85) | Not much news lately from Mr. Smith and his nephew. Drifts down one spot this week. |
| 5 | 7 | Medtronic | 31.37 | (0.58) | When Medtronic (31% margin) has a lower valuation than Orthofix, something is off kilter. |
| 6 | 6 | ArthroCare | 16.87 | 3.95 | Financials on the way? Triumph of hope versus experience, we suspect. |
| 7 | 5 | Exactech | 12.87 | 2.97 | Very low P/E to growth rate. Institutional investors are not enamored with smaller general ortho firms these days. |
| 8 | 10 | Integra LifeSciences | 12.32 | (10.60) | IART hit an air pocket this past month and is now the 3rd cheapest stock in orthopedics. |
| 9 | 8 | CONMED | 8.28 | 5.21 | Who would have thought that CNMD would perform so well given the recent spate of negative news. |
| 10 | 9 | Alphatec | (8.51) | (4.99) | NASS is looming and like all spine companies, ATEC is preparing for a strong meeting. |

# Robin Young's Orthopedic Universe

## Top Performers Last 30 Days

| | Company | Symbol | Price | Mkt Cap | 30-Day Chg |
|---|---|---|---|---|---|
| 1 | I Flow Corp | IFLO | $12.57 | $307 | 17.5% |
| 2 | Orthofix | OFIX | $31.58 | $542 | 10.2% |
| 3 | Osteotech | OSTE | $4.57 | $82 | 6.5% |
| 4 | Mako Surgical | MAKO | $8.90 | $224 | 6.1% |
| 5 | CONMED | CNMD | $21.19 | $616 | 5.2% |
| 6 | ArthroCare | ARTC | $20.55 | $551 | 3.9% |
| 7 | NuVasive | NUVA | $43.57 | $1,640 | 3.2% |
| 8 | Exactech | EXAC | $16.30 | $208 | 3.0% |
| 9 | Zimmer Holdings | ZMH | $51.92 | $11,130 | 1.3% |
| 10 | Johnson & Johnson | JNJ | $60.46 | $166,620 | 0.4% |

## Worst Performers Last 30 Days

| | Company | Symbol | Price | Mkt Cap | 30-Day Chg |
|---|---|---|---|---|---|
| 1 | Regen Biologics | RGBO.OB | $0.84 | $8 | -50.3% |
| 2 | Capstone Therapeutics | CAPS | $0.73 | $30 | -18.9% |
| 3 | RTI Biologics Inc | RTIX | $3.81 | $207 | -15.5% |
| 4 | Integra LifeSciences | IART | $31.87 | $906 | -10.6% |
| 5 | Symmetry Medical | SMA | $9.89 | $354 | -10.1% |
| 6 | TiGenix | TIG.BR | $6.18 | $152 | -8.3% |
| 7 | Smith & Nephew | SNN | $43.90 | $7,750 | -5.9% |
| 8 | Kensey Nash | KNSY | $26.50 | $295 | -5.6% |
| 9 | CryoLife | CRY | $7.90 | $224 | -5.5% |
| 10 | Alphatec Holdings | ATEC | $4.95 | $259 | -5.0% |

## Lowest Price / Earnings Ratio (TTM)

| | Company | Symbol | Price | Mkt Cap | P/E |
|---|---|---|---|---|---|
| 1 | Symmetry Medical | SMA | $9.89 | $354 | 9.02 |
| 2 | ArthroCare | ARTC | $20.55 | $551 | 12.15 |
| 3 | Medtronic | MDT | $37.42 | $41,420 | 12.44 |
| 4 | Zimmer Holdings | ZMH | $51.92 | $11,130 | 12.67 |
| 5 | Johnson & Johnson | JNJ | $60.46 | $166,620 | 13.27 |

## Highest Price / Earnings Ratio (TTM)

| | Company | Symbol | Price | Mkt Cap | P/E |
|---|---|---|---|---|---|
| 1 | I Flow Corp | IFLO | $12.57 | $307 | 120.65 |
| 2 | Smith & Nephew | SNN | $43.90 | $7,750 | 76.78 |
| 3 | RTI Biologics Inc | RTIX | $3.81 | $207 | 65.75 |
| 4 | NuVasive | NUVA | $43.57 | $1,640 | 41.97 |
| 5 | Synthes | SYST.VX | $122.52 | $14,540 | 38.10 |

## Lowest P/E to Growth Ratio (Earnings Estimates)

| | Company | Symbol | Price | Mkt Cap | PEG |
|---|---|---|---|---|---|
| 1 | ArthroCare | ARTC | $20.55 | $551 | 0.49 |
| 2 | Symmetry Medical | SMA | $9.89 | $354 | 0.84 |
| 3 | Exactech | EXAC | $16.30 | $208 | 0.97 |
| 4 | CryoLife | CRY | $7.90 | $224 | 0.97 |
| 5 | Orthofix | OFIX | $31.58 | $542 | 1.01 |

## Highest P/E to Growth Ratio (Earnings Estimates)

| | Company | Symbol | Price | Mkt Cap | PEG |
|---|---|---|---|---|---|
| 1 | NuVasive | NUVA | $43.57 | $1,640 | 4.40 |
| 2 | RTI Biologics Inc | RTIX | $3.81 | $207 | 1.85 |
| 3 | CONMED | CNMD | $21.19 | $616 | 1.80 |
| 4 | Johnson & Johnson | JNJ | $60.46 | $166,620 | 1.72 |
| ***5*** | ***Average*** | | | ***$10,277*** | ***1.57*** |

## Lowest Price to Sales Ratio (TTM)

| | Company | Symbol | Price | Mkt Cap | PSR |
|---|---|---|---|---|---|
| 1 | Osteotech | OSTE | $4.57 | $82 | 0.84 |
| 2 | Symmetry Medical | SMA | $9.89 | $354 | 0.87 |
| 3 | CONMED | CNMD | $21.19 | $616 | 0.88 |
| 4 | Orthofix | OFIX | $31.58 | $542 | 1.03 |
| 5 | Exactech | EXAC | $16.30 | $208 | 1.25 |

## Highest Price to Sales Ratio (TTM)

| | Company | Symbol | Price | Mkt Cap | PSR |
|---|---|---|---|---|---|
| 1 | TiGenix | TIG.BR | $6.18 | $152 | 212.36 |
| 2 | Mako Surgical | MAKO | $8.90 | $224 | 11.00 |
| 3 | Synthes | SYST.VX | $122.52 | $14,540 | 8.89 |
| 4 | NuVasive | NUVA | $43.57 | $1,640 | 5.25 |
| 5 | Regen Biologics | RGBO.OB | $0.84 | $8 | 4.89 |

# AAOS: Choose Evidence Over Opinion

**By Elizabeth Hofheinz, M.P.H., M.Ed**

It's a case of "I think" versus "The research shows that…"

So while Mrs. Jones in 3B probably wants her orthopedist's expert opinion, she will likely benefit from hard data even more. Such is the message being heralded by the thought leaders at the American Academy of Orthopaedic Surgeons (AAOS). Dr. Michael Keith,

Chair of the AAOS Evidence Based Practice Committee, explains, "From a philosophical standpoint, the goal is to convince our colleagues in orthopedics that evidence based medicine (EBM) is a better basis for practicing medicine than opinion, consensus or outside mandates such as cost containment. We aim to increase recognition of quality as the driving force behind change in healthcare policy, as well as to create solid standards. On the practical side, we are working to ensure that evidence based medicine penetrates education and training, clinical practice and other activities such as board certification, certificates, and leadership training."

While it may seem that opinion is being put under the microscope, orthopedists, having studied the hard sciences for many years, have a natural bent for evidence. Dr. Keith: "Orthopedists are naturally inclined toward science, so EBM should be a good fit. Those who are already accepting of this approach are interested because they want to be able to defend what they do as best practice and they want to be judged based on the correct standards. And to those holding out, I say, 'Opinion loses against a controlled, prospective, randomized study every time.'"

It is often the case that younger people are more open to change. With an eye toward influencing orthopedists in training, AAOS has instituted a program to change orthopedic education so as to emphasize evidence based medicine.



"We are beginning a program with the Residency Review Committee to include EBM as a foundation for education, meaning that it will be present throughout the curriculum for residents and fellows. For example, this will mean that journal clubs include an assessment of the level of evidence of all published reviews and that these reviews will be compared against the appropriate guidelines. The outcome, of course, is either that the old belief is supported or the new information rejects the formerly held belief."

In such a clear-thinking environment, there is no room for bias. Dr. Keith: "We are also working with

the Orthopaedic In-Training Exam Committee to include questions about EBM and to upgrade the way questions are written. It is important that the questions are not derived from the question writer's experience or his or her selected publications, but reflect what one would find in a systematic review of the literature. On our end, the Evidence Based Practice Committee takes several steps to eliminate bias, including that when we write clinical practice guidelines and reviews we don't even look at the abstract or the conclusions, we just look at the data."

## Hearing From Doctors and Patients

Also part of this continuous quality improvement process is an effort to develop self assessments for surgeons. "We are collaborating with the American Board of Orthopaedic Surgeons and the Council on Education to develop a practice improvement module that includes miniature versions of self assessments in which surgeons can study their practice relevant to one of the guidelines. This will enable surgeons to determine how well they performed, introduce changes and then follow up later to see if the quality of the results improved. At present there are two such modules under study, one on blood utilization and another on MRI utilization."

In an effort to get everyone on the same page, the AAOS Evidence Based Practice Committee is also reaching out to the leaders of the specialty societies. Dr. Keith notes, "We hope to partner with the specialty societies, and in fact are planning for a specialty society symposium on EBM. The fact is that the leadership of these organizations may not all be trained in EBM. But if we want only the best people heading up the societies, then we must bring everyone up to the same level of education on EBM."

When given the podium, Dr. Keith first of all stumps for the patients. "Our colleagues should understand that we use EBM to help express the patient's perspective. Even though most traditional publications don't speak from the patient's point of view, it is our objective to ensure that the patient's side is given a full hearing."

And a full hearing from patients, says Dr. Keith, means thousands of data points. "Part of outcomes research is that we now expect to have a patient's rating of how well the surgery worked. For example, take pain relief. In surveys done about patient priorities, they are asked how much change in pain is worth the operation. We want to look at thousands of patients and see what their collective patient experience is. That way, we will have data that says, for example, 'Well, if the surgery doesn't eliminate half of my pain then it is not worth the anesthesia, physical therapy, etc.'"

Dr. Keith's final point: "It is hard to imagine an orthopedic surgeon who doesn't believe in science…and if you believe in science, you can believe in the value of evidence-based medicine."

## Growing Pains: The Beginnings of EBM

Dr. William Watters, III, Chair of the AAOS Guideline and Technology Oversight Committee (GTOC), concurs, and gives a bit of history. "Great Britain and Canada began having a problem with healthcare resources long before we did; they began emphasizing evidence based medicine in the 1980s. It wasn't until the late '90s that American physicians and researchers began examining EBM. Since that time AAOS has restructured itself and has committed to promoting the concept of EBM."

But first they had to understand it. Dr. Watters: "When the GTOC was initiated in 2006 those of us involved had to educate ourselves on evidence based medicine by reading copious amounts of literature. We began to look at how to develop guidelines, and then the AAOS Board committed to fund the development of two initial guidelines, one of which was on pulmonary embolism in joint replacement patients. This was chosen because it was highly pertinent to the membership at large and was also an issue about which we were getting conflicting information. The other guideline was on the diagnosis of carpal tunnel syndrome, an important subject that affects several types of specialists."

They expected—and encountered—growing pains. "'Where do we get our evidence? How do we analyze the data?' were some of the questions that gave us pause at the outset. We retained an outside vendor, a university based group that had done this type of work for quite some time. Then AAOS decided to create its own such group, and chose veteran researcher Charlie Turkelson, Ph.D., to lead a new analysis group at AAOS. (This has been such a success that we have never again needed an outside vendor.) There were things to be worked out, of course, but the primary takeaway from this era was that the leadership of AAOS was extremely committed to advancing evidence based medicine."

Part of the strategy to be worked out was which, among the numerous possible topics, should be addressed. "Dr. Turkelson developed an invaluable topic prioritization matrix that we use as a guide to decide which health issues to study. It includes questions such as, 'Does the health problem carry a high individual or population burden of morbidity, mortality or disability? Is it something important to the membership at large and beyond? Does the problem, its treatment or diagnosis carry a high unit or aggregate cost?'"

"Based on that matrix," says Dr. Watters, "we can generate a hierarchy of topics. The committee typically develops three or four guidelines per year, with each topic having its own workgroup comprised of approximately six to eight people. While those in the workgroup should of course have experience with the topic, as well as be versed in EBM, they are not only orthopedists, but physical therapists, rheumatologists, etc." And all on board must be above board. "A major part of the process is full disclosure," states Dr. Watters. We must eliminate even perceived conflicts of interest. If we are putting out a guideline for treatment we don't want someone to say, 'Dr. X is on that committee and he was the co-developer of such and such product.'"



Once the decks are cleared of conflicts, the workgroup comes together in Chicago for a day long meeting. "During this time the questions to be addressed are chosen and the members of the evidence analysis group perform a literature search and rate the evidence. They and the workgroup then reconvene for two days to answer the questions with the best evidence available and to hammer out the initial draft."

## Which Issue Will Evidence Tackle Next?

And what is the Guideline and Technology Oversight Committee crafting at present? Dr. Watters: "Our workgroups are now developing guidelines for Achilles tendon rupture, ankle arthritis, distal radial fractures, and periprosthetic joint infections. In the past we have addressed, among other things, carpal tunnel syndrome, knee arthritis, and pediatric femoral fractures."

A torrent of possible topics, along with the need to stay current, means that the committee is always on duty. Dr. Watters explains, "The data for each guideline is reviewed every three or four years, with a new literature search to fill in any gaps. There may be nothing of substance to

add, or, there may be so much new information that we need to rewrite the guideline."

While nowadays those involved in evidence based medicine are not usually met with suspicion, it wasn't long ago that they had to fight an uphill battle. "The initial reaction to EBM amongst our colleagues was less than enthusiastic. To many, an evidence based approach was viewed as cookbook medicine that discounted the role of the doctor and his or her training. In fact, EBM values the training and experience of the physician, while taking into account the patient's expectations and desires and presenting the most recent evidence available."

"It is impossible for any doctor to read all of the available literature in his area of specialty. These guidelines take the 'cream' of the information and give the doctor and patients the best information with which to make joint decisions. They are not in any way meant to distance the patient from the physician or the physician from the decision making process. The guidelines are empowering for both the patient and doctor."

Commenting on another significant benefit of evidence based medicine, Dr. Watters concludes, "If you work from the goal of always behaving ethically, then the whole process of evidence based medicine is self correcting. If you are following the evidence then you are going to make an ethical decision. And we did take an oath to be ethical."

Orthopedics This Week

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# Stem Cell Nobel Prize and Other News

**By Robin Young**

This year's Nobel Prize for Medicine was given to three cellular researchers (Drs. Elizabeth Blackburn (University of California), Carol Greider (Johns Hopkins University) and Jack Szostak (Harvard Medical School)), each of whom made critical contributions to understanding one of the defining attributes of both stem cells and tumor cells—namely the urge to divide.

The three scientists demonstrated that cells will age if a particular string of code at the end of a DNA strand (telomere) is shortened. Telomeres protect the ends of DNA and are critical to cell division—which, of course, stem cells and tumor cells are known to perform quite impressively. Nobel Prize winner Elizabeth Blackburn compared telomeres to the tips on the ends of shoelaces that keep them from fraying.

Other stem cell pioneers, specifically Drs. McCulloch and Till—the two scientists who won the prestigious Lasker Award in 2005—were mentioned in the running for this year's Nobel Prize in Medicine.

While the Nobel Prize committee continues to watch and evaluate the stem cell arena, more news arrived on our desk last week of interesting and key new developments. Specifically, Spire Healthcare, a startup company in Manchester, United Kingdom, announced that it had successfully tested a new technique which uses stem cells to repair damaged bones. The leading investigator in the small study, orthopaedic surgeon

*Drs. Jack Szostak (Harvard Medical School), Elizabeth Blackburn (University of California), and Carol Greider (Johns Hopkins University)*

Dr. Douglas Dunlop, collected stem cells from a patient's bone marrow and mixed them with a composite of powdered bone from the patient's previous hip replacement operation. Dr. Dunlop and his team then used the stem cell packed bone to replace dead tissue from the ball of the patient's hip that had not been replaced.

The 39-year-old patient was suffering from necrosis of the hip. The doctor removed dead tissue from the ball joint and then filled it in with the mixture of autologous stem cells and powdered bone from the previous operation.

Dr. Dunlop has performed this procedure six times. While the information we've seen is only anecdotal, it is, nonetheless, very interesting for several reasons. First, it uses the patient's own materials. Second, all patients had necrosis of the hip and, according to Dr. Dunlop, the new material resulted in rejuvenated bone. According to Dr. Dunlop, the stem cell packed material successfully engrafted and all six patients are able to walk without pain. Quoting Dr. Dunlop, "If this new procedure works, he won't need a hip replacement. It will fix his hip for life."

In the U.S., PearlDiver estimates that there are approximately 427,000 cases of necrosis of the hip diagnosed annually.

## Stem Cell IPO in Russia?

The Moscow-based Human Stem Cell Institute ("HSCI") announced last week that it planned to complete

an initial public offering of stock. The IPO's price was set at 9 and 11 rubles per ordinary share ($0.30 per share). The company is planning to sell 15 million shares and raise about $4.5 million. Its market capitalization would be approximately $24 million.

The underwriting would put the shares onto the Innovative & Growing Companies (IGC) sub-sector of the Innovation and Investments Market on the Moscow Interbank Currency Exchange (MICEX).

The Human Stem Cell Institute was founded in 2003 to advance projects in stem cell technology. HSCI has laboratories and offices in Russia (Moscow and St. Petersburg), Ukraine and Germany. HSCI has processing laboratories and storage facilities for cellular materials, as well as research laboratories such as the Laboratory of Stem Cell Technologies in Moscow and the SymbioTec Co. biotechnological laboratory in Saarbrücken, Germany. HSCI is also the main publisher of the scientific journal Cellular Transplantation and Tissue Engineering.

This would be, by the way, Russia's first IPO this year.

## NIH Dollars for Stem Cells

We've all heard about the billions of new stimulus dollars being made available to young companies and technologies. Well, NeoStem, Inc. (NYSE Amex: NBS), which is developing a system of collecting, processing and storing adult stem cells, was awarded the princely sum of $108,746 for the repair of bone defects by human stem cells. The funds came to NeoStem as part of the American Recovery and Reinvestment Act (RRA) of 2009 from the National Institute of Arthritis and Musculoskeletal and Skin Disease (NIAMS) of the National Institutes of Health (NIH).

NeoStem plans to use the award to study the potential of very small embryonic-like stem cells to regenerate bone in an animal model. These very small embryonic-like stem cells are isolated from adults' own peripheral blood using NeoStem's proprietary isolation methods.

The principal investigator in the study is Dr. Russell Taichman, Professor of Dentistry, Department of Periodontics and Oral Medicine at the University of Michigan School of Dentistry, and his colleagues, Drs. Paul Kresbach and David Kohn.

Under the RRA, the NIH has established a new program entitled Research and Research Infrastructure "Grand Opportunities," also known as the "GO" grants program. This new program is designed to support large-scale research projects that accelerate critical breakthroughs, early and applied research on cutting-edge technologies, and new approaches to improve the synergy and interactions among multi- and interdisciplinary research teams. The program is intended for research activities that have high, short-term impact, and a high likelihood of enabling growth and investment in biomedical research and development in new fields of investigation.

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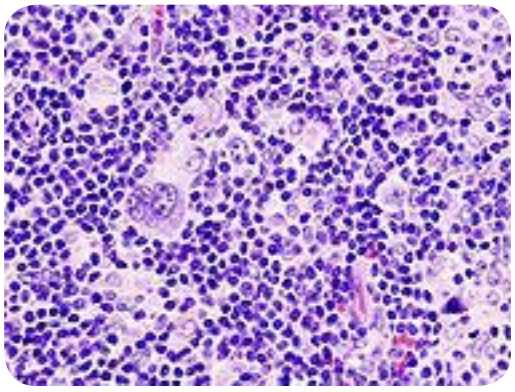
NeoStem is developing a network of adult stem cell collection centers that are focused on enabling people to donate and store their own (autologous) stem cells when they are young and healthy for their personal use in times of future medical need.

## Twenty-Year Results Reported of Autologous Stem Cell Transplants for Hodgkin's Lymphoma

It is rare to find 20-year follow-up results under any circumstances. To find it in stem cells was downright amazing. Yet, last week, across our desk came news that researchers from the Memorial Sloan-Kettering Cancer Center have reported on patients who'd received autologous stem cell transplants (ASCT) as part of a therapy regimen to treat refractory or relapsed Hodgkin's lymphoma (HL).



*Hodgkin's lymphoma/commons.wikipedia*

The results were presented at the Joint ECCO 15 – 34th ESMO Multidisciplinary Congress in Berlin this past September 20-24, 2009. Autologous stem cell treatment has been the treatment of choice for patients with responsive relapse of HL for more than two decades.

While a common treatment regimen for patients with HL and non-Hodgkin's lymphoma (NHL) is chemotherapy or high-dose total body irradiation (TBI), some researchers have argued that TBI is unnecessary and can be substituted with other treatments that are augmented with autologous stem cell transplants.

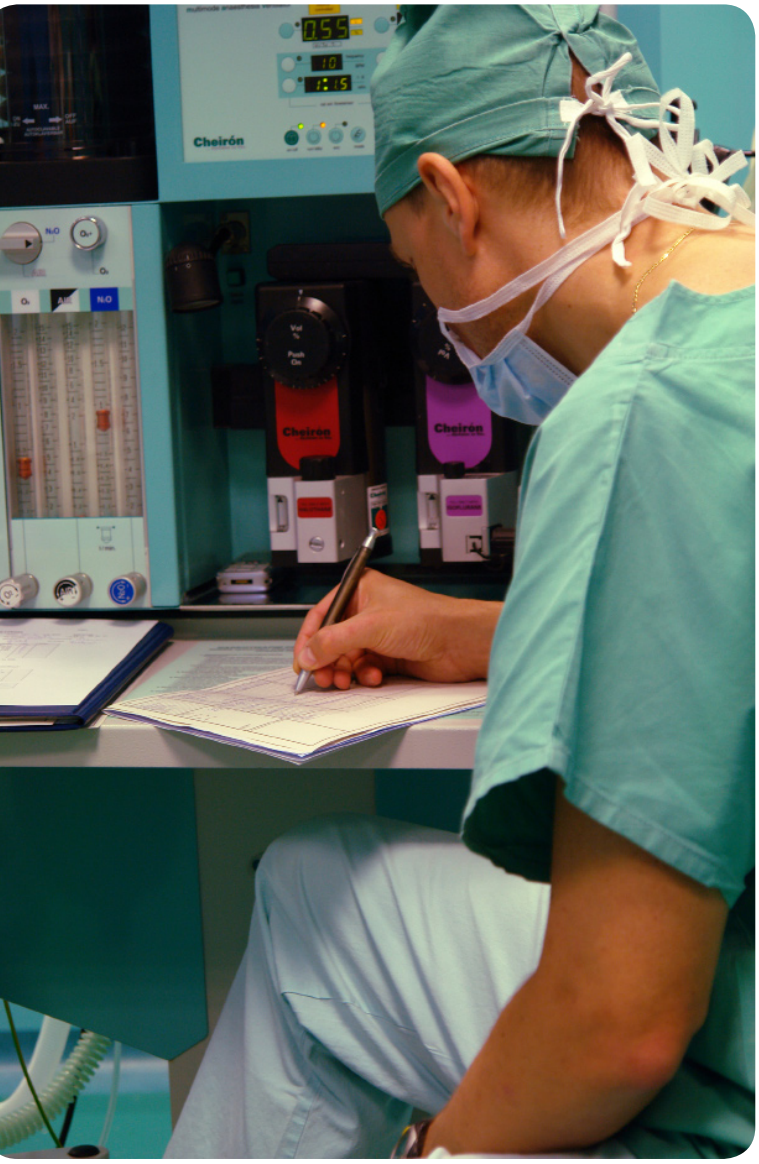
The study looked at 186 previously un-irradiated patients with relapsed or refractory HL who received a total lymphoid irradiation (TLI)-based regimen prior to ASCT. These patients were treated between 1985 and 2008. The researchers made the following observations:

- 5- and 10-year overall survivals were 68% and 56%, respectively.
- 5- and 10-year event-free survivals were 62% and 56%, respectively.
- 5- and 10-year HL-related deaths were 21% and 29%, respectively.
- 62% of patients were alive and free of disease at last follow-up.
- Patients who achieved a complete response to salvage therapy had improved outcomes.
- Primary refractory disease and extranodal disease predicted for poor outcomes.
- Introduction of peripheral blood stem cells in 1995 was associated with improved overall survival ($P$ = .06).
- Early mortality decreased over time with only one death since 1998 (1.2%).

**Conclusion:** The data confirmed the long-term benefits of autologous stem cell therapy for patients with relapsed or refractory HL. They also suggest that total body irradiation is not essential for cure, and patients can be treated with less radiation therapy.

# AAOS '08: Failure to Disclose

**By Walter Eisner**




There was no sugarcoating it. Joseph Zuckerman, M.D., the President of the American Academy of Orthopaedic Surgeons, was surprised and disappointed.

A study just published in the New England Journal of Medicine found that 95 of 344 physicians making presentations at the Academy's 2008 meeting in San Francisco failed to disclose their financial ties to industry.

This was at a meeting with a keynote address by Lew Morris, Chief Counsel, Office of Inspector General Department of Health and Human Services about federal investigations of industry/surgeon relationships. This was at a time when Congress was holding hearings titled "Surgeons for Sale" and a disclosure agreement was being reached between the U.S. Justice Department and the big five hip and knee device makers.

The findings of non-compliance with AAOS disclosure guidelines begs the question of whether or not physician self-reporting worked in 2008 to bring transparency to surgeon/industry relationships and gives additional fodder to "Sunshine" legislation proposed by Senators Chuck Grassley and Herb Kohl.

## Self-Reporting Shortcomings

Mininder Kocher, M.D., MPH, an associate professor of orthopedic surgery at Harvard Medical School in Boston and a lead author of the study, says their findings showed self-reporting doesn't necessarily yield complete transparency. "Disclosure is essential because such relationships may cause pro-industry bias," said Kocher after the release of the study.

Kocher and four colleagues looked at the 2007 payments made to physicians by Biomet, Stryker, DePuy, Smith & Nephew, and Zimmer. Those payments were made public as part of the deferred prosecution agreements with the government. The researchers then compared those payments to disclosures made by physicians presenting at the 2008 AAOS meeting or serving on boards or committees of the Academy.

Twenty-one percent of directly related payments and half of indirectly related payments weren't disclosed, the study found. The 43 directly related payments not disclosed amounted to $4.3 million, while the 16 indirectly related ones totaled $7.8 million.

AAOS policy at the time required physicians to disclose the receipt of

something of value from a commercial company or institution that related directly or indirectly to the subject of their presentations.

The leading reason given for nondisclosure was that physicians believed their payments didn't relate directly to the presentation topic. The study found this by sending a survey to the 91 physicians who didn't disclose payments in the final program of the meeting. Thirty-six of the 91 physicians responded to the survey.

Survey recipients were asked to choose from a list of potential reasons for nondisclosure that included the following: the payment was unrelated to the presentation topic, the payment was unknown at the time of disclosure, the payment had been received after the disclosure deadline, the payment was not large enough to warrant disclosure, the payment was unintentionally omitted, the payment was intentionally omitted, the payment was disclosed but was mistakenly omitted from the annual-meeting program.

The study found that payments were more likely to be disclosed if they were directly related to the topic of presentation, exceeded $10,000, and were directed to an individual recipient.

## New AAOS Policies

Joseph Zuckerman, M.D., told *OTW* in an October 8 interview that the Academy put a new disclosure policy into place following the San Francisco meeting. Zuckerman is also a professor and chair of the department of orthopedic surgery at the New York University Hospital for Joint Diseases.

The current AAOS Disclosure Policy reads as follows:

> *"The actions and expressions of Fellows or Members providing education of the highest quality or in shaping AAOS policy must be as free of outside influence as possible and any relevant potentially conflicting interests or commercial relationships must be disclosed. Because the AAOS depends upon voluntary service by Fellows and Members to conduct its educational programs and achieve its organizational goals, this disclosure policy has been designed to be realistic and workable."*

## 2007: The Disclosure Period

Zuckerman said the 2008 meeting in San Francisco was happening in the midst of an evolution of disclosure policies during the time of the Justice Department agreements. However, noted Zuckerman, the 2008 meeting reflected the Academy's disclosure policies of 2007.

Said Zuckerman, "2007 was the beginning of the 'Disclosure Period.' Medical centers and organizations, cardio and psychiatrists had issues [of disclosure]." We were in the midst of trying to 'refine' those policies."

## Transitioning to Online Disclosures

The AAOS leader said 2007 was also an important time because it was the last time AAOS members were allowed to submit their disclosure forms by paper. "In 2008, we transitioned to online disclosure. We took these steps without knowledge of this study and made the process tighter with respect to everyone disclosing their relationships," said Zuckerman. By going to an online system, Zuckerman says, there are mandatory

fields to be completed and the electronic form can't be sent without filling out all the fields. This will also make it easier for the Academy to track those documents for the next meeting in New Orleans in the spring of 2010.

In addition, Zuckerman said there are no longer any distinctions made between presentations that relate directly or indirectly to the presenter's relationship with a company, an item noted by physicians who had failed to report in 2007.

"It will now be left to the listener to decided for themselves if the presentation is related," added Zuckerman.

AAOS had symposia in 2008 and 2009 on industry relationships, and another is planned in 2010. The Academy is taking steps to educate members. For those not attending the meeting, multiple articles are being run in AAOS *NOW,* the Academy's in-house publication.

"Things have clearly changed since 2008, which reflected the policies from 2007," Zuckerman reiterated.

## No Retrospective Audits

Because some AAOS members violated Academy guidelines in 2008, we wondered if AAOS would try to find out who those physicians were. And would the Academy go back and audit the 2009 meeting in Las Vegas to measure compliance? Would what happened in Vegas stay in Vegas? [Sorry, we couldn't help ourselves.]

*Drs. Rankin and Zuckerman Building Playground in San Franciso/AAOS photo*

Zuckerman said the Academy has no plans to go back and audit the 2009 meeting to see if disclosures improved. "If someone didn't disclose retrospectively, what action would we take? Going prospectively is part of a project team review."

## Board Report in December

Last June, the Board of AAOS appointed a Board Project Team, chaired by the immediate past AAOS Board Chair, Anthony Rankin, M.D., to conduct a "complete analysis and review" of all Academy disclosure policies "at every level of the organization with anybody involved in any Academy activity," said Zuckerman. The AAOS Board had a preliminary report at its September meeting and will receive a final report in December.

"I expect they would make recommendations to incorporate in 2010," said Zuckerman. He continued:

> *"The last thing we want is to have any question related to our Annual Meetings or our members' participation in the Academy. We want 100% compliance of disclosure...that's something we're going to work towards."*

We asked Zuckerman if the Academy has considered a third-party audit of disclosures.



"At this point we cannot exclude any way to reach 100% compliance, but that's not a specific approach we've discussed," he said.

Asked if he sees any parallels to NASS' disclosure and divestiture policy which requires the disclosure of specific dollar amounts and possible divestiture of certain relationships with industry, Zuckerman said, "The requirements placed on any specific position you have is something the project team will address." For example, at NYU, Zuckerman says the IRB policies require that if a physician is in a relationship with a company, the physician can participate in the study, but can't be the principal investigator or be responsible for evaluating results.

Whether or not AAOS reaches its goal of 100% compliance will be hard to measure without auditing the public disclosures on company Web sites and the self-reported disclosures made by presenters on AAOS-mandated electronic forms.

However, the light shed on AAOS members by Kocher and his colleagues, and the new Academy disclosure guidelines, will certainly remove any excuses of confusion about the disclosure expectations for future presenters. We will watch closely for the AAOS Board Project Team report in December and see how the Academy responds to the "Disclosure Period."

# Extremities Device Market—Still Undefined!

**By Dev Joshi, PearlDiver Extremities Analyst**

The market for extremity repair products is one of the fastest growing markets in orthopedics with double-digit revenue growth rates over the past five years, but uncertainty still lingers around the question of how companies define extremities. Which body parts actually count as "extremities?"


The category of large joints includes hips and knees. Small joints include shoulders, elbows, hands, wrists, feet, ankles and toes. But not all device companies consider all types of small joint treatment as part of the extremities category. Instead, small joint treatment constitutes four different sectors of orthopedics:

1. Joint replacement and the reconstruction market
2. Small joint trauma market
3. Small joint sports medicine market
4. Extremity biologics market

Depending on the company, the category of extremities could include all, some, or none of those four small joint categories. When the extremities device market reported sales of over $900 million in 2008, some companies included joint replacement products within their reporting for extremities, and others included both joint replacement and small joint trauma products. A few companies also included small joints sports medicine products as being within the extremities device market. The trauma product market alone represented $4.7 billion (including treatment of large joint fractures), and sports medicine products earned close to $2.8 billion in sales. Without a standardized definition of extremities products, how can one really compare market share from one company to the next?

We can at least start with clearer definitions of the four small joint categories. Here is a closer look at these markets and how the orthopedics industry differentiates them:

1. Joint Replacement Market: This market represents implant devices that restore the joints of extremities such as shoulder arthroplasty, elbow arthroplasty, wrist arthroplasty and the new ankle replacement devices. These are implant devices that help restore the functionality of these small joints.

2. Small Joints Trauma Market: This could be its own joint reconstruction market, but companies tend to include sales related to small joint trauma in their reports of extremity product sales. This includes items used to treat fracture-related incidents such as fixation devices, screws and plates used to treat shoulders, wrist fractures, elbows and ankles.

3. Small Joints Sports Medicine Market: Sports medicine is a competitive market that includes hip and knee related sports injuries to the ACL (anterior cruciate ligament) and to the MCL (medial collateral ligament). However, a significant portion of the market is involved in arthroscopy and endoscopy procedures on small joints in the shoulder, wrist, elbow, foot and ankle. Sports medicine for small joints includes treatment of rotator cuff tears, tennis elbow, golfer's elbow and sports-related injuries.

4. Extremity Biologics Market: This sector includes all aspects of biological treatment for upper extremity, foot and ankle orthopedics. Products such as the GraftJacket from Wright Medical, the Rotator Cuff Repair Patch from Zimmer, and other biological products to treat soft tissue are reported as biologics sales. Biologics is still an evolving market, and it is too early to differentiate its market share from other extremity product categories.

Chart 1 shows the total orthopedic market for 2008 with extremity product sales of just over $900 million. Orthobiologics, the next largest market sector, more than doubled the sales figure from the extremities product market. Clearly, differences in categorization can create a large discrepancy between how extremity product companies report earnings and market share.

## How Do Companies Define Their Market?

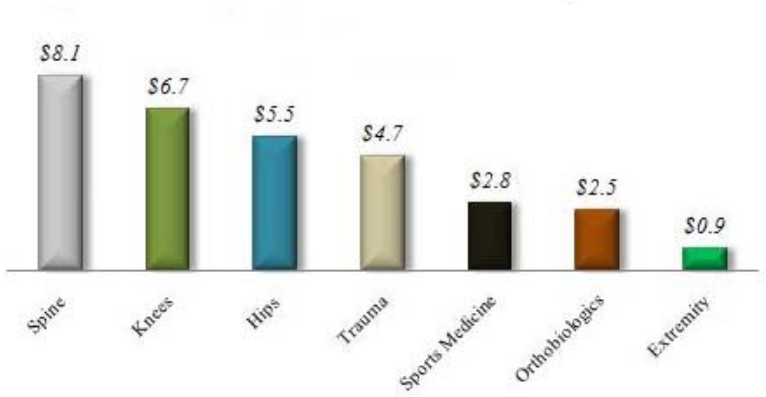
***Biomet, Inc.***

Biomet represents one of the largest orthopedic product suppliers in the world with over $2 billion in sales worldwide. The company offers a full line of trauma treatment products through its Biomet trauma division, and the company has a separate division for sports medicine where it includes soft tissue repair products. The product lines that Biomet currently includes as extremities products are:

Joint replacement and reconstruction products for shoulders, elbows, wrists and other small joints
Products like the Comprehensive Reverse Shoulder System (a second generation reverse shoulder prosthesis device) and the Maestro Wrist Reconstructive System (WRS)

Biomet is currently focused on the upper extremity area, and the company aims to provide a complete line of products for orthopedic surgeons performing upper extremity procedures. John McDaniel, Vice-President for upper extremities at Biomet Orthopedics, would like to see a universal approach that revolves around the surgeon's pattern for treatment for upper extremity joint replacement and the associated fracture fixation devices. According to PearlDiver research, Biomet holds close to 10% market share (in the second quarter of 2009) in the worldwide extremity product market, but that would increase significantly

**Chart 1: Worldwide Orthopedic Market**




*Source: PearlDiver Research and Estimates*

if all companies started reporting extremity sales from only joint replacement products.

***Wright Medical Technologies, Inc.***

Wright Medical develops products for the upper extremities, feet and ankles, with heavy emphasis on the foot and ankle side of the business. Extremity treatment offerings range from digit and joint arthroplasty, plating and screw fixation systems, and tissue fixation products (interference screws and bone anchors). Key products include the Evolve radial head and Micronail in the upper extremity segment and the Darco and Charlotte Plating lines and INbone Ankle replacement in the foot and ankle segment. The items that Wright Medical defines and reports in its public disclosures as extremity products are:

- Plates, staples, and rods for foot, wrist and elbow applications
- Stand alone screws for foot repair and fixation
- Interference screws and anchors for foot and ankle tendon repairs
- External fixation products
- Joint arthroplasty including total shoulder, total elbow and total ankle systems.

These products include devices and treatment from the categories of sports medicine, trauma and joint implants, all gathered under the extremities category. According to John Treace, Vice-President for Extremities and Biologics at Wright Medical, for reporting purposes, the company's definition of extremity products



includes all the hardware surgeons use to repair small joints. This includes arthroplasty, sports medicine and reconstructive or trauma plating products. Biologics dealing with soft tissue repair or extremities are reported separately in their biologics division. Currently, Wright Medical holds 10.6% of the market share for extremities worldwide according to PearlDiver research. However, Wright stands to lose quite a bit of market share if other companies started reporting fixation and instrumentation numbers in their extremities reporting.

***DePuy Orthopaedics, Inc***

DePuy Orthopaedics, as a subsidiary of Johnson and Johnson, is the leading extremity supplier in the world. Unlike Wright Medical, DePuy defines its extremity product market as joint replacement or the arthroplasty market for shoulders, feet, ankles and digits. DePuy has its own sports medicine division called DePuy Mitek, its own trauma division, and a separate biologics division serving the trauma and spine treatment businesses.

The product lines that DePuy defines as extremity products are:

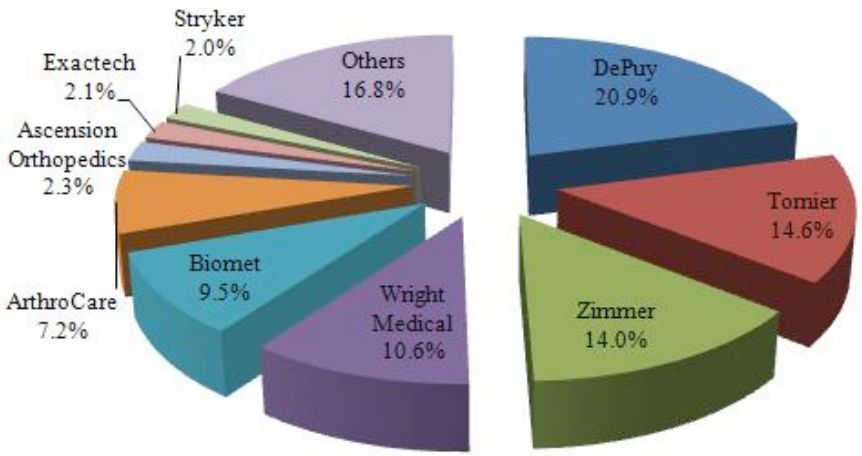
- Joint replacement and reconstruction products that include shoulders, ankles and digits.
- Hemi-arthroplasty shoulder fracture products, such as the Global FX Shoulder System
- Major products such as the Agility Ankle System, the Global Shoulder System, Delta XTEND Reverse Shoulder System and the Neuflex MCP/ICP Finger Implant System.

The product lines that DePuy defines as trauma and sports medicine in extremities are:

- External fixation products, staples, screw instrumentation, nails, rods and plates for trauma treatment
- General arthroscopic and endoscopic instruments, suture anchor products and cuff repair products to treat small joints are reported in the DePuy Mitek Sports Medicine division.

Dennis Cassell, U.S. Extremities Director at DePuy Orthopaedics, says that extremity means different things to different companies. DePuy defines extremity products only as joint replacement and arthroplasty products. Even with this limited reporting, DePuy remains the

**Chart 2: Extremities Market Share (2Q09)**




*Source: PearlDiver Research and Estimates*

number one extremity supplier in the world with over $200 million in product sales worldwide. Taking into consideration the variation in companies' definitions of extremities, DePuy holds close to 21% market share (from the second quarter of 2009). This could change dramatically if other companies reported extremity products as just the implant and arthroplasty market.

### *Other Companies*

Under the category of extremities, Zimmer Holdings and Exactech, Inc. distribute products only for upper extremity treatment. Zimmer's fracture products sales (part of its trauma division) represents close to 5% of the total trauma market worldwide. Zimmer's upper extremity line of products represents 14% (in the second quarter of 2009) of the total $900 million extremity device market. Exactech Inc., an emerging extremity company, has a similar product portfolio as Zimmer with just over 2% of the extremities product market share worldwide. Tornier includes sales of fracture treatment products within its extremity division, and Ascension Orthopedics reports all small joint products as extremity treatment. Integra Life Sciences includes endoscopic instruments for small joints, staples, screws, plates and fixation devices as extremities, and Orthofix International reports fixation devices and instruments for feet and ankle as extremities.

### *Summary*

How we define extremities could have huge effects on how companies and customers view this market's share of the orthopedics industry. If we limit our definition to implant products, we estimate the value of the extremity device market to be over $700 million. However, if we include trauma products and sports medicine products in our definition of extremities, we estimate the total market to be over $3 billion in sales world wide.

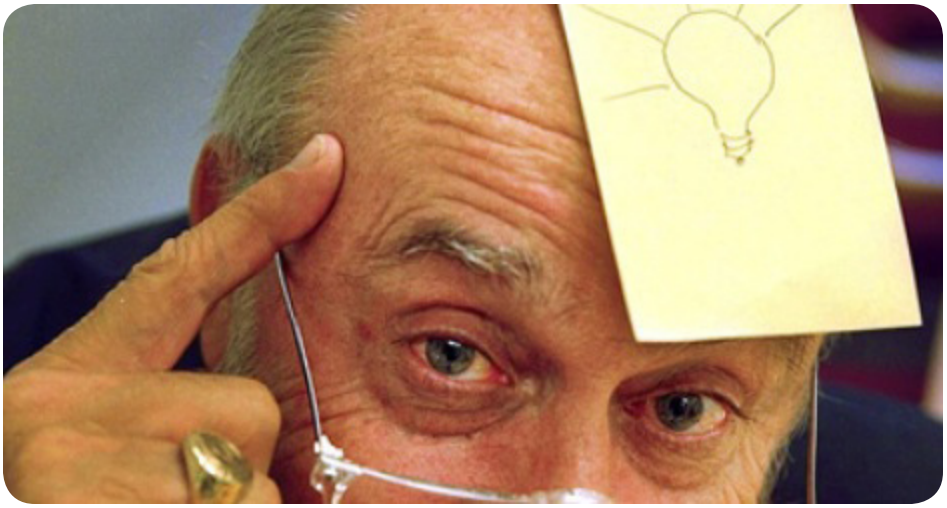
A change in categorization would also dramatically impact the market share for each company. For example, Synthes, with close to 50% market share worldwide in the trauma treatment market, would stand to make substantial gain in the extremities device market with a more inclusive definition of extremities. Smith and Nephew, ArthroCare, Arthrex and DePuy also play major roles in the sports medicine market which could add to their share of the extremities device market. Wright Medical might lead the foot and ankle device market in sales, but that could change if companies like DePuy start to report plating, screws and other fixation products as extremity devices. Based on how the extremities device market has been defined by each company, chart 2 shows the market shares for the second quarter of 2009.

So is there a solution to these discrepancies? In order to give companies (and customers) a true measure of market share, the leaders of the extremities device companies could meet to devise a standard definition of the small joint extremity device market in orthopedics. It might sound like a long shot, but it also might be in the best interest of these companies to work together to find a standard definition before one company defines extremities for everyone.

For other articles by this author, please select the following link: http://www.pearldiverinc.com/pdi/ext.jsp

# New Device Idea? Seek Help

**By Daniel Knowlton**



Eureka! You've just thought of a new way to improve that device you use in almost every surgery. Great. Now what?

Full-time physicians are busy people. And when a physician does come up with an idea for the advancement of a medical tool or device, that idea often ends up buried at the bottom of a long "to-do" list. Yet the relationship between physician inventors and industry remains at the core of medical device development. Doctors bring new ideas to companies (and vice versa), and this interchange brings new approaches to surgery and improvements to old technologies.

So how does an idea become a fully realized product? The development path can be full of speed bumps and dead ends, and it helps to have a guide along the way.

## Helping Ideas Become Reality

In an effort to move his own ideas into the market while also helping other physician inventors navigate the path of device development, Dr. Stephen Snyder co-founded a company called Redyns Medical, LLC with his son Nate Snyder and colleague George Rohlinger.

*Nate Snyder*
*Redyns Medical LLC*

Back in 2005, Redyns Medical was nothing more than a school project. Nate Snyder explains, "I was in business school at the time studying health care entrepreneurship, and I needed a thesis to work on for an assigned project. Dr. Snyder had a patent sitting in the back of his desk that he had shopped around to a bunch of companies but couldn't get any traction on it…So we took that patent and made a business plan around it." That plan resulted in the successful development of a whole line of post-operative dressings called ProWick, and Nate Snyder's school project became a budding new company.

If you consider Dr. Snyder's first contributions to device development, however, the roots of Redyns Medical go back much farther. Dr. Snyder: "I had the fortune, good or bad, of coming into the field of shoulder arthroscopy 25 or 30 years ago when there really wasn't any shoulder arthroscopy equipment or tools. There were very few people even dabbling in this technique. So I had the choice of either giving up and going back to the knee or helping develop equipment. The companies didn't yet know what we needed, so I got into the product development business right from the very beginning."

When it comes to getting a company's attention, however, even three decades of experience in device development might not count for much. "In many of these companies, it's almost like they have a revolving door. A new engineer comes in, he or she works for a few years, does a good job and then leaves. The next person to come in doesn't recognize the history I've had with the company, so any new ideas I bring in go right to the bottom of the list. Despite this history, I'm still part of the masses scrapping for a spot on the development ladder."

*Stephen Snyder, M.D.*
*Redyns Medical LLC*

"We realized," says Nate Snyder, "that if Dr. Snyder is having difficulty getting ideas evaluated and given a fair shake in industry, other inventors who don't yet have his experience must be struggling with many of the same issues. And we have found that to be true. Doctors are having a tough time getting to industry in this economy with just an idea. The engineering resources might be too slim or stretched, or the departments evaluating the technology don't have enough clinical experience to see the forward looking benefit of a technology."

Even if a company has all the resources in the world, physicians still might not have the means to move their ideas forward. "So often physicians will come up with an idea, and it might be left in their head or on a napkin," says George Rohlinger. "Then it gets stuck in the top drawer. When you have a day job and sometimes a night job, there isn't a lot of capacity in your day to advance these ideas. So we feel that Redyns Medical is like a catalyst to help physicians take their ideas beyond the top drawer of their desks." By helping physicians further develop their ideas and by helping companies understand why and how these ideas work, groups like Redyns can help physicians and industry see eye to eye.

*George RohlingerRedyns Medical LLC*

## A New Focus

When seeking guidance on a new device design, physicians and companies also need to consider how much the device development business has changed over the years. Newcomers to the field might find today's market to be significantly different from the one their mentors remember.

In Dr. Snyder's field of shoulder arthroscopy, for example, the focus has shifted from macro to micro. Dr. Snyder: "Many, many of the products that are necessary to do these reconstruction surgeries are now on the market, and each company seems to have their variation of anchors, stitchers and even suture material, but improvement still remains. Nothing is ever static. But now it's more difficult to get a company to see that this little change in the product or this improvement might be worthwhile."

Despite the difficulties, making even the smallest positive change in a device is vital to advancing the field. "We had dozens of wonderful products that allowed us to move forward in arthroscopy," adds Dr. Snyder, "but it's still a difficult surgery…Now the idea is to make it more available to general orthopedists who have a knowledge of arthroscopy and want to do a sophisticated surgery without having to open the shoulder. So it's now into the refinement mode rather than the gross development mode like it had been."

## Working Under Strict Scrutiny

Certain government offices are also focusing on refinement, not necessarily of medical devices but of the physician/industry relationships which produce those devices.

New oversight from the Department of Justice on physicians and orthopedic device companies opened the door on all the skeletons in the closet. Company budgets have become the object of strict scrutiny, and now every dime spent needs to get value in return. For example, companies can no longer legitimize paying for dinners and hotel rooms for a physician consultant's family during business trips. This of course seems honest and just in the midst of a recession where everyone is tightening their financial belts.

But all that scrutiny can be overwhelming.

Dr. Snyder fondly remembers a time when inventing new products seemed less complicated. "In the old days, we had freedom to get together at meetings or on weekends

and brainstorm new ideas for product development. It was a nice opportunity to work together with industry as well as some other creative physicians whom we may not have had an opportunity to interact with previously."

Unfortunately, in Dr. Snyder's opinion, "those days are over."

"The government oversight is going to make it really difficult to ever have the same type of relationship with industry that was present in the past for innovators," says Dr. Snyder. "Our project development meetings seldom occur and everyone is frightened of being implicated and/or indicted in a forbidden relationship. I'm hoping things will get better, but so far, I believe it has taken a toll on collective creativity."

So the physician/industry relationship has changed for the better and for the worse, but with plenty of new applications for approvals and clearances knocking at the FDA's door, there must still be a wealth of functioning physician/industry relationships. How do doctors and companies find ways to channel their creative ideas in today's challenging and scrutinized development business?

## Advice for Physicians

"The best advice is to seek advice," says George Rohlinger. "I know that sounds simple, but the product development pathway is not a straight path. It's riddled with choices and requirements. You can have a terrific idea or a new way of doing something, but can you engineer it? Can you manufacture it? Is it cost-effective? Is it an idea that's already out there?

Is there a customer for it? Finding someone with specific expertise in actually developing a product and getting it to the finish line is really important."

If you have a contact in a major device company, however, speaking with him or her about your new idea might actually be counterproductive. "Many inventors come up with an idea and call industry the next day," says Nate Snyder. "Without proper legal protection, you can lose the exclusive rights to your idea, and as a result, lose the ability to capture the full financial potential of your idea."

When you are ready to make the call, make sure you target the right companies and get the right person on the phone. "Getting the right access is important and really difficult," says Rohlinger. "Many of these companies are quite large now; they have hundreds and hundreds of products and hundreds and hundreds of employees. Understanding the nuances of all these companies is really important; every idea may not be right for every company. And if you wanted to call DePuy today, for example, who do you call? Gathering all of this information and networking takes a lot of time, but fortunately, we have the industry knowledge and know who to call."

Groups like Redyns can also help physician inventors turn that one phone call into several calls. "There's nothing better than competition to maximize the value of your idea," says Rohlinger. "If a surgeon calls company X and says 'I've got an idea,' now company X has that idea. Compare that to a scenario where the surgeon works with a firm like Redyns Medical, advances the product up the

value chain, and rather than simply calling company X, calls companies X, Y and Z. Now we've got multiple parties involved and we've created a competitive market dynamic to gain a better appreciation for what industry thinks your idea is worth."

## Advice for Industry

Physician inventors aren't the only ones who might seek guidance, and companies like Redyns can also give advice to industry. Nate Snyder advises companies to not limit their consultations to only the expert surgeons. "Industry primarily consults with the most skilled surgeons in the country. Dr. Snyder is one of them. There are things that Dr. Snyder can do that most surgeons can't do. But industry really isn't making products for the top 1%. They are trying to capture the broader market, who have a different skill level."

"You have to have the best and the brightest as some of your industry consultants," he continues. "I think that's really important, and that's where a lot of the innovation goes. But oftentimes if someone comes up with something that makes a difficult procedure easier for the masses, the top surgeon consultants don't get it. They think, 'well this is easy already. Why do we need that?' An example would be knotless suture anchors. If you've ever watched Dr. Snyder operate, tying knots is not a problem. But we've seen a huge proliferation of knotless suture anchors, and that's geared towards the masses."

Dr. Snyder couldn't agree more. "We have to gear things towards the masses because those are the people that are out there trying to do the work. If we don't do that, it will not only lead to patients having surgery that is not done well, but it will slow the growth of the entire specialty and limit it to people who have done fellowships or have had extra training."

Dr. Snyder imagines a future where new devices help general surgeons complete complex operations. "If you need a specialized surgery done in Smalltown, USA, you won't need to fly all the way to the big city because new technology will enable surgeons of all skill levels to perform the procedure. That's what I'm excited about."



## What's Next for the Device Development Business?

"The biologics are going to be a real big deal," says Dr. Snyder. And the physician/industry relationship will still be an important part of the development process. "Biologic development is going to be slow so we have to maximize what we can," he continues. "Without the means to apply these biologics and follow them clinically, they really don't have any value."

Dr. Snyder and his Redyns Medical team are working on their own ways to add value to a time tested biologic: allografts. "Allografts have been around for a while, but good allografts haven't been around that long," says Dr. Snyder. "There is now just a small handful of companies led by one (Wright Medical) who are capable of supplying us in the shoulder business with a cryopreserved (not freeze-dried) biologic graft from human dermis or skin. We can use these grafts to completely replace and/or augment, whichever is necessary, a massive non-repairable or minimally repairable rotator cuff. We do it arthroscopically using all these tools that we've been working on for 30 years. This is kind of the zenith now of the whole rotator cuff repair business."

"This allograft repair method is on-label for rotator cuff augmentation, but it still hasn't been blessed by the FDA for complete rotator cuff replacement," continues Dr. Snyder. "So we're developing the techniques, the technology, and the follow up to help the FDA see the bad and the good of it. So far the numbers are pretty phenomenal. Now we have people with a new rotator cuff who wouldn't have had one before, and that's the thing that I'm really excited about now."

Just as government oversight scrutinized the physician/industry

relationship, government policies will continue to alter the device development business. “Obamacare is going to make a big difference,” says Dr. Snyder. “It’s expensive to use biologics, and somebody’s going to have to tell the world where the cash is going to come from, or if it’s going to come. So medicine might undergo a great big change, and it may just be a change that flows down the development of these new products.”

In the meantime, while congress works out health care legislation, physicians and industry will continue to work together to bring new ideas into fruition. Companies might not realize when a new product or an improved device is worth development, and physicians may not think they have the time or the knowledge to develop their own ideas, but with the help of an expert guide, new inventors and budding companies alike can navigate the bumpy road of medical device development.

company news

## CONMED: Voluntary Recall

What could be better than proactivity paired with responsibility? In a recent display of such corporate accountability, CONMED Corporation's CONMED Linvatec unit recently instituted a voluntary recall for certain model numbers of the PRO5 and PRO6 series battery handpieces manufactured prior to May 31, 2008. They did the same for certain lots of the MC5057 Universal Cable manufactured prior to December 1, 2006 used with certain of CONMED Linvatec's electric powered handpieces. The company sent Medical Device Safety Alert letters to customers dated July 31, 2009 providing information on findings from its ongoing continuous quality improvement process.


As indicated by the company, those customers having purchased the PRO5 and PRO6 handpieces were notified about the unlikely possibility that units may self-activate. The letter also reminded customers that safe and effective use of the handpieces includes inserting the battery away from the operation site along with not touching or coming into contact with moving parts while inserting the battery, and to follow recommended handling and user instructions. These customers are also being provided with the affected serial numbers so that they might contact CONMED Linvatec to schedule the return and service of their units. Units manufactured and distributed AFTER May 31, 2008 are not affected.

In the MC5057 Medical Device Safety Alert Letter, CONMED Linvatec notified customers about the unlikely possibility that cables manufactured prior to December 1, 2006 might cause an electric powered handpiece to potentially self-activate. The letter instructed customers to avoid moving parts on the handpiece when the cable is inserted and to follow recommended handling and user instructions. The company is notifying customers that have the affected MC5057 Universal Cable so that they might contact CONMED Linvatec to schedule the return of their cables for replacements. MC5057 Universal Cables manufactured and distributed AFTER December 1, 2006 are not affected.

As indicated by the company, while there is the remote possibility that self-activation could cause injury, CONMED Linvatec has received no reports of any injuries with respect to the PRO5 or PRO6 handpieces; they have received no reports of injuries to patients from the cables. There were, however, two reports of non-serious injuries to medical personnel, with both reports occurring in 2006 in situations in which the users did not follow the instructions for use.

Robert Shallish, CFO of CONMED Corporation told *OTW,* "Customers using powered instruments need to be diligent and follow the manufacturers' recommendations on preventive maintenance procedures and schedules to ensure optimum performance of their devices. We need to break the 'use to failure' mentality around using it until it breaks. We would rather have a proactive approach toward powered instruments to avoid this type of situation."

The company recommends that anyone encountering a handpiece behaving erratically should cease using it and contact customer service at CONMED Linvatec; they should also refrain from using cables with excessive wear or damage, and engage in routine preventive maintenance

Regarding the company's quality improvement process, Shallish told *OTW,* "We trend user feedback as part of the voice of customer process to ensure we are optimizing performance of our products. We see this as an important consideration in the quality process and strive for a continuous improvement approach as a component of our CAPA [Corrective Action and Preventive Action] program."

*—EH (October 7, 2009)*

company news

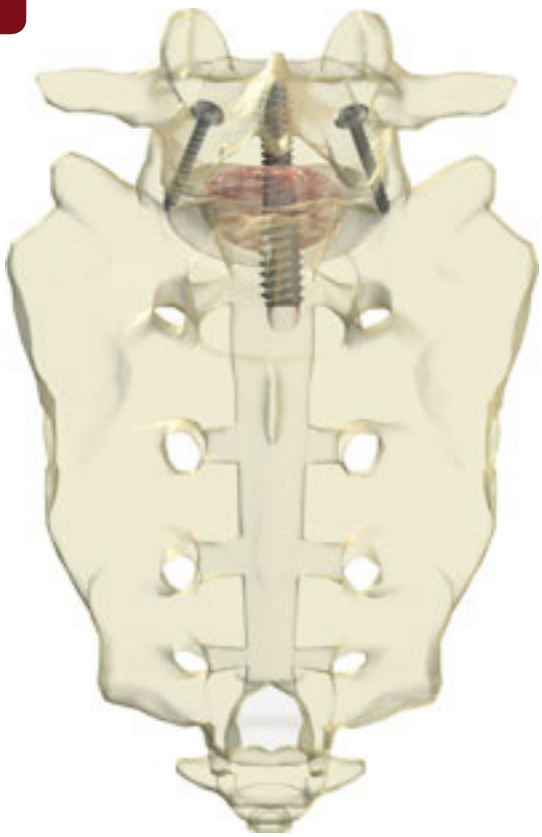
## TranS1's Reimbursement Uncertainty

TranS1, Inc. announced on October 6 that its 2009 third quarter revenues will be short by approximately $500,000 of previous guidance due to reimbursement uncertainty.

The company said it expects revenues to come in at $6.8 to $6.9 million. Previous guidance had pegged expected revenues from $7.4 to $7.9 million.

Rick Randall, President and CEO said, "Our results this quarter were impacted by continuing concerns and uncertainty in the marketplace surrounding reimbursement for our AxiaLIF procedure, which we are addressing with increased education and support resources for our current and prospective surgeon users. While we are disappointed that our third quarter revenues are below previously issued guidance we remain confident in our products, clinical benefits and prospects for future growth as the market for minimally invasive spine surgery continues to expand."

Wells Fargo Senior Analyst Mike Matson wrote in an investor note on October 7, "Management cited ongoing reimbursement challenges now that its AxiaLIF can no longer be billed as an anterior fusion (or ALIF) and must instead be billed as a Category III CPT code. Many insurers view Category III CPT Codes as experimental and will not pre-approve



*TranS1 AxiaLIF360/Courtesy TranS1*

the procedure or refuse to pay the code."

Matson expects reimbursement to continue to hamper growth until the company obtains a Category I CPT code which could, he says, take a year or more.

The new revenue numbers represent an approximate 15% growth rate over the previous year's quarter. While revenues will not meet expectations, Matson says that due to cost controls he expects the company to beat his 2009 earnings estimates.

TranS1 continues to have a strong cash balance and will end the third quarter with $61 million of cash after using around $5 million in the quarter. At this burn rate, estimates Matson, the company has 12 quarters worth of cash.

Full third quarter results will be provided after the close of trading on October 29, 2009.

*—WE (October 8, 2009)*

## US Spine Launches Phantom Plus

US Spine has announced the availability of its next generation of instrumentation and implants as a compliment to the company's posterior fixation systems.

The company launched the Phantom Plus Interbody Fusion System on October 6. The Phantom, along with the company's Facet Gun and upcoming Javelin MIS Locking Facet System, will be part of hands-on demonstrations at this year's North American Spine Society Meeting in San Francisco, California, in mid-November.

According to the company's announcement, features of the Phantom system include tapered leading edges for easy insertion, a higher degree of doming to more closely match endplate anatomy, anti-migration teeth, and advanced instrumentation for multiple insertion techniques. The implants are made from PEEK-OPTIMA polymer from Invibio and are available in several geometries.

company news

This is US Spine's proprietary entry to the interbody fusion cage market, which the company estimates to be nearly $1 billion in annual sales.

Paul Sendro, the company's Executive Vice President of Sales and Marketing, said:

> "Achieving product independence has always been a goal for us. This is an important milestone in our growth as a spine company. We now have full control over our entire product range."

While the company has achieved this milestone, there have been rumors regarding the company's management.

## Company Addresses Blog Rumors

*OTW* asked the company about a recent blog that reported that Paul Sendro was working as a consultant with a six-month contract. In addition the blogger wrote of rumors that all regional managers were terminated along with the educational staff and only East and West coast managers were left at the company. Finally, the blogger—the Spine Blogger—wrote that there was "scuttlebutt" about US Spine's board directors attempting to displace Doris Blake as the CEO of the company.

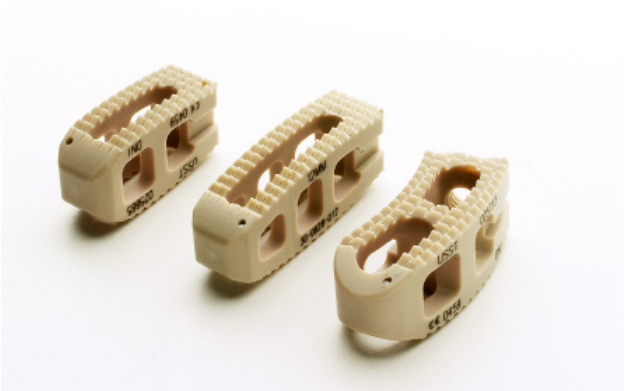
US Spine told *OTW* through a spokesperson, "Paul Sendro was brought to US Spine to help manage what the company considers a potentially rapid growth phase, with several new products about to be added to the company's product offering selection. Paul is indeed a consultant at present—while the company is finalizing his employment agreement. He was appointed a board member of the company in July 2009."

"Currently, US Spine has eight sales professionals, an increase of four from May, to support the company's growing sales. US Spine continues to have two professional education professionals."

"Doris Blake is involved in the company she helped create from a Vice Chairman position and has delegated day-to-day responsibilities to a team she trusts to take the company to the next step forward in its growth."

US Spine is a privately held company whose development efforts are focused on facet technologies that address open, MIS and motion preservation procedures.

*—WE (October 12, 2009)*



*US Spine's Phantom Plus Interbody Fusion System/Photo: US Spine*

## Biomet, Off To Fast Start in 2010

Biomet says it began its 2010 fiscal year highly encouraged and motivated by market share gains. As the first company to report quarterly sales, Biomet is always watched closely by competitors and analysts to see how orthopedics fared during the quarter.

Biomet's President and CEO Jeff Binder said in an October 9 press release, "We began fiscal year 2010 with an encouraging quarter. I'm particularly pleased with our global sales growth [constant currency] of 9% for orthopedic reconstructive devices, 10% growth for knees, 23% extremity sales growth and the 17% growth rate for spine. Additional product categories that recorded double–digit sales growth during the first quarter include craniomaxillofacial fixation, sports medicine devices and softgoods and bracing products."

The company's reported net debt balance at August 31, 2009, was

company news

$6.010 billion, with cash on hand of $226.4 million. Since going private in 2007, reported net debt has decreased $134.9 million.

| Biomet | 1Q10 Revenues (in millions) | % Change |
|---|---|---|
| Reported Revenues | $630.0 | up 4% |
| Reconstructive | $462.0 | up 5% |
| *Knees* | | *up 6%* |
| *Hips* | | *up 2%* |
| *Extremeties* | | *up 18%* |
| Spine | $59.3 | up 15% |

*Source: company reports*

## Knees

Knee revenues, on a reported basis, grew by 6% for the quarter. Key products during the quarter included the Oxford Partial Knee System, the primary and revision versions of the Vanguard Complete Knee System, E1 antioxidant infused tibial bearings and Regenerex porous titanium components, as well as the Signature Personalized Patient Care program.

## Hips

Hip revenues, on a reported basis, grew by only 2%. Key hip products were key press–fit stems, including the traditional and Microplasty versions of the Taperloc Hip Stem, the Echo Hip Stem options, and the Bi-Metric and Aura Hip Stems in Europe; key acetabular products included the Biolox delta Ceramic Femoral Heads, the M2a-Magnum Tri-Spike Cups, Ringloc and Regenerex Ringloc Cups, E1 antioxidant infused acetabular bearings, and Freedom Constrained Liners, as well as the Exceed ABT Advanced Bearing Technologies Acetabular System that is available in Europe.

## Extremities

Extremity device sales increased 18%, on a reported basis, as a result of "very strong demand" for the Comprehensive Shoulder System, the Discovery Elbow and the ExploR Modular Radial Head. In Europe, the T.E.S.S. Shoulder also contributed to extremity sales growth.

## Spine

Reported spine sales increased 15% due to balanced growth in both the spine hardware and spinal stimulation product categories during the first quarter. The key growth drivers for spine sales included the Solitaire Anterior Spine System, the Polaris Deformity System and the MaxAn Anterior Cervical Plate System, as well as non-invasive spinal stimulation devices.

## Patients and Taxes

During a question and answer session with analysts, Binder was asked about the catalysts needed to get patients back in for orthopedic procedures.

Binder noted that while procedure volumes have stabilized, knees had remained steady while hip procedures declined. He said it confounded conventional wisdom in that one would have expected knees to be more sensitive to market conditions. Binder cited four points that the company was watching to gauge future procedure volumes: consumer confidence; employment rates in the under-65 population; the slowing of procedures due to possibilities of healthcare reform; and positive demographics. He was confident that demand, which has been dampened, will be back.

When asked about a proposed $4 billion tax on device manufacturers, Binder said such a tax would "lead us to significant cost reductions." He was hopeful that the proposed tax would be eliminated or modified.

Encouraged and hopeful is a good way to start the year.

*—WE (October 14, 2009)*

# DePuy Pulls J&J's Wagon

Once again, DePuy pulled Johnson & Johnson's revenues along for the quarter.

J&J announced on October 13, that DePuy's reported revenues were up 4.3% for the third quarter, with knees rising 4%, hips up 6% and spine climbing 11%. Total DePuy revenues were $1,231 million.

| DePuy | 3Q09 Revenues (in millions) | % Change |
|---|---|---|
| Reported Revenues | $ 1,231 | up 4.3% |
| *Knees* | | *up 4%* |
| *Hips* | | *up 6%* |
| *Spine* | | *up 7%* |

*Source: company reports*

## company news

*Photo: Heufuhr im Engadin um 1900 / Wikimedia Commons*

J&J's total medical device sales of $5.8 billion exceeded Wall Street estimate by about $174 million. While J&J beat earnings expectations, investors were disappointed by total sales that came in below consensus by anywhere from $100 million to $200 million.

Dominic Caruso, J&J's CFO, was asked about pending legislation which would raise taxes on device manufacturers to cover more patients.

Caruso's moderate response was noticeably more nuanced then other device industry leaders who have warned of significant spending cuts if any tax is passed. Dominic told analysts on a conference call that J&J favors the Baucus bill over the other four bills currently approved by congressional committees. "We're supportive of sharing costs," said Caruso. But as currently written, the legislation is "unfair and excessive."

At a market size of $125 billion, Caruso said a 3%–4% tax is significant. "Hopefully the tax will be moderated."

The company would not comment on its ability to offset the fee with spending cuts or price increases. Senior analyst Larry Biegelsen of Wells Fargo wrote on October 13 that he believes the fee will eventually be reduced to about $2 billion per year. "This would negatively impact J&J's EPS by a manageable -1.4% in 2010."

DePuy's results follows Biomet's hip and knee results which were moderately below calendar 2Q due to tougher comps. Bank of America analyst Bob Hopkins wrote that, "Based on the Biomet and JNJ results our preliminary read on ortho is that we are unlikely to see any major changes in market growth this quarter, with constant currency growth remaining in the 3%–4% range."

*—WE (October 15, 2009)*

## legal & regulatory

### FDA Questions Dynamic Stabilization

The FDA is requiring manufacturers of 16 dynamic stabilization devices for spinal fusion to conduct new postmarket surveillance studies.

In an October 5 statement, the agency said: "Currently there is not enough clinical data to determine whether the devices provide enough spinal stability to allow for complete spinal fusion."

Industry executives contacted by *OTW* said this was not completely

unexpected as the agency attempts to clamp down on "off-label" marketing of 510(k) cleared devices that have not demonstrated successful fusion with their motion preservations devices. This action also follows an FDA announcement a week ago that it has asked the NIH (National Institute of Health) to review its entire 510(k) clearance program. The agency has been under heavy pressure from consumer groups, Congress and internal "whistleblowers" who believe the FDA has been too lax in clearing devices.

The FDA cleared the first dynamic stabilization system component in 1997 and has cleared numerous dynamic stabilization systems or components since then. FDA has only ordered postmarket surveillance studies for the class II dynamic stabilization systems and components, which are intended for bone fusion.

Dynamic stabilization systems are used in spinal surgery and some are intended to provide stabilizing support to the spinal column during bone fusion. However, the agency believes the system components may loosen, bend, or break over time. If fusion does not occur, a patient's condition could worsen and possibly require additional surgical procedures.

The FDA is requiring postmarket studies to address these potential risks for systems already on the market. In addition, the FDA is requesting manufacturers with new dynamic stabilization systems or components to submit clinical information for agency review prior to marketing.

## No Changes for Now

No changes are recommended regarding the use of systems until the FDA collects and reviews enough clinical data to have a better understanding of how the devices are used.

The timing of the announcement comes just one month before Zimmer is scheduled to present their Dynesys Spinal System before the FDA's orthopedic panel.

Zimmer spokesperson Brad Bishop told *OTW* that the FDA action does not directly impact the Dynesys PMA submission. "We are seeking approval for a 'non-fusion' indication and these letters address use in fusion procedures."

This announcement may be seen favorably by some dynamic stabilization makers currently conducting clinical trials and have not yet requested PMA approval from the FDA.

The FDA has required the manufacturers to address the following:

- the fusion rate for dynamic stabilization systems compared to traditional stabilization systems;
- the incidence rate, severity, and time course of adverse events for dynamic stabilization systems compared to traditional stabilization systems;
- the type, incidence rate, and time course of subsequent surgical procedures for dynamic stabilization systems compared to traditional stabilization systems;
- the cause of failure for dynamic stabilization systems based on analysis of all reasonable available systems that have been removed from patients, along with any association between the patient's demographic and clinical data and the device failure.


After the FDA reviews the clinical data gathered from the postmarket surveillance studies, it will consider whether labeling changes or additional preclinical and clinical testing requirements are required.

—*WE (October 6, 2009)*

## Dynasys Goes to Ortho Panel

The FDA's Orthopaedic and Rehabilitation Devices Panel of the Medical Devices Advisory Committee will hold one of their rare meetings on November 4 to consider Zimmer's Dynesys Spinal System.

## legal & regulatory

According to Zimmer's Web site, "The Dynesys Dynamic Stabilization System combines the surgical approach of traditional fusion with the philosophy of dynamic stabilization, using flexible materials to stabilize the spine while preserving anatomical structures. The result is dynamic stabilization that allows the surgeon to preserve much of the spinal anatomy. It accommodates a familiar surgical approach and minimally invasive techniques in a range of patients—including those with acute and chronic instabilities caused by degenerative changes in the intervertebral discs."

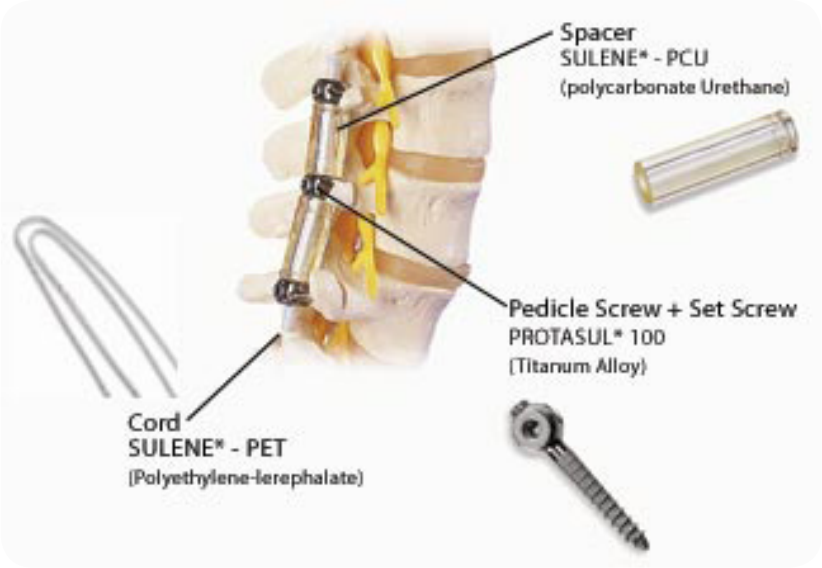
The Committee will discuss, make recommendations and vote on Zimmer's premarket approval application. The FDA will then make a final determination on approval of the device. Zimmer's application states the system is indicated to provide spinal alignment and stabilization in skeletally mature patients at one or two contiguous levels from L1-S1.

This Panel meeting takes place 30 days plus one after the FDA issued Post-Market Surveillance (section 522) orders to all companies with marketing clearance for "dynamic stabilization systems" intended to provide support to the spine during fusion. Zimmer received letters for the Dynesys System implants, which are cleared for use in fusion procedures.

Zimmer spokesperson Brad Bishop told *OTW* that the FDA order does not directly impact their PMA submission as they are seeking approval for a non-fusion indication. The FDA request addresses dynamic stabilization in fusion procedures.

The FDA will make background materials available to the public no later than two business days before the meeting on its Web site, www.fda.gov/AdvisoryCommittees/Calendar/default.htm. Scroll down to the appropriate advisory committee link.

—*WE (October 8, 2009)*




*Zimmer's Dynasys System/Zimmer Spine*



## biologics

### Bone Growth Breakthroughs

It has been an exciting few weeks for stem cells. Many biologic companies and research teams have found various ways to harvest mesenchymal stem cells and turn them into bone-forming cells to aid in healing bones, and some patients are now starting to enjoy the real benefits of the research.

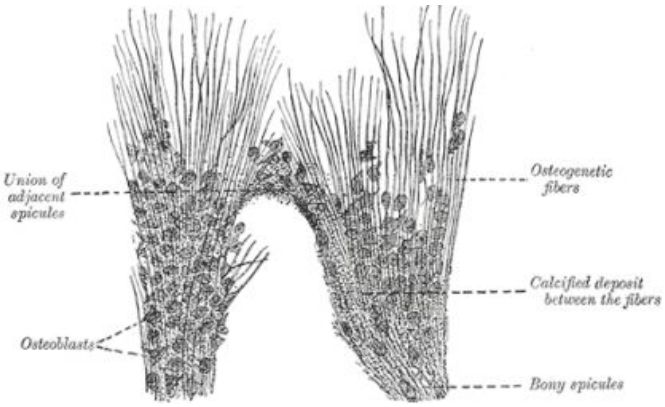
#### Two Patients With New Bone Tissue

In Southampton, England, Carl Millard, age 44, recently avoided a second hip replacement operation

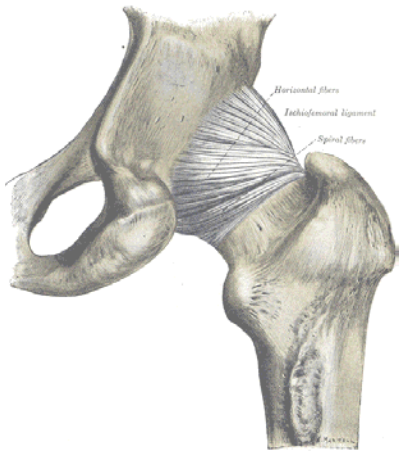
## biologics

with the help of a new stem cell procedure. Steroids used to treat his vasculitis slowly ate away at the bones in his joints until Millard needed to replace one hip with an artificial joint. When Millard's doctors realized that his other hip might face the same fate, Millard agreed to try a new stem cell based alternative.

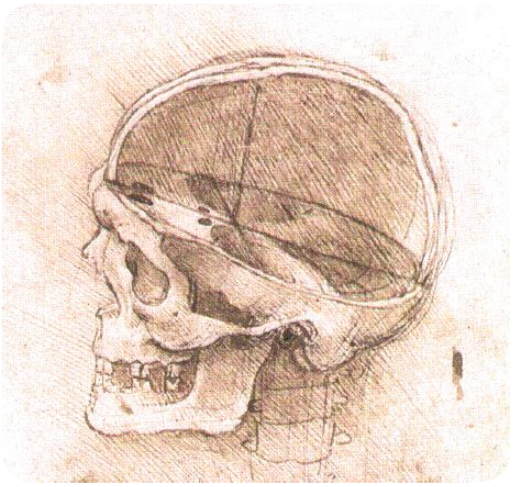
According to the *UK's Daily Express* ("My Surgery-Free Hip Replacement" September 29, 2009), Dr. Doug Dunlop harvested bone marrow stem cells from Millard's pelvis and mixed the purified stem cells with bone tissue donated from a hospital bone bank. He then cleaned out the dead bone tissue on the ball of Millard's hip joint and replaced the bone with the stem cell and bone mixture. So far, Millard is healing well. His hip bone grew a new blood supply and new bone marrow cells so that his body can continue to replace the bone he lost through his vasculitis treatment. This makes Carl Millard one of six NHS (UK's National Health Service) patients to receive this treatment at Southampton's Spire Hospital. The research team who developed the procedure, led by Professor Richard Oreffo of Southampton University, hopes to broaden their study with more patients in need of similar treatment.




Stateside at the Children's Hospital Medical Center in Cincinnati, another patient benefited from stem cell based bone growth. Brad Guilkey, age 15, was born with a genetic disorder called Treacher Collins Syndrome which stops bones from fully developing in the face and the skull. According to *Cinncinati News* ("Breakthrough in Growing Bones" October 12, 2009), Guilkey was born without the bones that form the outer part of the eye socket. Dr. Jesse Taylor, leading a team from the hospital's Division of Craniofacial and Pediatric Plastic Surgery, developed a way to restore Brad Guilkey's missing bones.




Dr. Taylor started with a model of Guilkey's missing facial bones carved from donated cadaver bone. He then harvested mesenchymal stem cells from the patient's stomach fat and a piece of periosteum membrane from Guilkey's thigh. The surgical team then injected the bone with the stem cells using bone morphogenic protein-2 to differentiate the stem cells into bone-forming cells. The harvested periosteum covered the bone implant and provided blood vessels to keep the tissue alive. The surgical team used surgical screws the hold the implant in place on the patient's skull, and a few months later, Brad Guilkey had new living bone and a working blood supply to help the tissue continue to grow.



### Two Laboratory Breakthroughs

In addition to these patient cases, two other U.S. biologic research groups reported recent success in growing bone tissue in the lab with stem cells.

A research team at Columbia University led by Dr. Gordana Vunjak-Novakovic successfully grew part of a human jaw bone in

biologics

their laboratory. The team injected bone marrow stem cells into a tissue scaffold and provided nutrients found in the body's natural bone development process. The result? A fully formed temporomandibular joint (TMJ).

Researchers at the Georgia Tech Center for Advanced Bioengineering for Soldier Survivability (see *OTW*'s "Military Medicine: Marching Ideas into Action"--June 30, 2009) also reported success with bone growth procedures in rats. Led by Dr. Barbara Boyan, the researchers used a nanofiber mesh covered with stem cells to regrow a section of a rat's femur bone in 12 weeks. The team hopes that in just a couple more years they could move on to human trials with some of their new bone growing techniques.

While these two patient cases are still experimental procedures and these laboratory successes haven't yet graduated to human patients, this research continues to move toward a day when stem cell procedures might become commonplace in orthopedic treatment.

*—DK (October 16, 2009)*

## BioMimetic: Positive Results for Augment

On autopilot no more… BioMimetic Therapeutics, Inc. today announced positive top-line results from its North American pivotal (Phase III) randomized controlled trial comparing its fully synthetic, off-the-shelf bone growth factor product, Augment Bone Graft, to autograft for use in hindfoot and ankle fusion surgery. While autograft is the traditional "tool" that orthopedic surgeons reach for, it must be obtained and transplanted from another bone in the patient's body, often requiring a second surgical procedure. Now, says BioMimetic, by using Augment, surgeons can spare patients this additional surgery.

A total of 434 patients at 37 sites in the United States and Canada participated in this prospective, blinded study. The researchers found that patients treated with Augment experienced a similar fusion rate (61.2%) compared with those receiving autograft (62.0%), which met non-inferiority. Since many patients had multiple joints treated, analysis was also performed on a per joint basis. Non-inferiority was also established on a per joint basis, with 66.5% of joints treated with Augment fused on CT scans compared to 62.6% of joints treated with autograft. According to the company, the healing (union) rate was 83.1% for Augment compared to 83.9% for autograft at 24 weeks. The delayed/nonunion rates were 8.8% for Augment and 10.2% for autograft. The remaining patients were judged by the investigators to be progressing to healing but were not able to be definitively diagnosed. Infection rates also tended to be lower for Augment (7.3%) compared to autograft (9.5%). Pain at the autograft donor site was present in 95.6% of autograft patients, while Augment patients do not require a donor site. Substantial pain at the autograft donor site was present at six months in 12.4% of the patients treated with autograft and none of the Augment patients.

A full 75% of patients in both groups had one or more risk factors for poor healing. There were no significant differences in the frequency of serious adverse events between the Augment and autograft treated patients. Analysis of human anti-PDGF antibodies indicated only 13% of Augment patients experienced


*Augment Bone Graft/BioMimetic Therapeutics, Inc.*

biologics

antibody formation at any time point, which dropped to 3.9% at six months. Additionally, 3.5% of autograft patients also had anti-PDGF antibodies. Most importantly, none of the antibodies in either group was neutralizing.

BioMimetic indicates that the data above reflect the results of the 397 patient "modified intent-to-treat" (mITT) study population. Thirty-seven patients were excluded from this analysis, 21 of whom were randomized but never treated and 16 who had major protocol deviations which were prospectively identified. Thus, the mITT population represents over 90% of all randomized patients and over 95% of all treated patients.

On a strict intent-to-treat (ITT) population in which those patients who were randomized but never treated are counted as automatic failures, 24-week fusion rates on CT scans were 57.9% for patients randomized to Augment and 60.4% for patients randomized to autograft. On a per joint basis the CT fusion rate was 65.2% for Augment compared to 64.6% for autograft. Clinical union rate for the ITT population was 79.6% for the Augment group and 79.2% for the autograft group. The delayed/nonunion rate on the ITT population was 8.1% in the Augment group and 10.7% for the autograft group.

"We are excited that our pioneering work at BioMimetic on ways to improve orthopedic and dental tissue regeneration has again translated into a potential new treatment option for patients with significant debilitating injuries or diseases" said Dr. Samuel Lynch, President and CEO of BioMimetic Therapeutics, in the news release. "These top-line data demonstrate a consistent picture that Augment is at least as efficacious as autograft, while also having the benefit of sparing patients the pain and potential morbidity resulting from autograft bone harvesting and transplantation to the fusion site. We look forward to sharing these positive pivotal trial data with the FDA. Finally, I'd like to once again acknowledge the work of our investigators and thank them for their excellent execution of this complex and rigorous trial."

"These top-line results are very exciting," added Dr. Christopher DiGiovanni, principal investigator for the Augment trial and professor of orthopaedic surgery and chief of the division of foot and ankle surgery in the department of orthopaedic surgery at the Warren Alpert School of Medicine at Brown University, Rhode Island Hospital. "The data available thus far support the primary objective of the study which is to find a safe and effective alternative to autograft in foot and ankle fusion surgeries. Should Augment receive FDA approval based on the full data set, I believe it will be widely used by practicing foot and ankle surgeons anxious to spare patients all the pain, potential morbidity, and extra surgical and anesthesia time associated with traditional autograft bone harvest. I look forward to having Augment available for use in patients."

Regarding the appropriate patient for Augment, Kearstin Patterson, Director of Corporate Communications, told *OTW*, "If approved, the product is for on-label use in patients 18 and older who are not pregnant. Also, as with any growth factor product, it should not be used in patients that have an active cancer. So, these three segments will most likely be contraindicated in the final labeling."

A substantial amount of data in addition to the top-line data announced today will be included in the company's PMA submission, which is expected to be filed with the FDA within the next three months.

Commenting to *OTW* on the PMA process, Patterson stated, "As we've previously announced, we submitted the first two PMA modules to FDA earlier this year (pre-clinical and quality/manufacturing). We are in the process of answering FDA questions on the first two modules now and are hoping to have FDA sign off on those when we submit (or shortly after) the clinical module. We plan to compile the recently announced clinical data and send the third and final module to FDA within the next three months. The clinical module will contain much more data than announced yesterday. We would expect to have a PMA Panel meeting scheduled for the 3rd quarter of next year. If all goes well, we expect product approval in late 2010, with commercialization in early 2011."

When asked if the company anticipates any issues with doctors

## biologics

transitioning to Augment, Patterson told *OTW*, "We had 60 clinicians involved in this study, and overall everyone has been pretty excited about the Augment product. In fact, many of them have agreed to be involved in the study for our second orthopedic product, Augment Injectable, which is based on the same technology as Augment. Our lead investigator has said on multiple occasions that, if approved, he thinks Augment will be widely accepted by foot and ankle surgeons. Based on feedback from our doctors, Augment handles very much like autograft (the current standard of care), and as a consequence it should not be a huge transition for the foot and ankle surgeons."

*—EH (October 15, 2009)*

## extremities

### Study: Injury Patterns Analyzed

They're getting their kicks from advancing a sport… researchers from the University of Iowa have dived into the details of injuries in swimmers. According to the news release, more than 42,000 male and female swimmers have competed at Division 1 universities in the past 25 years. The researchers in the study set out to close the information gap that exists on injury patterns for these athletes.

In a new study, published in the October issue of the *American Journal of Sports Medicine,* the investigators collected data from 2002-2007 to determine injury patterns and prevention strategies.

"Thirty-seven percent of the injuries suffered by the swimmers in our study resulted in missed time. By analyzing these injury patterns, we hope training programs can be modified to protect and strengthen those body areas that were most often injured, such as the shoulder," said Brian Wolf, M.D., in the news release. Dr. Wolf is lead author and Assistant Professor of orthopaedics at the University of Iowa Hospitals and Clinics.

Analyzing the overall injury rates from 44 male and 50 female collegiate swimmers, the researchers found that there were an estimated 4.00 injuries per 1,000 exposures for men and 3.78 injuries per 1,000 exposures for women. The shoulder/upper arm was the most commonly injured body part, followed by the neck and back. Those who specialized in a stroke other than freestyle had higher rates of injury; freshmen swimmers suffered the most injuries as well as the highest average number of injuries per swimmer. A significant pattern of fewer injuries was also observed during subsequent eligibility years for collegiate swimmers.

"Our research highlights the importance of properly preparing and transitioning freshmen athletes into collegiate swimming through strength training and gradual increases in distance. This is especially true for those athletes unaccustomed to collegiate level yardage requirements in practice and for those who have not previously done strength and cross training activities outside of the pool. Our study noted that 38% of injuries were the result of team activities outside of practice or competition," added Dr. Wolf.

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Regarding what type of modifications should be made to training programs, Dr. Wolf told *OTW,* "The message from our research is twofold. First, the prior training programs of freshmen and incoming new swimmers should be reviewed. Some incoming swimmers may have already been doing training regimens similar to the collegiate level. However, there are swimmers who come into college having never done dry-land cross training or weight work, or done in-pool yardage anywhere close to what is done in college. These athletes need to be gradually introduced to the collegiate training requirements. Secondly, training programs need to be monitored closely and adjusted as necessary when minor injuries occur in order to head off problems before they are significant. These adjustments can only occur if the coaching or training staff are vigilant and are getting feedback from the athletes."

As for the prospects for more surveillance and research, Dr. Wolf told *OTW,* "We are in the process of designing further research into swimming injuries. One study we hope to do would involve injury data from not only the University of Iowa, but many teams at the collegiate level. Secondly, we are looking into screening incoming freshman for information regarding prior training yardage and other training activities to study whether we can lower injury rates in our younger collegiate swimmers."

*—EH (October 5, 2009)*

## Extremity Medical: New Midfoot Fusion Device

Extremity Medical gets "back to nature." The company has just announced the release of the TarsX Intramedullary Midfoot Fusion Device, a product which replicates the natural arch of the foot while delivering significant compression and stability across the joints. As indicated by Extremity Medical, the TarsX system is an intraosseous fixation device that allows surgeons to create a variety of midfoot arthrodeses in each of the five rays while avoiding complications associated with plates.

Christopher W. DiGiovanni, M.D., Professor and Chief of the Division of Foot and Ankle Surgery in the Department of Orthopaedic Surgery, Brown University/Rhode Island Hospital in Providence, Rhode Island, led the design team for this product and commented in the news release, "The TarsX system is a very novel intramedullary device designed to expand the armamentarium of foot and ankle surgeons when faced with the many challenges associated with reconstructing complex midfoot deformity. The intervention is designed to simplify our approach to an historically difficult foot problem which has never been easy to treat."

Jamy Gannoe, President and co-Founder of Extremity Medical, further stated, "The introduction of the TarsX System is an example of Extremity Medical's commitment to delivering specialized solutions to the difficult challenges faced by extremities surgeons."

The TarsX Midfoot Fixation System was approved by the FDA this past April; the company is beginning the limited release of the product in selected centers across the country.

Commenting on the limited release, Scott Hunter, VP, U.S. Sales and Marketing for Extremity Medical, told *OTW,* "We plan to release the TarsX system to 15 centers across the U.S. This includes some of the leading foot and ankle centers in the United States such as Brown University/Rhode Island Hospital and The Cleveland Clinic. We will closely monitor user preferences by maintaining a detailed registry of all procedures."

When asked about the impetus behind the device, Hunter said to

*Extremity Medical: New Midfoot Fusion Device*

extremities

*OTW,* "The TarsX Intramedullary Midfoot Fusion device was designed to give the surgeon another tool to aid in reconstructing the complex midfoot deformities. It was conceived by Christopher W. DiGiovanni, M.D., Professor and Chief of the Division of Foot and Ankle Surgery in the Department of Orthopaedic Surgery, Brown University/Rhode Island Hospital in Providence. The device allows surgeons to fuse a variety of joints in the midfoot while avoiding the complications associated with plates and screws. The devise locks together to reproduce the natural arch of the foot while delivering compression across the joints being fused."

He added, "When designing the implant we set out to make an implant that achieves rigid stability through intramedullary fixation, minimizes wound complications by keeping all incisions on the dorsal side of the foot, and allowed the surgeon to fuse multiple joints where indicated. The devise can also be used in multiple rays across the midfoot to meet the different challenges surgeons face when reconstructing complex midfoot conditions. We also recognized the need to provide advanced instrumentation to make the procedure reproducible and simplify the technique."

As for details on sales and training, Hunter told *OTW,* "Extremity Medical products are sold through a network of independent orthopedic distributors in the United States and around the World. Our sales force in the United Sates includes approximately 40 distributors with roughly 200 sales representatives. Extremity Medical recognizes the need to provide detailed training to surgeons and our training program includes cadaveric workshops, sawbones training, and participation in workshops at major conferences including AOFAS and ACFAS."

*—EH (October 9, 2009)*

## Study: Hold Off on Opioids for Osteoarthritis

Should patients with severe joint creaking reach for what some would consider an extreme treatment? At issue: opioids. Researchers from Europe have just published a new review of the literature…the conclusion? For osteoarthritis patients, more problems than positives with opioids.

Eveline Nüesch, a lead author and research fellow at the University of Bern in Switzerland, told *OTW,* "We were surprised that opioids lead to only small to moderate reduction of osteoarthritis pain and would have expected larger effects. Increases in dosage did not seem to enhance the analgesic effect. In addition, the small to moderate benefits were outweighed by considerable increases in harms. Patients given opioids were much more likely to stop their treatment because of side effects, compared to patients who received placebo."

Also commenting to *OTW* was Peter Jüni, a Professor of Clinical Epidemiology at University of Bern and the senior author of the review, who noted, "In the US, osteoarthritis is the third most common diagnosis made by general practitioners in older patients, and osteoarthritis is the most common arthropathy to affect the knee. About 25% of adults aged over 55 years experience significant knee pain; and European data indicate that about 10% of these patients receive opioids, particularly if they did not respond sufficiently to other analgesics."

The review appears in the latest issue of *The Cochrane Library,* a publication of the Cochrane Collaboration, an international organization that evaluates medical research. The researchers analyzed 10 studies that included 2,268 patients, and compared the efficacy and safety of opioid pills and patches. Studies evaluated separately the use of oral codeine, fentanyl patches, oral morphine, oral oxycodone and oral oxymorphone in severe osteoarthritis.

The investigators also looked at whether opioid type, mode of administration, or any other factors could explain differences in outcomes. "The effects of different types of opioids on pain relief and improvement of function appeared to be comparable," Nüesch said in the news release. The reviewers found no significant differences in the effects of the drugs according to pain-killing potency, daily dose, treatment duration or follow up. They concluded that it is not advisable to use opioids routinely for these patients, even in the event of severe osteoarthritic pain.

## extremities


However, Roger Chou, M.D., associate professor of medicine at Oregon Health and Science University in Portland, isn't of the same opinion. In the news release, he indicated, "Taking a broader perspective, NSAIDs and acetaminophen aren't particularly effective for osteoarthritis, and other options are limited other than hip or knee replacement—which has its own risks and costs."

Dr. Chou added that it is not yet possible to generalize that potential harm from opioid treatment outweighs potential individual benefit. He said that more research could help enable clinicians "to better identify patients likely to benefit from opioids. We know responses vary, but at this time don't have a good way to predict who will respond better than others."

As for where we stand now in assessing which osteoarthritis patients might be appropriate for opioids, Dr. Chou told *OTW,* "Deciding which osteoarthritis patients might be appropriate for opioids is a challenge. In general, clinicians should consider the likelihood they will benefit (i.e., experience improvement in pain or function), the likelihood of abuse/misuse, and the likelihood of other side effects like nausea, constipation, sedation. The problem is that most of the data we have (and it isn't a lot) is in the area of predicting likelihood of abuse and misuse. We don't have a lot of information on identifying people more likely to benefit from opioids, or more likely to have other side effects. Efforts to predict who will respond to opioids based on demographic or clinical factors or doing things like intravenous test doses and testing pain thresholds haven't really panned out. One day we may be able to do genetic testing or have other ways to identify people likely to respond, but that's a long way away. So right now the general approach is, if a patient with osteoarthritis doesn't have risk factors for abuse/misuse (like prior history of substance abuse) and doesn't have worrisome comorbidities (like very bad sleep apnea) it's reasonable to consider a trial of opioids. The key is that it really should be a trial, meaning that patients who don't respond or who have side effects should be taken off them."

When asked how future research should be structured so as to capture such information, Dr. Chou told *OTW,* "There are a number of ways research could be designed to address this issue. One would be to incorporate evaluation of predictors of response into randomized trials. Of course we would need large trials to get interpretable data. Another would be to use large patient registries and collect information on potential predictors of response."

As for the researchers in Switzerland, Eveline Nüesch told *OTW,* "Currently we do not have and have not applied for funding to do more research on the subject."

*—EH (October 13, 2009)*

## large joints

### Platelet Rich Plasma: Positive Early Results

Round and round goes the centrifuge…but researchers would rather not go round and round…they'd like some definitive answers. According to a new study in the October issue of the Journal of the American Academy of Orthopaedic Surgeons (JAAOS), platelet -rich plasma (PRP), sometimes used in treating some sports medicine conditions, despite promising early outcomes, larger clinical studies are still needed to determine the benefits of its use.

"Some believe that PRP may catalyze the body's repair mechanisms at areas of injury, improve healing and shorten recovery time," said study co-author Michael Hall, M.D., in the news

## large joints

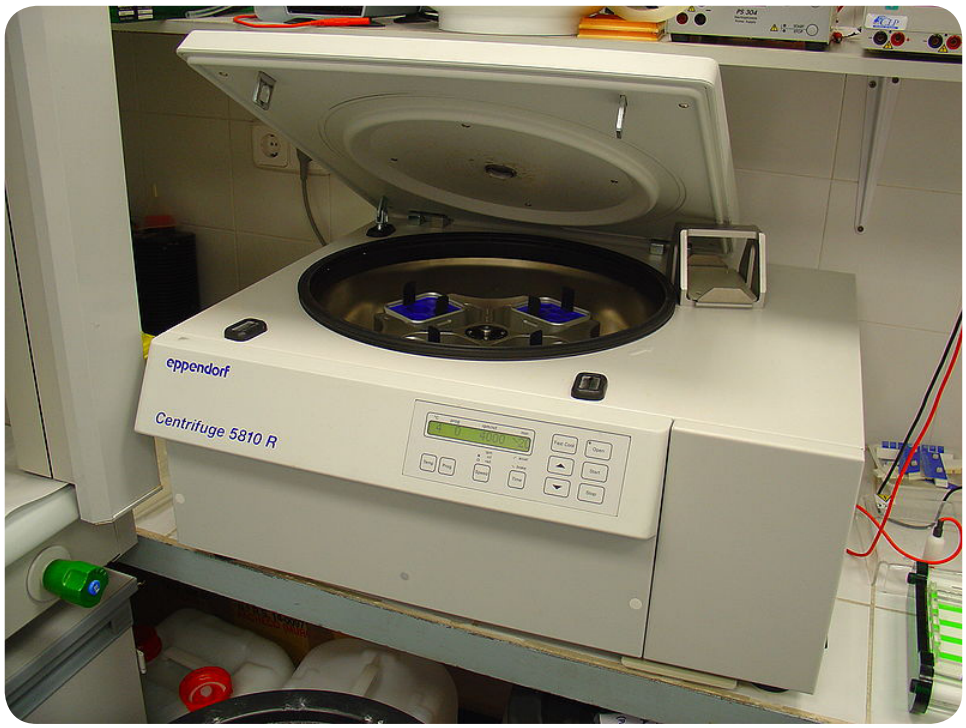
release. Dr. Hall is a senior orthopedic resident at the NYU Hospital for Joint Diseases in New York. He added, "However, there currently is minimal evidence of this clinically and more research must be performed."

PRP involves placing the patient's own blood into a centrifuge, which separates the red blood cells from the platelets. Next, the physician takes the platelet-rich portion of this blood (PRP) and injects it directly into the patient's injured area and the treatment is complete. Increasingly used by orthopedic surgeons, PRP treatments have been used for the past two decades to improve wound healing and bone grafting procedures by plastic and maxillofacial surgeons.

Dr. Hall told *OTW,* "At our institution, the authors have currently performed PRP injections for roughly 20-25 patients in the outpatient setting. We have not had any experience with surgical use. Dr. Dennis Cardone has had the most experience and reports modest improvement in symptomatology in about half of his treated patients."

PRP use in sports medicine primarily has been for the treatment of chronic tendon conditions, but also for acute muscle injuries and for the augmentation of tendon repair in the operating room. The most common applications include tennis elbow, Achilles tendonitis, patellar tendonitis, and rotator cuff tendonopathy.

In the news release, Dr. Hall said, "Use of PRP has increased, in large




part due to new devices that enable fast preparation in the outpatient setting. A patient gives a blood sample and 30 minutes later can receive their injection. There is always a risk of infection with any injection, and some have reported increased pain or inflammation at the injection site, but otherwise the risks with PRP appear minimal."

Also, before embarking on PRP, Dr. Hall suggests trying conventional treatments, such as anti-inflammatory medications, physical therapy, massage, activity modification, bracing and even cortisone injections.

"The bottom line is that there are some studies indicating that PRP may be beneficial in the healing process. Does it really have a positive effect clinically? We don't know," said Dr. Hall. "The good news is that there are a tremendous amount of studies underway. Hopefully, in the next few years, we will be able to help determine the true benefit of PRP."

As for details on these studies, Dr. Hall told *OTW,* "There are studies currently underway testing both non-surgical and surgical use of PRP. Many are being performed in Europe, are multicenter randomized controlled trials and can be found at www.clinicaltrials.gov."

Regarding how widespread PRP use is, Dr. Hall told *OTW,* "I believe PRP is currently an uncommon option to find 'in hospitals' (surgical use) or in the outpatient setting given its cost and lack of insurance reimbursement. It may be more common in large metropolitan areas and does seem to becoming more popular in use."

*—EH (October 6, 2009)*

# $950 for the most popular U.S. Orthopedic Market Reports

## From the Data Guys at PearlDiver

The end of the quarter is here and our boss, Robin Young, is pushing us to get these reports out the door. We just loaded Medicare data into the system. Then we cross-referenced Medicare with our Private Payer datasets. So now he wants us to start selling. With more than 200 million patient records we have the largest, most granular market studies available for U.S. markets. Robin's telling us that we have to move the inventory. Every report listed below is just $950. If you call us individually, we can give you volume discounts. The sooner we can get back to crunching numbers, the happier we'll be. These are great reports and we want to move them out.

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| Spine Procedure | Code |
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| Posterior dorsal fusion | 81.05 |
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| Lateral lumbar fusion | 81.07 |
| Posterior lumbar fusion | 81.08 |
| Posterior lumbar refusion | 81.38 |
| Discectomy | 80.51 |
| Spinal Decompression | 3.09 |

| Large Joint Reconstruction | Code |
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| Total Knee Replacement | 81.54 |
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| Extremity Implant Market Reports | Code |
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| Subtalar Fusion | 81.13 |
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| Rotator Cuff Repair | 83.63 |
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| Open Reduction of Fracture Radius & Ulna w/ Internal Fixation | 79.32 |
| Open Reduction of Fracture Humerus w/ Internal Fixation | 79.31 |
| Open Reduction of Fracture Tarsals & Metatarsals w/ Internal Fixation | 79.37 |

large joints

## More Tears, Surgery in Teen ACLs

"Pop" goes…the knee? Be it sudden torsion, dislocation, or some other insult to the knee, the result may be a tear in the anterior cruciate ligament (ACL). According to a new study published in the October 2009 issue of ***The Journal of Bone and Joint Surgery,*** researchers from Hospital for Special Surgery (HSS) have found that more people are undergoing ACL reconstruction, and that women and younger patients are more likely to need follow up surgery.

The team was working with a dataset with the largest number of patients ever included in a study of ACL surgery. It contained more than 70,000 patients who had ACL reconstruction surgery from 1997 to 2006 in the state of New York. The investigators learned that patients younger than 20 years old, who had an ACL reconstructive surgery, had an 82% increased risk for additional ACL surgery.

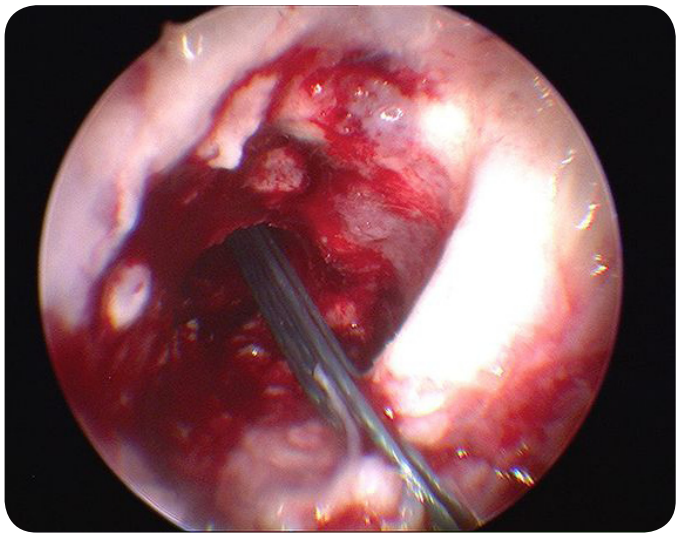
"We found that patients younger than age 40 and female patients are both more likely to have subsequent knee surgery after ACL reconstruction," said study author Stephen Lyman, Ph.D., in the news release. Dr. Lyman is Director of Epidemiology and Biostatistics at HSS in New York.

Lyman and his co-authors determined that the younger the patient is at the time of the procedure, the more likely they are to need additional ACL surgery within one year after having their initial ACL reconstruction. Specifically, they found that patients 30 to 39 years old had a 19% increased risk for additional ACL surgery, while patients 20 to 29 years old had a 43% increased risk for additional ACL surgery.

"We believe that younger patients may be at a higher risk for additional ACL surgery because they tend to be more active and this can lead to graft rupture," added Dr. Lyman. He added that younger patients may be less likely to adhere to rehabilitation restrictions when it comes to high-impact activity.

Regarding how to change this trend, Dr. Lyman told *OTW,* "It is likely that ACL reconstructed young people put more strain on their grafts, because young people are more likely to be involved in competitive, organized sports. Participation drops off substantially after high school/college and again by the time they've reached age 30. As such, they are less likely to attempt to play high demand sports soon after surgery. It is also possible that younger people are less likely to adhere to their rehabilitation protocols in an effort to return to sports quickly. This is not a school-based problem as a very small percentage of school-aged children or adolescents will have had their ACL reconstructed. The training programs for schools would be focused on ACL injury prevention, not treatment/rehabilitation."

One of the factors that contributed to an increased likelihood for subsequent surgery included age. Also, the researchers found that female patients are about 18% more likely than men to need subsequent knee surgery on one of their knees after ACL surgery. Additionally, patients treated by surgeons who don't do many ACL surgeries (fewer



*Arthroscopic reconstruction of the anterior cruciate ligament of the right knee.*

large joints

than six a year), and those treated at hospitals where comparatively few such surgeries are performed (fewer than 24 per year), are at a higher risk for having subsequent knee surgery.

"This trend has also been demonstrated in other surgical disciplines including cardiac and cancer surgery," explains Robert Marx, M.D., MSc, in the news release. Dr. Marx, a co-author of the study and Professor of Orthopedic Surgery at HSS, added, "ACL reconstruction is not an easy operation for someone who does not do it on a regular basis. Patients may wish to consider this information if they elect to undergo ACL reconstruction."

Understanding the risk factors is important because re-injury, requiring subsequent surgery, can be associated with the development of arthritis explained Dr. Lyman. "Just like any medical procedure, there are potential complications with ACL reconstruction and this study gives patients an idea of how frequent those complications can be."

*—EH (October 7, 2009)*

## Using EMG to Predict Knee Problems

Researchers (prognosticators) in Denmark have been active, well, measuring active and resting muscle cells. In a new study published in the October issue of the *American Journal of Sports Medicine,* the investigators found that screening the knee muscles of an uninjured female athlete with electromyography (EMG) technology can determine if they are at a high risk for an anterior cruciate ligament (ACL) rupture. The study is groundbreaking in that it is the first to define a specific muscle group activity that may put a female athlete at risk for an ACL injury.

"An ACL injury for a female athlete doesn't just affect them at the moment of injury; a high percentage of female athletes who suffer an ACL injury experience long-term consequences such as osteoarthritis and disability. This is unacceptable," said lead author, Mette K. Zebis, Ph.D., in the news release. Dr. Zebis, who works at the Institute of Sports Medicine Copenhagen and the Danish National Research Centre for the Working Environment, added, "Our research aimed to evaluate the possible use of EMG recording as a tool for ACL injury risk screening. If we can identify those at risk for the injury, we can help prevent it."

Dr. Zebis and her colleagues utilized EMG to screen 55 uninjured female athletes while they performed a standardized side-cutting maneuver (used to "fake" the defensive player to one direction while the athlete moves in the opposite direction). This particular motion was selected because it is highly common during a game, and a large number of non-contact ACL injuries appear to occur in this situation. Five of the athletes were found to have lower EMG signals in the medial hamstring muscle on the back of their thigh and higher activity in their quadriceps muscle. Those same athletes experienced an ACL rupture later on in the competitive season. Analysis was conducted on each subject's EMG signals and a high-risk zone was defined. Ten individuals initially fell into the high-risk zone, with five of those being the ones who subsequently experienced a non-contact ACL rupture.

*U.S. Women's National Basketball Team*

Dr. Zebis told *OTW,* "The study should be reproduced with a larger population at baseline and accordingly more events (i.e., ACL injuries) to confirm the present finding. The use of EMG is not straight forward. The implementation of the present method involves equipment and software to obtain data, and interpretation of data (i.e., time-consuming and costly). However, if the finding of our study is confirmed, the method should be used as a screening tool among athletes at risk. Implementation of the present method may at first be financed by institutions (e.g., insurance companies and/or sport associations/clubs) who have the interest and economy to help prevent this serious knee injury."

*—EH (October 13, 2009)*

## large joints

### Magnifi Launching Total Joint IEP

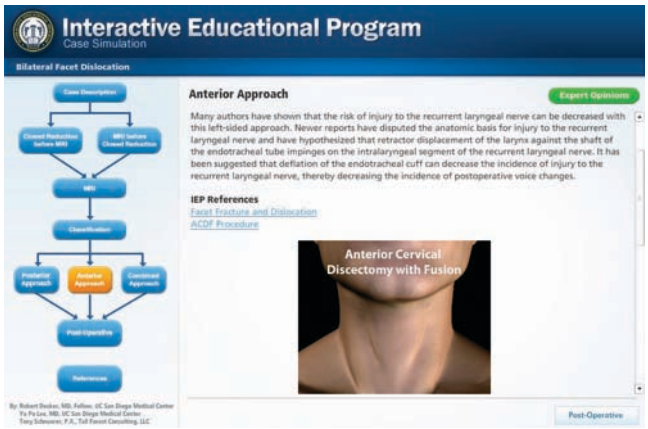
Continuing to knock online education out of the park… San Diego-based Magnifi Group is continuing its didactic hit parade with the rollout of the Interactive Educational Program (IEP) for Total Joint. Chock full of surgeon courses accredited by the Accreditation Council for Continuing Medical Education, the module includes sophisticated 3-D animations and images, and covers everything from basic science, to tumors, to inherited conditions.

Commenting to *OTW* was Andrew Wolpe, President and COO of Magnifi Group, who noted, "Magnifi Group's Interactive Educational Program is adding a Total Joint module in November 2009, a program which will be made available to over 75 fellows at 28 leading U.S. centers. The curriculum, developed by our esteemed Editorial Board—Doctors Thomas Schmalzried, Michael Mont, Javad Parvizi, Vincent Pellegrini, Giles Scuderi and David Hungerford—was developed specifically to meet the educational needs of fellows and includes chapters on hip and knee surgical management."

He added, "The IEP for Spine recently enrolled its second fellowship class, totaling 95 fellows from 38 U.S. spine centers. Through our partnership with the Spine Arthroplasty Society, the IEP Spine user base of practicing surgeons is now over 1,000 with approximately 50% from outside of the United States. The site content has been enhanced with interactive case simulations, courses on hospital guidelines and protocols, and over 15 surgical approach animations. The site includes over 75 CME credits that are available at no charge to surgeons."

The module contains a proprietary online notebook that allows surgeons to rapidly access their personal notes and materials from any computer at any time. Conveniently, surgeons are able to upload surgery notes, documents, images and videos directly into their private online notebook. Surgeons may also access the IEP's Image Library, download images and animations of their choosing, and utilize them for personal presentations as well as patient education.

There are interactive and rendered 3-D surgical animations featuring the latest FDA-approved, product-specific, surgical techniques, as well as a helpful dose of voice narration.




The Total Joint module also includes a forum in which surgeons can exchange ideas with their peers on a real time basis. Any goings on in the total joint universe may be accessed on the IEP Calendar—these events can then be downloaded to one's personal calendar. Those surgeons in the market for new employment can find assistance on the IEP Job Board, which includes listings of available total joint positions in the U.S. and abroad.

What haven't they thought of?

*—EH (October 16, 2009)*

## spine

### Vexim Develops New Spine Diagnostic

An 8.8 million EUR grant might seem like a lot of money to invest in a map, but this is no ordinary map. Vexim, creator of the SpineJack device for treating vertebral compression fractures, recently received these funds (currently about $12.9 million where 1 EUR = 1.46618 USD) to assist in the development of a new diagnostic tool which can show improvement in a fractured vertebra as a contour map.

#### Three Partners

The grant money came from OSEO, an organization set up by the French government

spine

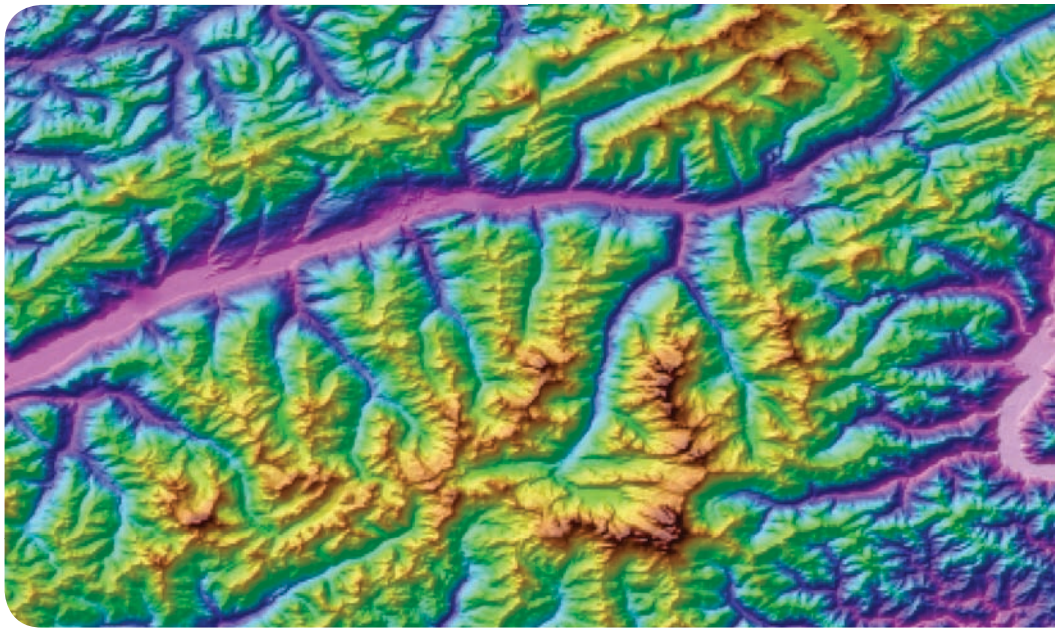
to motivate and award innovation, particularly in the medical field. More specifically, Vexim received its grant from OSEO's Strategic Industrial Innovation Programme which supports intermediate companies (with less than 5,000 staff members) and small companies (with less than 250 staff members). Vexim will share the funds with two other French partners; Biospace Medical will receive 2.2 million EUR of the grant money, and the Laboratory of Biomechanics (LBM) will receive 0.5 million EUR.

Together, these three partners will collaborate on what is now called the ILI project, or the "Implant Imagery Software" project (when translated into English). The partnership aims to create imaging software and post-treatment analysis tools for use with Vexim's SpineJack implant.

### How Does it Work?

Bruce de la Grange, Chief Executive Officer of Vexim, explains: "In a vertebral compression fracture, the end plates of the vertebrae frequently become concave; they collapse into themselves and into the vertebrae. The SpineJack is designed not only to raise the complete vertebrae but to raise the concave plateau so that the end plate becomes relatively flat once again."

"The new software is essentially a form of mapping similar to a contour map. It shows the extent to which the end plates of the vertebrae have been restored to their original height. By analyzing scans, the software can show on a relief map how many millimeters the end plates have been moved by. The most movement appears red, and then it goes through different shades of orange and yellow to green (no movement). This allows us to prove what we are doing with the SpineJack, which is restoring the morphology of the vertebrae."



*Contour Map of Valais*

Biospace Medical is focusing on developing the diagnostic imaging tools and the Laboratory of Biomechanics is creating the software. Bruce de la Grange adds, "the diagnostic tool will enable the surgeon to take images of the spine problem with the patient standing up rather than laying down, which will show the natural forces on the spine."

The software is specific to the SpineJack and not designed to map out changes in the vertebrae produced by any other device. However, as Matt Menze, PearlDiver analyst explains in his recent *OTW* series, "Spinal Motion Preservation," it's important to continually develop more diagnostic tools alongside the emerging spine treatment technologies so that doctors can evaluate just how effective these devices are. If the contour mapping software works for Vexim, maybe doctors and researchers should find ways to utilize this technique with other devices and procedures in the near future.

*—DK (October 5, 2009)*

## Sentinel: Life Spine's 20th 510(k)

Life Spine, Inc. has received 510(k) clearance for its Sentinel Occipito-Cervico-Thoracic (OCT) System.

spine

The OCT is a rigid stabilization system and promotes fusion from the occiput to thoracic spine. The company says the system features streamlined implants and instruments to address complicated procedures. Polyaxial screws are available in multiple diameters and lengths, and offer a generous cone angulation, which simplifies alignment with the rod and minimizes rod contouring.

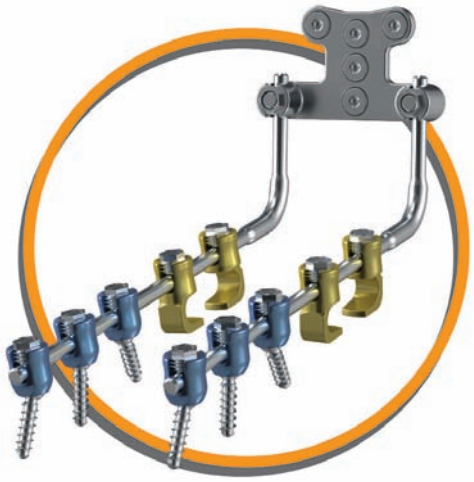
The company said on September 30 that the addition of the Sentinel is "a watershed event providing the ability to offer surgeons a full range of solutions to address spinal pathologies from the occiput to the sacrum." The system is Life Spine's 20th 510(k) clearance.

Privately-held Life Spine was founded in June 2003 by Michael S. Butler, President and Chief Executive Officer and is located in Hoffman Estates, Illinois.

*—WE (October 7, 2009)*

## SI-BONE at 200+ Sales Reps; Surgeon Training Milestone

At the base of the spine, there is the sacroiliac joint…at the base of SI-BONE, Inc., there is an increasingly strong sales and training program. This California-based company has announced that it has reached a milestone in training spine surgeons and distributors on their iFuse Implant System for minimally invasive treatment of sacroiliac (SI) joint dysfunction.



*Sentinel OCT System / Courtesy Life Spine, Inc.*

SI-BONE already has agreements with 12 spine surgery equipment distributors to introduce the iFuse, with more on the way. This trend has accelerated in the last four months, with its coast to coast sales team totaling 222 sales representatives.

Commenting on the appropriate number of distributors was Jeff Polack, VP Marketing and Clinical, who said to *OTW,* "There's no real ideal number of distributors. The ideal is to have all critical markets covered in depth to support the introduction of iFuse and the training and case support of surgeons."

Regarding entering different markets, Polack told *OTW,* "Our approach is a distributor model with some direct sales management to direct distribution efforts on a regional basis."

"We expect to have additional agreements in place within the next few weeks, and a significant ramp up in first surgical cases," said Jeffrey Dunn, CEO of SI-BONE, in the news release. He added, "We've trained over 20 spine surgeons in the last three months and have plans to train an additional 30 surgeons by year end."

Frank Tedesco, one of the principals at the New York-based distributor, Eclipse Surgical, said in the news release, "We're very pleased to be representing SI-BONE and its minimally invasive device, iFuse, for treatment of SI joint dysfunction. This is a significant clinical issue and we are in a unique position to promote the iFuse to spine surgeons as an effective minimally invasive treatment for this condition."

The company has conducted training sessions in numerous locales in the last few months including Indianapolis, Boston, Minneapolis, Detroit, Atlanta, Los Angeles, Buffalo, and has numerous additional training sessions scheduled. Cadaveric lab trainings are scheduled in October in Las Vegas, New York, Charleston, Denver, and San Francisco.

Surgeries using the company's patented, intramedullary implant are occurring all around the country. The procedure involves a minimal incision and small, titanium implants which are coated with a porous plasma spray that acts as an interference surface, designed to help decrease implant motion. As indicated by the company, these implants have substantial thickness and

spine

sophisticated metallurgy and are able to produce a much stronger construct than that of conventional pins or screws used to surgically fix boney structures. The implant technology from SI-BONE has been previously used successfully in approximately 1,000 cases of dysfunctional foot joints. The company plans to conduct a post-market multicenter study to determine the implant's effect over time on SI joint pathology and on symptoms associated with SI joint dysfunction.

As for the training, Jeff Polack told *OTW,* "Topics covered in training include market overview, diagnostic and therapeutic approaches to SI joint pathology, anatomy/pathology, SI-BONE technology and solution, surgical procedure, cadaveric lab (wet lab), dry lab and didactic, customer service."

*—EH (October 9, 2009)*

# The Picture of Success: Dr. John Bergfeld

**By Elizabeth Hofheinz, M.Ed., M.P.H.**

From bucolic farm life to rough urban areas to the Navy, Dr. John Bergfeld, Senior Physician in the Department of Orthopaedic Surgery at Cleveland Clinic, has had many colorful experiences. An Illinois native, his childhood was less than smooth. Dr. Bergfeld: "It was a pretty tumultuous upbringing. My parents divorced, my dad moved to Saudi Arabia, my mom went to California, and I attended a different school every year. My mother was so busy working that I spent most of my youth with my French grandmother, as well as my aunt and uncle, on a farm near Pittsburgh. While they emphasized the solid values of hard work and self reliance, the environment was a bit lonesome because there were few opportunities for social interaction."

When he later had the chance to socialize, he wasn't exactly keeping company with those bent on getting an education. "When I was in 7th grade my mother moved us to Philadelphia, but unfortunately we were in a pretty rough area. I was on the verge of getting into trouble, so my mom decided to see if the military could do anything with me. As it turned out, the Valley Forge Military Academy was the biggest influence of my young life. I was impressed and heartened to find there a level playing field…it didn't matter who your parents were or how much money you had."

But his beginning was still a bit rocky. "I had a chip on my shoulder and thought I was tough. I was taken down a couple of notches, however, when I got beaten up several times my freshman year. Over time, though, I grew to appreciate that there was no false environment there, i.e., you had your rank, you did your job and that's how you were judged. For the first time in my life, I had a social reference point. On the academic front, graduating 2nd in my military class drove home the point that if I applied myself I could progress in life."

Now a sports medicine specialist, Dr. Bergfeld treasures one letter more than any other he has ever received. "At Valley Forge we were required to participate in sports; my sophomore year I tried out for the varsity football team. I worked hard, and more than anything, I wanted to be invited back to football camp prior to my junior year. Receiving that letter from the coach asking me to football camp meant the world to me…I was part of the team."

As he would be at college. "I attended Bucknell University, played football, and met my roommate Denny Cox's family. They essentially introduced me to 'regular' family life."

## Finding Direction in Medicine

Now far from the uncertain future he once faced, a young John Bergfeld applied and gained acceptance into four medical schools. "I chose Temple University in Philadelphia because it was known for teaching practical, hands on medicine. There I was fortunate to meet my wife, Wilma, who was also a medical student."

Devoted to a future together, "Drs. Bergfeld" moved en masse…plus one. "Wilma was pregnant when we completed medical school, and so we wanted to be near her family in Cleveland. Cleveland Clinic was understanding about her condition, and allowed her to start her internship a bit later than everyone else. So in 1964, we both did our internships at Cleveland Clinic."

Although he was interested in cardiac surgery, Dr. Bergfeld didn't find enough heart in the field. "In cardiac surgery patients came in, had the operation and were gone. The surgeons didn't spend a lot of time actually talking to them. During this period I continued to play rugby and moonlighted as a team doctor for a local high school. It was through this work that I got to know the outstanding Dr. McCollister 'Mac' Evarts, and ended up doing an orthopedic rotation with him."

Intrigued, but not rushed, Dr. Bergfeld completed a year of general surgery. "This time at Cleveland Clinic gave me the experience I needed to become comfortable with soft tissue trauma, ruptured aneurisms, fluid balance… things of that nature. I feel badly for the students today because they have to decide on a specialty so early in training. I didn't have to commit to anything until I was finished with internship. These days, students must decide on a specialty by their third year of medical school."

Staying on at Cleveland Clinic for an orthopedic residency, Dr. Bergfeld dug deeper into a world that was not yet formalized—sports medicine. "I got to look on and learn as Dr. Evarts built the sports medicine division at Cleveland Clinic. He hired Dr. Royer Collins, a sports medicine pioneer, who taught us that sports medicine is more than surgery, that working with our primary care team physician colleagues was rewarding, and that education of our peers was an important part of 'academic' sports medicine."

Finishing up residency in 1970, Dr. Bergfeld would be taken down a notch by a military experience. "I had deferred my military service to attend medical school, but then it was time to get involved. When I signed on with the Navy they looked at my CV and saw that I had a lot of experience as a team physician. I was called to Washington, D.C. for an interview, and then sent to the Naval Academy to meet the football coach. This was when all of my friends were going to Vietnam, mind you. Upon returning to D.C., the officer in charge asked, 'What did you think?' Well, I had been trained at the renowned Cleveland Clinic and had my mind set on doing 'big' surgeries. His response? 'Boy, if you think Annapolis is not good enough for you we can send you other places whose names you can't even pronounce…like Da Nang.'"

"Epiphany!" says Dr. Bergfeld. "I told my wife that given my attitude I would likely be in Vietnam. As it turned out, I did receive orders from the Navy. I was sent to the US Naval Hospital Annapolis with an additional assignment to the US Naval Academy, where I built an orthopedic practice, treated athletes, and helped care for Vietnam casualties."



In the midst of all this, he shipped out and found his place in the chain of command at sea. "In 1972 I spent six months on a Navy ship in the Western Pacific, an experience which taught me where doctors fit into life. Our job as physicians was to support the team, but the real decisions were being made by the Captain and line officers. I recall going to an officers meeting and everyone was asked for input… with the exception of me. I've thought about this many times, and believe that this mirrors the role doctors have in society. We keep people healthy and those people keep things going. Some doctors become self centered and think that the world revolves around them. I tell my young trainees that they can easily be replaced."

## Mentors and Career Development

Back on dry land, a chance meeting then opened doors to the knee. "In 1970 as Navy team physician at the Army Navy football game, I met Dr. John Feagin, Army team physician, who would become a lifelong friend. We were seeing a lot of knee problems at the military academies, many of which Dr. Feagin said were torn anterior cruciate ligaments. I didn't know about these injuries at the time, but once I learned what they were I began to repair them. It was quite a challenge in those pre-arthroscope days."

Returning to Cleveland Clinic as staff in 1973, Dr. Bergfeld worked alongside colleagues and instituted a full sports medicine department and practice. "Along with Dr. Collins, Dr. Ken DeHaven and I were the first sports medicine staff. Although we were housed in the department of orthopedics, we could see that those around us wondered what exactly we were doing. But as television covered more and more professional

sports and played up the lives of the athletes, our burgeoning field grew. Suddenly, the young doctors applying for residency began to ask, 'Who is doing sports medicine here?' That's when the 'old' professors began to realize that they should pay attention to this subspecialty."

"In 1976 Art Model, owner of the Cleveland Browns, asked me to be the team doctor. I agreed, and began a terrific 28 year relationship with the team. Then in 1982 I signed on as team physician for the Cleveland Cavaliers basketball team. Working with these 'neuromuscular giants' was invigorating because they were very dedicated to physical fitness, followed instructions and were all talented athletes. With the basketball players we primarily saw overuse problems and stress fractures, whereas the football players experienced a lot of traumatic knee and hand injuries."

## Leading the Field with Research

Dr. Bergfeld, who went on to lead the American College of Sports Medicine and the American Orthopaedic Society for Sports Medicine, has always been committed to driving the field forward through research. He notes, "I am especially interested in problems of the posterior cruciate ligament (PCL). While it is a less common injury, the surgery to treat it is more complex. My research has involved looking at which types of surgeries are most effective for PCL issues; unfortunately, our first results were not very promising. Surgery on the back of the knee contains all the arteries, nerves, and blood vessels, unlike the front of the knee. It's just a much tougher environment back there."

Detailing his work, Dr. Bergfeld explains, "From 1985-98 my colleagues and I did a series of studies in which we showed that the posterior tibial inlay technique is the most effect biomechanical procedure for reconstructing a PCL. In this operation, the surgeon uses either the patient's own tendon or ligament from a cadaver. The procedure is done anatomically by placing the tendon or ligament in the anatomic position rather than through a drill hole. We showed in the lab that the procedure was more stable than other approaches, and in fact, as we followed the patients there were fewer reported cases of loosening. My work with the PCL has also led me to determine that 85% of these cases in athletes can be treated nonsurgically. It is really gratifying that today many team doctors follow the guidelines we have developed."

"The most satisfying part of my career is the young orthopedic surgeons and Primary Care Sports residents and fellows I have had an opportunity to train. I am particularly proud that five of these individuals have gone on to be department chairs and several serve as professional, college and high school team physicians."

A sportsman at heart, a proud Dr. Bergfeld says, "My wife, the first female President of the American Academy of Dermatology, is a long ball hitter in academics. While it is fantastic that she and I both work at Cleveland Clinic, one year I made the mistake of reading her review… the accolades went on for pages. We have two daughters, one who was a wonderful human being and attorney, but is now deceased. Our other daughter is an accomplished graphic designer who, among other things, creates personalized books about family biographies."

Also filling the pages of Dr. Bergfeld's life book are the pleasures of the outdoors. "My wife and I are avid sailors and enjoy backcountry skiing. Recently I have spent more time fly fishing, something which I see as a very academic sport. You must figure out what the fish are eating, and can fish in some spectacular places. I also love shooting sporting clays, something that harkens back to my days in rural Pennsylvania, where guns are not uncommon. It is a great way to focus and compete with oneself."

Dr. John Bergfeld…forged by obstacles and shaping the field.

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