VOLUME 6, ISSUE 29 | SEPTEMBER 14, 2010

# Orthopedics This Week

## week in review

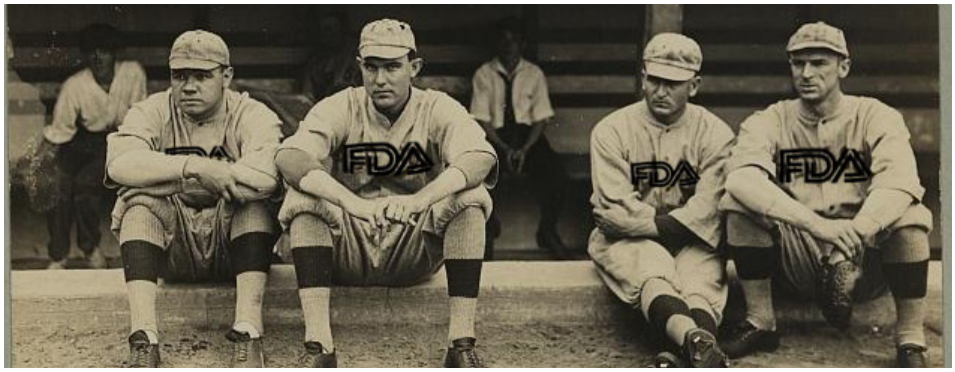
**7** 510(k) Retooling Part 3: Strengthening the Bench ◆ Jeff Shuren, M.D., the FDA's top device regulator, has improved his bench by appointing cardiologist Bill Maisel, M.D., to head up a new Science Council within the agency. Get to know Maisel and what the new Council will do here.

**12** Regenerating the Spine in FOUR Steps ◆ Can the degenerated spine disc be rehydrated? Yes, in four steps. Ok, not easy steps. But at the BioSpine3 meeting September 1-4 last week in Amsterdam a model for rehydrating the spine disc emerged. Read on for more about the cool stuff that came out of the Netherlands.

**16** Serving the Developing World: DePuy Spine and Dr. William Horton ◆ DePuy Spine and Dr. William Horton are bringing appropriate technologies and training to China… then, it's on to the rest of the world. Learn here about their novel, bold approach.

## picture of success

**4** Marc Viscogliosi ◆ Marc Viscogliosi, a Principal at Viscogliosi Brothers, LLC and the founder of more than 20 companies, has built his life around family and community. Now, Viscogliosi has been named a winner in the 40 UNDER 40 M&A Advisor Recognition Awards.




## breaking news



**For all news that is ortho, read on.**

Orthopedics This Week

VOLUME 6, ISSUE 29 | SEPTEMBER 14, 2010

# Orthopedic Power Rankings

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

**This Week:** The average orthopedic company today is trading at 12.6x trailing earnings. That's, in effect, an 8% earnings yield. Is that good or bad? The best way to put earnings yield into context is to compare it to earnings power. Big Ortho routinely earns 20-30% on sales. That means that the sheer business power of Ortho is 3x stronger than current valuations. No wonder Buffett is back buying.

| Rank | Last Week | Company | TTM Op Margin | 30-Day Price Change | Comment |
|---|---|---|---|---|---|
| 1 | 1 | Orthofix | 13.51% | (4.05%) | Just like that, OFIX raises EPS estimate by 5 cents for 4Q by swapping expensive debt for cheaper debt. Nothing but good news. |
| 2 | 2 | Kensey Nash | 38.72 | 14.33 | Best performing orthopedic stock (except for buy-out candidate OSTE) this last month. Why? Ummm…cash and high margins? |
| 3 | 5 | Alphatec | 1.59 | (14.80) | New buying gingerly stepping into ATEC. Up 8% in the last couple of weeks.Seventh lowest PSR. |
| 4 | 4 | Integra LifeSciences | 15.37 | 3.38 | Oppenheimer jumps in with an Outperform for IART. Three new products rolled out in as many weeks. |
| 5 | 3 | Johnson & Johnson | 27.1 | 1.89 | Warren Buffett is back! He is a buyer and is restoring his massive JNJ position. And why not?—3.70% dividend and low P/E. |
| 6 | 8 | Stryker | 24.71 | (2.02) | SYK made the biggest valuation pop of all big ortho this past week as value buyers went bargain hunting. |
| 7 | 6 | CONMED | 8.76 | (1.57) | CNMD is something else. Hits 52 week low, then reports chart topping earnings. Outlook for 3Q? More upside surprises. |
| 8 | 9 | Smith & Nephew | 22.83 | (7.37) | Not a lot of confidence in SNN this quarter. Consensus is for a down quarter. Yet, somehow management has beat consensus by an average of 12% each of last 4 quarters. |
| 9 | 9 | Zimmer | 27.69 | (9.11) | Stifel Nicholaus initiated coverage with a BUY. Oppenheimer with a Neutral. All we know ZMH has 2nd lowest P/E. |
| 10 | 5 | Medtronic | 32.48 | (10.50) | What's the secret of investing? Buy dollar bills for 40 cents. Value buyers starting to focus on MDT and its strong cash flows. |

# Robin Young's Orthopedic Universe

## Top Performers Last 30 Days

| | Company | Symbol | Price | Mkt Cap | 30-Day Chg |
|---|---|---|---|---|---|
| 1 | Osteotech | OSTE | $6.41 | $116 | 74.2% |
| 2 | Kensey Nash | KNSY | $27.13 | $256 | 14.3% |
| 3 | Integra LifeSciences | IART | $37.88 | $1,100 | 3.4% |
| 4 | Capstone Therapeutics | CAPS | $0.92 | $38 | 2.2% |
| 5 | Johnson & Johnson | JNJ | $59.98 | $165,210 | 1.9% |
| 6 | Synthes | SYST.VX | $120.09 | $14,252 | 1.3% |
| *7* | *Average* | | | *$10,760* | *-1.2%* |
| 8 | CONMED | CNMD | $19.39 | $558 | -1.6% |
| 9 | Stryker | SYK | $46.67 | $18,530 | -2.0% |
| 10 | Mako Surgical | MAKO | $10.81 | $365 | -2.3% |

## Worst Performers Last 30 Days

| | Company | Symbol | Price | Mkt Cap | 30-Day Chg |
|---|---|---|---|---|---|
| 1 | TiGenix | TIG.BR | $1.91 | $59 | -28.1% |
| 2 | Alphatec Holdings | ATEC | $2.13 | $186 | -14.8% |
| 3 | RTI Biologics Inc | RTIX | $2.25 | $123 | -11.8% |
| 4 | ArthroCare | ARTC | $25.79 | $697 | -11.7% |
| 5 | Medtronic | MDT | $33.34 | 36,210 | -10.5% |
| 6 | Orthovita | VITA | $1.77 | $136 | -10.2% |
| 7 | Zimmer Holdings | ZMH | $48.99 | $9,850 | -9.1% |
| 8 | NuVasive | NUVA | $30.06 | $1,180 | -7.5% |
| 9 | Smith & Nephew | SNN | $42.50 | $7,560 | -7.4% |
| 10 | Exactech | EXAC | $14.56 | $188 | -5.1% |

## Lowest Price / Earnings Ratio (TTM)

| | Company | Symbol | Price | Mkt Cap | P/E |
|---|---|---|---|---|---|
| 1 | Medtronic | MDT | $33.34 | $36,210 | 9.96 |
| 2 | Zimmer Holdings | ZMH | $48.99 | $9,850 | 11.66 |
| 3 | Exactech | EXAC | $14.56 | $188 | 11.77 |
| 4 | Kensey Nash | KNSY | $27.13 | $256 | 12.07 |
| 5 | Wright Medical | WMGI | $14.09 | $553 | 12.40 |

## Highest Price / Earnings Ratio (TTM)

| | Company | Symbol | Price | Mkt Cap | P/E |
|---|---|---|---|---|---|
| 1 | Smith & Nephew | SNN | $42.50 | $7,560 | 58.53 |
| 2 | Synthes | SYST.VX | $120.09 | $14,252 | 33.57 |
| 3 | RTI Biologics Inc | RTIX | $2.25 | $123 | 29.43 |
| 4 | NuVasive | NUVA | $30.06 | $1,180 | 24.70 |
| 5 | Symmetry Medical | SMA | $9.16 | $329 | 23.92 |

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

| | Company | Symbol | Price | Mkt Cap | PEG |
|---|---|---|---|---|---|
| 1 | Osteotech | OSTE | $6.41 | $116 | -5.82 |
| 2 | Orthovita | VITA | $1.77 | $136 | -4.58 |
| 3 | Mako Surgical | MAKO | $10.81 | $365 | -0.25 |
| 4 | TranS1 | TSON | $2.49 | $52 | -0.18 |
| 5 | Orthofix | OFIX | $29.58 | $522 | 0.61 |

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

| | Company | Symbol | Price | Mkt Cap | PEG |
|---|---|---|---|---|---|
| 1 | CONMED | CNMD | $19.39 | $558 | 14.30 |
| 2 | Johnson & Johnson | JNJ | $59.98 | 165,210 | 1.95 |
| 3 | Alphatec Holdings | ATEC | $2.13 | $186 | 1.73 |
| *4* | *Average* | | | *$10,760* | *1.70* |
| 5 | Symmetry Medical | SMA | $9.16 | $329 | 1.56 |

## Lowest Price to Sales Ratio (TTM)

| | Company | Symbol | Price | Mkt Cap | PSR |
|---|---|---|---|---|---|
| 1 | RTI Biologics Inc | RTIX | $2.25 | $123 | 0.74 |
| 2 | CONMED | CNMD | $19.39 | $558 | 0.77 |
| 3 | Orthofix | OFIX | $29.58 | $522 | 0.91 |
| 4 | Symmetry Medical | SMA | $9.16 | $329 | 0.98 |
| 5 | Exactech | EXAC | $14.56 | $188 | 1.01 |

## Highest Price to Sales Ratio (TTM)

| | Company | Symbol | Price | Mkt Cap | PSR |
|---|---|---|---|---|---|
| 1 | TiGenix | TIG.BR | $1.91 | $59 | 210.15 |
| 2 | Mako Surgical | MAKO | $10.81 | $365 | 10.99 |
| 3 | Synthes | SYST.VX | $120.09 | $14,252 | 7.90 |
| 4 | Kensey Nash | KNSY | $27.13 | $256 | 3.13 |
| 5 | NuVasive | NUVA | $30.06 | $1,180 | 2.81 |

# THE PICTURE OF SUCCESS

## Marc Viscogliosi

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

*Marc Viscogliosi*

When he had a heart attack at the age of 17, Marc Viscogliosi, now a Principal at Viscogliosi Brothers, LLC, and the founder of over 20 companies, deeply questioned the meaning—and the duration—of his life. Viscogliosi, who has just been named a winner of the '40 UNDER 40 M&A Advisor Recognition Awards,' had a youth centered around family and community. As he entered the world of work, Viscogliosi set out to bring these values into the business world. It was also during his youth that Marc Viscogliosi learned to take what many perceive as a deficiency—hearing loss—and turn it into an asset.



Marc Viscogliosi's sense of how human bonds can sustain and enrich grew out of his original community—his family. "My dad came to the U.S. from Italy in 1956, and although my mom was born here, her family arrived from Italy the year before her birth. My whole environment consisted of the strong family support network that my parents created for my two brothers, my sister, and me. When I was diagnosed with hearing loss in both ears my family rallied around me to teach me how to speak and read."

As he moved forward on the career path, Viscogliosi held on to how the right family, partner, and/or community can provide a foundation for success. "Being surrounded by people I trust gives me the strength to deal with daily challenges. Knowing that you're not facing your struggles alone lays a foundation for you to consider problems more thoroughly. Having such people in your life also means that you can rest assured that there will be no politicking or hidden agendas. At Viscogliosi Brothers (VB), which I run with Tony and John, all of our interests are aligned, and we are much stronger as a unit than as individuals."

When it comes to winning, Marc Viscogliosi knows that it involves hard work…and that one's success shouldn't be at the expense of others. "I watched my parents work 20 hour days. They taught us, 'As long as there is righteousness in your approach you will be rewarded.' This means that taking shortcuts is unacceptable. My bottom line: I never get involved in any project that could put a patient at risk."

With ethics as his guide, Marc Viscogliosi and his brothers have built a number of impressive businesses and introduced numerous highly successful products. "While we are most well-known for Spine Solutions and ProDisc, which is the market leading total disc replacement worldwide, we also founded Ascent Medical (which Stryker recently acquired). John, Tony, and I were also deeply involved with Spine Next, which Abbott acquired."

"Working with a stellar group of like-minded investment partners, VB has invested more than $70 million of its capital in several orthopedic device companies. Six exits have generated

**"Over the last 10 years, the funds that VB has managed have returned to its investor-partners 4.5x net cash-on-cash and a net annual IRR of 85%. We are also proud that we have been directly responsible for commercializing 100 different and new products which have been implanted in more than 250,000 patients worldwide."**

more than $1 billion in exit proceeds to VB and its investor-partners. Over the last 10 years, the funds that VB has managed have returned to its investor-partners 4.5x net cash-on-cash and a net annual IRR of 85%. We are also proud that we have been directly responsible for commercializing 100 different and new products which have been implanted in more than 250,000 patients worldwide."

Marc Viscogliosi the seasoned business icon muses about a time when little about his life was certain. "In my 17th year of life things seemed to come to a sudden halt. Having a heart attack at that early age was surreal…you're not supposed to think about dying when you are so young. I went from having a long-term perspective to having everything turned upside down in one day. In the same period I was diagnosed with Graves' disease, an aggressive form of hyperthyroidism that was linked to my heart attack."

A former political science major, Viscogliosi was at that time on track to make his mark in the diplomatic world. "I was accepted into a summer internship program at Georgetown University with Henry Kissinger. Then, my brother Tony asked me if I would like to work with him in New York for the summer. Given my health issues, my life was pretty tumultuous at the time…and I felt the need to be around family. Knowing that I would have much to learn from Tony, in 1992 I accepted his offer and put any thoughts of a political science career behind me."

Three years later Marc Viscogliosi would have a chance to give something back to his brother. "In 1995 Tony was diagnosed with Cutaneous T-Cell Lymphoma. I was enrolled at the University of Michigan, but decided to transfer to New York University. I couldn't let Tony be without family in New York."

Marc Viscogliosi's sense of compassion and ethics was born of a history of trials...and gifts. "The most valuable lesson that I have ever learned is something that my parents taught me… that my hearing loss is a wonderful advantage. So, I have always thought that whatever you have in life is a gift. When I remove my hearing aids I have an enormous ability to focus—there is no distraction of hearing what is going on in my environment."

And while Viscogliosi makes no claims of clairvoyance, he does have a certain gift. "My hearing loss means that I can pick up on the nuances of human interaction such as body language and other types of 'subconscious communication.' The way someone shifts in his

**"I don't believe the axiom, 'It's not personal, it's business.' People use that to justify unethical and/or callous behavior. There are things that a business must do to be successful and grow, but these can be done in an ethical manner. Egos always arise in business, and individualism is important. But we must be the bosses of our egos."**

seat, or how the person's focus shifts if they change how they hold their heads, for example. If you know someone well, and are attuned to these behavioral nuances, then you can see when something outside of work is bothering them. And most importantly, you can talk to them and try to help."

"Also, if you're discussing a contract, for example, you can notice when the inflection of someone's voice changes, as well as the strength of their word choice. To this latter point, as most people communicate their issues, they will choose the strongest language for those issues about which they feel most intensely. But there are people who do the opposite—as they take a firm position, they pull back and become less passionate (disconnected) and their word choice isn't as strong. You must know whether you're dealing with an emotional person who will correlate that with what they say."

For Marc Viscogliosi, success means not leaving your values at the boardroom door. "I don't believe the axiom, 'It's not personal, it's business.' People use that to justify unethical and/or callous behavior. There are things that a business must do to be successful and grow, but these can be done in an ethical manner. Egos always arise in business, and individualism is important. But we must be the bosses of our egos."

Surely the master of his own ego, Viscogliosi says, "I fail every day. If something goes wrong and we must cut back on staff then I take that personally and thoroughly evaluate what I did wrong. I think constant self evaluation is a critical ingredient of success. The key is to then apply that new knowledge in your future interactions."

Viscogliosi also succeeds every day… all around the world. "There is no better feeling than knowing that our work and products benefit millions of patients around the globe, and that I have fostered entrepreneurship and surgeon innovation. This is what I will leave behind."

A deep, broad, and flexible thinker, Viscogliosi says he still has much more to learn. "I know finance and accounting, but business success is predicated upon choosing talented and like minded people to work with. The more in touch I am with human nature the better business decisions I will make. Yes, the numbers have to work and the market has to exist, but the most important element—and where businesses stumble—is in the people realm."

When Marc Viscogliosi began this journey with his brothers, it was as someone who had seen not only stumbling, but people who regularly tripped others. "For years I worked at investment banking and Wall Street research firms, but in 1999 my brothers and I decided that we were tired of the Wall Street 'churn and burn' dynamic. We set out to establish a business in the legacy of the old European merchant banks where you build a business on trust and foster the creation of an industry. I am very proud that the surgeons we work with today are many of the same people we worked with 10 years ago. Another testament to what we have built is that many people who have worked here in the past and left, have come 'home.'"

"When we started Viscogliosi Brothers I was 24 years old. I thought, 'What do I need to build a firm that will be here for my children and grandchildren?' One of the best things I've ever learned is that a leader should hire talented people, give them clear directions, and liberate them. You get much further than if you take a controlling approach. I say to people, 'What barriers can I remove for you so that you can do your job?'"

For nearly 15 years, Marc Viscogliosi has had someone who understands what his life's work means to him. "My wife knows that because I care passionately about my job, there really is no division between my home and work life. She is originally from Colombia, and it is helpful that we have similar values—a shared work ethic, for example—that come from being raised in immigrant families. We now have two little ones, ages four and two. We hope to grow our family to four or six children and thus have the same large, warm family experience that we had."

Marc Viscogliosi…finding and creating meaning for himself and his community every day. ◆

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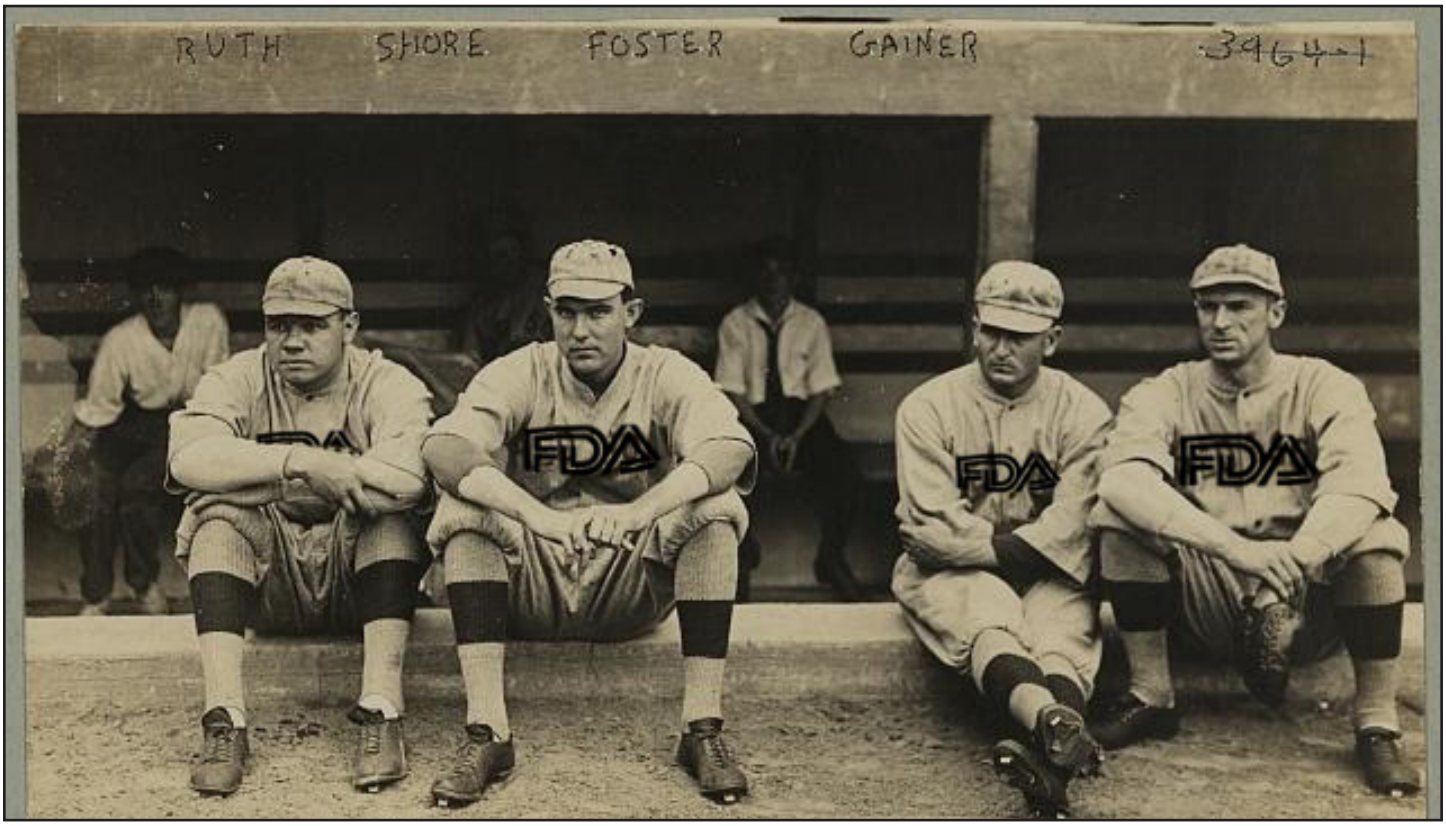
# 510(k) Retooling Part 3: Strengthening the Bench

By Walter Eisner




*Bain News Service/Wikimedia Commons/RRY Publications*

"I've got a thin bench," Jeff Shuren, M.D., Director of the FDA's Center for Devices and Radiological Health (CDRH), told the packed conference room in Minnesota at a Town Hall meeting early this summer.

*Jeff Shuren, M.D*

Shuren said the complexity of medical device science is increasing so quickly, it is difficult for the agency's reviewers to keep up. And when someone leaves for better paying jobs in industry or is temporarily out, it is very hard for a new reviewer to fill in.

## Inadequate Resources for Technologies of the Future

According to an August preliminary report by an internal CDRH task force:

"The Center's scientific staffing level is not optimal to meet the anticipated demands of the future, particularly the challenges presented by novel technologies.

"In 2007, the FDA Science Board's Subcommittee on Science and Technology reported that 'CDRH does not have the personnel or resources in place to adequately support the science needs in the regulatory review process for the planned technologies of the future….'"

These shortcomings have hampered the agency from fulfilling its mission of "promoting" medical innovation for the benefit of patients.

## 510(k) Retooling

To tackle this, as well as management problems within the agency's 510(k) clearance program, Shuren convened

*William Maisel, M.D., MPH, Deputy Director of the FDA's Center for Devices and Radiological Health./Washington.edu*

two internal work groups to come up with recommendations to improve the clearance program. He also asked the Institute of Medicine to review the program. The Institute's recommendations are expected next summer.

What did the internal task force recommend to strengthen Shuren's bench and tackle "technologies of the future"?

## CDRH Science Council

In this final installment of our three-part series where we've analyzed the agency's recommendations for retooling the 510(k) process, we look at one recommendation that has already been implemented: the establishment of the Center Science Council and the appointment of William H. Maisel, M.D., MPH, as its first Director. Maisel has become Shuren's right hand man for science. Technically, he is the newly appointed Deputy Director of the FDA's Center for Devices and Radiological Health.

The task force recommended the establishment of a Center Science Council as a new governance model to assure quality and consistency in CDRH's science-based decision making.

This standing body is responsible for overseeing science-based decision making across the Center.

Functions include:

- Premarket review
- Periodically auditing decisions
- Assessing program performance
- Acting as a resource for staff on scientific questions

## William Maisel, M.D., MPH

"Get to know Bill Maisel," said University of Minnesota Law Professor Ralph Hall. "Maisel and the Science Council have the potential to have a big impact on how devices will be evaluated and allowed onto the market."

Before getting drafted to shore up Shuren's bench, Maisel was the Director of the Medical Device Safety Institute at Beth Israel Deaconess Medical Center and assistant professor of medicine at



**"It is evident that to best protect the health of American medical device users, the FDA must promote and enforce a higher scientific standard for device clearance and approval—particularly for higher risk devices whose abnormal performance is likely to have adverse effects on patient health."**

Harvard Medical School. He had an active cardiology practice and also directed the Pacemaker and Defibrillator Service at Beth Israel Deaconess Medical Center.

His research interests, according to his biography, involve the safe and effective use of medical devices, and he has published extensively on the safety of pacemakers and defibrillators, drug-eluting stents and other cardiovascular devices.

Maisel received his M.D. from Cornell University, his MPH from the Harvard School of Public Health, and completed his internal medicine and cardiovascular training at Brigham and Women's Hospital. Maisel was also an FDA consultant and former Chairman of the FDA's Circulatory System Medical Device Advisory Panel.

## Maisel: "Higher Standard for Device Clearance"

Maisel's public statements regarding the FDA's success in protecting the public's health may shed some light on how he will act as Shuren's right hand science guy.

In testimony before Congress in May 2009, Maisel said:

"...Device malfunctions and software glitches have become modern 'diseases' that will continue to occur. The failure of manufacturers and the FDA to provide the public with timely, critical information about device performance, malfunctions, and 'fixes' enables potentially defective devices to reach unwary consumers."

And this testimony a month later:

"It is evident that to best protect the health of American medical device users, the FDA must promote and enforce a higher scientific standard for device clearance and approval—particularly for higher risk devices whose abnormal performance is likely to have adverse effects on patient health."

As we reported in Part One of our series, orthopedic devices have had a phenomenal safety record. Cardiovascular devices, according to Professor Hall's research, have not fared quite as well.

## Live-Saving vs. Life-Enhancing

Orthopedic physician leaders have urged the FDA to distinguish between "life-saving" and "live-enhancing" devices. Those leaders can hope that recommendations, supported by AdvaMed, to create a Class IIb category, will make getting new devices to patients more predictable and less burdensome.

In addition to the creation of a Science Council headed by Maisel, Shuren's science task force recommended further changes to the way CDRH will deal with a changing scientific landscape.

## Recommendations for Predictability

Shuren asked the task force to identify steps the agency should take to ensure regulatory predictability while adapting to emerging science.

This means helping CDRH become

more predictably adaptive, setting clearer guidelines about when new scientific information might prompt a change in how CDRH treats a given product, including how that product might be reviewed before it goes to market.

## Predicate and Substantial Equivalence

For example, the explosion of scientific advancements has challenged the agency's definition of terms like "predicate" and "substantial equivalence."

Shuren said a survey of agency staff found that employees didn't agree on "substantial equivalence," which led to "inconsistency in decision making." The agency proposes to clearly define the term, he said.

These tensions of definition and expertise played out during the last year of the Bush Administration as then FDA Commissioner von Eschenbach faced a rebellion from whistle blowing agency scientists who claimed senior managers were overriding their scientific judgment.

The agency was also challenged by ReGen Biologics' 510(k) application for its Menaflex surgical mesh. The application exposed a dysfunctional internal appeals process when reviewers applied an illegal predicate standard to the device. Even after two Orthopaedic Device Panels determined the device was safe, the agency still fumbled the application and likely denied the company due process.

## Other Recommendations

In addition to the creation of the CDRH Science Council, the task force also recommended the following:

**Enhance science-based professional development for CDRH staff.**

> Recommends that CDRH enhance training, professional development, and knowledge-sharing among Center staff, to assure that appropriate scientific expertise and regulatory experience are brought to bear in decision making. Both groups recommend that these efforts include providing greater opportunities for staff to stay abreast of recent scientific developments and current clinical practice.

**Establish a network of external experts to better inform the review of cutting-edge technologies.**

> Recommends that the Center continue ongoing efforts, in keeping with the Center's FY 2010 Strategic Priorities, to develop a network of external experts using web-based social media technology. Such a network would allow Center staff to more efficiently and effectively leverage outside knowledge in order to answer important scientific questions, but would not serve in an advisory capacity.

**Clarify the meaning of key terms in the 510(k) "substantial equivalence" review standard to improve the consistency, transparency, and timeliness of the review process.**

> Recommends that CDRH more clearly define these terms in guidance and training for review staff and industry.

In addition to these specific recommendations, the task force also noted a situation that has caused great friction between reviewers and applicants:

## Interpretation of the "Least Burdensome" Provisions

According to the CDRH Ombudsman, concerns about whether or not premarket evidentiary requirements are

consistent with the "least burdensome" provisions have consistently been a leading reason for complaints, disputes, and/or inquiries from industry.

The task force recommends that CDRH revise and clarify its 2002 "least burdensome" guidance.

"CDRH should clearly and consistently communicate that, while the 'least burdensome provisions' are, appropriately, meant to eliminate unjustified burdens on industry, such as limiting premarket information requests to those that are necessary to demonstrate reasonable assurance of safety and effectiveness or substantial equivalence, they are not intended to excuse industry from pertinent regulatory obligations nor to lower the agency's expectations with respect to what is necessary to demonstrate that a device meets the relevant statutory standard."

Agency reviewers expressed concern to the task force that the "least burdensome" provisions have created a culture in which it is "difficult for premarket reviewers to obtain evidence to consistently provide reasonable assurance of a device's safety and effectiveness. This is particularly challenging in the context of the 510(k) process, in which reviewers report that 510(k) submitters, relying on the substantial equivalence standard, are often reluctant to provide additional information that was not required for a predicate device."

## Shuren's Changes

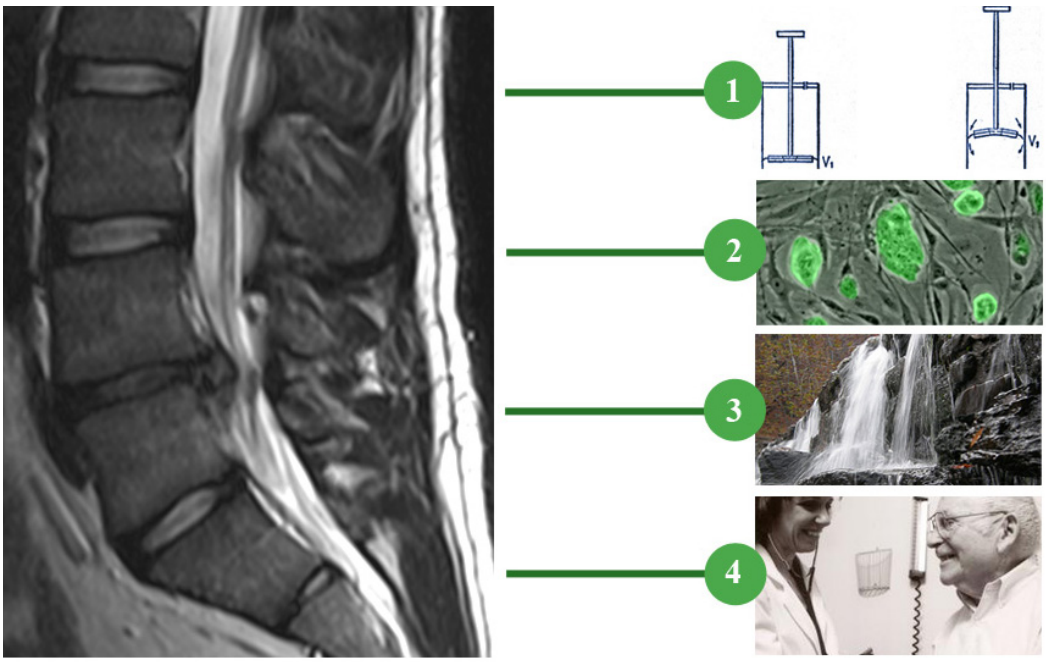
CDRH Director Shuren has been transparent, clear and explicit about the challenges he inherited to protect and promote public health. Clearly, many of the problems experienced by industry in trying to gain clearance for their devices can be traced back to disagreements with reviewers over science, definitions and authority.

Perhaps with Shuren strengthening his bench, this will be the change industry has been waiting for. ◆

# Regenerating the Spine in FOUR Steps

By Robin Young

Rehydrating the spine nucleus with stem cells, with or without bone morphogenic proteins, has been bouncing around the periphery of stem cell science for a decade or longer. Degradation of the spine disc from either acute or chronic disc injury and/or degeneration is the basis for most of today's spinal implant sales. If physicians could rehydrate a degenerated disc reliably it could transform the business of selling spinal fusion implants and instruments.




*Wikimedia Commons/RRY Publications*

But the nucleus is not a benign environment. Could, for example, stem cells survive the ph levels, the compressive and stress forces or avascular nature of the nucleus?

About 16 months ago data emerged from a small canine study (n=12) that adipose stem cells in a hyaluronic cocktail could rehydrate the disc to near normal levels. Then later that same year (September 10) a sheep study was presented at the Osteoarthritis Research Society International meeting in Montreal which seemed to show that a single, direct low-dose injection of allogeneic or "off-the-shelf" adult stem cells into the degenerated disc nucleus could rehydrate or regenerate the disc.

Earlier this month, at the BioSpine3 meeting in Amsterdam several researchers presented goat and canine studies that deconstructed the mechanisms of action for disc degeneration and then looked at strategies for rehydrating or regenerating the degenerated disc.

Incidentally, if you missed BioSpine3 you'll need to wait until 2012-2013 for BioSpine4 and the best overview of European biologics research for the spine.

Is disc rehydration or regeneration a fantasia or a potential reality? Last year's papers seem to indicate that, yes, cellular therapies COULD rehydrate the degenerated disc. BioSpine3's first six papers tackled this question head on. Here's what we learned:. There are four not-so-easy steps to successfully rehydrating the disc.

## Step One: Rapidly clear inflammatory and stimulatory factors

Of course, back pain is the whole point. Or back inflammation. Breaking down the components of inflammation or studying the chemical markers that correlate with disc degeneration provides tantalizing clues about what to do when disc degeneration is overwhelming the body's ability to repair itself.

Laura Creemers, Ph.D., Professor at the University Medical Center Utrecht in the Division of Surgical Specialties, Department of Orthopedics, described the many chemical signals (proteases and messenger RNA) that are correlated with disc degeneration. One very strong correlation she discussed in her presentation was between active MMP-2 and


*Dr. Laura Creemers*

human intervertebral disc degeneration. Other degeneration accelerators Dr. Creemers mentioned were MMP-14 and Interluken 6, 10 or 16. In other words, Dr. Creemers and many other researchers have been rather successful at identifying the chemical signals that support if not contribute to disc degeneration.

These markers are up-regulators of inflammation inside the disc. So, Step One, is to inhibit those chemical signals and other factors that support, if not also stimulate, disc degeneration—and to do so in a sustained manner—perhaps with microbeads or hydrogels, which would elute inhibitor compounds over time.

Easier said than done, of course!. Here is one area where progenitor cells, like mesenchymal cells, may have an impact since they are immune privileged and can down regulate inflammation. But other strategies are also called for and this, it seems to us, represents a major clinical opportunity.

Clearing out the chemical signals that support degeneration of the spinal disc lays the foundation for steps 2, 3 and 4.

### Step Two: Reverse the unfavorable biomechanical environment in the disc

There are five grades of disc degeneration—Grade I to Grade V—and where a patient's degeneration is on this scale determines (or should) what treatment strategies a surgeon might employ. As the cascade of degeneration progresses, the typical disc will move from a wet, spongy, healthy material (Grade 1) to a tough, dry and fibrous (Grade 5) material. The Grade 5 disc space has very different sheer forces, load-bearing tensions and other biomechanical attributes than the healthy, spongy, proteoglycan-rich Grade 1 disc.

What do biomechanics have to do with a healthy disc? A lot, said several of the podium speakers. A biomechanically healthy disc will create and maintain a constant flow of fluid, supporting a better nutrient environment.

Surprisingly (or, I guess, not) several researchers came to the topic of annular repair. A healthy annulus they said is vital to maintaining healthy biome-

chanics of the spine. "Repair the annulus." I was surprised by how often those words were spoken.

Finally, presenters at BioSpine3 kept returning to a fundamental truism of stem cell therapy. Stem cells (or progenitor cells) respond to the biomechanical environment of the human body as they move to differentiate. Different biomechanical signals prompt stem cells to differentiate into different tissues. So, as one researcher asked, if the biomechanical environment in the disc is not healthy, then why would we expect stem cells to differentiate into healthy disc tissue? Why indeed!

Step Two is essential. If the biomechanics of the disc can be restored, then the disc has a chance to rehydrate or regenerate.



## Step Three: Restore the osmotic pressure

Spine discs do not have a direct blood supply. There are no arteries to feed the disc tissues with oxygen or nutrients. Virtually all other tissues in the body rely on blood for oxygen and nutrients. If spine discs don't, then how do they stay healthy and vital? The answer is that normal, healthy discs are "fed" and oxygenated by the constant recycling of the disc fluid that occurs from everyday walking, stepping and lifting. The natural motion of the spine squeezes and releases the spine disc and creates a constant in and out flow of cerebral fluid, with oxygen and nutrients being added and waste fluids being released.

This process of sponging fluid in and out of the disc creates the healthy environment and reinforces the ability of the disc to maintain disc pressure.

So, after clearing out the chemical signals that support degeneration and then restoring the biomechanics the next logical step to regenerating the disc is to restore osmotic pressure. How to do that? Hydrogels may be one answer. A combination of materials including cells, growth factors along with hydrogels may be another answer.

Restoring osmotic pressure rehabilitates the disc's ability to rehydrate, maintain disc pressure, absorb shock, access nutrients and release waste materials. Obviously it's a good thing.

## Step Four: Identify ideal patient populations

Some patients with clear X-ray evidence of degenerative disc disease (DDD) feel no pain. Other patients with no X-ray or MRI evidence of disc degeneration feel debilitating pain. According to a recent paper in the New England Journal of Medicine: "Perhaps 85% of patients with isolated low back pain cannot be given a precise pathoanatomical diagnosis. The association between symptoms and imaging (e.g., MRI, X-ray, CT) results is weak. Thus, nonspecific terms such as strain, sprain, or degenerative processes, are commonly used. Strain and sprain have never been anatomically or histologically characterized and patients given these diagnoses might accurately be said to have idiopathic (source is unknown) low back pain."


*Kenneth M.C. Cheung*

Professor Kenneth M.C. Cheung from the University of Hong Kong, Queen Mary Hospital, presented his research into those markers that appear to predict which patients are likely to feel pain from degenerative disc disease and those who do not. Professor Cheung is the author of the first large-scale population study into whether first-time low back pain correlates with MRI findings. Among his findings is that increased disc degeneration on MRI correlated positively with the level of back pain reported.

Said Dr. Cheung, "We were able to demonstrate that when you have a more severe form of degeneration than expected for your age, you are much more likely to be symptomatic." Cheung and colleagues created a microsatellite marker analysis of 1,043 subjects from southern China between

the ages of 18 and 55 years who also underwent genetic evaluation for predisposition to back problems. Cheung and his co-investigator Jaro Karpinnen, M.D. of Oulu, Finland, read each subject's sagittal whole-spine MRI and then used that data to grade the severity of degeneration at the lumbar level.

The researchers then had their subjects complete Oswestry Disability Index (ODI), Visual Analog Scale (VAS), Roland Morris score (RM) and SF-36 low back pain (LBP) questionnaires. Using that data, Dr. Cheung and his colleagues correlated the reported pain with MRI findings.

Dr. Cheung's data is fascinating.

If it were possible to accurately predict which patients would feel pain, then surgeons could intervene earlier and, for example, inject cells or proteins into a healthier, nutrient rich disc where all the conditions exist to support cellular growth and disc regeneration.

## Conclusions:

We may have a model emerging for rehydrating the disc—although achieving those four steps is not a simple matter. This model could help improve the treatment of degenerative disease and change the standard of care from a type of salvage operation to a less disruptive preventative operation.



There is no question, if we can more accurately determine which patients are most susceptible to painful DDD, then those four steps to a rehydrated/regenerated spine might move from fantasia to reality after all.

Regenerating the Spine in Four Steps:

1. Pump you up
2. Add stem cells
3. Rehydrate the disc
4. Select the best patients ◆

# Serving the Developing World: DePuy Spine and Dr. William Horton

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

Most of us in the West live in an orthopedic bubble, taking for granted that the latest technology will be available if we need it. But for a Chinese farmer with a shoulder fracture, or an African mine worker with chronic foot pain, the best has (long been) yet to come. Change is in the air, however, because of the novel, worthy efforts of one extraordinary man and an equally extraordinary company.

In December 2009, Dr. William Horton, Professor Emeritus of Orthopaedic Surgery at Emory University, had to stop his work as a spine surgeon due to problems in both hands. But he was determined to continue working on his brainchild, The Emory Spine Center for Outreach and Medical Education (ESCOME).

*Dr. William Horton*

Dr. Horton: "I founded ESCOME in 2008 with the goals being to educate physicians and help to establish spine care centers in developing countries. We began in China, in part because the medical infrastructure there was fairly established. About the time that I was considering where my new professional home would be after having to stop surgery, DePuy Spine, a Johnson & Johnson company, (already an ESCOME sponsor) approached me about an exemplary new program they were putting together. DePuy had made an unusual and bold corporate decision—they wanted to focus a significant amount of resources on helping the developing world. I was hired as an international medical education consultant and moved the ESCOME project to DePuy because I could see that the chances of the program having maximal impact and success would be much higher under the industry umbrella."

And what about DePuy's efforts gave Dr. Horton confidence? "I could see that the business executives at the highest corporate levels were seriously examining the risks and benefits of creating technology for the developing world and fully appreciated the role that education plays in elevating the level of care. DePuy had looked at several specialties but decided that international spine issues were so widespread that they merited special attention. DePuy Spine committed to doing a Chinese pilot project in November 2009."

Determined to knock down barriers for those suffering around the world, the DePuy Spine team established three goals for its China program. Dr. Horton: "We are aiming for affordable and safe technologies that are intuitive enough so that healthcare professionals in developing countries with limited training can use them effectively. Additionally, we are optimizing training opportunities for doctors with strong fundamental skills but who work in quality second tier hospitals. Finally, we are wading through distribution issues

**"Maybe a well-meaning American teacher is explaining to a Chinese surgeon how to best retract the nerve root, saying 'the retraction should be light, easy and intermittent.' That student may not know the word 'intermittent' and may misinterpret the word 'easy' as 'simple' and 'light' as 'illumination'—which all makes no sense."**

in order to get affordable technology to people who need it."

As for the first goal, engineers spent many a late night around the table evaluating product designs and asking, "Would this work in a Szechuan village?" Dr. Horton explains, "The basic goal is to take existing technologies and reverse engineer them such that the cost is half of what it would normally be. A rural patient in a poor country has probably sold his last water buffalo to pay for his mother's implants. Then if she develops a complication such as an infection, where is the money going to come from for the follow up treatment? This means that we also have to focus on technologies and processes that minimize the potential for complications."



In a very real sense, the skilled, high-powered individuals leading this effort had to slow down, listen, and become learners. "In preparing the way to address our second goal—training surgeons—we had to learn the structure of Chinese healthcare. There are three tiers of patients: the wealthy, the middle class, and those in desperate poverty. Generally speaking, wealthy patients have ways to obtain excellent medical treatment, while those in the middle class have access to some medical services of inconsistent quality (although they live on the razor's edge financially). Additionally, the skill set of medical professionals is quite variable, which makes for real challenges and opportunities with education. The best trained doctors are outstanding but treat only about 10% of the patients at the highest quality hospitals, while the second tier physicians care for 50-60% of the population in those hospitals, with the poorest third of the populace often going without any care."

Despite its intense dedication and efforts, even DePuy Spine can't wave a wand and alter the internal dynamics of a nation. But a determined team *can* make a difference by being strategic. "Many of these issues are so embedded in the healthcare system that there are things we just cannot do. We took a hard look at where we could actually improve people's lives…and we decided to focus on training for the 'second tier' surgeons. We began by selecting a few leading Chinese surgeons with solid English skills to receive extremely valuable intensive training. They are becoming the future faculty for the courses that will be given largely in Chinese to those doctors in the second tier (where English cannot be relied on). These courses are designed for surgeons grappling with the issues of treatment indications, clinical decision making, and surgical technique. The courses involve 40-70 spine surgeons who present real cases they are struggling with. Over the next couple of years we and the Chinese faculty will observe the doctors' effectiveness and address any weak spots in the training…then they should be ready to take the reins at the second tier hospitals in China."

When working abroad, a nuanced and critical issue, says Dr. Horton, is language. "The well-meaning American surgeon who wants to work abroad can only go as far as language will take him or her. As a result, we decided to build our program using top tier Chinese surgeons who speak English well. The key to the program is that ultimately the teaching for tier two doctors will be in the Chinese language. More than any-

*Dr. William Horton*

where else, when working with cadaver labs and techniques, language skills are vital where double meanings of words or complex vocabulary often interact. Maybe a well-meaning American teacher is explaining to a Chinese surgeon how to best retract the nerve root, saying 'the retraction should be light, easy and intermittent.' That student may not know the word 'intermittent' and may misinterpret the word 'easy' as 'simple' and 'light' as 'illumination'—which all makes no sense."

So where are they now? "DePuy has established two teaching labs, one in central China and another in Shanghai with several courses for 2010 and 2011. We are addressing a twofold mission: one is to develop the top Chinese surgeons as faculty for the tier two teaching hospitals while also training them in such advanced procedures as cervical disc replacement and minimally invasive anterior lumbar corpectomy. The other goal is to help teach the 'second tier' surgeons how to do core spine procedures technically well. These particular courses are being taught in Chinese by the leading Chinese surgeons with two North American or European faculty there as guides and partners. Importantly, we have learned that if the cours-

**"China is our main focus initially, but as we move forward with our international education efforts we look forward to growth in other countries, such as our new training center in Brazil, and the one that is planned to open in India in 2011."**

es are in English then only one third of what is said will actually get through to people. You lose the nuances, which as we all know can lead to problems."

When dealing with the third leg of the stool—distribution—the team has to take into account local and national Chinese politics and market dynamics. Dr. Horton notes, "We can go at this project with gusto, but if we can't find a way to work within the existing system then things won't happen. Let's say we have a really safe product that is half the cost of current products… we must have a way to get the product to the surgeons and patients who need them--otherwise the education will be of limited impact. Sometimes, secondary agendas and arrangements are often in play at the hospital, city or province level that may impede the distribution of affordable technologies. We are trying to address this."

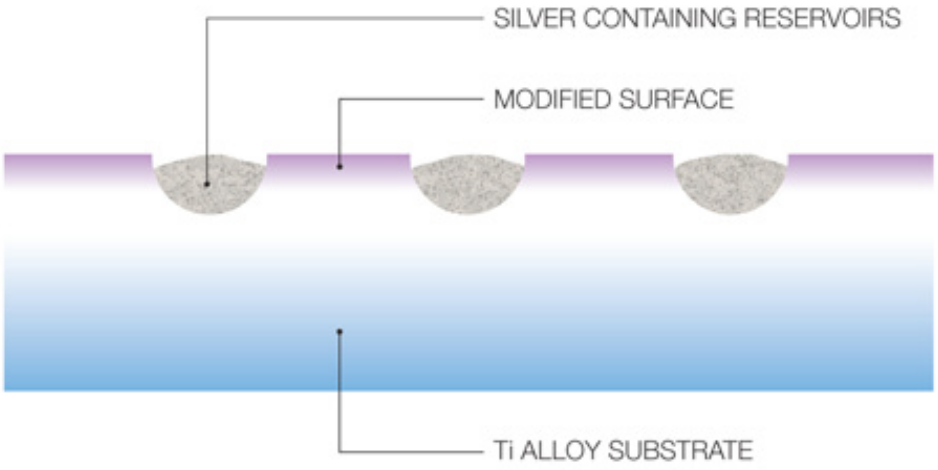
"And while in many cases those in the developing world are no longer sitting and waiting to get technology from the outside world, the average Chinese doctor and patient still recognize the differences in quality control and manufacturing standards. The bottom line is that in most cases, locally made, as opposed to foreign made, products will be used in tier two facilities until more affordable technologies are introduced. The doctors think, 'OK, now I am trained in procedure X, but half of my patients can't afford a name brand product, so I have to be able to offer them something.' So they end up using an inferior device which can be really bad for patients."



As for DePuy Spine, they are excited to be making progress on this challenging, but rewarding program. Debbie Williams, the company's Director of Communication states, "We are truly dedicated to increasing access to care in developing countries. We're scaling up professional, robust educational programs in China and matching these efforts to what specifically is needed by the surgeons and patients in that country. China is our main focus initially, but as we move forward with our international education efforts we look forward to growth in other countries, such as our new training center in Brazil, and the one that is planned to open in India in 2011. These programs will benefit patients throughout the developing world, building on the principles initiated in China, and incorporating features unique to each country as Dr. Horton and our entire education team refine the process." ◆

company

## Zimmer Acquires Anti-Infection Technology




*Agluna Treatment Process/Accentus Medical*

Zimmer Holdings has acquired exclusive global rights to English-based Accentus Medical's Agluna anti-infective technology.

*Cheryl Blanchard, Ph.D., Zimmer's chief scientist, said applying the Agluna technology to Zimmer's implants, "could lead to reductions in the occurrence of post-operative infections in joint replacement procedures."*

A September 3 announcement described Agluna as a patented surface modification technology applied to medical devices manufactured from titanium and its various alloys.

Medical device materials can be susceptible to rapid colonization by bacteria, which then produce a plaque or biofilm as protection against the body's defenses. According to the company, implants treated with Agluna technology have been shown to remain clear of such biofilm formation. In vitro testing has demonstrated that Agluna surface technology has bactericidal effects against bacteria known to cause post-operative, device-related infection, including drug-resistant strains.

### Silver Stitching

During the Agluna process, according to Accentus Medical's Web site, silver is "stitched" into the titanium surface in the form of positively charged ions and is therefore considered to be a surface modification and not a coating. Silver is well known for its bactericidal properties and the use of silver on medical devices has previously been approved by worldwide regulatory bodies on a large number of products. Silver ions at low doses will eliminate bacterial cells with no toxicological effect on the human patient. The treatment enables the steady release of silver ions from the implant's surface over several months by dissolution into body fluids, eventually leaving a silver-free implant that has long-term durability and biocompatibility.

Martin Pickford, Senior Vice-President of Business Development for Accentus Medical, said, "If successful in the long term, Agluna will help significantly reduce the estimated $5 billion in annual costs associated with infections resulting from primary joint replacement."

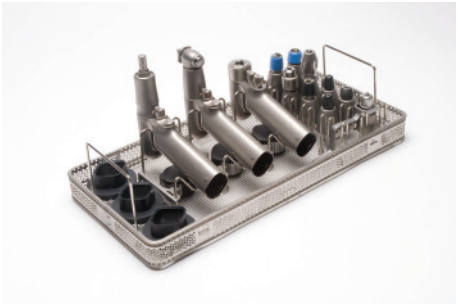
Under the terms of the agreement, Zimmer will acquire exclusive global rights to utilize Agluna for joint reconstruction and trauma products. In addition, the company will have an 18-month option to acquire additional exclusive rights for spinal devices, dental implants and sports medicine products. As part of the agreement, there will be an initial period of further development of Agluna. Accentus and Zimmer will collaborate to secure regulatory approval for products treated with the Agluna technology in both the E.U. and U.S. Financial details of the agreement were not disclosed.

*—WE (September 6, 2010)* ◆

## Cordless Power for Surgical Motors

More power? More convenience? That's what Aesculap is promising with its just released surgical motor system.

Meet the Acculan 3Ti, the latest surgical motor from Aesculap, the company that's been supplying operating rooms with motor systems for two decades. So what makes Acculan stand out from the Aesculap pack?



*Aesculap/Acculan*

Acculan is the latest generation of battery-powered motor systems from the company and can be used for orthopedic, traumatology and cardiothoracic surgeries. Aesculap is promising that this new version will offer even more in terms of precision, reliability and ergonomics than any other previous model from the company.

Because the Acculan 3Ti is all about battery power, let's take a close look at the power source here. The battery pack design is detachable which means the heat-sensitive battery cells and mechanisms escape steam sterilization. This along with the titanium and stainless steel housing are said to make the device last longer, thereby being a cost-effective purchase according to Aesculap.

Boasting 250 watts of peak power Acculan 3Ti is one of the few cordless motor systems to carry the power of pneumatic or cable systems and specific specs include drill modes, both clockwise and counterclockwise along with oscillating and tapping functions.

And you'll never run out of power with this design. Rechargeable batteries are checked with each charging to make sure you're working on full power. What happens when a battery replacement is needed mid-surgery? The non-sterile pack can be changed through a sterile funnel for easy added power.

Aesculap is also touting Acculan 3Ti's ergonomic shape. The design is said to offer excellent weight balance and handling characteristics. And the quick connect design was fashioned with surgeons in mind, giving an easy method for switching attachments and blades.

"Aesculap pioneered the concept of the non-sterile battery and has the most experience with this technology in the market. The battery compartment is completely sealed to the outer environment which allows for the product to be operated even if completely immersed underwater", said Sergej Kammerzell, Product Manager for Acculan at Aesculap.

*—JR (September 2, 2010)* ◆

legal

## AdvaMed Seeks 510(k) Comment Extension


*AdvaMed*

AdvaMed, the medical device industry's largest trade association, has asked the FDA to extend by 30 days the public comment period regarding recommendations to improve the 510(k) process.

A reason for the request is capsulated by one of the 70 recommendation from the 170-page report released August 3 calling for an improved agency database that would serve as a searchable one-stop source for detailed information about cleared devices, including photographs and design schematics.

**Proprietary Concerns**

The unspecified level of detail required of cleared devices is causing concern among device manufacturers that proprietary information will be released.

Janet Trunzo, Executive Vice President of Technology and Regulatory Affairs for AdvaMed, said the issue remains unresolved.

"Particularly of concern to us is the fact that the proposal suggests that detailed photos and design schematics for every 510(k) product would be put into this public database that would be searchable so that anybody, including competitors could get in there and get detailed information about a specific product."

AdvaMed is encouraging its members to express their opposition to the database. The FDA argues that an improved database will make it easier for 510(k) applicants to determine accurate predicate devices.

**Extension Request**

"We have asked FDA for an extension of the comment period because that report contains 170-plus pages of text to review," Trunzo said. "Yet, we only have a 60-day window to submit our comments. We have requested an extension for 30 days. We're not sure that FDA will grant us that extension of the comment period. We do know that many state medical device associations and regional associations have also requested an extension of the comment period."

Most of the agency's recommendations lack specific implementation details. Jeff Shuren, M.D., the agency's top device regulator has promised that the rule-making process that will put meat on recommendations will be transparent and will allow for industry and public input before being finalized.

With the glaring exception of transparency in the ReGen Biologic's case, Shuren has been a man of his word.

*—WE (September 4, 2010)* ◆

## Stryker Settles State OP-1 Complaint

Stryker has agreed to pay the state of Massachusetts $1.35 million to resolve allegations that the company marketed OP-1 without regulatory approval and withheld patient safety information from health care providers to boost sales.

Massachusetts' Democratic Attorney General Martha Coakley, who lost last year's U.S. Senate race to Republican Scott Brown, issued a statement saying that Stryker Biotech had compromised patient safety in pursuit of profits.

Stryker said the settlement was not an admission of liability.

The settlement came after Coakley filed a complaint last month accusing Stryker of falsifying hospital Institutional Review Board documents, subverting clinical review procedure, promoting an unapproved device and misleading physicians. Coakley first notified Stryker in March 2009 that the company was under state investigation.

*shutterstock.com*

Under the terms of the agreement, Stryker will pay $325,000 in civil penalties, $875,000 to fund efforts to combat unlawful marketing and other pro-

grams, and $150,000 to cover costs of the three-year investigation.

In October 2009, three sales managers and former Stryker executive Mark Philip were indicted by a federal grand jury for misleading the FDA about the use of OP-1. The three sales managers pled guilty while Philip pled not guilty.

While this settles Stryker's case with the State of Massachusetts, the federal issues are not concluded.

*—WE (September 1, 2010)* ◆

## DePuy Recalls ASR System

DePuy has voluntarily recalled the ASR XL Acetabular System and ASR Hip Resurfacing System used in hip replacement surgery due to the number of patients requiring revision surgery.


The recall announcement on August 26 said the company was advising patients with an ASR device to visit their surgeons for evaluation of their implant performance. Yearly monitoring is recommended to ensure the ASR hip replacement is functioning well, even in the absence of symptoms.

**March Field Safety Notice**

DePuy issued a Field Safety Notice in March 2010 after receiving new data from the UK that demonstrated the System had a higher-than-expected revision rate at 8-9% at three years when used with smaller head sizes.

The company said new, unpublished 2010 data from the National Joint Registry (NJR) of England and Wales showed a five-year revision rate of approximately 12% for the Hip Resurfacing System and approximately 13% for the XL Acetabular System. The revision rates are across the entire size range. The risk for revision was highest with ASR head sizes below 50 mm in diameter and among female patients.

According to the company, previous post-market surveillance data from a variety of sources, including national joint replacement registries, published literature, company sponsored clinical trials, internal complaints data and unpublished clinical research reports, had shown lower revision rates and that the ASR hip was performing in line with other devices in its class.

DePuy Orthopaedics' President David Floyd said, "We regret that this recall will be concerning for patients, their family members and surgeons. We are committed to assisting patients and health care providers by providing information through multiple channels and paying for the cost of doctor visits, tests and procedures associated with the recall."

**DePuy Covers Costs**

DePuy intends to cover reasonable and customary costs of monitoring and treatment for services, including revision surgeries, associated with the recall of ASR.

Patients and providers with questions related to this recall should visit depuy.com. Patients in the U.S. and Canada can contact DePuy by calling 888-627-2677 Monday-Saturday, 8 a.m. to 9 p.m. EST. Patients in other countries can place a collect call to the U.S. at +1 813-287-1651 24 hours a day, seven days a week.

The Hip Resurfacing System was introduced in 2003 and is only approved for use outside the U.S. The XL Acetabular System was first launched in 2004 and has been available worldwide.

**Discontinued in 2009**

According to the company statement, very few devices remain on the worldwide market because DePuy decided in 2009 to discontinuing the ASR System as a result of declining demand and the intention to focus on the development of next generation hip replacement and resurfacing technologies.

*—WE (September 1, 2010)* ◆

biologics

## Induced Pluripotent Stem Cells Down Under

*Kangaroo Crossing Road Sign/Wikimedia Commons*

G'day mate! Look out for the Australia to become a major player in the stem cell research race.

Is Australia positioning itself as the new hot spot for biologics? Well if the Bernard O'Brien Institute of Micro-surgery in Melbourne, Australia, succeeds with its stem cell work, "the land down under" could be the place to be.

The Institute is working with induced pluripotent stem cells to grow bone and cartilage in a controlled manner, to exact lengths and widths. There is also work there on regenerating organ tissue, like the heart and pancreas. The technology could help for disease, injury or deformity and there is already a clinical trial underway with five women participating to re-grow breasts after mastectomies.

But there are other research center in Australia too. The Monash University and Monash Medical Centre, Melbourne, for example, will be working in utero, injecting fetal stem cells into the fetus to stimulate development of kidneys and lungs in under-developed babies. These stem cells will be taken from the outside of the placenta.

The O'Brien Institute has also established the first dedicated stem cell bank in Australia to be used for research and medicine, in the hopes of sharing cell lines with other researchers and linking with other international banks. This not only could prove valuable to Australian researchers, but centers of study across the globe looking for reliable and affordable stem cell lines.

*—JR (September 1, 2010)* ◆

large joints

## A Better Brace?


*FUSION XT High Performance Knee Brace/Orthofix International*

A knee brace that touts more airflow and a better fit…sounds like Orthofix might on to something good.

Coming off a 30th birthday and opening a new operations and education center, Orthofix International just introduced the FUSION XT High Performance Knee Brace.

Springing out of Orthofix's sports medicine division, Breg, the new knee brace features a new innovation: the AirTech system.

AirTech is said to be a design that improves comfort and fit, boasting a construction that is said to increase air flow thanks to a full system of air mesh vents and grooved channel frame pads. This system is designed to allow cool air in and wick warm air and moisture away from the skin. Improving patient comfort appears to be paramount for this Breg design, with a new pad technology added to the design to take some of the pressure off of the knee and reduce those nagging pinches common with knee braces.

The success of this new technology will then rely heavily on patient feedback and if Orthofix has indeed created a more user-friendly brace word will spread. In fact the FUSION XT also has features to allow patients to give themselves a better fit, according to Orthofix developers.

Alan Milinazzo, Orthofix's President and CEO says about the new addition:

> "The FUSION XT brace is designed to provide significant advancements in performance and durability. The innovative new AirTech system represents our continued focus on making the FUSION line of braces the standard in patient comfort, fit and compliance.
>
> "FUSION XT is designed to provide support for ACL, PCL and collateral ligaments after the patient's recovery from knee surgery, and is also designed for prophylactic use."

Pivot-point strap tabs are longer and more flexible than previous model and are said to hold up better over time. The pivoting action also means patients can position straps for comfort and fit.

This introduction comes just as Jeffries & Company released a glowing recommendation for Orthofix, stating that "Refinancing widely expected but still positive." Raj Denhoy, Jeffries's analyst reports that with a new $300 million, five-year credit facility and earnings estimates on the rise, "We view the bias to estimates as squarely to the upside at Orthofix. We use 13x 2011 earnings for our $36 one-year target. We rate OFIX shares Buy."

With a $150+ million market for ligament braces and a growth rate that is predicted by many to rise over the new year, Orthofix should have a lot of potential patients for the device. Look for a woman's version of the FUSION XT coming out soon.

*—JR (September 9, 2010)* ◆

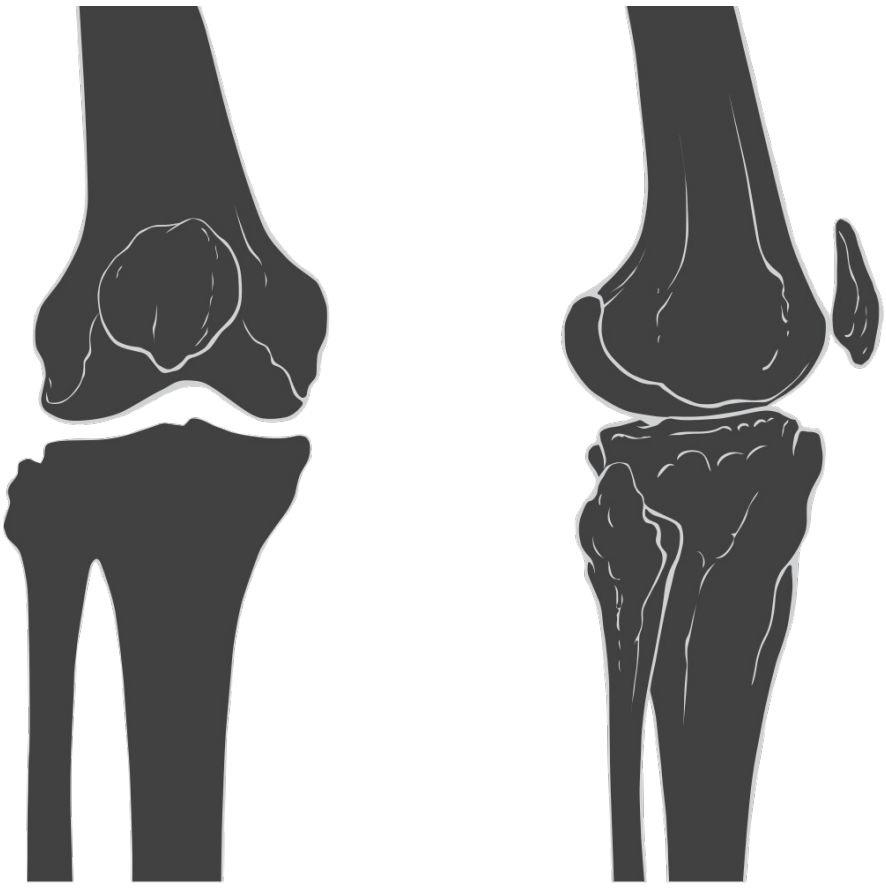
## Amedica Receives Knee Patent

Amedica announced on August 31 that the company has been assigned a U.S. patent for a knee implant that features a monoblock ceramic tibial component. This continues the company's shifting focus from spine to large joints.

The company uses silicon nitride ceramic technologies to develop and commercialize spine and total joint implants. It has commercialized various spinal implant products while developing reconstructive hip and knee implants.

**Patent No. 7,776,085 B2**

This patent (U.S. Patent No. 7,776,085 B2) is for an articulating tibial component with natural or prosthetic (resurfaced) femoral surfaces. The inventors are: John Bernero, Ashok Khandkar, Ramaswamy Lakshminarayanan, and Aaron Hofman. The patent is assigned to Amedica.



*Knee skeleton/Wikimedia Commons*
*Knee skeleton diagram/Source: Patrick J. Lynch, medical illustrator*

The tibial component is created from a silicon nitride monoblock adapted for fixation relative to a patient's tibial bone. Alternately, it can be affixed by a ceramic bearing insert component carried by a tibial baseplate member that is adapted for fixation relative to the tibial bone. In either form, the monoblock silicon nitride tibial component includes one or more upwardly concave articulation surfaces that promote movable bearing engagement with a generally convex or condylar-shaped femoral articulation surface.

Ben Shappley, Chief Executive Officer, President and Director of Amedica, said the monoblock silicon nitride technology with a bone-contacting Bioactive surface provides implants with, "remarkable wear characteristics and extended service life. In the long term, the technology helps surgeons achieve more successful outcomes in restoring patient function."

"Using monoblock silicon nitride with bio-ingrowth technology in the tibial component eliminate conventional polymer-based bearing inserts and the related, undesirable wear debris problems and revisions associated with the older technologies used in current implants," added Shappley.

**"Fracture Resistant, No Wear Debris, Enhances Bone Growth" - Amedica**

The company says its material is "remarkably fracture resistant, and its articulating surfaces do not produce the wear debris that is linked to osteolysis-related re-operations. Additionally, the Bioactive implants provide a hydrophilic surface and a conductive cancellous structure that enhances bone ingrowth and attachment."

Amedica recently entered into a Joint Venture Agreement with Orthopaedic Synergies Inc., a global reconstructive hip and knee company.

*—WE (September 7, 2010)* ◆

## Access to TJR Uneven in England

If you've got a bad hip and live in the hinterlands of England, well, that stiff upper lip might come in handy. Researchers from the UK and Canada have found that access across England to total joint replacement (TJR) of the hip or knee is uneven…women, elderly people, and those in deprived areas continue to be worse off.

Results showed that people aged 60-84 were more than twice as likely to have received an operation than people aged 50-59, despite all people in both groups having an equal need. People aged 85 and over, however, were less likely to have had the operations. Men received 31% more knee replacements relative to need than women and 8% more for hip replacements. People living in deprived areas were found to receive around 70% less provision relative to need compared with the most affluent areas for both knee and hip replacements.

Those living in urban areas got greater provision of knee replacement relative to need than people living in more isolated places, but the effect was different for hip replacement with people in villages or isolated areas getting the most provision relative to need.

The team used data from the Somerset and Avon Survey of Health (a small-area population-based survey), the English Hospital Episode Statistics (HES) database and the English Longitudinal Study of Ageing (ELSA)—a nationally representative population-based survey of 11,329 people aged 50 and over living in private households in England.

Andrew Judge, Senior Statistician at the National Institute for Health Research at the University of Oxford in the UK, told *OTW*, "We do not know the reasons why these inequities exist. Whilst hospital factors such as numbers of surgeons, beds and operating theatres were associated with overall levels of equity, they did not explain differences by age, sex and deprivation group. But it may be explained by patient-related factors such as willingness for surgery, or different thresholds for referral. Further research is required to enable the design of interventions that could ameliorate these patterns."

*—EH (September 2, 2010)* ◆



*Vaughan Leiberum/Wikimedia Commons*

extremities

## Inc. Magazine Ranks TMC Orthopedic

*TMC Orthopedic/Right: Prosthetist Ben Falls with patient Richard Lockley*

Every time this company grows, amputees have more hope than ever. TMC Orthopedic has just announced that Inc. Magazine has ranked the company 2,336 out of the 5,000 fastest growing companies in the U.S. For this honor, businesses were ranked according to their past three-year growth. This is a particular honor given that so many businesses are struggling.

Joe Sansone, CEO of TMC Orthopedic and the Amputee & Prosthetic Center, attributes the company's success to its commitment to patients and revolutionary approach to amputee care.

"We could not be more proud to be named one of the fastest growing companies in the U.S.," said Sansone in the news release. "It's a testament to the tremendous effort and success that we have achieved over the past nearly 19 years, but even more so a testament to how dedicated our team is to delivering the best in products and patient care."

TMC is the parent company to the Amputee & Prosthetic Center (TAPC), which has also seen tremendous growth since it was founded in 2005. TAPC was named #2 on the Houston Best Places to Work List for 2010 and #1 in 2008 and 2009. This part of the business has received multiple honors for its dedication to the amputee community, most notably through its charity Limbs of Love, which has provided over $1 million in prosthetic devices to amputees that would otherwise go without.

Sansone told *OTW,* "One of the most important projects we are trying to get off the ground is the Amanda McDaniel Fund. Amanda, a bright and vibrant teenager, was the recipient of a prosthetic leg from our TMC charity, Limbs of Love. Limbs of Love, which was founded in 2007, is a non-profit which provides prosthetic limbs for amputees in need all across the country. Unfortunately, Amanda later lost her battle with cancer, but in order to honor her memory, we are establishing the fund in her name to help other children. The money from the fund will go towards scholarships for amputees under the age of 18 to help them participate in camps or activities that they enjoy."

When asked about the progress of the fund, Sansone, the founder of Limbs of Love, told *OTW,* "The fund is still in the very early stages and we are working on securing sponsors, but we know how many children can be helped by this money. Programs like the Amanda McDaniel Fund and Limbs of Love are the lifeblood of our company, motivating employees by showing them how their hard work really does make a difference in the lives of others."

*—EH (September 8, 2010)* ◆

## Wright Medical Launches EVOLUTION

Anatomically, well, the knee pretty much stays the same. The technology to handle its issues, fortunately, evolves. And you might now say that Wright Medical Technology has the market on knee technology evolution. The company has announced the launch of the EVOLUTION Medial-Pivot Knee System, which features enhanced instrumentation, more sizing options and a posterior stabilized option.

David Blaha, M.D., in Ann Arbor, Michigan, explained in the news release, "The unique feature of both the ADVANCE and the EVOLUTION Medial Pivot knees is the 'ball-in-socket' mechanism on the medial side. The 'ball-in-socket' mechanism is designed to mimic the anatomy of the normal knee to promote more natural stability and motion."

As indicated by the company, studies have shown that Wright's medial-pivot technology has been consistently preferred by patients who received bilateral knee implants with a medial-pivot design in one knee and a traditionally-designed implant in the other knee.

The state-of-the-art engineering concepts and manufacturing technologies used to bring about the EVOLUTION

*The EVOLUTION Medial-Pivot Knee System/Wright Medical Technology*

included the use of CT-scans to produce implants which more accurately replicate natural knee anatomy, as well as features to aid in implantation through less-invasive surgical exposures. The resulting EVOLUTION Knee System is designed to ease rehabilitation and address stability concerns which may be experienced by some total knee replacement recipients.

Lowry Barnes, M.D., of Little Rock, Arkansas, noted in the news release, "Often, total knee replacement patients complain that their replaced knee does not feel normal, citing noises or a sensation of the joint slipping, especially as they descend stairs. The EVOLUTION implant's more refined medial-pivot design may feel more normal for patients."

Alex Winber, Director of OrthoRecon—Knees told OTW, "The EVOLUTION Knee is based on the ADVANCE Medial-Pivot Knee. The ADVANCE Medial-Pivot Knee was launched 12-years ago. In those 12 years, our customers began using less-invasive techniques for total knee replacement. They requested both implant and instrument modifications to help them. The EVOLUTION instruments have been reduced in size to more easily fit into a less invasive exposure. However, they incorporate several features which promote accuracy. For instance, several instruments allow surgeons to 'dial-in' the alignment of the implants to customize the implant fit for the patient."

Winber also told *OTW*, "The EVOLUTION implants have several features designed for less-invasive exposure. Of all the features, we are most excited about patent-pending tibial locking mechanism which was expressly designed to allow easier implantation through a smaller exposure. We tested this locking mechanism in our pre-market trial, and all participants were excited about this innovation. The EVOLUTION Knee is the second generation of medial-pivoting knee from Wright. What makes our total knees different is the ball-in-socket articulation on the medial side. This ball-in-socket allows the knee to be very stable and quiet because we've improved on things that could contribute to noise (such as instability)."

*—EH (September 10, 2010)* ◆

reimbursement

## Noridian Reconsidering VCF Coverage

Noridian, one of CMS's local coverage administrators is reconsidering whether or not vertebroplasty and vertebral augmentation procedures are reasonable and necessary or no better than a "sham procedure."

Noridian issued a draft Non-Coverage Local Coverage Determination (LCD) policy for vertebroplasty and vertebral augmentation earlier this summer. The company administers the Medicare program in several states under contract with the federal government.

A final decision regarding coverage will be made sometime after the September 6 comment deadline passes. The CPT codes under review are 22520 through 22525.

Vertebral compression fractures (VCF) represent significant morbidity to a large number of Medicare beneficiaries. Noridian believes that perhaps 250,000 individuals out of some 700,000 who suffer from this condition annually fail to respond adequately to conservative, symptom-directed care. Noridian has allowed coverage for the procedures since 2000.

**Noridian: "Absence of Literature"**

Noridian is basing its second thoughts on the, "ongoing absence of a body of literature that demonstrates the efficacy of either vertebroplasty or vertebral augmentation in the treatment of low back pain combined with utilization frequently aberrant from both the requirements of this policy and good medical practice."

The original coverage decision was based on the assumption that "initial, immature but highly positive, literature support would be augmented as experience with the procedure evolved. Such has not proven to be the case. As outlined in [a] recent *New England Journal of Medicine* article, results from these procedures have not met early expectations. In fact, the NEJM article reported on a clinical trial where the results of the procedure were no better than placebo (sham procedures)."

In effect, Noridian is saying they need more proof that the procedures are reasonable and necessary.

**Slosar: "Overwhelming Literature Supporting Effectiveness"**

Paul J. Slosar, M.D., President, SpineCare Medical Group at the San Francisco Spine Institute, wrote to his colleagues in mid August:

> "Contrary to two recent publications in the NEJM, the overwhelming body of published literature supports the effectiveness of vertebral augmentation (kyphoplasty and vertebroplasty) as do my personal clinical results and those in the medical community at large.
>
> "Most recent published results (Klazen, Lohle et al. Lancet 2010) reported on the VERTOSS II, a prospective randomized clinical study; support the clinical effectiveness of vertebroplasty. This 200+ patient study (almost twice that of the two NEJM articles combined) confirmed the significant near term and long term clinical advantage of stabilizing VCFs using vertebroplasty in patients with painful VCFs. Additionally, those data were consistent with the significant clinical advantage demonstrated in the prospective randomized 300 patient clinical study on kyphoplasty (Wardlaw et al. Lancet 2009)."

National coverage of the procedures may ultimately be the topic of a future Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) meeting.

*—WE (September 2, 2010)* ◆

*Wikimedia Commons*

# Would you call the same play for an entire game?

## Spinal fractures are different.

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Because no two patients or spinal fractures are the same, CareFusion has expanded the AVA*max*® Advanced Vertebral Augmentation system to include the tools you need to perform kyphoplasty or vertebroplasty. With AVA*max*, you have the right tools for the right approach at the point of care.

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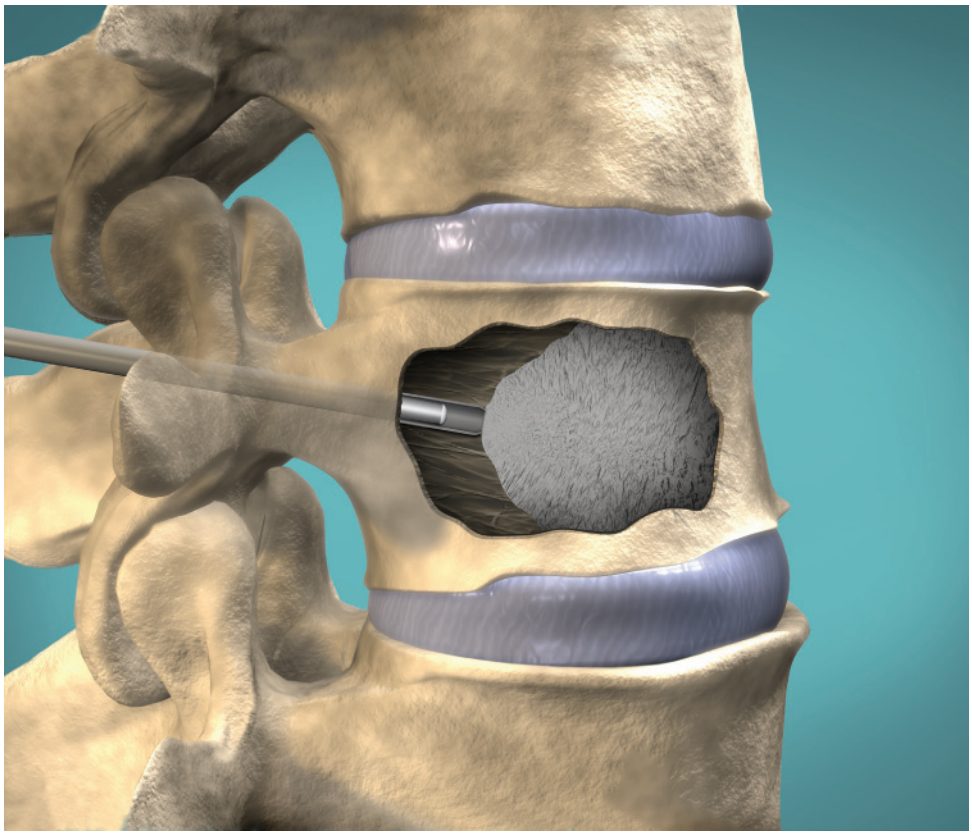
spine

## CareFusion Launches AVA*max* Vertebral Balloon



*AVAmax Vertebral Balloon/CareFusion Corp.*

Pop the champagne and don't forget the balloon release…CareFusion has announced the national commercial launch of the AVA*max* Vertebral Balloon, a minimally invasive device for use during kyphoplasty, a procedure for treating spinal compression fractures. As indicated by CareFusion, the AVA*max* Vertebral Balloon represents a competitive breakthrough and, along with its related components, costs up to 40% less than similar kyphoplasty products on the market today.

The AVA*max* Vertebral Balloon is part of an all-in-one system that includes an 8-gauge or 10-gauge needle, bone cement and delivery instruments for kyphoplasty or vertebroplasty, an alternate procedure to treat compression fractures. The all-in-one system gives doctors the choice and flexibility to perform either procedure at the time of patient care.

During the product's limited release period, CareFusion completed approximately 300 case studies with 8 in 10 physicians saying they would strongly consider switching to the AVA*max* product, according to post-product evaluation surveys.

"The AVA*max* Vertebral Balloon is easier to use and more efficiently designed than the system previously available to me," said C. Douglas Edmondson, M.D., FACR, interventional radiologist at Medical Center of South Arkansas, in the news release. "With one more tool in the AVA*max* toolbox, I can more selectively tailor spinal interventions with vertebropasty or kyphoplasty with a huge cost savings and no wasted materials."

The good news for radiologists? The AVA*max* PLUS vertebral augmentation system, which delivers cement for the procedure, allows the radiologist's hands to be out of the radiation field.

CareFusion has established a dedicated sales force for the AVA*max* Vertebral Balloon in order to drive product adoption and market penetration in the U.S. The company intends to expand commercial availability to Europe.

Elaborating on the development process was Jennifer Anderson, Vice President of Marketing, Surgical and Interventional Technologies at CareFusion, who told *OTW*, "CareFusion's product development team performed a thorough voice of customer analysis by viewing cases and interviewing clinicians to ensure a deep understanding of the procedure and the clinician needs in order to develop and introduce a new innovative, flexible, kyphoplasty product into the market."

Anderson also told *OTW*, "The majority of surgeons in the limited-commercial release case studies said they would consider switching to the AVA*Max* vertebral balloon product. Surgeons who indicated they wouldn't switch said it was because they had a prior agreement for another product."

*—EH (September 9, 2010)* ◆


# New Study of VCF and Mortality Rates Available

**The Study:** PearlDiver has just completed an extensive study of the VCF market with particular attention to patients who've received either vertebroplasty or Kyphoplasty treatment for vertebral compression fractures. Patients were tracked by age, gender, and select comorbidities. While the study does not attempt to correlate VCF procedures and mortality, it does track subsequent in-hospital mortality over time in these patients. Fully 41,000 VCF patients were tracked between 2006 and 2008 using the PearlDiver database of more than 1 billion patient records.

**The Price:** $3,900 (customers who've purchased a PearlDiver report in the last 12 months receive 20% discount to $3,120).

**To order:** Email dataguys@pearldiverinc.com or call 260-469-4161

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