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Orthopedics This Week

week in review

picture of success

breaking news

For all news that is Ortho, read on.

Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

This Week: Warren Buffet once said he buys stocks as if the stock market was going to stop working for five years. Translated: he buys companies with strong cash flows and low volatility. Wall Street is fickle. So keep your eye on cash flow and stable operations. Ortho demand is constant and cash flows remain comparatively high.

Rank	Last Week	Company	TTM Op Margin	30-Day Price Change	Comment
1	1	Orthofix	13.51%	(5.21%)	Cash balances have doubled in the last year while inventory is down 20%. Getting stronger and stronger.
2	2	Kensey Nash	38.72	(1.89)	KNSY kicks out 39% operating profit margin even with R&D spending at 22% of sales.
3	5	Johnson & Johnson	27.10	(3.88)	JNJ raises $1.1 billion in new debt. With $19 billion in cash, not a big deal really. Issue is ortho operations. Can DePuy shine inside JNJ?
4	3	Medtronic	32.48	(6.30)	The good news is that MDT has the lowest P/E ratio. Bad news is it reflects MDT's lack of growth prospects.
5	NR	Conmed	8.76	11.21	Did CNMD ever come roaring back! Up 11% in a month when every ortho stock sold off. Why? Monster earnings report.
6	8	Integra LifeSciences	15.37	(3.65)	IART signs three-year deal with GPO Amerinet and sets up a $600 million credit facility. Up two spots.
7	4	Zimmer	27.69	(9.63)	Big Blue is stable. That's a good thing. Now, it's time for some growth—organic or otherwise.
8	6	Smith & Nephew	22.83	(4.46)	SNN wins another patent suit in Germany. Margins are improving. But where's the growth?
9	10	Symmetry	11.48	(13.28)	Whew! That last quarter sucked. Now come the positive YOY comparisons? Maybe.
10	7	Stryker	24.71	(12.33)	The key for SYK is deployment of its cash. It is sitting on the balance sheet like an albatross dragging down ROA and ROE.

Robin Young's Orthopedic Universe

Top Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	Capstone Therapeutics	CAPS	$0.90	$37	32.4%
2	Osteotech	OSTE	$3.84	$69	24.7%
3	TiGenix	TIG.BR	$2.58	$80	18.7%
4	CONMED	CNMD	$19.64	$565	11.2%
5	Kensey Nash	KNSY	$22.79	$222	-1.9%
6	TranS1	TSON	$2.52	$52	-1.9%
7	Integra LifeSciences	IART	$36.17	$1,050	-3.6%
8	Johnson & Johnson	JNJ	$58.15	160,380	-3.9%
9	Smith & Nephew	SNN	$44.32	$7,880	-4.5%
10	Synthes	SYST.VX	$115.69	$13,729	-4.7%

Worst Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	Alphatec Holdings	ATEC	$1.97	$172	-58.5%
2	Exactech	EXAC	$14.34	$185	-18.7%
3	Wright Medical	WMGI	$13.97	$548	-18.4%
4	Mako Surgical	MAKO	$10.02	$339	-17.8%
5	RTI Biologics Inc	RTIX	$2.49	$136	-16.4%
6	Orthovita	VITA	$1.64	$126	-14.1%
7	Symmetry Medical	SMA	$9.53	$343	-13.3%
8	Stryker	SYK	$46.57	$18,490	-12.3%
9	NuVasive	NUVA	$31.92	$1,260	-10.8%
10	Zimmer Holdings	ZMH	$51.44	$10,340	-9.6%

Lowest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Medtronic	MDT	$35.57	$38,520	10.73
2	Exactech	EXAC	$14.34	$185	11.59
3	Zimmer Holdings	ZMH	$51.44	$10,340	12.24
4	Wright Medical	WMGI	$13.97	$548	12.29
5	Johnson & Johnson	JNJ	$58.15	$160,380	12.33

Highest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Smith & Nephew	SNN	$44.32	$7,880	61.03
2	RTI Biologics Inc	RTIX	$2.49	$136	32.57
3	Synthes	SYST.VX	$115.69	$13,729	32.33
4	NuVasive	NUVA	$31.92	$1,260	26.23
5	Symmetry Medical	SMA	$9.53	$343	24.89

Lowest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	Orthofix	OFIX	$30.22	$533	0.58
2	CryoLife	CRY	$5.30	$150	0.61
3	NuVasive	NUVA	$31.92	$1,260	0.64
4	Exactech	EXAC	$14.34	$185	0.73
5	Integra LifeSciences	IART	$36.17	$1,050	1.01

Highest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	CONMED	CNMD	$19.64	$565	15.22
2	Johnson & Johnson	JNJ	$58.15	$160,380	1.92
3	*Average*			*$10,664*	*1.67*
4	Symmetry Medical	SMA	$9.53	$343	1.64
5	Alphatec Holdings	ATEC	$1.97	$172	1.47

Lowest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	Osteotech	OSTE	$3.84	$69	0.70
2	CONMED	CNMD	$19.64	$565	0.78
3	RTI Biologics Inc	RTIX	$2.49	$136	0.86
4	Orthofix	OFIX	$30.22	$533	0.95
5	Symmetry Medical	SMA	$9.53	$343	1.02

Highest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	TiGenix	TIG.BR	$2.58	$80	77.25
2	Mako Surgical	MAKO	$10.02	$339	10.68
3	Synthes	SYST.VX	$115.69	$13,729	7.61
4	NuVasive	NUVA	$31.92	$1,260	2.89
5	Kensey Nash	KNSY	$22.79	$222	2.81

510(k) Retooling: Solution in Search of Problem

By Walter Eisner

On August 3, the FDA released a 120-page report which included CDRH Director Jeff Shuren's long-promised recommendations for overhauling the agency's 510(k) device clearance program.

The 70 recommendations included in the report address three areas: safety, predictability and innovation. Among the recommendations are calls to create a new Class IIb category, establish a Center Science Council and require more up-front safety and effectiveness data from industry in the submission process.

Will requiring more up front data from industry result in safer and more effective medical devices entering the market? Has the clearance program failed to protect public health?

Google Images

The Hall Report

Ralph Hall, a Distinguished Professor and Practitioner at the University of Minnesota Law School tried to find out.

Professor Hall and research assistants reviewed 510(k) data over a five-year period (2005 to 2009) to determine if the FDA review system was permitting products onto the market without a reasonable assurance of safety and effectiveness.

Given the pressure on the FDA from agency whistleblowing scientists, consumer advocates, high-profile media cases like ReGen Biologics and aggressive Congressional leaders, the answer may surprise you.

99.78% Success Rate

Of the 19,873 510(k) submissions made to the FDA over this five-year period, only .22% resulted in a Class 1 recall for premarket issues. Of those recalls, only two were for orthopedic implants.

In other words, the 510(k) clearance process works 99.78% of the time.

Here is what Professor Hall's study showed:

Total 510(k) Submissions in 10 years	39,747
Average Submissions in 5 year time period	19,873
Total 510(k) Recalls for 2005-2009	89
Total 510(k) Recalls for Pre-Market Issues for 2005-2009	43

Source: Ralph Hall

Solution in Search of Problem

Are the 70 recommendations to overhaul the 510(k) program put out by the FDA a solution in search of a problem?

We'll try to answer that question over the next few issues of *OTW*.

This is the first installment in a three-part series that looks at the effectiveness of the clearance program. The second installment will

Ralph Hall/reilly.nd.edu

consider the recommendations offered by the FDA and their likely impact on the orthopedic industry and surgeons. Finally, in part three, we'll focus on one of the recommendations already implemented by the agency: the establishment of the Center Science Council to be run by Bill Maisel, M.D., the newly appointed Deputy Director of the FDA's Center for Devices and Radiological Health.

This week we're digging into Professor Hall's research.

Research Methodology

Hall and his researchers classified an FDA clearance decision as "wrong" if the device was subsequently pulled off the market with a Class I recall. The researchers used Class I recalls instead of other measures (such as Adverse Events reports), because such recalls require mandatory reporting, are overseen by the FDA and permit researchers to separate review issues from non-review issues. Other measures may be inaccurate, unconnected to the reported event or anecdotal in nature.

Recalls occur because of one of three broad root causes:

- Premarket Issues
- Postmarket Issues
- Counterfeit or "quack" devices

The 510(k) clearance process is only relevant to premarket issues which deal with design problems and clinical data gaps before the product hits the market.

During the five-year period studied by Professor Hall, 116 Class I recalls were instituted.

There are 13 categories for a primary reason for a recall. Four are relevant to premarket concerns. Hall's research revealed the following results within these four areas:

- 32 recalls for design issues
- 10 recalls for software issues
- 8 for failure to warn
- 0 for failure to indentify risk

No Recalls Due to Clinical Risks

The evidence showed that **NO RECALLS** were identified as being related to newly discovered clinical risks. "This is a major difference compared to pharmaceutical recalls where human clinical trials are frequently used to identify clinical risk," said Hall.

As design/software issues are the major cause for recalls, Professor Hall says the best way to deal with those issues are through design controls. "The role of QSR (Quality System Regulations) is critical and could have substantial positive effects."

Some physicians such as Rita Redberg, M.D., a cardiologist specializing in heart disease in women, testified in front of the Institute of Medicine (IOM) that human clinical studies should be required for any device implanted in humans. Hall debated Redberg in front of the IOM and believes she has a sympathetic audience on the panel.

This is important because the IOM will offer its own recommendations for a 510(k) overhaul next summer. Hall says the FDA may institute less controversial recommendations immediately from its own report and let the IOM tackle the more contentious issues.

Would requiring additional human clinical studies have a significant impact on Class I safety recalls for cleared devices? "Our data indicates that it would have very little impact," says Hall.

"Industry and the FDA have done a great job of assuring safety. Given the need to balance safety and access and the inability to be all-knowing, can one expect more?" asked Hall.

It is clear that any recommendations to change the 510(k) process to provide greater assurance that unsafe implants

are not going to go into people's bodies is, in our opinion, a solution in search of a .22% problem.

Device Safety in Perspective

To put this .22% problem into perspective, Hall points out that 2.3% of Medicare hospitalizations result in a patient safety event; 2% to 4% of patients risk getting a hospital-acquired infection and 15% of patients over 65 receive unsafe prescriptions.

"If I were going into a hospital, I'd be worried about a lot of other things before I'd worry about the device that will be implanted in me," added Hall.

The professor should feel particularly safe if the device is an orthopedic device. Of the .22% of recalled cleared devices over the five-year study period, only 2.5% of those were for orthopedic devices. Infusion pumps and AED's (automated external device) were the highest percentage recalls of the device group, garnering 17.8% and 10.2% of the total recalls.

Given that some of the FDA recommendations include calls for more up front data and the creation of a new IIb device class, "PMA Light" as Hall agreed to call it, Hall says it would be hard to define a logical fourth class based on safety needs.

Physician Support

Professor Hall isn't the only one who thinks the clearance review process works.

In a March 22, 2010, letter to FDA Commissioner Margaret Hamburg, M.D., the American Academy of Orthopaedic Surgeons (AAOS) and 12 other medical societies (including the North American Spine Society) wrote:

With very few exceptions, the 510(k) process provides a reliable pathway for safe and effective devices to enter the market and aid in the treatment of patients in need in a relatively short time. We believe this program unites a least burdensome approach to the regulation of medical devices, a transparent process for the review and clearance of medical devices, and the use of the most expeditious pathway for bringing new products to market.

The AAOS exhorts the FDA to employ guidance documents and existing standards to further strengthen the 510(k) review process and transform it into a program that will continue to optimally serve the Agency, patients, physicians and the public into the future.

Untold Reasons for Overhaul

If the data clearly and irrefutably shows that the safety issues are a .22% concern, what is really driving the FDA's push for revamping the 510(k) process?

Hall says that he sees deeper levels at work here. How is the FDA working internally? How is the overall risk/benefit equation of new products and devices being evaluated and what does it mean for the physician and his or her ability to offer their patients new and innovative products?

Alice in Wonderland/John Tenniel, 1865/Wikimedia Commons

Next week we'll dig into those questions. We'll talk to Bill Mihalko, M.D., one of the AAOS representatives working with the FDA and Institute of Medicine to assure that orthopedic surgeons are heard and heeded.

Will the FDA recommendations result in patients getting faster access to life sustaining devices? Will it result in speeding innovation and keeping product development in the U.S.?

Click here to read the recommendations yourself. You've got until October 4, 2010 to let the agency know what you think. ◆

Who Will Control Osteotech?

By Robin Young

Osteotech, one of the oldest suppliers and developers of allograft implants for surgery is about to become, apparently, Medtronic's latest division. Spending a whopping 3% of its available cash (we think that qualifies as petty cash) $39 billion Medtronic is buying $123 million Osteotech.

Wikimedia Commons

Just yesterday, owners of nearly 30% of the shares of New Jersey-based Osteotech, Inc. were preparing to challenge the company's current management and board of directors charging that current management and board needed to be replaced.

Now, Osteotech's upcoming August 23 shareholder meeting at the Sheraton Hotel in Eatontown, New Jersey, will likely be a bit anti-climactic. Perhaps, instead of fighting, dissident shareholders Heartland Advisors, Inc., Spencer Capital Opportunity Fund, LP, Spencer Capital Management, LLC, Spencer Capital Partners, LLC and Boston Avenue Capital LLC can congratulate management and board for, finally, obtaining a price for the stock that is—well, the same as the price when most of these guys bought in.

Still, why would Medtronic buy Osteotech?

Here are four reasons:

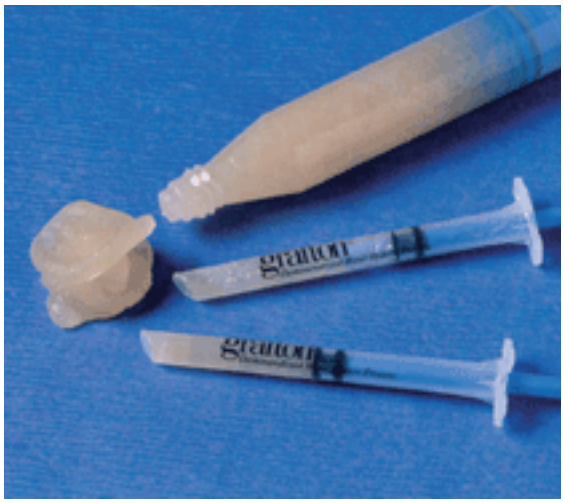
1. Exclusive access to DBM and other allograft bone and soft tissue products. Over the years Medtronic has purchased its allograft bone products from a variety of sources including Regeneration Technologies (now THAT was a tempestuous relationship) and even had its own allograft subsidiary. Some commentators have suggested that DBM is, in some way, a substitute for BMP. Right. The amount of BMP in a plug of DBM is roughly equivalent to a single drop of rain on the plain in Spain. Not much. Scott (Boden), back me up here.
2. Cheap revenues. Osteotech, at a market cap of about $80 million was one of the cheapest companies in all of orthopedics. But, as the dissident shareholders made very clear and as did Osteotech's management in their annual reports, you basically get what you pay for. Namely, a company that has always struggled to be profitable.
3. Control of their own allograft destiny. Or, density. This deal is particularly notable for the fact that a hardware supplier is finally buying an allograft company. No longer can anyone say that a hardware company won't buy an allograft company. Medtronic may have been in the body parts business, but it was fairly well under the radar. No more.
4. Exclusivity. Bye-bye to Osteotech's other customers who compete with Medtronic. Where will they go? Hello MTF, Allosource, Lifenet, TissueLink, RTI, etc.

But, why would Medtronic NOT want to buy Osteotech? Two reasons:

1. Lack of operating profit. Medtronic boasts one of the highest rates of operating profit in all of medicine—32.5% of sales. Osteotech's operating profit is (0.7)%.
2. Body parts. Approximately every seven years someone does something stupid and tries to circumvent established AATB or FDA rules. Like the funeral parlors in New Jersey that shipped parts around without consent or concern for rudimentary safety factors. Now Medtronic will be on reporter's speed dial for the next flare up

Bottom Line

Osteotech's dissident shareholders had six major concerns as they girded their loins for a fight with management on August 23.



1. **The Price of Osteotech's stock is too low**: Now it is 65% higher— roughly the same amount that dissident shareholders were claiming was lost due to management failures. The dissident group pointed out in their SEC filings that from April, 2007 to August 3, 2010, Osteotech's stock price had declined by approximately 55%. The dissident shareholders even pulled a chart from Osteotech's own annual report for 2009 to show that Osteotech's cumulative total stock return during the five-year period ended December 31, 2009, was worse than the NASDAQ Stock Market Index and the Dow Jones Medical Supplies Index. Specifically, an investment in Osteotech common stock on January 1, 2005 would have resulted in a nearly 42% loss. The Dow Jones Medical Supplies Index, which Osteotech has selected as the nearest comparable sector index, rose over 42% in that same period.

2. **Operating results and financial conditions have deteriorated:** Sure, but that's Medtronic's problem now. The dissident shareholders were pointing out that Osteotech's sales have stayed essentially flat between 2005, when the company generated $93.3 million, to 2009 when Osteotech reported $96.7 million in sales. They also stated that Osteotech lost a large customer in 2009 and, not entirely coincidentally, reported a $4.0 million loss that year versus a net income of $2.2 million in 2008. "Osteotech is also hemorrhaging cash,"wrote the dissident shareholders in their filing; "In the past two years, the company has burned over $12.0 million in cash, reducing its cash from $22.8 million as of December 31, 2007 to $10.7 million as of December 31, 2009."
3. **The core business is eroding:** Hey, after this deal it may erode further, but it could pick up from Medtronic's expanded business as well. Osteotech's DBM product line, which represents most of the company's sales, fell 6% in 2008 and fell another 8% in 2009. Sales from the client services segment fell a sobering 74% in 2009 which came after yet another large decline in 2008. Why the decline? Osteotech's largest

customer, Musculoskeletal Transplant Foundation, had decided NOT to renew their contracts with Osteotech. Ouch!

4. **Management hasn't met new product launch expectations:** Medtronic is now in charge of that. And there apparently is a lot to fix. According to the dissident shareholders's again,_Osteotech's initial launch date for its Plexur M product was mid-2007. On March 8, 2007, in the company's quarterly earnings call, Osteotech's CEO Sam Owusu-Akyaw announced that the product would not be released before 2008. On July 30, 2009, Osteotech said that there would be more delays and that the full product launch was pushed to the fourth quarter of 2009. Come November 6, 2009, Robert M. Wynalek, Osteotech's President Domestic, indicated that Plexur M's full release should happen in the second quarter of 2010, *three years* later than originally planned. Then for MagniFuse, Osteotech initially estimated that it would be released by 2008. Instead, Osteotech's management announced, in a May 10, 2010 press release that the national launch of MagniFuse products was more likely to occur in the second quarter of 2010. Finally, Osteotech's new Human Collagen Technology product, DuraTech BioRegeneration Matrix, was expected by management to roll into the market by mid-2010. We are still waiting. In fact in Osteotech's annual report to shareholders for the year ended December 31, 2007, filed with the SEC in March 2008, management said that DuraTech would be released in early 2009. On May 1, 2009, Osteotech's management then said that they expected to file a 510(k) submission to the FDA in the early third quarter of 2009, with a commercial product release expected late in the fourth quarter of that year. On December 17, 2009, the company announced the filing of its 510(k) application for FDA clearance of DuraTech.

5. **There is poor accountability to shareholders:** Ok. But there's about to be just one shareholder soo....Its academic now.

6. **Poor Corporate Governance**: Actually, this should be fascinating. According to SEC filings, senior management stands to walk away with several million dollars in change-of-control compensation. The dissident shareholders had drawn attention to these "poison pill" and "anti-takeover" provisions and now they will, we'd guess, likely be put into effect.

Osteotech Management's Response

Hey, we just sold the company for a 65% premium.

And, by the way, we think:

1. **Our Stock Price Performance Was Fine**: According to management the stock has performed well. Osteotech's total stockholder return increased, on a year-over-year basis, in 2006, 2007 and 2009. Osteotech's total cumulative stockholder return since 2005 has exceeded the returns of its primary competitors, RTI Biologics, Inc. and Orthovita, Inc.

2. **Our Operating Results Have Improved**: Osteotech returned to profitability in the second quarter of 2010 and increased its cash position in comparison to the first quarter. Osteotech's results of operations and financial condition have been improving since the current management team was put in place in 2006. In 2005, the company realized a net loss of $21.1 million. Mr. Owusu-Akyaw began leading the new management team as Chief Executive Officer in 2006, and Osteotech was profitable in 2006, 2007 and 2008.

3. **Our Core Business Is Improving:** Management doesn't argue with the point that sales declined in 2009 due to decisions by Smith & Nephew and MTF to end relationships with Osteotech, but it didn't significantly erode the business. With the launch of several new products, management has put Osteotech in the position to grow its sales. The three new products which have management excited are MagniFuse, Plexur and HCT (human collagen technology). In the first quarter of 2010, new products generated $1.8 million in sales, up 88% from 4Q09. In the second quarter, new product sales were $2.5 million, up 39% from the immediately preceding quarter.
4. **And we DID Launch a Review of Strategic Alternatives**: Osteotech's board of directors engaged Deutsche Bank Securities Inc. in 2009 to help it find and review strategic alternatives to raise stockholder value. Furthermore, Osteotech's board chairman spent a considerable amount of time in 2009 and 2010 on the ongoing evaluation and exploration of strategic alternatives for Osteotech that are focused on maximizing stockholder value.
5. **Finally, our Corporate Governance Practices Are Sound**: "The Dissident Stockholders claim that Osteotech ignores the concerns and interests of its stockholders. This claim is completely untrue, reflects the Dissident Stockholders' lack of information regarding communications the Company has had with other Osteotech stockholders, and completely discounts the numerous communications the Company has had with stockholders over the years. The Board has been actively working with an investment bank for months to evaluate strategic alternatives, bases a substantial portion of management's compensation on performance-based incentives and is involved with, and provides feedback and guidance on, the Company's strategies."

What Happens Next

Unless this deal falls apart, Osteotech is now part of Medtronic and, it would appear, all's well that ends well.

Orthofix Reaches the Big 3-0 in Style

By Jacqueline Rupp

Turning 30 doesn't scare the folks at Orthofix, in fact for them, it's reason to celebrate. Stop staring at the recent glowing revenue reports and you'll see the shiny, new North American Operations and Education Center, an impressive birthday present for any company, we'd say!

Orthofix International, N.V. is an international medical device company that creates and manufactures a wide range of minimally invasive surgical and non-surgical products. The main areas of focus are in the spine, orthopedic and sports medicine markets. Orthofix's self-described goal is to "address the lifelong bone and joint health needs of patients of all ages–helping them achieve a more active and mobile lifestyle."

To that end, the company has enjoyed consistent growth over its three decades, which can be attributed primarily to the internal R&D department as well as key acquisitions.

How about a quick look back at where it all began?

A "Dynamic" History

It was in 1980, Verona, Italy. Orthopedic researcher, Giovanni De Bastiani of the University of Verona had been working for several years on the concept of "dynamization." Or, as we say in Italiano "Dinamicansio." But when applied to orthopedics, dynamization refers to Bastiani's modular system of external fixators for fracture alignment that would allow for micromovement. That micromovement was necessary, according to Bastiani, to stimulate the bone to heal more rapidly and effectively. From there, Orthofix Srl was born. To this day, external fixation have been one of the core strengths of Orthofix and laid a foundation for 30 years of innovative designs and global manufacture of orthopedic medical devices.

In the last few decades, acquisitions became the company's main avenue for growth. Here's a timeline of the companies Orthofix was able to bring into the fold:

- 1992- Novamedix Ltd: Deep vein thrombosis prevention product, the A-V Impulse System. (Sold in 2010 to Covidien)
- 1993- Orthosonics: Ultrasound technology for joint replacement revisions
- 1995- American Medical Electronics Inc. (AME): established Orthofix's U.S. presence with a strong sales and distribution network and also created a new focus for the business: bone growth stimulators and substitutes
- 2004- BREG Inc: a privately held sports medicine company out of California that specialized in pain management devices and a line of orthopedic bracing devices
- 2006- Blackstone Medical, Inc.: Orthofix's largest acquisition, specializing in spinal implants along with cutting-edge biologics.

Orthofix's North American Operations and Education Center, Lewisville, Texas/Orthofix

"To that end, the company has enjoyed consistent growth over its three decades, which can be attributed primarily to the internal R&D department as well as key acquisitions."

"With this last acquisition," explains Dan Yarbrough, Vice President of Investor Relations, "We created a new spinal implants division which confirmed our commitment to this specialty and, along with our leadership position in the spine stimulation business, established Orthofix as a major participant in the spine industry."

Jerry Benjamin has served on Orthofix's board of directors for over 20 years and is the only member left from the original board. "As I have found over my long career, it is the people that make a company successful. We have been blessed with a succession of very talented and committed management teams that during their tenure brought the company through each step of its growth phase."

He says a critical component of Orthofix's story is how the company has changed its structure and management to respond to the new challenges and to ensure continued growth. "Over its history, Orthofix has had three CEO's, who have each made a tremendous contribution to the company at each stage of its development."

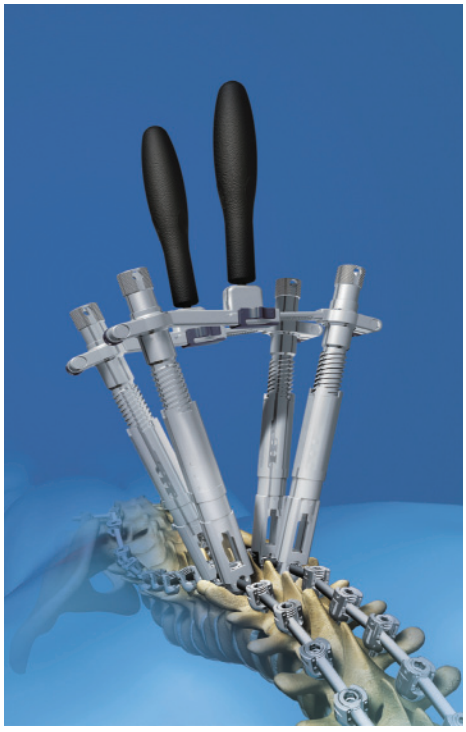
Many times it seems luck was on Orthofix's side. Benjamin describes a turning point in the company's growth that happened by chance. "In the mid-90s," recounts Benjamin, "it was becoming increasingly clear that Orthofix needed to take control of its U.S. sales and marketing if it was to continue to grow. A small Texas company focused on the stimulation market was identified as having a good sales and marketing organization that would satisfy the needs for Orthofix in the U.S. market…. We did not place any value on the stimulation business and the initial plan was that the stimulation business would be divested after the acquisition."

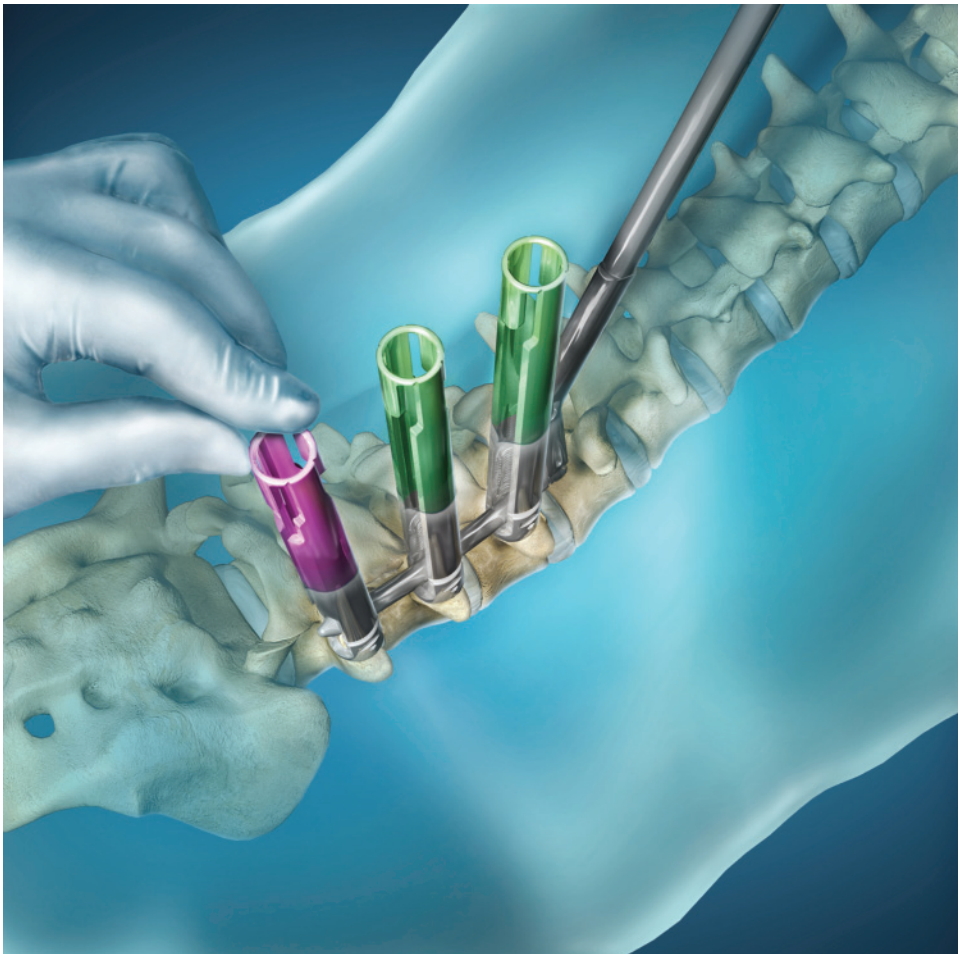
But post-acquisition Orthofix's new head of U.S. operations spotted heretofore hidden potential in the stimulation business. "The rest is history as the stimulation business helped propel Orthofix's share price from the low single-digits to over $30 per share over the next 10 years," says Benjamin.

Benjamin also points to a special environment created by the management team. "When Orthofix was initially set up in 1987, the management team chose to all sit in the same office together so that they could have open and close communication." He says this practice continued until the trio's retirement. "To me, this symbolized the very strong commitment to open communication and the sharing of the responsibilities in managing the company. I have sat on the board of over 40 companies and no other management team has ever operated in this way."

From Fixation to Biologics

Within Orthofix's product portfolio, there are several products that stand





New spine products/Orthofix

> **"Collaborating with the Musculoskeletal Transplant Foundation, Orthofix has moved into biologics to deliver an advanced stem cell-based biologic technology for bone healing. Called Trinity Evolution, it features a viable stem cell-based allograft with essential properties to generate bone growth in spinal and orthopedic procedures."**

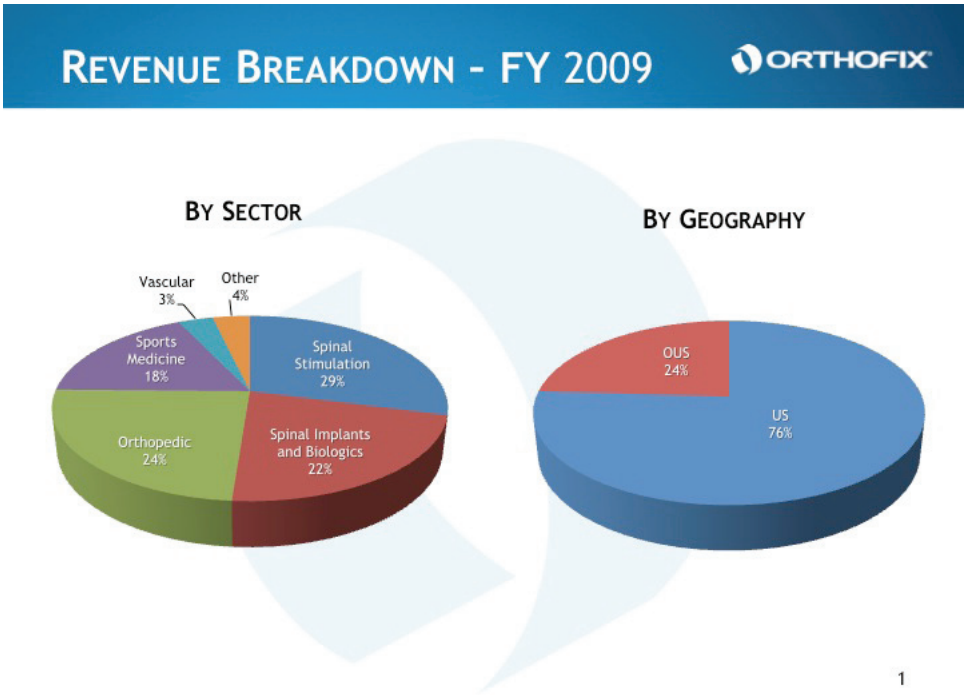
out. Cervical-Stim Bone Growth Stimulator, developed in-house, for instance is still the only FDA-approved stimulator for the cervical spine. Here are a few others:

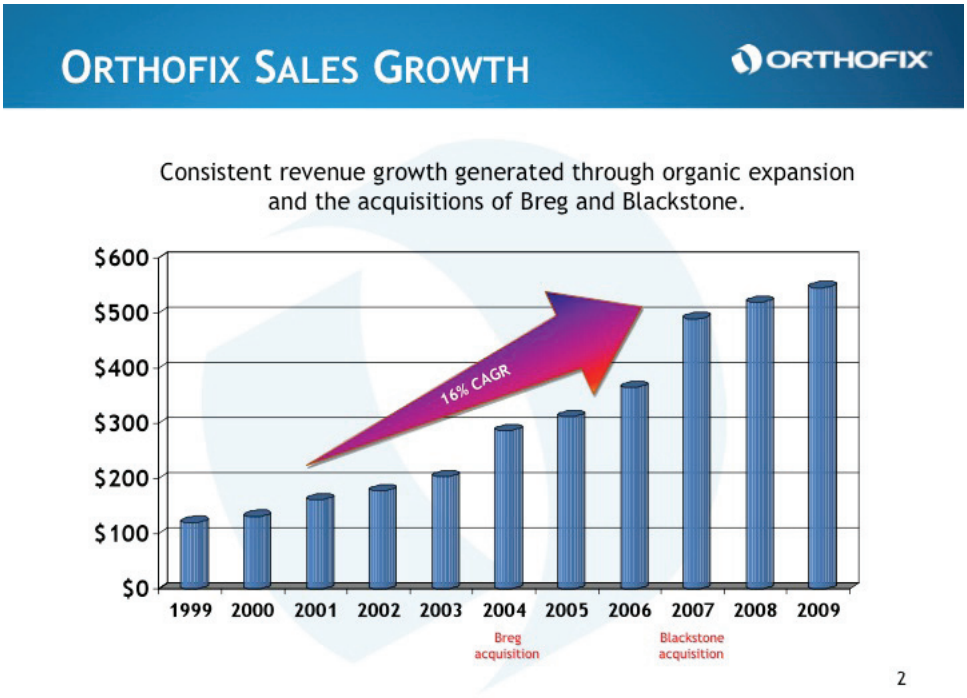
- The ISKD-only FDA-approved internal bone lengthener
- The Eight-Plate Guided Growth System for the correction of pediatric joint deformities, like bowed-legs and knock-knees
- Contours Volar Plating System for wrist fractures.

Orthofix partnered with Texas Scottish Rite Hospital for Children in Dallas for the licensing, training and clinical advancement of the TrueLok Ring Fixation System. This bone reconstruction system is used for foot and ankle deformity correction and has become a flagship product for the orthopedic division.

Collaborating with the Musculoskeletal Transplant Foundation, Orthofix has moved into biologics to deliver an advanced stem cell-based biologic technology for bone healing. Called Trinity Evolution, it features a viable stem cell-based allograft with essential properties to generate bone growth in spinal and orthopedic procedures.

"We launched several new products in 2009 that are helping drive growth in our spinal implants business," says Alan Milinazzo, President and Chief Executive Officer, "including our





Orthofix International

Firebird pedicle screw system, our Pillar SA interbody device, and Trinity Evolution, which is our adult stem cell-based bone growth allograft.

"We are launching new products in two of the faster growing sub-segments within the spinal implants industry. A deformity correction module based on the Firebird platform will for the first time give us the ability to offer surgeon customers a device to treat spinal deformities, such as scoliosis. This year we are also launching a new family of pedicle screws designed to be used in minimally invasive spine procedures."

Good Revenue News

Here are some highlights from Orthofix's 2Q10 earnings:

- **Adjusted total revenue** up 6% cc year-over-year, excluding vascular sale
- **Total spine revenue** up 11%
- **Total orthopedics** up 11%
- **Gross margin** up 160 bps on an adjusted basis from 2Q09, to 76.1%
- **Operating margin** up 220 bps on an adjusted basis from 2Q09, to 14.8%
- **Adjusted EPS** up 29% from 2Q09, to $0.54
- **Cash flow from operations** more than doubled year-over-year to $12.2 million; EBITDA up 23% to $28.9 million
- **Full year EPS guidance** increased by $0.10, new range $2.48 to 2.52
- **June 30, 2010 leverage** down to 1.9X from 2.6X at year-end 2009

Michael Mainelli, the newest board member says he was initially attracted to the company because of its ethics and integrity, but it's growth prospects aren't too shabby either. "I am excited about our future. We have top-notch distribution platforms in key markets to provide excellent service to our customers. Moreover, we still have significant growth

opportunities in relatively untapped and attractive European and Asian markets including Germany, UK, and Japan. Equally important, we have an excellent global management team that is very capable of executing the growth plans of the company."

Here are four observations PearlDiver has regarding Orthofix:

1. Ranks number 11 among the top orthopedic manufacturers worldwide with revenues raising from $365.4 million in 2006 to $519.7 million in 2008
2. Spine company market share estimated to rise from 3.4% to 3.6% by 2012
3. Spine implant and related biologics industry revenue forecast: from $243 million in 2007 to $357 million by 2012
4. Spinal implant market ranking: 6th largest supplier

And for the Next 30?

On August 12, a traditional ribbon-cutting served as both an anniversary celebration and the unveiling of the new North American Operations and Education Center in Lewisville, Texas. The 144,000 square foot facility boasts lots of bells and whistles for surgeons. The Orthofix Institute for Research, Training and Education features state-of-the-art facilities including a 7-station simulated operating room wet lab, 18-station dry lab and 50-seat lecture room, offering realistic surgical training opportunities.

An expanded R&D machine shop for the Spinal Implants Division means custom device and instrumentation requests can be addressed, while the Spinal Implants Division is now able to be housed in one locale, along with will the Spine Stimulation and North American Orthopedics Divisions.

"With the opening of our new facility in Texas," says Benjamin, "we have now fully integrated our spine, biologics and orthopedics businesses and are poised to take full advantage of the synergies that will bring with it."

Milinazzo adds the icing to this birthday cake."I really want to say happy birthday to our employees, who are primarily responsible for the success we have achieved over the last 30 years. They embody the innovation, the focus, and the loyalty that our customers see and appreciate every day." ◆

Scheduling and Tweeting: Reducing Wait Times

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

According to Dennis Kaldenberg, Ph.D., Chief Scientist at health care improvement firm Press Ganey Associates, wait times for orthopedic patients are, on average, longer than in other specialties. "Our data show that the median wait time in orthopedic practices is about two minutes longer than the wait time in practices for other medical specialties. This may reflect the growing demand for the services of orthopedic specialists in our aging population. If health care reform increases access to orthopedic services, this demand will be even greater."

When an orthopedist is in an exam room with a patient, all of his or her focus should be on that person. However, say researchers, the people tapping their feet in the waiting room should figure into your thinking as well. Apart from the courtesy aspect of it, the fact is that someone who waits too long to see the doctor is less likely to refer him to other patients.

Dr. Jordan Greenbaum, now an attending surgeon at New England Orthopedic Surgeons in Springfield, Massachusetts, and Dr. Chris Chiodo, Chief of Foot and Ankle Surgery at the Brigham and Women's Hospital, went looking for details. Dr. Greenbaum states, "In addition to wait times being a quality of care issue, I knew there was a burgeoning interest in patient centered outcomes such as patient satisfaction. While there is a substantial amount of literature on the impact of wait times on satisfaction in the emergency department and other subspecialties, I found that such information is really lacking in orthopedics."

Morguefile.com

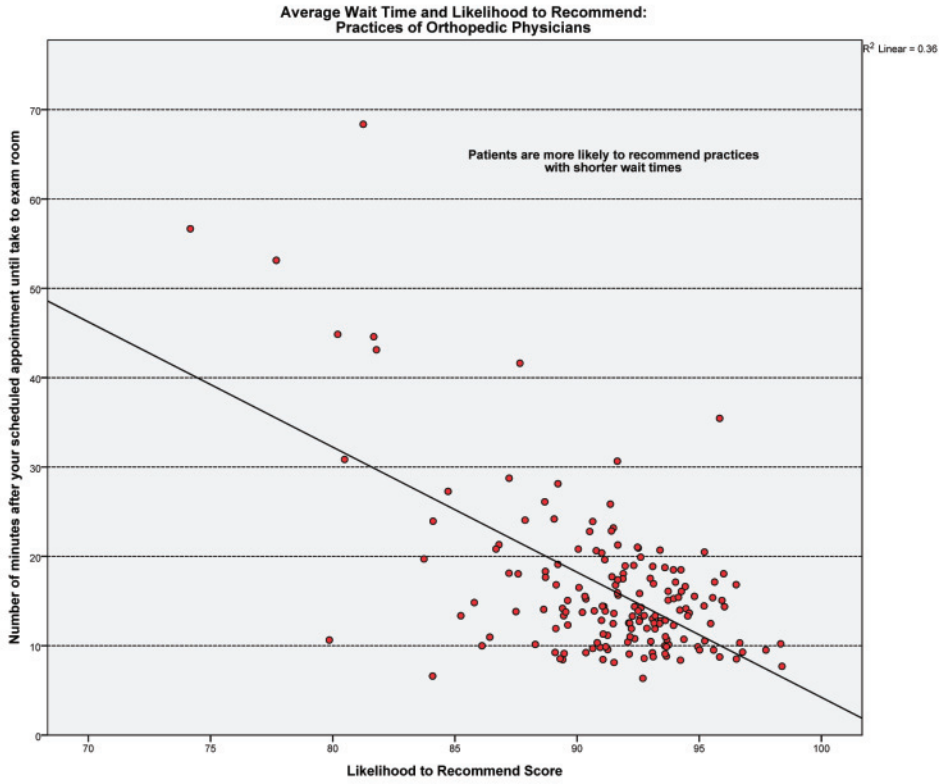
So like all good researchers do when they see a gap in the literature, Drs. Chiodo and Greenbaum and their team dove into it. Dr. Greenbaum: "Our starting point was data from a research firm, Press Ganey, who surveyed 2.4 million patients in 2008; through them we learned that orthopedic patients have the lowest satisfaction among 15 subspecialties and perhaps not coincidentally, the longest wait times. Armed with this information, we took two weeks and studied wait times at an orthopedic practice affiliated with Brigham and Women's Hospital. We measured how long patients spent in the waiting room and in the examination room, and how long the attending physician spent with the patient. After the patients emerged from the exam room they completed our survey on satisfaction with wait times and on the overall experience."

While orthopedists attended medical school, not magician school, it may behoove them to understand the power of perception. Dr. Greenbaum: "In at least one of our analyses, how long people thought they spent in

"In at least one of our analyses, how long people thought they spent in the waiting room was more important than how long they actually waited."

the waiting room was more important than how long they actually waited. Satisfied patients waited an average of 19.46 minutes; they thought they waited 20.41 minutes. The dissatisfied patients waited 40.21 minutes, but they thought they waited 48.26 minutes. In addition to patient estimated wait time, age and patient rated quality of the waiting room were also found on all analyses to be independent predictors of patient satisfaction. As far as age, older patients tend to be more satisfied than younger patients and perhaps less sensitive to a longer wait. Patients' opinions of the waiting room also impacted their satisfaction. While there are no evidence-based guidelines on what makes a successful waiting room, we know from the literature that any effort to improve the quality of the waiting room likely needs to be multifactorial, and may include using a professional decorator, nice music, soft colors, etc. In one study from the emergency medicine literature, simply putting a television in an examination room did not improve satisfaction."

He adds, "Those patients rated as 'satisfied' also spent another 18.04 minutes in the exam room before the senior orthopedist came to see them. Interestingly, we determined that dissatisfied patients waited 17.97 minutes, meaning that time in the exam room may not be predictive of satisfaction. This finding may be confounded by the fact that patients were seen by a resident or fellow prior to being seen by the attending physician. Also notable was that in some of our analyses, patients who were new to a practice were more sensitive to wait times. My impression is that patients with whom you have a relationship and who already have a favorable opinion of you may be more likely to forgive a long wait time."



Press Ganey Associates, Inc.

Dr. Chiodo was senior author on this study. He notes, "Patient satisfaction has never been more important than it is now. We are seeing more patients whose expectations are higher…all the while we have less time to spend with them."

Thus, says Dr. Chiodo, a bit of creativity is in order. "Many practices provide free internet service/Wi-Fi in the waiting room, accompanied by a pen and paper if people want to take notes on something. As for periodicals, we have found that magazines 'grow legs.' Every day I have my staff buy five newspapers, put a sticker with 'office copy' on them, and leave them floating around the waiting room. Also, you should offer patients coffee, tea, and water; you can also follow the restaurant example of giving people

"In orthopedics, the median wait time in the waiting room is 14 minutes, with a range of six to 68 minutes; the median wait time in the exam room is 10 minutes, with a range of five to 32 minutes."

buzzers that activate when they are ready to be served. If you're really running behind be prepared to give patients free parking and/or a gift card for coffee and a snack from the cafeteria or lobby kiosk."

While none of the above suggestions usually require a staff meeting, Dr. Chiodo's other idea may. "Strategic patient scheduling is critical when it comes to wait times. Patients are often scheduled/billed in 15 minute slots, and at times can be double or triple booked. In our practice we have found it helpful to realistically schedule patients so that an established patient needs less time than a new patient; a postop patients needs even less time. For example, instead of scheduling four people at 10:00, bring in two new patients at 10:15, one established patient at 10:30, and a postop patient at 10:30. You have a bit of leeway with the postop patient; you can have a physician assistant (PA) see them and then you can see them briefly afterwards. In the patient's mind, seeing a PA counts as 'face time.'"

Delving into the numbers, Press Ganey's Dr. Kaldenberg explains, "In orthopedics, the median wait time in the waiting room is 14 minutes, with a range of six to 68 minutes; the median wait time in the exam room is 10 minutes, with a range of five to 32 minutes. This means the total waiting time in orthopedic practices is about 24 minutes. The place of the wait doesn't matter; long waits in either the waiting room or the exam room will lead to dissatisfaction."

The bottom line for those concerned with their bottom lines? "There is," says Dr. Kaldenberg, "a clear relationship between wait times and the willingness to recommend a practice (orthopedic or otherwise). Making a patient wait influences the perceptions of the treatment experiences that follow. A

"My staff always advises patients to call before they come in to see how things are going. We also leave 'holes' in the schedule every hour to allow for some flexibility as well as the omnipresent same day emergency patient (6 or 7 a day). At present we are working on developing a new Twitter system to notify patients as well as an email alert."

'way forward' for physicians is to keep patients informed prior to bringing them into the exam room. We know that if they are waiting and they don't know why, then they are more dissatisfied. If you have a backlog because of an emergency or some other event, let your patients know."

So how to keep patients engaged instead of enraged? Follow the example of those who do it best, says Dr. Kaldenberg. "Look at Disney…they have figured out methods of keeping people involved and entertained, which has the effect of distracting them from how long they wait in line. Have a brainstorming session at your practice and discuss how you can adopt others' methods and/or create new ones."

Dr. Tom Grogan, an orthopedist in Santa Monica, California, is Tweeting his way to success in the wait time arena. He notes, "Because downtime in a practice produces no revenue, most practices like to have a full waiting room. The negative is that patients are vulnerable to a lot of factors that only increase waiting time. If one patient has a complex problem it backs everyone else up down the line. Add to that the issue of surgeons who operate in the morning and have their surgery run late."

The biggest issue, states Dr. Grogan, is how to keep patients informed about the flow of your day. "Most practices do not even try. In ours, if I am delayed in surgery, a staff member will try to contact patients downstream in the schedule to let them know of the delay. My staff always advises patients to call before they come in to see how things are going. We also leave 'holes' in the schedule every hour to allow for some flexibility as well as the omnipresent same day emergency patient (6 or 7 a day). At present we are working on developing a new Twitter system to notify patients as well as an email alert."

Use of new technology or not, the issue is only complicated by the issue of motivation, says Dr. Grogan. "Not only is the problem going to get worse as reimbursements shrink, but the trend towards physicians being hospital employees is also going to cause the problem to spiral out of control. Employed doctors have no reason to hustle and cut down on waiting times. Just think about the Post Office. Their job is to *deliver* the mail come rain or shine, nothing is said about customer service at the window. The job of an employed orthopedist is to do *surgery*. Keeping waiting times in the office in check is not their prime directive."

In those situations, it may end up being in the bailiwick of hospital administration as they see their patients either rate them lower or move their business. As for private or academic practices, Tweet me. ◆

company

MiMedx Group Announces First Earnings

Last December, MiMedx Group announced the launch of its first product, the HydroFix Vaso Shield.

On July 23, the company held its second earnings conference call and announced growing sales.

Company management highlighted four accomplishments during the second quarter of 2010.

Increases Revenue, Misses Expectations

First, revenue for the second quarter reached $322,000, up from $115,000 in the first quarter of the year. Company leaders forecast a "significant" increase for the upcoming third quarter. In a letter to shareholders, Parker H. Petit, Chairman and CEO wrote, "Our new forecast for the third quarter will be for revenues of approximately $800,000." Petit also noted in the letter that second quarter did not meet expectations.

Increases Distributorships

Second, management reported the company has 21 independent sales rep groups in the U.S., covering 32 states and 7 international dealers. The company is currently in final discussions with a number of additional dealers.

Production Facility Ramp Up

Third, the company made progress in the transition of the CollaFix manufacturing operations from the company's Tampa, Florida, facility to its Marietta, Georgia, facility and the transition of its Tampa office as the company's center of excellence for research and development. Management also noted progress in the selection of a larger facility in the Marietta area to house its expanded manufacturing operations.

FDA Clearance

Fourth, the company received clearance from the FDA for additional configurations for its HydroFix Vaso Shield.

MiMedx Group is a public biomaterials company that was formed by combining two early-stage medical device start-up companies, MiMedx Inc. and SpineMedica Corporation. The company's Medical Advisory Board includes Richard Guyer, M.D., a past president of the North American Spine Society.

The company's platform technologies HydroFix and CollaFix have, according to the company, such a vast number of potential applications in treating traumatized tissue and structures that it is too difficult to accurately quantify. The motto for company employees is: "Repair, Don't Replace."

Chairman Petit's letter to shareholders was refreshingly candid for its lack of hype and corporate speak. We look forward to hearing more from this company.

—*WE (August 13, 2010)* ◆

Symmetry 2Q10: Stabilizing and Improving

Symmetry Medical is one of orthopedics' canaries in the coal mine.

Symmetry Medical	2Q10	
	Sales ($ in millions)	% Change
Total Sales	$88.8	down 12%
Instruments	$35.4	down 25%
Implants	$28.5	down 5%
Cases	$19.8	up 5%
Other	$5.1	down 4%

Source: Symmetry Medical

Citing an overall economic environment which impacted demand from Symmetry Medical's major customers, the company reported a 12% revenue decline in the second quarter of 2010. Symmetry is the largest OEM provider of implants and instruments in orthopedics with a 55% market share.

Revenue of $88.8 million was down from the second quarter of 2009, but was up 5% over the first quarter of 2010. The company said it saw reduced revenue of 19.2% during the second quarter from their combined five largest OEM customers as those customers continue to manage inventory levels and the timing of their various product launches.

A Stabilizing and Improving Environment

Brian Moore, Symmetry's President and CEO, stated, "Total revenue in second quarter 2010 grew by 5% sequentially, providing further evidence of a stabilized and improving environment. We also achieved sequential expansion of gross margin and operating margin during the quarter, demonstrating better operational efficiency as we adjust to higher volume. Together, these positive results give us confidence that we are well positioned to benefit from a reacceleration of growth and to meet our 2010 revenue and EPS guidance."

Raising Guidance

For the full year 2010, the company is increasing revenue guidance to a range of $340 million to $350 million, up from the previously announced range of $330 million to $340 million. "The increase is based on actual results for the first half of 2010, current inventory levels and expected customer product launches," stated a company press release.

Zack Equity Research noted that Symmetry is, "poised for a rebound as its major customers such as DePuy, Stryker and Zimmer ramp up spending on orthopedic instruments and accelerates product launches."

—WE (August 11, 2010) ◆

Trans1 2Q10: Beating Expectations

Trans1 Inc.'s $7.2 million of revenue for the second quarter of 2010 beat consensus by $800,000. The sales

Working the Crowd/Wikimedia.org

number was 9% below the previous year's second quarter, but up 8% over the first quarter of this year.

Signs of Stabilization

Rick Randall, the company's CEO said, "We saw continued signs of stabilization in our AxiaLIF product line this quarter and our average revenue per case benefited both from a positive product mix shift and from the sale of newly launched TranS1 products into cases. We also achieved a significant corporate milestone in the quarter as the 10,000th worldwide patient was treated with the AxiaLIF implant."

The company reported that 667 AxiaLIF procedures were performed during the quarter. There were 540 procedures performed in the U.S., which was down 20% from the previous year.

Over the past three quarters U.S. procedures have been in the 540-550 range. Wells Fargo senior analyst Mike Matson said this is an indication that the company's base of customers has stabilized.

Raising Expectations

As a result, Matson said he was raising his 2010 and 2011 revenue

expectations from $26.7 million to $27.7 million and from $30.0 million to $30.6 million, respectively.

Matson wrote that Trans1's innovative axial approach for lumbar spinal surgery called the AxiaLIF, provides benefits to the patient, surgeon, and hospital. "However," continued Matson, "this revolutionary procedure is radically different from traditional spine surgery and has proven to be difficult to sell."

Set for Turnaround

Reimbursement, according to Matson, remains the key to a turnaround. "Trans1 has changed some of its management team, cut costs, and lowered its cash burn rate. Domestic procedure growth has stabilized and the company still has $47 million in cash. Given all this, we think that the scene has been set for a turnaround. The one thing left that needs to happen, in our view, is addressing the lack of physician reimbursement. Clinical data on the AxiaLIF has built to the point where the company now feels that it may be able to seek a Category I code."

—*WE (August 11, 2010)* ◆

SNN Crawls in 2Q10

Smith & Nephew posted a $959 million second quarter of 2010 while losing market share in the orthopedic reconstructive business.

Orthopedics came in with an anemic 1.1% increase, while the company's Endoscopy and Advance Wound Care Management units came in with 10.2% and 4.8% increases, respectively. Overall, revenue increased by 3.6% over the previous year's second quarter. Company Chief Executive David Illingworth said that within the company's orthopedics group, U.S. trauma and European orthopedic businesses are showing clear signs of progress. "Our customers are facing short-term budgetary pressures and challenges," added Illingworth. The company is assuming that healthcare budgets globally will remain challenging for the foreseeable future.

Smith & Nephew	2Q10	
	Sales ($ in millions)	% Change
Total Sales	$959.0	up 3.6%
Orthopedics	$372.0	up 1.1%
Trauma	$163.0	Flat
Endoscopy	$206.0	up 10.2%
Advanced Wound Mgmt	$218.0	up 4.8%

Source: BMO Capital

Hips and Knees Struggle

Geographically, orthopedics revenue fell 1% in the U.S. while growing 1% in Europe and 5% in the rest of the world.

The British-based manufacturer reported that the company's global hip franchise growth was flat, reflecting weaker sales from the Birmingham Hip Resurfacing System (BHR). With some concerns over metal-on-metal implants, the company said that the BHR has outstanding survivorship and metallurgy data and believes that an active program of support for the product, both with surgeons and patients, will be effective.

The company's other hip products, according to the company, continue to grow at above the market rate in aggregate.

The Low Crawl/U.S. Army/Wikimedia Commons

Global knees grew by 3%, with the Legion Knee System continuing to deliver strong growth, with volumes supported by some substitution from higher specification products. "We are confident that the increasing acceptance of Visionaire Patient Matched Instrumentation sets, and the 30-year wear claim for our Verilast bearing technology for knee replacement, will drive future growth," stated a company press release.

Taking It to the Air

The Verilast technology has been prominently featured in television ads in the U.S. recently, even gaining a mention on the NBC Nightly News.

Smith & Nephew's management told analysts that they continue to believe that the company's market share loss is a result of a focus on the younger, active patient population that is privately insured and has been hit harder economically.

The company believes that long-term industry growth drivers—including demographics, emerging markets and patients' desire to return to an active life—remain intact. In the second half of 2010, management expects the orthopedic and trauma businesses to benefit progressively from recent new product introductions and strong clinical data.

—*WE (August 11, 2010)* ◆

large joint

OA and Mental Health

Wikimedia Commons

Think happy thoughts and you won't feel as much pain?? Maybe. Researchers from the University of California Davis School of Medicine have found that osteoarthritis (OA) patients with better mental health felt less pain, and people with worse mental health felt more.

Barton Wise, M.D., a researcher with the UC Davis Center for Healthy Aging, said he and his colleagues conducted the research because of the episodic nature of osteoarthritic pain.

"Pain varies over time, both over extended periods and over shorter periods," Wise said in the news release. "The same person can feel little or no pain in their knee or hip, and later they can feel moderate-to-severe pain even when the extent of damage to the knee or hip joint as seen on x-ray imaging remains the same."

The researchers studied 266 subjects regarding the relationship between pain, fluctuations in pain and health outcomes. Wise said that part of the study's strength is that it gauged individuals' perceptions of their pain intensity at different times, as well as comparing different participants' pain experiences.

Dr. Wise added, "Pain is difficult to study in part because experiences and reporting of pain differ from one person to another. There can be differences in people's central or peripheral nervous systems, past experiences of pain or cultural differences in perceptions of pain, and these make it very complicated to look at differences in pain across individuals. Our study design helped eliminate some of those obstacles," he said. "But it's likely that people's pain is the result of a large group of different factors rather than something as simple as one specific physiological factor."

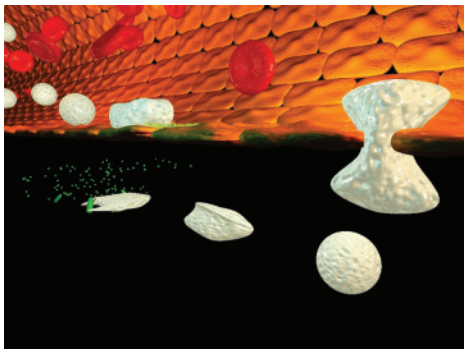
As for the prospects of getting mental health treatment for OA sufferers, Dr. Wise told *OTW*, "There is real hope for getting mental health treatment for OA sufferers. I would suggest that persons with pain from OA should be considered by their primary care physician for possible referral to a mental health specialist for evaluation and for work on mood and coping skills, as this may help improve their pain as well."

Regarding how a physician might convince someone to pursue such treatment, Dr. Wise commented to *OTW*, "A doctor might encourage a patient to pursue such treatment by reminding him or her that the mind and body work together, that pain is produced by an interaction between the two, and that work on mental health might improve both their outlook and their pain at the same time."

—*EH (August 13, 2010)* ◆

New Drug Target for RA

How *do* those immune cells get turned on? Researchers from Mount Sinai School of Medicine are



Greg Luerman/Immune Response/Wikimedia Commons

announcing that they have found a new mechanism that explains how certain immune cells are activated to create protective antibodies against infections or pathological antibodies such as those present in autoimmune diseases like rheumatoid arthritis and lupus.

Led by Dr. Andrea Cerutti, M.D., Professor of Medicine at Mount Sinai

School of Medicine, researchers studied human tissue and immune cells from people with mutations of TACI and MyD88, two proteins required to activate the immune system. MyD88 is a signaling protein that alerts the innate immune system—the immune system encoded at birth that remains unchanged—to the presence of pathogens. TACI is a receptor protein used to activate immune cells in the adaptive immune system, a more sophisticated immune system.

"Our research shows that TACI and MyD88 are part of an immune circuit that bridges the innate and adaptive immune systems. This circuit makes our immune response more flexible, allowing a more effective generation of protective antibodies during infections. Genetic defects of TACI and MyD88 cause immunodeficiencies characterized by recurrent, life-threatening infections. On the other hand, an abnormally strong TACI-MyD88 interaction may exacerbate autoimmune diseases like lupus or rheumatoid arthritis," said Dr. Cerutti in the news release. "Previous studies had suggested an involvement of TACI and MyD88 in lupus. Now that we have identified this interaction, we can figure out a way to inhibit it and prevent these diseases from getting worse."

"Our discovery provides a novel specific target, the signaling pathway between TACI and MyD88, to block the overreaction of the immune system and tissue damage in individuals with autoimmune disorders," added Dr. Cerutti. "We look forward to studying this discovery further and developing therapeutic targets that will inhibit the interaction between TACI and MyD88, preventing autoimmune diseases from progressing with fewer side effects than currently prescribed treatments."

As for how they might develop these therapeutic targets, Dr. Cerutti told *OTW*, "We plan to screen small molecule libraries and decoy peptides to identify inhibitors of TACI-MyD88 interaction. This screening is made possible by the fact that in this last work we have identified not only the molecular requirements for TACI-MyD88 interaction, but also a few biochemical and functional readouts to sort of measure the interaction. Putative inhibitors will be initially validated in vitro using B cell-based assays and then in vivo using suitable animal models."

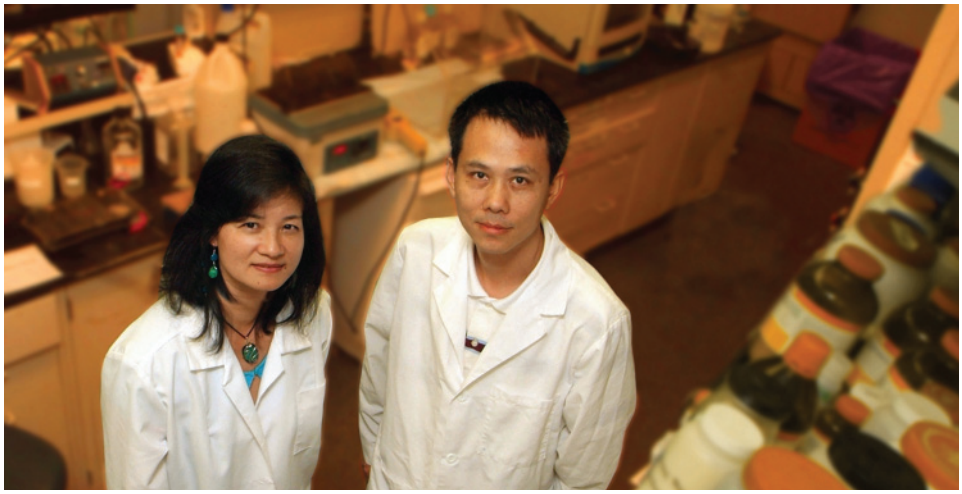
—*EH (August 11, 2010)* ◆

Neogenin, OA, and Osteoporosis

Another step toward cracking the osteoarthritis and osteoporosis codes? Researchers from Medical College of Georgia (MCG) have found that too little of a protein called neogenin results in a smaller skeleton during development and sets the stage for a more fragile bone framework lifelong. The team found that a developing mouse with neogenin deficits has poorly defined digits and is generally smaller, including having small growth plates. Dr. Zheng Zhou, MCG assistant research scientist, is first author. Dr. Wen-Cheng Xiong, developmental neurobiologist in the MCG Schools of Medicine and Graduate Studies, is a corresponding author of the study.

"Each cell type has a master gene. Neogenin is not that, it's more of a modulator," Dr. Xiong said in the news release. That's why, if it's mutated, like in the mouse, cartilage and bone formation is disrupted—not halted. It's also why neogenin could be a good therapeutic target for turning the tide on cartilage or bone loss that occurs in osteoarthritis, Dr. Xiong added.

Dr. Xiong told *OTW*, "My laboratory has been studying neogenin signaling for several years. Neogenin was initially identified as a receptor of netrin (neuronal axon guidance factor). However, its function in axon guidance seems minimal, as neogenin mutant embryo show relatively normal axon projections. We have studied neogenin signaling and function in several different cellular models, and have found that neogenin appears to be a regulator of BMP signaling in multiple cell types (Dae-Hoon Lee et



Dr. Wen-Cheng Xiong (left) and Dr. Zheng Zhou

al, Blood, 2010). This finding was also in light of the published observations of neogenin interacting with RGM proteins; RGMs appear to be BMP co-receptors. These observations led us to wonder if neogenin regulates cartilage development or chondrogenesis, which is largely dependent on BMP signaling. In addition, our studies were encouraged by the publications (by Cooper HM's lab) that neogenin is highly expressed in cartilage or chondrocytes during embryonic development and that neogenin deficient mice are smaller."

She also commented to *OTW*, "We also want to address: 1) if neogenin regulates articular chondrocyte differentiation and function, as neogenin is also highly expressed in this type of chondrocytes (in adult stage). Understanding how neogenin functions in those chondrocytes would provide insight into our understanding of adult joint function and pathogenesis of arthritis; 2) if neogenin regulates osteoblast differentiation and function. Addressing if and how neogenin regulates osteoblast function would help us to not only understand normal bone formation, but also pathogenesis of osteoporosis. Perhaps those studies will help us to determine if neogenin can be a new drug-able target for treatment of osteoarthritis and osteoporosis."

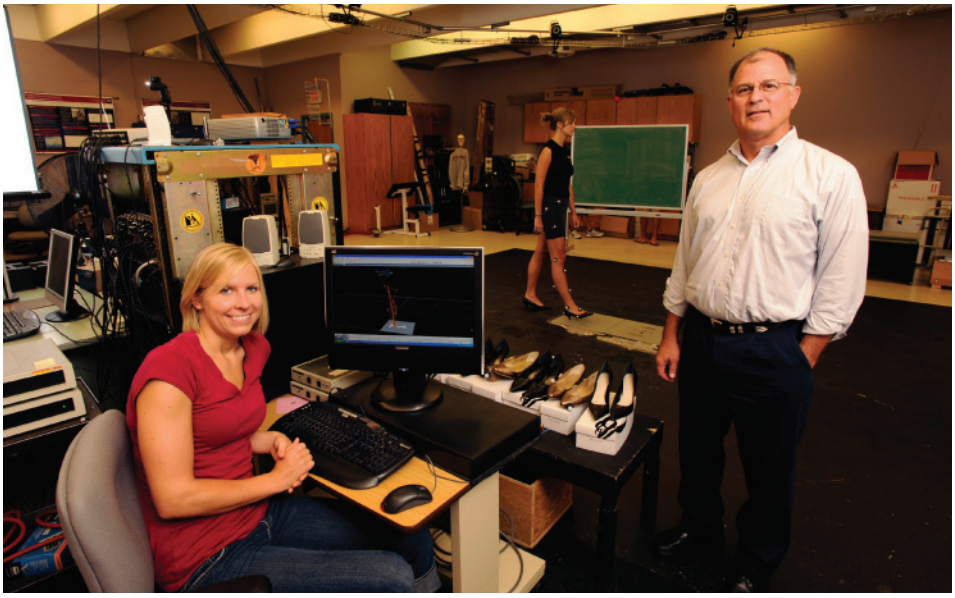
—*EH (August 10, 2010)* ◆

High Heels and Knee OA

Daily stiletto wearers, take heed…A new study by Iowa State University (ISU) kinesiology master's student, Danielle Barkema, has found that prolonged wearing of and walking in heels can contribute to joint degeneration and knee osteoarthritis.

"Obviously with research like this, you can't say with any certainty that if you wear high heels regularly you will develop osteoarthritis. We don't know that," Barkema said in the news release. "There are probably people [high heel wearers] who do and those who do not. However, based on this information, wearing high heels puts individuals at greater risk for developing osteoarthritis. And it seems to be that the higher the heel height, the greater the risk."

Using three heel heights, Barkema had 15 women complete walking trials. She measured the forces acting about the knee joint and the heelstrike-induced shock wave that travels up the body when walking in heels. Using sensors, accelerometers and lab equipment such as a force platform, she captured motion and force data.



Danielle Barkema and kinesiology professor and chair Phil Martin

"I think Danielle's exactly right," said Phil Martin, an ISU kinesiology professor and department head, in the news release. Dr. Martin, who assisted with the study, added, "Wearing high heels regularly puts a person at risk and the higher the heel, the greater the risk. The loading that's being produced in the joint with every step that they take

is higher—or at least, these data suggest that. These are not direct measures of loading within the joint, but they're an alternative way of looking at that kind of loading."

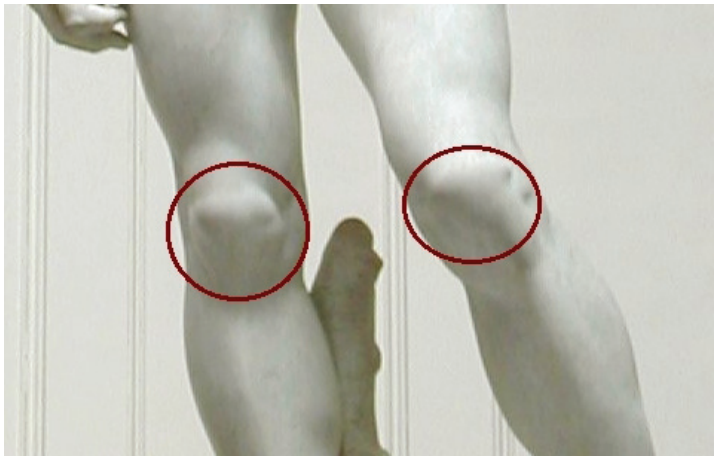
Barkema also found that heels—especially those two inches and higher—alters posture and can create strain on the lower back.

Barkema told *OTW*, "The outcomes of this study were not necessarily surprising to me, but certainly important and interesting. Previous high-heeled walking studies have shown unequal forces across the knee joint, which creates greater medial loading (or compression on the inner portion of the knee). Greater medial loads are associated with joint degeneration and the development of medial compartment knee osteoarthritis. We wanted to see if there was a systematic relationship between this medial loading and heel height. By looking at a flat, mid-heel, and high heel, we were able to establish that medial loading of the knee systematically increases with an increase in heel height. This is important because it means that consistently wearing high heels, and especially higher heels, puts individuals at a greater risk to develop knee osteoarthritis later in life."

—EH (August 9, 2010) ◆

Knee Lubrication and OA Development

While you can't drink something and have it go directly to your dried out knees, researchers *have* made progress in the knee lubrication area. A new study, led by Gregory Jay, M.D., Ph.D., an emergency medicine physician and researcher at Rhode Island Hospital, has identified options for restoring knee joint fluid to potentially prevent the development of osteoarthritis (OA). The researchers used animals with torn ACLs to test three fluids that could be injected into the joints and could serve as a substitute for lost synovial fluid.



Michelangelo's David - the patellae (kneecaps) highlighted/ Wikimedia Commons

Dr. Jay noted in the news release, "We know that acute ACL injury is a significant risk factor for the development of post-traumatic osteoarthritis. We also know why that occurs, due to the degeneration of the fluids in the joint and cartilage and joint instability, among other things. Our goal for this study was to determine an effective way to counter that process to prevent the development of OA."

The first fluid tested was human synoviocyte lubricin; the second was recombinant protein, with a change in the genetic make-up of the cell so that it makes a molecule of interest. The third was lubricin from human synovial fluid (purified before injection, and because it is more closely aligned with the natural lubricin, it is a positive control).

Dr. Jay stated in the news release, "First and foremost, we found that you can limit cartilage deterioration. This is evident by using a well-accepted OA biomarker which shows that the breakdown of cartilage collagen type 2 and recovered in the urine has been muted by treating the knee joint with lubricin."

Second, the study results indicate that when lubricin is placed back into the traumatized joint, it encourages the joint to make its own lubricin.

Dr. Jay added, "This is a huge advance over the existing technology of viscosupplementation injections. The concept was good, but the chemistry isn't there to support it. When viscosupplements were approved as devices in the '90s, it was thought then that hyaluronic acid used in this treatment was tied to joint lubrication because it was viscous. We now know that joint lubrication has little to do with viscosity. We are inventing a new type of joint lubrication strategy: Tribosupplementation, taken from the Greek, meaning to wear or to rub."

Dr. Jay told *OTW*, "As a result of these findings, we recommend replicating these findings in a large animal model. It is equally important to lobby the FDA to adopt surrogate markers for OA to help formulate studies for new drugs and devices that can be used to study the prevention of OA following injury—like MRI."

—EH (August 9, 2010) ◆

people

MacMillan Named to Manufacturing Council

Orthopedics now has a seat at the highest level of national manufacturing policymaking.

Steve MacMillan, Stryker's CPCEO (Chairman, President and CEO), has been named to the 2010 federal Manufacturing Council by U.S. Secretary of Commerce Gary Locke.

Steven MacMillan, CPCEO/Stryker Corporation

Advise on Competitiveness

The Department of Commerce established a 15-member council in 2004 to advise the Commerce Secretary on the competitiveness of the manufacturing sector and government policies and programs affecting American manufacturers. The agency said it recently re-chartered the group to include 25 members from a more diverse cross-section of the country's industries.

"As a country we need to promote job creation in the private sector." MacMillan said in a prepared statement. "I believe that this council can have a positive impact on policies that will spur greater growth."

The appointees represent a broad cross section of the industry and include steel, textile, superconductor, and solar panel manufacturers both large and small. Their products support a diverse range of industries such as the auto, aerospace, apparel and now, orthopedic devices

The Secretaries of Labor, Energy, and Treasury have also been added as ex officio members of the council to better collaborate on cross-cutting issues the council will address.

MacMillan

MacMillan joined Stryker in 2003 as President and Chief Operating Officer, and in 2005 became President and Chief Executive Officer. He recently added the Chairman title. He began his career at Procter & Gamble and later worked for Johnson & Johnson as well as the Pharmacia Corporation, where he was in charge of five global businesses with revenues of more than $2 billion.

The official government announcement described Stryker as a Fortune 500 company headquartered in Kalamazoo, Michigan, with 18,582 employees. Stryker's products are marketed globally to hospitals, doctors, and other health care facilities via direct sales personnel and distributors. Stryker's surgical products include such instruments as drills, saws, rasps, even cement mixers. The company's Orthopedic Implants category includes artificial joints, spinal rods and screws, artificial vertebral discs, bone cement,

and other orthopedic implants and supplies.

Congratulations Mr. Chairman. The industry will be well represented by the dean of orthopedic executives.

—*WE (August 13, 2010)* ◆

spine

"Eye Spy"/Creative Commons

Take a Peek…at PEKK!

Less stiff, less dense…meet OXPEKK-IG, the newest thermoplastic biocompatible polymer. The first medical device to utilize the substance just received FDA clearance, which means we could be seeing a lot more of PEKK soon.

OXPEKK-IG…It's a name with a lot of letters that doesn't give any clue to the nature of its make-up. But PEKK is actually a high-performance thermoplastic that's an ultra pure polymer. And, it just received FDA clearance in a long-term medical implant with the Kent Medical Devices product that is used to radiographically mark soft tissue sites during and after surgical procedures.

Manufactured by Oxford Performance Materials (OPM), this 510(k) clearance signals the first time a device using the proprietary barium-containing, radio-opaque polyaryletherketone polymer has been granted such approval in the U.S.

Having already had a presence in the commercial markets of Europe, the Middle East, South America and most recently Korea, PEKK is within the class of PAEK, so this is a material that already has a global following.

With properties similar to bone, the polymer is said to have a high level of biocompatibility according to Oxford's data. OXPEKK-IG has the potential for use in spinal cages, bone screws and hip and knee implants. Oxford says that some of the top features include OXPEKK-IG's density and stiffness, which is said to be lower than metallic biomaterials, resulting in better force distribution and creating an improved bone-implant interface and fusion rate.

—*JR August 5, 2010* ◆

THE PICTURE OF SUCCESS

Dr. Kristaps Keggi

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

Dr. Kristaps Keggi

Hiding all night in a Latvian forest waiting for a boat to safety in Sweden and deliverance from both Communist Russians and Nazi Germans, Kristaps Keggi had no idea if he would live to see the next day. Ultimately, Kristaps Keggi became the Elihu Professor of Orthopaedics and Rehabilitation at Yale University, Director of the Yale New Haven and Waterbury Hospital Joint Replacement Centers, and one of the most respected surgeons in the United States. But the memory of that boy in the woods is still a constant reminder of how fortunate he is to be practicing surgery in America.

Born in 1930s Latvia, Kristaps Keggi discovered a love of medicine from his surgeon-father. "My father was a surgeon and thought of medicine as one of life's highest callings. His feelings about medicine were very obvious to me, especially when I was trying to decide on a career. My maternal grandfather was a well known theologian, writer, poet, and educator; his ideals have left a profound impression on me. My mother, who was also a teacher, cared for us four children during many years of hardship."

Dr. Keggi: "In 1939, the Baltic States were overtaken by the Russians; for the Baltic people this meant a horrible five years of being caught between the Communists and the Germans, followed by fifty years of Russian rule. One of my most powerful memories is sitting in that Latvian forest waiting for a boat to Sweden. German patrols were nearby and my dad, concerned about the trustworthiness of the fishermen who were supposed to help us, decided against the plan and felt we would be safer in Germany until the end of the war. We did get to Germany, but once there we were taken to an SS Camp for Russians. My father hid us on the train that had taken us there, and we were able to escape. In 1949 we made it to the U.S. via the North Atlantic. The seasickness and cramped quarters were a welcome relief from the chaos we were leaving behind."

Such a tumultuous youth taught Dr. Keggi the value of life. "I consider myself very lucky. If my father hadn't been the only person qualified to take care of the communist mayor of our town, we would have been shot or deported. I recently treated a Puerto Rican woman with a complex hip problem. Her poverty and difficult life were things I understood and wanted to correct."

Arriving in New York, the 15-year-old Kristaps soon found himself on the educational fast track. "Our second day in the U.S. my mother took us to the nearest school—for me, it was the Manual Training High School in Brooklyn. My credits in French, Math, German, History, and Latin placed me in the senior class. I was introduced to a former GI who was helping Estonian and Latvian refugees through the American educational system. A month later the headmaster decreed, 'You're going to Yale'… and so it was."

"We did get to Germany, but once there we were taken to an SS Camp for Russians. My father hid us on the train that had taken us there, and we were able to escape. In 1949 we made it to the U.S. via the North Atlantic. The seasickness and cramped quarters were a welcome relief from the chaos we were leaving behind."

"I have come to learn that having read Victor Hugo, Camus, and others… you don't need psychiatry."

At Yale, Kristaps Keggi found wisdom in the pages of French literature, his major. "I took premed courses, but stuck to my literature track. I have come to learn that having read Victor Hugo, Camus, and others…you don't need psychiatry."

Remaining at Yale for medical school, Kristaps Keggi flirted with orthopedics early on, but didn't want to commit just yet. "My anatomy professor suggested that I study orthopedics; I had ruled out the other surgical specialties, but I was impressed by several cardiac surgeons and took some time to explore their work. Later, the inimitable Dr. Wayne Southwick arrived at Yale and my future was sealed—his enthusiasm for orthopedics was total and infectious. I wanted to be part of this vibrant, burgeoning field."

In many ways, the returning veterans from World War II put their stamp on both the practice of surgery in America and on Dr. Keggi. Following medical school, Dr. Keggi spent two years in general surgery at The Roosevelt Hospital in New York City. "I was put in charge of the ER as an intern. Among the senior surgeons on staff were those who had been in World War II and marched with General Patton…they brooked no nonsense. One of my mentors was the Chief of Surgery, Dr. Howard Patterson. He was a war surgeon, and impressed upon me the importance of being able to operate under any conditions."

Thoughts of Yale orthopedics stayed with Dr. Keggi, and in 1961 he returned there to work with Dr. Southwick. "Dr. Southwick thought us mature surgeons and expected us to do the right thing on our own. You could say that we were in a free country and could think freely about all aspects of surgery."

In reality as well, Dr. Keggi was committed to keeping his new country free. He volunteered for the Army and was commissioned as a second lieutenant in 1957; after his residency Dr. Keggi started two years of active duty. "Having survived Communism, I felt strongly about contributing to the U.S. military effort. My first year was in El Paso at the Beaumont General Hospital, where I worked with residents. The colonel in charge was only interested in knee injuries in soldiers, so I was in charge of spine, major trauma and almost all other reconstructive surgery."

But this couldn't fully prepare him for his future: the sound of helicopters and gunfire, the wounded, the heat, and once more, the chaos of war. "I was sent to a MASH hospital in Vietnam where the zeitgeist was, 'Forget the fancy stuff you learned…get back to the surgical basics learned in war surgery for thousands of years.' We were on our own in the Southeast Asian highlands—there was no Dr. Southwick. It was so new to be all alone in this environment and having to make quick decisions about the care of major wounds, amputations…."

To this day Dr. Keggi remembers the often terrifying reality of that war. "Mangled limbs from booby traps, AK-47 gunshot wounds…there was trauma everywhere. Nowadays we have improved ways of stopping a hemorrhage, as well as additional technology, but the basics of war surgery are the same and I teach it to all of my residents. Many of them may have to practice it since, as Plato said, 'Only the dead will not know war.'"

Returning to Yale in 1966, Dr. Keggi became an assistant professor of orthopedics…and among other duties was given the job of organizing a trauma service. "On a lark I drove to the headquarters of the Insurance Institute of Highway Safety in Hartford, arriving there with blood on my coat from having extracted an injured man from his crashed car. I was granted $20,000 to continue my work in trauma. This led to a larger grant, which later helped fund a Physician Assistant program at Yale. Another program I instituted involved sending medical students to follow the fire department and record emergency

"I was sent to a MASH hospital in Vietnam where the zeitgeist was, 'Forget the fancy stuff you learned…get back to the surgical basics learned in war surgery for thousands of years.' We were on our own in the Southeast Asian highlands—there was no Dr. Southwick. It was so new to be all alone in this environment and having to make quick decisions about the care of major wounds, amputations…."

"While this is quite an honor, I must say that I have perhaps derived the most satisfaction from teaching nearly 200 residents how to operate, how to deal with patients and how to think independently. I have encouraged them to question my work and everything else they may encounter in their training. They have rewarded me with their teaching Prize on six occasions."

care in the field. This revealed a significant number of mistakes that were being made in trauma care and helped further the Emergency Medical Technician Program."

Although his head had been set on becoming a Chair, Dr. Keggi increasingly realized that his heart was in doing and teaching surgery. "I began to dread administration. In 1969 I went to Wayne Southwick and told him that I was going into private practice. While maintaining teaching appointments at Yale and continuing clinical research, I operated at Waterbury Hospital."

But time would, in effect, pull out a Chair for him. "I maintained a clinical professorship at Yale all those years; now there is an endowed professorship in my name. While this is quite an honor, I must say that I have perhaps derived the most satisfaction from teaching nearly 200 residents how to operate, how to deal with patients and how to think independently. I have encouraged them to question my work and everything else they may encounter in their training. They have rewarded me with their teaching Prize on six occasions."

Some never forget where they came from…and some go beyond that. Dr. Keggi: "While attending the Goodwill Games in Moscow in 1986 I met several prominent Latvian orthopedists who then invited me to Riga. The next year I attended the first ever International Soviet Latvian orthopedic conference. During the event I met Dr. Viktor Kalnberz, a Latvian and the highest ranking Soviet academic surgeon, who invited me to perform an anterior approach to the hip. It was a rare surgery at the time, and they were thrilled. Viktor and I then started an exchange program, which evolved into the Keggi Orthopaedic Foundation. The goal is to promote the training of surgeons from the former Soviet Union and the Baltic States. More than 200 surgeons have trained with us and many are now in prominent positions in their home countries. One of our trainees has even served as the President of Latvia."

During the last 15 years Dr. Keggi has been primarily involved with teaching hip surgery to residents and fellows, his major area of expertise. "Years ago Dr. Terry Light worked with me on the anterior approach to total hip replacement. It is now accepted and considered a tissue sparing and minimally invasive operation. We used the Smith Peterson approach in which you do not cut muscles, but instead go through an internervous interval. This way you also preserve blood

supply to the muscles, thus allowing a faster recovery. All roads lead to Rome and many approaches to the hip work well. If the prosthesis is in the correct position, at the end of a year the result is the same. But, if you do a tissue saving internervous approach the initial recovery is faster (and there is less pain)."

On the homefront, Dr. Keggi takes pride in his marriage of 53 years. "My wife, a 'Smith gal,' is an award winning gardener and golfer who has also devoted much time to many civic activities. We have three daughters and five grandchildren, and much to my satisfaction and pride, our first grandson is now a sophomore at Yale."

Dr. Kristaps Keggi…an orthopedist against all odds. ◆

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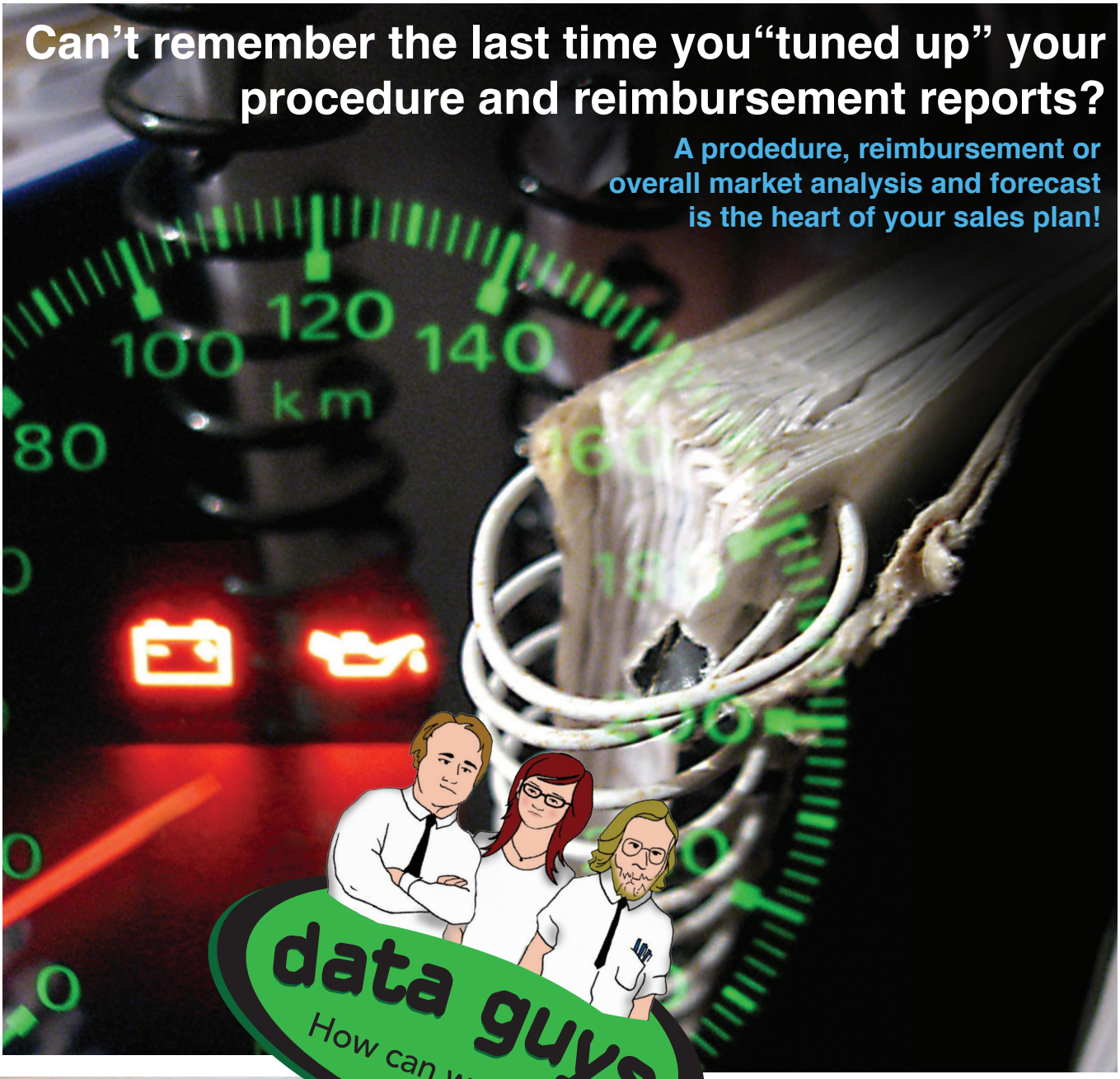

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