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Orthopedics This Week

WEEK IN REVIEW

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8 Who Is Buying the Kyphon (Medtronic) Patents? >> Six patent infringement lawsuits filed in Delaware disclosed that Medtronic sold over 500 kyphoplasty patents to an unknown company called Orthophoenix. Who are these guys? What did Medtronic get? What about the Kyphon Division? We find out.

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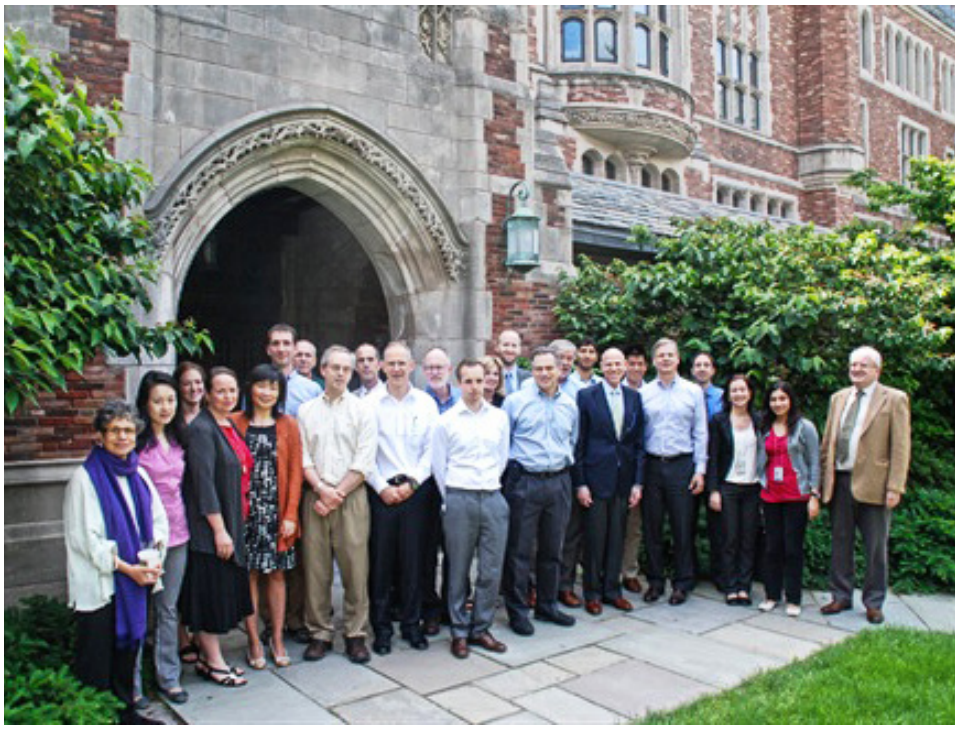
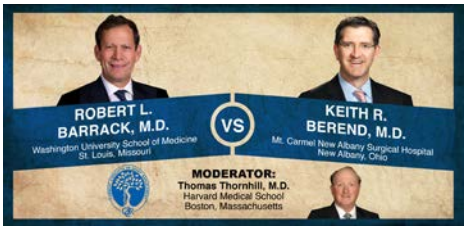




BREAKING NEWS

20 Small Stature? **K2M to the Rescue**

Spinal Elements: Patent Bonanza

Spine World Loses Luminary: **Harry Herkowitz, M.D.**

FDA Proposes **Sharing Clinical Data**

Judge Ups **Medtronic's Royalty Award** Over **NuVasive**

Nerve-Growth Factor Important in **Arthritis**

For all news that is ortho, read on.

Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

THIS WEEK: Interestingly, the big movers this past week were two companies who've yet to earn profits, MAKO Surgical and Baxano Surgical. MAKO's shareholders experienced a 16% rise in the last 30 days while Baxano's saw their equity value leap 20%. What does this mean? Investors want sales growth. When the rest of ortho is growing in low single digits, buyers seek out companies that are growing.

RANK	LAST WEEK	COMPANY	TTM OP MARGIN	30-DAY PRICE CHANGE	COMMENT
1	1	Medtronic	28.65%	5.82%	The s**t storm over Infuse started Monday. Clouds clear by Thursday. By week's end, it'll be history.
2	3	Stryker	23.68	(3.20)	How much of SYK's operating income is converted to free cash flow?—88%. Huge. And a big plus.
3	2	Zimmer	29.49	(3.86)	Like SYK, plenty of strong cash flow and lately Dvorak and Co. have been putting this cash to use via acquisitions. What else might be coming?
4	6	Integra LifeSciences	12.44	2.39	Key issue for IART is whether all the bad news is out. We think it is. Looking forward to pipeline products—which are impressive.
5	8	Orthofix	19.68	7.98	The recent run may be premature, but better to buy low than high. And the new management is just what the Dr. ordered for OFIX.
6	5	Wright Medical Group	6.84	1.36	The best estimates for this quarter and this year are for losses and flattish sales. Buyers have been picking up shares...but too soon?
7	4	Globus Medical	29.00	0.60	GMED "loses" appeal on Synthes patent suit, but, really, GMED won. The original verdict was the key win. This affirmed it.
8	7	NuVasive	7.53	(4.43)	Spine is simply out of favor at the moment and NUVA and GMED, as industry leaders, pay the price.
9	9	Alphatec	(4.29)	(1.03)	Postponing annual meeting? Raising stock options for board members—significantly? The market, if it is noticing, hasn't spoken yet.
10	10	Johnson & Johnson	25.58	(3.12)	Pyrrhic victory against GMED. Jury affirms previous $16 mm verdict for Synthes. The real loss was losing David Paul way back when.

Robin Young's Orthopedic Universe

TOP PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	Baxano Surgical Inc	BAXS	$2.24	$101	20.43%
2	MAKO Surgical	MAKO	$12.81	$601	16.35%
3	Orthofix	OFIX	$28.28	$550	7.98%
4	MiMedx Group	MDXG	$7.08	$679	6.31%
5	Medtronic	MDT	$52.92	$53,767	5.82%
6	Exactech	EXAC	$18.86	$253	3.40%
7	Integra LifeSciences	IART	$36.36	$1,020	2.39%
8	Wright Medical	WMGI	$25.27	$1,180	1.36%
9	ArthroCare	ARTC	$35.26	$994	0.83%
10	Globus Medical	GMED	$15.19	$1,398	0.60%

WORST PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	Bacterin Intl Holdings	BONE	$0.55	$24	-34.60%
2	Symmetry Medical	SMA	$8.03	$299	-23.01%
3	CryoLife	CRY	$6.09	$167	-5.43%
4	TiGenix	TIG.BR	$0.89	$90	-4.94%
5	NuVasive	NUVA	$21.79	$964	-4.43%
6	Tornier N.V.	TRNX	$16.17	$751	-4.21%
7	Zimmer Holdings	ZMH	$77.86	$13,109	-3.86%
8	Stryker	SYK	$67.21	$25,347	-3.20%
9	Johnson & Johnson	JNJ	$84.91	$238,503	-3.12%
10	Conmed	CNMD	$32.37	$909	-1.91%

LOWEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Orthofix	OFIX	$28.28	$550	11.00
2	Zimmer Holdings	ZMH	$77.86	$13,109	12.53
3	Globus Medical	GMED	$15.19	$1,398	13.31
4	Medtronic	MDT	$52.92	$53,767	14.26
5	Smith & Nephew	SNN	$58.88	$10,632	14.58

HIGHEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Wright Medical	WMGI	$25.27	$1,180	109.87
2	NuVasive	NUVA	$21.79	$964	57.34
3	Symmetry Medical	SMA	$8.03	$299	27.69
4	RTI Biologics Inc	RTIX	$4.25	$239	25.00
5	ArthroCare	ARTC	$35.26	$994	22.90

LOWEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Globus Medical	GMED	$15.19	$1,398	0.89
2	Conmed	CNMD	$32.37	$909	1.34
3	Zimmer Holdings	ZMH	$77.86	$13,109	1.34
4	Exactech	EXAC	$18.86	$253	1.35
5	Integra LifeSciences	IART	$36.36	$1,020	1.50

HIGHEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Wright Medical	WMGI	$25.27	$1,180	10.30
2	NuVasive	NUVA	$21.79	$964	4.91
3	CryoLife	CRY	$6.09	$167	4.23
4	Johnson & Johnson	JNJ	$84.91	$238,503	2.74
5	Symmetry Medical	SMA	$8.03	$299	2.31

LOWEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	Bacterin Intl Holdings	BONE	$0.55	$24	0.71
2	Symmetry Medical	SMA	$8.03	$299	0.73
3	Alphatec Holdings	ATEC	$1.93	$187	0.95
4	Exactech	EXAC	$18.86	$253	1.13
5	Conmed	CNMD	$32.37	$909	1.18

HIGHEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	MiMedx Group	MDXG	$7.08	$679	25.11
2	TiGenix	TIG.BR	$0.89	$90	21.92
3	Baxano Surgical Inc	BAXS	$2.24	$101	6.94
4	MAKO Surgical	MAKO	$12.81	$601	5.85
5	Globus Medical	GMED	$15.19	$1,398	3.62

PSR: Aggregate current market capitalization divided by aggregate sales and the calculation excluded the companies for which sales figures are not available.

Yale's Study Challenges Carragee's Mis-Measure of BMP-2

BY ROBIN YOUNG

The Spine Journal's editor, Eugene Carragee M.D., published a flawed and openly biased study of early Infuse studies in June 2011 and set in motion a series of responses one of which is the now completed Yale University Open Data Access review of Medtronic's BMP-2 patient study data. Carragee's June 2011 "study" also included a uncharacteristically aggressive attack on the authors of those early studies and in the process threw the spine surgeon community into polarized camps of conflicting and confused opinions regarding the use of recombinant BMP-2 (aka: Infuse) in spine fusion cases. What are the risks of retrograde ejaculation, cancer, ectopic bone formation and which patients are more or less at risk and is Infuse superior, same or worse than iliac bone crest graft (ICBG)?

Medtronic, sponsored most of the Infuse clinical studies, tried to address surgeon concerns by turning all patient level data in its possession over to Yale University's Open Data Access (YODA) program and providing $2.5 million of no-strings attached funding to support two independent, system reviews of the literature.

The YODA group, which was led by Harlan Krumholz, M.D., Joseph Ross, M.D. and Cary Gross, M.D., published the results of their work in the June Issue of the *Annals of Internal Medicine*. The issue was released Monday, June 17th. We received advance copies of the work last week.

Interestingly YODA has set up a web site for other researchers **and the public** to also access this same data-set.

Yale Open Data Access Steering Committee and other experts from government and academia

Here is our summary and analysis.

Conclusions:

- We're back where we were before *The Spine Journal's* assault on Infuse. Infuse works in certain patients and certain indications and not in others. And it is comparable to ICBG (the gold standard) in its ability to stimulate bone growth
- Retrograde ejaculation is a non-issue
- Cancer risk is exceedingly small
- The clearest case of where not to use Infuse is anterior cervical fusion
- Early Infuse research was biased.

In their own words, here are the physician editorial recommendations for surgeons who are considering Infuse for their spine fusion patients.

"These findings are important for guiding clinical decision making. On the basis of them, using either autograft or rhBMP-2 to enhance fusion rates in patients having anterior lumbar interbody fusion or posterolateral fusion seems clinically reasonable. Patients should be counseled on the relative benefits and harms of each option and should be allowed to actively participate in decision making. In some procedures, such as anterior lumbar interbody fusion, graft harvest is a separate procedure and avoiding a second incision and associated graft site pain may be well worth the exceedingly small increased risk for cancer. In posterolateral fusion procedures, locally harvested graft and ICBG are often available through the same incision. In these cases, it may not make sense to assume

any increased risk, no matter how small. Given the higher complication rates noted in anterior cervical surgery, rhBMP-2 should not be used in this setting without a compelling reason—for example, during a pseudarthrosis repair or other salvage procedure. For posterior interbody procedures, such as posterior lumbar interbody fusion or transforaminal lumbar interbody fusion, the use of rhBMP-2 is associated with ectopic bone formation, and strategies to minimize the clinical effect of excessive bone growth should be used."

"One caution in interpreting this information is that patients in the comparator group received autologous ICBG, the gold standard. One cannot assume that other graft materials (for example, allograft, demineralized bone matrix, or ceramic) would have results similar to those of autograft or rhBMP-2. Clinical decision making for cases where autograft is not available would have to take into account the probable lower fusion rates with these alternatives compared with autograft or rhBMP-2".

Methodology:

The methodology used in this review is clearly a step in the direction of more open and ultimately robust science. Specifically:

- Medtronic's data dump was systematically reviewed by TWO separate and independent sets of academic research teams. Their conclusions are available for side-by-side comparisons in the *Annals of Internal Medicine* issue. The fact that the two fully independent research teams came to largely the same conclusions lends strong internal validity to the meta-analysis.
- A steering committee which includes representatives from academia, government and industry as well as an additional group of experts guided the research methodologies and best practices approach. The committee did all it could to wring bias out of this review. There was no single Uber-Editor driving methodology and conclusions.
- The authors held a public comment period for review of their proposed methodology.

- All data and methodology is now available for review by other researchers and the public. It is, in other words, transparent.

Consider for a moment the ramifications of this historic approach.

If other research sponsors follow the YODA/Medtronic approach, then the days of a single research entity, like a company or an academic institution, monopolizing clinical data and its conclusions or interpretations could end.

Yes, there is comfort in working with the system we know. But as we saw with both the early Infuse studies and Carragee's own work, existing checks and balances for publication (peer review) or product approval (regulatory body review) and even the good intentions of researchers themselves can fall well short and even outright fail.

Here is the web site where anybody can apply for access to ALL of Medtronic's patient level Infuse data. http://medicine.yale.edu/core/projects/yodap

Benefit and Harm

The two independent research groups came to largely the same conclusions after reviewing the full data sets (the Simmonds, et al. group referenced 111 papers in its footnotes and the Fu, et al. group referenced 83 papers in its footnotes). Here is what the Simmonds group said:

> "Our principal analyses were based on data from 1408 individual participants in 11 eligible RCTs, including all trials sponsored by Medtronic (published and unpublished) and 1 additional trial. We found the randomization procedures to be adequate in all trials, but participants were not blinded to treatment. Although assessment of some outcomes, such as radiologic assessment of fusion, was blinded, patient-reported outcomes related to pain were not. Follow-up was reasonably complete up to our final analysis time point of 24 months. Although there is some potential for bias associated with patient-reported outcomes, in general, we consider the body of evidence for comparative effectiveness to be strong.
>
> We found clear evidence that rhBMP-2 improves rates of fusion compared with ICBG; however, the Medtronic definitions of fusion that we used may have been stringent given that only 69% of ICBG recipients achieved fusion within 24 months, which is lower than would be expected generally. Inconsistency across trials was high, with large $I2$ values at all time points.
>
> We also found that rhBMP-2 improves back pain and quality of life compared with ICBG at between 6 and 24 months after surgery. However, these improvements in pain fall below previously described, clinically meaningful thresholds (estimated as between 4 and 17 percentage points for ODI [Oswestry Disability Index] score and 5.4 points for SF-36 PCS [physical component summary]).
>
> The IPD also indicate that rhBMP-2 may be associated with an increased risk for cancer, with nearly double the number of new cancer cases compared with ICBG recipients. The overall absolute risk for cancer is low in both groups, however, so whether this increased risk is genuine is uncertain, but it is consistent with the literature suggesting a possible link between BMP [bone morphogenetic proteins] and cancer.
>
> Adverse event data in the literature raise concerns that rhBMP-2 may increase the risk for heterotopic bone formation, osteolysis, radiculitis, and retrograde ejaculation. However, these findings should be interpreted cautiously because they are based on only published nonrandomized studies, most of which provided little information about the comparability of groups.
>
> Our review differs from the existing review in that we had access to more extensive and detailed data than did Carragee and colleagues, who used aggregate data extracted from publications of industry-sponsored trials and publicly available FDA summaries and public meeting documents.
>
> The FDA materials seem to provide incomplete outcome data from a subset of trials evaluating rhBMP-2."

Here is what the Fu group said:

> "In spinal fusion, rhBMP-2 and ICBG seem to be similarly effective when used in ALIF and PLF, although the current evidence does not allow definitive conclusions about effectiveness in other surgical approaches. The Short Form-36 Physical Component Summary scores were slightly better with rhBMP-2 than with ICBG in ALIF patients through 24 months, but the difference was only 2 to 3 points on a 100-point scale and thus did not meet typical criteria for a clinically meaningful difference.

The use of rhBMP-2 in anterior cervical spine fusion was associated with statistically significant increases in overall adverse events, wound complications, and dysphagia or dysphonia. For lumbar fusion—both on-label and off-label—adverse events were common with rhBMP-2 and ICBG. Although our review raises concerns about a possible increased risk for retrograde ejaculation, urine retention, subsidence, and ectopic bone formation with rhBMP-2, the data on these harms were sparse and the quality of ascertainment was often poor. Our analysis underscores that more definitive evidence about harms was needed before rhBMP-2 became widely used.

We found that rhBMP-2 was associated with an increased risk for cancer through 24 months regardless of whether non–SEER-reportable cases were considered. This finding should be interpreted with caution because cancer cases were heterogeneous and, according to Medtronic, underreported. Seven Medtronic-sponsored trials (n =429 total) with no cancer cases in either group were not included in the meta-analysis but were not expected to affect the results. Animal studies do not suggest that rhBMP-2 is carcinogenic, but bone morphogenetic proteins are expressed by and promote the growth of some types of cancer. The development of cancer within 2 to 4 years also argues for a pro-oncogenic mechanism."

YODA Takes on Carragee

Finally, the authors could not let Carragee's scientifically unsound study from June 2011 go un-corrected. On page 877 of the York (Simmonds, et al.) paper, the authors reference Carragee's comment that "the risk of adverse events is 10 to 50 times higher than reported in trial publications."

Ten times to 50x higher. So the authors checked that claim. Here is their conclusion. "Our review differs from the existing review (*the authors then cited the Carragee study*) in that we had access to more extensive and detailed data than did Carragee and colleagues" and that after reviewing all of the data, the difference between the adverse events reported in the trial publications and actual adverse events was minimal.

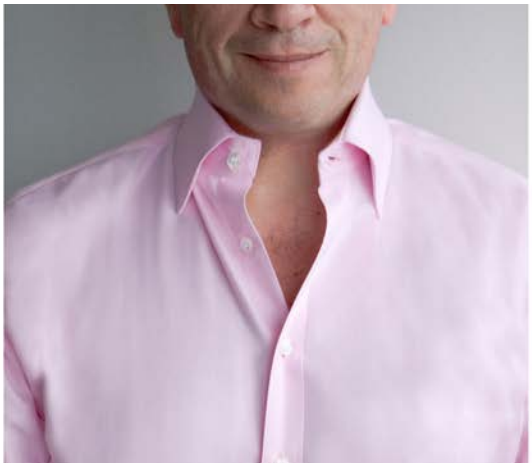
Quoting from page 883, the results of their analysis for adverse events was inconclusive and "The only clear evidence of a difference was for pain at or shortly after surgery, which was more common in the rhBMP-2 recipients (odds ratio, 1.78)."

Not exactly 10x-50x. Not even 2x.

That's a mis-measurement of a scale that approaches scientific malpractice. ♦

Who Is Buying the Kyphon (Medtronic) Patents?

BY WALTER EISNER


RRY Publications LLC

On April 25, 2013, a company named Orthophoenix, LLC registered itself in the state of Delaware and then, the following day, acquired over 500 of Medtronic, Inc.'s kyphoplasty patents.

Six years ago, Medtronic paid $4.1 billion for Kyphon Inc. Buried somewhere in those assets were these patents. Quietly and, perhaps, unexpectedly a mystery company emerged and with no fanfare, no press releases, bought these patents from Medtronic.

In May, Orthophoenix put a group of companies on notice that they may be infringing these just bought patents.

Who are these guys and what is going on?

Orthophoenix Lawsuits

Orthophoenix sent letters to at least six orthopedic companies and, in the process, claimed that their products infringed the just purchased Medtronic intellectual property (IP). On June 5, 2013, Orthophoenix filed lawsuits in Delaware against Sintea, LLC, Soteira Inc., Osseon Therapeutics, Inc., Ascendx, Dfine, Inc. and Wright Medical Technology, Inc. The lawsuits disclosed the acquisition of the Medtronic patents.

According to the lawsuits, Orthophoenix alleges those six companies are infringing on 12 separate kyphoplasty patents related to instruments and procedures.

The first question that comes to mind is: Who are these guys? The second, what patents did Medtronic sell and why?

Kyphoplasty

First, a little kyphoplasty and Kyphon history.

Kyphoplasty is an outpatient procedure used to treat painful compression fractures in the spine. In a compression fracture, all or part of a spine bone collapses. The procedure is also called balloon kyphoplasty. The doctor places a large needle through the skin and into the spine bone. Real-time x-ray images are used to guide the doctor to the correct area in the lower back.

A balloon is placed through the needle, into the bone, and then inflated. This restores the height of the vertebrae. Cement is then injected into the space to make sure it does not collapse again.

Kyphon Inc.

In 1994, Mark Reiley, M.D., an orthopedic surgeon from Berkeley, California, Arie Scholten, an engineer and inventor of surgical products, and Dr. Karen Talmadge, a Harvard University biochemist, founded Kyphon Inc. Funding followed in 1996. Two years later, the FDA cleared the company's inflatable bone tamps.

The company went public in 2002 and by 2003 surpassed $100 million in worldwide sales. By 2004, the FDA cleared Kyphon's bone cement for use in kyphoplasty, patient numbers reached 100,000 and another $100

Kyphon Building/ Courtesy of Kyphon

million in sales came through the cash register. The next year another 87,000 patients were treated and cumulative sales roared past $300 million.

In 2006, one of the company's sponsored clinical study wrapped up and the investigators were able to get their kyphoplasty results published and Medicare assigned it a reimbursement code. The company then launched a functional anesthetic discography procedure. Patient numbers reached 285,000. Cumulative sales topped $400 million.

$4.1 Billion Gamble

Medtronic bought Kyphon in 2007. The deal and price tag were not without controversy.

Industry insiders told *OTW* at the time that the price Medtronic paid for the technology was way too high and the patents were ripe for challenge. Shortly after the acquisition, Medtronic hired a new CEO and Chairman. The new CEO, Omar Ishrak, was openly critical of acquisition strategies pursued by his predecessor. He said the company would change the way it evaluated and executed future mergers and acquisitions.

The financial performance of the Kyphon division did not pan out as hoped. After the acquisition, Medtronic's management reported to its shareholders that Kyphon sales were flat and that the company was losing market share. Only recently with the company's core spine business (excluding Kyphon and Infuse) performing well, has the company become a market share gainer.

The Kallmes Effect

In 2009, two years after buying Kyphon, an orthopedic surgeon from the Mayo Clinic, David Kallmes, published the results of a study in which he claimed that he found no difference between vertebroplasty and a placebo procedure in treating patients with VCF (vertebral compression fractures). Dr. Kallmes completed another study in 2012 comparing kyphoplasty to vertebroplasty. The two procedures are similar except the balloon is used in kyphoplasty. Dr. Kallmes has not yet reported the results of his work, but, as Wells Fargo analyst Larry Biegelsen has noted, if the Kallmes study shows no difference between the two treatments, then the pressure on Medtronic's Kyphon division would probably increase. Considering everything, Biegelsen has advised his clients that Kyphon's sales in 2013 will likely reach $333 million (2.0% of total Medtronic sales). If Biegelsen is right, then Kyphon's sales would have declined another 5% from expected 2013 levels.

In 2011, Noridian Administrative Services, a Medicare contractor, determined there was no clear evidence that kyphoplasty was different from vertebroplasty.

According to Biegelsen, spine surgeons have told him that Dr. Kallmes' study is unlikely to show that kyphoplasty is superior to vertebroplasty on the primary outcome measures of pain and back specific functional status. He notes the Kallmes' study is relatively small (*n*=112) which makes it difficult to show a statistically significant difference.

"Nevertheless, Dr. Kallmes' study and the similar Australian study (also published in *NEJM* in August 2009)...resulted in about a 30% decline in combined kyphoplasty and vertebroplasty procedures in 2010 and about a 15% decline in Medtronic's Kyphon sales during the year following the [study] publication. If Dr. Kallmes' head-to-head study shows no difference between the two procedures, we believe some physicians and payers will…conclude that kyphoplasty is also no better than a sham procedure. If this is the case, Medtronic's Kyphon sales could decline further," added Biegelsen.

Medtronic is not talking about the sale of the patents. Biegelsen said it appears to him that the sale of the patents is an opportunity for Medtronic to leverage the Kyphon IP. Medtronic told him that it remains committed to the Kyphon business.

Who Are These Guys?

So back to the question of who is Orthophoenix?

Erich Spangenberg

Erich Spangenberg

We tracked down the Orthophoenix headquarters to a Dallas office building which also houses a company called IP Nav, a full service patent monetization firm headed by an attorney named Erich Spangenberg. That company is the licensing advisor to Orthophoenix.

Spangenberg and IP Nav

We reached Spangenberg in his London office on June 11, 2013.

Spangenberg said that Orthophoenix is made up of a group of investors experienced in medical devices. He said the group heard rumors in 2012 that Medtronic was interested in selling their patents. The Orthophoenix investors made an offer and Medtronic accepted. He did not disclose the price of the patents and Medtronic has not reported the sale in any SEC filings.

Medtronic did not confirm or deny the sale of the patents. But after rumors swirled that the company did not report the sale because it had an ownership interest in Orthophoenix, a Medtronic spokesperson denied any relationship with Orthophoenix. Spangenberg also confirmed that Medtronic had no interest in Orthophoenix.

We asked Spangenberg about Kyphon's uninspiring financial performance and why would his group want to buy such an asset. He candidly said that while the technology may not have performed well financially for Medtronic, numerous competitors were aggressively pushing the market. And hence, creating licensing opportunities for IP investors.

As IP Nav's founder, Spangenberg has advised patent owners in hundreds of enforcement, acquisition, commercialization and monetization transactions. Prior to founding IP Nav, he was a partner at the law firm of Jones Day (corporate), senior vice president of investment banking at Donaldson, Lufkin & Jenrette, and president of Smartalk Teleservices and also of Acclaim Ventures Group.

He's a Periclean Scholar from Skidmore College and holds an MSc from the London School of Economics. He received his law degree from Case Western Reserve University.

"Litigious, Patent-Holding Company"

According to his web site, Spangenberg owns companies that actively engage in enforcement, acquisition, commercialization and monetization transactions.

A November 2012 *Forbes* articles said Spangenberg has an "empire" of 247 IP-focused companies, "most of

which were created with the sole purpose of holding patents and filing lawsuits against those unlucky enough to infringe them."

The same article, according to *Forbes*, cites *PatentFreedom* as counting more than 500 suits filed by his corporations since 2005. "Spangenberg's lawsuits are so numerous that even he may not be able to track them: In 2008, a court awarded Mercedes-Benz and Chrysler $3.8 million when one of Spangenberg's companies sued the auto giants for patent infringement, violating a settlement they had already agreed to with another of his firms over the same issue," continued the *Forbes* article.

Corporate Counsel magazine described IP Nav, as one of the "largest, and most litigious, patent-holding companies" and writes that he advises a "sue first, ask questions later" approach.

Spangenberg doesn't disclose revenue of his business. But public records show that he and his wife, Audrey, also an IP lawyer, own a $9.3 million home in Dallas and two half-million dollar condominiums in Las Vegas.

Some critics call lawyers like Spangenberg "patent trolls." A February 2013 article in *InsideCounsel* says, "They don't make anything. Their sole business is to license their patents and sue those who resist purchasing licenses." The article continues that when a company sues for patent infringement, the defendant is likely to countersue with their own allegations of infringement.

The Spangenberg Defense

In the *Forbes* article, Spangenberg says his practice protects innovation in an age when it's especially crucial to America's future, as low-cost U.S. manufacturing becomes a thing of the past. "A strong protection of IP rights is important to protecting our economy. The world would be a better place if people understood intellectual property. I don't understand why just because it's prevalent, it should be free."

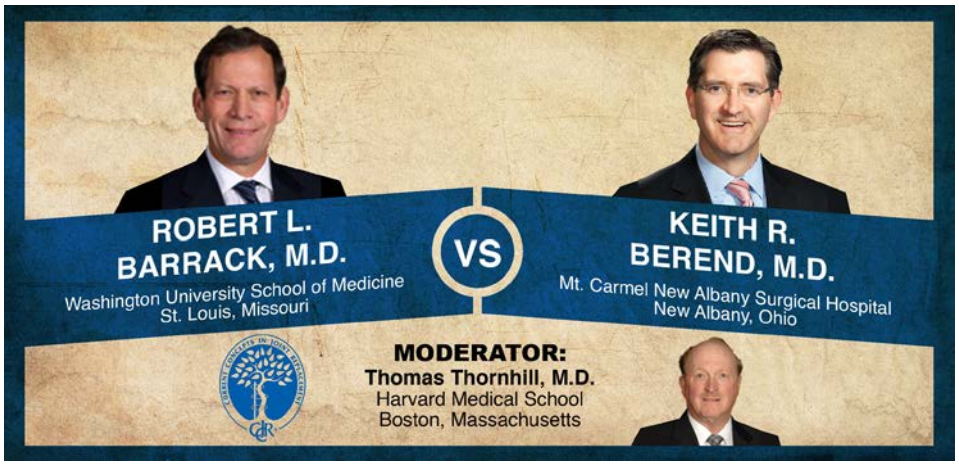
Did Medtronic get a good price for the patents for which it once paid over $4 billion? Are the patents defendable in court? For those answers we'll have to wait for Medtronic to disclose the price and terms of the deal in SEC documents and the outcome of Orthophoenix's lawsuit against the six orthopedic companies. For now we know a little more about Orthophoenix. Spangenberg promised to tell us more in the future. ♦

Barrack, Berend Debate Surface Replacement Arthroplasty

BY ELIZABETH HOFHEINZ, M.P.H., M.ED.

Robert Barrack says, "Our work has found significant differences favoring surface replacement." But, in Keith Berend's view: "This is not a viable option for most patients or surgeons."

This week's Orthopaedic Crossfire® debate is "Surface Replacement Arthroplasty: Still a Viable Option." For the proposition is Robert L. Barrack, M.D. from Washington University School of Medicine in St. Louis, Missouri; against the proposition is Keith R. Berend, M.D. from Mt. Carmel New Albany Surgical Hospital in Ohio. Moderating is Thomas Thornhill, M.D. from Harvard Medical School.



Current Concepts in Joint Replacement/RRY Photo Creation

Dr. Barrack: "Given the high rate of success of total hip arthroplasty (THA), high risk alternatives are not warranted. So surface replacement (SRA) must demonstrate a similar complication rate, there must be some clinical advantage, and there must be a reasonable learning curve to warrant continued use of this procedure."

"There are major short term complications with THA that lead to morbidity, dissatisfaction, and lawsuits. Where can we improve? Dislocation and limb lengthening are big problems; dislocation rates are generally accepted as being lower in SRA, but the lower incidence of perceived limb length discrepancy is among the potential advantages."

"Other potential advantages have been suggested and include a higher level of function/activity, less thigh pain, and less stress shielding. The problems with prior studies are that they've been low in numbers, been underpowered, and had a lot of potential for observer bias because of the absence of independent, blinded parties."

"We need to document: clinical advantage, a reasonable learning curve in the hands of a number of surgeons, and less stress shielding. Also, the clinical results…not just at specialty centers, but in large data sets."

"We did a national multicenter study to see if there was a discernible clinical difference among current THA implants with advanced bearings compared to surface replacements in young, active patients. We overcame observer bias by using an unbiased, blinded survey center that has expertise in administering questionnaires for federal and state agencies."

"There were over 800 patients; we found significant differences that favor surface replacement. There is a substantial difference in those that perceived a limb length discrepancy; thigh pain is perceived much more frequently by total hip patients than by SRA patients. THA patients even said that they limped more frequently than SRA patients; also, the SRA patients were much more active."

"Among the very high activity patients, surface replacements were much more likely to return to their most favored activity. We documented stress shielding in 90 patients, two-thirds with SRA, one-third who wanted SRA but either had a large cyst or limb length discrepancy; and we confirmed substantial stress shielding in the proximal femur for THA patients. At six months SRA has over 100% of the bone density preoperatively…and this is present even in the femoral neck at six months. Based on this, we now let our patients resume impact activities at six months. This study was recognized with the Marshall Urist Award."

"We have done two studies on the learning curve. After FDA approval we looked at 600 cases from 90 surgeons; then we compiled data from five total

joint specialists. Among all surgeons—who had done only an average of six cases—the total complication rate was 7%—which is almost the same complication rate as in a Medicare database for total hips. Among specialists, the complication rate was extremely low—2%—one-fourth that of the general population."

"Data from the Australian registry says that among young males with osteoarthritis (OA) the revision rate at five years is lower with resurfacing than conventional total hip. The facts speak for themselves. There's no doubt that this is a viable option. It's been identified by the American Academy of Orthopaedic Surgeons Technology Review as better or equivalent in some patient groups. And the same center that coined the term 'pseudotumors' in specific patient groups—Oxford—reported outstanding results in other patient groups."

"Superb SRA results have been reported from Oxford by Dr. Berend's mobile-bearing mentors. At their center, among males with OA, they had a 10-year survival rate of 99%. One disclaimer: it is dependent on the prosthesis. Most of this data is from one particular prosthesis; the results are highly variable depending on the device, patient selection, and surgeon. And much like mobile-bearing knees, it is a specialty procedure that isn't for all patients and not for all surgeons."

Dr. Berend: "This is not a viable option for most patients or surgeons. The first thing we always hear is that in the patient's perception is that this is a bone conserving operation. Clearly, if we cut the top of the femoral neck off we're discarding some bone, versus just capping off the top of the femoral head as we do with a resurfacing. Unfortunately there are multiple studies showing that there is more acetabular bone loss with resurfacing than with conventional total hip replacement. A study from Crawford found over 300% more bone loss on the acetabular side. This is something patients don't understand. They are told things like a surgical amputation of the femoral head, but they don't understand that in order to put in a big enough acetabular component and a big enough ball, it requires more bone loss, not less."

"What about the data Robert mentioned on dislocation rate and better range of motion? It's actually untrue. We all understand head/neck ratio, and clearly if we just put a cap on the end of the thigh bone, the head/neck ratio is significantly different than if we use even a 32mm head. In a computational study from Kluess the average range of motion with resurfacing was up to 50 degrees less than that of a 32mm total

hip. And in the model no resurfacings allowed for flexion of 90 degrees without impingement—either bony or mechanical."

"Lavigne's study showed that impingement was significantly higher with resurfacing and range of motion was significantly greater with total hip. Robert discussed functional outcomes, and in his phone survey of patients who had already received resurfacing and had undergone the receiver bias of having selected out a surgeon and an operation that they felt would benefit them, there were some significant advantages. In Lavigne's randomized, prospective study, there was no difference between either operative groups. In a similar study by Killampalli there were no differences in the level of function, and, interestingly, no differences in the level of activity pursued."

"In a study by Mont, the outcomes were significantly comparable in terms of satisfaction and activity score, with a slight bias towards a higher activity score in the resurfacing patients. In a meta-analysis by Singer the femoral revision rate was twice that with resurfacing as with total hip. Robert also mentioned the Australian registry; I would agree that in young men, and in the hands of well trained, experienced surgeons, with large diameter acetabular components, the operation is comparable to total hip replacement. It is not better than total hip replacement. When taken in aggregate, the revision rate for resurfacing in every registry study shows that resurfacing does worse than total hip replacement."

"In Graves' multinational assessment of the three largest registries (England and Wales, Australia, New Zealand) it is confirmed by all that with the exception of young men with large diameter femoral heads, the revision rate is significantly higher. Robert published a study with Della Valle where they had a 7.5% failure rate with 40 adverse events. The complication rate was higher in patients over 55 and in females. My study found the same thing, with an 8% failure rate, including infection, femoral neck frac-

tures, and loosenings of both the femoral and acetabular components. In our early experience we were concerned, and limited our use of this procedure to young men."

"I think it's indisputable that the broadest indications, the most reliable results, the least risk of an early reoperation, and the lowest risk of late mysterious complications, is with crosslinked polyethylene and a total hip replacement with a stem and an acetabular component."

Moderator Thornhill: "Keith, is it an arrow that you should have in your quiver for some patients?"

Dr. Berend: "In my quiver, no, because the indications are so limited that you're better off pulling the correct operation out of your bag every time and getting a good result nearly every time. The indications are clear: you must have bigger than a 54mm component, it must be well placed, and it needs to be a male patient under 55. Even with those patients, I'm still concerned about the second decade issues of metal-metal, and the fact that there is probably going to be a latency period. We're not seeing it early because these are patients that have well positioned components that have a large diameter. But we may see it late. They all have high levels of ions, and they are going to have extraordinarily high levels of ions in the joint itself."

Moderator Thornhill: "Who should get surface replacement?"

Dr. Barrack: "Males with osteoarthritis that are under 55 and want to be very active (doing activities that most total hip surgeons don't recommend for their total hip patients). In the last American Association of Hip and Knee Surgeons (AAHKS) survey 80% of hip surgeons either advise or prohibit their patients from impact activities. There's no evidence that at 10-15 years that this is detrimental for hip resurfacing."

Moderator Thornhill: "Robert, is there an indication for this in women?"

Dr. Barrack: "It's rare; it's an issue of size and morphology."

Moderator Thornhill: "Keith, Robert said the data show that this is a high activity implant (SRA). Do you agree?"

Dr. Berend: "There is no evidence that high activity levels are not obtainable nor are they bad in the second decade for a conventional total hip replacement. I'm in the 20% of surgeons in the AAHKS survey that don't restrict their patients. There's no data to the contrary."

Dr. Barrack: "You just heard the data to the contrary, and 200 of them were from your older brother. The statistical significance was so high that the high activity level data is supported."

Dr. Berend: "Those were patients that had already had the operation—meaning that they selected out a surgeon and an operation, and they met the criteria to have an operation…they felt like they were special. It isn't that the total hips were told they couldn't run, it's that the resurfacings had that operation specifically because they felt like they could run…and afterwards they could run."

Moderator Thornhill: "Boys, hang on! Robert, leg length discrepancy, limb and thigh pain…is that only in the first 6-12 months?"

Dr. Barrack: "These patients were 1-3 years out. Limb length has bias because it is a contraindication. But a patient saying they limp more or are less likely to walk 30 minutes…I don't think you can attribute that to selection bias."

Moderator Thornhill: "Thank you both." ♦

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Tricking Cells to Migrate to Fracture Sites...Don't Withhold Preop Antibiotics!

BY ELIZABETH HOFHEINZ, M.P.H., M.ED.

Making Autologous Cells Home in to Fracture Sites A former president of the Orthopaedic Trauma Association (OTA) is working to make it possible for healing cells to migrate to a fracture site. J. Tracy Watson, M.D. professor of orthopedic traumatology, fellowship director, and chief of the orthopedic trauma service at St. Louis University School of Medicine, tells *OTW*, "We just recently presented some our lab's work on cellular therapy at the recent OTA meeting in Minneapolis and are submitting this for publication. The project involves injecting stem cells, which have been harvested from intra-medullary reamings in humans. These bone forming cells were first collected, then isolated via a genetic marker which selects out for bone forming cells. These were then expanded in tissue culture and immuno-labeled. These cells were injected into the blood stream of an animal model femur fracture. We then analyzed the migration of these cells to determine to what extent theses allograft stem cells migrated to the site of injury. Which they did…and they subsequently augmented the fracture healing of the femoral shaft fractures. Clearly we have demonstrated that we can modulate cell populations to migrate to a site of injury. Our studies have also evaluated the healing potential utilizing placental cord blood cells as well."

"Such work holds a lot of promise. Imagine being able to harvest a patient's own cells…perhaps by plasmapheresis techniques, isolate and expand the bone forming cells and simply inject them back to the patient, much like a blood transfusion to help treat a severe fracture of a fracture that hasn't adequately healed. Currently we are simply trying to determine which cell lines exhibit the best migratory and osteogenic capabilities as this is just the first step in understanding this as a treatment modality to augment our surgical capabilities. It is hoped that eventually we can develop this technology to make it a reality for human use."

Wikimedia Commons and U.S. Navy photo by Fire Controlman 3rd Class Jovante L. Washington

It Is OK to Give Preoperative Antibiotics! Well, one million dollar question seems to have been answered. Should you be withholding prophylactic antibiotics prior to revision surgery? No, says a recent study that won the Knee Society Ranawat Award. Craig Della Valle, M.D. is an orthopedic surgeon at Midwest Orthopaedics at Rush and associate professor at Rush University Medical Center in Chicago. He tells

OTW, "Our prospective randomized study sought to determine if prophylactic antibiotics affect intraoperative culture results in patients undergoing revision hip or knee arthroplasty surgery. Many of us—myself included—were taught in residency to withhold preoperative antibiotics. Despite evidence that these drugs may be our most powerful weapon to prevent postoperative infections, many surgeons remain concerned that prophylactic preoperative antibiotics may alter intraoperative culture results and cloud the diagnosis of periprosthetic joint infection."

"I'm pleased to be able to provide evidence that—in the vast majority of cases—we can safely give preoperative prophylactic antibiotics without it affecting the cultures. This work, which builds on similar research by Robert Barrack, M.D., is making people reevaluate the practice of routinely holding antibiotics before revision. In the majority of cases the surgeon will probably know prior to the revision procedure whether or not there is an infection, and hence the decision to give the patient prophylactic antibiotics should be clear. However, in the rare case where the diagnosis is unclear preoperatively, the surgeon might consider holding them. However, our data suggests that they will not affect intraoperative culture results. This work has been presented at both the open and closed meetings of the Knee Society, and has just been accepted for publication by *Clinical Orthopaedics and Related Research*."

Military, Civilian Orthopedic Surgeons Collaborate for Disaster Response Col. James Ficke, M.D. was the Orthopaedic Surgery Consultant to the U.S. Army Surgeon General until April 2013. He co-chaired the Extremity War Injuries symposium for six years. Here, Dr. Ficke gives *OTW* an update on the collaborative work being done between military and civilian orthopedic surgeons. "Along with Lieutenant Colonel Warren Kadrmas from the Air Force and Navy Captains Daniel Unger and Eric Hofmeister, we have facilitated a coordinated military and civilian disaster response program. We learned much from the Haitian earthquake disaster, and are learning how to cut through the red tape and streamline processes so that doctors can help in an organized fashion. The military has recently completed test credentialing for two orthopedic surgeons at Keesler Air Force Base, where the commander

there is an orthopedic surgeon. It has been a success."

"Thus far, two civilian surgeons have gone through the program and several others have travelled overseas to help with either disasters or care of our wounded warriors. The intent of this program is to facilitate federal response in cooperation with these doctors. This effort concerns primarily major international events where U.S. government assistance is requested, but hopefully also across state boundaries when domestic events take place. We encourage all surgeons to get involved in disaster response, whether with non-governmental organizations, or to have them completely ready to board hospital ships or other military facilities at the centers of international disasters. Having all of the required training, certification, paperwork and preliminary credentialing procedures out of the way when disaster strikes saves time and lives."

"At present the federal government is working towards having an accepted, standardized credentialing process. They are doing fingerprinting and background checks on doctors interested in being credentialed during the Disaster Response Course, sponsored jointly by Society of Military Orthopaedic Surgeons (SOMOS) and the AAOS [American Academy of Orthopaedic Surgeons]. This course, directed jointly by Drs. Theodore Parsons, Chris Born, and Tad Gerlinger has sold out four times and has a standing waiting list for future courses. The next step is to have these volunteers privileged through the military. A year from now we hope to have the privileging process up and running; some issues remain, such as cross state recognition of surgeons, and medical liability. My message to anyone involved the process: You never know when a disaster will happen in your state, so it's in your best interest to help this program succeed."

Worldwide Push for Smallest Orthopedic Patients In 2008 Kaye Wilkins, M.D. received the Humanitarian Award from AAOS. Since receiving this honor he has continued his focus on trying to establish the availability of quality pediatric orthopedic services for children in countries with limited resources. This former president of the Pediatric Orthopaedic Society of North America (POSNA) is leaving a big mark on musculoskeletal care for the most vulnerable patients. Dr. Wilkins tells *OTW*, "I am continuing to focus primarily on providing outreach education in pediatric orthopedics. My philosophy is

to, 'leave skills not just scars.' During the past two years, I have worked on assisting selected orthopedic surgeons to establish pediatric orthopedic programs in Bangladesh, Nepal, and Sri Lanka. These orthopedic surgeons had previously traveled to established pediatric orthopedic training centers in North America where they observed the manner in which pediatric orthopedics was practiced and taught. Following these observerships, they then returned to their home orthopedic programs to implement what they had learned. I was especially proud in a return visit to Dhaka, Bangladesh, in 2012 to see that they had progressed to the point where they had established the Bangladesh Pediatric Orthopaedic Society, with its first meeting in late 2012. There were close to 20 individuals in attendance at that meeting."

"I have continued to visit Haiti to attempt to expose doctors there to pediatric orthopedic education. I arranged for seven members of their orthopedic society to travel to San Antonio and other pediatric orthopedic centers in North America to observe how the practice of pediatric orthopedics is now conducted. This was an effort to build some enthusiasm for their orthopedic surgeons to develop some expertise in pediatric orthopedics in their country. Prior to the 2010 earthquake there were no orthopedic surgeons with any pediatric orthopedic expertise. Two years ago they had their first fellowship trained orthopedic surgeon return to start his practice at the Adventist Hospital in a suburb of Port au Prince. A second orthopedic surgeon is now starting her training and will be ready to treat pediatric orthopedic conditions in Haiti in 2014. One of the few positive effects of the 2010 earthquake was that it opened up to the outside world the dire insufficiency of quality orthopedic care in Haiti. As a result, there is now an increased interest on the part of pediatric orthopedists from North America to travel to Haiti to participate in outreach educational projects."

Dr. Wilkin's also helped rebuild the orthopedic residency program at the State University Hospital in Port au Prince. "Fortunately, the residents have returned to the University Hospital and I am now able to resume the teaching conference in pediatric orthopedics. Overall, I think 'giving' is catching on… and I'm glad to find that POSNA's committee on outreach education is now one of the more popular committees."

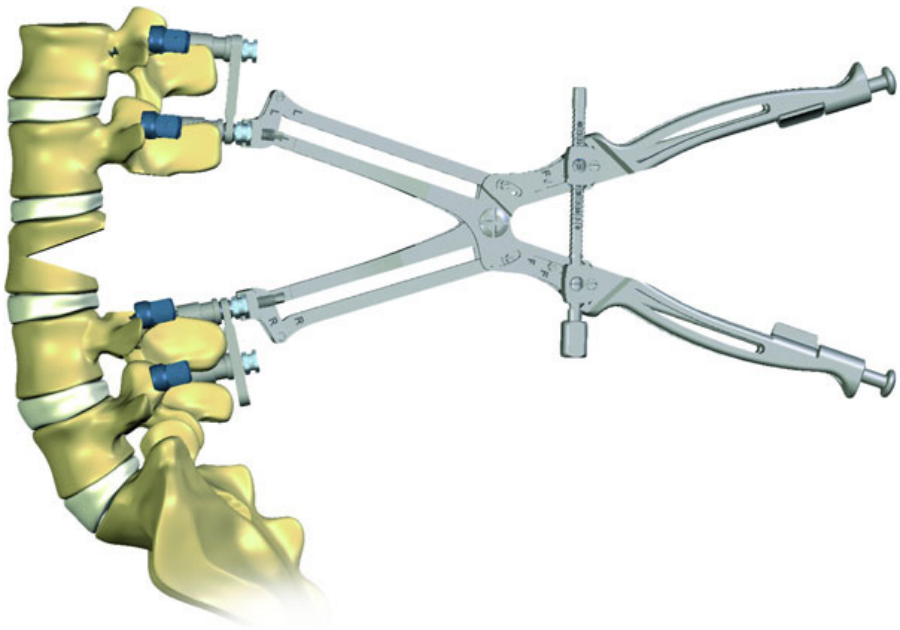
Matthew Scott New VP at ConforMIS ConforMIS Inc. has announced the appointment of Matthew Scott as the company's senior vice president of operations. Most recently the director of operations for Zimmer Dental, Scott oversaw all aspects of the operation and managed the rapid growth of the dental implant manufacturing facilities during his tenure. He also held several roles at Zimmer Orthopedics, where he started as the production manager for the knee femoral business, which led to leadership roles on teams responsible for lean process redesign, cost efficiencies and technology transfer, according to a company press release. Scott also helped establish a global network of manufacturing facilities to support the hip and knee implant business. He developed the business case for several overseas facilities, planned and executed the build out of the sites and served as interim general manager of a new production facility in Ireland before moving to Zimmer Dental. ♦

COMPANY

Medtronic Unveils Device to Restore Spine's S-Shape

Medtronic, Inc. has received CE Mark for a device used to treat patients with a severe form of spinal curvature to allow them to potentially stand up straighter without pain.

On June 13, 2013, the company announced the launch of the ReDux Plier calling it the "first specialty-designed surgical instrument" in the spinal orthopedic industry which allows physicians in the European Community to perform a more controlled osteotomy closure.



Medtronic, Inc./ReDux Plier

The instrument was developed by Medtronic European Product Development Office based in Tolochenaz, Switzerland, following an original invention by Professor Le Huec, chief of the Spine Unit and chair of the Department of Orthopaedics and Traumatology at the Bordeaux University Hospital, France.

Speaking at the SFCR (Société Française de Chirurgie Rachidienne) congress in Nice, France, Professor Le Huec commented: "The PSO (pedicle substraction osteotomy) procedure is an extremely powerful option for people with severe spinal curvatures, but the potential for complications has historically been very high. The instruments currently available were often too crude for the complex procedure, so working with Medtronic we have been able to produce specially-designed instruments which give surgeons greater control than ever before."

According to the company's statement, adult spinal deformity poses many challenges to spine surgeons. In particular, a substantial imbalance in the sagittal plane sometimes cannot be corrected solely with a standard arthrodesis procedure. In these cases, spinal osteotomies must be performed to restore balance in both the sagittal and the coronal planes.

Here is from the company press release:

> *PSO is a complex and delicate surgical procedure for patients with sagittal imbalance, a condition where the back has lost the characteristic S-shape that allows the skeleton to resist gravity and keep people standing upright. These patients can live in considerable pain, unable to stand or walk properly."*
>
> *During a PSO a triangular wedge of bone is removed from the middle of a vertebrae, allowing it to be angled backwards to re-align the spine by increasing the backward curve (lordosis) in the lower (lumbar) spine. This, according to the company, creates a more upright posture and relieves pain.*
>
> *Surgical procedures which remove bone from the spine, such as PSO, can be extensive and complicated. Problems can include the collapse of vertebrae when compression is applied to close the two sides left after the removal of bone. As the ReDuX Plier is connected directly to the implants, it aims to protect the front of the vertebrae from collapse by driving the kinematic of the closure and dissipating stress onto the bone screws.*

The device also provides a progressive correction, ensuring a more controlled procedure at every stage of the operation.

The device is not yet available in the U.S.

—WE (June 14, 2013)

LEGAL

Bone-Stim Investigation Nabs Virginia Doc

A Virginia podiatrist has been indicted in the ongoing investigation of fraudulent bone growth stimulator payments.

Ilene Terrell, M.D., of Fredericksburg was charged on June 12, 2013 with manipulating patient medical records and then lying about it to a grand jury. The indictment also claims Terrell lied to Orthofix, Inc. auditors.

Terrell allegedly prescribed an Orthofix stimulator device on numerous occasions for patients where the claim would not have met Medicare's guidelines. When this occurred, the Orthofix territory manager, Terrell, and an employee at Terrell's direction often manipulated patient medical records, making it appear as though the stimulator was not prescribed until three months had elapsed without healing, when in fact that was not true and Medicare should not have paid the claim.

On some occasions, Terrell allegedly prescribed a stimulator for a patient and the patient's bone healed within the prohibited three-month window. When that occurred, Terrell, an Orthofix representative, and an employee at Terrell's direction deleted references in chart notes that the patient was using the stimulator and was healing, and they created a new, fictitious note at the end of the 90-day period stating that the bone was still broken and that a stimulator would be ordered. Terrell also created fictitious prescriptions to support the bogus claims.

Podiatry Management Online/Ilene Terrell, M.D.

According to the complaint filed by Carmen Ortiz, the U.S. Attorney in Boston, on May 22, 2012, Terrell testified before the grand jury. She was asked several times if she was aware that patient records had been manipulated. Terrell lied to the grand jury, emphatically denying that she manipulated patient records or that she was even aware that anyone had done so. Terrell lied about other matters as well, including her communications with an Orthofix representative about the government's investigation and her role in obstructing an audit performed by Orthofix when the company requested that she provide medical records related to claims for bone growth stimulators.

The Foot Doctor of Rappahannock

According to her practice web site, "The Foot Doctor of Rappahannock, Ltd.", Terrell is board certified in foot surgery by the American Board of Podiatric Surgery. She provides conservative as well as surgical management of foot and ankle ailments for children, teens, adults and seniors, including diabetic patients.

She has been practicing in the Fredericksburg area since 1986 and has maintained Board certification in foot surgery since 1995. Terrell maintains privileges at Mary Washington hospital and the Fredericksburg Ambulatory Surgery Center. She has served as chairman of the podiatry department at Mary Washington Hospital.

Terrell attended the Pennsylvania College of Podiatric medicine and the Surgical Residency programs. "She is committed to providing the highest level of care, taking the time to explain your ailment and address your concerns. She believes that ongoing training and product knowledge assists her in her efforts to remain current with new trends in podiatric medicine and surgery," states the web site.

If convicted, Terrell faces a statutory maximum penalty of five years in prison, to be followed by three years of supervised release and a $250,000 fine on each count.

The details contained in the indictment are allegations. The U.S. Attorney said Terrell is presumed to be innocent unless and until proven guilty beyond a reasonable doubt in a court of law.

—WE (June 14, 2013)

Judge Ups Medtronic's Royalty Award Over NuVasive

A U.S. District Court has awarded Medtronic, Inc., a higher ongoing royalty rate than a jury had awarded the company previously in an ongoing patent fight with NuVasive, Inc. over NuVasive's CoRoent XL implants and certain MaXcess retractors and related products.

However, according to a June 12, 2013 announcement by NuVasive, the court awarded less than what Medtronic asked for after winning the first round of the patent fight

The jury verdict in Phase I of the litigation determined royalty rates of 10% on certain of the implants and 3% on certain of the retractors and related products.

The court was required to determine the ongoing royalty rates before a NuVasive's appeal could move forward. Medtronic, according to NuVasive, requested royalty rates of 36% and 11% for those products.

In the ruling received on June 12, the District Court ordered royalty rates of 13.75% on the applicable CoRoent XL implants and 8.25% on the applicable MaXcess retractors.

The company said it had expected litigation royalty expense of approximately $11 million for the full year 2013. The new royalty rates will increase that expected litigation royalty expense for 2013 by approximately $5 million.

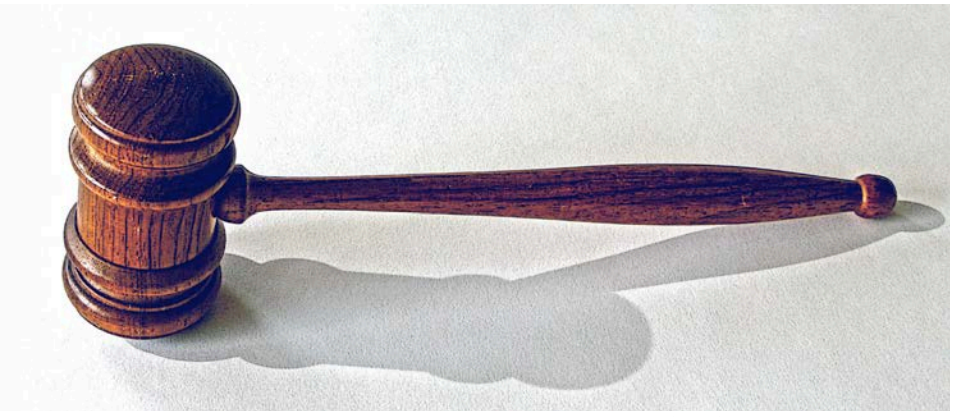
NuVasive Pursues Appeal

NuVasive Chairman and CEO, Alex Lukianov said he was pleased to have an outcome regarding the ongoing royalty issue so the company can finally begin the appellate process. "While we disagree with the Court-ordered royalty rates, they are significantly lower than those sought by Medtronic after its motion for an injunction following the verdict was denied. Today's ruling will have an immaterial impact on our liquidity and our ability to fund strategic initiatives," said Lukianov

He added that the company will "promptly and aggressively" appeal the verdict and damage award.

The majority of the royalty expense is related to patents that will expire in February 2015, according to Wells Fargo analyst Larry Biegelsen.

—WE (June 12, 2013)



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FDA Proposes Sharing Clinical Data

The FDA wants to share your clinical data with "non-FDA experts and other interested parties."

The agency says data gained from patients participating in clinical trials should be "maximized" for the benefit of society. So the agency is proposing to share clinical and preclinical data derived from marketing applications after de-identifying and masking that data.

regulations.gov

Safeguard Commercial Investments

However, the agency says it wants to do it in a way that would "both safeguard the privacy interests of patients enrolled in clinical trials, and appropriately protect the commercial investments of sponsors."

The proposal contemplates the availability of certain data after appropriate steps have been taken to de-identify it and remove the data's link to a specific product, study, or application.

The proposal, according to the FDA, does not pertain to unmasked safety and effectiveness data, (i.e., data that can be linked to a specific, identified application) including full study reports; the circumstances under which the disclosed information is already

specifically set forth in the Federal Food Drug and Cosmetic Act and FDA's regulations.

Further, FDA will not make available business-related confidential commercial information contained in product applications, including but not limited to information concerning licensing agreements and information identifying suppliers, unless such information has already been publicly disclosed by the sponsor. Nor will the Agency make available trade secret information under this proposal," stated the FDA announcement published in the Federal Register on June 4, 2013.

The agency invites comments on the issues to be considered with regard to such availability and on any limitations that should be placed on the availability of these data. You've got until August 5, 2013.

The agency says making that data available to non-FDA experts and other interested parties could make an important contribution to improving the efficiency and effectiveness of medical product development by providing scientific data that may be of value in the generation of new knowledge to facilitate innovation in the development and evaluation of critically needed medical products.

"Analysis of data from multiple clinical and preclinical studies has been used to identify potentially valid endpoints for clinical trials, understand the predictive value of preclinical models, clarify how medical products work in different diseases, and inform development of novel clinical designs and endpoints to the benefit of patients," continued the announcement.

The agency says it has considerable expertise in analyzing individual patient level and aggregated clinical trial data, but recognizes the potential to further advance regulatory science by allowing other experts the opportunity to contribute to these efforts. To fully realize the potential of these data, experts outside of FDA would need to become actively engaged in the research.

To read the notice and submit electronic comments, click here: http://www.regulations.gov/#!searchResults;rpp=25;po=0;s=Docket%252BNo.%252BFDA%25E2%2580%25932013%25E2%2580%2593N%25E2%2580%25930271;fp=true;ns=true

Written comments may be submitted to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, Maryland, 20852.

—WE (June 12, 2013)

LARGE JOINTS

Nerve-Growth Factor Important in Arthritis

Researchers at McGill University have just published a study in the *Journal of Neuroscience* that confirms prior research indicating that the nervous system and nerve-growth factor (NGF) play a major role in arthritis. The findings also support the idea that reducing elevated levels of NGF—a protein that promotes the growth and survival of nerves, but also causes pain—may be an important strategy for developing treatment of arthritis pain.

In particular, they investigated changes in the nerves and tissues around the arthritic joint in rats by using specific markers to label the different types of nerve fibers and allow them to be visualized with a fluorescence microscope.

Under normal conditions, sympathetic nerve fibers regulate blood flow in blood vessels. Following the onset of arthritis in the rats, however, these fibers began to sprout into the inflamed skin over the joint and wrap around the pain-sensing nerve fibers instead. More sympathetic fibers were detected in the arthritic joint tissues, as well.

The results also showed a higher level in the inflamed skin of NGF, which mirrors the findings of human studies that have shown considerable increases in NGF levels in arthritis patients. To investigate the role of these abnormal sympathetic fibers, the McGill researchers used an agent to block the fibers' function. They found that this reduced pain-related behavior in the animals.

"Our findings reinforce the idea that there is a neuropathic component to arthritis, and that sympathetic nerve fibers play a role in increasing the pain," said McGill doctoral student Geraldine Longo in the June 13, 2013 news release. Longo co-authored the paper with Professor Alfredo Ribeiro-da-Silva and postdoctoral fellow Maria Osikowicz.

"We are currently using drugs to prevent the production of elevated levels of NGF in arthritic rats; we hope that our research will serve as a basis for the development of a new treatment for arthritis in the clinic," said Professor Ribeiro-da-Silva.

—EH (June 14, 2013)

Wikimedia Commons and GerardM

SPINE

Steroid Injections: Approach With Caution

Researchers from Henry Ford Health System have found that a higher number of lumbar epidural steroid injections (LESI) is associated with an increased risk of vertebral fractures. The authors indicate that LESIs may lead to increased bone fragility over time, and while injection therapy is useful in some cases, it should be approached cautiously for patients at risk for fractures associated with osteoporosis. The retrospective study was just published in the *Journal of Bone and Joint Surgery* (*JBJS*).

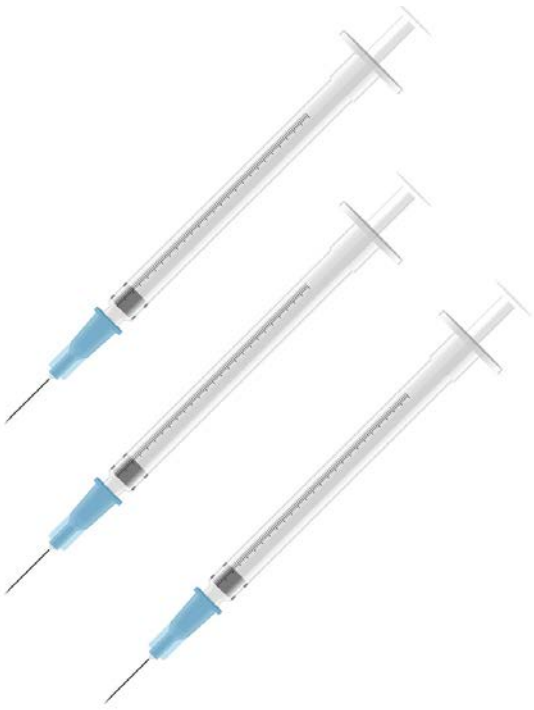
"In the appropriate setting, and for the right patient, LESI provides effective symptomatic relief and improved level of function, said Shlomo Mandel, M.D., M.P.H., lead author of the *JBJS* study and orthopedic surgeon at Henry Ford Health System, in the June 6, 2013 news release. "Through careful screening and monitoring steroid exposure, the risk of a fracture can be minimized. As orthopaedic surgeons who specialize in spine, we know there is a role for injection therapy, but the challenge is to make sure it is administered safely and still provide long-term benefits."

The researchers identified a total of 50,345 patients who had medical diagnosis codes involving the spine, and from that group, a total of 3,415 patients had received at least one LESI. From that subset, 3,000 patients were randomly selected, and then 3,000 patients from the non-injected group were selected as a control group. There was no significant difference between the injected and non-injected groups with respect to age, sex, race, hyperthyroidism, or corticosteroid use. An increasing number of injections were associated with an increasing likelihood of fractures, and each successive injection increased the risk of spinal fracture by 21%.

"It's important to remember that when contemplating an epidural steroid injection a physician should have a symptomatic history, physical findings and corresponding imaging of direct pressure on a single nerve," added Dr. Mandel. "Together with our patient, we review the benefits and risks of alternative treatments before selecting an epidural steroid injection."

Asked about his biggest concern about how these injections have been done in the past, Dr. Mandel told *OTW*, "My concern is the exposure to exogenous steroids, typically because of frequent injections and lack of attention to bone density."

As for future research, Dr. Mandel told *OTW*, "We need a larger prospective study to verify our findings. We are embarking on a prospective case-control project using bisphosphonates. It should shed some light on DEXA [dual-energy x-ray absorptiometry] and fractures, but the primary focus is prevention of fractures following ESI. Ultimately, if the study results are verified, guidelines like we have for other uses of exogenous steroids should be implemented."



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—EH (June 12, 2013)

Spinal Elements: Patent Bonanza

Spinal Elements, Inc. has announced that they have licensed a portfolio of patents essential for accessing the lumbar spine from a lateral approach and placing implants from that approach. The lateral approach to the spine provides the potential for less disruptive, minimally invasive surgical (MIS) access techniques to address numerous spinal pathologies.

Spinal Elements plans to use this newly licensed technology to develop access systems and implants for introduction later in the year. The company recently received 510(k) clearance from the FDA to market implants placed using the lateral access procedure. The clearance included the use of the company's Ti-Bond porous titanium coating on such laterally-placed implants.

Company President and co-founder Jason Blain remarked in the May 29, 2013 news release, "We are glad to add this portfolio of patents as a resource from which we can expand our product offerings as we move to make Spinal Elements an innovative leader in the MIS spine access and implant market. Over the course of the year we have introduced and will continue to introduce new technologies to offer spine surgeons the most advanced technologies for their patients."

Todd Andres, company CEO and co-founder, added, "The licensing of these patents and development of these systems is congruent with our culture of respecting the intellectual property of those who innovated before us while also developing our own technology and intellectual property to advance the field."

Jason Blain told *OTW*, "The decision to license the patents was easy. Spinal Elements is quickly expanding our MIS product portfolio and lateral access and implants will be an important part of that. We recognized that there is significant intellectual property (IP) already in the space. We want to protect our own IP while respecting that of others. The group that licensed the IP to us was extremely professional and pleasurable throughout the process."

"We will rapidly work to get our patented retractor system outfitted for lateral access over the course of the year. We will introduce a unique and advanced system for our customers while expanding our Ti-Bond titanium porous coating technology to the lateral platform."

—EH (June 11, 2013)

Spinal Elements, Inc.

Small Stature? K2M to the Rescue

Small persons with large back pain, take heart. K2M, Inc. is coming to the rescue. The company has announced the launch of the MESA Small Stature Spinal System in the Australian, New Zealand, and European

K2M, Inc.

spine markets. This is the company's first posterior spinal fixation product available for small stature patients. It boasts a 4.5 mm pedicle screw system, provides surgeons with the lowest profile alternative for treating small stature patients and, coupled with K2M's Zero-Torque Technology, it is designed to address the most difficult correction maneuvers.

"At last, a system powerful enough to get the job done and elegant enough to look the part. When used with the 4.5 mm MESA Rail, I have a more powerful system than with a 5.5 mm titanium rod and a lower profile than standard 3.5 mm top loading systems. It shares the load like a Luque construct, allowing coupled multi-planar correction," stated Dr. John Ferguson, Orthopedic Spine Surgeon in Auckland, New Zealand, in the May 29, 2013 news release.

According to Laurel Blakemore, M.D., Chief of Orthopedics and Sports Medicine at Children's National Medical Center in Washington, DC, "The MESA Small Stature Spinal System provides an extremely low profile, versatile construct option for my smaller patients."

stated Eric Major, K2M's president and CEO. "Providing innovative technologies to meet patient needs continues to be a top priority for K2M and this international growth reinforces our goal to offer the best solutions for the most complex spinal pathologies around the world."

A K2M representative told *OTW*, "We estimate the global small stature spinal device market to be over $400 million."

—EH (June 10, 2013)

PEOPLE

Spine World Loses Luminary: Harry Herkowitz, M.D.

On June 9, 2013 the orthopedic world was jolted by the sudden loss of Harry N. Herkowitz, M.D., the much-loved chairman of Orthopaedic Surgery at Beaumont Hospital in Royal Oak, Michigan. Dr. Herkowitz, who was 65 years old, is survived by his wife Jan, son Seth (Laura) and daughter Rachael (Michael – fiancé).

A luminary of the spine world, Dr. Herkowitz specialized in the surgical management of spinal disorders including spinal stenosis, herniated discs, deformity and trauma to the neck and back. Many who walk the halls of orthopedics programs nationwide continue to benefit from his extensive contributions to the field.

Dr. Herkowitz assumed the chairmanship of the department of Orthopaedic Surgery at Beaumont in 1991 and directed that institution's spine surgery fellowship program from 1987 to 2008. His talents and leadership insight also led him to prominence as president of the Cervical Spine Research Society, the International Society for the Study of the Lumbar Spine and the American Board of Orthopaedic Surgery.

Dr. Herkowitz's research legacies include contributions to degenerative solutions to aging discs and improving spinal implants. He gained renown with his 1991 landmark study on the treatment of degenerative spondylolisthesis, work which continues to influence current research. The name "Harry Herkowitz, M.D." appeared under the titles of many respected articles in the

Beaumont Health Systems

peer-reviewed literature; he also presented at hundreds of conferences. Dr. Herkowitz also edited a dozen major textbooks on the spine, and served as editor or on the editorial board of major orthopedic and spine journals. He was a graduate of Wayne State University School of Medicine, did his residency at Beaumont, and completed a spine surgery fellowship at Pennsylvania Hospital in Philadelphia.

Dr. Herkowitz was honored with an Outstanding Academic Excellence Award by Beaumont in 2011. He was also named among the 100 Best Spine Surgeons in America, recognized by Best Doctors in America, and was twice honored with the Volvo Award for Clinical Research in Low Back Pain.

Steve Garfin, M.D., chair of the department of orthopedic surgery at the University of California, San Diego, was a dear friend of Harry Herkowitz for 35 years. "He was a surgeon's surgeon, leader's leader, clinical scientist's clinical scientist, a great and loyal and true friend, beat everyone at hard work, but was a wonderful (and wonder as a) father, husband, family/friend, and respected/admired by all."

Remembering his friend with warmth, Dr. Garfin says, "He was very predictable and repetitive and had a touch of

obsessiveness. At meetings or events, no matter what restaurant, or style of it, he always got salmon if it was there—always. Then there was Sunday. As busy as he was, and how much he had a cast of people doing things for him, he always went to Costco, by himself, fighting Sunday crowds to look around and see what they had and what the bargains/specials were, but the bargains/specials didn't matter. He always bought the same things—water, Kleenex, and other surprisingly simple basics—always."

Todd Albert, M.D. is president of the Rothman Institute in Philadelphia and chair of the Department of Orthopaedic Surgery at Thomas Jefferson University. His thoughts: "Harry Herkowitz was a great friend, father, husband and an icon in orthopaedic surgery. While working in a private practice, he created sentinel scientific works on the treatment of degenerative spondylolithesis and degenerative cervical disease. He was a leader in multiple societies and on the American Board of Orthopaedic Surgery. Most importantly he was a thread that bound together a great tradition of those trained by Dick Rothman and their progeny. He made a huge effort to be welcoming and mentoring to all."

John Heller, M.D. is professor of orthopedic surgery at Emory University. He muses, "Dr. Herkowitz meant so much to so many. Words that come to mind include friendship, service, leadership, scholarship, excellence and loyalty. Whether you are among the countless patients he served, or those served by the surgeons he inspired or trained, Dr. Herkowitz simply changed lives. He changed the course of contemporary spine surgery through his research, his service to the American Board of Orthopaedic Surgery and leadership in numerous other professional organizations. He was the consummate mentor, a devoted family man and a true friend. We are all diminished by his passing. At ten years my senior, he was always cordial, supportive, willing to open doors, etc. His professional life was about paying forward the principles and behaviors of his primary mentor, Richard Rothman."

The spine world will go on, but is today a bit less rich in experience and ideas than before his passing.

Those who wish to further honor the memory of Dr. Harry Herkowitz may do so by making a contribution to:

Beaumont Foundation
Dr. Harry Herkowitz Fund
3711 West 13 Mile Road
Royal Oak, MI 48073
248-551-5330
http://foundation.beaumont.edu/

—OTW Staff

Villamil Named Lanx Latin America Education Director

Fernando Villamil, M.D., chief of the Orthopaedic Spine Service at Ashford Presbyterian Community Hospital in San Juan, Puerto Rico, is Lanx, Inc.'s new director of education for Latin America. He also joins the company's Surgeon Advisory Board.

Andrew Cappuccino, M.D., chairman of the company's advisory board and surgeon at the Buffalo Spine Surgery, Lockport, New York, said Villamil's surgical expertise "will be invaluable as we look to increase development and awareness of these unique fusion systems and further optimize minimally invasive spine care."

Villamil will oversee all training initiatives for Lanx in the region.

A native of Puerto Rico, Villamil completed his spine surgery fellowship at Harvard Medical School while working at Massachusetts General Hospital and Brigham and Women's Hospital in Boston, Massachusetts. A June 10, 2013, company announcement said Villamil has extensive experience in treating complex spinal conditions, having performed thousands of fusion surgeries.

Villamil said Lanx's technologies are among the most innovative available for spine care, enabling surgeons to perform truly minimally invasive fusion. "The Timberline Lateral Fusion System is an especially exciting offering, and in my experience, advances the efficiency of the lateral approach and associated patient outcomes. I look forward to working with my peers in Latin America to develop world class training programs for Latin America, as well as working with my international colleagues on the Surgeon Advisory Board to provide strategic direction to Lanx."

Lanx, Inc./Fernando Villamil, M.D.

In addition to the Timberline system, the company develops and markets a full line of fusion devices including the Aspen MIS Fusion System. Lanx is headquartered in Broomfield, Colorado, and distributes its products throughout the world via a network of direct sales representatives and exclusive distributor partners.

—WE (June 11, 2013)

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