VOLUME 10, ISSUE 9 | MARCH 18, 2014

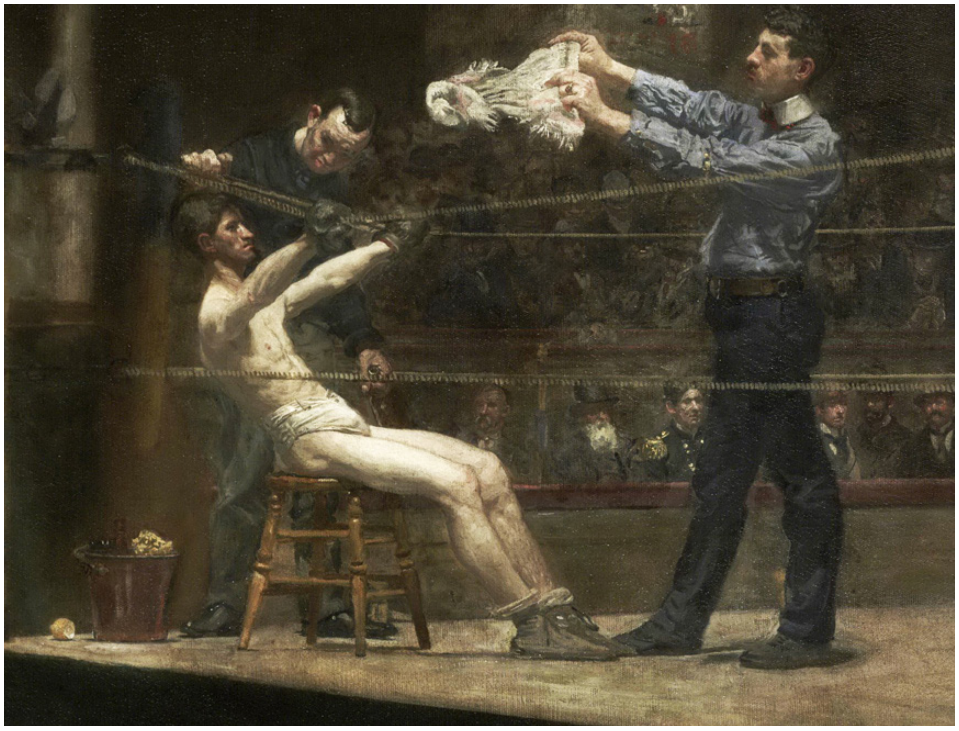
Orthopedics This Week

WEEK IN REVIEW

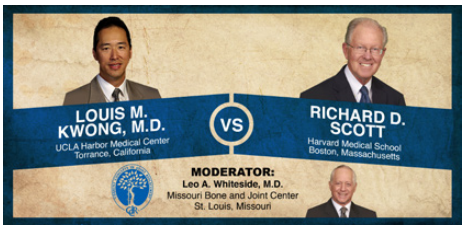
4 Can ConMed's Founding Family Survive? PART II >> ConMed's group of dissenting shareholders lost its largest member as Coppersmith Capital signed a standstill agreement and agreed to join the company board. Additionally, ConMed Founder and Chairman Eugene Corasanti agreed to resign as Chair and completely leave the board in 2015. Is the fat lady tuning up for Voce Capital?

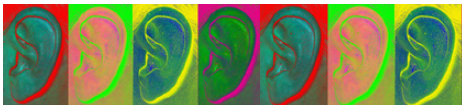
8 Infuse Off-Label Lawsuits Begin >> No product has generated more questions about off-label use than Medtronic's Infuse. From *The Spine Journal* to the U.S. Senate, partisan advocates have vilified Medtronic for their promotion of the product. Now the lawsuits have started and patients are claiming harm because Medtronic promoted off-label uses. Read what one patient has to say.

14 The Unexpected Rise of Hip Revisions and How to Handle Them // Notes from Sochi Olympics U.S. Team's CMO // Freddie Fu, M.D. Honored With Elizabeth Winston Lanier Award >> Geoffrey H. Westrich, M.D. from HSS discusses the exploding number of hip revisions and how to handle them well. Gloria Beim, M.D. talks about her incredible experience serving as chief medical officer for Team USA/Sochi. Freddie Fu, M.D. is honored with the Elizabeth Winston Lanier Award.



18 Cementless Fixation: Kwong v. Scott >> "Cementless fixation is an easy surgery with excellent intermediate to long term clinical performance," says Louis Kwong. Richard Scott counters, "Cemented TKA is state of the art and has a reoperation rate of 0.5% for the first 15 years. Cementless hasn't yet been proven to be as reliable as cemented fixation."





BREAKING NEWS

21 Promising New Stem Cell Data for **Osteoarthritis**

1,000 Spines Tested on **VMA System**

Bacterin Secures Loan

Elite Athletes Depressed, Tired as They Age

Wright and FDA Reach Procedure Agreement on PMA

Arthrosurface Toe Motion Preservation **System Cleared by FDA**

For all news that is ortho, read on.

Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

THIS WEEK: Many changes this week. On the plus side, Wall Street's analysts came out of AAOS uniformly positive. Investors, however, are trading as if risk is rising. Buyers favored higher quality ortho stocks (i.e., less sales variability) and earnings power. ConMed, which is in a shareholder fight, delayed its annual meeting—perhaps to settle with its dissenting shareholders or for other reasons. Either way, investors are more sellers of ConMed than buyers right now.

RANK	LAST WEEK	COMPANY	TTM OP MARGIN	30-DAY PRICE CHANGE	COMMENT
1	2	Stryker	15.71%	(0.84%)	SYK's bet on MAKO was in full display at AAOS and surgeons responded positively. SYK has momentum.
2	3	Zimmer	27.31	(1.31)	ZMH's answer to the accuracy and efficiency robot argument at AAOS was the iASSIST knee.
3	8	Integra LifeSciences	11.77	2.52	The least expensive equity in orthopedics these days. Adding sales reps aggressively in shoulder market. Up strongly in the rankings.
4	7	Johnson & Johnson	26.58	0.42	Almost NO attention to DePuy from Wall Street's analysts. Hard to fathom considering the new rotating platform for the ATTUNE knee.
5	5	Medtronic	28.84	4.31	Spine market back in favor. Head winds appear to have eased up due to new HTA study. Analysts see upside to 2014 growth rates.
6	4	Smith & Nephew	20.25	(0.17)	Talk about spiking the ball on the 2 yard line. Management implies Q4 sales bump was aberration. So 2014 will be slower?
7	10	Globus Medical	28.29	8.61	Riding two waves simultaneously: improving spine market outlook and the industry's profit leader. But valuations are clearly at the high end.
8	9	NuVasive	6.30	4.63	NUVA has two great strengths—longevity of management and strategic thinking up and down the ranks. Huge long-term advantage.
9	1	ConMed	10.37	(1.73)	Either dissident shareholders are selling or the market thinks the game is basically over. But ConMed has been affected—more outside influence.
10	6	Symmetry Medical	6.50	(2.18)	SMA's big news at AAOS was a femoral elevator for direct anterior hip arthroplasty. It's available under the well-known Bookwalter® brand.

Robin Young's Orthopedic Universe

TOP PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	Bacterin Intl Holdings	BONE	$0.74	$38	29.82%
2	RTI Biologics Inc	RTIX	$4.04	$229	23.93%
3	Orthofix	OFIX	$23.86	$464	12.39%
4	Globus Medical	GMED	$25.60	$2,390	8.61%
5	Wright Medical	WMGI	$33.40	$1,650	7.85%
6	MiMedx Group	MDXG	$7.32	$773	5.93%
7	NuVasive	NUVA	$37.75	$1,730	4.63%
8	Medtronic	MDT	$58.86	$58,910	4.31%
9	Exactech	EXAC	$23.47	$319	2.58%
10	Integra LifeSciences	IART	$47.14	$1,530	2.52%

WORST PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	Alphatec Holdings	ATEC	$1.39	$136	-23.20%
2	Baxano Surgical Inc	BAXS	$1.20	$57	-9.77%
3	Aurora Spine	ASG	$4.23	$66	-5.10%
4	Tornier N.V.	TRNX	$18.96	$920	-3.90%
5	CryoLife	CRY	$9.54	$266	-3.54%
6	Symmetry Medical	SMA	$9.86	$370	-2.18%
7	ConMed	CNMD	$44.83	$1,220	-1.73%
8	ArthroCare	ARTC	$48.12	$1,650	-1.35%
9	Zimmer Holdings	ZMH	$94.15	$15,940	-1.31%
10	Stryker	SYK	$80.27	$30,360	-0.84%

LOWEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Orthofix	OFIX	$23.86	$464	9.58
2	CryoLife	CRY	$9.54	$266	15.78
3	Medtronic	MDT	$58.86	$58,910	15.96
4	Zimmer Holdings	ZMH	$94.15	$15,940	16.39
5	Johnson & Johnson	JNJ	$92.81	$262,500	16.94

HIGHEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	NuVasive	NUVA	$37.75	$1,730	104.86
2	Symmetry Medical	SMA	$9.86	$370	74.25
3	ArthroCare	ARTC	$48.12	$1,650	31.78
4	Integra LifeSciences	IART	$47.14	$1,530	29.72
5	Smith & Nephew	SNN	$77.36	$13,830	24.87

LOWEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Exactech	EXAC	$23.47	$319	1.09
2	Orthofix	OFIX	$23.86	$464	1.37
3	Globus Medical	GMED	$25.60	$2,390	1.60
4	Zimmer Holdings	ZMH	$94.15	$15,940	1.70
5	ConMed	CNMD	$44.83	$1,220	1.89

HIGHEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Alphatec Holdings	ATEC	$1.39	$136	18.00
2	NuVasive	NUVA	$37.75	$1,730	10.10
3	Symmetry Medical	SMA	$9.86	$370	6.19
4	CryoLife	CRY	$9.54	$266	3.95
5	Integra LifeSciences	IART	$47.14	$1,530	3.13

LOWEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	Alphatec Holdings	ATEC	$1.39	$136	0.69
2	Symmetry Medical	SMA	$9.86	$370	0.92
3	Orthofix	OFIX	$23.86	$464	1.00
4	RTI Biologics Inc	RTIX	$4.04	$229	1.16
5	Bacterin Intl Holdings	BONE	$0.74	$38	1.16

HIGHEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	TiGenix	TIG.BR	$1.20	$192	44.60
2	MiMedx Group	MDXG	$7.32	$773	13.06
3	Wright Medical	WMGI	$33.40	$1,650	6.81
4	Globus Medical	GMED	$25.60	$2,390	5.50
5	ArthroCare	ARTC	$48.12	$1,650	4.37

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

Can ConMed's Founding Family Survive? PART II

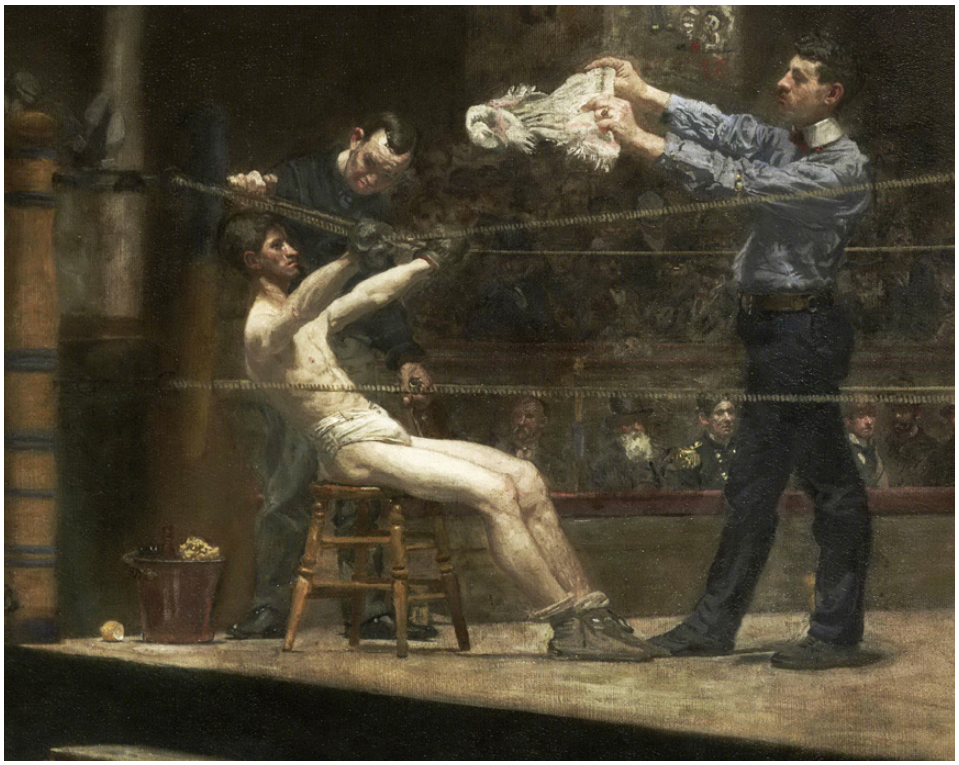
BY ROBIN YOUNG

A group of dissenting shareholders led by San Francisco-based Voce Capital and representing approximately 12% of ConMed, Inc. shares outstanding are making a determined effort to change the governance of ConMed and, quite likely, wrest management away from ConMed's founding family—the Corasantis.

Just a couple days before Valentine's Day, Voce Capital submitted for shareholder consideration names of four new directors to serve on ConMed's board.

ConMed's shareholders will be asked to vote on the new slate as well as management's nominees at ConMed's annual meeting—which originally had been scheduled for May 22 but was postponed late on Friday, March 14.

That meeting—whenever it is held—and this vote should be interesting.



Wikimedia Commons and Thomas Eakins

Who Are the Dissenters?

Leading the dissenters is J. Daniel Plants, managing partner of Voce Capital Management LLC. Despite owning a small (0.7%) of shares, Voce has successfully agitated ConMed's management to begin instituting changes and is largely responsible for a surge in buying interest in ConMed's stock.

Mr. Plants is a long-time Wall Street investment banker (law degree from University of Michigan) and has been employed at Goldman Sachs, JP Morgan, Needham & Company, ThinkEquity and HSBC. He is one of the founding members of Voce Capital.

Voce detailed its case against ConMed's management in a November 2013 letter and, in mid February 2014, filed papers with the SEC to replace four members of ConMed's board with a new slate.

Joining Voce in this effort were, at least initially, activist shareholders Camber Capital and Coppersmith Capital. Collectively the three investors own 12% of ConMed.

Boston-based Camber Capital Management, founded in 2006 by Stephen Rodney Du Bois, is a privately owned hedge fund which invests in micro-cap and small-cap companies—mostly in the health care sector.

By the end of 2013, Camber held almost 1.4 million shares of ConMed representing 5.02% of the company's stock. The total value of their shares is $56.6 million.

On February 6, Coppersmith Capital joined the fray announcing that they had amassed 5.9% of ConMed. By reputation, Coppersmith is an "event driven" fund founded in 2012 by Jerome Lande and claims to have significant activist experience.

Clearly, pressure on ConMed's management and the Corasantis was mounting.

At the time of its purchase, Coppersmith's founding partner, 37-year-old Jerome Lande said that he "knows the company well" and has been an on and off investor for over 10 years.

According to Coppersmith's press releases, it is a "long term value creation shareholder with more than one arrow in its quiver." At the same time Coppersmith announced their investment

and support for Voce's campaign to wrest ConMed's control away from the Corasanti family, Lande also said that he would "meet with management and try to implement the changes necessary to enhance value." But if sale of ConMed was the best option for value creation then, he said, he would "support that, at the right price."

ConMed Settles With Coppersmith and Adds Hartman and Lande to the BOD

Of the three dissenting and activist shareholders Coppersmith was both the largest holder of ConMed shares and the one who explicitly asked to meet with ConMed's management to implement changes.

Voce Capital had also met with ConMed's management many times before launching its bid to overhaul ConMed's governance.

Between February 7 and February 26, Coppersmith's Lande met with senior members of ConMed's management. On February 27 the two parties announced a settlement agreement.

Coppersmith agreed to vote all of its shares in favor of ConMed management's slate of directors.

And Eugene Corasanti, founder of ConMed and its long-time CEO, agreed to resign as Chairman of the Board and also agreed to NOT stand for re-election as a director in 2015.

The dissenters were now down to about 6% of ConMed.

With this, the odds that Voce might force a change in ConMed's governance, which were long to start with, got much longer.

Two New Independent Directors

As a result of the settlement with Coppersmith, two new independent directors are joining ConMed's board—they are Curt Hartman, former interim-CEO of Stryker, and Jerome Lande, founder of Coppersmith.

One of Voce Capital's main criticisms of ConMed's management is its insular management of ConMed and the per-

ceived lack of independent board oversight. Said Voce's Plant in his November letter to ConMed's management:

> "Any analysis of ConMed's corporate governance must begin with the recognition that, until July of this year, its Board of Directors has been inhabited exclusively by denizens of Utica, New York…. The Board's lack of alignment with shareholders, coddling of management and toothless oversight is highly relevant to the review of ConMed's strategic positioning and financial and operational performance."

With this agreement, ConMed would now have two independent members of the board both of whom hail from geographies well away from Utica, New York.

Voce Unimpressed

Voce Capital was not impressed with Coppersmith's standstill agreement nor with the new director nominees.

Said Voce's Plant:

> Mr. Hartman's "senior executive experience [consists] mostly as a financial officer, with CEO operating experience limited to eight months as interim CEO, no public company board service." And: "After a 22-year track record with Stryker, and eight months as interim CEO, Stryker board passed over Hartman for a full-time job in favor of another internal candidate with 18 months tenure at Stryker."

Voce also mentioned that they had interviewed Mr. Hartman as a potential nominee for ConMed's board but rejected him for two reasons. Said Voce: "First, we were (and still are) troubled by the gravity and specificity of the unrebutted allegations that Alere raised against him. Second, Mr. Hartman, who has been unemployed since his termination from Stryker in October 2012, made clear to us that he was pursuing board seats as a source of income and was interested in being appointed as ConMed's CEO if we were successful in electing directors."

As for the other board nominee (Jerome Lande), Voce has this comment: "Mr. Lande is an undistinguished 37-year-old investor with relatively narrow and junior experience."

Voce's Alternative Board Slate

And here are the four Board of Director candidates Voce is offering to ConMed's shareholders: *(See Table on page 7)*

Strong AAOS

The annual meeting of the American Academy of Orthopedic Surgeons was held last week in New Orleans. Initial reports from Wall Street analysts are that ConMed had one of its best meetings in years. Said Michael Matson, CFA of Needham & Company; "CNMD's (Buy) new products were impressive. CNMD is launching a number of new products during 2014, and after seeing these for

Name	Age	Principal Occupation for Past Five Years and Directorships
James W. Green	55	Mr. Green has been the president, CEO and a director of Analogic Corporation, a publicly traded manufacturer of advanced medical imaging and security systems, since May 2007. In addition to Analogic Corporation, Mr. Green sits on the board of directors of the Massachusetts High Tech Council.
Alan L. Kaganov, Sc.D.	75	Dr. Kaganov has been a partner of U.S. Venture Partners, a venture capital firm, where he focuses on medical devices and other health care industries, since 1996. From 1993 to 1996, Dr. Kaganov served as vice president, Business Development and Strategic Planning at Boston Scientific Corp., a leading medical device company, and spent six years in various positions at Baxter International, Inc., a globally diversified healthcare company.
Jeffrey M. Nugent	67	Mr. Nugent is the founder of Precision Dermatology, Inc., a privately held dermatology therapeutics company that was recently acquired by Valeant Pharmaceuticals International, Inc. He served as interim president and CEO of Ascension Orthopedics, Inc., an orthopedic extremities company. From 1999 to 2002, Mr. Nugent served as president, CEO and a director of Revlon, Inc., a publicly traded beauty care company. Mr. Nugent previously held a number of senior management positions within Johnson & Johnson for 25 years in R&D, operations, marketing and finance, including serving as worldwide president and CEO of Neutrogena Corp. from the time of its acquisition in 1994 until 1999. Mr. Nugent also serves on the boards of directors of several privately-held medical device companies.
J. Daniel Plants	47	Mr. Plants has been the managing partner of Voce Capital Management since founding the firm in 2009. Mr. Plants held a number of positions at leading Wall Street firms, including executive positions in investment banking at Goldman Sachs and JPMorgan Chase and as a corporate attorney with Sullivan & Cromwell.

Source: Voce Capital Management LLC

the first time at AAOS, we have greater conviction in CNMD's ability to reaccelerate its revenue growth this year and we reiterate our Buy rating."

What Happens Next?

Originally, ConMed's shareholders were expected to vote on both management's slate of board members—including the two new outside board members and Voce Capital's nominees—on May 22, 2014. But late last Friday (March 14, 2014) ConMed announced that it was delaying the annual meeting.

Whenever the annual is heal, odds favor management's slate. Because dissatisfied shareholders of a public company can simply sell their shares, there is a built-in inertia to shareholder votes at annual meetings.

Still, one way or the other, ConMed's board will now be comprised of at least two new outside members both of which have stated that they are interested in helping ConMed increase its value to shareholders.

One of Voce's most intriguing arguments is that ConMed is, in fact, a more valuable company than its current stock price would indicate.

Paraphrasing from Voce's November letter to ConMed's management:

> ConMed's is one of only three players with a full-line sports medicine business. Two-thirds of ConMed's revenues and three-fourths of its EBITDA is from sports medicine products. Eighty percent of revenues are from single-use disposables rather than capital equipment.
>
> Many companies believe ConMed is strategically attractive. Prime among them would be Zimmer, a small player in sports medicine today that has identified sports medicine as a corporate focus. Zimmer actually owned ConMed's Linvatec prior to Zimmer's spin-off from Bristol-Myers Squibb. Stryker, as well, would find that ConMed fills out its arthroscopy offerings. Smith & Nephew, on the other hand, has a strong arthroscopy franchise but lacks the depth in power tools offered by ConMed. Finally Biomet has a number of holes in its arthroscopy product line which ConMed could fill. ConMed's shoulder restoration system, for example, would be of particular value to Biomet. Other prospective acquirers include Arthrex, J&J, Covidien or even such diverse health companies as Bard, Boston Scientific, Danaher, Medtronic, Teleflex or 3M.

So, whatever happens at the eventual board meeting, this much is clear. Going forward this will not likely be the same ConMed Corporation. ♦

Infuse Off-Label Lawsuits Begin

BY WALTER EISNER

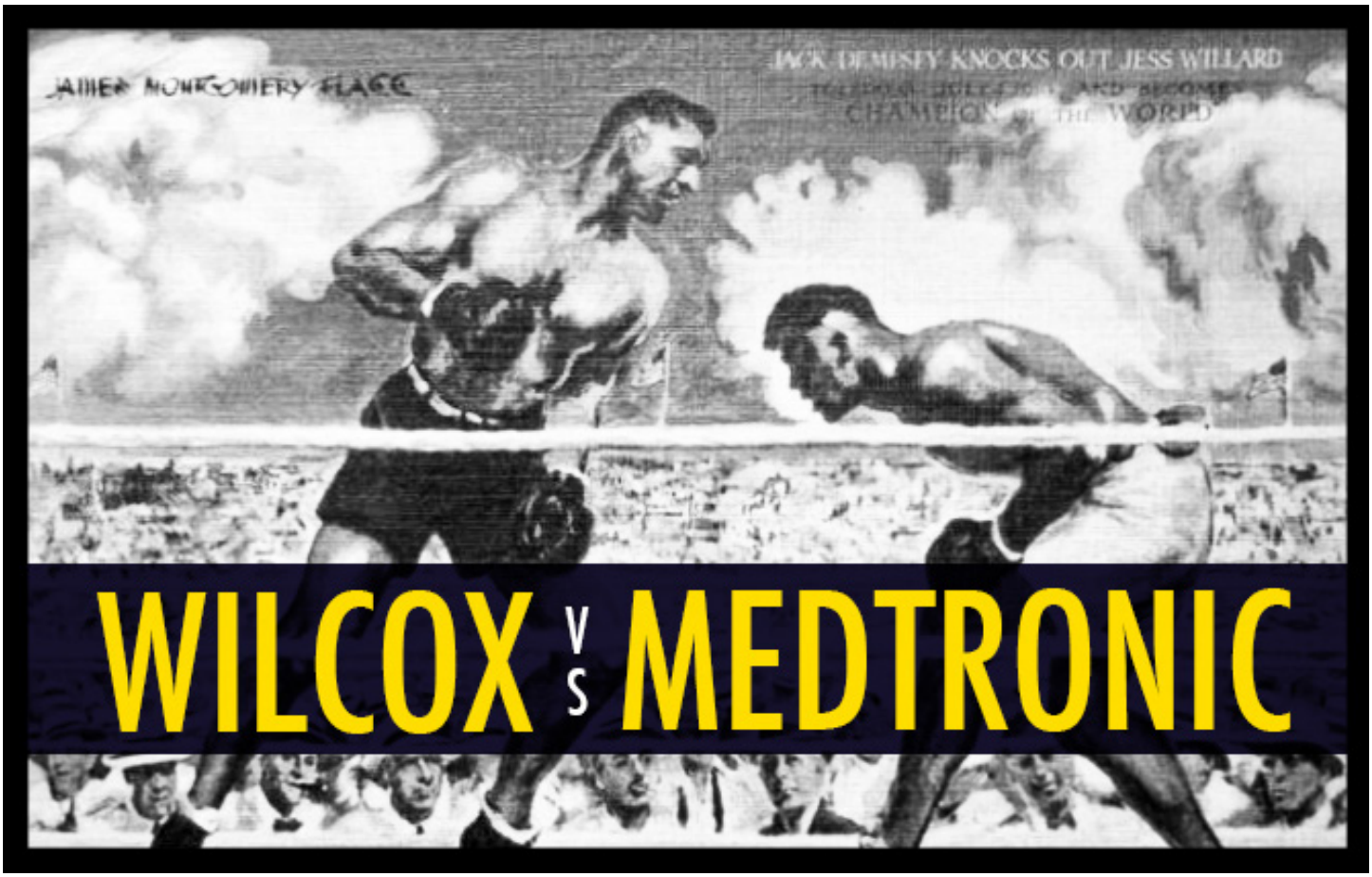


Photo creation by RRY publications/Wikimedia Commons

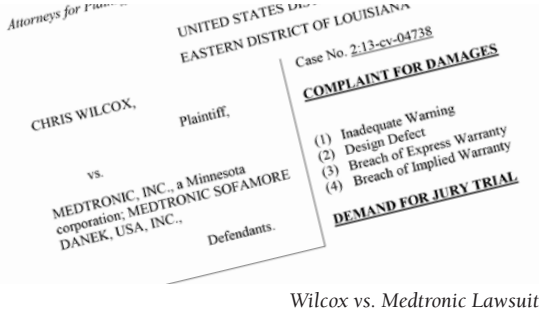
On May 20, 2008, Chris Wilcox underwent a decompressive hemilaminectomy and posterior lumbar fusion at levels L5-S1 in which Infuse was used. Off-label. The surgery was performed by Ralph Katz, M.D. The use of Infuse was off-label in this surgery because it was implanted by means of a posterior approach and the requisite LT-Cage was not used.

There were serious complications so the patient (Wilcox) sued Infuse manufacturer Medtronic, Inc., on June 2013 in the U.S. District Court, Eastern District of Louisiana. Wilcox is accusing the company of promoting Infuse to his and other surgeons for off-label uses when they knew it was dangerous and therefore is to blame for his complications.

Post-operative imaging studies, according to his attorneys, revealed that Wilcox had developed uncontrolled bone growth and resulting pseudoarthrosis and radiculopathy related to bone overgrowth at or near where the Infuse was implanted.

The Lawsuits Start

This isn't the first lawsuit that has been filed against Medtronic over complications arising from the off-label use of Infuse. Medtronic continues to defend itself by invoking its hard won Riegel Supreme Court decision which held that companies that have received FDA approval for their products are preempted from being sued in state courts for tort claims.


Attorneys for Plaintiff

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

Case No. 2:13-cv-04738

COMPLAINT FOR DAMAGES

CHRIS WILCOX, Plaintiff,

vs.

MEDTRONIC, INC., a Minnesota corporation; MEDTRONIC SOFAMOR DANEK, USA, INC., Defendants.

(1) Inadequate Warning
(2) Design Defect
(3) Breach of Express Warranty
(4) Breach of Implied Warranty

DEMAND FOR JURY TRIAL

Wilcox vs. Medtronic Lawsuit

But a recent decision by a Minnesota state judge pierced the preemption defense and allowed a defendant to proceed with his lawsuit against Medtronic.

Wilcox's "Complaint for Damages" charges Medtronic with: Inadequate Warning; Design Defect; Breach of Express Warranty and Breach of Implied Warranty.

Wilcox Allegations

Within the lawsuit are allegations that Medtronic improperly promoted off-label uses of Infuse. Wilcox's lawyers try to prove those allegations by presenting testimony of former Medtronic employees regarding off-label promotion in a shareholder derivative action, undisclosed payments to opinion leaders, letters from U.S. Senators regarding promotion and marketing of Infuse, the June 1, 2011 issue of *The Spine Journal* and the October 25, 2012 U.S. Senate Committee on Finance "Report on Medtronic's Manipulation of the Infuse Studies and Close Financial Ties with Researchers."

The case also brings in the settlement of two whistleblower lawsuits with the Department of Justice and the imposition of a Corporate Integrity Agreement (CIA).

While Wilcox's lawyers have thrown the kitchen sink into their 94-page Complaint, we focus only on specific allegations made by unnamed former Medtronic employees identified as "Confidential Witnesses" who claim first-hand knowledge of company actions. We will not recount the well-known political and controversial charges leveled by *The Spine Journal* and U.S. Senators.

The Off-Label Conundrum

The case boils down to one simple question: Did Medtronic promote Infuse for off-label uses? The case also raises important questions about who has a right to speak about off-label uses in light of a recent U.S. Appeals Court decision holding that a device sales rep has a First Amendment right to speak truthfully about a product to physicians and patients.

Wilcox's complaint says Medtronic employees and company consultants "thought leaders" acting in the name of the company conducted meetings, held seminars and published papers promoting the use of Infuse.

Medtronic directly and indirectly promoted, trained, and encouraged surgeons to perform spinal fusion procedures utilizing Infuse in a dangerous

off-label manner, claims Wilcox. The company "recklessly and/or fraudulently promoted and marketed Infuse."

Limited FDA Approval

Wilcox recounts that the initial FDA approved labeling for the product in 2002 indicates in bold underlined formatting: "These components must be used as a system. The Infuse Bone Graft component must not be used without the LT-Cage Lumbar Tapered Fusion Device component."

Medtronic, Wilcox points out, sells Infuse separately from the LT-Cage to surgeons who use the product off-label.

Soon after FDA approval, Medtronic issued a "Safety Alert" letter to surgeons on September 14, 2004, informing them that the company had received reports of complications associated with off-label use of Infuse in anterior cervical fusion procedures.

On July 1, 2008, the FDA issued a Public Health Notification to healthcare practitioners entitled "Life-threatening Complications Associated with Recombinant Human Bone Morphogenetic Protein in Cervical Spine Fusion".

In other words, says Wilcox, Medtronic had plenty of notice that the off-label use of Infuse was dangerous.

But, he continues, the company tried to find a way around the complications because sales of the product eventually exceeded $3.6 billion since the launch of the product and off-label uses accounted for 85% to 90% of all spine surgeries involving Infuse.

Confidential Witnesses

He cites a "Confidential Witness" (CW) who claims former COO Michael DeMane, former president of Medtronic Spinal and Biologics Pete Wehrly, and former worldwide vice president and General Manager, Biologics, Jon Serbousek, were all aware of the adverse events related to Infuse.

Confidential Witness # 13 (CW13) claims he was rebuffed for raising concerns about off-label promotion, and was told "we're paying you a lot of money to launch this. Shut your mouth and take the money. Let us worry about what is off-label or isn't."

Indeed, to set sales projections for Infuse, another confidential witness (CW2) stated that Medtronic's marketing department accounted for the scope

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and number of procedures performed, including the numbers of off label procedures, such as PLIFs and TLIFs, to predict sales projections.

Final sales quotas were dictated by senior management, and were far in excess of what the Spinal Division had projected, or could be achievable absent promotion of the product for off label uses, according to CW2.

"Aggressive" Sales Goals

Numerous confidential witnesses, including CWs 1, 9, 12 and 14 (a senior manager for Medtronic's Spinal and Biologics division from 2005 to 2008), allegedly confirm the intense pressure management placed on its sales representatives to meet the sales quotas. Like CW2, CW14 claims that sales goals were set by a handful of Medtronic executives, and that they were "very, very, very aggressive."

Wilcox goes on to allege that the company directed its own sales representatives to promote off-label uses of the product, "many of whom… guide[d] surgeons through off-label uses of the product during surgery."

"Although undisclosed by Medtronic, the first-hand accounts of its former employees demonstrate that this extraordinarily high off-label use was driven by Medtronic's sales force. Specifically, Medtronic's marketing and sales employees directed spine surgeons to Medtronic-compensated consultants or 'Opinion Leaders' or 'Thought Leaders'—other spine surgeons paid enormous sums of money by Medtronic—the sole purpose of which was to promote off-label uses of Infuse."

According to Wilcox, several spine surgeons have already testified under oath at depositions that Medtronic sales personnel overtly and directly promoted to them the off-label uses of Infuse in the spine.

Infuse Marketing

CW13 said he was brought into the company to develop a marketing plan; which included:

- Development of a "referral marketing" campaign designed to promote the product for off-label uses via a physician referral network;
- Identifying which surgeons should be targeted as part of Medtronic's off-label campaign and what claims Medtronic would make about the product;
- Development of a "cookie-cutter" CD series that outlined Medtronic's off-label campaign and included information on off-label procedures that was distributed to Medtronic sales representatives.

According to CW13, the referral marketing program involved having surgeons meet with other surgeons as a means of prompting discussion of off-label uses of Infuse among practitioners. CW13 also stated that Medtronic used a physician training program involving cadaver labs as a means to instruct surgeons regarding off-label applications.

Sales Rep Activity

Another confidential witness alleges the following actions by the company:

- Company sponsored physician meetings during which paid consultants made off-label presentations to local physicians.
- Instructions to sales representatives regarding various off-label uses of Infuse, including how much to use with cervical fusions when instructing physicians.
- Directions to sales representatives that they be present during off-label surgeries "to assist and direct and give advice when asked."
- Creation of sales quotas that were described by the CWs as impossible to reach without pushing off-label use.
- Sales representatives' references to data from published literature (presumably funded by Medtronic) when questioned by surgeons, the purpose of which was to provide surgeons with information regarding proffered techniques for off-label procedures and to educate them regarding off-label uses.
- Development of smaller-sized bone graft kits under the guise of selling them for FDA-approved uses, when, in actuality, the company had designed each kit to be used in an off–label cervical fusion surgery.

When questioned by a physician about how to use Infuse off-label, the witness claim sales representatives directed physicians to other surgeons who used the product off-label and also would demonstrate or explain how to do so.

The unnamed CW claims that during quarterly meetings in at least one sales region, a national biologics specialist would attend to explain how to conduct off-label applications of Infuse.

Sales representatives were also allegedly told to instruct physicians to use half the dose of rhBMP-2 during cervical fusion, and, aware of adverse events, instructed the representatives to tell physicians to use steroids to combat potential inflammation. They also directed physicians using the product in cervical spine fusion to throw away up to half of the rhBMP-2 dosage. Physicians were allegedly given a small book containing no reference to Medtronic, which contained information regarding the volume or dosage of rhBMP-2 that should be used for off-label applications of Infuse.

Finally, the CW claims the company instructed sales representatives and others during sales presentations regarding how to "get around" restrictions on off-label promotion.

Off-Label Information

Medtronic has demonstrated its willingness to push these cases to the highest court, so we don't see these Complaints going to a jury anytime soon. However, if the lawsuits are allowed to proceed, Wilcox and Medtronic may set new legal standards for how off-label information can get into the hands of patients and physicians. More information never hurt a patient. ♦

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The Unexpected Rise of Hip Revisions and How to Handle Them // Notes from Sochi Olympics U.S. Team's CMO // Freddie Fu, M.D. Honored With Elizabeth Winston Lanier Award

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

Explosion of Hip Revisions: How to Handle Them There is at least one doctor at Hospital for Special Surgery (HSS) who is righting an increasing number of surgical wrongs. Geoffrey H. Westrich, M.D. is Research Director of the Adult Reconstruction and Joint Replacement Service at HSS. Dr. Westrich has found himself being sought after for hip revisions, doing several per month on patients who fly in from all across the country. He told *OTW*, "I've just published an article in *Arthroplasty* on how to approach recalled hip replacements. The original idea was to allow surgeons to intraoperatively do more customization of hip replacements. We traditionally put in a stem which includes a neck; the only modularity we had before that was with the head. The newer designs allowed a modular neck that allowed surgeons to put in a stem and then put in a neck (with a choice of many different lengths and angles). It also came in neutral, anteverted, or retroverted. This allowed us to place the stem in a way that accommodates the patient's anatomy; it also allows us to intraoperatively select a neck that gave us the best chance of restoring leg length offset."

"The greatest risk is that of dislocation, which can happen if you don't restore offset. At HSS we had four surgeons doing this surgery with a dislocation rate of 1.2%. After modular neck prostheses initially came out, fractures of the metal neck (at the neck-stem junction) were reported."

Gloria Beim, M.D. with the Olypmic Rings

"Manufacturers switched to cobalt chromium, and although testing revealed no fractures, along came a new failure mechanism no one had ever seen—corrosion. This corrosion led to adverse local tissue reactions and elevated cobalt levels in the blood. The latter brings on systemic cobalt toxicity that causes problems like cardiomyopathy, renal problems, hair loss, rashes, etc. I've had patients showing up in my office with their teeth falling out because of this. Unfortunately, the manufacturers sold a lot of these implants before they realized it was a problem. My office constantly get calls from patients and even attorneys whose clients need to have the stem removed. This has greatly increased the amount of revision surgery that I am seeing on a monthly basis, not just for recall hip prostheses, but also for more revisions for other reasons as well."

"To best care for patients with these recalled hips, surgeons should make sure that their patients return to the office for follow up. Many doctors will say, 'Oh, I haven't heard from the patient so everything must be alright.' But this is an insidious process and not everyone has bad pain that brings

them into the office, and if the problem lingers there could be major tissue damage that can result in a very poor outcome in spite of revision surgery. Also, you must always check the blood work to assess metal ion levels. Third, you should use a high resolution metal artifact reduction sequence (MARS), a special MRI for metal suppression to rule out an adverse local tissue reaction. This can show us in the earlier stages if the person has an adverse tissue reaction; at the end stage it will show any destruction of the abductor muscles."

Notes From Sochi Olympics U.S. Team's CMO When Gloria Beim, M.D. founder of Alpine Orthopaedics, Sports Medicine & Regional Hand Center in Crested Butte, Colorado, started college at the age of 14 she could hardly imagine where her life would lead. Recently, Dr. Beim, chief medical officer (CMO) for the U.S. Olympic Team at the Sochi games, found herself staring down a mountain looking out at the Black Sea in the distance. Dr. Beim tells *OTW*, "There are no words to describe how thrilling this experience was. For eight months I studied Russian intensively, something which wasn't required of me, but that paid off immensely. Not only was it wonderful to be able to make those human connections, but it was downright practical. For example, it helped me get athletes get through the doping control stations seamlessly. In the village polyclinics—places set up at every Olympic games—I befriended the doctors, nurses, techs and volunteers with my Russian speaking, which resulted in incredibly good service when getting an athlete through X-ray or other medical services. It was also handy when using the pharmacy as all of the packaging was in Cyrillic letters. If you couldn't read Russian, you would have no idea what medication they just handed you!"

And her Russian got an 'A' from a certain higher up. "One day President Putin made a surprise visit to our facility. I wiggled my way through security and introduced myself to him in Russian. I received a great compliment from him…he said that I spoke 'perfect Russian.'"

"Our sports medicine clinic was specially built for Team USA athletes and staff. We brought our own diagnostic tools, including diagnostic ultrasound. We had a pharmacy, great recovery services, massage, physical therapy, sports chiropractors, etc. That way, when the athletes would walk into the sports medicine clinic they would feel right at home. The Russians set up clinics—

known as a 'polyclinic'—because a lot of countries don't bring along their own medical services and they did supply radiology equipment in addition to specialists in many fields including cardiology, ENT, dentistry, etc. The challenges are that the language is different, as is the practice of medicine. If we needed a CT/MRI then we took the athlete to a polyclinic, but we read the films and treated our own athletes."

"We treated ACL tears, shoulder dislocations, lacerations from ice hockey, and much more. Here is a really important message to my colleagues. When I was the CMO for the Pan American games in 2011 I got my first taste of a diagnostic musculoskeletal ultrasound. Although I had never been a big believer in this tool, I was blown away by its utility. The minute I returned to the U.S. I bought a machine, trained aggressively, and three years later I can't practice imagine practicing without one. It's much less expensive than an MRI, patients love it, and you have immediate results…three minutes! These are not just for traveling orthopedic surgeons."

"Being the chief medical officer for the Olympics was definitely a life changing and amazing experience. I also had the unique fortune of marching in the Opening Ceremonies. What an honor to be part of such energy and excitement."

Freddie Fu, M.D. Receives Elizabeth Winston Lanier Award Freddie Fu, M.D. has received the Elizabeth Winston Lanier Award for his career contribution to anterior cruciate ligament (ACL) reconstruction and advances in patient care. This honor comes from the Kappa Delta Society along with the Orthopaedic Research and Education Foundation, and was presented to Dr. Fu in New Orleans at the 2014 Annual Meeting of the American Academy of Orthopaedic Surgeons.

Dr. Fu, the David Silver Professor and Chairman of the University of Pittsburgh Department of Orthopaedic Surgery and founder of the UPMC Center for Sports Medicine, also will receive honors in Europe and Asia over the next four months. This includes an award being bestowed in Hiroshima, Japan, in July from the Japanese Orthopaedic Society of Knee, Arthroscopy and Sports Medicine (JOSKAS). Dr. Fu will be only the fourth surgeon—and second from the Western Hemisphere—recognized with the Masaki Watanabe Award for international achievement in arthroscopic surgery.

NASS Launches New Career Center NASS has launched a targeted career center where job seekers can home in on

spine-specific resources. Katie Szymaksi, sr. manager of Membership Services, told *OTW*, "In our ongoing attempts to help members further their spine careers, we realized that we needed greater attention to the area of practice management resources. Additionally, in the past several years, the online 'career center' market has changed drastically. Individuals are moving from searching for new positions through sites like Monster and are placing a greater emphasis on LinkedIn and other non-traditional sites to look for career opportunities. Through the new NASS Career Center, we are able to not only provide traditional job board functions, but are also able to capitalize on those newer social media resources; the new NASS Career Center is able to integrate on multiple formats, ensuring that our members and potential employers are able to connect."

"In mid-February, we launched a new website at www.spine.org which includes several features that will allow members to more easily find the information that they're looking for—including resources for career enhancement. That being said, it can be a challenge to launch a new website at the same time as we are looking to launch this new resource. Many of the features that are included in the new NASS Career Center have not yet been rolled out, including widgets on our social media pages and NASS home page as well as others."

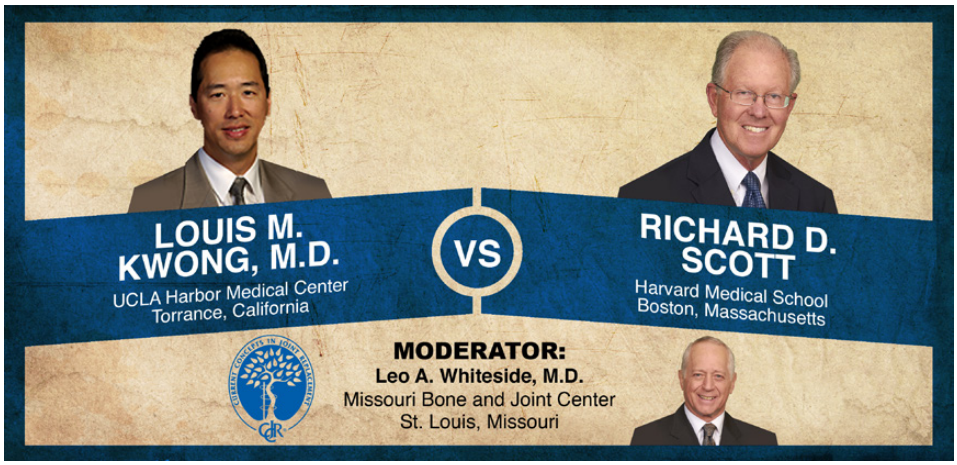
"Not only will the NASS Career Center be the go-to place for spine care providers and employers to connect exclusively about career opportunities in spine, but the site also goes beyond the "Monster" job search format to ensure that our members can both passively and actively keep an eye on job opportunities that they may be interested in. NASS Career Center users can also add their CV to a resume bank that allows them to anonymously be contacted by employers. Members also have exclusive access to new jobs for three days after posting, giving them an edge from other job seekers."

"Another key feature to the new NASS Career Center, which is provided as a partnership between NASS and JobTarget, is a career fair that will be held in conjunction with our Annual Meeting in San Francisco this November." ♦

Cementless Fixation: Kwong v. Scott

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

"Cementless fixation is an easy surgery with excellent intermediate to long term clinical performance," says Louis Kwong. Richard Scott counters, "Cemented TKA [total knee arthroplasty] is state of the art and has a reoperation rate of 0.5% for the first 15 years. Cementless hasn't yet been proven to be as reliable as cemented fixation."



Current Concepts in Joint Replacement/RRY Photo Creation

This week's Orthopaedic Crossfire® debate is "Cementless Fixation: A Contemporary Durable Solution." For the proposition is Louis M. Kwong, M.D. from UCLA Harbor Medical Center in California; against the proposition is Richard D. Scott from Harvard Medical School in Boston. Moderating is Leo A. Whiteside, M.D. of the Missouri Bone and Joint Center in St. Louis.

Dr. Kwong: "Cementless TKA was first explored 30 years ago with the primary goals of simplifying the operation, reducing the number of interfaces for failure, increasing the longevity of the implant, and addressing the needs of the younger, active population. But the early failures of first generation knee implants were plagued by aseptic loosening of the tibial and patellar components for several reasons: poor implant design, material failure, inferior polyethylene, thin patellar poly leading to high susceptibility to edge wear and osteolysis."

"Nevertheless, excellent survival in intermediate to long term follow-up has been seen in a number of series. Hoffman reported 93.4% survival at 12 years; Whiteside found 98.6% survival at 15-18 years (no cementless patella). And in Ritter's cementless series at 10 years there was 100% femoral component survival, 97.4% tibial component survival, but there was a patellar failure rate of 16.4% pointing to the continued need for improvement in this area."

"Substantial improvements have been made in both material composition and implant design. I think one of the most important biomaterials introduced in orthopedics in the last 30 years is porous tantalum. It has a reticulated trabecular geometry, an open cellular structure of 100% interconnecting pores. Each pore is shaped like a dodecahedron, a 12 sided figure with each side shaped like a pentagon. Each pore is 550 microns in size, and up to 85% of the material is porous by volume. Compared to other commonly used biomaterials such as smooth titanium, big and small sutured beads and fiber metal, porous tantalum has the highest surface friction against bone, thus imparting tremendous initial stability as a prerequisite for long term biologic fixation."

"The first total knee implant made with this material was a monoblock porous tantalum tibia, a single piece prosthesis with direct compression molded polyethylene into the porous tantalum. It achieves fixation with these two hexagonal pegs implanted into drill holes that are dimensionally smaller in size than the pegs themselves. Followed by this was a monoblock patellar component, also with the same geometry of direct compression molding poly into the porous tantalum, using a single hexagonal peg for interference fit."

"How have these implants performed? Mayo Clinic just reported their five year experience with the cementless tibia, and found no difference in survival against the cemented implant. There was a 3.5% overall reoperation rate and no revisions of the monoblock cementless tibia for aseptic loosening. In our own series at Harbor-UCLA we had 115 patients and 11 year follow-up of all cementless with an average BMI [body mass index] of 32.5. They all had cementless monoblock porous tantalum

tibia, a monoblock porous tantalum patella, and a cobalt-chromium fiber mesh femur. This was a non-selected series all done by orthopedic residents. We had 95.7% implant survival; four were revised for periprosthetic infection; one was revised for femoral component mismatch. There was one death due to pulmonary embolism, with no cases of osteolysis, no X-ray evidence of loosening, no revisions for aseptic loosening; patient satisfaction was 91%."

"The advantages of cementless TKA with porous tantalum are that you eliminate the concerns that exist with PMMA (polymethylmethacrylate) such as monomer induced hypotension, thermal necrosis of bone, third body wear from retained cement debris. You don't have the cost of cement, the mixing system, the cartridge for the cement gun, or lavage and irrigation. Also, there is an 18 minute reduction in OR time, a $3,000 reduction in hospital bill; at the end of the day of arthroplasty we typically save 1-1.5 hours, allowing us either to do an additional surgery or to finish the day early. There is also a savings in nursing and OR staff overtime. There is a reduction in anesthesia, a potential decrease in infection risk, a potential decrease in the risk of venous thromboembolism, and a decrease in overall morbidity and mortality."

"This is an easy surgery with excellent intermediate to long term clinical performance. Cementless fixation is the future and the future is now. Thank you."

Dr. Scott: "You have to admit that cemented TKA is the gold standard throughout most of the world. Long term survivorship is high, reoperation rates for any reason for the first 20 years run approximately .5-1% per year. Out of my own last roughly 4,500 knees I've had 244 reoperations. At an average of 14 year follow-up 5.5% had been re-operated for a rate of 0.4% per year. Half of the reoperations were for poly wear issues; most were implanted in 1995 and I hope most of those issues have been resolved."

"I have had experience with cementless patellar fixation. In the old days it required metal-backing with thinner poly with possible wear through. My personal incidence with one design is a 10% wear through rate at minimum 25 year follow up. Some metal-backed patellar designs (such as mobile bearing) are less vulnerable than others."

"I'm now going to shift a bit, and discuss hybrid fixation where there is a cementless femur, a cemented tibia—with or without patellar resurfacing. There are potential advantages of not cementing

the femoral component. There's the possibility of bone stock preservation should component removal be necessary. It's important, however, that fixation lugs are non-porous; otherwise extraction could be difficult. Also, there's the avoidance of possible cement debris from the femoral fixation. There's a shorter operating time should two cementings be utilized, and there is easy access to the back of the just-cemented tibial component (to check for extruded cement). With this procedure you have superior zone 4 integration sealing that interface from wear debris."

"We've studied zone 4 radiolucency in 17 paired cemented and cementless total knees; we saw 70% zone 4 radiolucency in the cemented femurs. These were all fluoroscopically controlled perfect laterals. There was 0% zone 4 radiolucency in the cementless femur. I now try to improve zone 4 interface when cementing by using what I call the smear technique. I pack and smear cement into the posterior condyles, put some on the back of the femoral component as well, and I cement with a trial rather than a real insert because I run the risk of snow plowing cement to the back of the knee with this process."

"The disadvantages of cementless femoral components are that more precise bone cuts are essential and the prosthesis is more expensive. Regarding bone cuts rigid primary fixation of the femoral trial is the key to a successful outcome. As for cementless femoral loosening, in my experience it is relatively rare. I've done about 1,200 of these with 1-26 year follow up and have had three loosenings for an incidence of .25%."

"Ancillary screw fixation is helpful in some designs, but it introduces a portal for wear debris and subsequent osteolysis. The newer trabecular metals may have promise, but follow-up is relatively short. Thank you."

Moderator Whiteside: "Louis?"

Dr. Kwong: "I agree with Dr. Scott in that the long term performance of the new cementless designs isn't proven. The results we have are 5-7 years and they are excellent. And while there's no question that Dr. Scott is an expert model of an arthroplasty surgeon when we look at a large market like the U.S., 75% of all arthroplasty is performed by a surgeon who does less than one total joint per month. So we look at the general orthopedic surgeon as performing the lion's share of the arthroplasty and how reproducible that is. The new designs of direct compression molded poly have the best long term performance of any poly in knee. They incorporate into the tibial and patellar designs a composition where the prosthesis is isoelastic with bone, allowing good physiologic transfer. We often look at the first two years, whether there are catastrophic failures that point to whether there was a problem with the design. We haven't seen that with the new generation type of prostheses that incorporate materials like porous tantalum."

Dr. Scott: "I have done about 40 cementless tibias. With some I thought that I should put some bone slurry to even out the cut if it wasn't perfect on the tibia. I don't think that's necessary on the femur. How do you both feel about that?"

Dr. Kwong: "Excellent point. The fact is that we want to achieve optimum contact on the interface between the cementless surface and the bone. So if it's not a perfectly flat cut I would recut that with minimal bone removal. I wouldn't advocate for putting any type of bone slurry in order to not interpose dead bone between the viable recipient bed and the porous surface."

Moderator Whiteside: "Dick, you seem to be happy with cementless fixation of the femoral component. If you had a tibial component that gave you reliable cementless fixation would you prefer that over cement?"

Dr. Scott: "I would be interested in using it then assessing the long-term results. Some of these systems…"

Moderator Whiteside: "Wait, let me go back to being the moderator! Where did you get this term, 'gold standard?' Did you major in economics?"

Dr. Scott: "I think platinum standard is better."

Moderator Whiteside: "Alright, alright! Do you ever see loosening between the cement and the metal?"

Dr. Scott: "I think that is design-related and technique-related…the actual femoral component and its surface… whether is has recesses or dovetails. I do see that."

Moderator Whiteside: "Look for that when you have a knee that keeps swelling and hurting, but the bone-cement interface looks good. Louis, do you ever do cemented knees anymore?"

Dr. Kwong: "Yes. When the bone quality is poor, when we have our patients with inflammatory types of arthritis where we're concerned about the compromised biologic potential."

Moderator Whiteside: "Thank you." ♦

Please visit www.CCJR.com to register for the 2014 CCJR Spring Meeting, May 18 - 21 in Las Vegas, Nevada.

COMPANY

DePuy Synthes Adds Features to Attune Knee at AAOS

DePuy Synthes Companies announced two new improvements to the company's Attune Knee System on March 12, 2014 at the annual American Academy of Orthopaedic Surgeons meeting in New Orleans, Louisiana.

After introducing the Attune system a year ago and implanting more than 31,000 of the devices during that time, the company added a rotating platform knee and anatomic patella. Both additions have received PMA Supplemental Approval from the FDA.

According to the company, the rotating platform design increases the level of conformity to provide stability while delivering freedom of mobility. In addition, the rotating platform design gives the tibial insert the freedom to self-align and track with the femoral component throughout the range of motion, allowing surgeons the ability to position the rotating platform tibial base on the proximal tibia for maximum bony coverage.

The knee, says the company, builds on the LCS Complete Knee System and the SIGMA Rotating Platform Knee System. More than one million rotating platform knees have been provided for surgeons and patients around the world.

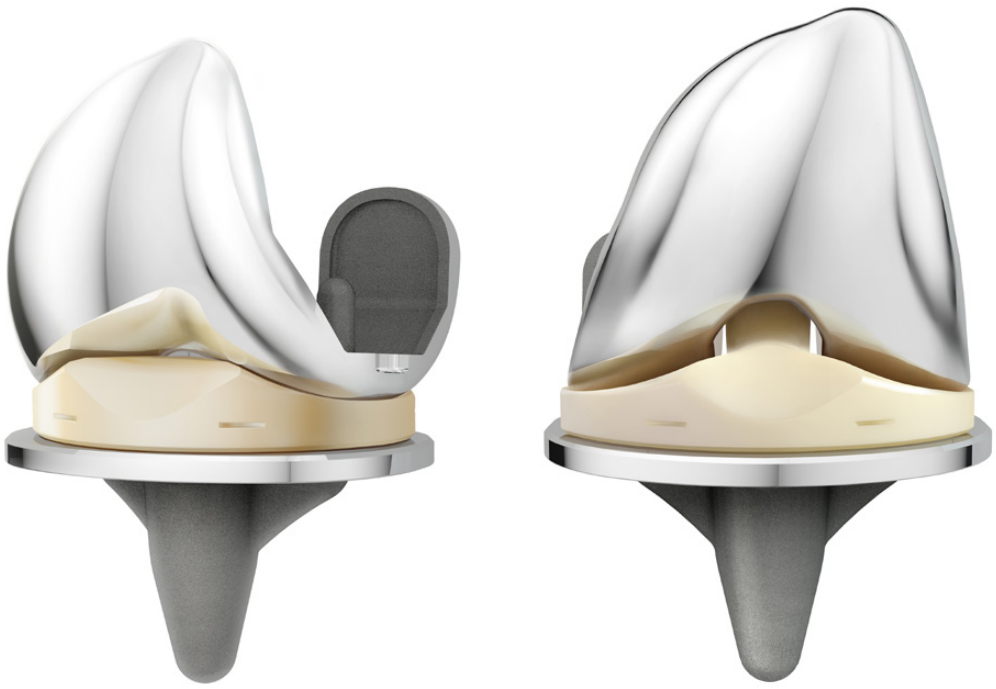
The anatomic patella works with the Attune knee femoral components, is unique to the company and is compatible with both the Attune fixed bearing and rotating platform knees. The patella, according to the company, is designed to have more natural sagittal plane kinematics than traditional dome style patella components. The more natural kinematics can reduce soft tissue interaction with the femoral component and thereby help prevent soft tissue irritation. Also, the unique kinematics of the anatomic patella can increase quadriceps efficiency in deep flexion, allowing the knee to more easily flex and extend.

For instance, studies show that between 10-20% of knee replacement patients are not completely satisfied with their knee replacement. A major contributing factor to this is anterior knee pain in the area of the patella. The anatomic patella was created to help address this need, and is designed to wrap around the knee in a more natural way and improve patella tracking.

Company officials told us that an early performance registry is showing "excellent" results. Multicenter studies are also being performed, but have not yet been completed. Early results, said the officials, are showing an improved range of motion and excellent stability.

Hannah McEwen, Ph.D., the company's joint reconstruction director for knee product development, said the company was looking to address an unmet patient need. "The introduction of the knee and patella bring new options for patient care."

—*WE (March 12, 2014)*



DePuy Synthes Companies

Millstone Medical Launches Oracle Application

Millstone Medical Outsourcing, LLC is excited to announce that the company has successfully launched and gone live with version 12.1.3 of Oracle's E-Business Suite application. As of Monday, February 24, Millstone has taken numerous clients aboard its new ERP (enterprise resource planning) system consisting of inventory and distribution modules as well as a customized portal for customer service, field reps, and ordering processes. With Oracle's capabilities, Millstone has developed a technology and hardware infrastructure that enhances and simplifies client interactions and maximizes online customer visibility.

To further enhance all aspects of its ERP system, Millstone has also contracted with cloud-based data center, Rackspace, to host all of its Oracle applications and provide high availability backup and redundancy. This combination of services delivers state of the art hardware and software that provides customers a high degree of assurance that orders will be fulfilled with no interruptions and product will be delivered with high reliability to hospitals and other providers.

"Oracle and Rackspace have provided a complete software solution for our business," said Brad Schwarz, vice president of operations at Millstone Medical, in the February 27, 2014 news release. "We are operating an ERP system built on advanced technology and security. Our new system streamlines capabilities and provides data access that our customers can't access on their own. We are very excited to bring all customers on board."

Tim Lucenti, director of process engineering, told *OTW,* "This system gives providers and sales representatives 24/7 access to initiate orders and see available inventory via wireless devices and other outlets. It allows us to efficiently fulfill orders at midnight that will be used for surgery that same day."

—EH (March 12, 2014)

Millstone Medical Outsourcing, LLC

Bacterin Secures Loan

Bacterin International Holdings, Inc. has secured access to an additional $4 million loan from ROS Acquisition Offshore (ROS).

Black Enterprise

The company entered into the loan agreement on March 6, 2014 and will pay an interest rate of LIBOR (London Interbank Offered Rates) plus 12.13%, subject to a LIBOR floor rate of 1%. Bacterin also agreed previously to pay a royalty of 1.75% on the first $45,000,000 of annual net sales, plus 1.0% of annual net sales in excess of $45,000,000. As additional consideration for ROS making the $4 million available, the company agreed to issue 1,500,000 shares of common stock to an affiliate of ROS.

Bacterin has the right to repurchase the loan and royalty interest at amounts to be determined based on the date of repurchase and the amount of prior principal, interest and royalty payments. The company plans to use the proceeds for working capital and general corporate purposes.

Bacterin Products

The company, located in Belgrade, Montana, develops bioactive coatings for medical applications and bone graft

material, processes and markets biologic allografts for transplantation. Bacterin's biologic scaffolds, OsteoSponge, OsteoSponge SC and OsteoWrap, are made from demineralized bone that is malleable and flexible, which enables efficient and precise handling. It also markets BacFast and OsteoLock, which are used in spine surgery, designed to minimize graft back-out, and increase osteoinductivity. Bacterin's latest allograft, OsteoSelect DBM Putty is distributed as a sterile product, with osteoinductivity testing completed on every lot after terminal sterilization.

Bacterin's Medical Device and Coatings Division focuses on the development of bioactive coating technologies for implantable devices. Its core competency is anti-microbial coatings designed to reduce potential infections associated with implants. This division also manages surgical kits necessary to support implantation of products processed by Bacterin's Biologics Division. Bacterin operates a 32,000 sq. ft., state-of-the-art, fully compliant and FDA registered facility, equipped with five "Class 100" clean rooms.

—WE (March 11, 2014)

Benvenue Medical Celebrating Results of Kiva Study

Benvenue Medical, Inc. has announced results of an independent, prospective, randomized study which found that the company's Kiva VCF Treatment System was as effective as balloon kyphoplasty (BKP) in reducing pain associated with osteolytic vertebral body metastases. The Kiva System also resulted in no extravasation (cement leakage) while BKP, the current standard of care, showed a nearly 10% leakage rate. The results of the first head-to-head study of Kiva and BKP for this patient population were published online and in the February 15 edition of the peer-reviewed journal *Spine*.

"Cement leakage is a common complication of balloon-assisted vertebral augmentation and can be disastrous for patients with bone metastases when it leaks into the spinal canal," said Panagiotis Korovessis, M.D., Ph.D., in the February 25, 2014 news release. Dr. Korovessis is Chief of the Department of Orthopaedic Surgery at General Hospital "Agios Andreas" in Patras, Greece, and lead author of the study. "This is the first study to show that the Kiva System is an effective alternative to BKP in providing spinal pain relief for these patients—and without the complication of cement leakage."

The study, titled "Is Kiva Implant Advantageous to Balloon Kyphoplasty in Treating Osteolytic Metastasis to the Spine? Comparison of 2 Percutaneous Minimal Invasive Spine Techniques," included 47 patients with 84 vertebral body osteolyses. Outcome measurements were vertebral body height, segmental kyphotic angle, extravasation rates, pain, function and quality of life. Results of the study include:

- Kiva and BKP provided equally significant spinal pain relief one month postoperatively, as measured by the Visual Analogue Scale and Oswestry Disability Index ($P<0.001$).
- No patients in the Kiva group experienced cement leakage, compared with 9.3 % in the BKP group.
- Kiva and BKP showed a tendency for restoration of anterior and posterior vertebral body height and kyphotic Gardner angle; only Kiva restored middle vertebral body height.
- Both Kiva and BKP safely augmented painful thoracic and lumbar vertebral osteolytic metastases; only Kiva additionally reinforced sacral metastases.

Asked where the company hopes to be in a year with Kiva, CEO Robert K. Weigle told *OTW*, "With our full commercial launch happening this month, it's hard to think about a year from now. What I can tell you is that the reception among physicians we've been talking to has been very positive and there is substantial interest in Kiva as a new, implant-based approach to vertebral augmentation."

"We look forward to presenting the results from KAST, our FDA-approved pivotal trial, at the Society for Interventional Radiology on March 26. In addition to KAST, this recently published study in *Spine* adds to the growing breadth of independent clinical data that demonstrates Kiva's effectiveness in treating VCFs, whether the fracture is caused by cancer, osteoporosis or trauma."

—EH (March 12, 2014)

Benvenue Medical, Inc.

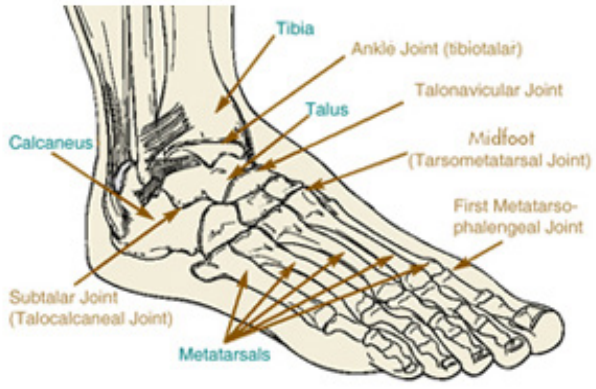
LEGAL

Arthrosurface Toe Motion Preservation System Cleared by FDA

There will be fewer toe fusions as Arthrosurface, Inc., founded in 2002, has received FDA clearance for its ToeMotion Total Toe Restoration System.

The company announcement on March 7, 2014, said the device will be launched at the AAOS (American Academy of Orthopaedic Surgeons) in New Orleans the week of March 10th.

The system consists of a metatarsal-based HemiCAP implant and a new inlay metal baseplate with a poly insert for the phalangeal side of the joint. Both sides of the metatarsal joint, according to the company, will now benefit from the tapered fixation post design which has been successfully used for almost 10 years. "The system provides proven fixation, while the inlay implants preserve bone. Because it is implanted by milling instead of by using saw cuts, the ToeMotion system avoids resecting the intrinsic tissues that provide stability to the toe," stated the company press release.



American Academy of Orthopaedic Surgeons

Thomas San Giovanni, M.D., from the University of Miami and the system's designer, said, "For many years we have been using the metatarsal-based HemiCAP with great success. However, there are patients that require an implant on both sides of the joint, rather than a fusion, so now we can offer a motion preserving option to those patients looking to maintain an active lifestyle. In Florida, our patients are active and outdoors all year long so they are looking for an active alternative to fusion. Never moving their toe again is not a very appealing option to them, so this is why I have been working with Arthrosurface to design a system that would be minimally invasive, stable and allow my patients to maintain their motion."

Steve Ek, CEO and co-founder of Arthrosurface stated "the extremities market is providing an excellent opportunity for growth over the next several years. As such, we are targeting to launch another five extremity products along with the new ToeMotion system. Our platform technology for rock-solid immediate fixation and inlay arthroplasty has been proven to work on many different joints. But, what is really exciting is how well suited inlay arthroplasty is for the extremity joints. These joints are inherently smaller, very mobile and traditionally have not done very well with larger more invasive implants that require a lot of bone removal. Smaller implants that restore anatomy and take away very little bone is the wave of the future."

—*WE (March 11, 2014)*

Wright and FDA Reach Procedure Agreement on PMA

Wright Medical Group, Inc.'s road for reaching FDA approval for its PMA (premarket application) for Augment Bone Graft has been rocky and highlighted by a contentious FDA orthopedic panel meeting in 2011.

On August 8, 2013, the company received an 18-page "not approvable" letter from the FDA for the product. The FDA said it was "concerned that the population enrolled was predominately low risk and, therefore, may not have warranted the use of either autograft or Augment Bone Graft."

But on March 10, 2014, the company announced it has reached an agreement with the FDA's Office of Device Evaluation (ODE) under which ODE will accept a further amendment to the PMA for the bone graft in lieu of proceeding with the Dispute Resolution Panel (DRP) that was scheduled for the week of May 19, 2014. The agreement with ODE remains subject to final approval by the FDA appeal authority. That approval is expected shortly.

The PMA amendment, which the company expects to submit on or about March 31, 2014, will consist of analyses of pre-existing radiographic films of clinical study patients at pre-operative and post-operative time points. ODE, according to the company announcement, has committed to an expeditious review of the PMA amendment and agreed to issue a determination on whether the PMA is approvable no later than 180 days after submission of the PMA amendment. The company intends to renew the DRP process if the PMA amendment fails to result in a reversal of ODE's previous not approvability determination.

Robert Palmisano, Wright's president and CEO, said while the development is cause for somewhat greater optimism than the company has thus far had reason to embrace, "It is important to reiterate that the parties' positions are still far apart and there is no guarantee this PMA amendment will result in an approval for Augment Bone Graft. Nevertheless, we are pleased we were able to work collaboratively with FDA to identify a path forward that does not require new clinical studies to get to the next approvability determination."

The agency had said the company would have to perform a new clinical study that evaluates the product as substitute for autograft in hindfoot and ankle fusion procedures in a well-defined high risk target population. The agency specifically had concerns about the "the patient population studied in the clinical study, the amount of graft material implanted, and the uncertainty as to whether any graft material would be needed or if the use of no graft material in a fusion procedure of the hindfoot and ankle in the population studied would have achieved similar results."

Contentious FDA Panel Meeting

At an FDA panel meeting in May 2011, panel member Brent Blumenstein, Ph.D., a statistical consultant said, "The [clinical] trial has no meaning." Augment was then owned by BioMimetic Therapeutics Inc. However, the final panel vote was 12-6 in favor of approving Augment as a safe treatment for ankle surgery after a rare public rebuke by panel members of FDA staff for failing to present safety evidence for the company's dental product. Panel members said they thought the agency came to the meeting with an agenda.

The panel then went on to vote 10-8 that Augment for ankle fusion surgery was effective and, finally, voted 10-8 that the product when used by surgeons in hindfoot and ankle surgery, delivered benefits that outweighed the risks.

Wright paid $380 million for BioMimetic in 2013.

Wright Medical Group, Inc. and FDA and RRY Publications

—WE (March 11, 2014)

BIOLOGICS

Brits Grow Ear From Fat

A team of doctors at Great Ormond Hospital in London are making serious plans to reconstruct an ear with stem cells taken from their patient's fat. They have already succeeded in growing cartilage in their laboratory and plan to proceed using a technique published in the journal *Nanomedicine*.

According to James Gallagher, writing for the *BBC Health News*, the doctors want to treat conditions like microtia, a situation where an ear fails to develop properly, is malformed or is missing altogether.

Microtia is presently treated by physicians taking cartilage from a child's ribs, sculpting it to make it resemble an ear and implanting it back into the child. The method is far from satisfactory as it requires multiple operations, leaves permanent scarring on the chest and the rib cartilage is said to never fully recover.

The team planning to reconstruct an ear using stem cells intends to take a tiny sample of fat from the child and extract stem cells from it. They plan to place an ear-shaped scaffold in the stem cell mixture so the cells could take on the desired shape and structure. They plan to use chemicals to persuade the stem cells to transform into cartilage cells. The researchers report that they have been able to create the cartilage in the scaffold, but want to do more safety testing before they use the technique on patients.

One of the researchers, Patrizia Ferretti, M.D., told the BBC: "It is really exciting to have the sort of cells that are not tumourogenic, which can go back into the same patient so we don't have the problem of immunosuppression and can do the job you want them to do. It would be the Holy Grail to do this procedure through a single surgery, so decreasing enormously the stress for the children and having a structure that hopefully will be growing as the child grows."

Martin Birchall, M.D. is a surgeon at University College, London, who was involved in the first operations to give patients lab-grown windpipes. He said of the ear project, "If you had something that was truly regenerative, that would be transformative."

—BY (March 11, 2014)

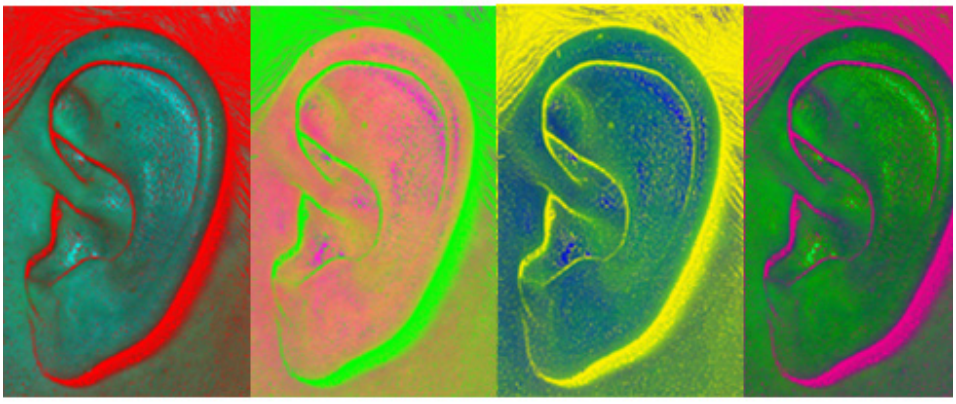
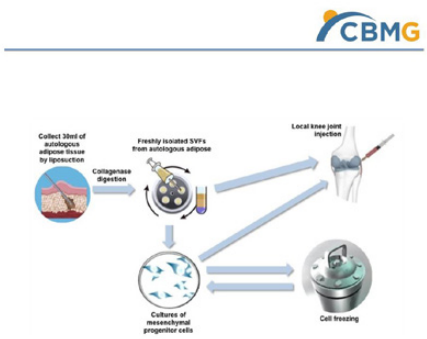


Image created by RRY Publications, LLC

Promising New Stem Cell Data for Osteoarthritis

An updated analysis of a Phase 1/11a clinical trial of adipose-derived mesenchymal precursor cell therapy for knee osteoarthritis (KOA) showed no serious adverse effects and some



Courtesy of Cellular Biomedicine Group

encouraging results. Participants experienced significantly reduced knee pain, improved knee mobility and prolonged walking distance.

Cellular Biomedicine Group, Inc. presented the results of its trial at the New York Stem Cell Summit in February. Shanghai's Renji Hospital, a tertiary hospital affiliated with Shanghai Jiao Tong University School of Medicine, conducted the trial. Researchers observed a reduction of bone lesions in some patients while MRI examination revealed an increase in cartilage thickness as early as three months after the therapy.

Data on three patients who completed the six-month follow-up confirmed the three-month findings. A full analysis of the six-month follow-up for all patients in the trial is still ongoing.

Wei Cao, PhD, BM, CEO of Cellular Biomedicine Group, Inc. said, "We

are very excited with the preliminary analysis of the trial. As far as we know this may be the first evidence that adipose derived stem cells can regenerate human cartilage in three months. Our preliminary conclusion from the three-month follow-up of the Phase I/IIa clinical trial is that ReJoin cell therapy for KOA patients is safe."

Cao noted that there are approximately 57 million people in China suffering from knee osteoarthritis. As drug-based methods of management are ineffective, life quality of KOA patients is compromised, and many patients with this disease will degenerate to the point of requiring invasive artificial joint replacement surgery.

—BY (March 10, 2014)

EXTREMITIES

Elite Athletes Depressed, Tired as They Age

An Indiana University (IU) study found that elite college athletes aren't in the greatest shape as they grow older. The team of researchers found that these previously vibrant athletes often face limitations to their day-to-day activities in middle age that could be a result of injuries during their athletic career.

Wikimedia Commons and Johnmaxmena

Lead investigator Janet Simon, a doctoral candidate in the IU School of Public Health-Bloomington's Department of Kinesiology, said researchers have long known that compared to non-athletes, college athletes experience more severe injuries—and long-term effects of those injuries. She was surprised, however, with her findings that the former elite athletes also scored worse on depression, fatigue and sleep scales. Her study—which focused on Division I athletes, considered the most competitive college athletes—was published in the *American Journal of Sports Medicine*.

"Division I athletes may sacrifice their future health-related quality of life for their brief athletic career in college," Simon said in the March 3, 2014 news release. "Also, when comparing former Division I athletes, non-athletes who were physically active in college and the general U.S. population, it appears that, in rank order of the three groups, non-athletes who were recreationally active in college had better health-related quality of life scores, followed by the general U.S. population. This may be because former Division I athletes sustain more injuries and possibly more severe injuries due to the rigor of their sport."

Here are more findings from the study, which analyzed questionnaires completed by 232 male and female former Division I athletes and 225 male and female non-collegiate athletes. The study participants were between 40 and 65 years old, and their scores were compared to a representative sample of the U.S. population in the same age range:

- Former Division I athletes were more than twice as likely as non-athletes to report physical activity limitations to daily activities and exercise.
- 67% of the athletes reported sustaining a major injury and 50% reported chronic injuries, compared to 28% and 26%, respectively, for non-athletes.
- 70% of athletes reported practicing or performing with an injury, compared to 33% on non-athletes.
- 40% of athletes reported being diagnosed with osteoarthritis after college compared to 24% of the non-athletes. Osteoarthritis has been linked to previous joint injuries.

Simon said athletes have access to a range of expertise during their college years, including strength and conditioning coaches and nutritionists, but they often find themselves on their own after graduating.

"Many of the Division I sports are not lifelong sports, so it is important for the athletes to find sports and activities that can keep them active as they age," Simon said. "The most important thing is to stay active. You may have been a former athlete, but unless you stay active your whole life, you may be decreasing your quality of life."

—EH (March 11, 2014)

TRAUMA

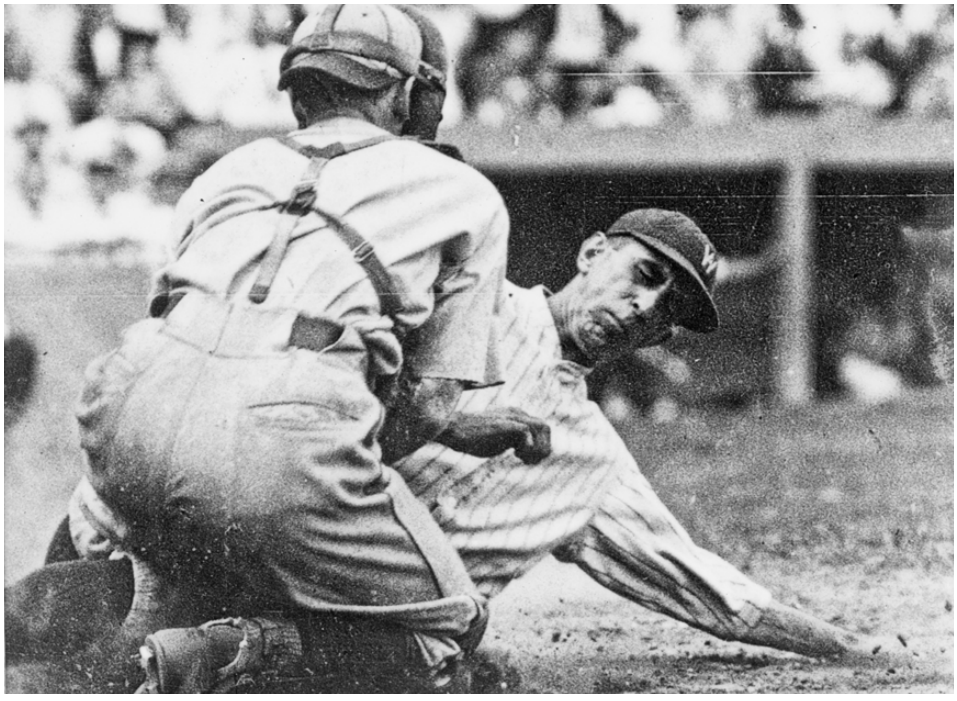
New Rules Protects Player's Heads

OTW recently reported on the hazards to the heads of runners trying to reach home plate in a baseball game and those of the catchers who try to block them. This week officials of Major League Baseball and the Major League Baseball Players Association have agreed on changing the rules. The change, while deemed "experimental," will take effect in the upcoming 2014 season. The rule reads, in part:

> "A runner attempting to score may not deviate from his direct pathway to the plate in order to initiate contact with the catcher (or other player covering home plate). If, in the judgment of the umpire, a runner attempting to score initiates contact with the catcher (or other player covering home plate) in such a manner, the umpire shall declare the runner out, even if the player covering home plate loses possession of the ball.
>
> "Unless the catcher is in possession of the ball, the catcher cannot block the pathway of a runner as he is attempting to score. If, in the judgment of the umpire, the catcher, without possession of the ball, blocks the pathway of the runner, the umpire shall call or signal the runner safe."

Not every player is in agreement with the change. *Ideastream*, in its report on the rule change, quoted Pete Rose who is reported to have said, "What's the game coming to? Evidently the guys making all these rules never played the game of baseball." The new rule is intended to cut the risk of injury, particularly concussions, taking place as a result of collisions at home plate.

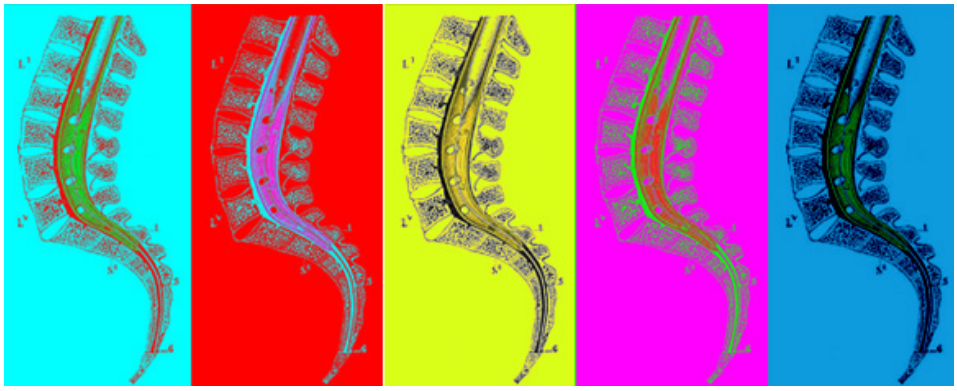
—BY (March 10, 2014)



Wikimedia Commons and David Shapinsky

SPINE

1,000 Spines Tested on VMA System



Wikimedia Commons and Grays' Anatomy

Physicians have tested over 1,000 patients with the Vertebral Motion Analysis (VMA) system since its limited commercial launch in 2013. Produced by Ortho Kinematics, Inc., the VMA is an automated, diagnostic alternative to the current test for assessing spinal instability, according to a company press release.

Company officials define spinal instability as a condition that can cause severe back and neck pain. They say that it is the number one most common primary diagnosis driving the 500,000 or more spine fusion surgeries done in the U.S. each year and that clinical studies have shown that this instability may be missed by the older, current test.

Ortho Kinematics CEO Paul Gunnoe said, "Spine surgeons are talking with their actions and prescribing the VMA. They recognize the value of the diagnostic insights they receive from the VMA."

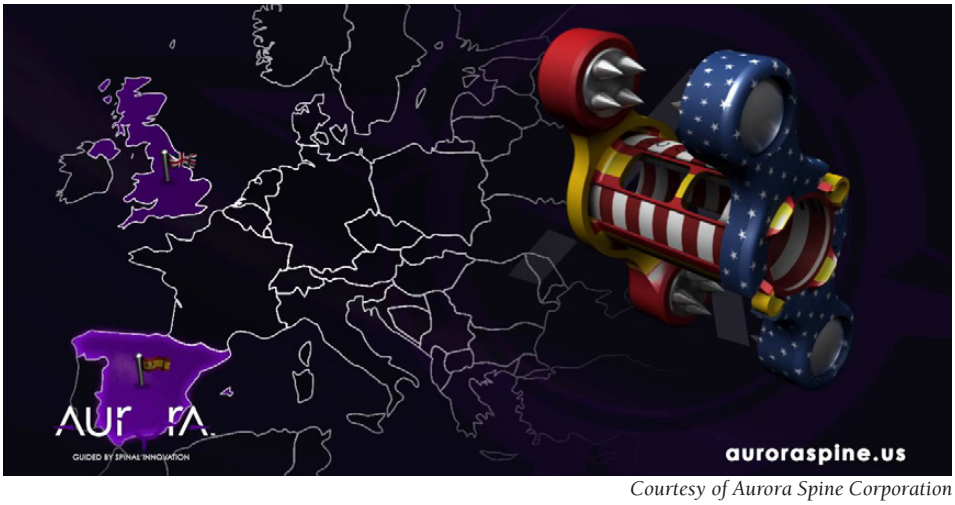
Gunnoe added that the company is focused on rolling out the VMA as quickly as possible so that all patients and surgeons have access to this technology. Ortho Kinematics, a privately held diagnostic technology company focused on spine imaging, is located in Austin, Texas.

—BY (March 11, 2014)

Aurora Spine ZIPS Into Britain

The first surgical implant in the United Kingdom of Aurora Spine Corporation's Zip Ultra, a minimally invasive interspinous device, took place in late February. Stuart James, M.D, performed the surgery at the University Hospital Llandough, a part of the Cardiff and Vale University Health Board.

"The ZIP MIS implant is very well designed. It is both stable and secure. Implanting the device was simple, easy and safe," said James who has completed a recognized spine fellowship in Bristol, UK, where he has gained extensive experience in all aspects of spinal disease and spinal conditions. The company's news release reports that James 'experience ranges from trauma and tumor work to adult and pediatric complex deformity of the spine. "I will be expanding my use of the product as I believe it has multiple spine fusion indications," he said.



Courtesy of Aurora Spine Corporation

James Trent Northcutt, Aurora Spine's president and CEO said, "We are absolutely thrilled that Aurora now offers our MIS portfolio in the United Kingdom, including the ZIP MIS Interspinous System. We believe that the ZIP device will change spine surgery in the U.S. with a true minimally invasive approach designed to achieve reproducible, superior patient outcomes."

Aurora Spine is an early stage company focused on bringing new solutions to the spinal implant market.

—BY (March 10, 2014)

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