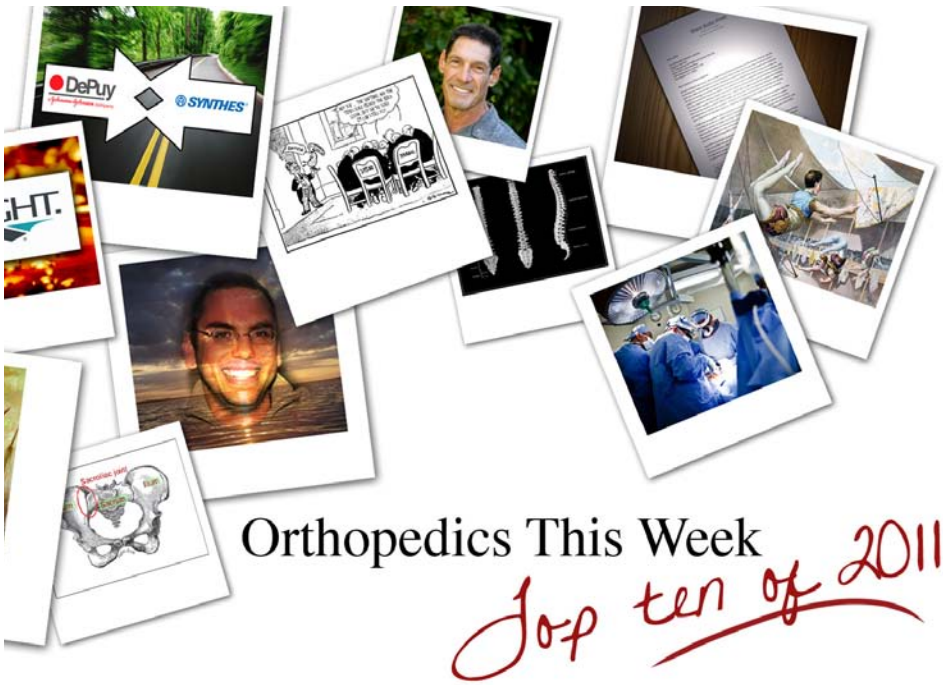
VOLUME 8, ISSUE 1 | JANUARY 3, 2012

Orthopedics This Week

week in review



breaking news

For all news that is ortho, read on.

Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

This Week: Over the last 30 days the value of the average orthopedic company equity rose 2.04%—which is the best monthly performance of 2011. Six out of ten of the Power Ranked companies beat the average. Overall, the Power Ranked firms rose 2.17% over the last month. 2012, we think, will substantially outperform 2011.

Rank	Last Week	Company	TTM Op Margin	30-Day Price Change	Comment
1	1	Zimmer	27.75%	5.68%	Japanese broker Muzuho upgrades to BUY from Neutral due to new cash dividend and management's large stock buyback program.
2	2	Medtronic	28.63	5.00	Citigroup advised its institutional investors that MDT is the top pick for 2012 among medical device companies.
3	3	Orthofix	14.72	2.80	Management tightening up operations, and, basically, turning OFIX into a chronic out performer.
4	4	Symmetry	6.45	2.04	Management is guiding the Street to expect $410-425 million in sales versus $400 million analyst consensus for 2012!!
5	6	Stryker	25.23	2.24	Stryker lands Synthes California sales force. Integration of Synthes into DePuy prompting some employees to jump ship.
6	10	Exactech	7.69	9.00	Plenty of new buyers adding EXAC to their portfolio. Looks like a bet on a small cap rally, frankly.
7	5	Integra	15.38	(4.05)	Stu Essig kicked upstairs after a 35% drop in the stock. New blood in the CEO spot. Street sees potential turmoil.
8	7	Smith & Nephew	22.8	5.25	SNN's key issue is profitability. Two things drive that—productivity and innovation. At SNN, innovation is especially difficult.
9	8	Johnson & Johnson	26.33	1.33	Every headline about JNJ reiterates the defensive nature of the investment. But still it underperformed last month.
10	9	Conmed	9.65	(2.36)	CNMD is all about improving profitability. Sales growth, at 1.5%, is nothing to write home about.

Robin Young's Orthopedic Universe

Top Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	Bacterin Intl Holdings	BONE	$2.86	$116	26.55%
2	CryoLife	CRY	$4.80	$135	16.50%
3	TranS1	TSON	$1.86	$51	12.73%
4	Wright Medical	WMGI	$16.50	$649	12.40%
5	Exactech	EXAC	$16.47	$216	9.00%
6	ArthroCare	ARTC	$31.68	$872	6.27%
7	Zimmer Holdings	ZMH	$53.42	$9,572	5.68%
8	Smith & Nephew	SNN	$48.15	$8,603	5.25%
9	TiGenix	TIG.BR	$0.95	$86	5.00%
10	Medtronic	MDT	$38.25	$40,367	5.00%

Worst Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	Kensey Nash	KNSY	$19.19	$166	-24.45%
2	Alphatec Holdings	ATEC	$1.72	$154	-15.69%
3	MAKO Surgical	MAKO	$25.21	$1,050	-12.47%
4	NuVasive	NUVA	$12.59	$532	-8.77%
5	Integra LifeSciences	IART	$30.83	$827	-4.05%
6	Conmed	CNMD	$25.67	$717	-2.36%
7	Tornier N.V.	TRNX	$18.00	$707	0.17%
8	Johnson & Johnson	JNJ	$65.58	179,089	1.33%
9	Synthes	SYST.VX	$167.79	$19,929	1.34%
10	Symmetry Medical	SMA	$7.99	$290	2.04%

Lowest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Zimmer Holdings	ZMH	$53.42	$9,572	11.34
2	Medtronic	MDT	$38.25	$40,367	11.49
3	Integra LifeSciences	IART	$30.83	$827	12.74
4	Johnson & Johnson	JNJ	$65.58	179,089	13.38
5	Kensey Nash	KNSY	$19.19	$166	13.61

Highest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Wright Medical	WMGI	$16.50	$649	35.11
2	RTI Biologics Inc	RTIX	$4.44	$245	27.75
3	ArthroCare	ARTC	$31.68	$872	22.15
4	Synthes	SYST.VX	$167.79	$19,929	21.24
5	Exactech	EXAC	$16.47	$216	20.85

Lowest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	Orthofix	OFIX	$35.23	$649	0.83
2	RTI Biologics Inc	RTIX	$4.44	$245	0.98
3	Zimmer Holdings	ZMH	$53.42	$9,572	1.22
4	Stryker	SYK	$49.71	$19,023	1.29
5	Exactech	EXAC	$16.47	$216	1.49

Highest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	NuVasive	NUVA	$12.59	$532	4.21
2	Wright Medical	WMGI	$16.50	$649	3.87
3	Kensey Nash	KNSY	$19.19	$166	2.27
4	Johnson & Johnson	JNJ	$65.58	179,089	2.23
5	Symmetry Medical	SMA	$7.99	$290	2.06

Lowest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	Symmetry Medical	SMA	$7.99	$290	0.80
2	Alphatec Holdings	ATEC	$1.72	$154	0.89
3	Conmed	CNMD	$25.67	$717	1.00
4	NuVasive	NUVA	$12.59	$532	1.11
5	Integra LifeSciences	IART	$30.83	$827	1.13

Highest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	TiGenix	TIG.BR	$0.95	$86	138.82
2	MAKO Surgical	MAKO	$25.21	$1,050	23.71
3	Synthes	SYST.VX	$167.79	$19,929	5.41
4	Bacterin Intl Holdings	BONE	$2.86	$116	4.41
5	Tornier N.V.	TRNX	$18.00	$707	3.11

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

Top Ten OTW Stories of 2011

By Walter Eisner

The birth of an orthopedic superpower, the death of a young engineer, dangerous accusations of clinical investigative bias, turmoil in markets and companies and reflections of an inventive genius were picked by our readers as the most popular stories on the pages of *Orthopedics This Week* in 2011

Readers clicked their way to over 6 million page views of stories during the year. Those clicks, tracked by Google Analytics, told us what readers found most interesting.

Before we list the top ten stories, one important story just barely missed the cutoff but was important to our readers because it reminded us of the humanity and purpose of our great orthopedics industry.

Hope and Love

On June 6, Jeff Guyer, a young orthopedic engineer asked us to "continue to breath in hope and breathe out love" in his last blog before peacefully passing away. The son of Rick and Shelly Guyer reminded us that engineers, surgeons, nurses and all the other providers love to go to work every day in the hope to improve patients' lives.

Jeff led a team that designed the GLIF (guided lumbar interbody fusion) procedure which won an *OTW Best Spine Technology Award* in 2009.

The Year's Top Ten Stories Picked by *OTW* Readers

– 10 –

The Wall Street Journal Bungles Surgeon Story

The *Wall Street Journal* reported in October that a patient died in April in Jackson, Mississippi, due to a surgeon's ownership in a medical device company. The neurosurgeon, Adam Lewis, M.D., is an investor in Spinal USA LLC.

We found the facts didn't match the accusation. It was another bungled, misleading story from *WSJ* about physician ownership in the business of healthcare. We set the record straight.

– 9 –

The Spine Blogger Unmasked?

In February 2009 an anonymous blogger began scorching surgeons for being greedy and spine companies for producing "me too" products. We were asked if we know his identity and in July we wrote what we found.

By September 2010, some of the blogger's followers began to call for his unmasking. A series of posted comments from his followers speculated that he was John Nieradka, a former colleague of ours at *OTW*.

In another posting on the blog, "John N." responded to followers that he was flattered, but that he wasn't the blogger.

– 8 –

An Overlooked Spine Market

While spine's innovation rate may no longer be the juggernaut it once was and independent auditing/actuarial firms like Milliman appeared to be trying to re-draw the boundaries of spine care, a small San Jose company which could be the next Kyphon, didn't seem to be affected.

In May we reported on SI-BONE, Inc., a three-year-old firm that appears to have uncovered an overlooked corner of the spinal implant market, the treatment of sacroiliac pain which, in size, maybe as large as 20% of all spine surgeries!

The new company is being directed by a few experienced medical device hands and one veteran of the Silicon Valley electronics world. None other than Mr. Kyphon himself, Mark Reiley, M.D., is SI-BONE's founder.

– 7 –

The Ten Most Disruptive Trends in Orthopedics

Ten potentially disruptive trends gathered momentum in 2011 that we believed would change orthopedics forever. From least to most, here were our picks in August.

- Everyday 10,000 baby boomers turn 65 in the United States.
- 125 million Americans suffer from a chronic medical condition.
- 3.6 billion prescriptions were filled last year in the U.S.—not counting medical marijuana.

- Pace of technology change is accelerating at an exponential rate.
- The smart phone is becoming a medical device.
- The number of robotic-assisted surgeries performed worldwide has increased three-fold over the past two years.
- Adult stem cells have been used in more than 190,000 patients in the U.S. since 2004 with no reported adverse events.
- Artificial intelligence systems are now beating humans in quiz shows.
- 50% of doctors are now employed by large healthcare corporations.
- The U.S. Government will pay less than it is paying now for healthcare in the United States.

— 6 —

Mutiny at Smith & Nephew

Nine former employees of Smith & Nephew's Visionaire team in Memphis got sued on March 11 by the company for conspiring to take company secrets and start their own business. A former colleague blew the whistle on them.

Three of the alleged "mutineers" fought back and claimed the company committed libel and owes them money.

— 5 —

Gary Michelson, M.D. Revisited and Surgeon/Industry Relationships

Seventeen years ago, Gary Michelson, M.D., called Sofamor Danek and asked if he could make some suggestions on improving one of their products. He was told, "No thanks," and if he thought he could a better job, he should do it himself.

He did exactly that, registering 955 patents and eventually winning a $1.35 billion dollar patent award from Medtronic, the largest in American history.

In June and July we revisited an earlier interview with the surgeon inventor and then talked with him about innovation, and the current state of the relationship between industry and surgeons. Michelson did not pull punches.

He told *OTW* that in the early '90s, many surgeons who were receiving money from implant suppliers and being called consultants were actually doing almost nothing other than influencing their colleagues to use that same supplier's products.

Gary Michelson, M.D.

— 4 —

Wright Medical in Turmoil

Perhaps no company in orthopedics had as much disruption to their business in 2011 as Wright Medical Group, Inc. from federal investigations into industry surgeon relationships.

Wright entered into a deferred prosecution agreement (DPA) with the government in 2010 and paid a $7.9 million fine.

But shortly before a Wright board meeting on May 4, 2011 to talk about compliance issues, the wheels came off. There was an unexpected and shocking announcement that Gary Henley, the CEO since 2006, resigned "without good reason."

Others were fired and other senior executives resigned. The company said it had found "credible evidence of serious wrongdoing" regarding its compliance with the DPA.

– 3 –

Physician-Owned Distributorships, Risks and Investigations

Nothing made device reps and manufacturers see red more in 2011 more than physician-owned distributorships (PODs), which reportedly have captured between 10-15% of the U.S. spinal market. Are they legal or not?

In June, a bipartisan group of U.S. Senators asked the Office of Inspector General (IOG) to investigate the growth of PODs and let them know if federal legislation is needed to keep them legal and ethical.

OTW laid out the legal arguments from lawyers by both sides. The verdict? PODs are legal until the government says they are not legal. In the meantime, everyone is waiting for the IOG report.

– 2 –

Carragee and NASS Living Dangerously

In June, *The Spine Journal* (*TSJ*), owned by publishing giant Elsevier and the official publication of The North American Spine Society (NASS) shocked the spine world by accusing well-known research physicians of omitting evidence in 13 clinical studies of Medtronic, Inc's INFUSE because of payments from the company.

OTW looked at the studies and discovered that Eugene Carragee, M.D, editor of *TSJ* had committed a number of deeply troubling mistakes, omissions, and what appeared to us to have been a systematic pattern of intellectual dishonesty in his accusations.

Carragee and his fellow authors embarked on an aggressive PR campaign to convince regulators, Centers for Medicare and Medicaid Services, and the general public that both patients and physicians who used INFUSE had been "living dangerously" over the past couple of decades.

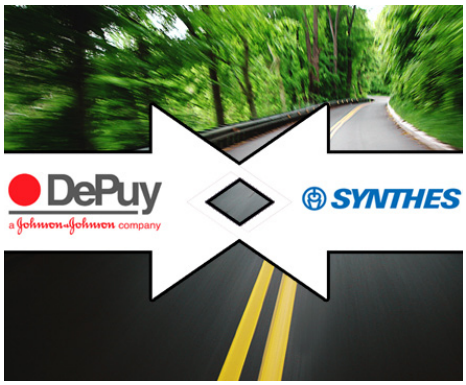
These actions prompted Charles Branch, M.D., former editor of *TSJ* to say in *OTW* that with the June journal issue and NASS press releases, "fanning the fire," the 2011 NASS meeting became more of a "professional society circus," and the chance for a true scientific debate "has been lost forever in the polarity of the accused and the accusers lining up to do battle."

– 1 –

An Orthopedic Superpower is Born, the Synthes/DePuy Merger

In April a new orthopedic superpower was born as Johnson & Johnson (owner of DePuy Orthopaedics, Inc.) announced it will acquire Swiss device maker, Synthes, Inc. for $21.3 billion.

The resulting firm will become the world's largest orthopedic company with annual orthopedic shipments of around $9.3 billion. In market share terms, the combined entity would have about 28% market share. The #2 and #3 companies would be Stryker Corporation at 14% and Zimmer Holdings, Inc. at 13%.



Morguefile/Wikimedi/RRY Publications

We reported the most important characteristic of this combination is the lack of overlapping products and sales personnel in four of the five major categories—knee, hip, trauma and extremities. As a result, integration of such large firms and their respective armies of sales, support, research and clinical personnel will be fairly painless.

In spine, however, we reported the opposite. DePuy Spine and Synthes have substantial and comprehensive overlap in terms of products, product categories and personnel. Indeed, in this case, we wondered who was really acquiring whom. Synthes, which markets its spinal implant products on a platform of direct sales personnel, may well emerge as the dominant surviving spinal implant organization.

We wrote that the merger will likely set in motion a massive game of musical chairs among spinal implant sales people throughout the industry as there is significant product and territory overlap between DePuy Spine and Synthes Spine.

So farewell 2011. We're eager to report on the new events of 2012. ◆

No Spine Care for Congress?

By Robin Young

How upset are spine surgeons in the United States? On a scale of 1 to 10—about 12.

Here is an excerpt from an email we received from a practicing spine surgeon:

"We should just not electively associate with or treat: attorneys, employees of MCO's or Medicare, government officials, Congress, the Supreme Court, President or bureaucrats or their families for a period of one year—effective 1-1-12."

And that's not all. "NO testimony or narrative reports for attorneys for personal injury or any other lawsuits as treating physician or expert witness. NO peer review for insurance companies, etc. Also no participation in ACO's , EHR meaningful use either."

Clearly this veteran clinician is mad as hell.

What could possibly have pushed this surgeon to urge his fellow physicians to, in effect, withdraw their talents and skills from attorneys, Medicare and so forth?

Wikimedia Commons and RRY Publications LLC. Photo Creation

Number One Concern of Spine Surgeons for 2012

In Becker's excellent *Orthopedic, Spine & Pain Management* web newsletter, writer Laura Miller asked six spine surgeons to discuss their number one concern for spine care in 2012. (Ms. Miller's entire article is available here: http://beckersorthopedicandspine.com/spine/item/10280-what-is-your-number-one-concern-for-spine-surgery-in-2012).

To a person, each surgeon said insurers are the #1 concern.

Here are two quotes from Ms. Miller's article in Beckers (the whole article is very good and we urge our readers to check it out):

> "Spine care in America is being destroyed by insurers at an unimaginable and unprecedented rate. Every day spine surgeons are discovering insurance company created roadblocks to their ability to care and provide for their patients.

Spine care is very complex and involves many conditions that are difficult to treat. The most common spinal conditions are those causing debilitating pain from the spine. The most common causes of this pain include muscle pain, facet joint pain and pain originating in the spinal disc (discogenic pain). The only treatments available for these types of conditions are medication, therapy, needle procedures and surgery. Every one of these avenues of treatment is currently (and has been for some time) under heavy attack by the insurance industry. Insurers simply don't want to pay for spine care so I predict we will see a dramatic reduction in elective spine care in

the near future." — **Ara Deukmedjian, M.D. (Founder, Deuk Spine Institute, Melbourne, Florida)**

"The ability to perform procedures due to insurance approval. I have had more denials in the past four months than I had total for the prior two years. Unfortunately, it puts the patients in the middle with nowhere to turn. Another issue is the continuing declining reimbursements while trying to maintain a practice where expenses continue to increase." — **J. Brian Gill, M.D. (Spine Surgeon, Nebraska Spine Center, Omaha)**

But Wait, There's Still More

Eleven months ago we opened *OTW* up to surgeons with first person accounts of the changing reimbursement landscape. The response was dramatic. The message was crystal clear. Spine patients and their surgeons are in a battle for control of their healthcare. And they are losing.

From Indiana: "We have been dealing with this for over a year. The increasing rate of denials for coverage has resulted in huge frustration for our patients. We have learned that the only way to get them approved is have the patient daily call them and bug them. The insurance companies constantly lie to the patients telling them that it is our fault for not sending appropriate info etc."

From Arizona: "65-year-old female (on Aetna) had undergone successful L3-5 laminectomy and fusion for stenosis and degenerative listhesis 2 years ago, achieving a pain free status for over a year. She presented with severe interval degeneration at L2-3 with back pain and stooped forward posture, decreased ability to walk for distance for 1 year. She tried physical therapy, medications, but the back pain and stooping slowly increased. CT scan showed L2-3 stenosis, inadequate lumbar lordosis (flatback), degenerative spondylosis at L5-S1 without stenosis. I recommended hardware removal, laminectomy L2-3, TLIF L2-3 and L5-S1, Ponte osteotomies L2-3 and L5-S1 to recover her lordosis, and posterior fusion with instrumentation L2-S1. — **Aetna denied the surgery, stating Milliman Care Criteria."**

"50-year-old male (Aetna) underwent Left L5-S1 laminectomy and discectomy for herniation, with complete pain relief for 5 months. His left leg pain returned though it was most severe along the posterior thigh only, and not down the S1 dermatome. He also developed severe mechanical back pain which was improved by rest. Flexion-extension Xrays did not show instability, but only degenerative disc at L5-S1. New MRI showed typical degenerative L-S1 disc and scar in the operative area but no recurrence of herniation. He tried PT, meds, epidural steroid injections with short term relief only. I recommended fusion at L5-S1, which **Aetna denied. 'This case does not meet the Milliman Criteria' was the reason."**

52-year-old male (Humana) with severe back pain for 2 years, bilateral leg pain and numbness, stooping posture, ambulatory with a

quad-cane, could walk less than 1/2 block. Xrays showed 18 degrees of degenerative scoliosis L2-5 with rotational listhesis L2-3, L3-4, and flatback. He was severely out of balance in the sagittal plane (stooping forward). MRI showed severe stenosis at L4-5 with less stenosis L2-3, L3-4. I recommended L2-5 laminectomies, Ponte osteotomies to regain lordosis and correct the curve, TLIF and posterior fusion L2-3. **Humana denied the surgery because the 'sports medicine orthopod' that reviewed it stated that 'TLIF is an experimental procedure'**. I pursued an appeal with someone with spine knowledge, and the reviewing neurosurgeon said 'there are too many of these fusions being done'. **Threatened legal action finally won approval for surgery."**

From Georgia: "I have a patient who is an international jazz singer. Due to L4-5, 5-S1 disc degeneration, she could no longer stand on stage. Her proposed 2-level ALIF was denied based on the Milliman criteria (BCBS). She waited until her husband could change the insurance carrier for his business so that she could proceed with the proposed treatment. She has had an excellent outcome, and is now back touring Europe. She has indicated her willingness to share her story, as she and her husband were suitably outraged over the whole mess."

From Oregon: "I was copied on an email this morning indicating that Regence BCBS has adopted the Milliman guidelines, which are perhaps causing surgeons to receive increased denials for fusions for degenerative conditions in Oregon."

From another surgeon in Arizona: "Today I was told by one of the Aetna reviewers that a patient with a Grade 1 isthmic spondylolisthesis with bilateral foraminal stenosis and bilateral progressive L5 EMG proven radiculopathy did not meet criteria for surgery because she did not have a Grade 2 spondy. It took significant work to get the surgery approved."

From Massachusetts: "I have just had a denial on a very solid gentleman in his 40s. He has had increasing pain for over 10 yrs. He has a normal lumbar MRI with the exception of prominent degenerative changes at L4-5. After exhausting conservative measures including injection therapy, he went through a discogram which confirmed L4-5 as his pain generator. After sitting with he and his wife, we decided to pursue an L4-5 fusion. The patient has been saving his vacation time and working in severe pain so that he can use those days for his recovery. MA BC/BS has denied his surgery (and denied his appeal). He will likely go on to lose the job he loves and endure pain with no end in sight. **At least the executives at MA BC/BS will get their bonuses."**

Who Decides Treatment?

Joining U.S. surgeons in an increasingly crowded operating room are attorneys, reimbursers, Medicare, Milliman, hospital administrators, Congress and the administration. Who decides treatment?

More often than the general public realizes, it is not the person trained for the job. The clinician.

The issue of course is money. The entities that control the purse strings are using that power to drive treatment plans—to the deep frustration and, we fear, detriment to both the patient and the front line surgeon.

Who Will Advocate for the Surgeon?

When Blue Cross Blue Shield of North Carolina proposed to, in effect, stop paying for degenerative disc disease (DDD), NASS (North American Spine Society) rallied eight of its fellow surgeon societies to present a unified

case for surgical intervention to treat DDD. It was a magnificent effort and for a while there was hope that rational minds would prevail. Last we heard, unfortunately, BCBS of North Carolina had not changed its policies.

Then in June, NASS's PR staff revved up the promotion for Dr. Eugene Carragee's flawed studies of BMP2 and put the phrase "living dangerously" into the popular lexicon when referencing spine surgeons.

The *Wall Street Journal* and the *New York Times* were just two of the many publications that picked up NASS's press releases and amplified the 'living dangerously" theme initiated by Carragee.

With the imprimatur of both NASS and *The Spine Journal* on the concept that spine surgeons were irresponsible in their treatment of patients, the effort to build support for spine surgeons among the reimbursing agencies took a heavy blow.

What if Atlas Shrugged?

The level of frustration at the hospital and clinic level is high and rising. These comments in Beckers and *OTW* are the tip of the iceberg. At some point, surgeons will find ways to reclaim some measure of control over the treatment of their patients.


Andrew Huth

Will surgeons have to start withholding treatment in order to restore sanity to clinical care?

That same surgeon who emailed his colleagues to suggest exactly that approach also offered the following three solutions which, in his view, would return reason and order to treatment of spine disease.

1. Comprehensive national tort reform is law

2. A multidisciplinary "stakeholder" panel consisting of spine care providers, researchers, patients, health insurers, medical device and pharmaceutical companies will convene to review EBM guidelines—such as NASS (some of them, anyway) and make National Coverage /Medical Necessity Guidelines by majority vote of the panel—the majority of voting members shall be physicians with recognized expertise in the subject voted upon and take this power of "right to determine Medical Necessity" out of the hands solely of for-profit insurers and the obvious conflict of interest/compliance issue this creates. The panel is elected by the members of the society they serve and have term limits...unlike the current proposed "Independent Advisory Board"

3. Medicare SGR payment reform is completed. No more year end "doc fix" band aids "

Too bad surgeons may have to shock the system into paying attention to such common sense proposals. ◆

Crosslinked Polymers in TKA: Aaron Hofmann Debates Jerry Engh

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

"In essence, Highlycrosslinked Polyethylene (HCLP) for total knees at this time is probably a bad idea." argues Dr. Engh. Not so, counters Dr. Hofmann. "We have nine years of clinical data and haven't seen any clinical problems with HCLP. As we said a few years ago, it was a wine before its time…I think it's time to drink the wine."

In an Orthopaedic Crossfire® debate titled, "Using Crosslinked Polymers in TKA: Surely Tough Enough," Dr. Gerard A. Engh of the Anderson Orthopaedic Institute argues that conventional PE (polyethylene) has its merits, while Dr. Aaron A. Hofmann of the University of Utah disagrees pointing out that HCLP has better long term wear. Both sides let the free radicals fly in this spirited Crossfire debate. Who comes out on top? You are the judge.

Wikimedia - KaihsuTai and Current Concepts in Joint Replacement/RRY Photo Creation

Dr. Hofmann: "We're going to be discussing smooth-running knees. The subject is Crosslinked Polyethylene (PE) in TKA…and I thought, 'Surely Engh is tough enough to listen to this talk and I'm sure he will agree with me at the end of this debate. So even Seth Greenwald said years ago that what we have is good enough…and if you agree then you can continue to use standard polyethylene, but if you don't think what we have is good enough you should consider changing to highly crosslinked."

"Every major manufacturer has made mistakes in trying to come up with new polyethylene…I would say that highly crosslinked polyethylene (HCLP)—just like in the hip—is not new, it's been around since 2001 and I've used it consistently since then."

"Gamma radiation is a good thing for PE wear. Unfortunately it causes free radicals, which can break down, oxygenate and cause oxidative degradation over time. If you look at the standard sterilization doses used versus wear, the more you radiate PE the better the wear. Unfortunately you still have these free radicals and we don't know when these PEs were born. I can drink my Bud Light and know exactly when it was made, but I can't look at my PE package and know how old it is and if it's degradated—even in the package."

"Every major manufacturer has developed HCLP or moderately CLP for knees. X3 is available and if you look at the manufacturer's data you see a remarkable decrease in wear. DePuy/JNJ shows moderately CLP…again, retaining mechanical integrity with oxidative stability. A manufacturer shows a marked decrease in wear characteristics with a newer PE. But you've got to get rid of the free radicals and that is done by most manufacturers by heating to stabilize those free radicals so they can't oxidate and combine with oxygen."

"If you look at some of the lab data, done by Muratoglu [Orhun Muratoglu, Ph.D.] looking at aged Durasul (HCLP), you don't see the subsurface cracks and delamination that you see in our standard PE or standard PE that was delaminated. He did another test looking at adverse wear, for example if you had a very high, very tight PCL, and what would happen if you got edge

loading. Standard PE, even at 500,000 cycles does not tolerate that. You get some damage with HCLP."

"A favorite subject of Jerry Engh is backside wear. This has been looked at by Muratoglu as well for Prolong, which is not as crosslinked as Durasul. If you reheat the deformations around the screw holes, the amount of backside wear is almost tenfold more with conventional than with HCLP. There are clinical papers available…two year minimum follow-up showing no problems with CLP [Minoda et al.]. Another study…out of Roy Bloebaum's lab in Utah looked at retrieved implants with a minimum two year follow-up showing that these things aren't falling apart early on."

"In our own clinical data published last year looking at our first 100 starting in February 2001 when this material became available, it really didn't show any fractures, revisions, osteolysis, or problems with the PE."

"When we looked at our standard versus our HCLP there was a marked difference…17% incidence of some lucencies under the tray with a standard PE and almost none with the HCLP. A patient that had one of each, had radiolucencies (on the right) under the screw. Another implant—just retrieved—patient that had after seven years a slightly loose knee was unhappy with that…gave me a chance to look at this PE as we put a thicker one in. We saw a bit of surface damage on the articular side. On the back side you can still read the fine print—the serial number and how thick the PE is, so there is almost zero backside wear."

"In conclusion we have nine year clinical results and haven't seen any clinical problems with it. As we said a few years ago it was a wine before its time… I think it's time to drink the wine."

Dr. Engh: "I think we all realize that we had a problem in the '80s and '90s with accelerated PE wear that was caused by gamma irradiation in air, but this was not a material problem. Then there was carbon fiber reinforcement, heat pressing, changing the molecular structure of the material. All of these failed horribly. The solution came by changing the method of sterilization to either non-gamma or gamma in inert."

"The largest retrieval study is from Dartmouth. They had over 1,600 implants; 32 of these were sterilized by ethylene oxide…non gamma, no delamination, minimal penetration rates. These are six implants that were in situ for more than 15 years and they showed negligible wear. Out of our own institution… retrieved AMK [Anatomic Modular Knee] implants, low dose gamma in barrier, linear wear rates of .02 mm per year. This would take 50 years to wear one millimeter."

"In a small number of retrieved implants the wear rates for cubic millimeters is quite low. If we look at wear of conventionally sterilized inserts versus acetabular cups, the wear rates of the former is less than a quarter in terms of linear wear of acetabular cups and less than half in terms of volumetric wear. But the problem with HCLP is not only that we don't have a wear problem as long as we don't sterilize with gamma in air, but we've reduced the tensile strength of the material, and this can cause fatigue problems. We get smaller wear particles that are more bioreactive…and I would argue that there aren't any clinical studies to date proving that there is reduced wear."

"If we look at retrieved inserts….again from our institution…gamma irradiated versus gas plasma with low dose

gamma irradiation. When we get out after five years those that have been irradiated are showing considerably greater pitting on both the top side and on the back side of the implants compared to non irradiated implants. With increasing radiation doses we decrease the toughness; in more constrained devices such as posterior stabilized implants we open the problem of potential implant fracture."

"Looking at HCLP and reduced strength when we increase the dose of radiation, we decrease the material strength. Also, the wear debris is smaller and more bioreactive. The wear debris from HCLP is less than a micron in diameter, and these particles have a more robust inflammatory response."

"If we look at retrieval wear scores… HCL versus low dose (sterilized in) inert (conditions), there is no difference in the percent of pre- or post-melt surface damage. Other studies show the same thing…HCL material, no statistical difference in terms of wear scores compared to conventional material. We have FDA reports of implant fractures using this HCL material. Tibial PE fractures: pegs wearing or breaking off the back side of these implants as reasons for revision. Or if we look at osteolysis-there are already cases reported of osteolysis with very short term follow-up reports."

"In essence, HCLP for total knees at this time is probably a bad idea."

Moderator Duncan: "So Aaron, it seems that from Dr. Engh's standpoint, if we're careful with sterilization there's no reason to change, particularly when you take into account the potential downside of reduced fracture toughness of HCLP."

Dr. Hofmann: "Maybe it's performing well in his hands…it hasn't performed well in mine, nor in our own implant retrievals, nor in our clinical follow-up of our patients with conventional versus standard."

Dr. Engh: "I have not retrieved an implant in the last nine years that was not sterilized by gamma radiation in air for either wear or osteolysis. It's so dramatically different because I had enormous problems when it was sterilized with gamma in air *and* if it had a long shelf life. There's another problem, and we can never really compare what Aaron is telling us with HCLP because after they highly cross link poly they quench the free radicals, but for every one of you in the audience, when you use conventional poly that has low dose gamma and is placed in a barrier, for some reason manufacturers don't quench the free radicals. Why—if it's important to do that in the highly cross-linked material—is it not important to do that in the conventional material? And that's why we won't be able to compare these two because oxidation may happen after we put it in the patient."

Moderator Duncan: "What about the future of the HCLP in which Vitamin E has been used in the manufacturing process?"

Dr. Hofmann: "HCLP is available with every manufacturer and I think we're gong to be seeing that with every implantation. The only confusing thing is guys like Jerry who say that conventional PE is still a good thing, and so that's why some surgeons have continued to use it. You asked why don't the manufacturers squelch all the free radicals in all the PE…it's because people still want conventional. And it's certainly driven by economics. You get conventional PE being priced at one price and HCLP as the state of the art and it's $100-$200 more…that drives what surgeons use."

Dr. Engh: "At my institution it's more like $1,000 more for the HCLP. I wish a manufacturer was here to tell me why that's so important. Now we use Vitamin E to quench it…we use other methods. Why, if it's so important in the HCLP isn't it in the conventional—and most of us today are putting in the conventional? We've been using conventional PE in barrier a lot in our institution and the wear rates are quite low even with that. But I don't have 10-20 year results to find out if oxidation in vivo is a problem."

Moderator Duncan: "Thank you, gentlemen." ◆

Please visit www.CCJR.com to register for the 2012 CCJR Spring Meeting, May 20-23 in Las Vegas, Nevada.

On (and Off) the Record

By Elizabeth Hofheinz

Dear *OTW* Reader: An anonymous spine surgeon muses, "Are the **side effects of InFuse over or under stated**?"… Mike Franz discusses the **International Spine and Orthopedic Institute …Dr. Scott Levin, the Chair at Penn, reports on the region's first bilateral arm and hand transplant**… and more.

Carragee Out to Make a Name for Himself? A spine surgeon who requested anonymity told *OTW*, "First of all, is the increased retrograde ejaculation related to Infuse, to surgical exposure, or to the technique? In many people's minds, Infuse is not at fault; and there is increasing data to suggest that this problem is not related to Infuse. The other issue is the increased incidence of malignancy that Dr. Carragee raised. There is some concern that he based his conclusions on incomplete data that was publicly available—rather than on the full data set. The information from the statistics at the company suggests no increased risk related to Infuse. There is some concern whether a higher dose amplifies the incidence or is just a spike. The fundamental issue is, 'Are you going to believe the company or Dr. Carragee, who many think is on a mission to make a name for himself?' The FDA has found Infuse to be safe and effective…and they have access to all of the data. There is just not enough data at present to change practice."

David Veino, Tom Kennedy New VPs at Globus Globus Medical, Inc. has added two new vice presidents to its executive team: **David Veino**, vice president of Marketing, and Tom Kennedy, vice president of Surgeon Relations and Education. David Veino will lead Globus' worldwide marketing efforts. Prior to joining Globus, he spent five years as global director of sales and marketing for the Interventional Spine division of Stryker. Prior to Stryker, Veino spent five years in sales with Atherotech culminating as vice president of sales. Prior to that, he held roles of increasing

responsibility in sales and marketing at HeartGen Centers, Philips Medical Systems, Cor Therapeutics, and Parke Davis Pharmaceuticals. **Tom Kennedy** will be responsible for Globus' Musculoskeletal Education and Research Center (MERC) as well as the Surgeon Relations Group. Previously Tom was vice president of professional affairs and medical education for Smith + Nephew's Biologics and Clinical Therapies Division. Prior to that he was director, Professional Programs with Stryker Spine. Additionally, Tom has over 15 years experience in various sales and marketing positions, including those with C.R. Bard, Maxxim Medical and Johnson and Johnson Medical.

"Marrying" Chinese and Western Surgeons MikeFranz is CEO of the International Spine and Orthopedic Institute (ISOI), a high-level, unprecedented cultural exchange of sorts. Franz, who is also CEO Emeritus and Chief Strategy Officer of the Texas Back Institute (TBI), tells *OTW*, "The Kerlan Jobe Clinic and TBI have jointly founded the International Spine and Orthopedic Institute (ISOI) with a goal of establishing orthopedic surgery hospitals in China. We are focusing on affluent Chinese patients, expatriates, and medical tourists. We have a unique partnering of Western and Chinese surgeons; to access the surgeons in China, we are relying on our existing relationships with senior orthopedic professors in that country. Through their introductions we are meeting skilled Chinese surgeons and are conducting training programs here and in China. Having established these relationships, we can thereby seek out affluent Chinese patients. The perception in China is that Western medicine is in a more advanced state than Chinese medicine, so there is quite a demand for what we are offering. Our U.S. training hubs are TBI (for spine), and Kerlan Jobe (for sports medicine and total joints). We are proud to have already created a partnership with the First Affiliated Hospital of Suzhou University last March, whereby we renovated a VIP orthopedic center and now send U.S. surgeons there. The next project is a private hospital where we have ownership in the orthopedic department and we will put our model into it. Our ultimate objective will be for ISOI to have majority ownership in standalone orthopedic surgery hospitals in China, something we expect will start to occur in 2013."

Spine Wave Has New Product Developer Spine Wave, Inc. has announced that it has entered into an agreement with MB Innovations (MBI), a newly formed product development company based in Memphis, Tennessee. MBI will initially develop products exclusively for Spine Wave while they expand their infrastructure in anticipation of taking on additional medical device clients. MBI will assemble an accomplished team of engineers and advisors who have experience in developing commercially successful medical devices. The team will be led by Troy Drewry, President of MBI, who began his career in product development at Medtronic Sofamor Danek and most recently held the position as VP of U.S. Operations for Paradigm Spine. Mike Sherman, a partner at MB Venture Partners, will serve as executive chairman of MBI. Mike's product development career spans over 20 years at Synthes, Smith + Nephew and Medtronic Sofamor Danek where he generated over 90 issued U.S. patents.

$50,000 to Develop MI Bone Tissue Device Jay Khanna, M.D., associate professor of orthopedic surgery and biomedical engineering at Johns Hopkins University, has been awarded $50,000 to develop a minimally-invasive bone tissue harvesting device with a softer drill. Dr. Khanna's device allows for the collection of more bone tissue, a safer autograft, reduction of pain and better grafting. This technology is the core of a startup company, BOSS Medical, LLC.

Vascularized Composite Allograft Transplantation—Opportunity for Orthopedics? L. Scott Levin, M.D., FACS chair of Orthopaedic Surgery at the University of Pennsylvania, is pleased with the progress they are making with transplantation. Dr. Levin, professor of surgery (plastic surgery), is the only orthopedic surgeon to direct a university-based transplant team. He tells *OTW*, "We did the first bilateral arm and hand transplant in the region

two months ago; the patient is doing extremely well, and is regaining the functions of daily living that she didn't have before transplant. This complex procedure involved orthopedic surgeons, plastic surgeons, hand surgeons, etc. From an orthopedic perspective vascularized composite allograft transplantation represents a future opportunity for living joint repair and replacement of other body parts that until now were impossible or relied on prosthetics that have limited life expectancy as a device. We are moving forward, and have several patients who have undergone evaluation and will be listed for surgery in early 2012."

Luke Faulstick Leaves DJO Luke Faulstick has moved on from DJO Global. The former executive vice president and chief operating officer will leave the company in early February, 2012 to join Power Partners, Inc., a privately-owned power transmission manufacturer, as Co-owner, President and CEO. Faulstick has served as a member of the board of advisors of Power Partners, Inc. since 2003.

Closer Than Ever to Arresting Degeneration Dr. Isador Lieberman of the Texas Back Institute has "no doubt" that biologics is the future of spine surgery. He tells *OTW*, "We are seeing more information these days on regeneration and alteration of the degenerative cascade—and the reversal of the degenerative cascade. This is stuff that will put us heavy metal spine surgeons out of business…and that is a good thing. The FDA has already starting shaking the trees with companies, and having them come out with stem cell possibilities. But the slowness of the regulatory process will ultimately delay the availability of this technology for patients. *The good news is that we are closer than ever to arresting the degenerative process so that we'll be able to manipulate that process with targeted therapeutics like growth proteins or something that is part of the BMP group.* Many researchers are looking at various applications and trying to reassign them to another application. As for the regulators, somebody has to step up and point the FDA in the right direction. We need a point person who will say, 'This is what you need to do; this is how to handle this opportunity. Why are they so hesitant?' Because they look at this stuff and say, 'We don't know how to categorize it… is it a pill, an implant, or a procedure'… and no one wants take responsibility for this process." ◆

company

TranS1 Snags Medicare Coverage

TranS1 Inc. has snagged another coverage victory, this time with Medicare.

The company announced on December 14, that Palmetto GBA, a Medicare Administrative Contractor, has removed its Non-Coverage policy for AxiaLIF effective January 1, 2012.

In its letter, Palmetto indicated that its medical directors had reviewed the AxiaLIF clinical information and decided "...the benefits are well supported by high-quality evidence, and has clinical value." Palmetto provides care to approximately nine million Medicare beneficiaries in California, Virginia, North Carolina, South Carolina, Nevada, West Virginia and Hawaii.

Ken Reali, TranS1's president and CEO, was happy. "We believe that this decision further validates the safety and effectiveness of the AxiaLIF procedure and our ability to work with payors to adopt policies that support reimbursement for the procedure. We look forward to being able to work with spine surgeons to provide the minimally invasive AxiaLIF approach to Medicare beneficiaries in these covered states."

In addition to announcing the company's first local coverage decision with Medicare where the insurer has agreed to cover the AxiaLIF specific t-code in seven states, the company also announced coverage this past year with private payors Humana and Horizon (BCBS of New Jersey). All told, theose insurers cover 23 million lives. Reali told *OTW* that the procedure is gaining ground with payors as the company increases the number of peer reviewed publications. "Over 25 new papers have been published in 2011 that demonstrate safety and efficacy," said Reali.

TranS1 currently markets the AxiaLIF family of products for single and two level lumbar fusion and the Vectre and Avatar posterior fixation systems for lumbar fixation supplemental to AxiaLIF fusion. TranS1 was founded in May 2000 and is headquartered in Wilmington, North Carolina.

—WE (December 29, 2011)

TranS1 and Medicare/Morguefile and RRY Publications LLC Photo Creation

Do Biomet's Rising Sales Beckon a New Ortho Dawn?

Biomet, Inc. reported a preliminary 4% rise in second quarter 2012 sales after the markets closed on December 19. Total revenues totaled $725.1 million.

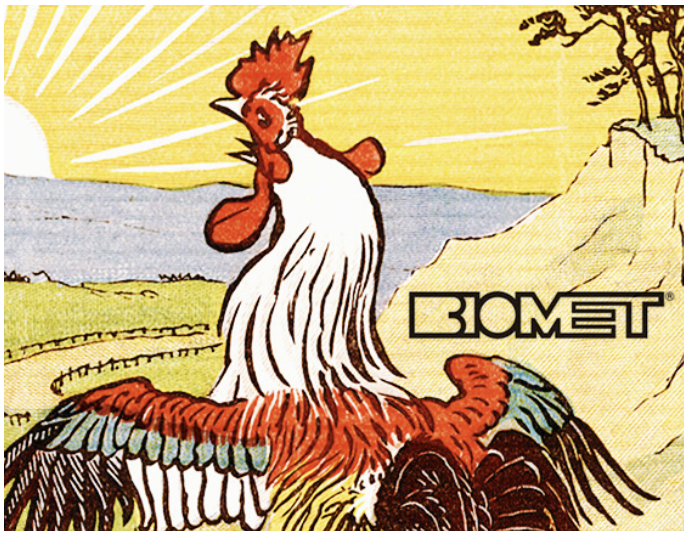
The next day, orthopedic stocks shot through the roof. Zimmer climbed almost 7%, while Stryker and Medtronic were up close to 3% to 4%.

"We would view the Biomet large joint reconstruction results with cautious optimism for the broader hip and knee markets," wrote Derrick Sung, an analyst with Sanford C. Bernstein & Co., in a note to investors. "Investors are generally pricing in no expectation for an orthopedic market recovery in 2012, so we would view any signs of such as incrementally positive for Stryker and Zimmer, the pure-play orthopedic companies."

Like the rooster crowing at dawn, Biomet is the first of the large orthopedic device companies to report quarterly sales. The company's results are thus closely watched for what their sales volumes mean to the rest of the industry. Reported hip sales rose 7%, knees were up 2%, and extremities and trauma rose 13%. Only spine sales continued their downward trend, dropping 5%.

The company reported that worldwide large joint reconstructive sales increased 5% to $442.3 million and increased 3% in the U.S. Knee sales decreased 1% and hip sales increased 7% in the U.S.

Jeff Binder, the company's president and CEO, said the company was "pleased" with the overall sales performance and was "particularly happy" to see acceleration in year-over-year quarterly growth rates compared to the last couple of quarters in the company's major product categories, including knees and hips.



Rooster Cropped/Randolph Caldecott/Wikimedia Commons

Biomet 2Q 2012	Sales ($ in millions)	% Change
Total Reported Sales	**$725.1**	**4%**
Large Joints	442.3	5%
Knees		2%
Hips		7%
Sports, Extremities, Trauma	85.4	13.0%
Spine & Bone Healing	77.3	down 5%
Dental	73.6	3.0%
Other	46.5	down 1%

Source: Biomet, Inc.

"Positive Sign" – Wall Street

Wells Fargo's analyst Larry Biegelsen cautioned against reading too much into these results in an investor note because Biomet's growth this quarter was on easier comps and the company's results may not be representative of the rest of the sector because its knee and hip market share is modest (low double digits).

Biegelsen, however, said the large joint growth could signal improvement in the orthopedic market. He said Biomet's reported large joint recon growth was the company's first quarter with positive growth since fiscal FQ2 2011.

"Biomet's U.S. knee growth of is a move in the right direction after three quarters of negative mid-single-digit growth. Worldwide knee growth is encouraging after three straight quarters of declines. The acceleration of U.S. hip growth is a strong signal for the U.S. hip market. Worldwide hip growth also jumped significantly compared to last quarter and flat growth for the previous three quarters. Despite easier comps, we believe Biomet's growth is a positive sign for the large joint markets. Assuming Biomet has not taken market share; Biomet's results should be a positive for the ortho companies such as Zimmer, Stryker, Wright Medical and, to a lesser extent, Johnson & Johnson," concluded Biegelsen.

While Biomet is the rooster crowing at this dawn of rising orthopedic sales, it's yet to be seen whether or not this rooster gets credit for the sunrise.

—WE (December 21, 2011)

legal

November 2011 FDA Approval Summary

The FDA granted six original Premarket Approvals (PMAs) during the month of November 2011. None were for orthopedic devices. The approvals were for:

- MELA Sciences, Inc.'s MelaFind is for use on clinically atypical cutaneous pigmented lesions with one or more clinical or historical characteristics of melanoma.
- Merz Pharmaceuticals, LLC's BELOTERO Balance device is indicated for injection into the mid-to-deep dermis for correction of moderate-to-severe facial wrinkles and folds such as nasolabial folds.
- Dako Denmark's HER2 CISH pharmDx Kit is intended for dual-color chromogenic visualization of signals achieved with directly labeled in situ hybridization probes targeting the HER2 gene and centromeric region of chromosome 17.
- Edward Lifesciences, LLC's SAPIEN Transcatheter Heart Valve is indicated for transfemoral delivery in patients with severe symptomatic native aortic valve stenosis
- Boston Scientific Corporation's PROMUS Element Plus Everolimus-Eluting Platinum Chromium Coronary Stent System (Monorail and Over-The-Wire) is indicated for improving luminal diameter in patients with symptomatic heart disease due to de novo lesions in native coronary arteries ≥ 2.25 mm to ≤ 4.00 mm in diameter in lesions ≤ 28 mm in length.
- Abbott Vascular, Inc.'s XIENCE PRIME and XIENCE PRIME LL Everolimus Eluting Coronary Stent System is indicated for improving coronary luminal diameter in patients with symptomatic heart disease due to de novo native coronary artery lesions (length ≤ 32 mm) with reference vessel diameters of ≥ 2.25 mm to ≤ 4.25 mm.

Four orthopedic related Supplemental approvals were granted. Those approvals were for:

- DePuy Orthopaedics, Inc.'s LCS Total Knee System. To manufacture the subject components from GUR 1020 polyethylene with an antioxidant (AOX), to change the packaging components and materials, and to request approval of a shelf-life testing protocol for the subject P.F.C Sigma RP Curved and Stabilized Tibial Inserts.
- Zimmer, Inc.'s Trilogy AB Acetabular System received approval of the post-approval study protocol.
- DePuy Orthopaedics, Inc.'s Pinnacle CoMplete Acetabular System received approval of the post-approval study protocol.
- Orthofix, Inc.'s Physio-Stim, Spinal-Stim and Cervical-Stim received approval for the addition of an alternate battery pack supplier.

A summary of the FDA's November 2011 PMA/Supplemental activity was as follows:

- Total of 81 PMA Originals under review—33 are active and 48 are on hold. Three applications have been under consideration more than 180 days.
- Total of 599 PMA Supplements under review—473 are active and 126 are on hold. Tne are older than 180 days.
- The FDA received 1 new PMA and 88 Supplement submissions during the month.

To read the approvals in detail, click here:
http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/ucm285155.htm?source=govdelivery

—WE (December 28, 2011)

Image creation by RRY Publications, LLC. Wikimedia Commons and FD

Spinal Kinetic Beats Synthes in Patent Fight

A federal jury in northern California has found that Spinal Kinetics, Inc.'s M6 artificial cervical and lumbar discs do not infringe on Synthes USA's '270 patent. In fact, according to a December 13 announcement by Spinal Kinetics, the jury found the Synthes patent invalid.

The M6-C (cervical) and the M6-L (lumbar) artificial discs were introduced internationally in 2006 and are available in 17 countries. Over 13,500 implants have been used in patients in that time, according to the company.

Synthes' artificial spinal disc, the ProDisc, is not covered by the '270 patent. Spinal Kinetics argued in court that Synthes never commercialize the '270 patent. However, Synthes still claimed it lost ProDisc sales as a result of Spinal Kinetics' alleged infringement. Synthes claimed that its market share had fallen "significantly" within two years of the introduction of the M6 in the German market.

Synthes originally filed suit in November 2008 in federal court in Delaware. The case was transferred to northern California in February 2009.

Tom Afzal, president and CEO of Spinal Kinetics, says the verdict allows the company to focus resources on making the devices available to more patients, including in future clinical trials in the U.S.

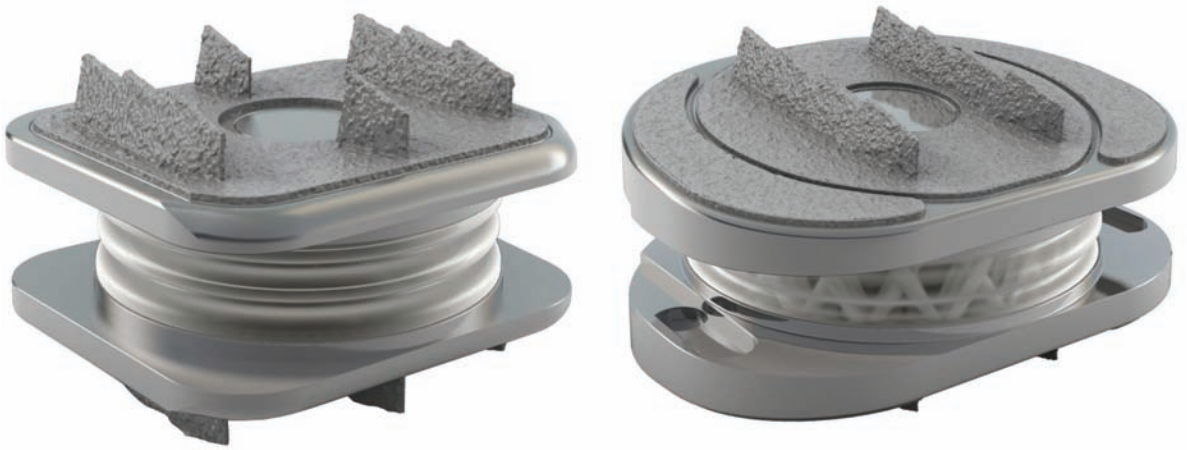
The M6, says the company, is the only artificial disc that replicates the anatomic structure and biomechanics of a natural disc by incorporating both an artificial nucleus and annulus. In the U.S., Spinal Kinetics has successfully completed an FDA IDE (investigational device exemption) Pilot Study of the M6-C in patients with both single and two-level disease, and has received approval from the FDA to initiate an IDE Pivotal Study.

The abstract for the '270 filed in 2003 states:

"Disclosed is an intervertebral implant comprising a central axis, a bottom cover plate and a top cover plate, which are respectively provided with an exterior surface that extends transversal to the central axis, and a central part. Said central part is located between the cover plates and is provided with a sleeve encompassing a fiber system that is connected to the cover plates and is embedded in an enveloping body made of a homogeneous material. In analogy with the anatomic structure of the natural disk, the inventive intervertebral implant can transfer occurring compressive forces onto the cover plates thereof as tensile forces that are applied to the individual fibers of the fiber system thereof."

Spinal Kinetics, located in Sunnyvale, California, is a privately held company founded in 2003. The company says it is focused on partnering with spine surgeons to develop motion preservation systems for the spine.

—WE (December 19, 2011)



Spinal Kinetic M6 Artificial Discs/Spinal Kinetics, Inc.

large joints

Missing Link for Arthritis?

Scientists have discovered a missing link between the body's biological clock and sugar metabolism system, a finding that may help avoid the serious side effects of drugs used for treating arthritis, asthma, and allergies. In a paper published last week in *Nature*, scientists at the Salk Institute for Biological Studies report finding that proteins that control the body's biological rhythms—cryptochromes—also interact with metabolic switches that are targeted by certain anti-inflammatory drugs.

"We knew that our sleep and wake cycle are tied to when our bodies process nutrients, but how this happened at the genetic and molecular level was a complete mystery," says Ronald M. Evans, a professor in Salk's Gene Expression Laboratory, in the December 19, 2011 news release. Dr. Evans, who led the research team, added "Now we've found the link between these two important systems, which could serve as a model for how other cellular processes are linked and could hold promise for better therapies."

Glucocorticoids also play a role in regulating inflammation and are used as anti-inflammatory drugs for diseases caused by an overactive immune system. However, because of their role in sugar metabolism, the steroids can disrupt a person's normal metabolism, resulting in dangerous side effects, including excessively high blood sugar levels, insulin resistance and diabetic complications.

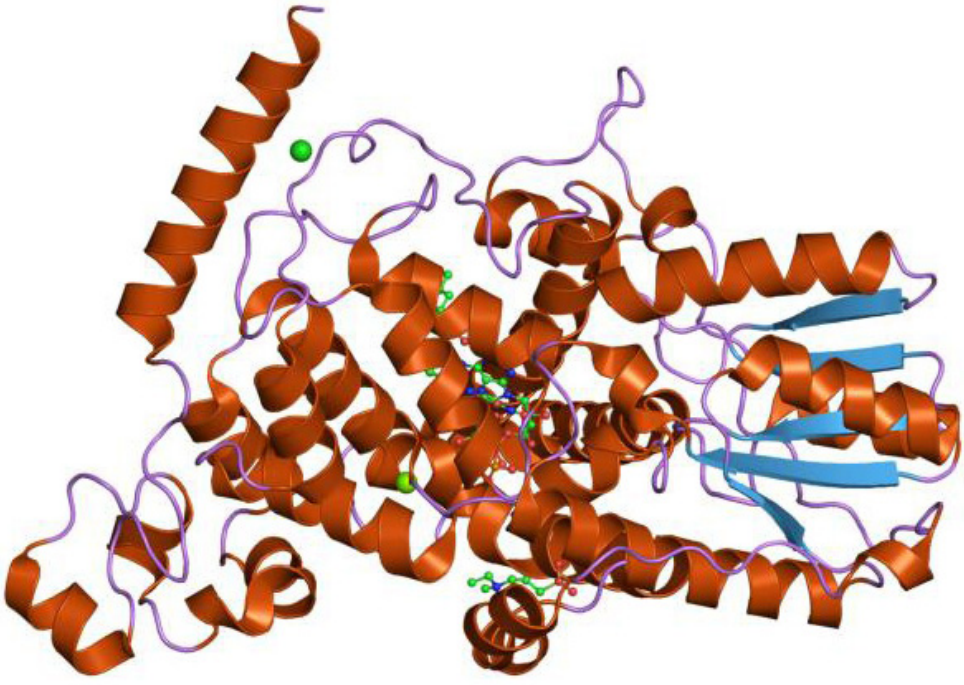
The Salk researchers may have found a way around these side effects by discovering a new function for cryptochromes 1 and 2, proteins that were previously known for their function in the biological clock.

The cryptochromes serve as breaks to slow the clock's activity, signaling our biological systems to wind down each evening. In the morning, they stop inhibiting the clock's activity, helping our physiology ramp up for the coming day. In their new study on mouse cells, Evans and his colleagues made the surprising discovery that cryptochromes also interact with glucocorticoid receptors, helping to regulate how the body stores and uses sugar.

"We found that not only are the crytopchromes essential to the functioning of the circadian clock, they regulate glucocorticoid action, and thus are central to how the clock interacts with our daily metabolism of nutrients," says Katja A. Lamia, an assistant professor at The Scripps Research Institute and former post-doctoral researcher in Evan's laboratory at Salk.

The discovery also raises the possibility of developing new anti-inflammatory drugs that avoid some side effects by targeting cryptochromes instead of directly targeting the glucocorticoid switches.

"Disrupting the normal day-night cycle of activity may prevent a person's biological clock from synchronizing correctly with their daily patterns of nutrient metabolism," Evans added. "As a result, the body might not store and process sugar normally, leading to metabolic disease."



Wikimedia Commons and Jawahar Swaminathan and MSD staff at the European Bioinformatics Institute

—EH (December 27, 2011)

Exactech Initiates Cartilage Repair Study

Exactech, Inc./Note: this includes two images of the base and one plug

Exactech, Inc. has announced that it has initiated a prospective, randomized, multi-center, clinical trial to evaluate the safety and effectiveness of a new cartilage repair technology. According to the company, the new technology incorporates a novel tissue processing system that allows for preparation of a patient's own cartilage for delivery to the site of a cartilage defect in a single-stage procedure. The system uses both mechanical and chemical processing to increase the potential for cartilage regeneration.

The first of 92 surgeries planned for the study was successfully performed December 1, 2011, by Professor Ching-Chuan Jiang, M.D., and Dr. Hong-Sen Chiang, at the National Taiwan University Hospital (NTUH) in Taipei, Taiwan. The study will include one-year follow-up of patients treated for focal chondral or osteochondral lesions of the knee, and will provide the basis for a premarket approval application to the Taiwan Food and Drug Administration upon its completion.

"Cartilage repair has become a strategic focus of Exactech's biologic research and development efforts," said Bruce Thompson, senior vice president and general manager of Exactech's Spine and Biologics Division, in the December 19, 2011 news release. "Exactech believes cartilage repair can offer an early intervention, regenerative approach to treating patients who present with cartilage defects, which is often a precursor to osteoarthritis."

"This is the first time a one-step, single-surgery system has allowed transplantation of a patient's own cartilage processed to facilitate regeneration of focal defects," added Professor Jiang. "It is our hope that this clinical trial will prove our implant technique to be effective in regenerating native cartilage."

Exactech licensed the technology in 2008 from Industrial Technology and Research Institute of Taiwan (ITRI) and NTUH and has spent three years conducting research and development.

Initiation of this clinical trial represents a major milestone in Exactech's plan for commercialization of its cartilage regeneration technology in multiple global markets, including the United States and Europe. Exactech will follow the particular regulatory requirements of the intended markets to assure the most timely introduction of the technology for the benefit of patients in these markets.

When asked about the development process, Bruce Thompson, told *OTW,* "Since the acquisition of the technology, the company has worked diligently to transfer the research from the Taiwanese non-profit R&D organization, although certain aspects of the project are still contracted to the Institute. The product system includes a cartilage processing kit which prepares the patient's own cartilage for reimplantation inside the chamber of a resorbable implant. Work is ongoing to optimize the cartilage preparation process, process development for manufacturing commercial quantities of product, and instrumentation development for implanting the device."

—EH (December 23, 2011)

MedShape: Shape Memory Polymer Patent

Flexibility…a good quality in people *and* in medical devices…MedShape, Inc. has announced that it has been granted a patent from the United States Copyright and Patent Office for its shape memory polymer-based technology. The patent was granted for a "Method and Apparatus for Deploying a Shape Memory Polymer."

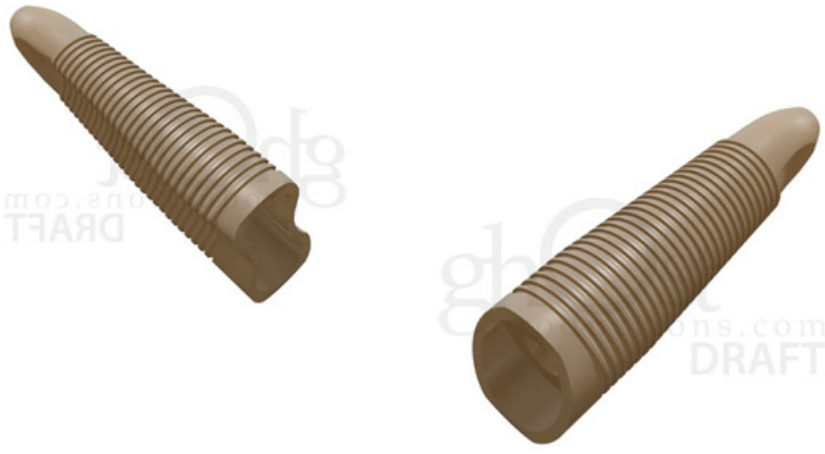
As indicated by the company, unlike traditional static implants, shape memory devices can adapt to changes in the site of implantation, such as local bone resorption, and can respond positively to implant loading to maintain secure fixation even under challenging conditions.

Devices manufactured from MedShape's primary shape memory biopolymer, PEEK Altera, have already been cleared by the FDA for human use. These devices include the Morphix Suture Anchor and the ExoShape Soft Tissue Fastener. PEEK Altera was developed by MedShape to allow the design and manufacture of unique shape-changing medical devices with excellent biocompatibility, long-term biostability and uncompromised postoperative imaging options.

"This latest issued patent is a key addition to our intellectual property portfolio and serves to consolidate the leadership position created by MedShape in the field of shape memory biopolymer medical devices," stated Ken Gall, Ph.D., chief technology officer, in the December 15, 2011 news release. "MedShape has successfully introduced new shape memory biopolymer devices that deliver tangible benefits to surgeons and patients. This patent recognizes the proprietary nature of our platform technology and is a testament to MedShape's world class research and development team."

Dr. Gall told *OTW*, "MedShape's shape memory biopolymer, PEEK Altera, has broad potential applications in numerous medical specialties, including orthopedics, cardiovascular surgery and general surgery. The issuance of this latest patent will serve to further protect our intellectual property rights as we continue to enhance surgical procedures through smarter, shape-changing biopolymer devices."

—EH (December 22, 2011)



MedShape, Inc.

It's the Pain, Stupid

Researchers looking for the cause of the dramatic increase in knee replacement surgeries in recent years have held that the aging of the population and its increasing obesity is largely responsible. Now Dr. Uyen-Sa D.T. Nguyen, DSc, of the Clinical Epidemiology Research & Training Unit of Boston University School of Medicine, and Brigham and Women's Hospital, Boston, says, in effect, "Not so fast."

Morguefile and dtl

He and his colleagues suggest that the rise in knee surgeries may be linked more to increasing knee pain or an increased awareness of knee pain, according to a December 15 article in *MedScape Today* by Steven Fox.

To understand what is driving the increase in total knee replacements, Nguyen and colleagues evaluated results from six National Health and Nutrition Examination Surveys (NHANES) conducted between 1971 and 2004, and from three exam periods in the Fram-

ingham Osteoarthritis (FOA) Study carried out between 1983 and 2005.

"We examined whether a change in the prevalence of knee pain and symptomatic knee osteoarthritis could be attributed to age, BMI [body mass index], or radiographic knee osteoarthritis," Nguyen wrote.

Participants in the NHANES surveys were between 60 and 74 years of age and there were more than 6,900 people included in the study. Participants in the FOA study were predominately Caucasian and at least 70 years old. The number of people evaluated in the FOA study were 902, 1,132, and 671 from the 3 exam periods, respectively.

Researchers asked participants in both studies whether they experienced knee pain most days. In addition, participants in the FOA study underwent bilateral weight-bearing radiographs of their knees to assess the presence and extent of osteoarthritis. Radiographs were combined with self-reported knee pain to define symptomatic knee osteoarthritis.

The researchers found that from 1974 to 1994, non-Hispanic white and Mexican-American men and women and black women, in the NHANES study experienced a 65% increase in age and BMI-adjusted knee pain.

Among FOA participants, the prevalence of age and BMI-adjusted knee pain and symptomatic osteoarthritis approximately doubled in 20 years among women, and tripled among men.

"These increases may explain the surge in knee replacement surgeries and suggest a bigger burden of knee pain in our society than previously thought," the researchers wrote.

The researchers saw no such trend among FOA participants in terms of the prevalence of radiographic evidence of osteoarthritis. "Age and BMI-adjusted prevalence of radiographic knee osteoarthritis did not substantially change over this same period for men and actually may have decreased for women "the authors noted.

The researchers conclude that even though the prevalence of knee pain, independent of increasing age and rates of obesity, has risen during the last 20 years, obesity accounted for only part of the increase. The study is published in the December issue of the *Annals of Internal Medicine*.

—BY (December 21, 2011)

Death or Revision – Which Comes First?

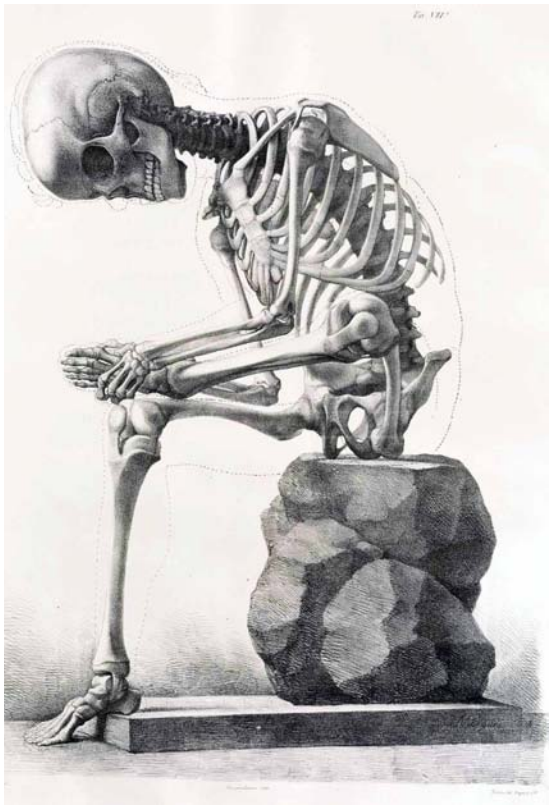
Patients about to undergo hip or knee replacement surgery often ask their doctors how long their implant will last. And surgeons, when asked that question by patients, often wonder what to tell them.

Now a study in New Zealand, published in the *British Journal of Bone and Joint Surgery* involving 4,668 patients undergoing primary total hip and knee replacements at a university hospital between 1989 and 2007, offers some answers.

Researchers found that patients younger than age 50 at the time of surgery have a greater chance of requiring a revision than they do of dying. Patients around 58 years of age have a 50-50 chance of needing a revision. In patients older than 62 years the prosthesis will normally outlast the patient. Patients who are over 77 years of age have a greater than 90% chance of dying before requiring a revision whereas those around 47 years old are, on average, twice as likely to require a revision as they are to die.

The average age of the patients in the study was 69 years old. A total of 1,175 patients (25%) had died at follow-up at a mean of ten years post-operatively. The mean age of those who died within ten years of surgery was 74.4 years (29 to 97) at the time of their surgery. There was no association of revision or death with higher comorbidity scoring of patients, grade of surgeon, or patient gender.

—BY (December 21, 2011)



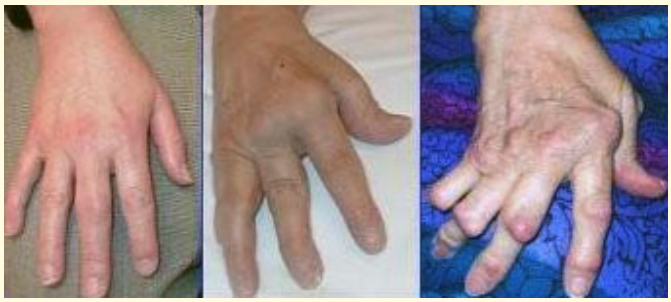
Wikimedia Commons and Francesco Bertinatti and Mecco Leone

RA Drug: FDA Accepts NDA

A beginning nod…Pfizer Inc. has announced that the FDA has accepted for review the New Drug Application (NDA) for tofacitinib, an investigational novel, oral JAK inhibitor being studied for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA). The FDA has provided an anticipated Prescription Drug User Fee Act (PDUFA) action date in August 2012 for the NDA. Pfizer has also submitted an application for this indication for tofacitinib to regulatory authorities in Japan. The European Medicines Agency is already reviewing an application for tofacitinib for the treatment of adult patients with moderate-to-severe active RA.

"Pfizer is pleased to have achieved this regulatory milestone, which reflects our commitment to advancing treatments for inflammatory conditions, and constitutes a significant step toward bringing tofacitinib to RA patients who are in need of additional therapeutic options," said Geno Germano, president and general manager, Specialty Care and Oncology, Pfizer Inc., in the December 20, 2011 news release. "We are proud of the comprehensive Phase 3 clinical program that we have completed and believe that, if approved by the FDA, tofacitinib has the potential to improve the lives of people with RA."

—EH (December 21, 2011)



Wikimedia Commons and Arnavaz

spine

Soteira Inc. of Natick, Massachusetts, has received clearance from the Food and Drug Administration (FDA) to market the company's Shield Kyphoplasty System in the U.S.

In the December 12 press release, Larry Jasinski, Soteira's president and CEO, said the system includes a "unilateral, steerable cavity creator and a self expanding stent-like implant designed to direct PMMA cement flow for optimal placement during vertebral augmentation." Jasinski also said the technology is the "first of its kind" to obtain 510(k) clearance from the FDA.

The new system, in addition to the company's existing portfolio and an "active short-cycle pipeline," allows Soteira to "work toward offering the most comprehensive product portfolio for VCF (vertebral compression fracture) treatment in the global market," continued Jasinski.

Shield Kyphoplasty System cover with cement beads/Soteira, Inc.

Michael Marks, M.D., MBA, a spine surgeon and chief of staff at Norwalk Hospital in Norwalk, Connecticut, said the

system is an exciting new development for spine surgery. "The Shield System allows me to successfully inject cement into an implant within the vertebral body which will give the structural support required while helping me to limit cement inadvertently getting into the spinal canal. The control gained from this technology will allow me to treat patients which have posed challenges in the past due to complicated fractured anatomy."

"The system has the added advantage of being a unilateral treatment which reduced the invasiveness of the procedure and has the potential to reduce radiation exposure for the patient and our surgical team," added Marks.

The company's existing portfolio includes the C3 Curved Osteotome Kit, which the company says, uses a unilateral, curving cavity creator to create a central cavity which spans the sagittal midline, or target areas for cavity creation. An adjustable blade is used to create the cavity. Degree of blade adjustment allows for the creation of cavities with a diameter to match the anatomical requirements of each fracture.

Soteira is a privately held venture-backed company incorporated in 2004 to develop and market a new generation of technologies for the treatment of vertebral compression fractures. In 2008, the company established a subsidiary company, Soteira GmbH, to lead the company's European commercialization efforts. Sotiera GmbH currently manages distribution of the Soteira products in Germany, Spain, Italy, Belgium, and Austria.

—WE (December 22, 2011)

Oregon and York, England Join Yale for Infuse Study

Yale University's review of the clinical data relating to Medtronic's Infuse bone growth protein will be conducted by two separate research organizations, one located in Oregon and the other in the United Kingdom. The West Coast team is from the *Oregon Evidence-based Practice Center at Oregon Health & Science University* in Portland. The UK team is from the *Centre for Reviews and Dissemination* at the University of York. Each team will issue separate reports, which are expected to be completed by the summer of 2012, according to a release from *Mass Device*.

The Yale investigation is led by rock-star scientist Dr. Harlan Krumholz and is underwritten by a $2.5 million grant by Medtronic to Yale University. The Minneapolis firm is providing access to the entire data set from its trials of the Infuse compound, called recombinant bone morphogenic protein-2 (rhBMP-2).

"This project is setting a new standard of transparency and will ensure that all data about this product is made publicly available and scrutinized by those with an interest in the drug," Krumholz said.

The controversy over the Infuse product, including allegations of underreporting of adverse events, arose during the summer when *The Spine Journal* dedicated its entire June 2011 issue to exposing what it claimed were problems with growth proteins, including a repudiation of some of the research surrounding Infuse.

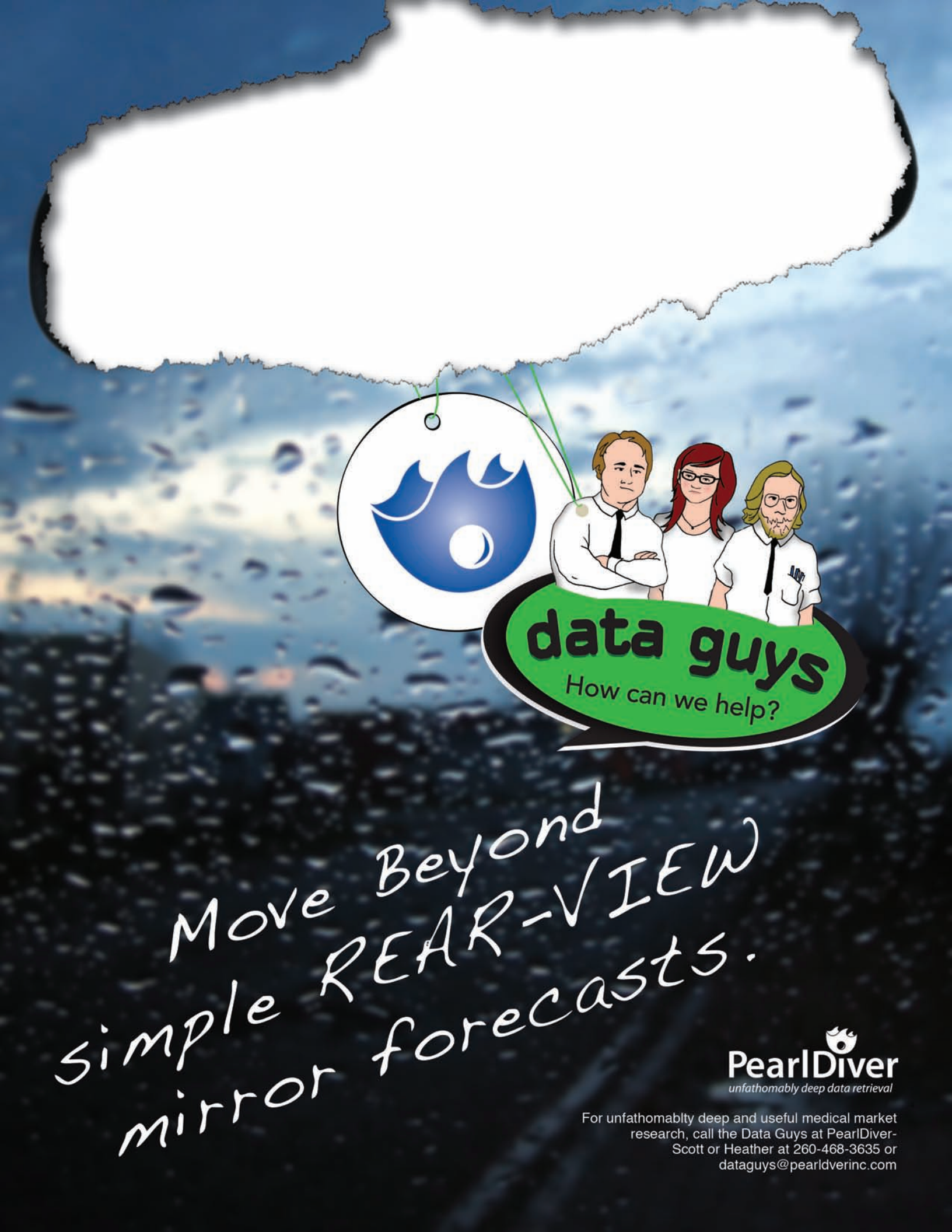
The journal's investigation claimed to have found that 13 studies (published by authors who collectively received millions from Medtronic) downplayed or omitted entirely evidence of safety risks from Infuse.

Many of those claims are being disputed by *OTW*.

In a June statement, Medtronic CEO Omar Ishrak said, "For several years Medtronic has been leading the industry in reforms designed to eliminate or mitigate conflicts of interest. We will continue to investigate questions surrounding researchers' potential conflicts of interest, refine our policies as warranted, and strive to lead the industry in ethical and transparent business practices."

—BY (December 19, 2011)

Compliments of: University of York England and Oregon Health & Science University


data guys
How can we help?
Move Beyond simple REAR-VIEW mirror forecasts.
PearlDiver
unfathomably deep data retrieval
For unfathomablty deep and useful medical market research, call the Data Guys at PearlDiver- Scott or Heather at 260-468-3635 or dataguys@pearldverinc.com

Orthopedics This Week | RRY Publications LLC

Main Contact Information:
RRY Publications LLC
116 Ivywood Lane • Wayne, PA 19087
TOLL FREE: 1-888-749-2153
Fax: 610-260-6451

Robin R. Young, CFA
Editor and Publisher
robin@ryortho.com

Elizabeth Hofheinz, M.P.H., M.Ed.
Senior Writer
elizabeth@ryortho.com

Walter Eisner
Senior Writer
walter@ryortho.com

Tom Bishow
Vice President of Sales
tom@ryortho.com

Biloine W. Young
Writer
bgwy@msn.com

Suzanne Kirchner
Production Manager
suzanne@ryortho.com

Jayme Johnson
Production Coordinator
jayme@ryortho.com

Dana Bader
Graphic Designer
dana@ryortho.com