VOLUME 5, ISSUE 19 | JUNE 23, 2009

Orthopedics This Week

week in review

the picture of success

breaking news

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Orthopedics • This Week
VOLUME 5, ISSUE 19 | JUNE 23, 2009

Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

This Week: How will healthcare reform affect sales and earnings of orthopedic companies? The chattering class in Washington will talk about revenue caps. DRG's on steroids. Reconciliation is likely dead as Democratic leadership backs away. No question, though, trend is toward less variability in medical care.

Rank	Last Week	Company	TTM Op Margin	30-Day Price Change	Comment
1	1	Integra LifeSciences	12.35%	7.24%	2nd least expensive orthopedic stock as measured by P/E, PEG and PSR. P/E is 80% of expected earnings growth rate.
2	4	Symmetry	11.05	18.56	#1 least expensive orthopedic stock AND insiders are buying stock…again. Could they possibly know something we don't?
3	2	Exactech	13.42	0.00	Amazingly diversified small orthopedic company. Spine, shoulder, hip, knee, biologics plus distribution all over the world.
4	5	ArthroCare	16.87	12.26	Settled with State Farm but lost an arbitration decision with Gyrus Medical for $11.7 million—2 steps forward and 1 step back.
5	8	Stryker	23.18	2.60	Barron's picks SYK for a sharp rebound. 8th least expensive stock in ortho, certainly the price is right.
6	7	CONMED	9.80	12.11	"Sell" rating issued by Zacks. We disagree. Hospital spending will recover in coming 12 months. Good news for Linvatec/CONMED.
7	3	Orthofix	8.14	10.50	After nearly a 60% run since the first of the year but with only 1.9% sales growth forecast in 2Q, stock is losing steam.
8	6	Zimmer	29.96	(6.33)	We have faith in big blue Z's products and distribution but, oh my, the soft, people issues remain ZMH's greatest challenge.
9	10	Medtronic	31.68	6.93	When was the last new spine product that made surgeons go, "wow"? It's been a very long while.
10	9	Johnson & Johnson	25.36	1.25	The Republic of JNJ is expected to report a 9% decline in sales for 2Q. DePuy, however, should report decent sales growth.

Robin Young's Orthopedic Universe

Top Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	Alphatec Holdings	ATEC	$3.15	$150	54.4%
2	Orthovita	VITA	$5.02	$382	52.1%
3	I Flow Corp	IFLO	$6.70	$164	27.1%
4	NuVasive	NUVA	$43.48	$1,580	23.0%
5	Symmetry Medical	SMA	$8.88	$318	18.6%
6	Capstone Therapeutics	CAPS	$0.82	$33	17.1%
7	RTI Biologics Inc	RTIX	$4.54	$246	17.0%
8	CryoLife	CRY	$5.77	$163	15.9%
9	TiGenix	TIG.BR	$6.26	$152	13.6%
10	Kensey Nash	KNSY	$25.96	$295	12.5%

Worst Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	Regen Biologics	RGBO.OB	$2.09	$20	-16.4%
2	TranS1	TSON	$6.80	$140	-13.8%
3	Zimmer Holdings	ZMH	$42.47	$9,140	-6.3%
4	Synthes	SYST.VX	$101.36	$12,033	-1.6%
5	Exactech	EXAC	$14.61	$187	0.0%
6	Johnson & Johnson	JNJ	$56.09	$154,560	1.2%
7	*Average*			*$9,344*	*2.2%*
8	Stryker	SYK	$40.32	$16,010	2.6%
9	Mako Surgical	MAKO	$8.75	$219	3.1%
10	Medtronic	MDT	$33.96	$37,870	6.9%

Lowest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	ArthroCare	ARTC	$11.00	$293	6.46
2	Symmetry Medical	SMA	$8.88	$318	7.70
3	Zimmer Holdings	ZMH	$42.47	$9,140	10.43
4	Medtronic	MDT	$33.96	$37,870	11.58
5	CONMED	CNMD	$16.29	$473	12.20

Highest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Osteotech	OSTE	$4.34	$78	140.28
2	I Flow Corp	IFLO	$6.70	$164	69.60
3	Smith & Nephew	SNN	$37.56	$6,630	67.15
4	NuVasive	NUVA	$43.48	$1,580	50.01
5	RTI Biologics Inc	RTIX	$4.54	$246	38.97

Lowest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	ArthroCare	ARTC	$11.00	$293	0.26
2	Symmetry Medical	SMA	$8.88	$318	0.76
3	Integra LifeSciences	IART	$26.35	$748	0.80
4	Exactech	EXAC	$14.61	$187	0.81
5	CryoLife	CRY	$5.77	$163	0.92

Highest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	NuVasive	NUVA	$43.48	$1,580	9.90
2	RTI Biologics Inc	RTIX	$4.54	$246	2.26
3	Johnson & Johnson	JNJ	$56.09	$154,560	1.59
4	*Average*			*$9,344*	*1.48*
5	CONMED	CNMD	$16.29	$473	1.46

Lowest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	CONMED	CNMD	$16.29	$473	0.66
2	Osteotech	OSTE	$4.34	$78	0.72
3	Symmetry Medical	SMA	$8.88	$318	0.74
4	ArthroCare	ARTC	$11.00	$293	0.87
5	Orthofix	OFIX	$25.89	$443	0.88

Highest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	TiGenix	TIG.BR	$6.26	$152	345.77
2	Mako Surgical	MAKO	$8.75	$219	34.59
3	Regen Biologics	RGBO.OB	$2.09	$20	15.46
4	NuVasive	NUVA	$43.48	$1,580	5.67
5	TranS1	TSON	$6.80	$140	5.10

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Inside the Synthes Indictment

By Walter Eisner

Did Synthes, its Norian subsidiary, and four senior company executives conspire to conduct an illegal clinical trial, promote off-label use of a bone void filler and lie to the FDA about what they had done?

U.S. Attorney Michael Levy

Michael Levy, the U.S. Attorney in Philadelphia, thinks so and has convinced a federal grand jury that there is enough evidence available of criminal activity to let a jury decide.

The grand jury returned a 58-page criminal indictment on June 16 against Synthes, Inc., Norian Corporation and four Synthes executives: Mike Huggins, Tom Higgins, Richard Bohner, and John Walsh.

Huggins was the President of Synthes North America during the time of the alleged felonies, and in February 2004 he became the President of Synthes Spine.

Higgins was the President of Synthes Spine and reported to Huggins. He left that position in February 2004 to become Synthes' Senior Vice President of Global Strategy.

Bohner was Synthes' Vice President of Operations and reported to Huggins.

Walsh started as Synthes' Director of Regulatory and Clinical Affairs, Spine Division in 2003 and reported to Bohner and later Huggins.

The Charges

The defendants are being charged with conducting clinical trials without authorization of the FDA which, prosecutors say, resulted in the deaths of three patients.

Norian is charged with a total of 52 felony counts: one count of conspiracy to impair and impede the lawful function of the FDA and to commit crimes against the U.S., seven counts of making false statements in connection with an FDA inspection, and 44 counts of shipping adulterated and misbranded Norian XR in interstate commerce with intent to defraud.

The parent company, Synthes, is charged with 44 misdemeanor counts of shipping adulterated and misbranded Norian XR in interstate commerce.

The four executives are each charged with one misdemeanor count of shipping adulterated and misbranded Norian XR in interstate commerce.

The Investigation

Synthes received a grand jury subpoena in early 2006 regarding off-label use of Norian XR. The indictments resulted from the nearly three-year-long investigation.

The case was investigated by the United States Food and Drug Administration (FDA) Office of Criminal Investigations; the United States Department of Health and Human Services (HHS) Office of Inspector General (OIG); the Department of Defense Criminal Investigative Service (DCIS), and the Veterans Administration OIG.

U.S. Attorney Michael Levy in announcing the indictments said, "The defendants charged today bypassed the [FDA] process, with the knowledge that the product that they were marketing posed potentially significant risks. When predictable bad results occurred, they lied to the FDA investigators. They put their profits ahead of responsible business practices and the truth."

The HHS' OIG Office of Investigations Special Agent-in-Charge Patrick Doyle said, "It is never acceptable for the health care industry to place the profit motive over people's wellbeing…. Should these companies and executives ultimately be found guilty, they will have to pay a price for placing at risk the very people for whom they purported to provide relief."

The U.S. Department of Veterans Affairs was involved in the investigation because some of the procedures were performed at VA hospitals. Officials did not release the names of the hospitals.

"The Department of Defense is outraged by a company that potentially puts our military personnel, their family members, and veterans at undue risk for serious medical complications or even death, just to increase their corporate bottom line," Assistant Special Agent-in-Charge Kenneth Maupin, of the Defense Criminal Investigative Service, said in a statement.

Synthes Responds

Indictments are always one side of the story. Prosecutors get to make their case public while the accused usually have to hold their powder dry and wait to defend themselves in court. However, Synthes spokesperson Gilgian Eisner told OTW on June 19 that the picture painted by the Department of Justice is very distorted and has misled the media and the public.

He says Synthes will dispute many of the facts alleged by the government and the indictment is full of statements with which the company disagrees.

Synthes is particularly adamant that there is no conclusive evidence either way that the use of its bone filler product contributed in any way to the deaths of the three patients. Eisner says Synthes will defend itself vigorously to the charges of conducting an unauthorized clinical trial and promoting the off-label use of a device that was not approved or cleared by the FDA for the uses described in the indictment.

This is the third widely publicized biologic bone product that has attracted the attention of federal prosecutors and officials. The U.S. Attorney in Boston filed criminal charges against Stryker this past year over the marketing of its OP-1 product, and Medtronic continues to be pestered by Senator Charles Grassley's ongoing investigation of the off-label use of Medtronic's InFuse® product and the company's relationship with surgeon consultants.

What is notable in these cases is that they are bringing criminal indictments instead of civil suits. It is one thing to get sued and quite another to tell your shareholders that prosecutors think you are a possible criminal.

Norian Bone Cements

Synthes acquired Norian Corporation in July 1999. Before that, Synthes did not have a presence in osteobiologic products to go along with its wide array of mechanical implant devices and instruments.

Prior to its acquisition by Synthes, Norian had developed, manufactured and sold two calcium phosphate bone cements, called Norian Cranial Repair System (CRS) and Norian Skeletal Repair System (SRS).

The cranial product was a Class II device and had been cleared by the FDA to be marketed for filling defects in the skull. SRS was a Class III device that had been approved by the FDA to be marketed for use in the distal radius, a long bone in the arm.

Norian System (Bone Cement)

From the beginning, says Levy, the intended market for the successor product of CRS, Norian XR, was the unapproved use in surgeries to treat vertebral compression fractures (VCFs).

New Uses and Markets

In the spring of 2000, say prosecutors, Synthes Spine's product development team interviewed orthopedic surgeons and others who used PMMA (polymethylmethacrylate) off-label to treat VCFs, inquiring as to whether they had used SRS in such surgeries. Prosecutors say the purpose of those interviews was to create a market for the SRS with radiopaque barium sulfate. This product was eventually brought to market as Norian XR.

In June 2000, company employees, at the direction of Tom Higgins, summarized the results of the interviews in an Executive Summary distributed to Synthes management. The Summary, according to prosecutors, stated that there was "excitement about using Norian for vertebroplasties" among the surgeons and the market potential for Synthes was considerable.

By late summer 2000, Synthes began development of the Synthes Vertebroplasty System for treating VCFs. The system consisted of SRS-R and a group of Class I instruments to inject the SRS-R.

Norian XR was cleared for sale by the FDA in 2002 as a medical device to treat bone voids or defects in the skeletal system. Synthes marketed Norian XR from 2002 to 2004, only selling approximately 200 units and realizing total net sales of approximately $400,000.

The marketing clearance by the FDA made it clear that Norian XR was not intended for use in the spine. Prosecutors say that Synthes always had its eye on obtaining an indication for use in the spine.

IDE or "Test Market"

The indictment says that the company recognized early on that there were two possible solutions to accomplish this strategy:

First, the legal solution, which was to disclose to the FDA the intended use of the product and then to try to secure FDA approval of XR for use in surgeries to treat VCFs after obtaining an investigational device exemption ("IDE") to investigate the safety and efficacy of the product. Or, second,

Person No. 7

the illegal solution, which was to promote XR for use in VCFs through a limited so-called "test market," during which the company would evaluate the safety and efficacy of the product in unapproved clinical trials and judge the success according to its own standards. The indictment charges that the company and its coconspirators consciously and deliberately chose the illegal solution.

Starting as soon as late summer 2002, the company allegedly approached selected spine surgeons and asked them to use the predecessor device, SRS, in VCF procedures as part of an initial Synthes "test market" for SRS.

While the FDA had approved Norian XR for some uses, the agency insisted in its clearance to treat bone voids and defects, that Synthes needed to conduct clinical trials if it wanted to expand the uses of Norian XR to treat spinal fractures.

However, a company executive identified in the indictment as "Person No. 7" decided not to conduct clinical trials. Instead, No. 7 said the company should "get a few sites to perform 60–80 procedures and help them publish their clinical results," according to the indictment.

The indictment does not identify "Person No. 7," but it says he was the chief executive officer and a large shareholder. The Philadelphia Inquirer reported on June 17 that a company spokesman identified Hansjörg Wyss as the CEO while the tests occurred.

Synthes did not confirm or deny to *OTW* that Wyss was Person No. 7.

The "Test Market" Campaign

According to the indictment, the company conducted two XR "Test Market Kick-Off" surgeon meetings, and one surgeon forum from August 2003 through mid-January 2004, training approximately 52 spine surgeons how to use Norian XR to treat VCFs.

Huggins, Higgins and Bohner attended the first surgeon meeting on August 15 and 16, 2003, held in San Diego with spine surgeons selected by Synthes. Surgeon travel expenses were paid by Synthes. It's alleged in the indictment that lectures and PowerPoint presentations were given concerning the use of Norian XR in vertebroplasty to treat VCFs, and that a lab was held during which the surgeons injected Norian XR into the vertebral bodies of cadavers.

A second training meeting was held in Charlotte, North Carolina, on September 19 and 20, 2003.

Brent Constantz, the founder and former CEO of Norian, told us during a phone interview on June 18 that the San Diego meeting showed the **"most blatant disregard for FDA regulations in promoting off-label use"** he had ever seen.

Patient Deaths

The indictment charges that after the death of a third person (this time on January 22, 2004) during a surgery in which a Norian cement was used to treat VCFs, the company cancelled future surgeon forums.

The two previous deaths also occurred on the operating table with patients suffering from a rapid drop of blood pressure. Synthes sales reps were present at each surgery. No definitive evidence was presented to determine whether or not the Synthes device was the cause of death.

The indictment alleges that the company considered, but rejected, the idea of recalling or removing XR from the market. Either action would have required Synthes to notify the FDA of the patient deaths.

FDA Inspection

But the FDA was already watching and conducted an unannounced inspection at the Norian plant in West Chester, Pennsylvania, from May 11 through June 18, 2004.

The inspection focused on whether or not Norian and Synthes had conducted an unauthorized clinical trial of XR. The indictment alleges that a number of Synthes employees, including Huggins, Bohner and Walsh, made materially false and misleading statements to the FDA investigator during that inspection period.

The indictment says that on May 19, 2004, Norian and Synthes made false and fraudulent statements to the FDA investigator by stating that, in August 2003, Synthes did not have a vertebroplasty system. Another Synthes employee allegedly made a false statement on May 27, 2004, by characterizing the summer 2002 "test market" for SRS in the spine as surgeons mixing SRS with barium sulfate "on their own."

On June 16, 2004, say prosecutors, Bohner told the investigator that he knew nothing about a vertebroplasty "test market" for SRS. Bohner also told the FDA that the 34 "test market" cases discussed at a July 18, 2003, safety meeting involved only data that Synthes had collected from what surgeons were doing on their own, rather than a test market conducted by Synthes.

Prosecutors say that the July 18, 2003, "safety meeting" detailed the adverse events and first death. They say Huggins, Higgins and Bohner decided to continue the illegal XR "test market" that had begun in the summer of 2002 with SRS-R, in order to assess whether the level of risk from using Norian XR was acceptable or too high.

The indictment states that the following month, Huggins noted that Synthes had a "poor record of PMA approvals" and Huggins and Higgins directed that the "test market" would continue.

FDA Observations

At the close of the inspection, the investigator for the FDA issued the agency's observations to Norian. Among other things, the FDA observed that Norian:

- Did not submit an IDE application to the FDA prior to initiating the Norian XR "test market."
- Shipped Norian XR for the purpose of use in vertebroplasty and kyphoplasty procedures to treat fractures of the vertebrae, an indication for which Norian XR had not been cleared or approved by the FDA.

Final Warnings

The criminal indictment is filled with lists and transcripts of meetings, emails and grand jury testimony that paint a disturbing picture of Synthes executives suppressing and ignoring warnings from physicians and employees that the company needed to pursue a different regulatory track.

For example, on September 26, 2003, prosecutors say a spine surgeon told Synthes that, because the Norian XR "test market" was collecting information from surgeons performing vertebroplasty and kyphoplasty surgeries to treat VCFs, he believed that Synthes was required to go to each IRB of each hospital participating in the "test market." He also told them that, in his view, Synthes had risk management problems and needed more oversight of its clinical and compliance issues.

A month later, Huggins, Higgins and Bohner allegedly received an email from a Synthes employee with an attachment of Synthes' initial proposal for obtaining an IDE from the FDA that was never submitted.

"Synthes is at an increased legal risk."

The IDE proposal (which is detailed in the indictment) discussed the Norian XR "test market" and the fact that two patient deaths had occurred. The proposal went on to state:

"Currently, Norian XR is being used off-label to treat VCFs. The FDA has been very conservative regarding the treatment of VCFs and has issued numerous statements...cautioning companies...that the use of any material in vertebroplasty/kyphoplasty is off-label. The present state of the approved indication of Norian XR and the FDA bulletin puts Synthes in a compromising position. Synthes is at an increased legal risk with regards to product liability and medical malpractice.... We recommend that Synthes pursue an IDE for the usage of Norian XR in treating VCFs...."

Synthes' Reputation on Trial

The financial impact of this indictment on Synthes is likely to be small. "We believe even if Synthes is held liable for off-label promotion, it would probably only apply to a small number of these patients which would make the potential economic exposure quite manageable for a company with $1 billion in cash on its balance sheet," Kepler Capital Markets analyst Florian Gaiser told Reuters on June 17.

"Synthes and the [U.S.] attorney might settle the case for between $1 million and $10 million, or 0.1% to 1.0% of estimated 2010 group profit," said Vontobel analyst Christoph Gubler. "The realized sales are extremely small. The court case will probably take several years to conclude," continued Gubler.

While the financial impact on Synthes may be small relative to its size, the company's reputation, which is founded in the oldest orthopedic traditions of Europe, is clearly at stake. It's hard to believe that the company would risk its reputation on a relatively small market niche. Perhaps this was simply a horrendous strategic blunder in getting a new product on the market or a case of rogue employees who acted outside company guidelines.

Or, perhaps this is another case of a company caught in the murky and confusing FDA regulatory scheme regarding the off-label use of devices.

Whether this indictment will find its way to a jury is unknown. Whatever happens, we hope the resolution of this case is transparent, informative and will serve to offer a guide to companies who want to bring new devices to the market.

Pass/Fail: Fellowships and Patient Safety

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

Is he ready? Are her hands sufficiently dexterous? Is he fluent in the details of this procedure? Such are the questions that veteran surgeons must address when handing responsibility—and surgical drills—to fellows.

Advice From Dr. Bray

Dr. Robert Bray, Founding Director and CEO of Diagnostic and Interventional Spinal Care (D.I.S.C.) in Marina del Rey, California, has had fellows of all talents and characteristics pass through his doors. He says, "Fellows, like fellowships, differ widely. Most of the fellows I work with start out by thinking that they're ready to do the procedure themselves. They are often frustrated, however, because I start them out very slowly and at first let them do almost nothing. They observe me first, and then I gradually allow them to do pieces of the surgery—first exposure, then drilling, etc.—all based on their competency levels. In general, fellowship mentors differ in how quickly they bring fellows along in the OR."

So you can't just hand things off to a fellow, thinking, "Great. That's one less thing I have to do." Dr. Bray explains, "What a lot of people don't know is that it's actually a lot of work to have a fellow. There are many surgeons who view having fellows as a chance to withdraw themselves from the 'grunt work' of things such as labs, putting a chart together, doing a history and physical, surgery prep, and weekend rounds. The problem with this is that many of those things are integral to patient care. I have to know my patient…and the only way I'm going to do that is to have 'face time' with them."

"I am involved in labs, do rounds with the patients, etc. Fellows really need to be observed by a mentor every step of the way. I have seen cases where fellows have been allowed to operate without much supervision—or no supervision—and got into trouble with the nerve linings and screw placement."

Advocating for staying involved, Dr. Bray says, "Take the old adage that to get a good outcome you need to have the right patient, the right surgery, done right. If you offload a number of responsibilities then how will you know you are hitting these marks? There is a careful decision making process involving patient evaluation

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and the selection of the appropriate procedure. When the wrong procedure is done it is sometimes because the mentor didn't put enough time into choosing the right procedure."

One thing is for sure. Surgeons didn't become surgeons to have their hands tied behind their backs. Dr. Bray: "There are two types of fellowships, one in which trainees are active and one in which they just observe. You can't ever completely learn just by observing. At some point before you are 'let loose' on the public you should have hands-on experience that is properly supervised. Actually, I am of the opinion that there should be a totally different certificate for those individuals who have done an observational only fellowship."

A patient may think that because Dr. X has completed a fellowship, he or she is fully trained and competent. Speaking to this issue of quality, Dr. Bray states, "The fact that there is no rating system for fellows is controversial and is something that needs to be worked out. It's usually a pass/fail designation…and hardly anyone is designated as failing. When someone gets a certificate at the end of the year it doesn't say that the person is competent or got a high score. I have had frank discussions with some fellows who have completed the fellowship year, but needed more time to master different concepts/procedures. I've advised them to do more time somewhere else. Fortunately, they have taken this advice."

"Where is the umbrella and the measuring stick?" asks Dr. Bray. "At present we have no superstructure that regulates fellowships. Nor do we have any type of ranking of the programs for spine. It seems to go by subspecialty, i.e., for spine surgery there is no approving structure, whereas for sports medicine there is an AAOS approved fellowship. Having oversight and solid guidelines would help ensure high quality training. For example, we need a guideline saying that you must be present at every case your fellow does. And, as the situation is now, any orthopedist or neurosurgeon in private practice can take out an ad saying, 'I do spine surgery and am accepting fellows.' Then at the end of the year he or she just prints a certificate off the computer. That is just too random."

And now to the less tangible, but important topic of vainglory. Even if the fellow who casts his shadow upon your doorstep is short of stature, his ego may be large. "While fellows can and should have a healthy ego, they have to be open to learning new things," says Dr. Bray. "On occasion I have a new fellow who wants to show everyone 'how it's done,' at which point I make it clear that this is not the reason they're here. Fortunately, with years of experience behind me, I can demonstrate to them there is still a lot to learn. Once the fellow realizes this they usually move forward quickly. It really depends on the individual. I have some people doing a lot by the three month mark, but with others I have to take things more slowly. And yes, for those who have to wait longer, it's tough on their egos. But they do catch up at some point."

Dr. Wolf Weighs In

For Dr. Brian R. Wolf, the Director of the Sports Medicine Fellowship at the University of Iowa, "preparation" is the mantra. "First of all, you must thoroughly assess each fellow's capabilities and knowledge levels. I sit down with the fellows before each case and talk about the plan and how we'll fix xyz problem should it arise. I go into the OR knowing exactly how hands-on I will be. Having weekly case conferences is also an important part of planning. Reviewing, for example, 'Here is a shoulder injury and here is what I'm thinking needs to be done. This is what you need to think about from an anatomical viewpoint, from a technical viewpoint and a post operative plan viewpoint.'"

And if the fellow finds himself in dire straights? Dr. Wolf: "Let's say we're ready to start arthroscopically fixing a rotator cuff and we're allowing the fellow to actively participate. He is passing the main sutures, but having some difficulty. The patient's shoulder is getting more swollen and we need to be finishing up to avoid having prolonged anesthesia time. At that juncture the roles are exchanged and instead of being the fellow's assistant I become the primary surgeon. Later there is a post-op meeting about what went wrong. During this time I have to help the fellow understand that dragging out the procedure means that suture management and repair gets more difficult the longer the case goes on. Plus, there is a risk that the patient's hospital or recovery room stay will be lengthened when you have a longer anesthesia time."

For a fellow who is struggling, the most important thing, says Dr. Wolf, is that you don't set him or her up for further failure. "If necessary, we need to provide fellows with avenues other than the operating room suite to improve their skills. For example, we have an arthroscopy and surgery teaching lab where they have access to cadaveric specimens. Our fellows are scheduled to spend time in the learning lab every week working on surgical skills and approaches. This is a great setting for getting more familiar with new instruments and practice procedures in a low pressure environment. If we identify some deficient skills for a particular fellow we will have them spend extra time working on things in the training lab."

While it's informative to talk to fellows, it's even better, says Dr. Wolf, to closely watch their actions when you first begin working with them. "Some fellows talk a big game but when it comes time to display their knowledge, they have not yet mastered the skill. At the same time there are always silent superstars out there who don't say too much, but are highly talented. The only way to get a grasp on what exactly they can do is to watch them closely."

"Every fellow has basic things that he or she has learned in residency… and all cases have simple and complex aspects. This means that you can gauge their skill levels right away, early in the fellowship year, no matter what they tell you. I will ask them, 'Have you seen or done this in residency, learned about this in the lab, or read about it?' Within 5 minutes of them participating in the simple parts of the case I can get a good idea of their

talent/skill level. That then also plays into how much involvement they'll have in the more challenging parts of a case. This evaluation continues throughout the fellowship training year, and as the fellow masters more skills he or she becomes more involved."

At certain times, says Dr. Wolf, observation has its place. "I've come to the conclusion that if you're a good learner then you can learn by watching—your hands don't necessarily have to be active in the case. Observation would be appropriate when fellows are seeing a technique or procedure for the first time. Then as they become familiar with the skills and techniques needed they gradually are involved more actively in cases as the fellowship year proceeds."

As for any formal assessment of trainees, Dr. Wolf calls upon images emanating from the Middle Ages: "Medicine and surgery remain bound to the tradition of apprenticeships. A more structured way of determining fellows' readiness for the world is likely coming down the pike, but as of yet there is no surgical skill test to pass other than their mentors' subjective assessment. The onus is on the educators to ensure that their protégés are truly prepared to undertake high level surgery. Orthopedic surgery and neurosurgery are two of the most highly sought after fields for medical students, so I do feel that we're getting the best and brightest."

In the end, it's up to the student to find the right mentor, and it's up to the mentor to take full responsibility for his or her apprentice. And, it's the mentor who should be doing most of the observing…of the fellow.

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Stem Cell Debate Is History

By Robin Young

The only stem cell that has NOT been associated with a cure of some disease or affliction is, ironically enough, the embryonic stem cell. We could not find in the literature a single case of any patient—*not one*—that has been cured of anything using embryonic stem cells. On the other hand, the number of case reports where adult stem cells reportedly cured patients is in the hundreds.

Probably the most famous of these is Osiris Therapeutics' GVHD (graft-versus-host disease) patients. In the Phase II trial completed last year, the company reported that of the 32 patients enrolled in the trial, 94% responded after receiving two infusions of adult stem cells (Prochymal), and 74% of these respondents had total clinical resolution of the disease. In addition, those patients who experienced a complete response rate by day 28 had a statistically significant improvement in survival as compared to patients experiencing a partial or non-response.

Dr. Anthony Atala

Why, therefore, are the press and most of the general public still talking about embryonic stem cells?

Dr. Anthony Atala, Director of Wake Forest's Institute of Regenerative Medicine and the leading researcher of using birth tissues to supply stem cells for therapeutic use, said, "When compared with embryonic stem cells, amniotic fluid stem cells (AFS) have two main advantages: First, no embryo needs to be harmed in harvesting the cells, sidestepping a major hot-button political issue, and [second] AFS cells will not form tumor cells, as the considerably more raw embryo-derived cells can."

"They're not as early and they're not as wild," he explains. "The cells are further along the line of development—and you don't see fetuses developing tumors—so these cells are much more controlled."

Embryonic stem cells are harvested from two sources: 1) Embryos – harvesting living embryos that are 5–7 days old. This method results in the death of the embryo. 2) Fetuses – stem cells are harvested from miscarriages or aborted babies.

Adult stem cells, on the other hand, seem to be popping up everywhere. *The Journal of Translational Medicine* (Jazedje T, Perin PM, Czeresnia CE, et al. Human fallopian tube: a new source of multipotent adult mesenchymal stem cells discarded in surgical procedures. J *Transl Med.* 2009;7:46 Epub) reported last week that Fallopian tubes removed from fertile women of child-bearing age during hysterectomies or other procedures are an amazingly rich source of stem cells or, more accurately stated, limited lineage progenitor cells.

These are not embryonic cells. Instead, these cells have already progressed down a particularly evolutionary pathway—specifically, the lineage that leads to muscles, bones, nerves, or blood vessels. These cells, for example, won't evolve into eyes or brain or teeth.

Researchers from the University of Sao Paulo in Brazil found that human fallopian tubes are rich in mesenchymal stem cells. The team isolated and grew these cells in a laboratory and differentiated them into muscle, fat, cartilage, and bone cell lines.

"In addition to providing an additional potential source for regenerative medicine, these findings might contribute to reproductive science as a whole," study leader Tatiana Jazedje, of the university's Human Genome Research Center, said in a news release from the journal's publisher.

Past studies have also shown success with isolating and differentiating mesenchymal stem cells harvested from umbilical cords, dental pulp and body fat.

Then we ran across Dr. Angela Christiano's paper in *Cell*. Dr. Christiano is the Director of the Basic Science Research Group as well as the Richard and Mildred Rhodebeck Professor of Dermatology and Professor of Genetics at Columbia University. Her research has shown that two subpopulations of cells exist **within the hair follicle**, including stem cells.

Dr. Angela Christiano

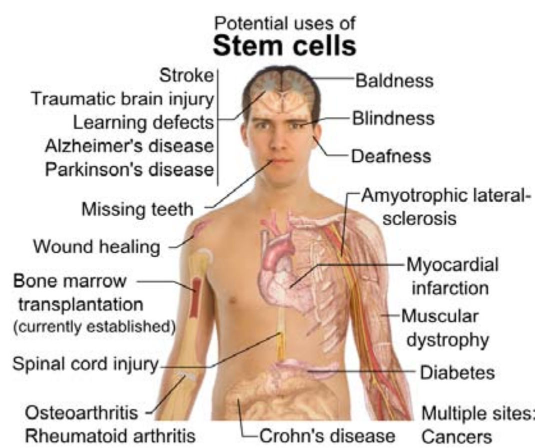
These progenitor cells, Dr. Christiano showed, have significant plasticity and can differentiate into bone marrow, muscle, bone, fat, and neural cells. The neuronal differentiation of hair follicle stem cells, together with their ease of access as adult stem cells, prompted Dr. Christiano and her team to study the use of hair follicle stem cells for neurological and degenerative diseases.

Birth tissues, hair follicles, bone marrow, retina, intestines, teeth enamel, and fat. Where will it end? In fact, we have even found articles that describe harvesting neural stem cells from areas of cadaver brains as part of standard allograft recovery processes.

The contrast with embryonic research is startling. So much so that any debate about the relative merits of adult versus embryonic stem cells is settled. Done. Stick a fork in it. Embryonic stem cell research is still looking for its first cure without, incidentally, triggering a tumor.

Embryonic cells can be tumorigenic. This past February, an online article detailed the case of a 9-year-old boy suffering from ataxia-telangiectasia, a childhood disease that causes degeneration of parts of the brain. The condition has no cure. So the child's parents went to the Soviet Union for embryonic stem cell injections. A benign brain tumor resulted. Surgeons in Israel removed the tumor, wrote the case up and published it in the February 2009 online version of *Scientific American*.

Adult stem cells, also known as limited lineage progenitor cells, have overwhelming advantages over embryonic stem cells including:



Source: Wikimedia Commons images, author Mikael Haggstrom, Public Domain

Orthopedics This Week
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1. Plentiful supply
2. Thousands of relevant case histories
3. Rich clinical history with more than 100,000 patients treated
4. Easy to harvest or purchase (allograft or autologous)
5. Non-tumorigenic
6. Ease of implantation

This year, we estimate, limited lineage progenitor cells whether in allograft form or autologous forms (bone marrow or adipose tissues) will be used in more than 20,000 patients and generate more than $85 million in revenues. By the end of this year, four companies will be offering products with limited lineage progenitor cells. By the end of 2010, that number could double.

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Cerebral Palsy Surgery Lagging Research?

By Scott Ellison, PearlDiver Large Joints Analyst

Patients with cerebral palsy (CP) present special problems to their orthopedists. Often a single patient must be treated for numerous issues involving spasticity, problems with gait, large joints, the spine and extremities. Therein lies the question: since so many CP patients are children, should they be treated with multiple procedures spaced throughout their adolescence to take into account their growing bodies, or should multiple procedures be done all at once?

According to United Cerebral Palsy 1.5 to 2 million children and adults have CP in the United States. An additional 10,000 infants are diagnosed each year along with an estimated 1,500 pre-school children. Their diagnoses fall into five areas:

1. Hemiplegic Cerebral Palsy – affects one side of the body
2. Diplegic Cerebral Palsy – affects all four limbs, although weakness and spasticity are more severe in the lower limbs
3. Quadriplegic Cerebral Palsy – affects all four limbs to an equal extent
4. Monoplegic Cerebral Palsy – affects a single limb
5. Unspecified Cerebral Palsy – extent affected is not specified

Patients with CP are further classified by their level of severity under the Gross Motor Function Classification System (GMFCS). This ranges from Level 1, very few symptoms of cerebral palsy, to Level 5, which covers severe physical restrictions requiring full assistance.

The levels are:
1. Patient has few indications of CP
2. Patient uses an orthotic and may have trouble with stairs
3. Patient needs crutches or walkers
4. Patient needs an electric wheelchair
5. Patient requires full time care

The treatment goal for ambulatory children at levels 1 and 2 is to improve the patient's ability to walk. For those classified in levels 4 or 5, the goal is to increase comfort and improve posture. Physicians have traditionally achieved these goals by performing standard tenotomy (cutting of a tendon) and osteotomy (division of bone to reposition or adjust alignment) procedures numerous times throughout adolescence as patients mature.

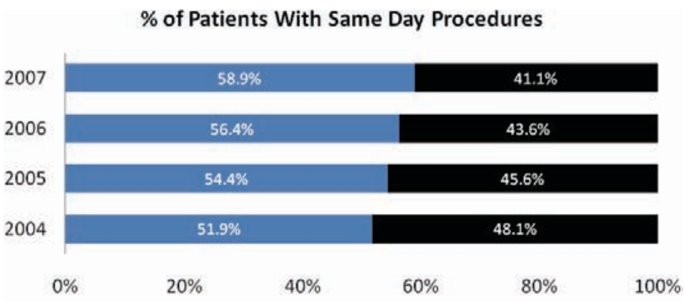
This treatment involves many trips to the hospital, an increased amount of physical therapy, interruption of schooling and a diminished quality of life. Mercer Rang, Ph.D., has termed these multiple interventions on children with CP a dreaded "Birthday Syndrome" because the lengthy procedures and recovery times often keep children in the hospital even during their birthdays when they end up celebrating with nurses instead of with family and friends. It seems increasingly evident that the alternative of performing multiple procedures at once would greatly increase a CP patient's quality of life, but would it still effectively treat the patient's condition?

Research conducted over the past decade indicates that instead of spacing out multiple surgeries over a period of years, performing a single-event, multilevel surgical (SEMS) procedure can actually yield better results. Most recently, researchers like Spiro et al (who studied 84 children with spastic CP who underwent SEMS procedures) and Otsuko et al (who studied 57 patients treated for sagittal imbalance and gait disturbance) published in the article "What's New in Pediatric Orthopaedics", in the *Journal of Bone and Joint Surgery,* May, 2007, both concluded that their results validated the use of SEMS.

With the help of advanced gait analysis and computer-based systems which are continually improving the ability to break down motion and study it in detail, physicians are now more able to diagnose various CP conditions. In many of the recent studies, both motor function and walking scores—along with quality of life—improved for children treated with a SEMS procedure.

Despite these promising studies, one look into the PearlDiver Patient Records Database reveals that physician practice has been slow to reflect the research. Chart 1 shows the percentage of 389 patients who underwent multiple tenotomies and osteotomies versus those who had SEMS procedures.

Chart 1: Single Event Multilevel Surgical Procedure Frequency



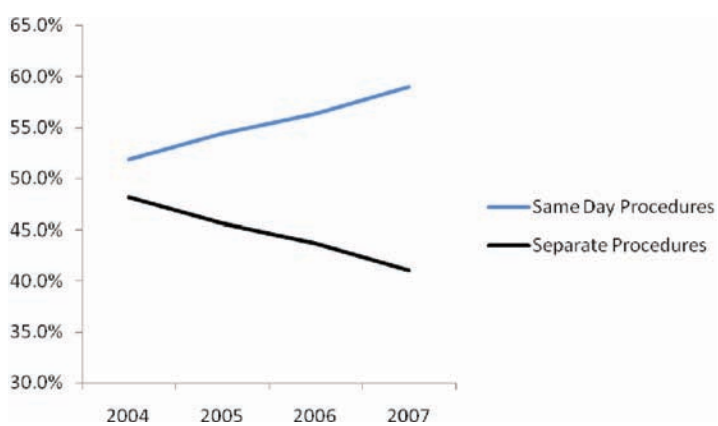
Source: PearlDiver Patient Records Database 2004 – 2007

In 2004, 51.9% of children with cerebral palsy underwent a SEMS procedure. Despite the fact that researchers continued to release studies noting the effectiveness of SEMS procedures over the alternative of multiple procedures over a period of time, by 2007 the number of SEMS procedures had increased only seven percentage points to 58.9% over the course of three years. With the potential to drastically improve a CP patient's quality of life, one would instead hope to see an equally drastic shift toward SEMS procedures.

This graph shows the trend as research continues to bolster the practice of SEMS procedures, though 41.1% are still being treated with multiple procedures.

Fortunately, the push toward the single-event multilevel surgical procedure has led physicians to improve spasticity management and delay the surgical procedure until patients are older. Dr. Hank Chambers, President of the American Academy for Cerebral Palsy and Development Medicine says, "Our goal with spasticity management, physical therapy and bracing is to delay the surgery as long as we can...until about age seven or eight." He believes that by using gait analysis and spasticity

Graph 2: Single Event Multilevel Surgical Procedure Trend



Source: PearlDiver Patient Records Database 2004 – 2007 management, physicians can decrease the number of procedures, increase quality of life and improve patient results when patients have a SEMS procedure.

Dr. Chambers notes that children will usually have one more growth spurt and several more procedures may have to be done. This is in sharp contrast to the older school of thought that starts procedures as early as age two because of the belief that early corrections will allow children to grow and develop more like those without CP.

The key to successfully delaying surgery lies in the new forms of spasticity management. In the ambulant patients, typically GMFCS levels 1 through 3 with focal spasticity (spasticity which creates a focal problem treatable by local means), surgeons can now inject Botulinum toxin typa A (BTX-A) directly into problematic muscles, blocking the neurotransmitter acetylcholine which initiates involuntary muscle contractions. For patients with pure spasticity (having limited or no dystonia, muscle contractions causing a twisting of the affected body part), an additional option used in patients level 2 or 3 is the selective dorsal rhizotomy. This procedure involves severing problematic nerves that don't receive gamma amino butyric acid, which helps to control nerve impulses.

For non-ambulatory patients—GMFCS levels 4 or 5 who also suffer from involuntary muscle contractions, an additional option is the intrathecal baclofen pump—which delivers medication directly to the spinal fluid.

These additional options allow for better spasticity management and the delay of major procedures, which further opens the door for the single-event, multilevel surgical procedure.

Table 1 shows that the number of tenotomy procedures for children under the age of five has decreased since 2004. Table 2 shows that changes in the number of patients who underwent osteotomies were far more dramatic, dropping from 23% for children under five in 2004 to 8% in 2007. Looking forward, the number of osteotomy procedures performed on patients under five will have little room to decrease further, and the number of tenotomies performed on this age group also seems to have leveled off.

Surprisingly, while the percentage of children under the age of five being treated with tenotomy and osteotomy procedures has dropped substantially, the percentage increases in other age groups has not followed the expected pattern. From 2004 through 2007 children between the ages of five and nine receiving an osteotomy, tenotomy or both, increased only slightly. For both procedures, the largest increase was in the age group of 15 to 19 and not in the expected five to nine group. The advances in spasticity management are clearly helping physicians delay surgery for patients under age five.

So the dramatic change in CP surgery trends is happening not in the number of SEMS procedures over multiple, separate procedures but in the timing of the surgeries. The majority of patients still undergo tenotomy and osteotomy procedures in the five to nine age group, and with continued growth spurts, many of these patients may need more than one procedure to fully treat their condition. However, the fact that physicians can delay surgery should help increase the number of successful SEMS procedures. The numbers may not be increasing as sharply as one might hope, but the door is open for continued progress. Physicians will hopefully be able to continue on this trend so that the treatment of cerebral palsy will make fewer interruptions in patients' lives, allowing them more time—and more birthdays—with friends and family.

For more articles by this author, please select the following link: http://www.pearldiverinc.com/pdi/large.jsp

Table1: Age Trend of Tenotomy Procedures Procedure Frequency

Age	2004	2005	2006	2007
Under 5	27%	18%	21%	18%
5 to 9	42%	40%	34%	45%
10 to 14	25%	32%	32%	23%
15 to 19	5%	11%	13%	13%

Source: PearlDiver Patient Records Database 2004 – 2007

Table 2: Age Trend of Osteotomy Procedures

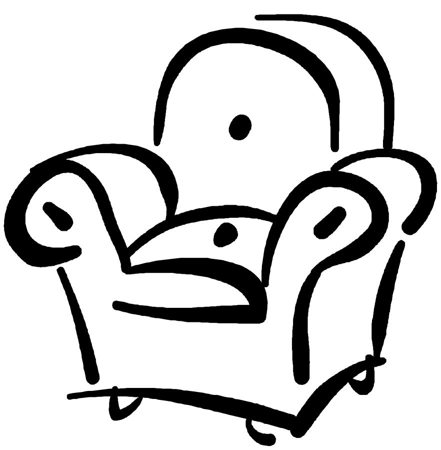
Age	2004	2005	2006	2007
Under 5	23%	14%	15%	8%
5 to 9	44%	44%	38%	46%
10 to 14	26%	34%	32%	32%
15 to 19	7%	7%	16%	15%

Source: PearlDiver Patient Records Database 2004 – 2007 company news

$1.5 Million for Chair at Case Western

A very large chair…The Figgie Foundation, a private foundation based in Pepper Pike, Ohio, has made a $1.5 million gift to endow the Harry E. Figgie III, M.D. Professorship in Orthopaedics at the Case Western Reserve University School of Medicine. The gift was provided in memory of Harry E. Figgie III, M.D., who died in 1999.

Dr. Figgie graduated from the Case Western Reserve University School of Medicine in 1979, and was an orthopedic surgeon at University Hospitals who found his calling in the realm of joint replacement. His talents also lay in the engineering arena; Dr. Figgie also received degrees in biomedical engineering and industrial engineering from Rensselaer Polytechnic Institute. Additionally, he was an industrial entrepreneur who served as vice chairman of technology and strategic planning of the Willoughby, Ohio-based Figgie International Inc.



"This new chair reinforces the importance of recruiting and retaining stellar research faculty who will take medical innovation and education at the School of Medicine to even higher levels of excellence," said Pamela B. Davis, M.D., Ph.D., dean of the School of Medicine, in the news release.

A university spokesperson told *OTW,* "The gift will allow the university to fund a position and thus hire a new professor in orthopaedics. This individual will teach and conduct research, specifically in innovative areas of orthopaedics."

"Harry was a remarkable person who made significant contributions to our profession," said Randall E. Marcus, Charles H. Herndon Professor and chairman of the Department of Orthopaedics, in the news release. "His love and enthusiasm for orthopaedic surgery was obvious to his colleagues, friends and patients. We are very grateful to the Figgie family for their generous gift that has allowed us to create this professorship as a lasting tribute to his legacy."

—EH (June 9, 2009)

Impliant 1, Archus 0

Impliant, Inc. has successfully defended a patent in Europe against a challenge from Archus Orthopedics and has received two additional patents in the United States.

On June 9 the company announced that the European Patent Office confirmed the validity of one of its key patents after the challenge from Archus Orthopedics. The patent was originally issued to Impliant in 2007 and involves the company's flagship product, the TOPS System.

TOPS System

The system is a total posterior arthroplasty device designed to treat lumbar spinal stenosis with or without facet arthrosis and spondylolisthesis. Archus challenged the patent on the grounds of being too broad. The European court rejected that argument and upheld every claim of the patent.

It was reported in Seattle media on May 18 that Archus had laid off most of its 45 employees and significantly scaled back its operations to conserve its remaining cash. Archus is sponsoring a study of 450 patients with its spinal implants, although it's no longer recruiting patients, according to a posting on clinicaltrials.gov.

In addition to successfully fighting off the Archus challenge, Impliant also announced that it had been granted two additional patents in the U.S. The company

first (U.S. 7537613), granted on May 26, is another patent that's related to the TOPS system. The second (U.S. 20050197705), already a patent in Europe (EP1646338), entails a unique translateral spinal disc replacement.

Impliant President and CEO Todd Potokar said these developments strengthen the company's "robust" IP portfolio.

These announcements continue the good news for Impliant after voluntarily suspending their pivotal clinical trial a couple of years ago. After some engineering work that trial continued in May 2008. Impliant had given *OTW* readers a detailed insider view of their experience with the FDA and surgeon community. Such examples of transparency are serving the company well.

—*WE (June 11, 2009)*

DJO Chattanooga Moves to Tijuana

DJO Chattanooga is packing up and moving to Tijuana.

DJO Tijuana

"These transitions are never easy, but over the past several years, we have completed many successfully," said DJO spokesman Mark Francois in comments to *Orthopedics This Week*.

The manufacturing facility, which has operated for more than 60 years under different owners, will be shut down and more than 300 jobs will be cut. Francois told *OTW* "Consolidation of our Chattanooga facility represents the next phase of our cost savings initiatives and will leverage the scalable infrastructure at DJO.

"Over the course of the next nine to twelve months, Chattanooga's manufacturing operations will move to our award winning facility in Mexico, distribution operations will transition to our new facility in Indianapolis and customer service will transition into DJO's Vista headquarters.

Francois said the plant probably will be put up for sale. All employees will be offered severance packages and can apply for positions within the company if they're willing to relocate.

The plant was acquired in early 2002 by Texas-based Encore Medical Corp. In 2007, Encore, now called ReAble Therapeutics, was bought by the Blackstone Group. Blackstone is also the primary private equity group which took Biomet private.

According to DJO's Web site, Chattanooga was the world's largest manufacturer of clinical rehabilitation equipment and supplies for treating skeletal, muscular, neurological, and soft tissue disorders. Brands include the Hydrocollator hot and cold therapy products; Adapta treatment platforms; a comprehensive family of Intelect and Vectra Genisys electrotherapy which include ultrasound, laser and light therapy; Triton DTS traction systems; and OptiFlex continuous passive motion devices.

The Chattanooga plant also made the Moveo, which was named the 2009 winner of the Kruesi Spirit of Innovation Award. The Spirit of Innovation Award is awarded annually for outstanding innovation in new products, services and/or business practices in the Chattanooga area.

DJO's primary manufacturing facilities are located in Tijuana, Mexico; Austin, Texas; Chattanooga, Tennessee; Clear Lake, South Dakota; Vista, California; and Sfax, Tunisia. The Tijuana plant was built in late 2004 and covers 225,000 square feet. Adjacent to the plant is a new 60,000 square foot distribution center that ships worldwide daily.

—*WE (June 11, 2009)*

Orthomimetics: Finalist in UK Engineering Award

While some finalists for the prestigious Royal Academy of Engineering MacRobert Award are rewarded for their contributions to air and sea, Orthomimetics, the UK-based regenerative medicine aficionados, were chosen because of their

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company

Andrew Lynn (Founder and CEO) and Bill Bonfield (Founder and Non-Exec Director) with Sir Garth Morrison, Chairman of the MacRobert Trusts, receiving their finalist certificate. Credit is Steve Forward.

commitment to the edification of the human body—and ultimately...spirit.

Those presented with the MacRobert Award, established in 1969, are recognized as having successfully developed innovative ideas in engineering and have demonstrated the role of engineers and scientists in contributing to national prosperity and international prestige. Orthomimetics (OM) has been selected as a finalist for its successful development of Chondromimetic, a dual-layered medical implant that supports the natural regeneration of bone and soft tissue in injured joints, aiding recovery and avoiding or delaying the need for joint replacement surgery. OM achieved CE Mark approval for Chondromimetic in December 2008 and has launched a comprehensive a clinical trial program.

Also included in this prestigious group are:

- Rolls-Royce plc for the Trent 900 gas turbine aero engine, providing efficient power for the Airbus A380, the world's largest passenger aircraft.
- The Arup Group Ltd for the Beijing National Aquatics Centre—the Water Cube—built for the 2008 Olympics but now providing a legacy as a vast integrated water venue.
- QinetiQ Group plc for the Tarsier system which automatically detects debris on airport runways, saving time and improving safety.

Dr. Geoffrey Robinson, CBE FREng, chairman of the judging panel and formerly Director of Technology, IBM UK said in the news release: "The challenge of picking a winner from such a strong field is heightened by the breadth of engineering excellence on offer: from technologies that have undergone revolutionary change since 1969, to those that would then have seemed inconceivable. The diversity of the engineering is matched by that of the organisations in which it is being developed: from those that have re-invented themselves, sometimes more than once, over the past 40 years, to those led by people who weren't even born when the MacRobert Award was first presented. Whichever team emerges the winner, we can be confident that British engineering innovation will emerge in winning form from the current downturn."

Commenting on the selection, Andrew Lynn, CEO of Orthomimetics added, "It is an honour to have been chosen as a finalist for the MacRobert Award. To have been nominated alongside companies with such exceptional track records is a tremendous endorsement of our technology, our products and the efforts of our talented and dedicated team."

Lynn told *OTW*, "The MacRobert Award is presented following an intensive three-month evaluation process by a panel of 10 of the most successful and respected engineers in UK industry and academia. To have had our flagship product selected as a finalist by such an informed and esteemed panel is a great endorsement of our technology, particularly alongside such high-profile co-finalists as Rolls Royce and Arup."

—EH (June 18, 2009)

company

Lay-Offs at Big Blue Z

The Big Blue Z, aka Zimmer, announced this past week that 450 employees would be laid off and that health benefits for its retirees would be cut. In terms of Zimmer's global employment, these layoffs represent less than 5% of the workforce. Among the 2,800 employees in Warsaw, Indiana, roughly 100 got the pink slip last week.

Over the past decade, Zimmer's employment base has grown 21% and sales per employee (a rough measure of productivity) has decreased from $513,000 per employee in 2007 to about $480,000 per employee now.

Bradley Bishop, Zimmer's spokesperson, mentioned that the lay-offs were not about cost cutting but rather about a realignment of the company's priorities. From the coffee shops in Warsaw we heard that the lay-offs affected employees in spine, trauma, osteobiologics and total joints.

Each laid-off employee will be receiving, we heard, about one year's severance and will be signing an 18-month non-compete agreement. So if Biomet or DePuy were hoping to snare some former Zimmer employees, they will have to wait a year and a half.

Healthcare benefits were also cut for Zimmer's retirees. The other issue for many of those laid off is the state of their Zimmer stock options, 401(k) and pension plan. With Zimmer's stock now at the lowest levels in roughly seven years, those assets are largely underwater.

But the primary issue remains as it has for a while at Zimmer—namely its relations with its surgeons. The company's relations with its core surgeons took a significant hit over the past two years and despite the new sales and marketing executive from GE, the cloud over Big Blue Z has still not lifted. Market share erosion continues.

Finally, with these lay-offs, the cut back in health coverage and other pension concerns, rumblings of union organizing activities have started to emerge. Could traditionally non-union Zimmer go union? All we know that the times, they are a'changing.

—RRY (June 18, 2009)

Symmetry: $5 Million for Precision Equipment

It's a clear-cut issue…to be competitive these days you must have the latest equipment. To that end, Symmetry Medical Inc. has announced an investment of over $5 million in high precision design, development and manufacturing equipment at its 30,000-square-foot Design and Development Center (DDC) in Warsaw, Indiana.

In the news release, Brian Moore, President and CEO, said, "The spine, trauma and reconstructive orthopedic markets are being increasingly driven by computerized systems and demand for high precision design, development and manufacturing capabilities. The addition of this highly sophisticated equipment further strengthens our competitive position and allows us to meet this growing customer demand for computer generated technology. This strategic initiative ensures that we continue to provide the highest available technology for implants and medical instruments that keep our customers competitive and ensure speed to market for their products. We look forward to the growth opportunities these expanded capabilities will provide."

Symmetry has ramped up its capabilities and expertise at the DDC to include multiple high precision implant and instrument machining cells which provide high speed machining processes with up to five times more precision than traditional equipment.

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A company representative provided *OTW* with the following details on the new equipment:

- Highly accurate milling (precision to ±0.005mm (5 micron))
- Laser tool setting
- High speed machining up to and including 5-axis with capabilities to mill features as small as Ø0.4mm
- Pallet loading systems for unattended machining and high volume machining
- Turning – "Swiss style" including multi-axis machining up to and including 10 axis (the Swiss style turning allows the machine to turn at a higher RPM, enabling them to create finer detail)
- Bar feed machines for unattended machining and high volume machining
- Metrology equipment including a Mycrona Altera SL-600 (silver line 600) with precision capabilities to ±0.0006mm (6/10 of a micron); this includes a quality assurance device. It features precision capabilities that can measure of up to 6/10 of a micron, ensuring accurate print design specification.
- Ability and experience in machining multiple types of medical device materials such as: Various Stainless Steels, Titanium, Cobalt Chrome, Various Plastics (Radel R and PEEK)

—*EH (June 19, 2009)*

Dr. Haber Wins Caspari in Japan

Professor Mark Haber, an orthopedic surgeon from Wollongong, Australia, won big in Japan at the International Society of Arthroscopy, Knee Surgery & Orthopaedic Sports Medicine's (ISAKOS) seventh biennial congress in Osaka (April 5–9, 2009). A panel composed of members of the ISAKOS Upper Extremity Committee selected Dr. Haber's work out of 1,200 other abstracts to award him the Richard B. Caspari Award for his research on repairing torn rotator cuffs in the shoulder.

Dr. Haber conducted his research, titled "Biomechanical Contact Properties of Rotator Cuff Repairs During Passive Arm Movement: Perilously Low Levels Occur with Single versus Double-row Repairs," at the Royal North Shore Hospital's Murray Maxwell Biomechanics Laboratory in Sydney in conjunction with Drs. Richard Appleyard and Eran Dolev, and the series was co-authored by Dr. Daniel Biggs.

The research clearly shows that too many rotator cuff repairs end in failure. According to Global Orthopaedic Technology, which partly funded Dr. Haber's work, surgeons perform 12,000 rotator cuff repairs in Australia every year, but almost half of those repairs fail structurally, often in the first 18 months. Fortunately, Dr. Haber found a way to improve on the traditional approach.

Using the Opus TwinLock Knotless Fixation System from ArthroCare Corp., which also partly funded the research, Dr. Haber developed a new technique now called "transosseous equivalent" or the "Perfect Print." This new technique more securely attaches tendon to bone and could result in longer-lasting, more stable rotator cuff

Dr. Roderich Heikenfeld of Germany, Dr. Haber and Dr. Benno Ejnisman of Brazil

company

repairs. Dr. Haber's team analyzed the strength of traditional rotator cuff repairs during and after surgery, as well as into the rehabilitation phase. They found that rotator cuff repairs have a period of "relaxation" which can result in poor fixation of tendon to bone. The "Perfect Print" technique, however, involves retightening the knotless repair before completing surgery. This method may allow patients to safely begin the rehabilitation process earlier which could improve healing and decrease recovery time.

ArthroCare's Opus technology for rotator cuff repairs originally launched in 2007, and quickly earned the Frost & Sullivan Award for Product Innovation in 2008. Dr. Haber's research shows that this line of technology still has the potential to aid further surgical innovations.

As for Dr. Haber, the award was a great moment of both personal and national pride. "This award is a great recognition of the outstanding work done by our whole research team," he said in a press release. "It also shows that although Australia has a small population, we are well represented among the world's medical and surgical achievements by relying on originality. This prize is the greatest achievement in my professional life."

—DK (June 19, 2009)

Alphatec Spine's OsseoFix Gaining Strength

Alphatec Spine is having a month-long streak of good news. Today this small but fast-growing company announced that as of June 1, 2009, over 115 patients in eight European countries have been treated with the OsseoFix Spinal Fracture Reduction System. Although this device is not yet cleared for sale in the U.S., it is currently under 501(K) review with the FDA.

OsseoFix is designed to treat vertebral compression fractures usually caused by osteoporosis, trauma, or a pre-existing disease at the fracture site. Compared to other products on the market today, OsseoFix should allow physicians to treat fractures with less cement, which may help reduce surgical complications and improve healing.

According to Dirk Kuyper, Alphatec Spine's President and Chief Executive Officer, OsseoFix represents the company's initial launch into the aging spine market. "Our next training lab, which will be held in July in Vienna, is oversubscribed, with 50 surgeons and over 70 total participants already enrolled in what will be our third training session," said Mr. Kuyper in a press release.

Earlier this month, Alphatec Spine announced their successful completion of a private placement of $10 million of its common stock shares to one of its existing shareholders, HealthpointCapital Partners II, L.P. This move should help Alphatec Spine obtain the capital they need to keep their fast-growing pace. PearlDiver analyst Matt Menze singled out Alphatec Spine as one of the stand out orthopedic companies during the first financial quarter, and with a month like this, we can only expect to see them continue this trend through the year.

—DK (June 19, 2009)

legal & regulatory

Medtronic's Disclosure Bumbling

Medtronic's awkward efforts to shake loose from Senator Chuck Grassley's investigative grip just don't seem to end.

Medtronic Chairman and CEO Bill Hawkins was asked on June 8 by legal & regulatory

CNBC about the company's financial relationship with former Army surgeon, Dr. Tim Kuklo. Kuklo has been accused by the Army of falsifying results of studies conducted on soldiers using InFuse.

CNBC's Mike Huckman asked Hawkins about the extent of Medtronic's financial relationship with Kuklo and whether the company would fully cooperate with an investigation of that relationship by Senator Grassley.

This *OTW* writer was watching the live interview and was shocked to hear Hawkins respond that, "Our relationship began after he [Kuklo] left the Walter Reed Medical Center and went to Wash U [Washington University in St. Louis]."

Oopsy.

Medtronic send out a "clarification" a couple of days later.

"Bill (Hawkins) indicated that our relationship began with Dr. Kuklo when he joined Washington University. The correct answer is that while we began a consulting relationship with Dr. Kuklo in August 2006, Dr. Kuklo did perform a number of reimbursable functions, including training and education, for the company while he was a practicing physician at Walter Reed...."

At best, the chairman received a bad staff briefing since he probably doesn't personally monitor all physician consulting agreements.

However, the issue here isn't that Hawkins got an important detail wrong, but that the issue of Medtronic's consulting agreements with surgeons keeps getting in the way of company business. Senator Grassley has Medtronic by the ankles like a pit-bull and he's not going to let go until he's satisfied that Medtronic has disclosed all of their consulting contracts and has a system in place to disclose and monitor all such contracts in the future.

Grassley initially got into the Kuklo controversy because Medtronic didn't include Kuklo's name on a list of consultants that the senator had previously requested from Medtronic of surgeons involved with InFuse.

A Medtronic spokesperson told us that Medtronic had submitted the names of all surgeons who had specific consulting contracts that only involved work on InFuse. The company also has other general consulting agreements, some of which include InFuse work. They did not disclose those contracts.

We're convinced that Grassley's investigative staff doesn't believe that Medtronic has complied with the letter and spirit of their requests. Medtronic's "technical" compliance with Grassley's requests is only inviting additional scrutiny and more requests for information.

Surgeon Fears

Medtronic is not going to win a battle with a U.S. Senator over the meaning of what "is" is.

We're starting to hear from surgeons that they are very concerned about working with companies that are inviting such scrutiny. We're convinced that companies biting the bullet with enhanced compliance programs are going to benefit in the long run by attracting top surgeons who want to do research in the lab, not in their lawyer's libraries. Zimmer's Dave Dvorak and other companies that have taken such steps look more prescient every day.

Senator Grassley is clearly building a case for passage of his "Sunshine Act".

We urge Medtronic to pull the curtains wide open and let the sun blind the senator into loosening his grip on their ankles and surgeon's fears.

—*WE (June 10, 2009)*

OTW Senior Writer Ejected From AdvaMed Meeting

On June 12 *Orthopedics This Week* senior writer Walter Eisner was ejected from an investment bank meeting hosted by Wachovia Capital to discuss health care reform.

Eisner had been invited by the investment firm to listen to a presentation by AdvaMed boss Steve Ubl.

Fifteen minutes into Ubl's presentation on the likely impacts on the medical technology device sector of proposed health care reform legislation, Eisner was ejected for being a member of the media.

Ubl had told attendees that proposed health care legislation would likely "be a wash" for medical technology companies due to increased coverage of the uninsured and a slowing of the increase of health care spending by the government.

In fact, said Ubl, proposals such as "comparative effectiveness" might even benefit the sector as there will be an increase in demand for medical technology. He believed that industry will adapt to any changes in health care policy and reimbursements.

OTW writers have participated in numerous investor meetings with investment firms in the past, including Wachovia. We assume Boss Ubl requested that no media be allowed to listen to his comments. It seems that while AdvaMed gives public support to legislative measures to require transparency and disclosure of surgeon relationships with industry, those measures do not extend to the trade association.

Eisner had hoped to find out how much space exists between what the AdvaMed leader tells investors and what he tells members of Congress and the media.

Eisner was heard to shout as he was being dragged out…."Let the sun shine in Mr. Ubl."

—*WE (June 15, 2009)*

Medtronic Discloses Payments to Kuklo

Medtronic has finally told Senator Charles Grassley how much it paid former Army surgeon Timothy Kuklo, M.D.

legal & regulatory

Over $850,000 between 2001 and 2009.

The company did not disclose those payments when the Senator had previously requested a list of surgeons who had worked on the company's InFuse bone growth product.

Kuklo has been accused by the Army of fabricating data and forging signatures on studies related to the product.

Timothy Kuklo, M.D.

Medtronic said that the payments were not related to the discredited study nor was the company involved in any way with the study. That was also some of the reasoning used by the company to explain why it didn't disclose Kuklo's payments previously.

That would mean that Kuklo conducted his InFuse study without any involvement by the company of any kind and was funded by the Army, Kuklo or another party. It would also mean that Kuklo received almost $800,000 for other work with the company.

The company identified those payments as either reimbursements for travel expenses, or payments for speaking or training other doctors on

legal & regulatory

Medtronic's behalf, or for consulting. The company said that those consulting services included working on the design of new or existing orthopedic products and surgical instruments. Reports did not identify those products or instruments.

Medtronic continues to dribble out details that raise more questions than answers.

It's certainly possible but astonishing that an Army surgeon receiving that much money from Medtronic would not have spent one dime on a study about their InFuse product or that the study would not have come up during any of the times Kuklo spoke to other doctors on Medtronic's behalf.

But that's Medtronic's story and they are sticking to it.

Kuklo has repeatedly declined to comment on the matter.

Machiavelli advised his prince to get all the bad news out at once and dribble out the good news. It would be good advice for Medtronic to heed.

—*WE (June 18, 2009)*

biologics

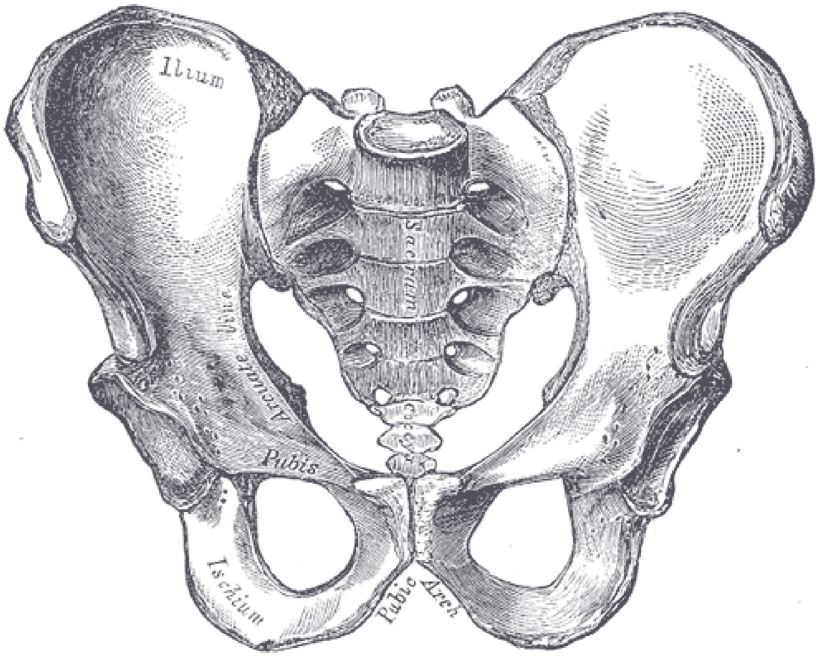
Highway Patching Material Heals Bones

Shoveling cement into a fracture might not be the most delicate way to heal a broken bone, but the technology behind the new bone void filler from Bone Solutions Inc (BSI) works on cracks in the pavement just as well as it works on cracks in the pelvis. This device, called OsteoCrete, is the first in the company's technology pipeline, and it has a key difference from the standard bone void fillers available today.

Rather than develop another calcium-based bone void filler similar to most of the products on the market, BSI based their device on magnesium. According to Tom Lally, President of BSI, most calcium-based products can't match the compressive strength, expandability, and strong binding quality of a magnesium-based bone void filler. And Mr. Lally would know. He's also the co-owner of Bindan Corp, which first developed this magnesium-based technology as a quick-setting cement to patch roads and as a fire-resistant coating.

With the OsteoCrete kit, physicians can mix the solution themselves and then inject the filler into the bone or mold it to the proper shape. OsteoCrete reabsorbs into the body as bone regrows naturally to fill in the void.

BSI recently received FDA 510(k) clearance for the use of OsteoCrete in long-bone and pelvis applications, but the company certainly does not plan to stop there. "We have had discussions with companies that comprise more than 90% of the orthopedic industry worldwide to explore the opportunity for strategic alliances," said Lally in a recent press release. "Initial target vertical markets include all extremities, maxillofacial/cranial, shoulder and knee-related surgical procedures and initially non-load-bearing spinal applications and musculoskeletal allograft uses. These will require



BSI recently received FDA 510(k) clearance for the use of OsteoCrete in long-bone and pelvis applications future FDA and other governmental regulatory certification for global sales."

BSI ultimately hopes to become a "one stop shop" for every physician's bone, ligament, and tendon mending needs. The OsteoCrete solution is also Ph neutral, and, according to the BSI website, they may seek separate FDA clearance to use this product as a delivery system for stem cells, growth hormones, protein, and other biologics.

This may be only the first device in the company's technology pipeline, but the pipeline appears to be very, very long. We'll watch BSI, and the highway repair crews, to see if OsteoCrete can go the distance.

—DK (June 15, 2009)

large joints

Treat RA-Caused Disease Via Surgery Sooner

What do we want? Joint replacement! When do we want it? Now! Well, at least sooner than it's been happening in some cases. According to an article on *Medical News TODAY* ("Earlier Surgery Recommended for RA Patients," June 3, 2009), researchers from Michigan, Maryland, and the United Kingdom have found that metacarpophalangeal joint disease, a condition caused by rheumatoid arthritis (RA), is best treated with surgery—and best treated sooner as opposed to later.

Researchers determined that while customary treatment for this condition involves replacing the knuckle joints with solid silicone joints, this and similar courses of action are controversial. There are disagreements between hand surgeons and rheumatologists regarding the indications, timing and perceived outcomes of the procedure; rheumatologists typically refer late-stage patients for surgery whereas hand surgeons are more apt to "go in" earlier. The study, published by the American Society of Plastic Surgeons in the June issue of their journal, *Plastic and Reconstructive Surgery,* is the largest cohort study of its kind.

As indicated in the article, the researchers examined the outcomes of 70 RA patients who underwent surgery after suffering from hand deformities. Two groups based on the degree of deformity were established, and the outcomes of the reconstruction were assessed at six months and at years one, two and three. After reconstruction, both groups had positive self-reported hand outcomes and showed statistically significant improvement. Nonetheless, the more severe group still had significant deformities, showing that the more serious the malformation, the more difficult it is to correct.

Commenting to *OTW* was Dr. Kevin Chung, Professor of Plastic Surgery at the University of Michigan. A hand

Kevin Chung, M.D.

and upper extremity surgeon, and the study's lead author, Dr. Chung noted, "This is the first collaborative multicenter international study on a common rheumatoid hand surgery procedure. Hand surgeons and rheumatologists from the U.S. and UK are working together to derive evidence based on meticulous data collection effort in order to understand the outcomes of surgical and nonsurgical treatments. The support from the National Institutes of Health is critical in this large scale, long-term study and we hope to continue following this important cohort of patients beyond the three-year time frame initially stipulated for this project. In essence, joint replacement surgery for the rheumatoid patients with severe hand deformities does work. For rheumatoid patients with incapacitating hand deformities, consultation with hand surgeons is mandatory to determine the most effective treatment."

—EH (June 8, 2009)

Hip and Knee Joint Registry Proposed

After waiting for industry and professional societies to act, Democratic House members Bill Pascrell, Jr. of New Jersey and Lloyd Doggett of Texas have introduced legislation to create a national registry of artificial hips and knees.

Pascrell said that the registry will improve patient safety and outcomes and get rid of poorly performing devices. Such a registry could play an important role as the $1.1 billion Comparative Effectiveness Research Center gears up. By being able to track devices on a long-term basis, providers would be able to track patients' results over time and help detect ineffective surgical practices and faulty devices.

Henrik Malchau, M.D., an orthopedic surgeon at Massachusetts General Hospital in Boston, says in a June 10 New York Times article, "A patient here (U.S.) faces double the risk that a patient in a country with a registry faces of needing to have an artificial hip or knee replaced earlier than expected.

AAOS Efforts

The American Academy of Orthopaedic Surgeons (AAOS) had previously written Pascrell saying it preferred a privately run registry that would include both Medicare and non-Medicare patients.

AAOS has tried for more than a decade to set up such an independent registry but device manufacturers have been reluctant to pay for it. The Academy, along with another orthopedic organization, recently earmarked $450,000 to pay for start-up funding.

No long-term financing has been secured yet and device makers have not agreed to pay for it.

Pascrell told *The Times* that he believed that patients had waited long enough for the groups to act. He also said that, given the Justice Department settlements with device makers and allegations of kickbacks to surgeons it was important for the government to be involved.

AAOS First Vice President John Callaghan, M.D., has made establishing a registry a top priority.

When he took office a few months ago he acknowledged that building a national joint registry in the U.S. will be a complex task, but was optimistic that it can be accomplished.

John Callaghan, M.D.

He told members at their annual meeting that when he assumes the presidency of the AAOS in 2010, he would put a special emphasis on continuing the development of a national joint registry.

Worldwide Registries

"Approximately 15 countries around the world have joint registries," said Callaghan. "All of them combined are only tracking 150,000 to 200,000 joint replacements each year. In the United States, however, we're performing about 750,000 joint replacements every year, which means large joints

that our registry would need to be three to four times the size of all the other joint registries combined. Tracking that many joint replacements will be a massive undertaking."

But the extra emphasis on quality by government and consumers as part of health care reform is increasing the likelihood of creating such a registry. Callaghan noted that this attention has resulted in the FDA's renewed effort regarding a unique identification system for medical devices.

The Pascrell/Doggett proposed joint registry would be established under the Agency for Health Care Research and Quality, a part of the Department of Health and Human Services.

The bill estimates that it would take three years to set up the mechanisms needed for the registry to operate and that it would begin producing data two years after that.

—*WE (June 16, 2009)*

RA Patients: 63% Have Psychiatric Issues

Inflamed joints, deflated spirits… the European League Against Rheumatism (EULAR) has announced that researchers have learned that over half (63%) of patients with rheumatoid arthritis (RA) also suffer from psychiatric disorders, with the majority of these (87%) occurring in the depressive spectrum.

The study, recently presented at the 2009 EULAR conference, also contained findings that over half (52%) of the patients studied had experienced stressors prior to the onset of RA.

Other points of interest from the study include:

- 23% of patients were diagnosed with cognitive dysfunction, with 16% of this attributed to depression
- 33% suffered from sleep disorders
- Those with depression had more severe RA and greater functional insufficiency and pain; they also received less aggressive treatment than patients without depression. (No significant differences in age, duration of illness, gender or DAS28[1] scores were noted between the two groups)
- Significantly, cognitive impairments were found more often in patients older than 50 years (39% vs. 9%)
- The age of the first prednisone intake was significantly higher in patients with depression compared to those without (48 vs. 30 years)

Dr. Tatiana Lisitsyna from the State Institute of Rheumatology RAMS, Russian Federation, who conducted the study, said in the news release: "Psychiatric disorders are a very common comorbidity for people with RA, and they tend to be stress-related and associated with disease activity and chronic pain. Evaluating and addressing the mental health of those with RA should be a regular feature of rheumatology practice to improve quality of life and reduce the potentially distressing psychological burden of RA."

Seventy-five patients with RA—as defined by the American College of Rheumatology (ACR)—were included in the study. The vast majority (96%) were female, had a median age of 52 years, and median disease duration of 12 years. The median DAS28 score was 4.98. Median prednisone intake duration was 34 months and 80% of patients were taking DMARDs (disease-modifying antirheumatic drugs). Using the Brief Pain Inventory (BPI) scale to assess pain, 74% were considered to have either severe or moderate pain.

The International Classification of Disease scale was used to diagnose psychiatric disorders; also used were the Hospital Anxiety and Depression Scale for screening, the Hamilton Anxiety Rating Scale and large joints

the Montgomery-Asberg Depression Rating Scale. Projective psychological methods were employed for evaluation of cognitive function.

[1]*Mark DAS28 (Disease Activity Score) is an index used by physicians to measure how active an individual's RA is. It assesses number of tender and swollen joints (out of a total of 28), the erythrocyte sedimentation rate (ESR, a blood marker of inf ammation), and the patient's 'global assessment of global health.' A higher score indicates more active disease.*

—*EH (June 12, 2009)*

Funding for Residency Training

As government and industry close their wallets on funding for graduate medical education (GME), it becomes more imperative for orthopedic residency programs to seek out alternative sources of support. So say the authors of a recent article published in the *Journal of Bone and Joint Surgery* (Funding of Educational Opportunities in Orthopaedic Surgery Residency Training; A Survey of Residency Program Directors and Chairs 2009;91:1542-1545).

Drs. A. Alex Jahangir (Hennepin County Medical Center), John H. Flint (University of Iowa Hospitals and Clinics), and Samir Mehta (University of Pennsylvania) invited 149 residency directors and chairs to complete a survey on program funding; 80 of these individuals returned surveys. The findings include the following:

- 86% of the programs provided research funding to residents and 90% of the programs provided a "book fund," which residents could use for books, travel to meetings or courses, or to buy equipment.
- Contributors to the book fund were the faculty (38%), the institution (30%), and industry (19%), with other sources (alumni donations and endowments) contributing the remaining 13% of the funding.

A full 88% of responding programs stated that industry support paid for books at their programs; 83% of the programs had held industry-supported sawbones courses for the residents; 67% of the programs had received industry funding for courses and meetings off campus for their residents; and 65% of the programs had journal club sponsored by industry.

Commenting to *OTW,* Dr. Jahangir noted, "Our study demonstrated that nearly half of the respondents (residency program directors and chairmen) believed that if industry funding was decreased or eliminated without any other funding to replace the current level of financial support, their programs would be unable to provide their residents with the current level of educational resources. This finding clearly demonstrates the lack of federal funding available for graduate medical education and the perceived importance of industry financial support for many of these institutions, even though industry contributed to only a small portion of the overall residency expenses. With decreases in industry funding for graduate medical education (GME), it is imperative that industry and academic programs continue to work towards a common methodology so that funding from industry can still occur, and yet remain ethical and transparent. Furthermore, it is equally important that the federal government, in health care reform legislation, addresses and increase GME funding in order to assure that future orthopaedic residents have high quality educational opportunities and are able to deliver quality patient care."

He also told *OTW,* "A surprising finding from this study was that when the respondents were asked about potential sources of funding to replace industry funding, many respondents believe that financial contributions will have to be made by the existing

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faculty, alumni, and/or a departmental residency foundation, while only a small percentage (9%) believed that government support would be increased. This raises the issue that if industry funding is no longer available for GME, responsibility may fall upon the shoulders of faculty who already donate their time and likely contribute to a university or dean's tax. The potential for cannibalization of research funding or private donations or endowments for capital improvement may also occur. This may result in less faculty participation in residency training and less research funding."

He added, "As a person who is at the beginning of my academic orthopaedic career, and had many great educational resources and opportunities in residency and fellowship to develop as an orthopaedic surgeon, I am concerned that the educational experience that my current and future residents receive may be jeopardized because of decreased GME funding. As our population ages and increases in size, without continued support of GME, there will be a shortage of orthopaedic surgeons to serve this population. My hope is that this study serves as an eye opener to both orthopaedic surgeons and policy makers demonstrating the importance of continuing to improve and fund graduate medical education. Our plan is to work on additional studies which objectively demonstrate the importance of this support to the future of our specialty and our patients. It is with this objective data that policy makers, especially in this time of health care reform, can make the appropriate funding decisions to keep the future of our specialty strong not just for us as surgeons, but for our patients."

—EH (June 18, 2009)

people

Randal Clarke: New VP at Custom Spine

There's a new startup sheriff out west. New Jersey-based Custom Spine (CSI) has announced that Randal Clarke, who started out years ago as a sales rep for Zimmer, is the new Vice President of Sales for the Western region. His 27 years in the orthopedic medical device market includes broad expertise in developing markets for new products and building successful start-up organizations.

Clarke's history includes a sales career at Linvatec, followed by a launch of Advanced Orthopedic Systems. This entity, a distribution company for orthopedic products from Linvatec sports medicine, Bionx and Hall Surgical Power, had revenue in excess of $11 million.

Randy Clarke told *OTW,* "CSI is my third start up company. The first two were Osteobiologics, for one year, and ConforMIS for the last two years. OBI was acquired by Smith & Nephew in January of 2007 and ConforMIS is continuing to ramp up sales volume in a very competitive total joint market. I was brought on to establish and develop a sales distribution network for both companies, primarily in the western region of the US. Once the sales groups were set up, my responsibility was to manage and motivate a mostly independent group of sales reps to support them with the challenges of establishing some sales and relationships with local surgeons. It takes a very entrepreneurial approach and spirit to take on a company and produce where there are no existing sales. Not everyone can do it. I can look back at both assignments and know that we were highly successful in both markets."

Detailing his move to Custom Spine, Clarke told *OTW,* "ConforMIS has great technology and I really enjoyed the group of individuals there. But when the opportunity came along to work with Lew Bennett and Mahmoud Abdelgany, I knew that something special was about to happen at Custom Spine. Mahmoud is a thought leader, well ahead of his time with regards to research and product development. His passion and enthusiasm is contagious. On the other hand, a chance to work alongside of Lew Bennett is like a

people

football player getting the chance to be coached by Vince Lombardi or Lou Holtz. He has seen at all, done it all, and his record speaks for himself."

In the news release, Lew Bennett, President of Custom Spine, was quoted as saying, "Randy will be a great asset to our management team. His vast knowledge of the orthopedic industry combined with his experience of distributorships and management of developing markets, will further support Custom Spine's growth initiative."

—EH (June 4, 2009)

spine

Biostat System Reports Pilot Study

Spinal Restoration, Inc. has submitted its Biostat six-month primary endpoint results to the FDA.

The company announced the submission of the results from an ongoing, two-year IDE (Investigational Device Exemption) pilot study of the Biostat System for the treatment of chronic low back pain due to symptomatic internal disc disruptions on June 9.

The results are from a three-site, 15-patient pilot study and are a key milestone for the company's petition to initiate a larger pivotal trial.

Company President and CEO Gary Sabin said he believes the safety and efficacy measures obtained in the pilot study are supportive of moving into the pivotal study.

The results of the pilot study will be presented at the International Spine Intervention Society (ISIS) annual meeting in Toronto this July. In addition, complementary results from an animal model investigation of the Biostat System have been accepted for presentation at the North American Spine Society (NASS) annual meeting in November.

The Biostat System consists of the Biostat Biologx Fibrin Sealant, a human-derived, resorbable biologic tissue sealant, and a proprietary application system designed to deliver the biologic to the intervertebral disc. The company believes the application of the sealant to the disc may alleviate discogenic pain by sealing the painful disruptions, reducing inflammation, and enhancing tissue repair.

The Biostat System is an investigational device and is limited by federal law to investigational use only.

—WE (June 10, 2009)

CORTOSS Cleared by FDA

Those with vertebral compression fractures normally experience tingling… now they can tingle with excitement. Orthovita has announced receipt of 510(k) clearance from the FDA to

market CORTOSS Bone Augmentation Material for treatment of vertebral compression fractures (VCF). An injectable, bioactive composite that mimics the physiological properties of human cortical bone, CORTOSS is the first alternative to polymethylmethacrlyate (PMMA) cement that has been evaluated in a large-scale, multi-center, randomized, controlled clinical study and cleared in the U.S. for VCF.

spine

"Every year roughly 250,000 people in the United States undergo augmentation procedures such as vertebroplasty and kyphoplasty for painful fractures in the spine. Since the inception of the vertebroplasty procedure in the mid-1980s, PMMA has been the only viable implant for vertebral augmentation," stated Antony Koblish, President and CEO of Orthovita, in the news release. "CORTOSS is the first FDA-cleared alternative in this product category. Our experience and research to date shows that physicians and their staff are pleased with the innovative handling and biomechanical characteristics that CORTOSS offers. We believe these features, supported by our extensive human clinical data demonstrating safety and effectiveness, offer physicians and facilities substantial value and a clear rationale for adopting CORTOSS."

Just this past April Orthovita submitted the two-year follow-up clinical data comparing the efficacy of PMMA to CORTOSS. In this 256-patient pivotal trial conducted under an investigational device exemption, CORTOSS, a blend of cross-linking resins and reinforcing fillers, achieved its primary end-point of non-inferiority to the PMMA control at 24-months. Success was measured by improvement in the Visual Analogue Pain Scale (VAS) pain score, maintenance or improvement in Oswestry Disability Index (ODI) function assessment, maintenance of vertebral height and alignment, and no subsequent device-related surgical intervention at the index treatment level. At 24 months: The composite endpoint success rate was 76.9% for patients treated with CORTOSS and 73.4% for PMMA patients; With an ODI success rate of 96.7%, the CORTOSS patient group experienced a statistically significant benefit in function success over the PMMA group, which had an ODI success rate of 88.4%. Also, the CORTOSS patients required an average of 30% less material to achieve fracture fill.

John Mathis, M.D., of The Center for Advanced Imaging in Roanoke, Virginia, and editor of the original textbook entitled *"Percutaneous Vertebroplasty and Kyphoplasty,"* commented in the news release, "For over 20 years, the treatment of vertebral fractures relied on the application of a foreign material without much consideration for the mechanical, and none for the biological conditions. CORTOSS is a material that was designed to restore mechanical conditions and match the properties of natural bone. I believe that its introduction marks the beginning of the next phase in the treatment of vertebral fractures which will be concentrated on the patients' physiology."

With 83% follow-up at the 24-month time point, says the company, the study also represents a significant piece of clinical research in this field. The pivotal study, in combination with various clinical trials previously completed in the U.S. and Europe, brings the total number of patients studied for CORTOSS in vertebral compression fractures to 527.

"Orthovita's commercial success has been grounded in our ability to effectively present the value of our basic science and human clinical data throughout a hospital," stated Christopher Smith, Senior Vice President of Sales and Marketing. "VITOSS Bone Graft Substitute is now the leading synthetic bone graft for spine surgery and our hemostat business, led by our VITAGEL product, has experienced brisk growth since its inception in 2005. We believe that CORTOSS will benefit significantly from the commercial infrastructure, core competencies and call patterns we have established.

spine

Further, we estimate that our current coverage addresses roughly 80% of the surgical market for vertebral compression fractures, which gives us a strong position to launch CORTOSS while we continue plans to grow our current product lines."

Orthovita will focus its initial commercialization strategy on supporting and ensuring continued clinical success with CORTOSS in vertebral compression fractures. Commenting on the strategy, Koblish told OTW, "Our plans for the U.S. commercial launch of CORTOSS include a controlled roll out starting in about 30 days. This roll out will last about 90 days and then we will progressively broaden the scope of the release with the intention of a full launch by the end of 2009."

Koblish also told *OTW,* "Our initial success will be measured by a solid platform of routine clinical success. We believe that will drive long-term commercial success and that patients will benefit in the same way they did in the clinical trial, with measurable improvement in pain, function and adjacent fractures."

—EH (June 8, 2009)

trauma

New Genetic Disorder in Children

A time of ultimate joy is sometimes marred by the shock and sadness of discovering that one's newborn has a serious medical problem. Researchers, including those from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), part of the National Institutes of Health, have discovered a new autoinflammatory syndrome, a rare genetic condition that affects children at birth or shortly afterwards. The findings appear in the June 2009 issue of the *New England Journal of Medicine.*

Dubbed DIRA (deficiency of the interleukin-1 receptor antagonist) by the researchers, the potentially fatal symptoms include swelling of bone tissue, bone pain and deformity, inflammation of the periosteum, and a rash that can span from small individual pustules to extensive pustulosis that covers most of the patient's body.

"We knew when we saw these children that we were dealing with a previously unrecognized autoinflammatory syndrome. The clinical characteristics were distinct from other diseases we had seen before," said NIAMS researcher and lead author Raphaela Goldbach-Mansky, M.D., M.H.S., in the news release.

All the children had inherited mutations in IL1RN, a gene that encodes a protein known as interleukin-1 receptor antagonist (IL-1Ra). IL-1Ra binds to the same cell receptors as the inflammatory protein interleukin-1, and acts as a brake on this inflammatory protein. Without IL-1Ra, the children's bodies cannot control systemic inflammation that can be caused by interleukin-1.

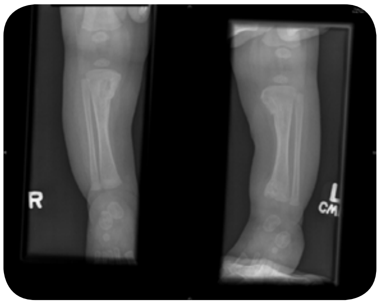
Nine patients from six families with DIRA were found in Newfoundland, the Netherlands, Lebanon, and Puerto Rico. Those alive at the time of diagnosis (six) were treated with anakinra, a synthetic form of human IL-1Ra normally used for rheumatoid arthritis; most responded successfully and immediately to anakinra. "Our first patient had been unresponsive to trauma

several treatments, and his health care team had almost given up. But with anakinra, he was out of the hospital in 10 days and his symptoms resolved," Dr. Goldbach-Mansky said in the news release.

"The beauty of this discovery is that the symptoms of this devastating disease can now be treated," added NIAMS director and immunodermatologist, Stephen I. Katz, M.D., Ph.D. "The abnormal inflammatory pathways seen in this disease may also help us understand other common diseases that share clinical features, such as psoriasis, as well as other autoinflammatory disorders."

Regarding the swelling of the bone tissue, Dr. Goldbach-Mansky told *OTW*, "There are four forms of bone lesions that we have seen in DIRA so far:

1. **Osteolytic bone lesions**-in most children biopsies are used to rule out septic osteomyelitis, however the children usually do not have fever and the lesions are sterile, antibiotic treatment is not effective.



2. **Periosteitis,** swelling and inflammation of the tissue surrounding the bone with new bone formation mainly around the hips. This finding has been

confused in the literature with a benign condition called infantile cortical hyperostosis. However it is crucial to make the proper diagnosis of DIRA, as it is a different disease and failure to treat appropriately with anakinra or at least corticosteroids can lead to death due to an escalating inflammatory syndrome called SIRS, systemic inflammatory response syndrome. The periosteal swelling is also seen around the lesions of the bone-cartilage junction of the ribs and were present in all children we have seen so far. These rib lesions are not healing fractures. These lesions are painful and infants often hurt when they are picked up from their bed.

3. The **bony overgrowth** originating in the proximal and distal growth plates of the long bones seen in one child of Puerto Rican ancestry is clinically the most impressive bone manifestation. This finding is also seen about 50% of children born with another IL-1 mediated disease called NOMID, neonatal-onset multisystem inflammatory disease. In contrast to DIRA children with NOMID have an urticaria like rash, aseptic meningitis and progressive sensorineural hearing loss. These lesions are disfiguring, can lead to contractures, inability to walk and are painful as long as the bone grows. Once the growth plates are fused the bone of these lesions is histologically "normal" and also fractures heal normally, osteotomies that have been performed in NOMID children to correct these lesions have healed well.

4. DIRA and also NOMID patients, both syndromes of IL-1 mediated inflammation, develop **osteopenia/ osteoporosis** that actually improves significantly with anakinra (IL-1 blocking) therapy."

Directing several comments toward orthopedists, Dr. Goldbach-Mansky said to *OTW*, "The disease starts early in life but some children who survive the initial perinatal period can present with aseptic osteolytic lesions at frequent intervals. One of our children had three bone biopsies to rule out osteomyelitis over six years. When a rash is present and the cultures are negative then testing for DIRA should be done and respective treatment should be initiated."

She also said, "We are recruiting patients into a study which aims to determine their outcome on treatment. We are in the process of setting up

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a study with a longer acting IL-1 blocking agent which does not have to be given by daily injections which can be traumatic in little children. We are also interested in better understanding which inflammatory pathways are involved in causing the inflammatory bone lesions including the osteolytic bone lesions. As there are other spontaneous diseases in children and adults that present with sterile osteolytic lesions and periosteitis/ osteitis such as CRMO [chronic recurrent multifocal osteomyelitis] and possibly SAPHO [synovitis-acne-pustulosis-hyperostosis osteomyelitis syndrome], understanding whether the pathways that drive these lesions overlap may help us to also find effective therapies for these disorders that are currently not well understood."

—EH (June 8, 2009)

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The Picture of Success: Dr. Lisa Cannada

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

Whether it was the drama of childbirth or the trauma of the ER, Dr. Lisa Cannada, Associate Professor in the Department of Orthopaedic Surgery at St. Louis University, was exposed to medicine early in life. "My dad, an OB/GYN, brought me around our hometown of Steubenville, Ohio, when he delivered babies. My grandfather was a general practitioner who let me visit his office and watch him see patients. Later on he let me come to the local ER and observe. I was so impressed by how both my dad and grandfather evoked such love and appreciation from patients…and how they genuinely improved people's lives."

Her appreciation for the workings of the human body, however, took a detour prior to settling on medicine. "I was heavily into sports during college and told my parents that I wanted to become a physical education teacher. They basically said that this was not something they wanted for me. I became an athletic trainer, majored in health and sports sciences, and worked with athletes 40 hours a week at Ohio University. And I was constantly working with orthopedic surgeons."

Busy, but not stretching her intellectual muscles, Lisa Cannada began to look elsewhere for something that would engage her mind. "Within three months of earning a masters degree in athletic training I realized that the work wasn't sufficiently challenging. 'I should go to medical school,' said the resounding voice in my head. I waited awhile, both because I needed to take several classes, and because my husband, a track athlete in training for the Olympics, needed me to wait for him. At least I knew before starting medical school that I was going to be an orthopedic surgeon. From my days as a trainer I could see that it would be a perfect fit."

Learning Through Trauma

Lisa Cannada did her medical training at the University of Maryland at Baltimore, and, while reveling in the unpredictable, she found her professional love. "As soon as I spent 10 minutes at the acclaimed Shock Trauma Center I knew what my future entailed. The busy, stimulating environment was so exciting. I liked that fact that you never knew what was coming in the door, had to think on your feet, and got to work with different specialists."

Agog at all there was to learn about trauma, Dr. Cannada delved into her residency at Case Western Reserve University and squeezed the most knowledge out of every minute. "During residency I took my vacation time to do research and attend trauma meetings. We had to teach an anatomy class for medical students, something that led to my strong interest in education. New learners are like sponges, always asking questions and keeping the teacher on top of things. It was in this period that Dr. Jack Wilber came into my world and taught me his sophisticated reduction techniques and handling of soft tissue. I also enjoyed learning from Dr. Brendan Patterson, a strong leader who supported my work and showed me how important leadership qualities are for success. On a personal note, it was good to be back near family. My grandfather had died and I had been away from everyone for quite some time."

Her mind never far from the nerve center of urgent care, Shock Trauma, Dr. Cannada completed her residency in 2001 and then returned to that esteemed facility for a fellowship. "I had worked toward a fellowship at Shock Trauma my entire residency. The volume and breadth of trauma was so compelling; they get 7500 trauma admits per year so you could essentially operate around the clock. In my first week there I only went home twice to grab fresh clothes. We had so many mangled extremities come in the door that a great part of the education was related to saving limbs or deciding when to amputate. I recall one particularly unusual and challenging case of a person trying to race a train on his ATV. The train won, and he was tossed into a sewerage pool. This resulted in an upper extremity amputation, and was complicated by the fact that we had to contend with infection issues."

Working alongside senior trauma surgeons propelled Dr. Cannada into new realms. "A clinical ace, Dr. Andy Burgess taught me basic things that would make, for example, sacroilliac screw placement, easier. Dr. Andy Pollack, who will head the Orthopaedic Trauma Association (OTA) in a few years, taught me the finer points of leadership. For example, he let me know how to ask for something without feeling like I'm asking for everything. Dr. Alan Jones served as a model of meticulousness, and was the only attending that scrubbed in on every case."

Rapid fire trauma coupled with the rigors of practice building would give Dr. Cannada a new understanding of her profession. "After finishing my fellowship in 2002, I then went to Grady, a county trauma center in Atlanta. We were incredibly busy with caring for a large underserved population. When I got there more than 90% of the patients were uninsured, so I learned about trying to build a practice in a very challenging setting. In particular, I learned how to get people who were just putting in time at work to help you out. The socioeconomic impact of trauma, both for the hospital and the patient, was also made clear."

Following the advice of one's mentors is often easy; actually following them can be tricky. Dr. Cannada: "In 2004 I was hired by Drs. Alan Jones and Dr. Bob Bucholz at the University of Texas Southwestern Medical Center at Dallas. I was eight months pregnant and on bedrest when I got a call that Bob was no longer Chair and Alan had just left. I had gone there for the opportunity to work with my mentors, but fate had other plans. I did accept the position, which afforded me the chance to work with Dr. Maureen Finergan, a talented trauma specialist who encouraged my efforts to become a leadership fellow through the American Academy of Orthopaedic Surgeons. I also learned from Dr. Charlie Reinert, who had such an incredible work ethic that at times he would stay up all night long. He was very supportive of me; in fact, he was my professional 'rock.'"

Advocating for Families and Mothers

Several years later Dr. Cannada joined a family of orthopedists who had, for the most part, known each other for years. "In 2008 I began working at St. Louis University with some of the 'giants' of trauma. We have seven traumatologists, including Roy Moed, the Chair of the Department and Tracy Watson, former President of the OTA. Roy recruited Tracy, along with three other trauma surgeons from another institution; they have been together for10 years. This group of surgeons is truly showing me what it's like to have partners who are thoroughly encouraging and supportive."

Helping to create the wave of the future in education, Dr. Cannada has worked to establish the fellowship match process for trauma programs. "I have worked on the OTA fellowship committee with Tracy Watson since 2002. We had always been working toward the goal of a fellowship match, but we knew that in order to get everyone's agreement, the right circumstances would have to be present. We took baby steps, beginning with a computer application process, followed by holding interviews at the OTA meeting, and then demonstrating the need for match due to the increased interest in trauma. All of orthopedics is going towards a fellowship match process but I think we have set a good example for other subspecialty societies."

Digging into important, but under-appreciated topics, Dr. Cannada has put substantial effort toward understanding the nuances of treating the pregnant patient who experiences an orthopedic trauma. “Interestingly, my results indicate that even with a minor distal radius fracture the pregnancy becomes a high risk trauma, with a significant chance of preterm delivery. Some of my related work, childbirth after pelvic fracture, has been accepted as a podium presentation at the fall OTA meeting. There is a real complexity in this multicenter project in identifying patients who have had a pelvic fracture…and then getting them, as well as their OBs, to respond to a questionnaire. I began working on this topic during my fellowship, and was assisted by Dr. Carol Copeland, also at Shock Trauma. She was a true role model, in the sense that she was a female faculty member at one of the largest trauma centers in the U.S. She was also raising a son.”

Discussing her other current research, she notes, “I have started getting studies together for a multicenter, retrospective look at retrograde femoral nailing, something which hadn’t been accepted as the norm but is now more popular. The results of retrograde nailing are promising, in particular the fact that you don’t increase the risk of infection if you do it in an open fracture or gunshot wound.”

Having gained so much from mentoring through the years, Dr. Cannada believes in the importance of helping one special ‘mentee.’ “My husband and I have one child, a daughter. My very adaptable husband supports my career so that I can travel to meetings and work at home when I need to. In the mornings I leave before the nanny arrives and then return after the nanny leaves, so he is a very involved dad. On the whole, I’m a much better mom because of my work. Not only does it mean that my daughter has a role model for what is possible for women today…it also shows medical students and residents what they can accomplish.”

Dr. Lisa Cannada…for when trauma needs an advocate.

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