VOLUME 5, ISSUE 36 | NOVEMBER 24, 2009

Orthopedics This Week

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Spine Procedure U.S. Market Reports	Code
Spine Fusion	
Anterior cervical fusion	81.02
Posterior cervical fusion	81.03
Anterior dorsal and dorsolumbar fusion	81.04
Posterior dorsal and dorsolumbar fusion	81.05
Anterior lumbar fusion	81.06
Lateral lumbar fusion	81.07
Posterior lumbar fusion	81.08
Spine Refusion	
Posterior lumbar refusion	81.38
Other Spine Procedure	
Discectomy	80.51
Decompression	03.09

Large Joint Reconstruction	Code
Total Hip Replacement	81.51
Total Knee Replacement	81.54
Revision of Hip Replacement	81.53
Revision of Knee Replacement	81.55
Excision of Semilunar Cartilage	80.6
Cruciate Ligament Repair	81.45
Synovectomy of the Knee	80.76
Removal of Implanted Device Tibia/Fibula	78.67
Hemiarthroplasty	81.52
Hip Resurfacing	00.85

Extremity Market Reports	Code
Ankle Fusion	81.11
Triple Arthrodesis	81.12
Subtalar Fusion	81.13
Total Shoulder Replacement	81.80
Partial Shoulder Replacement	81.81
Rotator Cuff Repair	83.63
Total Ankle Replacement	81.56
Open Reduction of Fracture Radius & Ulna w/ Internal Fixation	79.32
Open Reduction of Fracture Humerus w/ Internal Fixation	79.31
Open Reduction of Fracture Tarsals & Metatarsals w/ Internal Fixation	79.37

(2004-2008 U.S. Procedure, Sales, Charging and Demographic Data as derived from Medicare AND Private Payer datasets)

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Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

This Week: There was a decided shift in market sentiment last week to large cap orthopedic stocks. To us this does NOT feel like a flight to quality, rather we think institutional investors are rotating sectors and coming back towards orthopedic stocks. Usually, large caps are first in a sector rotation, then medium, then small caps.

Rank	Last Week	Company	TTM Op Margin	30-Day Price Change	Comment
1	3	Smith & Nephew	22.42%	9.36%	SNN buys Nucryst for $21 million and launches new technology for battlefield injuries and wound covering.
2	4	Zimmer	28.10	11.72	Upgraded by UBS. $1 billion in notes sold. New war chest?
3	1	Stryker	23.50	7.83	Interesting positioning. Acquisitions combined with higher dividend payout. How about a stock buyback?
4	9	Integra LifeSciences	15.37	1.65	Second best value in the orthopedics. Top-line growth has always been good. As ortho's most prolific consolidator, what's next?
5	8	Medtronic	31.09	8.10	Is Sofamor Danek giving MDT stability while the other cardio companies (BSX & STJ) stumble?
6	5	Orthofix	10.33	(6.00)	Upgrade from Wells Fargo. Trinity stem cells has the analysts excited. Me? Cash flow, baby, cash flow.
7	7	Exactech	12.61	(1.70)	Third-best value in orthopedics. Historically, EXAC has outperformed the industry by 2x.
8	10	Johnson & Johnson	26.94	3.66	Barron's featured JNJ for its dividends. We're noticing that JNJ is setting a 52-week high.
9	6	CONMED	6.92	(3.38)	CNMD announced two new products, a cruciate recon system and a novel biocomposite. Key is sales rebound.
10	2	Alphatec	(2.01)	(11.97)	The market has always had a volatile take on ATEC. Huge swings both ways. Market is irrational at the moment.

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Robin Young's Orthopedic Universe

Top Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	ArthroCare	ARTC	$21.80	$584	13.5%
2	Zimmer Holdings	ZMH	$56.92	$12,120	11.7%
3	Wright Medical	WMGI	$18.39	$710	9.9%
4	Smith & Nephew	SNN	$47.53	$8,390	9.4%
5	Synthes	SYST.VX	$130.50	$15,488	9.2%
6	Medtronic	MDT	$39.62	$43,850	8.1%
7	Stryker	SYK	$48.73	$19,380	7.8%
8	TiGenix	TIG.BR	$6.63	$163	6.2%
9	***Average***			***$10,706***	***5.1%***
10	RTI Biologics Inc	RTIX	$3.89	$212	4.9%

Worst Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	Osteotech	OSTE	$3.04	$55	-35.0%
2	Regen Biologics	RGBO.OB	$0.50	$5	-28.3%
3	TranS1	TSON	$3.54	$73	-24.7%
4	NuVasive	NUVA	$33.80	$1,290	-22.8%
5	CryoLife	CRY	$6.11	$174	-20.4%
6	Symmetry Medical	SMA	$8.16	$292	-17.4%
7	Alphatec Holdings	ATEC	$4.19	$220	-12.0%
8	Capstone Therapeutics	CAPS	$0.67	$27	-11.8%
9	Orthovita	VITA	$3.75	$287	-11.3%
10	Kensey Nash	KNSY	$23.30	$258	-10.2%

Lowest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Symmetry Medical	SMA	$8.16	$292	8.89
2	ArthroCare	ARTC	$21.80	$584	12.89
3	Johnson & Johnson	JNJ	$62.31	$171,920	13.61
4	Kensey Nash	KNSY	$23.30	$258	13.82
5	***Average***			***$10,706***	***14.35***

Highest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	I Flow Corp	IFLO	$12.64	$309	292.33
2	NuVasive	NUVA	$33.80	$1,290	176.96
3	RTI Biologics Inc	RTIX	$3.89	$212	47.65
4	Synthes	SYST.VX	$130.50	$15,488	40.58
5	Medtronic	MDT	$39.62	$43,850	23.46

Lowest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	ArthroCare	ARTC	$21.80	$584	0.52
2	CryoLife	CRY	$6.11	$174	0.80
3	Orthofix	OFIX	$29.77	$510	0.84
4	Symmetry Medical	SMA	$8.16	$292	1.05
5	Exactech	EXAC	$16.16	$207	1.07

Highest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	NuVasive	NUVA	$33.80	$1,290	3.30
2	RTI Biologics Inc	RTIX	$3.89	$212	1.97
3	Johnson & Johnson	JNJ	$62.31	$171,920	1.84
4	Zimmer Holdings	ZMH	$56.92	$12,120	1.76
5	***Average***			***$10,706***	***1.69***

Lowest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	Osteotech	OSTE	$3.04	$55	0.62
2	Symmetry Medical	SMA	$8.16	$292	0.74
3	CONMED	CNMD	$21.46	$625	0.92
4	Orthofix	OFIX	$29.77	$510	0.98
5	Exactech	EXAC	$16.16	$207	1.22

Highest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	TiGenix	TIG.BR	$6.63	$163	227.88
2	Mako Surgical	MAKO	$8.80	$292	10.96
3	Synthes	SYST.VX	$130.50	$15,488	9.47
4	NuVasive	NUVA	$33.80	$1,290	4.20
5	Regen Biologics	RGBO.OB	$0.50	$5	3.22

Extremity Market Aims for $1 Billion

By Dev Joshi, PearlDiver Extremities Analyst

Extremity industry suppliers sold $250.1 million dollars worth of products in the third quarter (3Q09), exceeding our forecast by $4.6 million, or close to 1.8%. As a result, we have raised our extremity industry revenue forecast for the fourth quarter to $282.5 million, which would represent a 13.9% year-over-year (YOY) growth. We have also raised our forecast of extremity product sales for 2009 from $1.028 billion to $1.037 billion. Though the growth of extremity product sales lost some momentum during the last few quarters due to the economic recession, the industry still reported growth of close to 12% each quarter. This strong and consistent revenue growth across the whole extremity product market is moving the industry towards the psychologically important mark of $1billion in total annual revenue.

Top reasons why we believe the extremity product market has been consistently increasing sales revenues are as follows:

- Procedure volumes continue to grow
- Extremity treatment is still a relatively new area when compared to large joint and spine treatment, and there is plenty of room for medical advancement

New treatment options such as the reverse shoulder arthroplasty and new ankle replacement products have helped create a surge in procedure volumes in recent years. Revenue increase in 3Q09 of 13.9% was the highest reported since 3Q08. Domestic sales continued its upward trend, but sales in international markets were almost nonexistent due to changes in foreign exchange rates. The companies which reported the highest, double-digit growth percentages were Biomet, Inc, Wright Medical Inc. and Zimmer, Inc. Zimmer, which struggled since 4Q08 with flat or low single-digit growth in the extremity product market, has rebounded with a solid, high double-digit revenue sales..

Table 1 (next page) illustrates the quarterly sales performance of each of the extremity companies. The 3Q09 growth of 13.9% was surprisingly higher than our estimate of 12.3%. Innovation and increased demand have been the keys of success for this market.

As in quarters one and two, DePuy continues to hold the #1 spot as the

Table 1: Worldwide Extremity Product Earnings (in millions) by Company (2009-2012E)

Extremities	2009E							
Market	1Q09	2Q09	3Q09E	4Q09E	2009E	2010E	2011E	2012E
DePuy	$65.6	$50.4	$55.5	$64.0	$235.5	$260.0	$292.5	$328.0
Tornier	$39.2	$35.3	$38.8	$44.2	$157.5	$182.0	$205.8	$234.0
Zimmer	$33.3	$33.7	$32.6	$34.0	$133.6	$145.0	$159.5	$177.0
Wright Medical	$25.9	$25.6	$25.5	$29.4	$106.4	$128.2	$151.6	$177.7
Biomet	$20.3	$22.9	$20.6	$21.8	$85.6	$98.2	$116.2	$135.3
ArthroCare	$16.2	$17.3	$17.0	$18.0	$68.5	$78.7	$87.0	$94.5
Ascension Orthopedics	$6.1	$5.5	$5.8	$6.8	$24.2	$31.0	$40.8	$50.6
Exactech	$5.8	$5.1	$5.5	$6.5	$22.9	$31.2	$41.0	$52.8
Stryker	$5.8	$4.8	$5.4	$6.4	$22.4	$24.8	$26.7	$28.9
Others	$45.2	$40.4	$43.4	$51.4	$180.4	$203.5	$234.8	$268.2
Total	$263.4	$241.0	$250.1	$282.5	$1,037.0	$1,182.6	$1,355.9	$1,547.0
YOY Growth	*11.8%*	*11.6%*	*13.9%*	*14.0%*	*12.8%*	*14.0%*	*14.7%*	*14.1%*

Source: SEC filings, PearlDiver estimates and press releases. ArthroCare has not reported sales since 1Q08. Stryker sales represent only shoulder sales. Ascension and Tornier are estimates.

worldwide extremity product market leader in terms of total revenue.

Tornier, a privately held company from France, is #2 and Zimmer, Inc. is holding on to the #3 spot. Chart 1 illustrates the market share by company for 3Q09.

Individual Company Breakdown

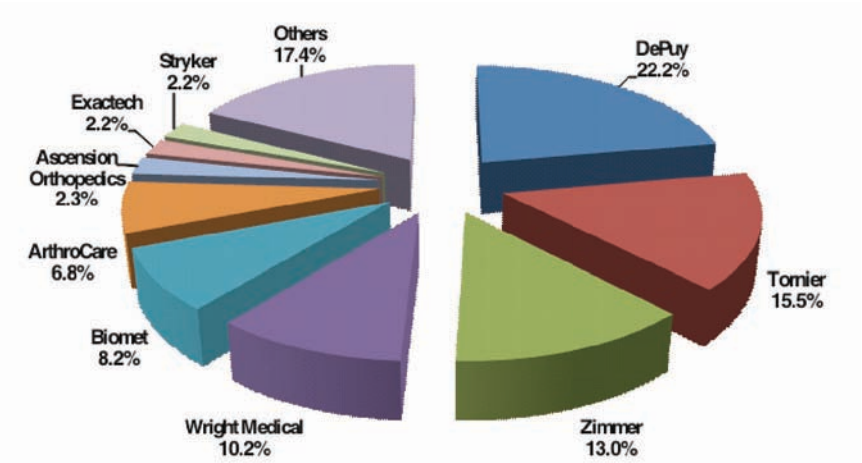
Zimmer Holdings, Inc.

Zimmer Holdings had a surprisingly strong third quarter. Following poor performances in the past two quarters, 3Q09 sales of $32.6 million, a 19% increase YOY, has given the company momentum again. The company's extremity product sales now represent 3.4% of its total sales—an increase from 2.9% in 3Q08. The total sales for the nine months ending September 30, 2009 are $99 million, an increase of 10% compared to total sales of the prior year's nine-month period.

Zimmer's domestic sales for the quarter represented 77.6% of its total extremity product sales with a growth of 25% YOY. The Bigliani/Flatow Shoulder Solution and the Zimmer Trabecular Metal Reverse Shoulder System led its extremity product sales in the U.S.

The European market, which holds 16.3% of Zimmer's extremity product sales, reported a 5% decline from 3Q08. The Asia-Pacific market, which holds just 6.1% of Zimmer's total extremity product sales, reported a 33% growth from 3Q08.

Chart 1: 3Q09 Extremity Product Market Share



Source: Sec filings and PearlDiver estimates

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Extremity products were the second best performing market for Zimmer behind products for the spine, which helped raise revenue 24% YOY due to the acquisition of Abbott Spine in 4Q08. For 4Q09 we estimate that Zimmer will report its second quarter of double-digit growth for the year at 13% YOY, bringing in $34 million in sales.

Biomet, Inc.

Privately held Biomet again had a highly successful quarter. In 3Q09 extremity product sales totaled $20.6 million, a 17.9% YOY worldwide growth from 3Q08. Sales in the domestic market grew by a whopping 39%. Biomet now holds about 8.2% market share, a slight increase from 8.0% in 3Q08.

The shoulder surgeon community has also strongly received Biomet products, especially the second-generation reverse shoulder prosthesis device which the company rolled out in May 2009. Worldwide demand has been strong for the comprehensive reverse shoulder system as well as the primary shoulder system. Other products showing strong demand are the Discovery Elbow and the ExploR Modular Radial Head.

Biomet has become one of the top manufacturers in the upper extremity product market, and we expect the company to report double-digit growth in the fourth quarter as it did in the third. For 4Q09 we estimate that Biomet will report 19.8% YOY growth from sales of $21.8 million. The reverse shoulder device will be a key factor for the future success of Biomet.

Wright Medical Technology, Inc.

Wright Medical is one of the top foot and ankle product suppliers in the world, distinguishing itself from other companies that focus primarily on the upper extremities. However, Wright Medical has not completely written off upper extremity products, and the company also has a shoulder system (Olympia) in the market. The company's extremity division represents 21.6% of its net sales worldwide, an increase from 19.5% in 3Q08.

For 3Q09 Wright Medical reported a growth of 17.7%, taking in $25.5 million in extremity product sales. While this is nowhere near the 38% growth in the prior 3Q08, it is still a significant increase, making Wright Medical one of the top three foot and ankle product suppliers in the world (next to DePuy and Tornier).

Wright Medical's success in the third quarter was primarily due to the 24% increase in its domestic sales of products such as INBONE, the CHARLOTTE Foot and Ankle System and the acquisition of Rayhack in 2008. International sales, however, dropped 10% in the third quarter. The previous quarter also showed an 8% decline in international sales due to a distributor transition in Australia and the unfavorable foreign exchange rates.

Wright Medical's extremity sales for 3Q09 represent 10.2% of the total extremity product market worldwide, which is up from 9.9% in 3Q08. Taking into account the slight decline in growth over the last three quarters, we estimate that 4Q09 will bring the company's total sales to $29.4 million with a growth rate of 18.5% for the fourth quarter. We estimate that total extremity sales for the year will be around $106.4 million, which represents an annual growth of 19.7%.

DePuy Orthopaedics, Inc.

For 3Q09, Johnson & Johnson's DePuy, the leading extremity product company worldwide, reported $55.5 million in product sales. This represents just over an 11% YOY growth, consistent with the last two quarters of 2009. DePuy experienced exceptional growth and brand acceptance with their Delta Xtend (reverse shoulder prosthesis) and Global AP (anatomical shoulder system).

DePuy's share of the extremity product market for 3Q09 is, we estimate, 22.2%, down from 22.8% in 3Q08. DePuy's major market is its upper extremities product line, especially the shoulder system, which represents around 80% of DePuy's total sales and is the driving force behind the company's growth. DePuy still reigns as the number one upper extremity product supplier in the world in terms of revenue and is one of the top three foot and ankle product suppliers.

DePuy, however, faces stiff competition from Tornier, Biomet, and Zimmer within its shoulder market while Wright Medical continues to be the one of the top three supplier in the foot and ankle arena. For 4Q09, we estimate that DePuy's extremity sales will continue to grow at a consistent double-digit rate just over 12% —buoyed by a strong shoulder device market. For 2009 we estimate slightly over 10% growth with total annual sales of $235.5 million.

Exactech, Inc.

Exactech holds a tiny portion of the extremities market, but the company's innovative line of shoulder products is getting attention and gathering momentum. For 3Q09 Exactech reported a growth of 31% in its shoulder division, which is exactly similar to the 31% growth in 2Q09. Sales for the quarter increased to $5.5 million from $4.2 million in 3Q08.

For the first nine months of 2009, sales of Exactech extremity products were up by 38% to $16.4 million, compared to $11.8 million for the same period of 2008. This was due to the continued success of the Equinoxe Shoulder System. We estimate that the shoulder division for 4Q09 will grow in the neighborhood of 30%, bringing in $6.5 million in sales. Extremity product sales for 3Q09 are now 2.2% of the total extremity market share worldwide, up from 1.9% in 3Q08.

Other Extremity Companies

Tornier, Inc., the second largest extremity product manufacturer, is still maintaining double-digit growth in the range of 15% for the quarter. We estimate that Tornier will report around $157.5 million in total extremity sales for 2009, a solid 12% annual growth rate. Tornier's lead products are the Aequalis Shoulder System and the NexFix MTP Fusion System.

Integra LifeSciences Holding Corporation reported low double-digit sales growth for the 3Q09 in its extremity reconstruction sales. According to management, forefoot product sales were weaker compared to its hindfoot and midfoot products, which were the stronger components in its extremity reconstruction market. Integra's international extremity market growth improved on both a dollar basis and in constant currency. We estimate that Integra LifeSciences' annual extremity product sales for 2009 to be at $75 million.

Small Bone Innovation, Inc. (SBi), Arthrex, Inc., Orthofix International N.V. and Acumed LLC have also reported strong double-digit growth for 3Q09. **Stryker Corporation,** which does not play a significant role in extremity treatment, reported an estimated 2% quarterly growth in its shoulder division sales.

Looking Forward

The extremity reconstruction market continues to be a small yet exciting slice of the orthopedic industry. Companies are posting strong results and will continue to do so. We expect the fourth quarter will be similar to the third quarter with growth of about 14% bringing the sales to $282.5 million.

PearlDiver research indicates that with the fourth quarter total, the extremity market will cross the billion dollar mark and report $1.04 billion in sales for 2009. Management of the extremity product companies sees strong growth potential and believes that their sector may become one of the fastest growing sectors in orthopedics.

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A Marriage Made in…the OR: Orthoplastic

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

Wedding of the Virgin:Raffael 1504/wikimedia.commons

If a plastic surgeon who later studied orthopedics had thought of this idea, the field might be called "Plastortho." Instead, Dr. L. Scott Levin, Paul B. Magnuson Professor of Orthopaedic Surgery at the University of Pennsylvania, an orthopedist who became a board certified plastic surgeon, had the eureka moment.

Melding Two Fields of Medicine

Dr. Levin, formerly a professor of both orthopedic surgery and plastic surgery at Duke University Medical Center, as well as Chief of the Division of Maxillofacial and Oral Surgery at that institution, explains his background: "When I began my residency in orthopedic surgery at Duke in 1982 we were required to do two years of general and thoracic surgery. This experience greatly broadened my understanding of surgery. I was accepted into the Duke orthopedic residency program by Dr. J. Leonard Goldner, who served as President of the American Society for Surgery of the Hand and was an extraordinary educator."

"I had always been interested in hand surgery," continues Dr. Levin,. "In part this was because after my undergraduate work, I went to Japan and studied reconstructive microsurgery with Yoshikazu Ikuta and Kenya Tsuge. In the late 1980s it was evident that the surgeons who were developing advances in microsurgery and free tissue transfer were plastic surgeons. In 1987 I went to the orthopedic Chair at Duke, Dr. James Urbanick, and told him that I wanted to do a plastic surgery residency. He was somewhat shocked as I had just spent six years doing general, thoracic, and orthopedic surgery. I explained that becoming a board certified plastic surgeon would give me additional skills to become a better hand surgeon."

A bit of an oracle, Dr. Levin could see that thinking big in orthopedics would increasingly mean thinking small. "In 1988 I began training at the Christine M. Kleinert Institute for Hand and Microsurgery in Louisville, Kentucky. I also spent time as an AO Fellow in Switzerland with Dr. Reinholdt Ganz (1988); I also did a period of study at the acclaimed Center for Reconstructive Microsurgery in Taipei, Taiwan (1991). Following this I was invited to remain on faculty at Duke, and was appointed to both orthopedics and plastic surgery by Dr. David Sabiston.

"I began my practice in 1991 and since that time have performed a variety of reconstructive procedures using the operating microscope to transfer tissue. For example, we often remove muscle from a patient's back and place it on the tibia to cover open fractures. This and other similar

procedures are powerful techniques that solve orthopedic problems. To be able to transfer living bone and tissue is just astounding. Other examples include transplanting a great toe to the hand of someone who had lost a thumb, as well as reconstructing head and neck defects in cancer patients. The bottom line: I took my knowledge of orthopedics and plastic surgery and applied the principles and practices of both disciplines to clinical problems simultaneously. The result: orthoplastic surgery."

Training Others in Joint Study

So has his work been met with a red carpet or a grimace? "These efforts were well received at Duke because orthopedic surgeons could readily see that I was providing a need for wound issues that arose during orthoplastic surgery. They relied on me to solve their complications. It went very well because when speaking with them, I was thinking like an orthopedist…as well as a plastic surgeon."

And the reception in the wider world? "Unfortunately, despite an immense need for microvascular surgery in the world of orthopedics, reconstructive microsurgery is not of much interest to orthopedists. It is not particularly well compensated and takes a long time to learn. It is technically demanding and involves such complexities as replantation and reattaching hands, fingers and arms. In the early 1970s it had an air of 'sexiness' that some found alluring. Due to reimbursement and tort reform issues, however, the vast majority of orthopedists now leave such work to plastic surgeons."

But there are those whose interest runs deep enough to assume this challenge. Dr. Levin: "I have trained many hand and microvascular fellows who want to use orthoplastic techniques for extremity reconstruction. I have seen them go on to perform free flaps and other microvascular procedures."

And regardless of which "camp" they come from, orthopedics or plastic surgery, they turn to Dr. Levin. "When I served as Chief of plastic surgery at Duke there were no turf battles because my background meant that I was a bridge between the two fields. Here at Penn I have been given the opportunity to create the same integrated hand service that combines orthopedics and plastic surgery. This cutting edge work involves exciting new ideas about soft tissue reconstruction that will help save limbs. Actually, we are in the process of creating a limb salvage and reconstruction center at Penn that will combine foot and ankle, trauma, tumor work, psychiatry, pain management, etc. This program has been created, and will be managed, by the Penn Health System. It was easy to sell the concept to such a collaborative institution."

The Future of Orthoplastic Surgery

Dr. Levin, who can be found at both orthopedic and plastic surgery meetings around the world, is now bringing his expertise and foresight to

the University of Pennsylvania. "One of my undertakings is to replicate the cadaver lab that I established at Duke, something that will allow residents and fellows to learn about new tissue flaps and the anatomy of new free tissue transfers, among other things. These trainees will also be able to take advantage of another new project here at Penn—composite tissue allograft (CTA) transplantation, the next frontier in orthopedics. Along with Dr. Abraham Shaked, Director of the Penn Transplant Center, I am creating the Penn CTA program, an effort that will be up and running in several months."

Revolutions happen at all levels… such is the case with composite tissue allograft (CTA) transplantation. Dr. Levin: "Applying orthoplastic principles to CTA will reshape the field of orthopedic surgery and change the lives of patients in dramatic ways. For example, let's say you lost an arm. The only thing I can offer you now is a prosthesis. With CTA you can actually have a new, 'living' arm. Or, if someone has a totally destroyed knee the only alternative at present is knee replacement. With CTA you could have a new knee. How? We remove the knee joint out of a donor and put it in your knee. Take elbow and shoulder work, an area where we know that the longevity in joint replacement is fairly short lived. If I can take a living elbow joint and transplant it, that will last the rest of the patient's life—assuming it is not rejected."

To address this last point, says Dr. Levin, researchers are increasingly looking at the basic science and immunology of implant rejection. "The fact is that orthoplastic CTA may improve the quality of life, but it is not life saving. If you needed a heart transplant you would accept the risk of immunosuppression. But you may not be open to this risk for a CTA elbow replacement because you have to take drugs the rest of your life—drugs that may contribute to cancer, diabetes, etc. Thus, the basic science research underway now is looking at ways to make patients tolerant of transplants. Our first patient will be someone who lost both arms and legs to infection—that person is in line for bilateral hand transplants."

These and other traumatic injuries often occur in the military arena. Because of this, Dr. Levin was invited to be a visiting scholar at Landstuhl Regional Medical Center in Germany, a staging center for soldiers brought in from Iraq and Afghanistan. "In Iraq and Afghanistan we have seen the most devastating soft tissue trauma ever because of Improvised Explosive Devices and Rocket Propelled Grenades. As a result, soft tissue techniques to save extremities have never been needed more than they are now. We are so fortunate to have advanced microvascular techniques that allow us to reconstruct shattered limbs. Unfortunately, most orthopedic trauma fellowships don't offer instruction on free flaps or microsurgery."

Dr. Levin concludes, "Reconstructive microsurgery needs to be present in orthopedic surgery because if not, the optimization of patient care in all subspecialties in orthopedics will be comprised. Knowledge of soft tissue handling and procedures should be part of orthopedic education. You should at least be aware of what is happening in the field and the possible treatment solutions that are available."

Leaving the U.S.

By Robin Young

My medical entrepreneur friends are spending so much time outside the U.S. that this country, for them, has become a kind of bedroom community. They sleep here, but go to work in Europe, China or Latin America. They still pay taxes in the U.S., but their medical technologies are, increasingly, gone, baby, gone. Since just this past July, four companies have told me that they plan to stop their applications at the FDA and shift resources to clinical studies and product launches in the EU, China or Brazil.

Here's a verbatim email I received last week from one particularly well known and famous U.S. inventor:

> "We are bringing our technology to China, as we find that going through the FDA has become prohibitive cost wise. The unpredictability of getting ultimate approval has caused us and many other U.S. companies looking for alternatives in bringing their advances to patients."

At a surgeon meeting just eight weeks ago, one young implant entrepreneur stood up and said that it costs him $2 million and a few years to get into the European market while costing $70 million and seven years to get into the U.S. market. He told the group of about 100 surgeons and business people that he has decided to avoid the U.S. market.

The strength of free markets, of course, is that it allows the unfettered movement of capital, technology and people—even if it means leaving the U.S. Well, the free market is operating. A couple decades ago, Rick Scott, then CEO of HCA could make a statement like, "The first words out of the mouth of U.S. tourists in Europe when they have a health problem is; 'Get me to the United States'." Most everyone would have agreed.

Today, if a patient wants the latest technology, they go to Cologne, Germany's stem cell hospital, or India's Wockhardt hospital system or the United Kingdom's Queens Medical Centre in Nottingham or South Korea's Wooridul hospital in Seoul.

All four use technologies that are more advanced than those available in the United States.

Because of the way the U.S. regulatory system is designed, U.S. companies have to seek predicates to pre-1976 devices in order to get indications for clearance under the 510(k) rules. The rest of the world has no such constraint.

Because U.S. surgeons are presented with devices that have been cleared according to pre-1976 technologies,

South Korea's Wooridul Hospital

they often find themselves in the position of going "off-label" in order to deliver proper patient care. If their European or Korean or Brazilian colleagues have data showing the proper, legitimate and successful use of a device that is NEW and if the U.S. surgeon decides to follow where the data is leading, they are then risking litigation, censure from politicians and, potentially, from their own surgeon societies for such "unapproved" indications.

Broken FDA

ReGen Biologics/Menaflex

The classic example is InFuse. This recombinant bone morphogenic protein was approved for use in the U.S. with Medtronic's LT spine cage in the lumbar spine using an anterior approach. Every time a surgeon uses Infuse in two levels, in a manner that is not with an LT Cage or is not in the lumbar region or with a posterior approach, he/she is going "off-label." We estimate that upwards of 70% of InFuse use is off-label.

Probably the poster child for what is wrong with the FDA/CMS system is the Menaflex story. Is the FDA really going to retract a 510(k) clearance—*not because the product in question was unsafe or in any way failed to perform in the market place*—but rather because their process is, to paraphrase the FDA, "broken"?

In 2004, after about a decade of conducting a clinical trial under the FDA's PMA (premarket approval) guidelines, a New Jersey company named ReGen Biologics submitted the first module of a PMA application for a product called Menaflex. Menaflex is a collagen implant to treat partial menisectomies. In 2005, the company decided to switch from a PMA submission to a 510(k) approach. The company believed that a pre-1976 predicate device existed that was substantially similar to Menaflex and therefore, could form the basis for 510(k) clearance. The FDA, with the PMA data in hand, twice refused to grant clearance under the 510(k) approach saying that the device was not substantially equivalent to other legally marketed devices.

Believing that its treatment by the FDA was capricious and, potentially, purposefully unfair, the company reached out to its congressional representatives. The Congressmen and Senator then signed and sent a letter urging FDA Commissioner von Eschenbach to review ReGen's submission to ensure a "fair and equitable process."

The accusation on the table is that ReGen, by going to its congressional representatives, applied excessive pressure on the FDA. But ReGen argues that the letter, which was vetted by the Senate Ethics Committee ***before*** being sent to the FDA, was not a request to clear the product; rather it was a request for a fair process.

Finally, at no time during the entire process was the safety of Menaflex in question. Nor, as it turns out, was its efficacy in question. Instead, this technology, which has now been studied for more than 15 years, is at risk of being pulled from the U.S. market. Given this risk, what is ReGen doing? It is focusing its Menaflex sales effort in Europe.

Going to Europe

The EU model is very different from the U.S. model. The EU, surprisingly we guess, appears to be quite comfortable with private industry involvement, specifically, through the

Notified Bodies process. The European FDA-like entities are referred to as "Competent Authorities" and they determined risk categories for devices—basically, low, middle, and high. The high-risk devices require clinical trials, which are governed like FDA trials. Lower-risk devices however, are farmed out for approval (or clearance) to private organizations that are responsible to the Competent Authorities. These private organizations are audited on a regular basis and are ***paid by the companies to do an evaluation of the product*** as well as make sure the company is in compliance with European regulations for manufacturers of medical products.

Compared to the fundamentally adversarial system in the U.S., this is a breath of fresh air.

The European model of medical technology review has proven to be faster, less expensive and more receptive of physician input with regards to technology evaluation than the U.S. system. Who benefits? The patients for starters. EU patients get access to the latest medical innovation. U.S. patients who want access to the latest technology or biologics either go overseas or go without.

The situation may be worsening. Such common and critical surgical products as bone cements, interbody cages, vertebral body implants and similar technologies, which have no material design or composite changes from technology predicates and were cleared years ago, are now being asked by the FDA to submit to NEW supplemental studies or biomechanical testing.

Routine 510(k) applications are now taking 6 to 18 months to complete and add cost burdens that routinely exceed $1,000,000 per device.

Lumbar Disc Arthroplasty Example

Lumbar disc arthroplasty (LDA) is one of the most advanced technologies for spine care and it was approved in the U.S. a couple of years ago. Patients who suffer from severe spinal disability and receive disc arthroplasty have reported substantial, long-term benefits, including minimal disability. Four U.S. pivotal trials were completed to study LDA. Each showed similar patient outcomes, at an estimated cost of $200,000,000 and cumulatively, 20 years of patient experience. Here's the kicker. While companies were spending such huge sums in the U.S. to approve the early generations of this new technology, European surgeons had progressed beyond these early versions and are now using fourth and fifth generation disc arthroplasty devices.

In fact, there are now 15 new lumbar disc technologies currently under development or study in Europe. **If these were all in the U.S., it would require, we estimate, an increase in clinical study costs of at least $750,000,000, and require five to seven more cumulative years of experience for each of these technologies!** Costs will likely be passed along to the consumer, with no meaningful gain to be realized by the clinical community.

The U.S. regulatory pathway today is more un-predictable and non-transparent than it was five years ago. Today's FDA is a large and onerous tax on the U.S. medical system and, taking the migrating entrepreneurs and scientists at their word, is the most powerful reason they are moving their business and technologies to Asia and Europe.

How can this system be fixed? Here are three simple reforms that came from another good friend, Charles E. Schneider, Vice President of Reimbursement at the Musculoskeletal Clinical Regulatory Advisers, LLC in Washington, D.C.

- First, the FDA must restructure its current 510(k) and PMA approval process to reduce cost and time to market. The European model which incorporates MORE clinician and manufacturer input is a great

first step. The system must find a way to combine clinical study requirements so that they can meet both FDA and Medicare evidence needs.

- Second, FDA staff must not treat industry or clinicians as the "enemy" and find ways to work more interactively with surgeon/scientists and the technology industry. Under the current system time is sincerely wasted because of recurring requests from FDA. The requests can clearly be more efficiently addressed by agency personnel with phone calls and, sad to say, a better understanding of technology and anatomy.

- Third, FDA staff must be better trained. At a minimum, FDA staff should spend time in actual clinical practice. Reviewers who are just entering the review process almost always lack relevant clinical or technical experience and therefore the capacity to make informed decisions, or even ask the right questions!

Candidly, I suspect it will take the exodus of a fair number of the best and brightest of our medical entrepreneurs before change can occur. It's called the Brain Drain and it refers to intellectual capital moving from one location to another. In this case, out of the U.S. and towards the EU, China and elsewhere. Companies, engineers and scientists are going to those markets that encourage medical technology innovation and advancement. Until the current FDA system can fix these issues, the U.S. appears to be destined to become the equivalent of a medical technology bedroom community to the world.

Brain Drain

NASS: Interesting Times

By Walter Eisner

The North American Spine Society (NASS) is entering its 25th year.

The organization's last two years have been about refining who and what the society represents, confronting ethical challenges that have disrupted the surgeon/industry relationships that drive innovation and, attempting to move the society into to what newly installed President Ray Baker, M.D., calls the "Intel Era of Spine Care."

It's not been an easy journey. Some former society leaders and members have openly criticized new NASS leaders for abandoning the cause of representing spine surgeons and instituting the profession's toughest disclosure and divestiture requirements.

Some spine companies are wary of the society's positions on coding and fear the organization is favoring existing procedures at the expense of new technologies to protect payments to surgeons. Sometimes the society seems it's between a rock and a hard place.

Baker told *OTW* during an extensive interview during the recent NASS meeting in San Francisco that the society's board has spent a lot of time on these issues, as well as redefining NASS' mission statement and central operating principle.

Who Represents Spine Surgeons?

Ray Baker, M.D., President of NASS

"The question came up, 'Are we primarily a member-based or a patient-based society?' The consensus was that, for NASS to be successful over the long run, we have to be patient centered. If we lose the patient at the center, then we're going to lose any chance that we have to affect policy or to advocate for change and our members will ultimately lose," said Baker.

> ***"Now, at times, that might put us at perceived odds with the short-term interest of our members on a specific issue. But if we look at the bigger picture, we can see that in the long run we're preserving the specialty and we're preserving it for generations to come."***

At last year's NASS meeting in Toronto, the society's then outgoing president, Tom Faciszewsk, M.D., announced the organization's central operating principle would be to promote quality spine care. That announcement begged the question, "Who will represent the best interest of spine surgeons?"

NASS' Executive Director Eric Muehlbauer, M.J., C.A.E., told OTW during the recent interview,

> ***"It's a bad rap for somebody to say we don't represent surgeons, because we do. We just don't spend 100% of our time on spine surgery issues. Not everything in spine relates to surgery. Spine care is a broad field. There is also a very distinct difference with how NASS operates compared to some other medical societies. We're a 501(c)(3) charitable, scientific, educational, non-profit organization. We have the tax exemption from the IRS because we are supposed to do something for the betterment of society in the U.S.A."***

Muehlbauer says some medical associations act like trade associations and are out to promote the interest of their distinct membership. "Not that we're not out to promote our members' interests, but we also have a larger purpose and we take it seriously."

"Does NASS represent spine surgeons?" asked Baker, an

anesthesiologist before answering his own question.

"Although surgeons represent the largest constituency in NASS, we are a multidisciplinary society. By maintaining a multi-disciplinary focus we actually strengthen our seat at the table. We are one of the few societies that can come before a panel and say we aren't a surgery-based society or an intervention-based society—we are a spine care society. We look after all interests."

"In the short-term," asks Baker, "does that put us at odds with one particular group?"

"At times," he admitted. "With a vocal minority," added Muehlbauer.

"Best Year Ever"

Both men say that NASS has never been stronger and credible with payers, regulators, other medical societies, its members, and the public to be able to face the coming challenges and to be able to take advantage of the coming opportunities.

Ray Baker, M.D., President of NASS

"We are not slowing down," said Baker. "In fact, we are probably going to have our best year ever this year. This year we have gained over 700 new members. We have over 5,500 members, and are on track to beat 6,000 by next year."

The change of mission, institution of new ethics rules and criticism doesn't appear to have changed the way NASS members vote with their feet.

"We have a 97% retention rate of our existing membership," noted Baker.

> ***"You know it is important to say there is a vocal minority of people who get upset at NASS—usually people who have a lot to lose. For instance, some are very upset about transparency. But when we look at the rank and file, they are not upset about this. In fact, they are expecting this. They are saying, 'We want credible voices as our spokespeople. We don't want to have this tied to industry anymore.'"***

Even with a tough new disclosure and divestiture policy, Baker says he is personally very gratified that the society has a 100% board retention rate. "When you look at our board, you're talking about thought leaders who I think are recognizable names. People can look and say we're not having to scrape the bottom of the barrel. We have really top-notch board members."

Reigniting Innovation

Baker hopes his term as head of NASS will be seen as a time when innovation is "reignited."

"I think one of our challenges is to reignite innovation in a different way."

Baker said he recently spoke to the CEO of a small spine company and said, "You know, innovation has stalled." The CEO responded that innovation has not just stalled, but stopped. He told Baker that it was not just in spine, but also in cardiac, in pharma, and in other areas. "There's nothing coming out anywhere and venture capital is sitting on the sidelines. So our challenge is, how we reignite innovation?" asked Baker.

Muehlbauer added,

> ***"Companies have been risk averse and not sure what they can do."***

"If I'm their attorney, I'm saying, sit on your hands, do nothing. But now that there is a better understanding based on corporate integrity agreement and other pronouncements indicating what's allowable and these third-party mechanisms are being formed for research, etc. and so on. Hopefully there is a backlog of interest in funding research and development activities, but doing it through the right mechanisms, in the right ways with the right processes."

Values

Baker agreed that the word "value" will be added to the current coverage framework of CMS [Centers for Medicare and Medicaid Services] that asks if a device or procedure is "reasonable and necessary."

He believes NASS can attempt to bring clarity and certainty to the situation by doing the following:

- Define value
- Work on proving value (registry, clarify CER (Comparative Effectiveness Research) parameters especially with regard to cost issues)
- Make sure that (CER) is not merely cost containment
- Work with the FDA to clarify what is needed to pass a new device (PMA versus 510(k))
- Work with CMS and insurers to provide industry with a stable 'bar' to achieve payment. (CER, RCT, Registry, some combination).

"Although these are not areas that NASS (or any other medical society) usually enters, who is better at defining quality and assessing new technologies than NASS, and who would you rather have do it, NASS or the government?" asks Baker.

Codes

Defining and proving value is where the society's mission will cause some stress. As an example, Baker cited NASS' activities in creating separate CPT codes.

"Say you make a new device that will decompress the spine, but will do it percutaneously and take one-third of the time of a standard open decompression. In addition it has very little associated risk. But you're billing it as if it were the more expensive, work-intensive, risky procedure."

"In the short term, that may be very good for the device company," continued Baker. "But in the long term, it puts all decompression procedures on the insurer's radar. The decompression CPT code gets on the radar for CMS and the whole family of CPT codes gets revalued and often down valued."

> ***"There are times that we have to lose some of the low-hanging fruit in order to maintain credibility for the big things. We are just trying to protect the things that are the bread and butter of our surgeons and other members."***

Vertebroplasty vs. Kyphoplasty – A Precursor

Another example of NASS' willingness to act in defining value was its recommendation to CMS over the relative value of kyphoplasty and

vertebroplasty. NASS and four other spine societies told CMS, in essence, they believed both procedures offered the same value and should be reimbursed at the same rate.

Baker said, "If you go back to that Intel model, you have two really fast processors. One costs more. We are saying, 'Shouldn't we call that question at some point?' I don't think we looked at it necessarily by saying, 'This is going to raise our credibility, so we're going to pick on this technology.' But, it came up, and we had to deal with it as we saw fit. The panel that went over this did a very good job of looking at all the literature and they really could not come up with any safety or efficacy data that distinguished these two technologies. And so, in the absence of safety or efficacy data, how do we separate them?"

"This was really, in many ways, the precursor to the value question," added Muehlbauer

Supporting Wang

While the new society leaders have received their share of criticism in pursuing a new mission, tough ethics policies and questions of whether or not they represent the best interest of surgeons, one has to note their standing shoulder-to-shoulder with board member and spine surgeon Jeff Wang, M.D., when he came under attack by Senator Chuck Grassley earlier in the year.

We asked Baker about the high profile investigations of spine surgeons David Polly, M.D. and Wang and the roles of societies in standing up for their members.

Regarding Polly, who resigned from the board of AAOS, Baker said, "That was a much more pressing issue for them. I know that we have taken the tact with Jeff Wang that we're going to stand by Jeff, and he has always complied with NASS' disclosure policies. We've talked with him and said that we can await the final verdict of the independent investigation."

While innovation may be at a standstill in the U.S. and Ray Baker and his society may have a perilous walk across the bridge to the "Intel Era of Spine Care," no one will be able to say it wasn't with eyes wide open.

Ultimately spine care professionals will decide with their membership dollars who best represents their interests. For now, the leadership at NASS is confident that their decisions and actions will help reignite innovation in spine.

company news

OtisMed "Custom-Fit" for Stryker

Alfred W. Elmore - The proposal/Wikimedia

Stryker's Stephen MacMillan told analysts during the company's last quarterly earnings conference call that it was looking to spend some of its cash on an acquisition.

On November 10, the company announced that it had acquired OtisMed, developer of a custom-fit knee technology.

OtisMed will operate as part of Stryker's Orthopaedics division and will remain located in Alameda, California. Stryker also announced that it had signed deals with Japan's Mutoh Co. Ltd. and Synergetics USA Inc. to acquire assets used to produce the Sonopet Ultrasonic Aspirator control consoles, hand pieces and accessories.

Specific terms of the two separate deals were not disclosed. Stryker said it expects to pay $67 million in upfront payments as well as up to an additional $36 million in future milestone and royalty payments.

Both deals are expected to close before December 31.

OtisMed developed the OtisKnee, which is based on the company's patent pending, proprietary ShapeMatch technology. Using 3-D software, the ShapeMatch technique attempts to optimize the size and placement of the Custom Fit Knee before surgery, based on the patient's own normal (non-arthritic) knee anatomy. From this 3-D image, custom cutting guides are created to assist the surgeon in making bone cuts that are specific to the individual patient. This, says the company, allows for a "customized" implant fit and placement.

—WE (November 13, 2009)

DePuy Spine's NASS Launches

DePuy Spine's stated mission is to "Never Stop Moving."

The company took its own advice and launched a new cervical allograft and cervical plate system at the just completed NASS (North American Spine Society) meeting in San Francisco.

The Uniplate 2 Anterior Cervical Plate System is a next generation single-screw midline fixation system. The Vertigraft VG2 Allograft incorporates Preservon technology and is, according to the company, the first allograft that can be stored at room temperature in a fully hydrated state.

The company says it has introduced 30 new products over the past three years, including eight this year, addressing spinal disorders.

Gary Fischetti, Worldwide President, DePuy Spine, said,

> "DePuy Spine is committed to continued innovation and filling patient and clinical needs across the entire spectrum of spinal disorders…This means offering solutions, not just products."

Cervical Plate

The Uniplate 2 is used for one- or two-level anterior cervical discectomy and fusion (ACDF). Single-screw midline fixation allows the surgeon to affix an implant using one screw per vertebral body.

According to the company, the device has a thinner profile between screw holes and flexible "bend zones" that allow surgeons to customize the plate to fit a patient's anatomy, and has less material on both ends to reduce the risk of adjacent level impingement. The device also has posterior cleats designed to reduce slippage and fourth generation Cam-Loc technology.

company news

Uniplate 2 / DePuy Spine

Preservon Technology

The Vertigraft VG2 allograft with Preservon technology is made of a composite of cortical and cancellous bone. Preservon is a new, proprietary glycerol-based preservation solution developed by LifeNet Health exclusively for DePuy Spine. The company says the solution eliminates the need to freeze or freeze-dry the allograft and avoids the lengthy thawing and rehydration process, which saves time in the operating room.

—WE (November 17, 2009)

Pioneer and Bonovo Storm Into China

Pioneer Surgical Technology and Bonovo Orthopedics have received permission from the Chinese government to market Pioneer's full portfolio of spinal fusion products in the country.

Pioneer spokesperson Jim Parks said on November 17:

> "For the past few years, the two companies have been quietly working through the arduous product approval process with the Chinese government. With that process now complete, Bonovo Orthopedics, Inc. will introduce Pioneer Surgical Technology's portfolio of spinal fusion products at China's largest orthopaedic meeting in two days."

The Pioneer/Bonovo partnership includes two American spine surgeons with legendary reputations in China. Hansen Yuan, M.D., Ph.D., serves on Pioneer's Medical Advisory Board and Anthony Yeung, M.D., a leader in minimally invasive surgery, is an early investor in Bonovo.

Parks says that China has the fastest growing spine market in the world. "The distribution agreement between Pioneer and Bonovo will boost American exports to China while helping to bolster the regional economy by keeping and growing jobs at home," added Parks. Pioneer Surgical is based in Marquette on the Upper Peninsula of Michigan.

Pioneer's Chief Marketing Officer and General Manager of Spinal Operations, Thomas McLeer said, "While it has taken a long time to get these products approved, there is an interesting advantage to have all of these products gaining approval at approximately the same time in that we are hitting the market in 2010 with a complete Pioneer 'fusion system'...not just individual products."

Shanghai at Night / Wikimedia

Bonovo's CEO Peter Slate said:

> "With Pioneer's leading-edge technology and Bonovo's customer service and support, we are confident that Pioneer Surgical will become the preferred brand by leading orthopedic surgeons throughout China. We are excited to get started."

Pioneer and Bonovo signed a comprehensive agreement in 2008 for the distribution and sale of Pioneer products in China with Bonovo serving as Pioneer's exclusive distributor of its products for the Chinese spine market.

—WE (November 18, 2009)

New Products and Buildings for Medtronic

Medtronic's spine and biologics unit has launched a new pedicle screw system

company news

and a ceramic scaffold used for fusion. The company can distribute these new products from a new $65 million distribution center opened on November 17 in Memphis.

TSRH 3Dx Spinal System

The new pedicel screw system is the TSRH 3Dx Spinal System, which according to the company, is designed "with procedural efficiency in mind, the TSRH 3Dx Spinal System offers two screws designed to address multiple pathologies. The Multi Planar Adjusting (MPA) Screw option provides surgeons a variable angle posted screw for targeted, controlled correction maneuvers."

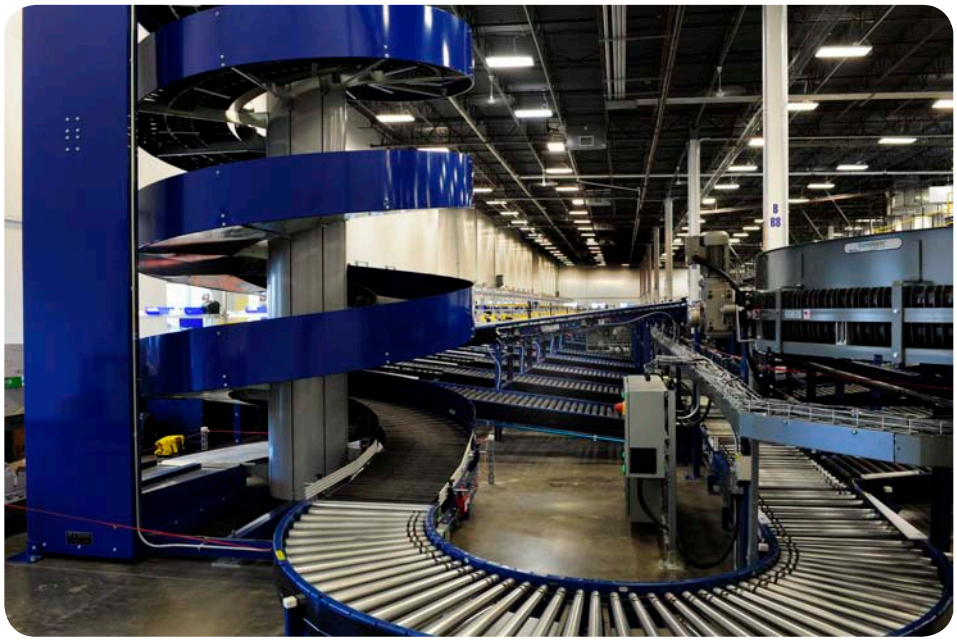
In 1987, Medtronic's collaboration with the Texas Scottish Rite Hospital for Children in Dallas, Texas, to develop a system to treat scoliosis, led to the development of the TSRH Spinal System—a hook, rod, and screw system used in spinal procedures.

Mastergraft Strip

Medtronic launched the Mastergraft Strip at the recent NASS (North American Spine Society) meeting and announced the full U.S. market release on November 18.

The Strip is a flexible ceramic scaffold that can be used in combination with a patient's bone tissue for fusing multiple levels of the spine. The company says the device helps patients whose spines have lost stability or their natural shape.

The strip provides a platform that allows surgeons to perform graft procedures with greater simplicity, eliminating the need to use multiple units of a synthetic product for a long fusion.



Spiral Conveyor and Loaner Processing Sorter/Medtronic Memphis

New Distribution Center

The company's new $65 million distribution center includes two buildings that will house around 260 employees and distributed spinal implants, instruments and other medical devices.

One building, newly constructed, is 157,000 square feet and is designed to accommodate an expansion of 300,000 to 400,000 square feet.

The other, was an existing 118,000 square feet building. It was renovated

company news

by adding a 34,000-square-foot mezzanine, bringing the total building to 152,000 square feet.

"It is important to grow this facility in Memphis because it is critical to our business model because of the strategic geographical location of Memphis and our partnership with FedEx and the FedEx air hub," company spokesperson Victor Rocha said. "There is a significant distribution talent pool to pull from in the city and the surrounding area."

Medtronic's spinal and biologics business is based in Memphis, where it employs 1,500.

—WE (November 19, 2009)

legal & regulatory

Synthes' Ti Synex II Recalled

The FDA has ordered surgeons and hospitals to immediately stop implanting the Synthes USA, Ti Synex II Vertebral Body Replacement device.

The agency initiated a Class 1 recall of the device on September 14, 2009.

Synex II/Synthes

The device is used in the T1-L5 portion of the spine to replace a collapsed, damaged, or unstable vertebral body. The company issued a statement stating the recall was related to a global voluntary recall of the device, which was initiated after receiving six adverse event reports.

The agency was responding to reports of moderate to severe loss of vertebral body replacement height, caused by failure of the central body component, in-situ at 6 to 15 months after implementation of the device. Potential adverse events include neural injury, increased pain, spinal kyphosis, failure of supplementary fixation, and need for revision surgery.

Physicians who have questions may contact the company at 1-800-620-7025 extension 5375. Patients who experienced adverse reactions/events with this device should report to Synthes at 800-752-0128 or email: ComplaintUnit@synthes.com.

The company notified hospitals and sales consultants about this recall by mail on September 23, 2009. On November 9, 2009, the company sent physicians a follow-up letter for their patients.

Synthes says it recommends annual monitoring of implanted patients by their physicians through radiographs and pain assessment. Radiographic changes and/or an increase in pain or other symptoms may be indicators of loss of device height and device failure. If patients have an increase in pain or other symptoms, they should contact their surgeons. This monitoring may or may not fall within Synex II surgeon users' routine postoperative care plan, and more frequent monitoring may be indicated depending on the patient's clinical profile.

—WE (November 13, 2009)

biologics

TiGenix Acquires Orthomimetics

Spinning out synergy…TiGenix, a biomedical company built around technologies developed at two Belgian universities, has announced the acquisition of Orthomimetics, a privately held medical technology company based in Cambridge, the United Kingdom. Orthomimetics, founded in 2005 as a spin-out from the University of Cambridge and the Massachusetts Institute of Technology, has products based on a collagen biomaterials platform for the production of scaffolds for cartilage, meniscus, ligament and tendon repair.

Orthomimetics' flagship product, Chondromimetic, is an off-the-shelf, resorbable implant for the minimally invasive repair of small osteochondral defects; it has received CE-Mark approval and is close to entering the European market. These types of osteochondral defects are not something that TiGenix has to date addressed in its product line. Thus, says TiGenix, Chondromimetic is an excellent fit with the former's lead product, ChondroCelect (both

biologics

products target the same customer base in complementary indications).

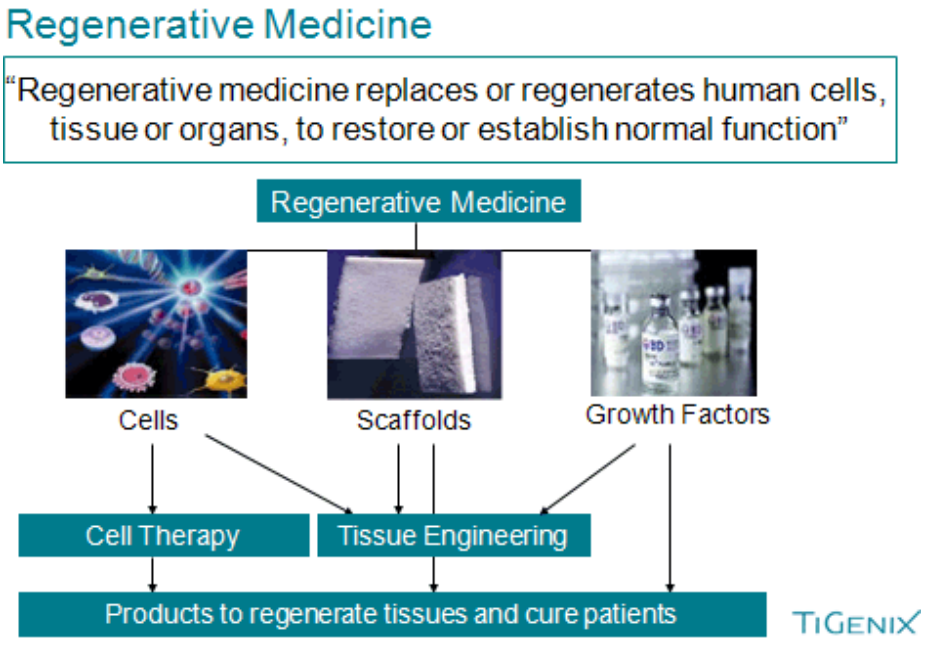
This agreement means that TiGenix moves more solidly into the biomaterials market. Orthomimetics' boasts a patent-protected ability to combine three natural biomaterials—collagen, glycosaminoglycans and calcium phosphate—into bioresorbable tissue regeneration scaffolds. The combination of Orthomimetics' biomaterials know-how with TiGenix' cell-based platform, says TiGenix, allows the company to broaden its development focus towards regenerative medicine products for meniscus, tendon, and ligaments.

In the news release, Gil Beyen, CEO of TiGenix, stated, "This consolidation represents a natural extension of our core business strategy to provide the best regenerative medicine solutions to orthopaedic surgeons worldwide. The synergies between Chondromimetic and ChondroCelect allow us to leverage our existing European infrastructure and commercial capabilities, and provide the opportunity to increase our near-term revenue growth with limited impact on our cash needs."

Beyen told *OTW*, "By combining Orthomimetics' collagen biomaterials platform with our expertise in cell-based approaches we will first focus on developing new combination products based on characterized cells and collagen scaffolds for meniscus repair."

Commenting on the strategic fit between the companies, Andrew Lynn, CEO of Orthomimetics, said in the news release, "The ability to equip a single sales force with two approved products that have the same point of sale is a clear and immediate commercial benefit."

Lynn, who will assume lead business-development responsibilities at TiGenix as Chief Business Officer, went on to add: "By bringing together key expertise and market-ready products based on cells, biomaterials and minimally invasive delivery systems, TiGenix has put itself in a strong position to drive the market uptake of regenerative medical treatments in orthopaedics. It is an honour for all of us at Orthomimetics to become part of this innovative and exciting effort."



Regenerative Medicine/TiGenix

biologics

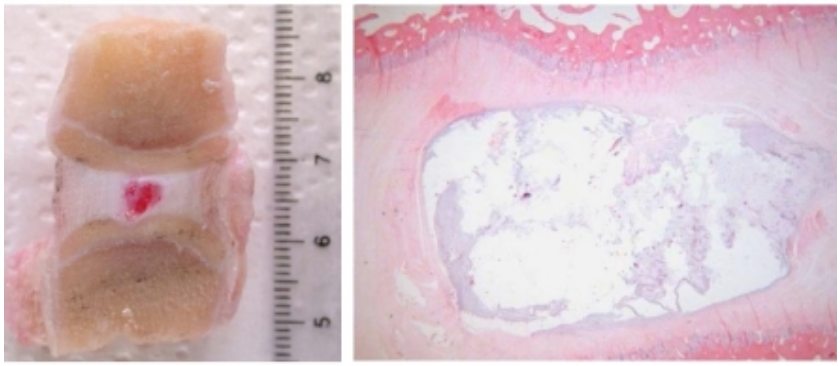
Lynn told *OTW*, "A strong cash position, two near-term product launches and a track record for delivering operational milestones are key elements of the sound fundamental position that the combined company will benefit from immediately. These sound fundamentals hold the potential to underpin a focused effort to consolidate some of the leading products and technologies in regenerative medicine. A priority of my remit as Chief Business Officer will be to work with Gil, Frank [Hazevoets, CFO] and the rest of the management team to identify and execute transactions that have the same key characteristics as the acquisition announced today, namely, contribution to TiGenix' near-term revenue generation, clear technological synergies and innovative potential, and a capital structure that preserves a strong cash position."

—EH (November 17, 2009)

Award-Winning Biomaterial Heals Discs

This biomaterial managed to win a 2009 Spine Technology Award without even having an official product name. Here are the details on a new potential treatment option for aging or damaged intervertebral discs.

A group of researchers in the UK have developed a biomaterial that could help save aging or damaged intervertebral discs without requiring a lengthy surgery or an implant. This hydrogel, a polymer swollen with water, is still in the gestation phase; the researchers have yet to give it a name or test it in human trials. Yet some spine specialists already see much potential in this technology—enough potential, in fact, to give these researchers a Spine Technology Award for one of the best regenerative technologies of 2009.



Biomaterial in Bovine Discs/Aston University

How Does it Work?

Professor Brian Tighe of Aston University has helped lead the project for over three years with colleagues from Oxford University and Keele University. The Aston biomaterials research unit combined their experience with artificial tissues with the expert disc physiologists at Oxford University and the top spinal surgeons at The Robert Jones and Agnes Hunt Orthopaedic and District Hospital NHS Trust at Keele University. After putting their heads together, the team came up with a biomaterial that closely mimics the natural tissue found inside intervertebral discs.

The nucleus of a spinal disc contains mostly water, and keeping those discs hydrated is the key to maintaining a normal disc height and spinal support. If a disc becomes injured or wears thin over time, it may lose the ability to stay hydrated which leads to serious pain and potentially osteoarthritis and spinal stenosis. There are some other minimally invasive, non-surgical treatment options which involve injecting material into the disc, but these procedures often require full or partial nucleotomy and use implants which may not fully restore disc flexibility. The hydrogel from the Aston-Oxford-Keele team, however, requires no nucleotomy, and physicians can inject the biomaterial directly into the disc. According to the researchers, this material could reduce some spinal surgery to a day procedure as well as offer a solution to the large number of patients deemed otherwise unsuitable for spinal surgery.

The Aston Biomaterials research unit first worked with artificial tissues in a completely different area—artificial corneas, the surface of contact lenses and chronic wound

biologics

areas. "This was a great stepping stone," says Professor Tighe, "that made us realize there are no long term biocompatibility problems or even short term biocompatibility problems in putting this material in contact with real tissue because the body uses very similar approaches to keep the tissue hydrated. Think of the way the cornea remains hydrated during the day and the way that the disk recovers so well overnight—the underlying mechanism remains exactly the same. And that is what we sought to mimic."

Funding, Research and Commercialization

The first chunk of funding for the research came from the UK government's Engineering and Physical Sciences Research Council (EPSRC). The team received about £750 thousand in grant money which was split evenly among the three universities. As for the initial tests of the biomaterial, according to Professor Tighe, "What we have done and have been doing continuously from the beginning is in vitro mechanical testing on various spine models using cow segments and sheep spine. We have done quite a lot of in vitro testing which has been all very successful."

"Following that initial grant," explains Professor Tighe, "which was really a three-year grant, we at Aston applied for a one-year follow-up grant from the research council in order to optimize the functioning of the material and to look at the commercial exploitation of the material. And that 12-month period is just about up now and we're writing up our research and results. So I think all of the fundamental work is done, and we feel that's it's now ready to go into the hands of people who will exploit it more widely than we are able to."

According to Darian Brookes, the team's Business Development Manager, "We have some contacts with firms, mostly in the US, and we are in the extremely early phases of what will hopefully lead to actual testing in humans."

And the research team's recent SpineTechnology Award might just help this project get the attention of potential partners. Professor Tighe adds, "This is a very welcome recognition, especially because we hadn't really set out for great recognition. It's the first time we've put our head above the parapet, and it's good to have it in such a prestigious area of awards."

—DK (November 20, 2009)

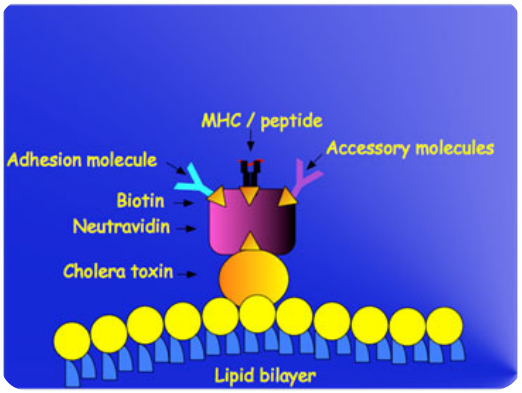
large joints

Study: Adeona's RA Tx Is Safe

Sending the immune system back to school...Adeona Pharmaceuticals, Inc. has announced results from a double-blind, placebo-controlled Phase 2 clinical trial using its oral dnaJP1 for the treatment of rheumatoid arthritis (RA)—the drug was safe and well tolerated. The six-month study, published in *Arthritis & Rheumatism*, involved 160 patients and was sponsored by the National Institutes of Health.

Oral dnaJP1 is an orally active epitope-specific immunotherapeutic molecule derived from a family of heat shock proteins that contribute to autoimmune inflammation in RA patients.

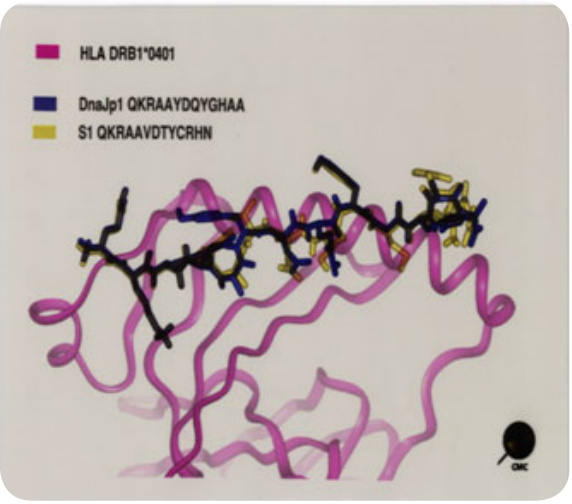
When asked for details on how heat shock proteins contribute to autoimmune inflammation in RA patients, Max Lyon, Adeona's President and CEO told *OTW*, "Heat shock proteins are evolutionarily conserved proteins expressed by all organisms during periods of cellular stress, especially during inflammation. When recognized by humans, they are recognized by the immune system and have the effect of further upregulating and perpetuating the inflammatory response. dnaJP1 is a heat shock protein subunit expressed in the



HLA - peptide complex is bound by the T cell receptor on the surface of T cells

large joints

synovial fluid of 75% of RA patients, and is therefore believed to be involved in the upregulation of the tcells that inappropriately become activated in RA leading to the inappropriate attack and destruction of cartilage. dnaJP1 is similar to the same antigen expressed by the bacteria e.coli. So in laymans's terms you can think of the immune system in the joints thinking that it is attacking e.coli, but instead is not; it is the human antigen and is misguided. When antigens that the body recognizes are consumed orally as opposed to via injectable vaccine, the gastrointestinal immune system teaches the immune system to not attack such antigens, (otherwise we would be attacking all of the food we eat). So by giving dnaJP1 orally, we are educating the immune system to NOT attack dnaJP1, a process known as immune tolerance. Immune tolerance represents the holy grail and potential future of autoimmune disease therapy, since it is disease modifying and can hopefully like a vaccine eliminate the need to take chronic therapies which are only symptomatic and have a lot of problems."



HLA molecule on the surface of antigen presenting cells (APC)is the immune receptor for the peptide

The randomized trial, held at 11 centers, found that there was a significant reduction in the percentage of T cells producing the porinflammatory cytokine tumor necrosis factor alpha (TNF-alpha). The primary efficacy end point (meeting the American College of Rheumatology 20% improvement criteria at least once on day 112, 140, or 168) showed a difference between treatment groups that became significant in post hoc analysis using generalized estimating equations. Differences in clinical responses were also found between treatment groups on day 140 and at follow up, which, says the company, is indicative of a durable response following discontinuation of therapy. Post hoc analysis showed that the combination of dnaJP1 and the commercially available RA agent, hydroxychloroquine (HCQ), was superior to the combination of HCQ and placebo, demonstrating potential synergy of dnaJP1 with HCQ.

In the news release Max Lyon commented, "We are pleased that this important study is receiving the scientific attention it deserves and believe that dnaJP1 has significant potential to improve the course of treatment for RA patients. We are currently engaged in a variety of activities required to support further clinical trials of dnaJP1 while simultaneously actively seeking U.S. and international licensing and corporate partnerships for this potentially important new therapy for RA."

Lyons also commented to *OTW*, "We were pleased to learn that this immune tolerance approach appears to have effectiveness for RA, a condition that causes a lot of pain and permanent disability for millions of people (and one for which current therapies sell $13 billion a year). This is the first study we believe to show the potential of this approach in RA. We think we learned a lot about which patients are more likely to respond; the biomarkers all seemed to go in the right direction, and this gives us confidence in the design and planning of further trials."

—EH (November 18, 2009)

Blue Belt: Super Cutter on the Way

A cut above…Pittsburgh-based Blue Belt Technologies, Inc. is going for technological gold. This Carnegie Mellon spinoff, formed in 2003 to focus on the commercialization of innovative devices, says that its Precision Freehand Sculptor is on the way to market, and on the way through the FDA. (In process, in process!)

Blue Belt's CEO, Craig Markovitz, told *OTW,* "When artificial joint components are installed, precise shapes must be cut in bone to insure proper biomechanics. Precision

large joints

Freehand Sculpting (PFS) provides a handheld tool that enables the surgeon to accurately cut these shapes without the need for the complicated jigs and guides currently used in surgery. Utilizing PFS, surgeons can perform minimally invasive procedures not possible with current surgical tools."

As indicated by the company, PFS belongs to a category of "semi-active" robotics that analyzes the surgeon's cutting motion and intelligently cuts bone. A preplanned target shape divides the bone into waste bone, which should be removed, and healthy bone to be preserved. When the surgeon moves the cutter over the bone, the PFS system determines whether it is over waste bone or healthy bone and cuts accordingly. PFS works by coupling the cutting tool to a computer system and a position tracking system. The tracking system monitors the position of the tool relative to the bone and feeds this information to the computer system. Software running on the computer determines, based on the tracking information and the surgical plan, if the bone should be cut or not and adjusts the cutter accordingly.

This method combines the advantages of robotic technology (such as accurate positioning and fast reaction times) with the skill and experience of a surgeon. Blue Belt indicates that PFS allows a much smaller footprint compared to other robotic systems, which is a welcome convenience in a crowded operating room. The

Precision Freehand Sculptor/Blue Belt Technologies, Inc.

company also noted that PFS provides a significant cost advantage over other surgical robots, and can often leverage surgical navigation technology that is already present in the hospital.

The company stresses that the product increases safety, saying that PFS provides a layer of safety through intelligent extension or retraction of a high-speed cutting bur relative to a surrounding guard. This guard allows precise exposure of the bur, accurately controlling depth of cut, and also provides protection to surrounding tissue structures. With this protection and added safety, the surgeon can work with less visibility, allowing for smaller incisions.

On the efficiency front, Blue Belt indicates that the continual switching of instruments is eliminated with PFS, and that the surgeon can use PFS to confidently pinpoint and address only the parts of the bone that matter.

Regarding any issues with adoption, Markovitz told *OTW,* "Surgical navigation and robotics have been growing in both recognition and market share. Our solution represents the addition of unique and powerful capability to existing instrumentation, is very cost effective and is adaptable to individual surgeon preference."

As for training, Markovitz commented to *OTW,* "Details on familiarizing surgeons with the technology are under development but we expect to conduct cadaver sessions as well as utilize a select group of early adoptors to begin the market education process. Since our technology leverages existing instrumentation

large joints

and navigation platforms, the learning curve has proven to be very short. Surgeons have been immediately able to understand how the technology works and can use the technology immediately in surgical procedures."

The company, a finalist in the recent Life Sciences category for the Pittsburgh Technology Council's annual Tech 50 awards, aims to have the PFS ready for sales within a year.

—EH (November 19, 2009)

Older Athlete? Get Moving!

Petr Novák/Wikipedia

"You take it easy, *I* have a hockey game," said the 65-year-old to her doctor. Researchers from the University of Pittsburgh Medical Center (UPMC) are reporting new findings that highlight the importance of higher impact athletics for older individuals. The study, which involved 560 athletes who took part in the 2005 National Senior Games (the Senior Olympics), is published in the November/December issue of ***Sports Health: A Multidisciplinary Approach***.

"Our study represents the largest sample of bone mineral density (BMD) data in mature athletes to date. My colleagues and I were surprised to see that active adult participation in the high-impact sports had such a positive influence on bone health, even in the most oldest athletes," said Vonda Wright, M.D., Assistant Professor of Orthopaedic Surgery at the University of Pittsburgh Medical Center, in the news release.

Participants in the games, which included basketball, road race running, track and field, triathlon, and volleyball, were on average 65.9 years old; there were 298 women and 289 men. Each athlete completed a Senior Athlete Health Registry Questionnaire with registration materials which requested general medical information. All respondents were then invited to participate in BMD testing via a calcaneal quantitative ultrasound of the heel of their dominant foot. After age, sex, obesity and use of osteoporosis medication were controlled, participation in high-impact sports was found to be a significant predictor of improved BMD compared to those individuals who participated in lower impact sports.

Dr. Wright told *OTW*, "We set out to ask, 'In the best of the best examples of active aging, would high-impact

large joints

exercise indeed be better for BMD than low impact…and low impact better than nothing.' Our hypothesis was confirmed. High-impact exercise was as important as the other top 5 predictors in maintaining bone density. Our conclusion for patients was that if they are going to do something for 30 minutes, make sure it is high impact."

"It is clear that not every mature adult can participate in high-impact sports, especially those with hip or knee osteoarthritis. However, this study suggests that high-impact sports can play a significant part in healthy bone aging. With a multi-part approach and the appropriate use of high-impact exercises individuals may be able to make greater strides against bone loss than the current treatment strategies imply," added Wright in the news release."

As for what orthopedists should tell their patients about this study, Dr. Wright commented to *OTW,* "Most orthopedists have focused on the young athlete while overlooking the largest growing group of active people in the country, the aging athlete. Instead of finding ways to keep mature athletes on the road, they are passed off with the advice to essentially, 'slow down and act your age.' One school of thought is that older athletes are wearing out the warranties on their bodies so they should stop using them at a high pace. I strongly disagree—telling people to slow down or stop is encouraging a sedentary lifestyle which we know is so dangerous to health. Instead, we should help them modify their programs to maximize performance while minimizing injury. I just completed a study on muscle mass in older athletes which involves a group of high-level runners. Because they only run, they have numerous musculoskeletal injuries from overuse. They need to expand beyond their sport of interest."

Specifying what can help older athletes, Dr. Wright stated to *OTW,* "Four things make the difference: flexibility(stretch the muscles and tendons daily); aerobic(intensity is more important than repetition); carrying a load (resistance training); equilibrium exercises (stand on one foot, do Pilates or Tai Chi)."

Fundamentally, said Dr. Wright to *OTW,* "I am trying to answer the question, 'What are we capable of as we age?' To put things in perspective, in the 2005 Senior Olympic Games, the 50-year-old male winner of the mile race won in 4 minutes 34 second, while the 18-year-old winner of the Pennsylvania state track and field mile won in around 4:11. That is a 30-year age span with not a lot of difference between their times."

—EH (November 20, 2009)

spine

USOC and D.I.S.C. Team Up

Whether a star pole vaulter needs a bone scan or a behavioral assessment, he or she can now get it under one roof. The United States Olympic Committee (USOC) and D.I.S.C. Sports and Spine Center have made it official: they have formed a strategic partnership in which D.I.S.C. will become an Official Medical Services Provider through the 2012 Olympic Games.

"The addition of D.I.S.C. to the USOC's sports medicine program is significant as we strive to provide first class, consistent medical care to America's Olympic and Paralympic athletes and hopefuls," said USOC Acting CEO Stephanie Streeter, in the news release. "With D.I.S.C. as Team USA's partner, we will be able to provide world class surgical care as well as state of the art rehabilitation and preventive care services to keep athletes in the best condition possible to compete at the highest levels.

1920s Olympics Poster/Wikimedia Commons

spine

The USOC is proud to partner with D.I.S.C. and looks forward to a long relationship."

Those athletes needing virtually any type of sports medicine care can avail themselves of D.I.S.C.'s specialists, who can provide comprehensive outpatient care in fields including spine and orthopedic surgery, chiropractic care, acupuncture, performance psychology, nutrition, and rehabilitation.

D.I.S.C. will be responsible for administering USOC medical records and streamlining medical care. This enables the athlete, the physicians and USOC medical personnel to easily track and follow, in real time, the care of the athlete from any location in the world.

Commenting on the real-time program was Dr. Robert S. Bray, Jr., D.I.S.C. CEO and Founding Director, who told *OTW,* "We intend to set up a medical records system that will allow total access to both USOC-qualified medical personnel and/or D.I.S.C. doctors as consultants that allows access to the USOC athletes for their medical history and any treatments or rehabilitation they have received and coordinate their care. Having access to past medical history and medical data as well as being able to update any treatments that are rendered provides for a continuity of their medical care from any location in the world.

"We are honored that the USOC has entered into this partnership with D.I.S.C. Sports and Spine Center as we embark on this progressive endeavor," said Dr. Bray in the news release. "Our philosophy at D.I.S.C. has always been to set a higher standard of medical care for our patients and we are committed to bringing this approach to the Olympic family. American athletes deserve every chance to go for the gold and we intend to do everything in our power to help them live their dreams."

As for what they are doing "out of the gate," Dr. Bray told *OTW,* "This is a combined effort to have in place by the time that the Winter Games start in Vancouver a basic computer system registering all of the active participants for their medical histories and bringing the first phase of the medical records system online. The second phase is to set up a regional referral system that is centered around D.I.S.C. Sports and Spine Center which will allow complete access to multidisciplinary care to any physicians in the practice and provide access for the Olympic athletes at a V.I.P. level for any of the services that are needed."

Dr. Bray also provided details to *OTW* on how the D.I.S.C. model translates to the USOC. He noted, "The USOC has historically worked with in-house limited medical and trainers with rehab as their model. The physicians and surgeons as consultants have simply been on a volunteer basis and there was no complete continuity either between these volunteer doctors repeating from Olympic games to Olympic games or availability in between. Furthermore, most of the Olympic athletes were left to obtain on their own referrals outside for treatment of their injuries. Under the D.I.S.C. model, we will serve as the first regional referral center

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for an Olympic athlete to come to and receive all aspects of care whether they are chiropractic, soft tissue, physiatry, pain management, neurological, or orthopaedic sports injuries. In addition, D.I.S.C. physicians will likewise be giving time and effort to Olympic, Paralympic and authorized games as well as participating as volunteers in training. This system will provide medical access to across the board specialties for the first time on a consolidated basis where all medical records will be kept consolidated as necessary information to be used for rehabilitation and training. This sets a new standard for sports medicine with a full integration of all aspects of care which had previously not been done at the USOC and is really not the standard even across the country where most groups are not integrated with all the aspects of care into a single practice so that they can look across the board at all the injuries from a conservative, training, rehab, soft tissue and/or surgical point of view. This brings the highest level of care in a consolidated fashion, with real-time tracking of medical records and outcomes and serves as a standard on which we hope to build on for the USOC and Olympic athletes."

—EH (November 13, 2009)

Biospace med Now in Virginia

Instilling—and installing—excellence…The visionaries at Biospace med, a medical technology company based in Massachusetts, and Paris, France, have announced that Spinal Surgery Associates of Charlottesville, Virginia, is the first healthcare facility in that state to install the *'EOS'* x-ray imager, the world's first ultra-low-dose x-ray technology.

The FDA-cleared EOS can capture head-to-toe images of patients in a standing, weight-bearing position with quite a reduction in radiation dose—up to 10 times less than a conventional X-ray and up to 1000 times less than a CT scan. Additionally, says the company, EOS images are designed to provide incredible detail and enable physicians to better diagnose and plan an effective course of treatment.

"High-quality spine-imaging is critical to my surgery-planning yet very difficult to obtain," said William Sukovich, M.D., in the news release. Dr. Sukovich, a spinal surgery specialist and founder of Spinal Surgery Associates, also said, "Until now, I have not been able to obtain an x-ray image quality that is suitable for my needs. But when I saw the superb image quality from EOS output in spine exams-***and*** at such reduced irradiation compared to conventional x-ray imaging-my decision to acquire EOS was immediate. EOS is exactly what a single-surgeon spine practice like mine needs."

EOS/Biospace med

William Sukovich, M.D.

Dr. Sukovich told ***OTW,*** "With EOS, I have access to vital information that was either previously unavailable or difficult to obtain—information that helps me to improve my surgical planning while limiting, to the very minimum, the amount of radiation to which my patient is exposed. I strongly believe that EOS can become the new gold standard in orthopedic imaging."

"We are tremendously pleased to announce the first installation of our ultra-low-dose EOS x-ray imager in one of the leading spine centers in the state of Virginia," added Marie Meynadier, Ph.D., CEO of Biospace

spine

med. "EOS represents an entirely new paradigm for the safe and effective imaging of patients, and we are looking forward to rolling out this revolutionary technology throughout the state of Virginia and across the United States."

Regarding their expansion, Dr. Meynadier told *OTW,* "We are not targeting specific states in the U.S. We believe that every patient in the U.S., when prescribed an X-ray, should have access to an ultra low dose, high quality exam made possible by EOS. To date we have started with east coast installations, but we already have midwest and west coast installations planned for early 2010 installation."

—EH (November 16, 2009)

The Picture of Success: Dr. Jo Hannafin

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

If her life had taken a different turn, she could have been digging ponds to raise fish in Asia. Instead, Dr. Jo Hannafin, Director of Orthopedic Research at Hospital for Special Surgery (HSS) in New York, ended up in a lecture hall at medical school.

"I was raised in Fall River, Massachusetts, an old mill town," says Jo Hannafin. "Our family was Irish Catholic, and both of my parents were born in the town and lived there all their lives. It is a town of traditions, and as such, I was baptized in the same church as my father. Education was hugely important to my parents, and my siblings and I were the first ones in the family to attend college. My dad worked as an X-ray technician and my mom stayed home to care for me and my two siblings. Because my dad worked with physicians and had them as mentors, he understood the importance of education for his children."

Far from human patients, Jo Hannafin began her scientific adventure in the realm of freshwater algae and plankton. "As an undergraduate at Brown University I considered premed, but it seemed overwhelming. So I became an aquatic biology major, something which opened doors to science that I might not have otherwise pursued. My faculty mentor, Dr. Leon Goldstein, invited me to spend the summer in his lab at the Mt. Desert Island Biological Laboratory (MDIBL) to study the physiology of osmoregulation in skates and dogfish sharks which were used as models for human disease. It was a life enhancing experience and I subsequently had the opportunity to spend several summers there."

Eager to apply her lab work to the field(s), Jo Hannafin considered joining the Peace Corps. "I wanted to sign on as a fisheries biologist, but there were no available openings in the Peace Corps at the time. I was fortunate to secure a position working with Roy P. Forster in the Department of Biology at Dartmouth College. Dr. Forster also taught in the medical school physiology program and invited me to attend physiology lectures in the medical school. While I had grown up seeing medicine through the eyes of my father, I thought it would be useful to see an approach based on science."

Embarking on a Career in Medicine

When Jo Hannafin decided to see medicine through her own eyes, she looked for a program where she could build upon her previous biological research. "After working in a research lab for two years I decided to apply to a M.D., Ph.D. program, and was pleased to be accepted at Albert Einstein College of Medicine in the Bronx. I had set my sights on this program in part because of the opportunity to do my thesis research with Dr. Rolf Kinne, whose work I knew from MDIBL. I decided to pursue a Ph.D. in physiology, and did my doctoral thesis in Dr. Kinne's lab where I studied membrane transport systems in mammalian kidney and the rectal gland of the dogfish shark."

Her head was still in the lab…then came the rotations. "Once I hit the wards, any thoughts of pursuing a career in nephrology or a related area began to fade. I was first exposed to internal medicine, but, while I intellectually enjoyed the complexity of the diseases that we were treating, I didn't like managing chronic disease. I then did an elective rotation with Dr. Martin Levy, an orthopedist who had operated on my knee when I was in medical school. I had been in training for the national rowing team and had a significant injury that he treated. Several years later I had to schedule an elective which overlapped with the trials for the world championship

team. I called Marty and he said that I could rotate with him and take time off to race in the trials."

"The sports medicine rotation opened my eyes to a potential career in orthopedic surgery. It was then that I realized it was possible to combine my intellectual side with my love of athletics. It was a visceral decision after just one elective…a leap of faith."

Dr. Hannafin continues, "I raced at the world championships that year, then returned to medical school and began my surgical electives. I was struck by the many different kinds of personalities there were in surgery. The surgeons and medical students I had met thus far were very strong willed and outspoken. I, on the other hand, was rather quiet. But no matter. I could see that I had found a field where I could correct patients' problems…and I knew that it was going to be in the realm of sports medicine."

Award-Winning Research

After completing medical school in 1985, Dr. Hannafin continued her surgical and orthopedic training at Montefiore Medical Center and the Albert Einstein College of Medicine. "It was a very busy residency as we staffed two public hospitals (one level 1 and one level 2 trauma hospitals) in the Bronx, as well as two private hospitals. Our surgical training was trauma intensive, and we rarely slept when on call (this was before the 80 hr work week). I was one of eight residents in my year and the only woman; it was a great bunch of guys who I remain friendly with to this day. The program was unusual for its time in that there were eight female residents spread out over the four year program. Ed Habermann, our chairman, was forward thinking in that way."

She continues, "My primary mentor was Martin Levy, who was also my medical school mentor. My other significant teachers were Leonard Seimon (spine and pediatrics), Neil Cobelli (trauma), David Hirsch (arthroplasty) and Neal Macy (pediatrics). They all had a very good balance between teaching us how to care for the patients in the clinic and hospital and developing our surgical skills."

Dr. Hannafin then began a two-year sports medicine and shoulder fellowship at HSS. "The first year was dedicated to research, during which time I worked with Dr. Steven Arnoczky in the Laboratory for Comparative Orthopedic Research developing models to examine the effect of mechanical load on soft tissue. My second year there set the stage to remain at HSS. Dr. Russell Warren, the Chief of the Sports Medicine and Shoulder Service and Surgeon in Chief of the hospital, offered me a position as the first clinician-scientist at the hospital. He could see that I was dedicated to research, and that the future of sports medicine would involve basic, translational and clinical research."

The visionary Dr. Russell wasn't the only one to take notice of Dr. Hannafin's achievements. "My first major award at HSS was the Philip D. Wilson award for excellence in fellowship research. The Orthopaedic Research Society also honored me with a Young Investigator Award for

that research. This particular work was among the first to demonstrate that collagenous tissues respond to the surrounding mechanical environment. Application of mechanical load to tissues such as tendon and ligament are critical for the normal maintenance of tissue—and the tissue can maintain its strength and elasticity. This work opened the door to several grants, including a Development and Feasibility grant from the NIH."

"Four years ago, I was awarded an R01 grant to look at the cellular responses to mechanical loading. Using both an animal model and 3D cell culture based systems I have studied ligament fibroblast response to loading and the possibility of

improving the potential healing response of a ligament that doesn't heal on its own. That grant, which is in its final stages, has been significant for my own sense of personal success and the results of our work will set the stage for future grant submissions."

With 40% of her week spent in the lab, Dr. Hannafin has time to take the ideas churning in her head and say, "what if…?" Detailing her other research, she notes, "I am also interested in the pathology and treatment of adhesive capsulitis, also known as frozen shoulder. This condition occurs primarily in women between the ages of 40 and 60, and involves the development of inflammation in the shoulder joint. This gradual process results in scarring and loss of motion in the joint. My students and I are interested in trying to characterize what happens to that tissue, why there is scarring, and what inflammatory mediators are involved."

She continues, "We have a study underway now looking at the efficiency of ultrasound guided cortisone injections in the shoulder joint at different stages of the disease. At this point we are collecting surgical biopsy specimens from those patients to look at what pathways are activated in the capsule (in the synovium) that cause the scarring. Our results thus far indicate that early injections in stage one can stop the progression of frozen shoulder. We have studied this area for many years, but in the past did not perform the injections under ultrasound or x-ray guidance. In order for these results to be accepted for publication, it is necessary to document that we are in the joint and that medication is being delivered to the site of the pathology."

An Expert Communicator

The only guidance she needs for her other work, however, is her gut instinct and the power to observe how others communicate. Dr. Hannafin: "I tend to be drawn to mentoring female medical students and residents because there are still different issues that women in medicine face that men don't usually have to deal with…such as about the timing of starting family. It also strikes me that there are real cultural differences in the ways that men and women convey information *and* receive information. This is often the case for patients, as well as medical professionals. It does not necessarily apply to all men and women, but we still need to be aware of the differences in all of our patients."

"To generalize, it appears that women often expect more detailed information concerning their condition and their options for treatment. They often will arrive having done an internet search or will be seeking additional opinions because they do not feel that they have received adequate information to make an informed decision. My thoughts in this area have changed dramatically over the years. If you had asked me 20 years ago about the differences between men and women, I would have said that we are all the same."

Whether guiding male or female students, Dr. Hannafin insists on a patient first approach. "It may be tempting to crank through the voluminous number of patients, but they deserve our undivided attention. I also emphasize to students that they shouldn't prejudge patients. When people come to see us, they are often in pain, and may be angry. And yes, it's harder to be kind and take time with someone like that. I try to teach by example and take the extra time to let someone vent—they usually feel better once they are heard. Then you can get down to the underlying problem and map out a plan."

And Dr. Hannafin makes sure that the patients understand that plan. "I try to educate patients about anatomy, as well as the underlying cause of their problem. If I come up with a treatment plan that doesn't fit in with their schedule, then they won't do it because they don't understand why it is important. You might be a technical genius in the OR, but if the patient doesn't understand what

you did, they may not approach their postop period correctly. For example, they may not make the appropriate lifestyle modifications, they might remove their sling prematurely, or they might use their arm or knee before they should. All in all this means that you *and* the patient didn't get a good result. Teaching the technical skills of surgery is fairly straightforward…it's the communication area that often gets us into trouble."

Preventing Injuries

Her breadth of knowledge also still makes its way to the water, field, or court. "I covered the 2004 Athens Olympic games for the U.S. rowing team, an amazing, once-in-a-lifetime experience. Just going to the dining hall and being surrounded by the best athletes from all over the world was incredible. I continue to provide care for the US Rowing team on an intermittent basis and stay involved in rowing through my position on the Board of Trustees of the National Rowing Foundation. This year I was honored by the US Rowing team when the Women's 8 was named for me. The women raced the Hannafin at the 2009 World Championships…winning the gold!"

"Closer to home, I spend time working with young athletes who experience sports injuries. My hope is that high school athletes will begin to move away from a single sport. I take care of a lot of female soccer players who often began the sport around the age of five. By the time they are 8 or 9, they're in a travel league, on regional teams, etc. From the frequency of play alone, the risk of injury is greatly increased. And if, for example, a 13 year old tears her ACL, that's the beginning of a lifetime of change for that kid."

Speculating about a "wish list" for her program, Dr. Hannafin notes, "If I were ever awarded a substantial amount of funding, I would target a portion of the funds to support our sports medicine patient registries at HSS. The members of the Sports Medicine Service at the Hospital for Special Surgery have committed time and resources to establish a series of prospective patient registries in the areas of ACL reconstruction, cartilage restoration, rotator cuff repair and shoulder instability."

"These registries over the years to come will provide an extensive data base to answer research questions concerning patient outcomes following the surgical procedures under study. I would target the remainder of the funds to the support of community rowing programs and injury prevention programs. Rowing programs such as Row New York and The Foundation for Rowing Education are designed to bring the sport of rowing to communities and students that are underserved. The Row New York program is a model for others as it combines rowing, mentorship, tutoring and SAT prep for their athletes."

There is another program that is turning Dr. Hannafin's head. "The American Orthopaedic Society for Sports Medicine (AOSSM) is developing a program entitled STOP: Sports Trauma and Overuse Prevention. It will be a comprehensive public outreach program focusing on the importance of sports safety—specifically as it relates to overuse and trauma injury in children and adolescents."

Dr. Hannafin is concerned that some in her field are forgetting an old aphorism…An ounce of prevention is worth a pound of cure. "I think that the field of orthopedic sports medicine is evolving toward the surgical care of the injured athlete and that less emphasis is being placed on the non-surgical care and the prevention of sports related injury. As sports medicine orthopedic surgeons we need to remain involved in all aspects of the treatment of our athletes."

Dr. Hannafin lives by the motto, "Find your balance between work, family and fitness and enjoy each day as it comes." She adds, "I am part of a family of athletes, having met my husband John Brisson while training as a competitive rower at the New York Athletic Club. John is now the Director of Youth Rowing at the Pelham Community Rowing Association in Pelham, NY. We have three children, Andrew, a collegiate swimmer and artist at Alfred University, Caitlin, a collegiate rower and student at Brown University and Connor, a high school diver and student at Greenwich HS."

Dr. Jo Hannafin…preventing injuries and researching new solutions.

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