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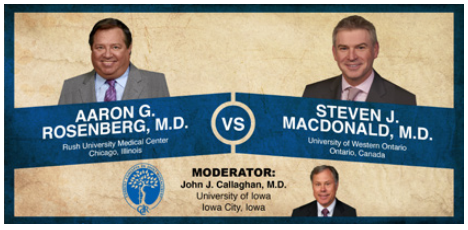
Orthopedics This Week

WEEK IN REVIEW

5 Zimmer/Biomet Deal in the FTC Gears >> It's been more than 60 days since Zimmer announced it was acquiring Biomet. The FTC has 30 days to decide if they want to block the deal. What's happening? The former FTC antitrust lawyer who negotiated the consent decree which allowed Synthes and DePuy to merge, gives his opinion. Read it here.

8 Surprising MicroPort Orthopedics >> Simply put, MicroPort is the most interesting company in large joint recon. With the big guys pushing scale economics, MicroPort is betting on innovation economics—and geographic expansion. Think #1 ortho company in China on top of a powerful innovation engine—all from Memphis, USA. These guys are on to something.

11 Rosenberg, McDonald Debate Tourniquet-less TKA >> "Pain is lower without a tourniquet, and non-tourniquet patients have better ROM," says Aaron Rosenberg. "Hold up," says Steve MacDonald. "Do you really want to increase OR time and cost when there is no evidence to support the supposed downsides of using a tourniquet?"



15 Health Care Happenings at the World Cup // Rush University: OA Pain is Lower With PRP AND HA // Columbine-Tested Doctor Advises Orthopedic Colleagues on Behavior During Mass Casualties// Navy Seals' Orthopedic Surgeon Discusses Massachusetts General, Sports Medicine >> Bert Mandelbaum, M.D. is on site at the World Cup and lets us know the structure and challenges of health care at this massive event. Brian Cole, M.D. of Rush details findings of his new study on OA, PRP, and HA. Up-close lessons for orthopedic surgeons from the Columbine and Aurora theater shootings. And Matt Provencher, M.D. talks about his new role at Mass General, and gives his thoughts on sports medicine.

BREAKING NEWS

20 Expanding Orthopedics Awarded Chinese Patent

Olympus Halts **OP-1** Effort

$1.7 Million to **Case Western Engineer** for Growing Tissue

Frustrated Canadian **Surgeon Opens Own Clinic**

Top 11 Recommendations to Improve the FDA

Boeing and ACOs Dump Insurance Middle Man

For all news that is ortho, read on.

Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

THIS WEEK: Orthopedic supplier consolidation puts the top-tier competitors (ZMH/Biomet, SYK, DePuy) in a stronger position. The risk of being left out of hospital contracts falls when the number of vendors falls. Large hospitals like a Zimmer/Biomet, DePuy, and Stryker oligopoly. One more key point: hospital-employee surgeons who are expert on implant systems that are widely used across different hospitals become more marketable, valuable and geographically flexible.

RANK	LAST WEEK	COMPANY	TTM OP MARGIN	30-DAY PRICE CHANGE	COMMENT
1	6	Orthofix	6.75%	11.91%	As CEO Mason makes the rounds (JMP and Jefferies most recently) the number of institutional buyers is rising.
2	3	Exactech	10.15	9.83	EXAC's new computer-guided knee system getting very broad exposure at key meetings in June and July.
3	4	Integra LifeSciences	11.77	4.75	Get this: IART's Q1 earnings jump 84%, but miss ZACK's estimate by a penny. So they downgrade to a "sell." Really?
4	8	Medtronic	28.84	6.58	Medtronic's deal to merge with Covidien has more than its fair share of political and FTC issues. But so far, so good.
5	1	Zimmer	28.42	1.40	Zimmer's long tenure at the top of the Power Rankings finally ends. Valuation is why. Plus the next six months is all about closing BMET.
6	2	Stryker	15.71	1.61	With the idea of buying SNN percolating in the background, SYK's highest priority now is digesting what it already bought.
7	5	Symmetry Medical	6.55	0.57	From an earnings perspective, this year should be a very good year for SMA. Sales, however, look flat, flat, flat.
8	10	Johnson & Johnson	26.58	4.68	Ironically, Zimmer's purchase of Biomet helps DePuy. It moves the industry to a rational oligopoly and fits with the new economic model of medicine.
9	9	MicroPort Scientific	35.16	(9.77)	We really like MicroPort's focus on innovation and geographic expansion. It can eventually drive well above average sales growth rates.
10	NR	NuVasive	6.05	4.09	Goldman Sachs upgraded NUVA saying that the company's natural operating leverage will drive profit margins up.

Robin Young's Orthopedic Universe

TOP PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	MiMedx Group	MDXG	$6.94	$733	23.05%
2	Orthofix	OFIX	$35.80	$660	11.91%
3	Exactech	EXAC	$25.25	$345	9.83%
4	LDR Holding Corp.	LDRH	$24.78	$646	8.92%
5	Tornier N.V.	TRNX	$23.76	$1,154	8.20%
6	Smith & Nephew	SNN	$88.65	$15,832	6.74%
7	Aurora Spine	ASG	$2.75	$43	6.69%
8	Medtronic	MDT	$64.12	$63,848	6.58%
9	Integra LifeSciences	IART	$47.15	$1,536	4.75%
10	Johnson & Johnson	JNJ	$104.99	$297,027	4.68%

WORST PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	Baxano Surgical Inc	BAXS	$0.56	$27	-15.17%
2	MicroPort Scientific	853	$0.63	$892	-9.77%
3	K2M Group Holdings	KTWO	$14.05	$535	-5.70%
4	Alphatec Holdings	ATEC	$1.44	$141	-4.00%
5	Globus Medical	GMED	$24.09	$2,251	-1.91%
6	ConMed	CNMD	$43.91	$1,195	-1.57%
7	TiGenix	TIG.BR	$0.88	$141	-0.41%
8	Bacterin Intl Holdings	BONE	$0.68	$37	0.00%
9	Symmetry Medical	SMA	$8.87	$333	0.57%
10	Zimmer Holdings	ZMH	$104.35	$17,512	1.40%

LOWEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Medtronic	MDT	$64.12	$63,848	16.92
2	Zimmer Holdings	ZMH	$104.35	$17,512	17.64
3	Johnson & Johnson	JNJ	$104.99	$297,027	18.62
4	Stryker	SYK	$83.97	$31,833	20.14
5	Exactech	EXAC	$25.25	$345	20.78

HIGHEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Orthofix	OFIX	$35.80	$660	298.66
2	NuVasive	NUVA	$35.11	$1,636	113.27
3	Symmetry Medical	SMA	$8.87	$333	79.90
4	MicroPort Scientific	853	$0.63	$892	35.24
5	Smith & Nephew	SNN	$88.65	$15,832	28.12

LOWEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Exactech	EXAC	$25.25	$345	1.15
2	Globus Medical	GMED	$24.09	$2,251	1.54
3	ConMed	CNMD	$43.91	$1,195	1.91
4	Zimmer Holdings	ZMH	$104.35	$17,512	2.11
5	Stryker	SYK	$83.97	$31,833	2.22

HIGHEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Orthofix	OFIX	$35.80	$660	16.23
2	NuVasive	NUVA	$35.11	$1,636	10.13
3	CryoLife	CRY	$9.02	$253	6.80
4	Symmetry Medical	SMA	$8.87	$333	6.66
5	Smith & Nephew	SNN	$88.65	$15,832	2.84

LOWEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	Alphatec Holdings	ATEC	$1.44	$141	0.69
2	Symmetry Medical	SMA	$8.87	$333	0.83
3	Bacterin Intl Holdings	BONE	$0.68	$37	1.12
4	RTI Biologics Inc	RTIX	$4.37	$247	1.13
5	Baxano Surgical Inc	BAXS	$0.56	$27	1.37

HIGHEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	TiGenix	TIG.BR	$0.88	$141	24.71
2	MiMedx Group	MDXG	$6.94	$733	10.91
3	Wright Medical	WMGI	$31.09	$1,552	6.03
4	MicroPort Scientific	853	$0.63	$892	5.84
5	LDR Holding Corp.	LDRH	$24.78	$646	5.79

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

MicroPort Orthopedics

Integrity In Motion™

Your *New* Global Partner, with 60 Years of Orthopedic Excellence.

Quality

Our talented manufacturing team, built on 60 years of experience in Arlington, TN, remains focused on Quality

We're only as good as the last patient experience.

Our mission is to get patients back to a state of mobility that feels as natural as possible.

Innovation

Our investment in the future fuels our relentless pursuit of technology to keep us ahead of the market and you ahead of your patient's expectations.

Responsiveness

We are driven to provide you and all our customers around the world with the most responsive, reliable service in the industry.

To Learn More About Microport Orthopedics Visit Us at www.ortho.microport.com

Zimmer/Biomet Deal in the FTC Gears

BY WALTER EISNER

The phones on the desks of hospital purchasing agents who buy hip and knee implants from Zimmer Holdings, Inc. and Biomet, Inc. are ringing right now.

On the other end of the line are investigators from the Federal Trade Commission (FTC). The investigators are asking the purchasing agents, among other things, if they believe the prices they pay for medical devices will go up if Zimmer is allowed to acquire Warsaw hometown rival Biomet.

Darren Tucker/Bingham McCutchen LLP

According to Darren Tucker, the former FTC antitrust lawyer who handled the Johnson & Johnson/Synthes merger while working for the agency, if the answer is no, that's pretty much the end of the story and the FTC will allow the Zimmer/Biomet deal to proceed. If the answer is maybe, the investigators will look for more data. If the answer is yes, the agency kicks into a high gear that could doom the deal.

Hart-Scott-Rodino Waiting Period

The Hart-Scott-Rodino (HSR) Act requires companies to file a premerger notification to both the FTC and the Department of Justice (DOJ). The agencies then agree who will review the case, but in ortho transactions it is usually the FTC. The premerger notification is full of information about each company's business. The parties may not close the deal until a 30-day waiting period has passed, or the government has granted early termination of the waiting period.

Photo creation by RRY Publications LLC

Good Timing for Ortho

Tucker told investors during a Bank of America conference call hosted by analyst Bob Hopkins on June 19, 2014, that Zimmer is going to the FTC at a good time. The FTC staffers believe the marketplace in orthopedics is made up of highly sophisticated purchasers who have enough interchangeable products to choose from. Furthermore, going from five major suppliers to four does not set off antitrust alarm bells at the FTC.

Hospital mergers are the big deal at the agency at the moment with antitrust experts sitting on pretty good evidence that those mergers are driving up healthcare prices. Tucker also said that the agency, which looks for regulatory victories to tout to Congress and the media, will be unlikely to find them in orthopedics.

Tucker is surprised that since the deal was announced back in April, there has been no announcement from Zimmer. The HSR Act does not require the premerger notification to be filed at any particular time after a public announcement of intention to merge. A Zimmer spokesperson could not confirm or deny to us whether or not a premerger notification has been filed with the FTC.

The only public response to the merger so far has come from European regulators who put a halt to their review of

the merger because Zimmer didn't supply the needed information. Zimmer said it is responding aggressively to the request for more information.

"Pull and File"

Because the agency has 30 days to act and nothing has been made public, Tucker suspects Zimmer may have performed a "pull and refile" maneuver. After the company files the pre-merger notification documents, one of three things happens as the FTC looks at a deal.

First, says Tucker, the preliminary investigation with customers in the market might show that there is little fear of rising prices. In that case, the agency allows the HSR period to close and the deal proceeds.

Second, there may be some very limited questions on the minds of the investigators, but the company has a strong belief that the deal will be allowed to proceed. By "pulling and refiling," the company is giving agency another 30 days to settle their questions.

The Dreaded "Second Request"

Companies have a strong incentive to do that because if the staff questions are wide and deep enough, the agency will proceed to the third option: a "Second Request" order. Then all hell breaks loose as this sets up a massive roadblock which will extend the review period for many months. Only 4% of deals get a second request. Following the second request, there is a massive discovery request with depositions and subpoenas for documents from the parties as well as third parties. This can take as long as four to five months.

If a "Second Request" order is issued, there is a very heavy reliance on ordinary course of business documents to make the FTC case. That's where investigators uncover, what Tucker called, "hot docs," where parties sometimes say things they really wish they hadn't said. Investigators will dissect ordinary day-to-day documents which show things like who they view as their competitors including win/loss records, bidding records, marketing plans and strategies and strategic plans; all of which is designed to look at or to get at the idea of who is really competing against each other in the marketplace.

Search for Unilateral Effects

In the initial 30 or 60 day review period, Tucker says FTC lawyers and economists are looking for "unilateral effects." That is, are the merging firms' products particularly close to competi-

tive products? Will a significant number of customers consider the Zimmer/Biomet products to be their first and second choices?

The investigators will want to know that if the merged company raises prices, are the purchasing agents going to continue to buy from the merged company and will they consider other competitors' products to be very distant substitutes.

They'll want to understand how customers actually purchase the products and how many suppliers they feel they need to maintain competitive pricing. Do they do things through RFPs (requests for proposals) or other types of formal bidding processes? Do hospitals limit it to two or three suppliers? They will want to talk to surgeons and other medical professionals to better understand to what extent the different suppliers in the market offer unique products or the extent to which, for example, Zimmer and Biomet's products are unique in any way; this gets back to the idea of looking at the closeness of competition between the parties.

Product Differentiation

If there are a number of surgeons that state Zimmer and Biomet are offering the best products, that is potentially a concern. If, on the other hand, the surgeons say that they like all of the products on the market or if they weren't able to turn to Zimmer, they would be happy with J&J's or Stryker's…hat would be very helpful for the transaction.

The FTC will also look at whether or not there are other companies that might replace the competition that would be lost from the merger. That new competition can come from two places. It could come from new entrants into a market, or it could come from an existing competitor. Agency investigators will ask if other players in the marketplace might reposition their products or might make other changes to make headway with customers that might be dissatisfied from the transaction.

In short, Zimmer and Biomet's fate lies in the hands of their customers.

Five to Three and Market Share

That proposed consolidation will reduce the number of major U.S.-based hip and knee makers from four to three, with only Zimmer/Biomet, DePuy Synthes and Stryker remaining. Stryker has made it clear it is considering an acquisition of Smith & Nephew, which is based in England but makes its implants in Memphis, Tennessee.

Going from five to three major market competitors in a marketplace raises antitrust concerns. It was a consent agreement negotiated by Tucker that required DePuy to divest itself of its wrist trauma business before the FTC allowed the Synthes merger to proceed.

With JNJ/Synthes, Tucker said the FTC was concerned about the market for wrist fracture treatment systems and found that the merging parties would have over 70% share in that market. However, Tucker believes that non-industry outsiders often mistakenly place too much emphasis on overall market share statistics.

Market shares are not the only consideration. Yet, said Tucker, 70% is high and a merging party would have a hefty burden to convince the FTC that there is not a problem with the merged companies having a 70% share of most any market.

Dave Dvorak, Zimmer's president and CEO, told analysts on April 24, 2014 that it was important to keep in mind that the orthopedics market is a $45 billion industry. He noted that Zimmer's market share in knees is in the mid 20% range, while Biomet is in the lower teens. In hips, Zimmer is close to 20%, while Biomet has a similar share.

According to Tucker, the market shares in ortho are high with Zimmer/Biomet but certainly not showstoppers. With sophisticated customers doing everything they can to drive down costs, you typically don't need to have five competitors for the customers to maintain competitive price levels. Four would certainly seem to be adequate and maybe even three, according to Tucker.

The other thing the FTC will look at is how many suppliers are needed to maintain competitive price levels, and this is very much an industry specific issue. There is no magic number of how many competitors you need in an industry to remain competitive. There have been some industries where the FTC has actually allowed deals to go from three to two, for example, without there being a problem because customers said they only need two suppliers because they can hammer the two against each other or play them off each other.

Clearance Expected

Tucker believes the FTC will want to clear the case quickly because he does not see the agency wanting to push to make a big case in ortho transactions right now. They are more interested in the hospitals for which the purchasing agents work. Maybe FTC staff is taking the opportunity to ask those purchasing agents some questions about their own competitors. ◆

Surprising MicroPort Orthopedics

BY ROBIN YOUNG

Courtesy of MicroPort Orthopedics, Wikimedia Commons and Yassine Mrabet

Orthopedics is simply one of the foundational pillars of all medicine. Demand for orthopedic medical products and services will likely never, ever decline. Whether the issue is trauma (fractures, wars, auto accidents) or arthritis or congenital defects like cerebral palsy or back pain…global demand currently exceeds supply and will be rising for as long as anyone cares to forecast.

Any company that aspires to be a diversified provider of medical products and services eventually comes to orthopedics. The only other sector that could arguably approach orthopedics in terms of universality and rising demand is wound care. But even wound care doesn't reach the sheer patient volume and diversity of orthopedics.

So when MicroPort, the Shanghai-based (and Hong Kong exchange traded) medical device company decided to diversify it went to orthopedics AND the United States.

This impressive two-fer is, in retrospect, a notably smart strategic coup. Since MicroPort's purchase, Smith & Nephew plc bought ArthroCare Corporation, Zimmer Holdings, Inc. bid for Biomet, Inc. and Stryker Corporation is evaluating the purchase of Smith & Nephew. Orthopedic equity values are rising as buyers are realizing that the number of large joint recon suppliers is rapidly shrinking.

There is a ***scarcity value*** to large joint reconstruction companies.

Who Is MicroPort?

Simply put, MicroPort is the most interesting company in large joint recon.

This 16-year-old company was founded by the former VP of R&D for Atlanta-based Cryomedical Sciences, Inc.—Dr. Zhaohua Chang. Dr. Chang was raised in China where he earned a master's degree in cryogenics (his Ph.D. degree in biological science is from the State University of New York) and realized the clear need for a Chinese-based medical device company.

So in 1998 this scientist, author of more than 40 peer-reviewed articles and holder, at the time, of five patents, founded MicroPort Scientific Corp.

MicroPort's first products were devices for cardiac catheterization and stent implantation. At the time, only 3,000 patients in China had had coronary stents implanted (vs. 700,000 in the U.S.).

With the backing of the Chinese government MicroPort launched a balloon dilation catheter. The company would not turn a profit until 2002—

but Chinese hospitals began to learn that MicroPort was capable of supplying high quality and reliable implants and instruments. Before then, Chinese hospitals were nearly 100% dependent on imported cardiac instruments and implants.

In 2003, MicroPort received a license to sell its coronary products in Japan—which was a major milestone for the company since it meant that its products were of sufficient quality to compete in the very demanding international markets.

Also in 2003, MicroPort introduced the first Chinese produced drug-eluting stent (DES). Chinese physicians were openly skeptical that a domestically produced implant could match JNJ's or Medtronic, Inc.'s or Boston Scientific Corporation's quality. Very few physicians were willing to use such a technically complex and advanced domestic product. So MicroPort made clinical studies a particular focus. The resulting clinical data demonstrated the quality of MicroPort's DES. MicroPort was one of the first Chinese medical device companies to overcome the country's deep rooted prejudice against domestically produced complex implants.

Today, it holds the #1 share in China's DES market. Eventually it hopes to hold the #1 share in China's orthopedic market.

In 2010, in order to fund its expansion into markets outside of cardiovascular (electrophysiology (EP), diabetes and orthopedics) the company sold $198 million of its stock on the Hong Kong Stock Exchange.

As befits a company whose founder comes out of research about 20% of MicroPort's employees are in research & development and the company invests 16-18% of revenue on R&D.

Innovation Economics, Not Scale Economics

In the five months since MicroPort (MPO) closed on its $290 million purchase of Wright Medical's large joint recon business, a clear (and increasingly unique) direction is emerging—innovation over scale.

Said Ted Davis, CEO of MicroPort Orthopedics and Chairman of MicroPort's InterContinental Executive Committee (IEC) responsible for businesses outside of China: "This is the time to turn the innovation engine back on. This year we doubled our historic rate of R&D spending. Wright Medical had a strong history of innovation in large joint reconstruction. But in recent years that was shifted in favor of increased investment in extremities."

Indeed, for the past several years, it seemed as though Wright Medical, as it was investing in foot and ankle, biologics or hand and wrist technologies, was harvesting the large joint recon business to fund extremity R&D.

Such an explicit commitment to innovation stands in contrast to what appears to be scale economics driving decisions at the larger hip and knee recon firms. Indeed, hip and knee reconstruction appears to be consolidating into three firms—Zimmer, DePuy and Stryker.

Commenting on his industry's recent urge to merge, Davis said: "Orthopedics is seeing price compression for the first time in 20 years. How to deal with price pressure? Larger players with larger infrastructures are cutting pay for distributors and looking for ways to economize wherever they can, for example with synergies from mergers."

Added Jonathan Chen who leads MicroPort's International Businesses and is co-chair along with Davis of MicroPort's IEC, "for MicroPort this is a great opportunity. Our purchase of Wright's large joint business was the first of the current merger wave and we've had a full year to bring these two companies (MicroPort and Wright's large joint recon) together. We can now play offense."

MicroPort's Growth Plan – Innovation and Geographic Leadership

In 2013, Wright's sales of hip and knee implants were $231 million (FYI - 2012 was $269 million). The brands are DYNASTY and CONSERVE hip implants, PROFEMUR stems, SUPERPATH minimally invasive hip surgical instrumentation and ADVANCE and EVOLUTION medial-pivot knee systems.

Considering that the global hip and knee recon market is about $14 billion, MicroPort starts with just under 2% share of that market.

Leveraging off MicroPort's strong reputation in China, these former Wright Medical large joint implants and instruments should attract, at a minimum, an equivalent share of the $1.3 billion projected Chinese recon market in 2018 for another $30+ million, bringing the total business size, prospectively, to $300 million.

Added Chen, "Geographic expansion of the Wright Medical's brands was part of our original thesis for the acquisition and it is coming to fruition—especially in the Chinese orthopedic market. Demand for MicroPort Orthopedics in China is strong and exceeding our forecasts. We can't produce instruments fast enough to meet demand."

MPO's biggest challenge, said Chen, was access to Western surgeons with familiarity of the Wright instruments and implants to train the Chinese sur-

geons. While the company only has 2% global hip and knee market share currently, according to Davis and Chen, there is 98% upside.

THE Fast Recovery Company

According to Davis, MPO's vision is to use innovation to drive market penetration and, at the hospital level, economics and improved outcomes. There are two elements to MPO's vision:

1. Design implants, instruments and procedures which speed up hip surgery recovery. In this vision, the sale is less about the "widget" and more about the procedure. MPO's focus is on becoming THE fast recovery hip surgery company via innovative implants, instruments and procedural innovation.
2. MPO begins with a strong medial pivot knee platform. Wright Medical made a strategic decision to invest in its extremities business and didn't allocate the resources to push the medial pivot since the development of the EVOLUTION system. As a result it never really captivated the U.S. market. That's changing under MPO, said Davis. The key is data and, Davis told *OTW*, the company is approaching 15-year data on its medial pivot knee. Fifteen-year data is indeed a strong platform upon which to launch a renewed effort to capture knee market share.

#1 Chinese Ortho Company: Made in Memphis

Every company in orthopedics has a China strategy. But MicroPort IS China.

Both Davis and Chen made it clear that MicroPort's goal is to become the orthopedics market leader in domestic China—currently the second largest economy but if growth continues at current rates, could soon be #1.

Wright Medical's large joint recon business had a presence in approximately 60 countries, including China, before MicroPort. With MicroPort, these implants could quite possibly become the largest selling hip and knee implants in China. That those implants would be designed, forged and packaged within hailing distance of Beale Street is, well, quite the deal.

To support this long term plan, MicroPort announced this past week that it would expand its Arlington, Tennessee, headquarters operations to include a surgeon training facility and invest $100 million over the next five years "in product design, manufacturing capability, and world-class training and education facilities."

The expansion is expected to create 171 jobs.

Said CEO Davis: "The team at MicroPort Orthopedics is excited to partner with the state of Tennessee to expand our operations. Together, MicroPort and Tennessee will create high-quality jobs, attract and retain top caliber employees, and manufacture world-class medical devices for the global orthopedic market. We truly appreciate the support we have received from our state and local officials, especially those working in the Department of Economic and Community Development."

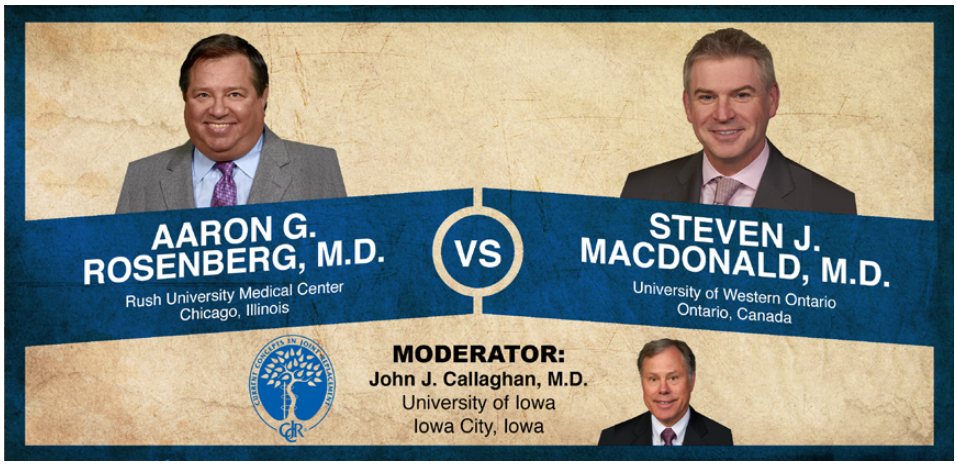
MicroPort Orthopedics: the most interesting hip and knee company in orthopedics. ♦

Rosenberg, McDonald Debate Tourniquet-less TKA

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

"Pain is lower without a tourniquet, and non-tourniquet patients have better ROM [range of motion]," says Aaron Rosenberg. "Hold up," says Steve MacDonald. "Do you really want to increase OR time and cost when there is no evidence to support the supposed downsides of using a tourniquet?"

This week's Orthopaedic Crossfire® debate is "Tourniquet-less TKA: Let it Bleed." For the proposition is Aaron G. Rosenberg, M.D. from Rush University Medical Center; against the proposition is Steven J. MacDonald, M.D. from the University of Western Ontario. Moderating is John J. Callaghan, M.D. from the University of Iowa.



Current Concepts in Joint Replacement/RRY Photo Creation

Dr. Rosenberg: "We're all trying to get to an operative experience that will results in a pain-free, fully functional knee. We have recently had improvements in peri-operative analgesia and rehab techniques, as well as certain biomechanical things to improve alignment and component design. We've also used closure in flexion and cryotherapy. And we've been focusing on the consistency that comes from reducing outliers and complications. Avoiding the tourniquet helps you accomplish all of these things."

"First of all, it allows you to get the bleeding vessels as they come up, as opposed to obliterating them with the tourniquet and then ignoring them when the tourniquet comes down…allowing the blood to accumulate in the knee. Several studies have looked at tourniquet versus no tourniquet TKA [total knee arthroplasty], and almost all show a benefit. In 1997 there was a study in the *Journal of Arthroplasty* showing less thigh pain postop; in 2001 the *Canadian Journal of Surgery* had a study showing less overall blood loss and a trend toward fewer complications. A 2009 article in the *Journal of Thrombolysis* showed reduced local thrombogenic/fibrinolytic activity; it also found that the tourniquet release, after being up for a period of time, causes systemic activity. Finally, a 1998 study in *Anesthesia and Analgesia* revealed fewer DVTs [deep vein thrombosis]."

"The biggest concern has been blood loss. A meta-analysis from 2011 (Tai et al., *Knee Surgery, Sports Traumatology, Arthroscopy*) compared tourniquet to tourniquet-less and found that the total measure of blood loss favored the use of a tourniquet. Many of the other measures show no significant difference between the two…or a slight favoring of the tourniquet (but primarily only for intraoperative blood loss)."

"A 2010 meta-analysis (Smith et al., *Knee*) involved 15 studies and 1,040 TKRs [total knee replacement]. The researchers found that no tourniquet use led to greater intraoperative blood loss, but there was no difference in total blood loss or transfusion rate, or any other measure assessed. And there was a trend to more complications with a tourniquet."

"In 2013 Li et al. published a study in the *European Journal of Orthopedic Surgery and Traumatology* comparing TKA with and without a tourniquet. It involved 15 studies and 804 patients; there was no significant difference in calculated and measured total blood loss. Use of a tourniquet decreased intraoperative blood loss, but increased postoperative blood loss. My contention is that this blood frequently ends up in the knee, causing hemarthrosis and a reduced rate of return of flexion. There was no significant difference in operative time."

"We now have several modalities available to us to help reduce perioperative blood loss. Tranexamic acid is probably the most widely studied in TKA, and it seems to be safe and effective. Also, there is a device by Medtronic (for whom I am a consultant) that uses bipolar radio frequency and saline, and

shrinks the blood vessel collagen in the soft tissue and bone."

"In a study published in 2012 (Ledin et al., *Acta Orthopaedica*) the researchers were looking to see whether or not tourniquet use improved fixation in patients with cemented knees. They randomized 50 patients to TKA with or without a tourniquet, and they used RSA (radiostereometric analysis) at regular intervals to measure fixation quality. They found no difference in motion of the components with RSA, and total bleeding at day four was slightly less in the tourniquet patients. However, pain was lower in the non-tourniquet group, and the non-tourniquet group had better ROM at two years (11 degrees greater). So consider going without a tourniquet…get the bleeders as you go. Use adjunctive means to reduce blood loss, avoid hemarthrosis, thigh pain, and other deleterious sequelae."

Dr. MacDonald: "I have performed TKAs without tourniquets; there are pros and cons. There are a few randomized clinical trials (RCTs), many opinion pieces…but there is no registry data."

"There can be no argument that a tourniquet reduces intraoperative blood loss. The 2010 meta-analysis mentioned by Aaron showed significantly greater intraoperative blood loss without a tourniquet. However, overall blood loss—intraoperative and postoperative—was not different between tourniquet and tourniquet-less groups. So the question becomes, 'Do you want it in your field, or later, when you're finished?'"

"Several studies do show decreased blood loss. In an RCT of 72 patients, the tourniquet group showed much less overall blood loss than those who didn't have a tourniquet. But there is that short, transient postoperative pain that some people get in their thigh."

"So if you're going to use a tourniquet, how much of the procedure should you use it for? An RCT published in 2012 in the *ANZ Journal of Surgery* recommend-

ed—as I do—that if you're using a tourniquet, use it for the whole procedure."

"It's a given that we want a dry bone surface for cementing. If you don't have that there is a potential for increased risk of late loosening. There are techniques around that (to get a dry bone surface): meticulous hemostasis, pulsatile lavage, and filtered carbon dioxide."

"But they all come with costs: dollars and time. A 2010 study in the *Journal of Bone and Joint Surgery* (Willis-Owen, et al.) with 3,500 patients found a direct correlation between OR time and infection rate in TKA. This paper concluded that 'steps to minimize intraoperative delay should be instigated,' and that 'care should be exercised when introducing measures which prolong the duration of joint replacement.' Be cautious in telling anyone to do something that's going to increase your OR time."

"As for the proposed downsides to a tourniquet, they're either basic science theories or are rare or short term. One thing you hear all the time is 'vessel wall damage leading to increased DVT.' Is there a single clinical paper supporting this? No! Fukuda, et al. conducted a study involving tourniquet versus tourniquet-less (*Archives of Orthopaedic and Trauma*, 2007) where they gave all patients ultrasounds pre and postop. They found no difference in the incidence of DVT between these groups."

"What about increase in wound healing disturbances? There is no evidence of that. Delay in muscle function recovery? No evidence of that. As for nerve damage, I think everyone who has done knees or used tourniquets for a long time will see transient nerve damage. I don't think they're permanent."

"So don't use a tourniquet if: you are concerned about the theoretical risks, you have alternatives to a dry field, if they are cost neutral, you don't increase the OR time, and you don't need published data on long term results."

Moderator Callaghan: "Aaron, after that diatribe, do you have any other rebuttals?"

Dr. Rosenberg: "We use a tourniquet because it provides us with a bloodless field and makes the operation easier to perform in some respects. There are areas where that is vitally important, such as upper extremity surgery and flexor tendon repair in the hand. In the knee, where the landmarks are much larger, the amount of bleeding that one encounters isn't sufficient to warrant the downside effects. And there are the occasional findings that you get in someone who has a swollen thigh or a postop decrease in ROM because of the effect of the tourniquet. Also, most of us have gone to not getting the bleeders as you go, letting the bleeding occur after we've closed the knee…and we end up with more blood in the knee than we'd like. By getting the bleeders and being meticulous in your approach, the morning after surgery when you remove the compressive bandage and begin ROM, I find the knees to be flatter, less full of fluid. The thigh is much softer and more amenable to the first day of physical therapy. Occasionally you need to do a TKA without a tourniquet; as you get more experienced with this it become much easier."

Moderator Callaghan: "Steve, anything else?"

Dr. MacDonald: "Use a tourniquet."

Moderator Callaghan: "Aaron, sometimes people say, 'I don't use a tourniquet, but I put it up when I'm cementing, etc.'"

Dr. Rosenberg: "I generally put the tourniquet up during the cementing process. So I will almost always put the tourniquet up unless the patient is a vasculopath. Also, it does allow you to see when you've got a significant lateral geniculate vessel should you encounter a significant trauma. Having the tourniquet in place is useful in case you have a vascular accident of significance. Some patients have a very dry field and we don't need to put the tourniquet up to cement the knees; in cementless knees I don't think it matters very much. "

Moderator Callaghan: "Aaron, you and I are a decade older than Steve, so seeing bleeders is a bit more difficult for you and I. The other point is, if it's the vasculopath or the person that you don't put the tourniquet up for, do you do any preparation on the bone?"

Dr. Rosenberg: "The one thing that I haven't used to clean the bone is the CarboJet; however, I'm very meticulous in my preparation of the bone—regardless of whether or not I use a tourniquet. I'm also meticulous about injecting the cement, and if I don't get a good injection then I pressurize it with my thumb over the entire surface of the femur and the tibia so that it has a stippled appearance."

Moderator Callaghan: "Steve, is there a tourniquet time that you get more concerned about?"

Dr. MacDonald: "I use tourniquets for my revisions as well…then it's a bit more of a timing issue. I think, 'Am I going to be able to get the whole revision done and cemented in place by the 120 minutes?' Sometimes we'll let it down for a period of time, but I want it up when I cement in a revision. What I don't know is what the pressure should be. I put it up to 300 (350 if they are obese). But there is probably an ideal pressure, and

it may be quite a bit lower than 300… that may mitigate the downsides."

Dr. Rosenberg: "I think that's true. It's shocking that so many of my colleagues have that tourniquet up to 300/350. I generally try to pick 100mm of mercury above the mean arterial pressure."

Dr. MacDonald: "Some complications—like thigh pain—are related to time."

Moderator Callaghan: "If you let down a tourniquet on a bad revision, how long do you have to keep it down?"

Dr. MacDonald: "There's no data on that, but I do a minimum of 30 minutes."

Moderator Callaghan: "Thanks, guys." ♦

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

Health Care Happenings at the World Cup // Rush University: OA Pain is Lower With PRP AND HA // Columbine-Tested Doctor Advises Orthopedic Colleagues on Behavior During Mass Casualties// Navy Seals' Orthopedic Surgeon Discusses Massachusetts General, Sports Medicine

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

Left image: Created by RRY Publications LLC/Wikimedia Commons. Middle image: Jo Hannafin, M.D., Ph.D. with Dr. Russell Warren, M.D. (left) and Thomas Sculco, M.D. (right) of HSS. Right image: William Salomon received a standing ovation at the Hospital for Special for Surgery Tribute Dinner.

World Cup: Bert Mandelbaum, M.D. Providing Medical Excellence When the best soccer players in the world tear on to the field in Brazil over these next few weeks, Bert Mandelbaum, M.D., an orthopedic surgeon and co-chair of medical affairs at the Institute for Sports Sciences in Los Angeles, will be there to ensure that things are going according to plan…at least from a medical perspective. Dr. Mandelbaum, medical director for the FIFA Medical Center of Excellence in Santa Monica, is the FIFA Venue Medical Officer at the Fortaleza Venue. He told *OTW*, "I have learned much from working on the last five World Cups, and am thrilled to be applying this knowledge to these games. My role is to oversee the medical systems involved, and to connect World Cup doctors to the local emergency system. This involves supervising care of all 700+ athletes, understanding the nuances of doping control, etc."

"A major part of this is understanding how medicine is practiced in Brazil. It is a complex system; there is a private system alongside a national health system. For the games, each of the 12 stadiums around the country is connected to a health system, and each venue has a medical director. Aside from his or her medical duties, these individuals work to organize major service providers such as security, police, and fire professionals. One of the challenges is security as Brazil has had some issues with high crime areas surrounding the venues. If there are protests they will establish buffers around the stadium(s) in order to ensure that those involved with the games are not exposed to this."

"On the first day we had orientation meetings where we were introduced to the Brazilian doctors. We reviewed all of the systems and ensured that the medical director for each venue understands the importance of communicating exactly what happening at each critical

moment. Everyone must understand what we do when and how it should be done. I think our area of vulnerability will be the connectivity between some of the venues, such as between me and any given venue medical director and between them and the hospitals."

"Running through it all is the smell and the feel of immense excitement. And when the whistle goes off there is a crescendo of intensity and everything goes from 0-110 MPH."

Physical Therapy NOT Helpful With Hip OA A new study published in the *Journal of the American Medical Association* (*JAMA*) has found that among adults with hip osteoarthritis (OA), physical therapy does not produce greater improvements in pain or function as compared to a placebo treatment. Kim Bennell, Professor and Director of the Centre for Health, Exercise and Sports Medicine, in Physiotherapy at the School of Health Sciences, University of Melbourne, led the study. Patients with hip OA were randomly assigned to attend 10 sessions of either active physiotherapy treatment (which included education and advice, manual therapy, home exercise and walking with an aid, if needed) or placebo treatments (inactive ultrasound and gel). The researchers found that patient outcomes were about the same at the 13 and 36 week intervals.

Professor Bennell commented to *OTW*, "We had expected that 'real' physical therapy would have greater benefits for pain and function than placebo physical therapy—in actual fact, while both treatments did improve pain and function, there was no difference in these benefits between the two groups. I think this highlights the very powerful 'placebo' effects of seeing a caring therapist who listens, shows empathy and lays hands on the affected part together with the patient's beliefs and positive expectations around the treatment."

"We have a number of other trials for people with hip osteoarthritis and others for people with knee osteoarthritis. We are testing a range of different interventions including knee unloading shoes, pain coping skills training and use of a walking stick as well as other studies looking at what factors trigger increases in pain to help us design better treatments."

Harry N. Herkowitz, M.D. Distinguished Chair in Orthopaedics Created Beaumont Health System has announced the creation of the Harry N. Herkowitz, M.D. Distinguished Chair in Orthopaedics. This effort was made possible because a cadre of about 300 physicians, friends, family, and former students contributed more than $2.2 million to honor Dr. Herkowitz and Beaumont Health System.

In the June 12, 2014 news release, Jeffrey Fischgrund, M.D., chairman of the department of Orthopaedic Surgery at Beaumont and the first Herkowitz Distinguished Chair appointee said, "If you made a tree of spine surgery, all the branches lead to Harry Herkowitz." Dr. Fischgrund will use the funds to support ongoing education and research at Beaumont, two areas of utmost importance to Dr. Herkowitz.

Dr. Herkowitz did his orthopedic residency at Beaumont Health System in 1975, followed by a spine fellowship at Pennsylvania Hospital. He was named Chairman of the Department of Orthopaedic Surgery at Beaumont, Royal Oak in 1991.

Rush University: Pain, Function Superior Using PRP over HA Rush University researchers have recently un-blinded their results from a double-blind prospective randomized controlled trial comparing clinical outcomes and intra-articular biology in patients injected with leukocyte poor platelet-rich plasma (PRP) to those injected with hyaluronic acid (HA) for the treatment of knee arthritis. Brian Cole, M.D., professor in the Departments of Orthopaedic Surgery and Anatomy & Cell Biology at Rush University Medical Center, told *OTW*, "There has been a great deal of discussion surrounding the idea that platelet-rich plasma PRP is a biologic alternative to HA. Some think that it may cause changes in the intra-articular biologic milieu and thus mitigate the symptoms of osteoarthritis (OA). In our study, a double-blind prospective clinical trial, we randomized 111 patients into either the HA or PRP cohort. We found statistically significant improvements in pain and function at six months in those patients who received PRP as well as HA, with PRP demonstrating superiority for some outcome measures at six months. It was also interesting to note that some patients who initially failed to respond to HA injections administered prior to initiating the study actually responded favorably to PRP in the study."

"Our study followed many of the existing requirements provided in the guidance document from the FDA that describes the basic tenants of methodology and outcomes when comparing two treatments in patients with osteoarthritis. Each patient underwent a blood draw so they did not know which arm of treatment they were assigned to, were blinded as to the nature of their injection and did not receive any insurance charges or explanations of benefits that would otherwise alert them as to the treatment received. It's important to note that whoever got PRP also underwent a CBC [complete blood count] to quantitate the platelets in the PRP. We also did a unique biologic assay,

an ELISA analysis of the synovial fluid, something that has not been done to date for both patient groups. This allowed us to understand the characteristics of the biology of the joint. We saw that those who received PRP had a significant improvement in the overall biologic milieu in the joint."

"At this point we are still going through the data, and will be submitting this work for presentation at several upcoming meetings. The biggest challenge is that payers will look at this and ask, 'Is there FDA biologic labeling?' And, in absence of that, payers often challenge it. Going forward we may include a saline control to get this properly labeled for OA. Hopefully we will make enough progress in order to make a difference with payers…patients with OA really need more options that are safe and cost-effective."

Dr. Cole's co-authors on this study were Dr. Lisa Fortier, Ph.D., D.V.M., Vasili Karas, M.D., M.S.; David B. Merkow, B.A.; Kristen Hussey, B.S.; Angela Stuckey, B.S.; Nikhil Verma, M.D.; Bernard Bach Jr., M.D.; Bryan Forsythe, M.D.

Matt Provencher, M.D. Talks Comprehensive Care, New Role at Mass General How to take something terrific and make it even better? That is the challenge facing the new head of sports medicine at Massachusetts General Hospital. But Matt Provencher, M.D., the medical director for the New England Patriots and a visiting professor at Harvard Medical School, has a plan. He tells *OTW*, "In considering the future of our program I turn toward trends in the field of sports medicine. It is becoming clear to my colleagues and I that people are athletes *for life*, whether your pursuits are a professional, occasional, or collegiate in nature. We have an emerging young, healthy population that wants to stay that way…and we must consider treatment concepts that do not involve surgery. I can't think of a better word than 'comprehensive' when it comes to the future of sports medicine. We will increasingly see a team care approach that will take into account things such as core strengthening, better nutrition, less inflammatory food, adrenal access disorders, etc. Thus far, we have not done a great job with looking at these and other nonoperative, often nuanced, issues."

"Take, for example, caring for a sprained ankle. If you focus solely on the ankle then you miss an opportunity to take 'the high road' of care. What exactly is wrong with this ankle? Is there something going on in the lower extremity? Is it a kinetic chain problem? A neurocognitive or proprioceptive issue? Is there muscle imbalance? It is vital to be able to consider these details. The challenge, however, is finding a way to provide episodic but longitudinal care and have payers recognize why we are having patients see all these experts."

"Given that payers need to become more educated about injury prevention at some point we will be bringing a number of insurance representatives in for seminars on this topic. They must understand the value that these patients get from not only the healing treatment but also the preventative care the insurers are covering. For example, if you have a teenage female with a torn ACL [anterior cruciate ligament], we know that she is at a higher risk of tearing her other ACL. The payers need to know that preventing such an occurrence would save them tens of thousands of dollars."

Dr. Provencher, a retired Navy Commander who is in charge of medical care of the Navy Seals, added, "Our goal is to be *the* comprehensive sports medicine center around…one that has a laser focus on the ultimate needs of the athlete at any level. We are continuing to strengthen relationships with neurology, physical medicine, and rehabilitation. In addition, we are now beginning to do community outreach for younger athletes in order to give them top notch care. We will also continue to strengthen our concussion clinic, work that is enhanced by the recent award of a $10 million NFL grant."

Asked what he learned from his years in the military, Dr. Provencher noted, "It was in the Navy that my team building skills were honed. I learned the importance of crafting a vision, exhibiting fairness, ensuring transparency and treating people with the utmost respect. In the military you learn to rely on one another, and that everyone plays a role. It is this mentality that stays with me and will influence everything I do here at Mass General."

Columbine-Tested Doctor Has Advice for Orthopedic Colleagues

There is no room for ad libbing in a mass casualty event, says Christopher Colwell, M.D., medical director of the Denver Paramedic Division and Denver Fire Department and the director of the Department of Emergency Medicine at Denver Health. Dr. Colwell, who was called upon during the Columbine tragedy, the Aurora theater shooting, and other mass casualty events, believes that orthopedic surgeons have a vital role in these events. He tells *OTW*, "The most important message I have for my orthopedic colleagues is that you must be prepared in advance for something of this nature and magnitude. When such a tragedy strikes that is not the time to 'figure it out.' If your hospital does not have an adequate disaster plan with regular drills that involve all of you then you should initiate improvements in the system."

"Disaster planning is a team effort and should at no point become a turf issue. You must communicate early and discuss who has what role. In a traumatic event such as a mass shooting or explosion there are usually orthopedic injuries that must be addressed. There must be a structured approach to their management, however, and recognition that the first injuries seen may not be the injuries most urgently in need of intervention. As this is not something that is seen every day it requires a focus on team management, working with others to determine which patients have the greatest need for limited resources, including operative management."

Asked what he learned from the Columbine experience, Dr. Colwell stated, "Our goal was to empty the emergency department…communication and getting organized at the scene were also vital. The early radio announcements indicated that help was needed at the scene, but in fact there were plenty of providers already there…the problem became that so many medical professionals arrived that a number of them actually got in the way. Well-intentioned providers showed up and didn't know anyone and didn't understand our system or know their way around. This chaos occurred in the ED as well and became a real problem when it was so crowded there that we couldn't find the key people we needed. When this happens you have essentially transferred the disaster from the scene to the emergency department! A clear system of identification was needed so we were able to clearly recognize the senior decision maker for orthopedic surgery as well as other specialties.

"In many cases we like to set up a triage and establish groups of red, yellow, green at the scene that will be transported to the ED in the order of need. Then at the ED the most experienced surgeons and emergency physicians will be making the decisions as to who gets priority for CT scan, the OR, and other limited resources. The best scenario is to have a couple of orthopedic surgeons in the OR, with the most experienced orthopedic surgeon in the triage area working with the trauma surgeon and emergency physician to prioritize patient care. And it is impor-

tant to empty the ED in order to address the needs of the mass casualty victims coming in and this may require creative methods such as moving current ED patients to outpatient clinics or other less acute areas of the hospital."

"I understand that orthopedic surgeons want to be in the middle of the action and be the decision makers. As physicians we are pulled to that role, but believe me, too much of that thinking can cause real problems. After Columbine we began setting up a command system with an incident commander. Responsibilities of the incident commander can include addressing issues like making sure the cafeteria is open in the middle of the night, or resources in short supply are obtained, so it would rarely make any sense to have a physician in this role. As with all disaster preparedness, a clear plan that is arranged before a disaster occurs of how to set up a command center and who will be incident command is essential to smooth management of these events."

"Again, prepare, communicate, know your roles…we can definitely do better for future victims of these horrible events."

HSS at Waldorf Astoria…Honors William Salomon, Jo Hannafin, M.D.

On Monday, June 16, 2014 Hospital for Special Surgery (HSS) held its 31st Annual Tribute Dinner 2014 at The Waldorf Astoria in New York. The event, hosted by Brian Williams, anchor and managing editor of NBC Nightly News, honored William R. Salomon, the Honorary Chairman of Citigroup in celebration of his 100th birthday. Jo A. Hannafin, M.D., Ph.D., attending orthopedic surgeon and director of Orthopedic Research at HSS, received the Lifetime Achievement Award.

The event was attended by distinguished medical staff, celebrities, and outstanding athletes who have had their mobility restored by HSS. Also present were hundreds of leaders from the worlds of business, health, finance, media, sports, the arts, and government. ♦

COMPANY

Expanding Orthopedics Awarded Chinese Patent

It's celebration time for the spine gurus at Expanding Orthopedics Inc. (EOI). The company is announcing that it has been granted a Chinese patent for its XPED System, an expandable pedicle screw with instrumentation.

Mark Levy, M.D. an orthopedic surgeon, founder and chief technology officer of Expanding Orthopedics, said in the June 16, 2014 news release, "I am very proud of this achievement as this rewards our extensive research and development efforts and confirms the uniqueness of the XPED System and the innovation brought by our team to the medical community. This is the sixth granted Chinese patent for our extensive expanding devices platform, which demonstrates our focus and commitment to this market for several years now."

Ofer Bokobza, CEO of Expanding Orthopedics said, "The Chinese market is one of the fastest growing markets in the world with large concentration of the ageing population (over 65) which is expected to reach 25% of population by the year 2050. EOI is setting itself for the Chinese market by designing and delivering innovative products at an affordable price, to access both the higher and lower ends Chinese healthcare markets. "We intend to execute this strategy, starting with the XPED expandable pedicle screw technology platform, which addresses the growing need of the ageing population for enhanced anchoring solutions in low bone quality. Other innovative products from our rich IP portfolio, such as the FLXfit, our unique expandable cage, will follow, fulfilling our vision of providing novel solutions to improve spinal health."

Dr. Levy told *OTW*, "The patent process is always exciting, as you try to combine your innovative ideas, mechanical and physical constraints and existing intellectual property (IP). Still, during our IP process we always keep in mind the clinical benefit for the patient as well as the features required by the surgeons, which is why our fantastic scientific advisory board is already closely involved at these early stages. At EOI we already have a broad IP portfolio (12 issued patents and 8 pending patents), but it's always a great recognition and achievement to obtain a new grant."

"The XPED is already used by numerous leading centers in Europe and so far close to 2,500 expandable screws have been successfully implanted worldwide. One year from today we hope to be in the U.S. market with the XPED, which will be a tremendous disruptive opportunity as there is no FDA approved solution today for patients with compromised bone. As for China, we are starting the China Food and Drug Administration registration process these days and believe to be able to obtain approval within 24 months." — *EH*

Expanding Orthopedics Inc.

Olympus Halts OP-1 Effort

Olympus Biotech Corporation has put a fork into its efforts to commercialize OP-1.

After paying $60 million to Stryker Corporation in 2010 for the biologic product that has snake-bitten everyone who has attempted to commercialize the protein, Olympus announced on June 18, 2014 that it will close its 120-employee manufacturing plant in West Lebanon, New Hampshire, because it has been unable to find a buyer for the past four months.

OP-1 was a disaster for Stryker as the company failed to get FDA approval for the product, paid millions in fines for the way it marketed the product and several former employees received jail time for lying about those marketing practices. It was an albatross around former Stryker CEO Steve MacMillan's neck when Olympus Biotech came along to try and breathe life into the product.

The product was even part of a U.S. Senate investigation as Senator Chuck Grassley tried to exercise his uninformed medical clinical judgment by saying that OP-1 could have been used as a substitute for Infuse in a clinical trial at the University of Minnesota.

Olympus Corp: Cameras to Bio

Olympus Biotech was formed four years ago by the Japanese camera giant, Olympus Corp. to focus on products for regenerative medicine. It bought the rights to the protein-based putty used to regenerate bones for treating spinal, hip and knee conditions. Shortly after the purchase, Olympus underwent its own investigation by securities regulators in Japan. OP-1 left no one unscathed.

The company reportedly said the closure was "purely a financial decision… and is not related to the performance, quality or safety of our OP-1 family of products." The regenerative medicine industry took a hit late last year when a change in the Medicare and Medicaid reimbursement drastically lowered rates for many wound treatments.

In March, company officials continued to defend OP-1 even while announcing the pending shutdown of Olympus Biotech.

"We are proud of OP-1's legacy in the market and its significant contributions to regenerative medicine and the quality of life in patients worldwide," David Renker, company chief operating officer, said in a news release. The company is providing severance benefits and access to outplacement services to its employees, as well as making them aware of open positions at other Olympus Corp. locations.

While this specific effort to commercialize bone morphogenetic protein 7 (OP-1) has fizzled, it's unlikely that the science which explains the key role the protein plays in the transformation of mesenchymal cells into bone and cartilage will be discarded. The International Society for Molecular and Cell Biology and Biotechnology Protocols and Research named bone morphogenetic protein 7 as the 2011 Molecule of the Year.

The question isn't whether another commercial effort will be made, but who will have the courage to take another bite of the apple? — *WE*

OP-1 Putty/Olympus Biotech Corporation and RRY Publication LLC

LEGAL

Top 11 Recommendations to Improve the FDA

When Congress passed the Food and Drug Administration Safety and Innovation Act in 2012 to reauthorize the FDA to collect user fees from device manufacturers, the FDA and the medical device industry agreed to an independent, comprehensive assessment of the agencies medical device submission review process.

That assessment has been completed and recommendations have been made to improve the agency's review process.

A June 11, 2014, Booz Allen Hamilton 147-page report offers 11 recommendations, including the need for the agency to conduct a retrospective study of withdrawn premarket approval applications to determine ways to curb such withdrawals. The report also recommends that the FDA clarify the administrative standards for 510(k) clearance applications to minimize rejections.

The recommendations cover the following five wide areas and include:

Quality Management

1. Adopt a holistic, multi-pronged approach to address five quality component areas to standardize process lifecycle management activities and improve consistency of reviews (Priority Recommendation)

Evaluation of Review Process

2. Develop criteria and establish mechanisms to improve consistency in decision-making throughout the review process (Priority Recommendation)

3. Optimize RTA (Refuse to Accept) process by improving awareness of and clarity around Administrative requirements for 510(k) submissions

4. Perform a retrospective root cause analysis of withdrawn submissions and develop a mechanism to minimize their occurrence

5. Implement a consistent practice for communicating early and frequently with Sponsors during the Substantive Review phase to address and resolve potential issues prior to Substantive Interaction

Evaluation of IT Infrastructure and Workload Management Tools

6. Provide mandatory training for the three primary IT systems that support MDUFA III (Medical Device User Fee Amendments) reviews (Priority Recommendation)

7. Provide increased clarity to applicants beyond existing eCopy guidance to enhance organized submission structure

8. Evaluate tools for providing a comprehensive view of staff workload

Evaluation of Training Programs

9. FDA should identify metrics and incorporate methods to better assess review process training satisfaction, learning, and staff behavior changes (Priority Recommendation)

10. Promote informal training and knowledge sharing by seasoned staff for review staff and management to share division or science-specific review processes, lessons learned, and best practices

Assessment of Staff Turnover

11. Develop CDRH-wide (Center for Devices and Radiological Health) staff transition and succession plans to mitigate the impact of turnover on submission reviews

For each recommendation, Booz Allen provided suggestions for specific actions that the agency might take to address

Image created by RRY Publications, LLC / Source: FDA

the recommendation, as resources are available. The FDA may determine at its discretion to take action on these recommendations in alternative ways.

To read the entire report, click here: http://www.pharmamedtechbi.com/~/media/Supporting%20Documents/The%20Gray%20Sheet/40/24/D10%20MDUFA%20III%20Evaluation%20Final%20Report%20on%20Findings%20and%20Recommendations%20vFinal.pdf —*WE*

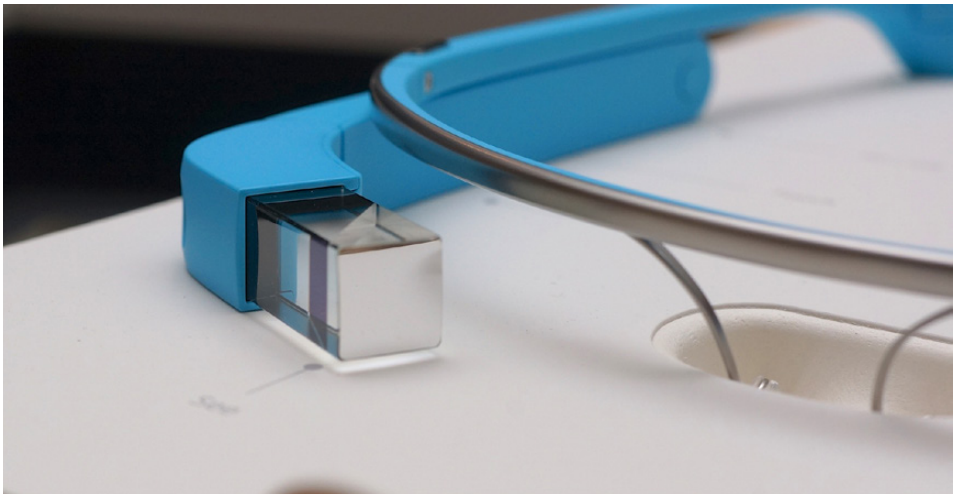
Google Glass for Medical Record Keeping

That geeky-looking Google Glass hanging to the side of a pair of spectacles is appearing on more and more of the brows of physicians. Christina Farr, writing for *Reuters*, reports that a company in Mountain View, California, has developed what it calls the "first wearable health record." The company is drchrono, Inc. and it specializes in the recording and preserving of patients' medical records.

The company has developed an app that doctors can wear that allows them to automatically record a consultation with a patient without having to type the information on an iPad or computer. Photos, videos and the conversation are all recorded and stored in a cloud-based storage service that can be shared with the patient and other doctors.

Farr quoted Bill J. Metaxax, M.D., a podiatrist in San Francisco who uses the device in the operating room and in consultations with his patients, who says that 99% of his patients agree to his use of the Glass. Doctors, however, are moving slower. Metaxax believes that only a minority of physicians have adopted Google Glass in their practice.

That will change if drchrono co-founder Daniel Kivatinos has his way. Farr quoted him as saying, "Google is still in the early-stages of determining the most viable use-cases for Google Glass. But some doctors are demanding Glass, so Google is providing resources and support to developers." He says that as many as 60,000 health care professionals have registered to use his company's Glass-based medical record service and the free app. Former Google Health employee Missy Krasner told Farr that she knows of about 20 startups that are looking to provide Glass record-keeping services to this group of forward-looking physicians. — *BY*



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Get On FDA's Cloud

The FDA's collective heads are in the clouds when it comes to "Big Data." And the agency wants you to get on their cloud.

openFDA

On June 2, 2014, the agency launched openFDA, a system designed to make it easier for web developers, researchers, and the public to access and use health data sets collected by the agency.

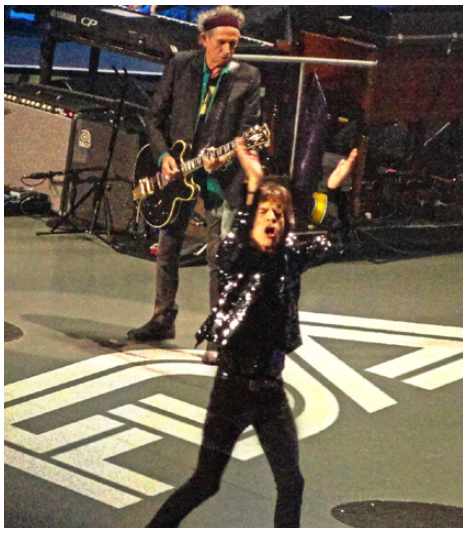


Image created by RRY Publications, LLC / Sources: FDA and Wikimedia

For example, over 3 million reports of drug adverse reactions or medication errors have been submitted to the FDA Adverse Event Reporting System (FAERS) since 2004. But obtaining that information hasn't been easy. Companies send hundreds of Freedom of Information Act (FOIA) requests to the FDA every year to get the data. Other methods required downloading large amounts of files encoded in a variety of formats that were slow and labor intensive.

This year alone, the FDA expects to receive somewhere between 1.5 and 2 million submissions through its eSub-

mission Gateway—and some submissions can now be as large as a terabyte (one trillion bytes) in size. This is the very definition of a big data.

openFDA will make publicly available data accessible in a structured, computer-readable format. It provides a "search-based" application programming interface that makes it possible to find both structured and unstructured content online.

Build Your Own Apps

Software developers can now build their own applications (such as a mobile phone app or an interactive website) that can quickly search, query or pull massive amounts of public information instantaneously and directly from FDA datasets in real time on an "as-needed" basis. Additionally, with this approach, applications can be built on one common platform that is free and open to use. Publicly available data provided through openFDA are in the public domain with a CC0 Public Domain Dedication.

Drug adverse events is the first dataset—with reports submitted from 2004 through 2013 available now.

The agency says Big Data is important to the agency carries out regulatory science, which is the science of developing new tools and approaches to assess the safety, efficacy, quality, and performance of FDA-regulated products. "Through innovative methods such as cloud computing, we are taking advantage of this flood tide of new information to continue to protect and promote the public health," said the agency through FDA Voice blog.

You can visit FDA's cloud here: https://open.fda.gov/ — *WE*

LARGE JOINTS

Biomarkers May Predict Osteoarthritis

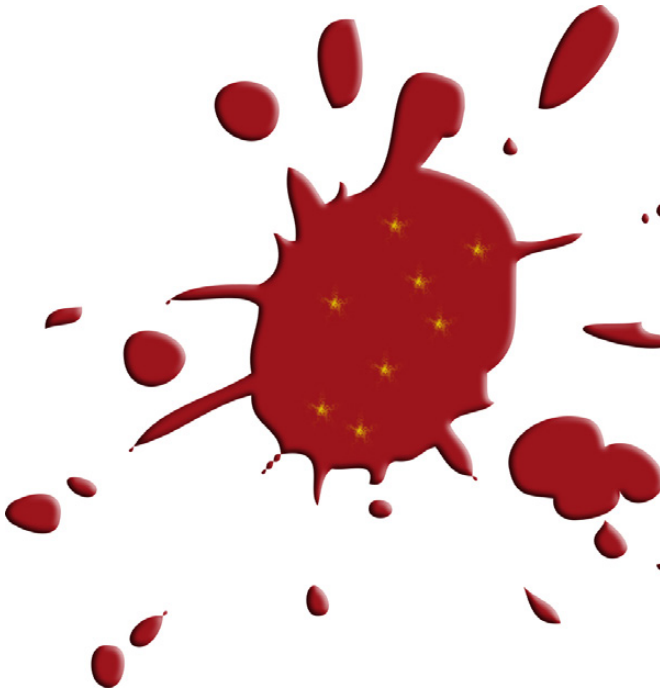
Researchers have found a correlation between the presence of biomarkers in the blood, known as micro RNAs (miRNAs), and the development of severe osteoarthritis (OA) of the knee or hip joint.

This is the first study of a large population-based cohort to identify differentially expressed miRNAs in osteoarthritis patients. It was led by Christian Beyer, M.D., from the University of Erlangen-Nuremberg, Germany and presented June 11 at the European League Against Rheumatism Annual Congress (EULAR 2014).

The study followed 816 patients over 15 years and screened existing serum samples of people with OA, through which they identified three potential miRNA markers. They used joint replacement as a definitive outcome of severe OA in the knee or hip. Of the 816 patients, 67 patients had one or more total joint replacements for severe knee or hip OA. The results of serum analysis showed a correlation between severe knee or hip OA and three miRNA molecules known as let-7e, miR-454 and miR-885-5p. These findings indicate those miRNAs could be used as biomarkers to predict severe OA.

"These results indicate that for the first time we will be able to predict the risk of severe osteoarthritis before the disease starts to significantly impact a person's life, allowing us to take preventative action early on. Through the early identification of osteoarthritis we can decrease both the impact of the disease on individuals and the major socio-economic burden severe disease poses," said Beyer.

"OA is a common musculoskeletal disorder affecting ten percent of the world's population. It is characterized by pain and stiffness in the joints and is one of the top ten most disabling diseases in developed countries. OA is a major cause of knee or hip replacements and disability from the disease has a great impact on individuals, healthcare systems and society. With risk factors including advancing age and obesity, researchers expect the burden of the disease to grow," according to the EULAR news release. — *BY*



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Frustrated Canadian Surgeon Opens Own Clinic

It was frustration over long patient wait times in the public health care system that prompted Dr. Nicolas Duval and his wife Dr. Pauine Lavoie to drop out of the public system and go private in 2002. "I had patients waiting up to two years for a hip replacement," said Duval.

The two now own Canada's only private clinic that offers total knee and hip replacements. On average, Duval performs around 400 hip and knee replacements a year at their clinic in Laval, Quebec, a stone's throw from Hôpital de la Cité-de-la-santé. Duval owns the clinic jointly with his physician wife who ensures pre-op and post-op patient care, and does the paperwork.

Now Duval exults in the gratitude of his patients. He said, "For me, as a surgeon, the best reward is hearing people say, 'Thank you for taking the risk of opening this clinic and helping me not lose a couple of years of my life waiting for surgery.'"

"I was very upset," recalled Duval, who worked as a surgeon and teacher at the McGill University-affiliated Queen Elizabeth Hospital and the Centre hospitalier de l'Université de Montréal between 1996 and 2002.

Courtesy of the Duval Clinic, Laval, Quebec

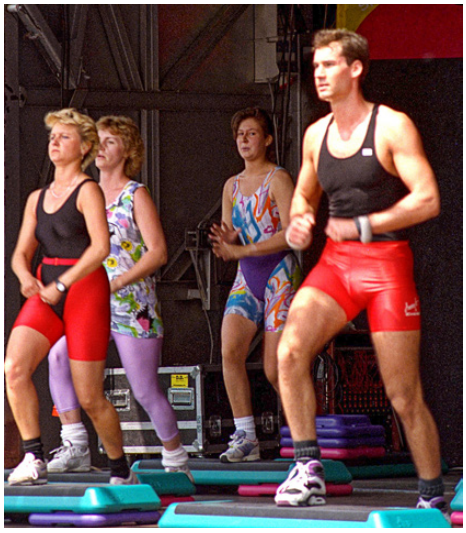
The most expensive procedure Duval performs is hip replacement surgery for which he charges $19,000 a hip. That fee includes the surgery in one of the clinic's two new cutting-edge operating rooms, pre-op tests, post-op care, and a six-night stay with round-the-clock nursing care in one of the clinic's five acute or nine convalescence beds. Knee replacements cost $18,000 with the same package of services.

The patients pay for all of the charges and neither doctor receives fees or deals with the province's medical health insurance board. Like all doctors in Canada, their professional practice is authorized by and is accountable to Quebec's college of physicians. "There is an almost endless supply of patients," Duval said. "And demand will continue because many people now live into their 90s."

David Zukor, M.D., FRCSC, chief of the department of orthopedic surgery at the Jewish General Hospital, Montreal, said his hospital is "one of the busiest places" in the province, doing 600 to 700 replacements a year. Two other Montreal hospitals are likely to do as many replacements, said Zukor. At Jewish General, the waiting list for hip and knee replacement is about six months once the patient has been seen by doctors, Zukor said. However, he added that it can take another six months for patients to get that first pre-op meeting. — *BY*

Regular Exercise Helps Suppress Inflammation

Research from Ohio State University has found that regular exercise suppresses local and systemic inflammation. The findings from the in vivo study were recently presented at the European League Against Rheumatism Annual Congress (EULAR 2014).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"As the inflammatory process in rheumatic diseases is a major cause of disability, we are excited to uncover the process by which exercise works on a molecular level to decrease this inflammation. Our results show the benefits that exercise could have in decreasing the great burden of rheumatic diseases. They also highlight the need for frequent exercise in order to create clinically significant results," said Dr. Nicholas Young in the June 12, 2014 news release. Dr. Young was the presenting author from The Ohio State University Wexner Medical Center, Columbus, Ohio.

Working with mice, the researchers looked at the regulation and activation

of NF-kB, a protein complex that controls many genes involved in inflammation. The team used lipopolysaccharides (LPS) to create an inflammatory response in the mice before and after exercise. The researchers indicate finding a strong systemic and local inflammatory response upon injection of LPS, which was strongest at two hours post-injection.

As noted in the news release, "NF-kB activation was seen as a result of the LPS and was detected in lymphatic tissues throughout the mouse. In those groups where mice were exercised pre- and post-LPS injection, the NF-kB activation was significantly inhibited in whole-body systemic analysis. The effect of exercise on the inhibition of NF-kB activation was identified as a transient effect, lasting only 24 hours after exercise. The role of exercise in inhibiting NF-kB activation was linked to the suppression of multiple pro-inflammatory cytokines. Cytokines are produced by a wide range of cells including macrophages and are involved in cell signaling."

Dr. Young told *OTW*, "Since rehabilitation plays a significant role in the recovery of patients following orthopedic surgery, the effects of exercise over inflammation are a tremendously important influence to consider. Our results indicate that moderate levels of exercise on a daily basis can function as a systemic biological response modifier to regulate inflammation. In an acute model of inflammation, our data showed that a moderate daily exercise regimen suppressed the induction of inflammation stimulated by bacterial components, but that these results were transient and lost after 24 hours. Considering that epidemiological data suggests that regular exercise translates to a decreased prevalence of infectious disease and is efficacious in patient rehabilitation following surgery, our results suggest that exercise modulates the immune system to optimize inflammatory responses and that the greatest benefits may be observed in rehabilitation following orthopedic surgery with daily, moderate exercise. Importantly, this immuno-optimization is a result of daily moderate exercise; exhaustive or excessive exercise can be detrimental to immune system regulation. Thus, the exercise regimen prescribed in rehabilitation following surgery must be individually determined based on the age, activity level, and type of surgery for each patient." —*EH*

Waiting Too Long for TJR is a Bad Idea

Is there an optimum time—a window of opportunity—for a patient to get a hip or knee joint replaced? Data from a joint replacement monitoring program and database at UMass Medical School says "yes" and that waiting too long will reduce the benefits of surgery.

"Don't wait until you can't walk or take the pain any longer," said David Ayers, M.D., the Arthur M. Pappas Chair in Orthopedics, professor of orthopedics and physical rehabilitation and director of the Musculoskeletal Center of Excellence. "That's what we hear a lot from patients and doctors—to wait until you can't take it anymore. But the data is telling us that for typical patients, there's only a fixed amount of improvement you can get from surgery. So if you wait too long, you don't get the full value."

Wikimedia Commons and Before My Ken

Ayers said that this is not about having surgery too early, either. Instead he says that doctors now have objective, data-driven tools that can help patients decide, together with their surgeons, where they are with pain and function and when to have surgery.

The nationally-recognized physical composite score for an individual with no joint pain or functional difficulty is 50. The new data, based on a study of 17,000 patients, reveals that typical patient scores improve an average of 12 points after total joint replacement (TJR) surgery. Because patients on average experience the same change in functional improvement after surgery, a typical patient who waits until his function is extremely impaired will not achieve the same degree of post-operative function as will a typical patient who chooses surgery at the ideal time.

"What we're seeing is that the average person who chooses total joint replacement has an average pre-total joint replacement function score of 32," said Patricia Franklin, M.D., professor of orthopedics and physical rehabilitations. "On average, TJR patients can achieve scores of 44 or greater and approach the function of non-arthritic patients after surgery. But, 20% of patients who wait until their score is 25 or lower generally don't get the full 12 points of improvement. In fact, 40% of those who wait this long only achieve post-surgery function at the arthritis level of 32. If 50 is the goal, these are important measures for patients and surgeons to monitor when deciding on joint replacement surgery timing," said Franklin. — *BY*

EXTREMITIES

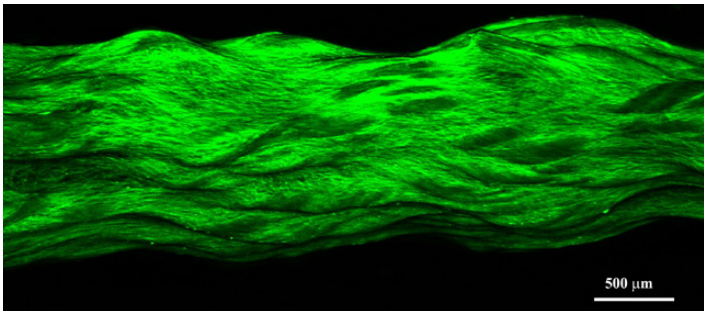
$1.7 Million to Case Western Engineer for Growing Tissue

Ozan Akkus, Ph.D., a professor of mechanical and aerospace engineering at Case Western Reserve University, has been awarded a $1.7 million grant from the National Institutes of Health (NIH) to grow replacement rotator cuffs and other large tendon groups. His work will impact injured soldiers and athletes, accident victims and the wider population.

Dr. Akkus, who created a way to reconstitute collagen into tough fibers and induce adult stem cells to grow into tendons on those fibers, will be focusing on basic science and translational work over the next five years.

According to the June 16, 2014 news release, "His lab uses electrical currents to align collagen threads, mimicking the natural tendon and making the threads dense and strong as a tendon. And his team can make threads in bulk, which would enable manufacturers to make spools of the material—enough to accommodate hundreds of thousands of surgeries."

"Woven threads are sufficiently strong to be surgically handled and sutured in place and be fully load-bearing," Dr. Akkus said. "This would enable a patient to begin physical therapy and remobilization quickly," he added. "The threads alone could be used as sutures to repair simple tears. But when more tendon material is needed, adult mesenchymal stem cells placed on the aligned collagen differentiate toward tendon cells without highly regulated growth factors, which also carry undesirable side effects or other chemicals."



Case Western Reserve University

Dr. Akkus told *OTW*, "The most striking feature of this product is its ability to induce growth-factor free differentiation of adult stem cells into tendon cells by mimicking the topography of the natural tendon. This is probably the first time a fully-load bearing pure collagen repair scaffold is fabricated as a woven biotextile for bulk-repair of tendon. Unlike 'collagen rich' decellularized xenografts, the 100% pure collagen nature of this scaffold will have consistent performance."

Regarding his most important message for orthopedic surgeons, Dr. Akkus stated, "The complication rates in rotator cuff repairs are still unacceptably high. Furthermore, the number of solutions for functional repair of advanced stage rotator cuff degenerations is limited."

Asked about the challenges of this work, Dr. Akkus noted, "Like any biomaterial based repair strategy, patient to patient variations in the regenerative capacity of stem cells is one of the biggest challenges in the regenerative medicine. Some stem cells thrive magnificiently in the body whereas other sources may not." — *EH*

New Study: Infection Risk 7x Greater With Diabetes

Complications from diabetes increase the risk of infection after surgery on feet and ankles, according to a study that appeared in a recent issue of the *Journal of Bone & Joint Surgery*. As reported by Brenda Naugent in *Diabetes Health*, type 2 diabetes patients with complications that include such ailments as diabetic peripheral neuropathy or an A1C of 8 or higher are more likely to experience surgical site infections following ankle or foot surgery than are non-diabetics.


Wikimedia Commons and Ujb98

Researchers from the University of Pittsburgh Medical Center examined 2,060 surgical cases. They divided the cases into four groups, patients without diabetes and neuropathy, patients without diabetes but with neuropathy, diabetic patients with no complications and diabetics with at least one complication.

They found that 3.1% of the cases studied developed surgical site infections and the diabetic group with complications was 7.25 times more likely than the other three groups to develop infections.

Nugent quotes the researchers as writing, "Complicated diabetes increases the risk of surgical site infection after

foot and ankle surgery. Patients who had diabetes without complications did not have a greater risk of surgical site infection compared with non-diabetic patients without neuropathy."

They found that the presence of neuropathy, even in patients without diabetes, increases the risk of surgical site infection. Poor long-term glycemic control was also associated with an increased risk of surgical site infection. — *BY*

REIMBURSEMENT

Boeing and ACOs Dump Insurance Middle Man

Boeing and healthcare providers in the Seattle area have dumped the insurance middle man.

On June 13, 2014, the giant aerospace company and two accountable care organizations (ACOs) formed by UW Medicine and Providence Health & Services and Swedish Health Services, formed a partnership to provide care for the employer. No insurance company is involved. Boeing has separate contracts with each provider.

"The advantage for Boeing will be that they can take the middle man out of the equation between the patients and the health system. It may be able to reduce cost, in part because of the simplification of not having the insurance mechanism in the middle," said Dr. Elliott Fisher, director of the Dartmouth Institute for Health Policy and Clinical Practice in New Hampshire.

"It's a very interesting model and worth pursuing," Fisher said in an article published in the *Seattle Times* on June 17, 2013.

30,000 Patients

Boeing has "created a flight plan for a new era of health care," said Paul Ramsey, M.D., chief executive officer of UW Medicine. Starting in January, 2015, 27,000 Boeing employees and some 3,000 retirees will begin the program. Eligible participants—who include nonunion workers and certain union-bargaining units—will also have the option of keeping their current plans or choosing another non-ACO plan. Those signing up for Preferred Partnership will select between Providence-Swedish or UW Medicine.

In the deals, the contracts set goals for the employees' medical costs. If the costs are higher or lower, the provider either foots the bill or reaps the savings.

The contracts allow patients the ability to schedule appointments in a timely manner and require the providers to maintain patient safety and satisfaction information. There are additional benchmarks tied to costs, including reducing readmissions to hospitals after treatments and effectively managing chronic conditions such as diabetes and heart disease.

Patient Benefits

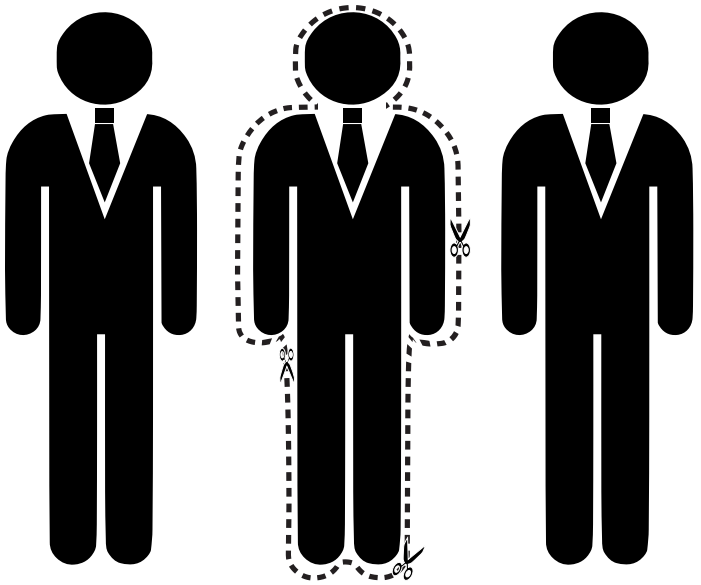
According to the *Times*, Boeing officials said there are numerous incentives for using Preferred Partnership, including lower paycheck deductions to pay for care, larger company contributions to Health Savings Accounts, no co-payments in many cases for visiting primary-care doctors and 100% coverage for generic-drug prescriptions.

Provider Efficiencies

One benefit to the providers is access to more patient data. Because Boeing is paying the costs, the company can share that data with providers, which can then try to determine the cheapest, most effective approaches.

The Providence-Swedish ACO includes the network's clinics and hospitals, as well as The Everett Clinic, Pacific Medical Centers clinics, The Polyclinic, Proliance Surgeons and others. Some members of the UW Medicine network are Seattle Children's Hospital, Seattle Cancer Care Alliance and the Overlake and Northwest Hospital centers and clinics.

The disintermediation of healthcare delivery continues. — *WE*



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

WRITERS

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

Walter Eisner
Senior Writer
walter@ryortho.com

Biloine W. Young
Senior Writer
bgwy@msn.com

ADVERTISING

Tom Bishow
Vice President of Sales
tom@ryortho.com

PRODUCTION

Suzanne Kirchner
Production Manager
suzanne@ryortho.com

Jayme Johnson
Email, Web, & Conference Coordinator
jayme@ryortho.com

Dana Bader
Graphic Designer
dana@ryortho.com

---

116 Ivywood Lane • Wayne, PA 19087
TOLL FREE: 1-888-749-2153
www.ryortho.com