VOLUME 11, ISSUE 26 | AUGUST 18, 2015

Orthopedics This Week

WEEK IN REVIEW

4 The Ultra Patient >> Who ARE these people? They are your ultra-patients. Like Ellen Miller, who climbed Everest, Nuptse and Lhotse after her hip replacement, or Roy Wyatt who climbed Kilimanjaro at age 75 after his hip surgery or Scotland's John Matthews or Don Healey who climbed Mount Everest courtesy of an HSS installed hip.

8 Toledo (?) A Center of Orthopedic Innovation >> More than three dozen orthopedic companies had already made the trek to test their ideas, make a product or find new products in, of all places, Toledo, Ohio. Is there something in water here? No, just tons of cool lab equipment and some highly talented professors. Maybe you should get to Toledo too.

13 Breathtaking: World's First Bilateral Hand Transplant in a Child// Nonunion Rate in Subtalar Fusions… Mysteries Remain // Study: Medial Chondrosis Associated with BMI, Alignment, and Medial Meniscal Status >> 18 months, 3 hospitals, 40 medical personnel, and 10 hours for the first bilateral hand transplant. New Study: **no** difference between stem cells and autologous bone graft for treating nonunion subtalar fusions. Finally—Wash U researchers link status of articular cartilage in the tibiofemoral compartments at the time of rACLR to meniscal status.

17 Reverse Shoulder or Not? Crosby and Gobezie Debate Contained Cuff Arthropathy >> According to Lynn Crosby: "When treating cuff tear arthropathy with loss of acromial-humeral distance; pain with or without activity; good deltoid tone and strength, reverse is the best option. Not so fast, says Reuben Gobezie: "Don't do these reverse replacements on patients who have these types of tears because they have pre-op range of motion greater than 90. It is not a good outcome." Who wins this great debate? You decide.

BREAKING NEWS

21 Orchid Design Tapped by FDA for **Submission Tracking Project**

Total Knee **FDA Cleared** for **Stryker's MAKO**

Dr. Carson Rising in **Iowa**

FDA on Record **Approval Pace in 2015**

FDA User **Fees Rise** 4.2% for **2016**

Could Simple **Protein Reduce Head Injuries**?

For all news that is ortho, read on.

Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

THIS WEEK: Lots of orthopedic equity repricing these last few trading sessions. There were more sellers than buyers of Zimmer Biomet as most institutional investors hunker down for a year of integration. Dvorak and his team will try to beat expectations (see Dvorak's Playbook article). This week we add Orthofix to the Power Rankings in place of ConMed and Xtant (aka: Bacterin) Medical moves up smartly on the strength of both rising sales and the merger with X-Spine.

RANK	LAST WEEK	COMPANY	TTM OP MARGIN	30-DAY PRICE CHANGE	COMMENT
1	1	Stryker	22.78%	6.29%	Will China's woes affect Stryker's Trauson sub? Unlikely. China's aging population plus modernizing healthcare system prevail over currency drop.
2	3	Smith & Nephew	20.19	4.49	Buys Russian trauma and orthopedics businesses, DeOst LLC and DC LLC. Russia has actually been a growth market for SNN since 2005.
3	4	Medtronic	27.92	2.15	MDT upcoming sales report will be one bright spot in these dog days of August. Can MDT spine beat $715 million in sales for the quarter?
4	10	Bacterin/ Xtant	(16.41)	10.12	Revenue for the combined Bacterin/X-Spine rose 12.6% in the first half of 2014. Pro-forma EBITDA was $1.2 million. Not bad.
5	5	RTI Biologics	7.50	1.09	Zacks rated RTIX a "Buy" and said that the company has an expected earnings growth rate of 93.9% for this year.
6	6	Globus Medical	30.87	0.80	The fascinating dichotomy of GMED is its very low P/E to expected earnings growth rate vs its stratospheric Price-to-sales ratio. Why? Profitability.
7	2	Integra LifeSciences	13.74	(2.10)	Strong international sales in Q2 plus acquisition of MicroFrance have the flip side of raising currency concerns because of this international exposure.
8	9	Zimmer Biomet	30.35	(1.49)	Institutional investors have notoriously short memories. To them ZBH looks like DePuy Synthes. Can Dvorak et al. change those perceptions?
9	NR	Orthofix	2.35	16.65	Sales up 5%, constant currency, and EBITDA marched higher by a very respectable 17%. Management raised guidance for the year. Is OFIX back?
10	7	Johnson & Johnson	28.44	(1.60)	As we noted last week, JNJ has the most consistent record of growth, dividends and earnings in all of medicine—53 years in a row.

Robin Young's Orthopedic Universe

TOP PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	Orthofix	OFIX	$38.95	$734	16.65%
2	Bacterin Intl Holdings	BONE	$3.70	$43	10.12%
3	NuVasive	NUVA	$53.07	$2,597	7.15%
4	Stryker	SYK	$103.64	$39,026	6.29%
5	Smith & Nephew	SNN	$37.26	$16,665	4.49%
6	Medtronic	MDT	$77.58	$109,713	2.15%
7	RTI Biologics Inc	RTIX	$6.52	$376	1.09%
8	Globus Medical	GMED	$26.52	$2,521	0.80%
9	Zimmer Biomet	ZBH	$105.53	$21,461	-1.49%
10	Johnson & Johnson	JNJ	$98.81	$273,615	-1.60%

WORST PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	Aurora Spine	ASG	$0.22	$4	-50.43%
2	Alphatec Holdings	ATEC	$0.69	$69	-50.36%
3	MiMedx Group	MDXG	$9.34	$1,017	-24.00%
4	Exactech	EXAC	$18.29	$257	-13.85%
5	K2M Group Holdings	KTWO	$21.14	$874	-12.17%
6	CryoLife	CRY	$10.56	$313	-8.41%
7	LDR Holding Corp.	LDRH	$40.54	$1,163	-7.53%
8	MicroPort Scientific	853	$0.40	$575	-6.90%
9	Tornier N.V.	TRNX	$24.10	$1,187	-6.70%
10	Wright Medical	WMGI	$25.16	$1,294	-6.22%

LOWEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Exactech	EXAC	$18.29	$257	16.33
2	Johnson & Johnson	JNJ	$98.81	$273,615	16.78
3	Zimmer Biomet	ZBH	$105.53	$21,461	19.19
4	Globus Medical	GMED	$26.52	$2,521	20.41
5	Stryker	SYK	$103.64	$39,026	23.03

HIGHEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	CryoLife	CRY	$10.56	$313	88.29
2	NuVasive	NUVA	$53.07	$2,597	84.75
3	MiMedx Group	MDXG	$9.34	$1,017	62.27
4	RTI Biologics Inc	RTIX	$6.52	$376	37.73
5	Smith & Nephew	SNN	$37.26	$16,665	33.26

LOWEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Globus Medical	GMED	$26.52	$2,521	1.67
2	Zimmer Biomet	ZBH	$105.53	$21,461	1.71
3	Exactech	EXAC	$18.29	$257	1.83
4	ConMed	CNMD	$56.07	$1,553	2.23
5	RTI Biologics Inc	RTIX	$6.52	$376	2.52

HIGHEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	NuVasive	NUVA	$53.07	$2,597	5.66
2	MiMedx Group	MDXG	$9.34	$1,017	4.15
3	Medtronic	MDT	$77.58	$109,713	3.52
4	Johnson & Johnson	JNJ	$98.81	$273,615	3.47
5	Smith & Nephew	SNN	$37.26	$16,665	3.02

LOWEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	Alphatec Holdings	ATEC	$0.69	$69	0.33
2	Exactech	EXAC	$18.29	$257	1.04
3	Bacterin Intl Holdings	BONE	$3.70	$43	1.23
4	RTI Biologics Inc	RTIX	$6.52	$376	1.43
5	MicroPort Scientific	853	$0.40	$575	1.62

HIGHEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	TiGenix	TIG.BR	$0.82	$132	20.99
2	MiMedx Group	MDXG	$9.34	$1,017	8.60
3	LDR Holding Corp.	LDRH	$40.54	$1,163	7.79
4	Medtronic	MDT	$77.58	$109,713	5.41
5	Globus Medical	GMED	$26.52	$2,521	5.31

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

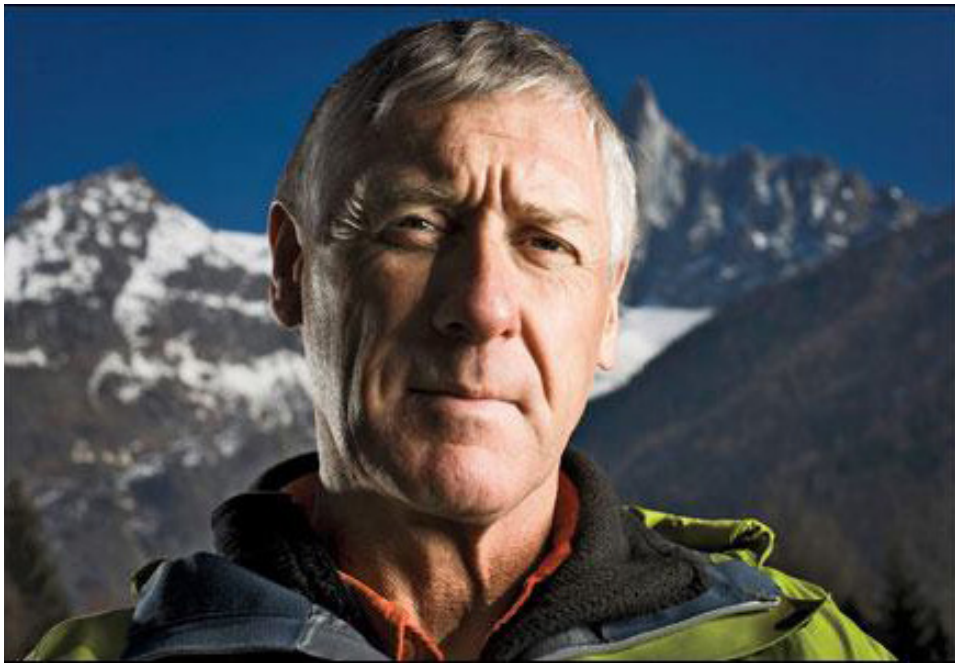
The Ultra Patient

BY BILOINE YOUNG AND ROBIN YOUNG

Who ARE these people?

They are your ultra-patients—like Ellen Miller, who climbed Everest, Nuptse and Lhotse after her hip replacement, or Roy Wyatt who climbed Kilimanjaro at age 75 after his hip surgery, or Scotland's John Matthews who at age 71 is taking on Ben Macdui mountain or Don Healey, who at the comparatively young age of 62 climbed Mount Everest. All these patients (and more) were able to accomplish these incredible feats with artificial hips.

Thomas Sculco, M.D., said this about his ultra-patient, Don Healy: "With the increased knowledge we have today regarding joint replacement techniques, a patient like Don Healy can expect a full recovery. And, as seen in Don's case, if a patient is motivated and determined, he or she can do just about anything following hip arthroplasty."



Wikimedia Commons and Alexander Roumega

Doctor, Can I Climb a Mountain?

Ellen Miller, who at the young age of 54 became the first American woman to climb the three highest mountains in Nepal—the so-called Everest trilogy of Nuptse, Lhotse and Everest—did the final leg of her remarkable achievement with the benefit of an artificial hip.

Roy Wyatt had his hip replacement surgery when he was 74 years old. In 2007, the retired banker but active runner, biker and hiker climbed Mount Kilimanjaro. Then he went back to his surgeon, had ANOTHER hip replacement and proceeded to celebrate his new joint by hiking up Denali in 2008, the highest peak in North America at 20,320 feet. Later that same year he and his 55-year-old son flew to La Paz, Bolivia, and climbed two of the tallest peaks in the Andes.

This year, 71-year old John Matthews announced that he planned to climb Great Britain's second highest peak, Ben Macdui, with the CEO of the manufacturer of his implant. (Interesting precedent. Wonder if other implant company CEO's would do the same?).

And finally, one of Tom Sculco' s patients, Don Healy famously climbed Mount Washington in spring of 2007, then Mount Baker in the Northern Cascades, then Mount Rainier, Denali, Kilimanjaro and finally Everest in the years following his surgery.

What do all of these ultra patients have in common?

In a nutshell, they don't take "no" for an answer—and they won't believe you if you say they can't climb a mountain with an artificial hip.

If at First You Don't Succeed…Get Another Surgeon

Don Healy was a candidate for a hip replacement after breaking his hip in a biking accident in New Hampshire. Nine months after having his hip pinned and hobbling around on crutches with no discernible improvement he sought advice from an orthopedist near his home in New York City. That doctor recommended a hip replacement. When Healy asked if he could still go after his life time goal of climbing Mount Everest, that doctor said "no." Furthermore, said the surgeon, Healy would probably have his range of motion limited to such an extent that he could not squat.

So Healy went for a second opinion.

He visited Dr. Thomas Sculco at Hospital for Special Surgery (HSS) in New York. Dr. Sculco, a frequent debater at the CCJR meetings and ranked as one of the most proficient and safest orthopedic surgeons in New York City, pored over Healy's X-rays and then told Healy that post-surgery, climbing mountains was not necessarily out of the question. In fact, Sculco assured Healy, he would be able to squat.

John Matthews, the Scottish hiker who wanted to climb Great Britain's second highest peak, asked Mike Tuke, chairman of MatOrtho, a British medical device manufacturer based in Leatherhead, Surrey, to join him. When a local reporter asked Tuke about his ambitious hip replacement friend he said, "Generally speaking we don't encourage patients to do more than they should, but actually what happens is that patients go and do what they feel they can do and if you tell them not to do something that sets up a challenge."

"Staying active is the best way to live longer so joint replacement is a vital life extender and it is very satisfying to be in a business that is a life changing operation."

Probably the best reaction came from Roy Wyatt's surgeon, Dr. David J. Covall, who was quoted as saying this about his very unusual patient: "Obviously, Mr. Wyatt is not our typical hip replacement patient. He's an amazing guy. The fact that he was so active before his surgery and so motivated played an important role in his recovery afterwards."

Less Risky Than Driving on the Interstate

Of course, total joint reconstruction is not only one of the most commonly performed surgeries in the world but one of the most routinely successful. Said Dr. Covall, "Almost 95% of my patients go home from the hospital the day after surgery." It is, he said, "probably less risky than driving on Interstate 285."

And if your patient is athletic and interested in extreme sports, then, as a physician, it may well be a good opportunity to let your patient be your guide.

Ellen Miller, who was a mountain *runner* and fitness coach before her

Courtesy of Vitality Center, Vail, Colorado

hip replacement, was certainly a very unusual patient. As she described it to *Denver Post* writer John Meyer in August 2013 "The trilogy was kind of my final hurrah," said Miller. "At my age, I simply can't manage the discomforts of an extreme high-altitude expedition as well as I used to be able to. The cold… the discomfort, it's just gotten harder for me as I've gotten older. I don't feel like I've gotten much slower climbing the mountain, but managing that discomfort has become more difficult." (http://www.denverpost.com/boxing/ci_23801557/vail-climber-is-first-american-woman-complete-everest)

The trilogy she is describing is the Everest trilogy—which means climbing the two mountains adjacent to Everest in addition to Everest. She climbed Everest via the north face in 2001 and the southeast ridge in 2002. She had hip replacement surgery in 2008, climbed Lhotse (27,940 feet) in 2009 and had the other hip replaced later that year. She climbed Nuptse (25,791 feet) on May 16, five years to the day after her first hip replacement.

"It's very interesting; as soon as you get off the Everest highway and hang that right, very few signs of people at all," Miller said. "The views of Everest and Lhotse from there were incredible, and I realized that's a view that very few people have had the opportunity to see because not many people walk over there. That, in and of itself, was a magnificent experience."

A Pattern of Embracing Challenge

Looking back, Roy Wyatt of Lilburn, Georgia didn't think hip replacement was such a big deal. As he characterized it for the Resurgens Orthopaedics Clinic website, it was as quick and easy as having a tooth pulled. Approximately a week after his first THR, he was exercising at the "Y" and about six months later running in the 10K Peachtree Road Race (the largest in the world and now 46 years running). Again, it was Roy's 14th in a row.

Roy Wyatt/Courtesy of Resurgeons Orthopaedics

Later, he completed the six-day, 440-mile bicycle ride in September along the Natchez Trace from Nashville, Tennessee, to Natchez, Mississippi.

As he told the Resurgeons clinic newsletter; "When you get old, you have two choices. You either do it, or you sit. I've always flown airplanes, raced motorcycles, and exercised, and I have no intention of slowing down."

Don Healy's Story

Here is Don Healy's story as covered in the Hospital for Special Surgery website. (http://www.hss.edu/newsroom_don-healy-climbs-everest.asp)

> Don Healy had lived the sedentary life of a business owner until he turned 60 in May of 2005. Suddenly he felt like a couch potato. "I had gone up a couple of waist sizes and

I started to feel sluggish," he recalls. A year later he began seriously working out. He shed 25 pounds and set the goal of scaling Mt. Everest, which had been a childhood dream, by the time he reached his 65th birthday. He mapped out the peaks he'd need to scale in preparation, and began training in earnest. He made his first journey above the tree line on a. Five days before the expedition, a broken hip from a bicycle accident stopped him in his tracks. The day of the accident Don feared he wouldn't be able to walk again, much less climb high peaks.

Two weeks after his meeting with Dr. Sculco, Don went in for surgery. During the total hip replacement, the cup-shaped hip socket and the ball of the thigh bone were replaced with a ceramic ball and titanium stem and a socket. Within a day, he was walking with a cane and working with a physical therapist. After two weeks of therapy, Don was taking short walks around the block. Soon he was adding training to his physical therapy sessions. "I would complete my therapy and then stay for an extra hour and work on my upper body strength to maintain my fitness," he continues. After six weeks, Dr. Sculco lifted his hip precautions. "He said, 'You are free to do whatever you want,'" recalls Don. "At first I didn't feel comfortable trying to do too much so I paced myself," he continues. Three months following his surgery, Don resumed climbing and scaled the Gros Piton, an elevation of 2,600 feet in St. Lucia in the Caribbean. "My hip was fine,' he said.

Several weeks later, he'd made it up Mt. Adams in New Hampshire and then within a year of his accident, he'd climbed Mount Rainier. "My broken hip made me more determined than ever," he says. "I wanted to demonstrate that neither age nor physical setbacks need to limit one's goals."

In 2009, he reached the summit of Mount Kilimanjaro in Tanzania and then Denali, in Alaska, (formerly called Mount McKinley) a requirement before attempting Mt. Everest. In May 2010, Don Healy became one of the oldest Americans to reach the top of Mount Everest. Says Don, "Even though Dr. Sculco said I'd be able to make the climb, I think even he was surprised to learn that I had done it."

Don Healy/Courtesy of Hospital for Special Surgery

Don dedicated his climb to the Hospital and Rehabilitation Center for Disabled Children in Katmandu, Nepal. The Center specializes in orthopedic surgery for children from rural areas and treats congenital deformities such as clubbed feet, as well as improperly healing broken bones, burns and metabolic bone disease. Don has pledged $29,035 (one dollar for every foot he climbed) with the help of family and friends to the American Himalayan Foundation, an organization that provides education, health care and preservation services in the Himalayan region. The donation will support the Hospital, which also treats young patients through three satellite centers and makes visits to children to provide needed physical therapy"

What Ultra Patients Mean for You

They are a mixed bag. Any physician who approaches these patients with an authoritarian, omniscient approach will be disappointed. Yes, honest communication would seem to demand that the physician fully disclose all risks and limitations inherent in large joint reconstruction surgery. Further, after thousands of cases, any experienced surgeon will speak with well-earned authority. But ultra-patients are accustomed to uncharted territory. They present an intriguing shift in the patient/physician communication model. To them even the tallest mountains are mere obstacles to overcome. What's a surgeon by comparison? The key, naturally, is to collaborate and help them scale their personal mountains so they can later tackle even greater challenges courtesy of your excellent treatment. ♦

Toledo (?) A Center of Orthopedic Innovation

BY ROBIN YOUNG

Wikimedia Commons and Magnus Manske

The paradox of innovation is that it is largely immune to dollars, place or pedigree. Why did orthopedics take hold originally in Warsaw, Indiana? Or Memphis or Cleveland?

The answer is people.

Not money. Not fancy degrees. Not offices in major cities.

People. Like Dane Miller, Art Stefee, Edwin Ryerson, Willis Campbell, Norman Kirk, Gavriil Ilizarov, John Charnley, Charles Ray, Lewis Sayre, Sterling Bunnell, Homer Stryker, Paul Harrington or Gerhard Kuntscher.

And they worked in some of the most unlikely places—between corn fields in Indiana, in Siberian outposts, in remote corners of England and even POW camps in Germany during World War II.

So it was exciting to uncover a new center of orthopedic innovation roughly 2-½ hours northeast of Warsaw, Indiana, and that, to our pleasant surprise, more than three dozen orthopedic companies had already made the trek to test their ideas, make a product or find a new products in, of all places, Toledo, Ohio.

Companies like K2M, Inc.; DePuy Spine, Osteotech, Inc.; Disc Dynamics, Inc.; Orthovita, Inc.; Synthes, Inc; Stryker Spine, Inc.; Biomet, Inc.; Spine Wave, Inc; Spinal Concept, Inc; Medtronic; Globus, Inc; Advance Spinal Technologies, Inc.; LANX, Inc; Alphatec, Inc; Applied Spine Technology; Invibio, Inc.; Osseon, LLC; Pioneer Surgical Technologies, Inc; Interventional Spine, Inc.; SI BONE, Inc. and Paradigm Spine, Inc.

Innovation on the Maumee River

The Maumee River starts in Fort Wayne, Indiana, and meanders northeast through the corn and soybean fields of Indiana and Ohio to Toledo where it empties into Lake Erie. The Maumee River made Toledo a port city and gave the factories in Toledo access to Detroit, Pittsburgh, Cleveland and points east. Autos dominated the local economy for years. Making cars, but more importantly making the glass for cars, became Toledo's comparative advantage.

Toledo is the "glass city" and home to Corning Glass Works.

Like most rust belt cities, the last few decades have been difficult. Two auto manufacturers (Jeep and GM) are left. When we visited Toledo this summer we often heard the question; Will Jeep Stay?

Tellingly, the largest employer on the Maumee River in the great port city of Toledo is, in fact, the University of Toledo.

And it is the University that is shaping the future of not only Toledo but, we learned, orthopedics.

E-CORE

Toledo's university and, more specifically, the Engineering Center for Orthopaedic Research Excellence or E-CORE, is leading this small city into a knowledge-based economy. ECORE was founded by Vijay K. Goel, Ph.D. and Nabil Ebraheim, M.D. Neither of whom grew up fishing for walleye on the Maumee.

Joining Drs. Goel and Ebraheim are Anand K. Agarwal, M.D., Sarit Bhaduri, Ph.D., Edward Nyman Jr. Ph.D., Hossein Elgafy, M.D., Christian Schultz, M.D., Kamal Deep, M.D., Mohamed S. Hefzy, Ph.D., and Eda Yildirim-Ayan, Ph.D. ECORE started in 2006 and in the intervening years it has put up a record of orthopedic innovation – based on original bioengineering research.

Here's a sample of what has emerged from the ECORE group:

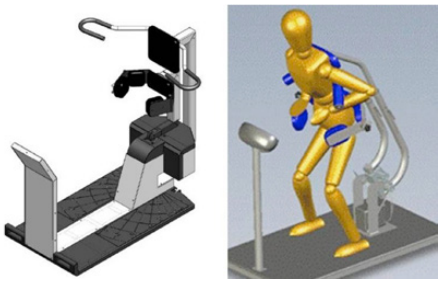
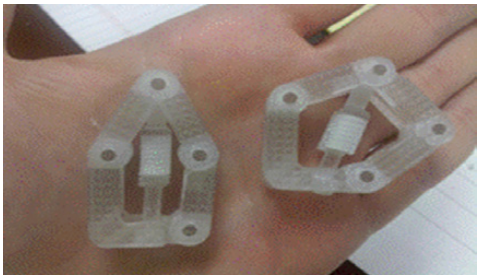
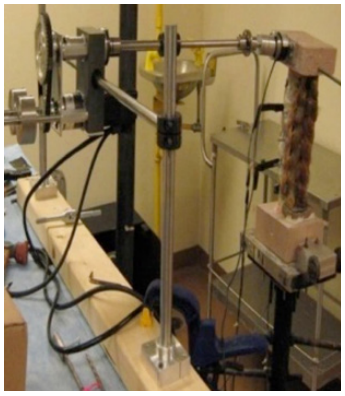
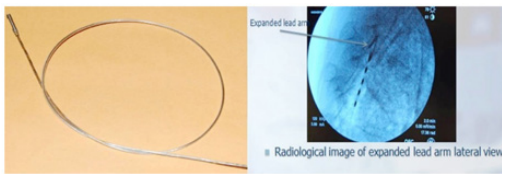
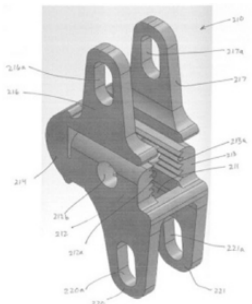
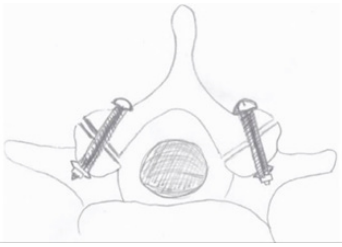
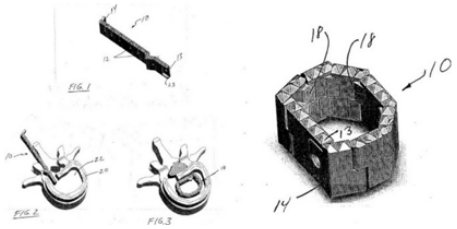
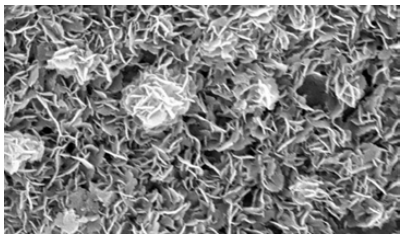
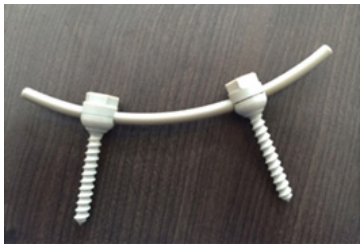
Trainer TP 4.0 Back/Core Muscles Exercise Machine **Inventors:** Goel VK, Dick D, Jaegly J, et al. **Licensed to:** Turning Point LLC, Toledo, OH **Manufactured:** Lokrey Manufacturing, Toledo, OH	
MIS Cage Articulating Interbody Fusion Cage **Inventors:** Goel VK, Matyas A. **Licensed to:** GAMMA Spine LLC, Toledo, OH **Sub-licensed to:** X-Spine, Inc. Miamisburg, OH	
Automated Spine Testing System **Inventors:** Goel VK, Friis (Univ. of Kansas), ATS. **Licensed to:** Applied Test Systems - ATS, Inc., Butler, PA	
Neuromodulation Lead Electrical Stimulation Lead for a Neurostimulation System that Resists Relative Movement after Implantation **Inventors:** Atallah, Goel VK, Agarwal AK, Kodigudla M. **Provisional Application:** Ref # D2012-2, U.S., May 3, 2012	

Table continues on page 10...

Hybrid Multifunctional Posterior Interspinous Fusion Device **Inventors:** Agarwal AK, Goel VK. **Provisional Application:** Serial No. 61/599,988, May, 2012 **Licensed to:** Butterfly LLC, Toledo, OH **Sub-licensed to:** Paradigm Spine Inc. New York, NY	
Bioactive Facet Fusion Device **Inventors:** Goel VK, Agarwal AK. **Provisional Application:** Ser. No. 61/593,270, January 31, 2012 **Licensed to:** Butterfly LLC, Toledo, OH	
Smart Intervertebral Fusion Cage **Inventors:** Elahinia M, Chapman C, Anderson W, Goel VK, Agarwal AK. **Licensed to:** EndoSphere Spine LLC, Toledo, OH **Sub-licensed to:** joimax Inc., Karlsruhe, Germany	
Method for Modifying Surfaces for Better Osseointegration **Inventors:** Bhaduri S, Goel VK, Zhou. **Companies:** Exclusive option with Orchid Inc., MI, June 2012	
Polymer Pedicle Screw and Rod System **Inventor:** Agarwal Anand	

Source: University of Toledo

OsteoNovus and Spinal Balance

In July 16 of this year two companies officially emerged from this hothouse of product testing—OsteoNovus and Spinal Balance, Inc.

The two startup companies are part of a new program from the University of Toledo called Launch Pad Incubation.

OsteoNovus and Spinal Balance are early-stage orthopedic medical device companies which were founded by members of the UT faculty—specifically Dr. Anand Agarwal, professor of bioengineering and orthopedic surgery at the University of Toledo and Dr. Vijay Goel, UT Distinguished University Pro-

fessor Endowed Chair and McMaster-Gardner Professor of Orthopaedic Bioengineering, bioengineering and orthopedic surgery along with Arthur Karas, co-founder of Spinal Balance, and Dr. Sarit Bhaduri, UT professor of mechanical engineering/dentistry and co-founder of OsteoNovus. Dr. Agarwal manages both of the companies as president and CEO.

Biologics

OsteoNovus is developing innovative biologic materials which are demonstrating the ability to support and regenerate bone at impressive speed and quality. The company's lead product, NovoGro, grows robust bone in six weeks. Best of all, it will be available as a moldable putty or injectable bone substitute. NovoGro is designed for use in multiple clinical applications, including bone voids, treatment of various fractures and spinal disorders.

Hardware

Spinal Balance has designed, developed and is starting to manufacture advanced spinal hardware including the Libra Pedicle Screw System, a facet screw system and interbody cages. The implants came from the work at UT and include several highly novel and unique attributes. One that caught our eye was a combination metal and allograft facet screw. The implants are targeting degenerative disc disease and spine deformity indications.

University of Toledo Engineering

Being part of the larger UT engineering complex has allowed these startup firms to accomplish much more with much less. Already the two companies have established research, development and manufacturing facilities, including a lab space, a custom clean room, and a controlled inventory storage area.

Finally, leveraging the UT resources has helped these startups to secure funding grants and investor equity support. Investors appreciate the ability of LaunchPad Incubation to provide entrepreneurial assistance, state-of-the-art facilities, and other valuable resources.

The Secret of UT's Success

The secret behind Toledo's success are the labs that Drs: Goel, Agarwal, Bhaduri, Hefzy, Demetropoulos, Nyman, et al have painstakingly put together over the years. These labs have attracted all the top spine and orthopedic compa-

nies and now, are pumping out a stream of innovative products as well.

These well-equipped labs can conduct research at the cellular level, bench and cadaver tests, analytical modeling and even clinical and patient follow up after surgery or rehabilitation.

Companies using UT have access to spine biomechanics labs, joint biomechanics labs, computational labs, whiplash and impact trauma diagnostic labs, biomechanics and assistive technology labs, material processing labs, tissue engineering and regenerative labs and bone biology labs.

The equipment includes automated spine testing systems, two Optotrak Motion Traking Systems, three MTS Bionix bi-axial Universal Testing Systems, Bose Micro-Mechanical testing system, a 6-station MTS Bionix Spine Simulator and so much more. The labs even have an in-house machine shop along with complete sets of surgical instruments, digital video fluoroscopy, digital video cameras, optical microscopes and more and more.

In addition, the labs can perform high end computer aided design (CAD) work as well as simulations. The software available includes: ABAQUS, COMSOL, MSC Adams, OpenSim, Solidworks, AutoCAD, Mimics, 3D-Doctor, Slicr3D, 3-Matic. TrueGRID, MeshLAB, IA-FEMesh, LabView and Matlab.

From a practical standpoint, that means that the ideas percolating from these engineers can be fabricated, tested, modeled and simulated very quickly and affordably.

How many orthopedic startup companies can say that they have access to such rich talent and equipment?

The Future

Not surprisingly, a growing list of companies (and investors) are finding their way to the University of Toledo and the guys with long last names (except Vijay) in the bioengineering building.

If the lessons of Warsaw, Memphis, Cleveland and the Twin Cities are any clue, this port city at the mouth of the Maumee River is well on its to becoming a major center for orthopedic innovation and commercialization. ♦

Breathtaking: World's First Bilateral Hand Transplant in a Child// Nonunion Rate in Subtalar Fusions…Mysteries Remain // Study: Medial Chondrosis Associated with BMI, Alignment, and Medial Meniscal Status

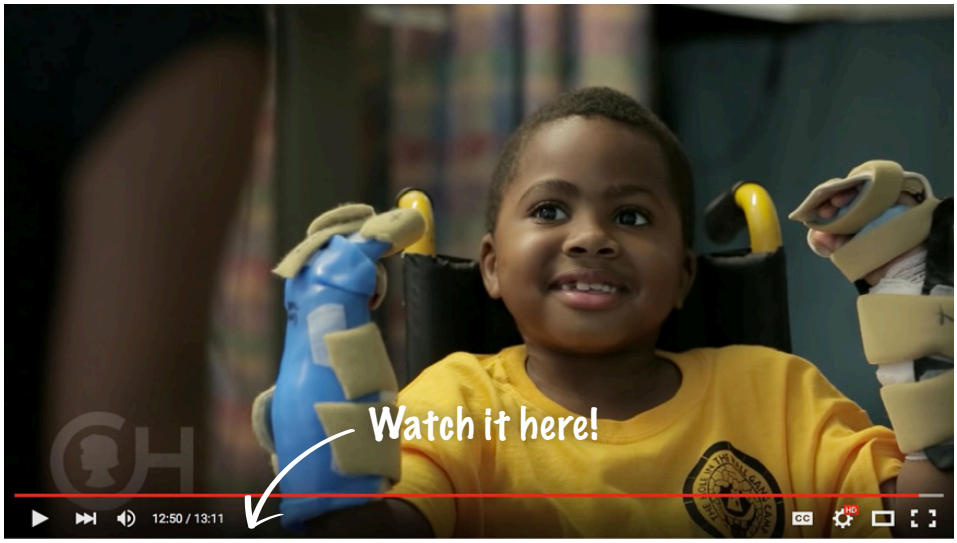
BY ELIZABETH HOFHEINZ, M.P.H., M.ED.

Breathtaking: World's First Bilateral Hand Transplant in a Child

What kind of surgery could involve 18 months of planning, 3 hospitals, 40 medical personnel, and last for 10 hours? A world's first…a bilateral hand transplant in a child.

The transplant team, led by L. Scott Levin M.D., FACS, chair of orthopaedic surgery at the University of Pennsylvania and professor of surgery (division of plastic surgery), also included medical personnel from the Children's Hospital of Philadelphia and Shriners Hospital for Children in Philadelphia. Dr. Levin, told *OTW*, "This brave young boy, Zion Harvey, was referred to us by Scott Kozin and Dan Zlotolow, two talented hand surgeons at Shriners. He had lost his hands at the age of two due to an infection. Now, he has a second chance."

Dr. Levin is the only U.S. orthopedic surgeon to ever lead a Vascularized Composite Allotransplantation team. He noted, "Zion's surgery required, among many other individuals, five orthopedic surgeons and five plastic surgeons. The planning was very complex, with involvement required by pharmacy, ICU, nursing, OR, anesthesia, the internal medicine etc.…as well as numerous meetings to explain what was being done. We created extensive checklists and practiced the operation several times at the Penn Human Tissue Laboratory. We utilized CT generated cutting guides for the osteotomies and



http://youtu.be/pFyP_R6wPr8

we used 3D printing to create models of the patient's hands (based on MRI data) and thus increase efficiency in the OR."

"We closely followed our protocols and checklists in order to ensure that no step was eliminated, and that what we had rehearsed was exactly what we did during the surgery. Things moved along very efficiently in the OR and we had excellent communication between the entire surgical team. It was a big orchestra. It helped immensely that the technical aspects, such as connecting the donor's forearm bones to Zion's arms, were worked out in advance."

"One sign of success as the operation progressed was that Zion's new hand was revascularized in the appropriate amount of time. The color and size matching was excellent because we had created models of his ideal hand based on his MRI and CT data. The 3D printing helped us select and confirm that the size of the donor hand was acceptable to transplant onto Zion's forearm."

"This has been an unusual, emotional experience…and it must be said that while one little boy has new hands, there is a family that is mourning the loss of their little boy. They deserve the utmost respect."

"We check in on Zion two to three times a day to ensure that things are progressing as they should. He is already moving his fingers and picking up objects; he will continue with hand therapy for some time."

"We have made a lifelong commitment to this patient and his family. Because

Zion lost his hands at such a young age, we will be doing functional MRI scans of his brain to determine how his brain responds to having hands and how the brain will grow and adapt."

"In order to do this kind of case you need microvascular experience in free tissue transfer and pediatric microsurgery. Unfortunately, these skills have been lost in American orthopedics; modern microvascular surgery is now predominately the domain of reconstructive plastic surgery. I have been privileged to train a few orthopedic hand and microsurgery fellows who are doing elective reconstructive microsurgery. But this is intensive, and not for everyone. There are not, for example, a lot of joint replacements or arthroscopies that you have to take back in the middle of the night." This can happen and does happen occasionally in free tissue transfer if there is a vascular thrombosis.

"Zion required urgent return to the operating room due to arterial thrombosis one of his blood vessels. We fixed the problem without incident, but it demonstrates that there is a high degree of vigilance and postop intensity that is required particularly in microsurgery."

"Zion will be the first of many children to have this surgery; it holds great promise."

Subtalar Fusions: Digging Into the Nonunion Rate What is behind the nonunion rate in the subtalar joint? Famed foot and ankle specialist, Chris Coetzee, M.D., wanted to find out. He tells *OTW,* "I am the primary investigator on a current multicenter study looking at subtalar fusions; we know the nonunion rate is roughly 10% for these procedures, which is pretty high for an orthopedic procedure rate."

"The fact that the subtalar joint has a fairly poor blood supply may be one thing that contributes to the high nonunion rate. Also, this is a joint with high load sharing…and it's a small joint, so every time you walk it is absorbing your full body weight. There is also a shear component to load, not only axial"

Dr. Coetzee, noting that this is a prospective randomized controlled trial, added, "To see which treatment would result in a higher fusion rate, in one arm of the study we used stem cells and in the other arm we used autologous bone graft. While we were hoping that the

stem cells would be the missing link, it looks like there is no difference between the two groups. Once all the data is collected we will stratify the data to see if there are specific situations were stem cells might be beneficial or superior to autologous graft."

"We took x-rays at 6 weeks, 3 months, 6 months, and one year; we did CT scans at 6 months. The one thing we learned early on during the study is that the specificity of an x-ray to show fusion is only 30%. The subtalar joint looks like a saddle, so depending on the direction of the x-ray beam things can be unclear. If there is flatfoot involved, then you have to aim the beam perpendicular to the joint in order to determine if it is fused. You really must use a CT scan. While they used to be expensive and a bit challenging to access, you can now have them done just about anywhere—and have them done without a substantial cost."

If not stem cells, then what is the missing link? Dr. Coetzee says, "It might be that there will just be a certain percentage of subtalar fusions that will result in nonunions. We need to determine if there are different fixation methods that are more effective. At this point we use screws; in theory that is static compression, so if there is a bit of bone resorption then you lose your compression. The idea would be to have something that is ongoing, i.e., dynamic compression such that even if you get bone resorption you will obtain compression across the joint. As for this study, it is ongoing, and we will have the final results by the end of the year."

Medial Chondrosis Associated with BMI, Alignment, and Medial Meniscal Status It looks like those patients having to undergo revision ACL [anterior cruciate ligament] reconstruction (rACLR) could be at a disadvantage when it comes to their cartilage. Robert H. Brophy, M.D. is an associate professor of orthopedic surgery at Washington University School of Medicine in St. Louis. Dr. Brophy told *OTW*, "Patients who undergo rACLR often experience damage to the articular cartilage (chondrosis). We thought that malalignment could overload one compartment of the knee and be associated with a higher rate of chondrosis in that compartment."

"In one of our previous studies we looked at patients who had undergone a prior meniscus repair and how that related to cartilage wear. We showed that if the patient had had the meniscus removed then they fared worse than if they had undergone a repair. We didn't know whether it mattered if the repair resulted in a healed meniscus, we were just basing the results on the previous surgery."

"Using data from the Multicenter ACL Revision Study (MARS) study, a prospective cohort, we were able to identify 246 patients who could be included in the study. We suspected that body mass index (BMI) would be related to chondrosis in the medial compartment; here, the average BMI was 26.4. We found that the medial compartment had more chondrosis than the lateral compartment. Disruption of the meniscus was noted in 35% of patients on the medial side and 16% in the lateral side. Medial compartment chondrosis was associated with BMI, alignment, and medial meniscal status. Lateral compartment chondrosis was significantly associated with age and lateral meniscal status. Patients who had an intact meniscus decreased their odds of having chondrosis by 64% to 84%."

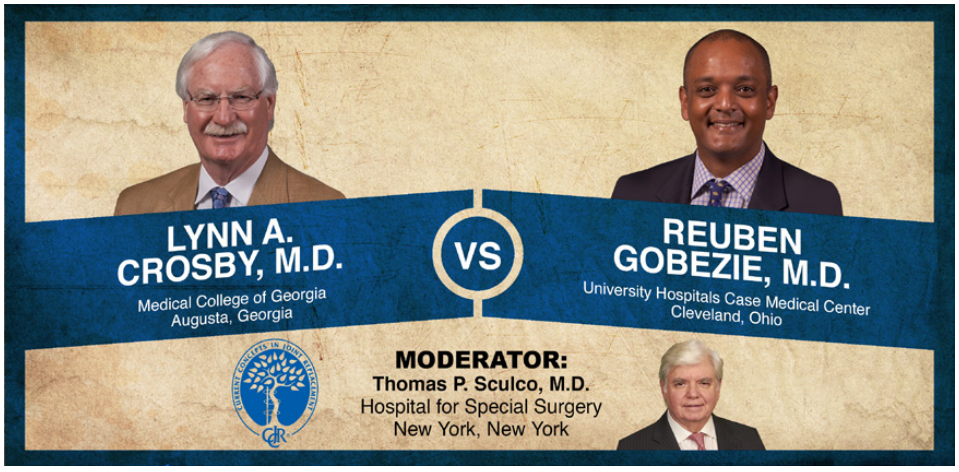
"While we found no significant association of chondrosis in the lateral compartment with alignment it is possible that the study was underpowered. The study design can show association but not causation, and we're still talking about a single snapshot of data."

"We still don't know if we should correct malalignment in people undergoing ACL reconstruction to prevent arthritis. This needs to be examined prospectively, but this is a challenging study to conduct in adequate numbers." ♦

Reverse Shoulder or Not? Crosby and Gobezie Debate Contained Cuff Arthropathy

BY OTW STAFF

According to Lynn Crosby; "When treating cuff tear arthropathy with loss of acromial-humeral distance; pain with or without activity; good deltoid tone and strength, reverse is the best option. Not so fast, says Reuben Gobezie; "don't do these reverse replacements on patients who have these types of tears because they have pre-op range of motion greater than 90. It is not a good outcome." Who wins this great debate? You decide.



Current Concepts in Joint Replacement/RRY Photo Creation

This week's Orthopaedic Crossfire® debate was part of the 16th Annual Current Concepts in Joint Replacement® (CCJR) – Spring meeting, which took place in Las Vegas this past May. This week's topic is "Contained Cuff Tear Arthropathy – Best Treated with a Reverse Shoulder." For the proposition is Lynn A. Crosby, M.D., Medical College of Georgia. Reuben Gobezie, M.D., University Hospitals Case Medical Center, is in opposition. Moderating is Thomas P. Sculco, M.D. from the Hospital for Special Surgery.

Dr. Crosby: Cuff tear arthropathy was first coined by Neer and Craig in 1972. A massive rotator cuff tear leads to a superior migrated humeral head, which then causes an arthritic change where there's erosion and collapse of the glenohumeral joint. Grammont, in 1985 used the inverted version of the constrained designs of the '70s that have since been removed from the U.S. market. He lowered and medialized the center of rotation, increasing the moment arm of the deltoid that limited the shear forces responsible for glenoid failure. And these were brought back in the U.S. market in 2004.

At that point [2004] the indications for the reverse shoulder were rotator cuff tear arthropathy. Reverse shoulder has since morphed into a lot more different diagnoses that we use it for. Today we're talking about rotator cuff tear arthropathy.

Dr. Rockwood in 2006, shortly after it was re-released into the U.S. warned in a *JBJS* article about the potential downsides of using this prosthesis. If we look at these complications independently, post-operative hematoma is certainly the most common. If you take the patients off their anticoagulant, use a hemovac or drain post-operatively, I think this can be completely prevented. Glenosphere dissociation is basically a technical error at the time of surgery, and so if you're careful and put your components together, I think this can be eliminated.

Another potential complication is glenoid subluxation/dislocation, I think we're getting a handle on that. It's proper tensioning, and we certainly can't control the trauma events that occur. Dissociation of polyethylene component, is probably after a trauma event. Acromial or scapular fracture certainly is the black cloud on the horizon. We haven't got that completely under control, but are working on it and I think there's been some nice moves to help prevent and treat these when they do occur. Infection, I think we're getting a handle on *P acnes* which is a major cause and I think we're on the way to maybe decreasing the infection rate in these prostheses. Scapular notching, I think we've almost eliminated that as a potential problem.

If we look at a plain X-ray, acromial descent is normal at 7mm to 14mm and if we get an MRI, we expect then that the supraspinatus will fill the fossa. If it's less than 7mm but greater than 5mm usually the supraspinatus is retracted and the fossa would show fatty atrophy. If it is less than 5mm then we have a massive tear including the infraspinatus and the head will be high. And these are the cases that go on…if they're not arthropathy already, they're going to be soon, and those are the ones we're dealing with. You can't just deal with that MRI find-

ing. You need to look at the coronal view and if there's muscle above the tangential line, then these patients can still have a rotator cuff repair. You have to treat the patient and maybe do an arthroscopy to see if they're repairable.

If the repair's impossible, it's less than 5mm, conservative treatment is still an option. Injections. Deltoid rehab. They can get some significant relief. Arthroscopy can be a powerful tool early with debridement and biceps tenotomy, especially if they're a male with an active range of motion above 100 degrees and good deltoid tone. If repair's impossible then we start talking about arthroplasty. Then our options are hemi, standard stem or reverse. We used to think if the head was centered, then a hemiarthroplasty could be potentially helpful to the patient. So if we go from a type 1a to a type 1b…and this is really a progression...these are the ones that we felt maybe a hemiarthroplasty might work. But what you have to realize is the erosion doesn't stop just because you put a piece of metal in there. The erosion under the acromion and under the superior aspect of the glenoid continues to happen. Then you get into these patients who have massive bone loss and they have very difficult reconstructive options. Certainly in decentered ones where you have pseudoparalysis there's really no option of a hemiarthroplasty and a reverse is really the option for them.

When treating cuff tear arthropathy with loss of acromial-humeral distance; pain with or without activity; good deltoid tone and strength with a failed nonoperative treatment, I feel the reverse is the best option.

Dr. Gobezie: What is a contained massive cuff tear? In my mind it's a massive cuff tear, that's centered on the glenoid. Hence, it's contained within the glenohumeral joint. This is a unique group of patients. Usually they have preserved range of motion, oftentimes they're younger or they're very active patients because they have retained range of motion, and their typical complaint is night pain. In other words, they feel weak, but they move their arm and they have night pain.

I want to start off with showing what the literature says about this because this has been looked at. In terms of people who are not pseudoparalytic, who can still move their arms, but have massive cuff tears, there are two big series—one from Frankle and one from Boileau—showing that if you look at these patients, while you can get good results with regards to range of motion, they're not satisfied. Both of the papers concluded - don't do these reverse replacements on patients who have these types of tears because they have pre-op range

of motion greater than 90. It is not a good outcome; neither from satisfaction…in some cases even decrease in range of motion.

What are the options for irreparable cuff tears? You have debridement, partial repair, tenotomy, muscle transfer, CTA head and…then of course if you have a hammer everything is a nail… reverse arthroplasty.

I want to share with you something that's relativity new, called a superior capsular reconstruction [SCR]. Essentially it's made and designed specifically for the patient with a contained cuff tear, and sometimes even a little superior migration and you want to avoid a reverse arthroplasty.

What is a superior capsular reconstruction? It can be done open or arthroscopically as an outpatient and involves a graft material…either fascia lata or allograft. The difference is that in typical grafts that we've talked about before—augmentation grafts—you'll see that the augmentation graft is sewn into the muscle tendon and then inserted with screws into the greater tuberosity. In the SCR, the fixation of the graft is medial on the superior aspect of the glenoid rim and it's fixed with a lateral row of anchors laterally.

You've all heard the expression 'necessity is the mother of invention'. This approach came about because surgeons in Japan **did not** have the reverse arthroplasty until 2014. Dr. Mahata developed this technique to address the massive cuff tears in patients where he didn't have the opportunity to do a reverse. And these are often young patients with good range of motion. They use fascia lata grafts, but not allografts as we have before. The concept of SCR is to reduce superior translation …in other words to keep the cuff of the humeral head contained within the glenohumeral joint and allow the deltoid and the other surrounding muscles to operate and move the arm.

I want to share with you what Mark Frankle told me when I asked him 'how does the lateralized reverse work?' Dr. Crosby shared with you about the Grammont style where you dislodge the arm and you make the deltoid lever arm greater. Mark said to me, 'Any implant that stabilizes the fulcrum of the glenohumeral joint in rotator cuff arthropathy will work. The quest is how well and for how long.' That's just the point.

The whole SCR is made to stabilize the humeral head in the glenoid and allow the other muscles to work. Biomechanically this has been shown by Mahata et al. If you compare the superior capsu-

lar reconstruction to the intact cuff, it actually resists superior forces as well as an intact cuff and better than a tendon patch and better than a rotator cuff tear would do otherwise.

The clinical outcome Mahata reported was on 24 shoulders over a two-year minimum follow-up using fascia lata and showed he could reduce the acromial humeral distance significantly. The ASES scores improved significantly. And there was only a 15% instance of graft tear. Superior capsular reconstruction offers good outcomes, quick rehab, and outpatient surgery; does not burn any bridges and that's the key. A lot of these young people who can still move their arm, don't want to have something that burns bridges and I would tell you that it doesn't burn any bridges and to me reverse replacement for a contained cuff tear is more like the wild west.

Moderator Sculco: Who would not be a good candidate for reverse shoulder, in your opinion?

Dr. Crosby: Someone who has pain, number one. Certainly if they're pseudoparalytic—that's a different group. They're disabled because of their inability to use the arm, so I think that's a separate group. But certainly pain is still the major driving indication. Then the secondary arthritic changes…there are still some conservative treatments that work very well with these people who have excellent elevation above 100 degrees, have good deltoid function, and injection is still a very good option for these people early with a physical therapy program on their deltoid. If they still have excellent elevation but some pain is their complaint, then an arthroscopy in the biceps, either tenotomy or tenodesis, can be very helpful in those people to eliminate their pain.

Moderator Sculco: And what's your feeling about Reuben's operation—the superior capsular reconstruction?

Dr. Crosby: I think it's coming along. I actually was in Liverpool on Thursday at the Liverpool Shoulder Symposium and Peter Minton, who is Reuben's mentor, presented this and said 'I did this, I do this and I did one just recently. I spent 2.5 hours trying…dropped the arm down to the side and it fell apart, so I did a reverse in the operating room the same setting.' I don't think we're quite there yet, but I think it's coming.

Moderator Sculco: So Reuben, you have a patient who has arthritic changes in the joint, as well as this massive rotator cuff tear. Aren't you going to do a reverse shoulder in that patient or are you going to try to do your reconstruction?

Dr. Gobezie: I think it's about how the patient presents. Part of the story—they have a massive cuff tear and they have a little bit of arthritis, but the patient's functional range of motion is very important and the symptoms. Oftentimes contained massive cuff tears… those are the people who are being told 'Hey, look you need a replacement.' Oftentimes I see them and they say, 'Hey, doc I saw this guy, said replacement. I can move my arm blah, blah, blah' and their weakness is the biggest issue. I think if someone is not pseudoparalytic, the MRI's nice, the arthritis is nice, they have good function, I want to keep it that way.

Moderator Sculco: I want to thank the speakers for an outstanding session. ♦

Please visit www.CCJR.com to register for the 2015 CCJR Winter Meeting, December 9 - 12 in Orlando, Florida.

COMPANY

Orchid Design Tapped by FDA for Submission Tracking Project

Orchid Design has been selected by the FDA to be the sole regulatory consulting firm to participate in their submission tracking initiative. The FDA is piloting a web-based program to track the status and key details of 510(k) submissions in an effort to add transparency and eliminate confusion surrounding the often misunderstood "FDA Review Clock."

Kellen Hills, senior quality and regulatory consultant for Orchid Design commented in the August 06, 2015 news release, "The insights gained from working directly with the FDA on this project will allow us to efficiently and effectively navigate the regulatory submission process, as well as bring important issues to the FDA's attention from a perspective they may otherwise not have considered in the development of the Submission Tracker program."

A representative from Orchid Design told *OTW*, "Orchid Design responded to FDA's request for participants by sharing our regulatory team's prior experiences with other global regulators submission tracking processes. We also work with multiple branches within FDA and are not restricted to a single device type. Orchid Orthopedics is also a key contract manufacturer to many of the major OEMs [original equipment manufacturer], so the relationship between FDA/OEM/Contract Manufacturer is already established."

"We bring a unique perspective, in that we work with various size OEM's, from single physicians to small start-ups, to midsize OEMs to multi-billion dollar global companies. The size of the organization brings unique challenges when working with FDA, from a resource standpoint, from a knowledge standpoint, and from an expectation standpoint. We also work with multiple branches within FDA and are not restricted to a single device type (from large joint orthopedics, to spine, to dental, to neuro, to endoscopy, to urology, etc.)."

"Many smaller companies still feel that the entire 510(k) submission process is a 'black box;' you send something to FDA and hope to hear back in 90 days. The FDA has put out guidance documents to help explain the review clock, but there is still uncertainty when trying to determine exactly where in the review process you are, when the clock starts and stops, and when you should expect feedback." — *EH*

Logos courtesy of Orchid Design and FDA

Total Knee FDA Cleared for Stryker's MAKO

The FDA has added total knee clearance to the previously cleared total hip application of Stryker Orthopaedics' MAKO robotic system.

Courtesy of MAKO Surgical Corp.

An August 6, 2015 company announcement states that the clearance expands on current MAKO partial knee and total hip applications of the robotic reconstructive service line. In March, the FDA cleared the company's use of the robotic system for total hip replacement procedures.

David Floyd, the group president of Stryker's orthopedic business, said, "The ability to include a MAKO total knee application with our market leading Triathlon Total Knee System represents a key milestone in reconstructive surgery. We are excited about the opportunity to transform orthopaedics by furthering the growth of robotic-arm assisted surgery, and by enhancing the surgeon and patient experience."

Limited Launch

The company is preparing to initiate a limited market release of the new application by the end of the year.

During a conference call with analysts on July 23, company Vice President Katherine Owen told the analysts to keep in mind that it was going to take three to four quarters before they've

gone through the necessary training and upgrades needed to optimize the launch.

According to the company, over 50,000 MAKO procedures have been performed since 2006, with the first total hip procedure performed in 2010. Since then, over 7,000 total hip procedures have been performed with the MAKO system using various surgical approaches including direct anterior, postero-lateral, and antero-lateral.

Rise of Robotics

In March, RBC Capital markets analyst Glenn Novarro wrote, "In total knees, U.S. surgeons expect robotics to represent ~10% of total knee procedures two years from now, ~18% of procedures five years from now, and ~23% of procedures ten years from now."

Stryker sure hopes so as the company seeks to capitalize on its $1.65 billion acquisition of MAKO Surgical in 2013. — *WE*

LEGAL

Dr. Carson Rising in Iowa

They say you can hear the corn grow in Iowa in late summer. After the Republicans held their first presidential debate in early August, you could hear Dr. Ben Carson's support grow as he moved into second place in the polls in Iowa.

A new *CNN/ORC* poll out after the first Republican debate showed that Dr. Carson now trails only Donald Trump by 22% to 14% in Iowa. Dr. Carson has also caught U.S. Senator Marco Rubio to tie for fourth place in national polls of potential Republican voters. Trump still leads national polls with 22.8%, Jeb Bush at 12% and Wisconsin Governor Scott Walker at 9.4%. Rubio and Dr. Carson are at 6.2%.

Dr. Ben Carson

Best Line of the Night

Dr. Carson had the best line of the night at the end of the early August debate when he said, "Well, I haven't said anything about me being the only one to do anything, so let me try that: I am the only one to separate Siamese twins, the only one to operate on babies while they were still in their mothers' womb, the only one to take out half of a brain although you would think, if you go to Washington, that someone had beat me to it."

Nate Silver's online publication, *FiveThirtyEight*, said Dr. Carson "continues to poll fairly well and is well-liked by voters. Depending on which poll you look at, he was rated as either the most impressive or the second most impressive candidate in the varsity debate."

Winners and Losers

Silver tracked changes in polls, pre-debate to post-debate. Carly Fiorina, the former Hewlett-Packard CEO, until being fired by her board, had the biggest jump, rising 6.0%. Rubio and Carson each rose 2.4%. Scott Walker was the big loser, dropping 4.6%.

Healthcare? What Healthcare?

Perhaps the most surprising thing about the debate was the absence of talk about healthcare. They all said they wanted to "Repeal and Replace" Obamacare. But no one offered an alternative.

The only ones to give more than a sound bite about healthcare were Ohio Governor John Kasich, as he explained why he expanded his state's Medicaid program with Obamacare money, and Donald Trump, who claimed that even though he'd said good things about the single payers systems in Canada and Scotland, he preferred a "private system" for the U.S. "without the artificial lines around every state."

Polls and the Nate Silver Scorecard

Silver urged people not to get too wound up about polls right now.

"Twelve years ago, in August 2003, Joe Lieberman led in most polls of the Democratic primary. Eight years ago, in August 2007, Rudy Giuliani maintained a clear lead in polls of Republicans, while Hillary Clinton led in polls of the Democratic nomination contest. Four years ago, in August 2011, Mitt Romney began with the lead in polls of Republican voters, but he would be surpassed by the end of the month by Rick Perry, the first of four Republican rivals who would at some point overtake Romney in national polling averages," wrote Silver.

Silver says the polls have "some correlation" with election outcomes. It's better to be near the top than near the bottom. But polls right now are "like projecting a major league pitcher's numbers from high school stats: Sure, you'd rather draft a random 17-year-old with a 2.14 ERA than another one with a 3.31 ERA if that's all the information you have to go by. But that data doesn't reveal very much, and its predictive power tends to be swamped by other indicators (everything from the pitcher's strikeout-to-walk ratio to his scouting reports)."

Endorsements Matter

The best indicators in the case of presidential primaries, says Silver, are "endorsements and support from party elites tend to be more reliable indicators of eventual success."

If that's the case, place your bets on Jeb Bush.

FiveThirtyEight keeps track and weighs endorsements on a numerical scale of Governors (10 points), U.S. Senators (5 points) and U.S. Representatives (1 point.) In that race Bush leads with 31 points, followed by New Jersey Governor Chris Christie with 25 and Huckabee with 15. Dr. Carson stands at 0. — *WE*

FDA on Record Approval Pace in 2015

A new report from EP Vantage says that in the first half of 2015, the FDA has already approved 26 devices with either premarket approval (PMA) or a humanitarian device exemption (HDE). That's more PMAs and HDEs for new devices than for all of 2009, 2010 or 2013, said the report.

Photo creation by RRY Publications, LLC, logo courtesy of FDA and image from Pixabay

At this rate, the agency is on target to approve more such devices than in any individual year in the past decade.

One Ortho Device Approved

We checked the FDA PMA record for orthopedic devices. Only one Original PMA has been granted so far this year. That was in May for Vertiflex Inc.'s Superion Inter Spinous Spacer. There have been 16 Supplemental Approvals granted for orthopedic devices for things such as post-approval studies, changes in vendors and updates in packaging or manufacturing processes. DePuy Synthes and Medtronic plc led the way in Supplemental Approvals with eight and five respectively.

According to EP Vantage, the average review for devices granted a PMA or HDE took 17.1 and 16.7 months, respectively.

In April, the FDA finalized a new expedited pathway for medium- and high-risk devices that meet an unmet need for certain serious medical conditions. Then, in June, the agency announced it would exempt some 120 classes of low-risk devices from premarket notification requirements, making it substantially easier to bring devices in those classes to market.

Unfortunately, none of those classes included orthopedic devices. — WE

Whistleblower Earns $2.2 Million in NuVasive/DOJ Settlement

A whistleblower will receive $2.2 million of the $13.5 million dollar settlement announced in late July between NuVasive, Inc. and the U.S. Department of Justice.

The company did not admit to any wrongdoing in the settlement, nor did the Justice Department require the usual Corporate Integrity Agreement (CIA) that allows the government to continue monitoring activities from inside the company.

The Corporate Whistleblower Center issued a press release on August 12, 2015, divulging the whistleblower amount. The Center also said the settlement "resolves allegations that NuVasive knowingly offered and paid illegal remuneration to certain physicians to induce them to use the CoRoent System in spine fusion surgeries, in violation of the federal Anti-Kickback Statute." The Center also said the marketing of the system was not approved by the FDA.

SOLAS Noted

"The alleged illegal remuneration consisted of promotional speaker fees, honoraria and expenses relating to physicians' attendance at events sponsored by a group known as the Society of Lateral Access Surgery (SOLAS). SOLAS was allegedly created, funded and operated solely by NuVasive, despite its outward appearance of independence," continued the press release.

The government issued a federal administrative subpoena to the company in the second quarter of 2013. The subpoena sought discovery of documents for the period January 2007 through April 2013. The exact details of the investigation were never disclosed by the government or the company. However, former CEO Alex Lukianov previously stated that the subpoena was a very broad document request, "focused on interbody with regard to Quadrant and biologics, both Osteocel and FormaGraft, but it's very broad."

When a preliminary agreement between NuVasive and the government was announced in March, Wells Fargo analyst Larry Biegelsen said he believed the amount of the settlement was relatively immaterial, saves the expense and impact of a CIA on selling operations and makes it easier for the company to "participate in industry consolidation."

The government said NuVasive cooperated fully with the investigation and the new leadership team at NuVasive appears to have finally put this episode behind them. — *WE*

Photo creation by RRY Publications, LLC/ Logos courtesy of NuVasive, Inc. and U.S. Department of Justice

FDA User Fees Rise 4.2% for 2016

Starting October 1, 2015, your FDA user fees are going up by 4.2%. The FDA expects to collect a total of almost $130 million from industry over the course of fiscal 2016.

A notice by the FDA in the *Federal Register* on August 3, 2015 announced the fee rates and payment procedures for medical device user fees for fiscal year 2016. The rates will apply from October 1, 2015, through September 30, 2016. The 4.2% increase comes after a 2.9% fee cut in fiscal 2015. Fees climbed 4.2% in fiscal 2014.

For 510(k) clearances, the fee rises from $5,018 to $5,228. For premarket applications (PMAs), the fee goes from $250,895 to $261,385.

Small Business Break

There is a break for small businesses.

If your business has gross receipts or sales of no more than $100 million for the most recent tax year, you may qualify for reduced small business fees. If your business has gross sales or receipts of no more than $30 million, you may also qualify for a waiver of the fee for your first premarket application or premarket report.

Important Links

To pay the annual establishment fee, firms must access the Device Facility User Fee (DFUF) Web site at https://userfees.fda.gov/OA_HTML/furls.jsp.

To read the entire Federal Registry Notice, including payment levels and procedures, click here: https://www.federalregister.gov/articles/2015/08/03/2015-18907/medical-device-user-fee-rates-for-fiscal-year-2016#page-46036. — *WE*

Photo creation by RRY Publications, LLC / Logo courtesy of FDA

LARGE JOINTS

OrthAlign, Lima Corporate Sign Distribution Agreement

OrthAlign, Inc. has entered into a European distribution agreement with Lima Corporate for KneeAlign, its total knee arthroplasty (TKA) technology.

"As Lima embarked on building a best-in-class platform to provide surgeons with a complete range of solutions in TKA, we were convinced that OrthAlign's precision alignment technology should be included in our offering," said Luigi Ferrari, Lima Corporate's chief executive officer, in the August 6, 2015 news release.

As indicated in the news release, "In a published clinical study by Denis Nam, M.D. (Washington University in St. Louis), significant differences favoring the use of KneeAlign vs. CAS were found with regard to the accuracy of femoral component alignment, with 94.9% of patients in the KneeAlign cohort having an alignment within 2° of neutral vs. 92.5% in the CAS cohort. There was also a significant difference in overall mechanical alignment of the limb, with 92.5% of patients within 3° of neutral mechanical axis in the KneeAlign cohort vs. 86.3% in the CAS cohort."

"We are pleased to partner with Lima in further expanding our award-winning KneeAlign technology to surgeons and patients throughout the European continent," said William E. Maya, OrthAlign's chief executive officer. "There were approximately 540,000 TKAs in Europe during 2014 and this number will likely increase as the population ages, so this is a very important mar-

Logos courtesy of OrthAlign, Inc. and Lima Corporate

ket for us in our international growth strategy. Lima's forward-thinking vision in providing surgeons with a best-in-class platform of technologies resonated with us and we are honored to be a key part of the offering. Ultimately, we hope it helps to raise the standard of care throughout Europe for TKAs".

Luigi Ferrari told *OTW*, "As technology continues to advance in orthopedics, surgeons are now demanding a complete range of solutions for their TKAs. A Lima-OrthAlign partnership makes sense because surgeons throughout Europe will now have easy access to a world-class knee, combined with the most practical precision alignment tool in the marketplace, all from one single source. OrthAlign technology takes all of the gold standard benefits of computer assisted surgery systems and puts them in a handheld device, without all of the drawbacks that stunted CAS adoption. In confirming our decision to partner with OrthAlign, Lima surveyed a strong sample of European-based surgeons and the feedback received was very positive. We are looking forward to working together with OrthAlign in providing surgeons with best-in-class solutions."

William Maya told *OTW* "There were approximately 540,000 TKAs in Europe during 2014 and this number will continue to grow. However, as Europe faces increased price constraints, countered with increasing market demands for the latest in technology, products like OrthAlign will play an even more important role in raising the standard of care for TKAs. We hope that every surgeon and patient will be able to experience the enormous benefits of OrthAlign, seeing firsthand why it's already been used, worldwide, in over 35,000 cases." — *EH*

Transplant Successful for Most Young Patients With Damaged Menisci

According to a new study, the majority of patients younger than age 50 who had a torn or severely damaged meniscus experienced reduced pain and improved knee function following transplant surgery. The study, just published in the *Journal of Bone and Joint Surgery*, also found that many patients had to undergo another surgery within 10 years.

Findings include: 63% of meniscal transplants were viable at 10 years; 11% of patients with successful transplants had pain during daily activities; 72% were able to take part in low-impact sports. In patients who required additional surgery, the meniscal transplants lasted between 7 and 8 years after surgery.

Frank R. Noyes, M.D., lead study author and founder of the Noyes Knee Institute at the Cincinnati Sports Medicine & Orthopaedic Center, told *OTW*, "Meniscus transplantation has been performed at our center for over 25 years and all patients are entered into our prospective studies of this procedure. I believed it was important from the very beginning to follow patients for the first few years after surgery with serial MRI studies to determine if the operative procedure realized its initial goal, which was to achieve adequate fixation of the transplant (preventing extrusion) to allow healing. Then, with longer follow-up, the assessment of knee symptoms, activity levels, and tibiofemoral compartment joint space (with weight-bearing posteroanterior radiographs) is required to determine the procedure's impact on knee function. The final, 10+ year survivorship

Photo courtesy of Frank R. Noyes, M.D.

analysis allows the clinician to counsel patients on realistic long-term outcomes. I always understood and expressed to all patient candidates that the procedure is not curative, but that it may 'buy' several years before other operations may be required."

"Before the operation, 70% of the patients had moderate pain with daily activities. An average of 11 years had elapsed from the original injury to the meniscus transplant, during which time, this group of 38 patients had undergone a total of 139 operations. At the time of the transplant procedure, abnormal articular cartilage surfaces were found in the majority of knees, including subchondral bone exposure in 53% and extensive fissuring and fragmentation in 37%. Therefore, the level of pain was not surprising."

Asked which patients would not be candidates for this procedure, Dr. Noyes noted, "Contraindications for this operation include advanced knee joint arthritis with flattening of the femoral condyle, concavity of the tibial plateau, and osteophytes that prevent anatomic seating of the transplant. Patients with untreated lower limb axial malalignment (varus or valgus) who are not willing to undergo a corrective osteotomy, and patients with anterior cruciate ligament deficiency who are not willing to undergo a reconstruction are not candidates. Other contraindications include pre-existing knee arthrofibrosis, significant lower limb muscular atrophy, and a history of prior joint infection with subsequent arthritis. Symptom-

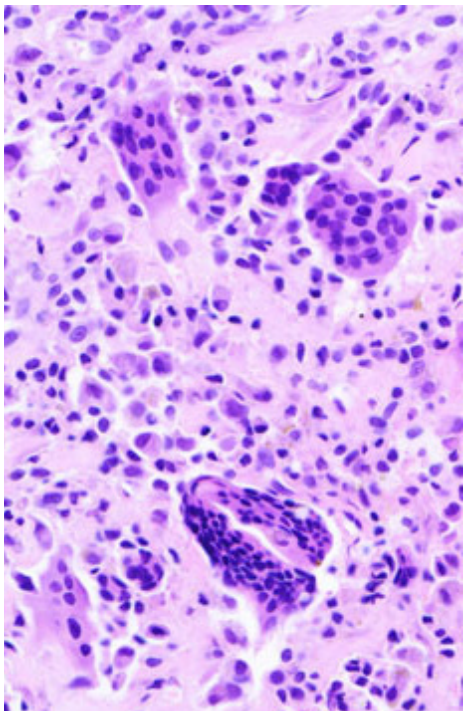
atic noteworthy patellofemoral articular cartilage deterioration (subchondral bone exposure) and obesity (body mass index > 30) are also contraindications. Finally, prophylactic meniscus transplantation following total meniscectomy is not recommended in asymptomatic patients who do not have articular cartilage deterioration."

"The goals of meniscal transplantation are to restore partial load-bearing meniscus function, decrease symptoms, and provide some chondroprotective effects. However, it is important to note that the procedure continues to evolve, as investigations of tissue-processing, secondary sterilization, and long-term function evaluate its effectiveness. Unfortunately, many investigations report that most transplants gradually deteriorate, tear, extrude from their normal position, or shrink in size, thereby loosing the ability to provide function. Accordingly, the goal is to provide short-term benefits until a more suitable meniscus transplant is clinically available. At best, the transplant provides only partial function, and therefore, strenuous sports and high-impact activities are not advised postoperatively. Education of the patient and family is required so that all understand and accept the current limitations of the procedure. Importantly, I have promoted for many years repair of meniscus tears that extend into the central third region, including double-longitudinal, triple-longitudinal, radial, and flap tears that are too often removed. Preservation of meniscal tissue through repair is preferred over transplantation whenever possible." — *EH*

EXTREMITIES

Study: CSF-1R Inhibitor Induced Tumor Regressions

An investigational drug for a rare orthopedic tumor is showing promise, says a new study in *The New England Journal of Medicine* (*NEJM*). According to this research, PLX3397, an oral targeted CSF-1R inhibitor, led to prolonged tumor regressions in most patients with tenosynovial giant cell tumor (TGCT), a disease that affects the joint or tendon sheath. The research was performed at Memorial Sloan Kettering Cancer Center.


Histopathology of giant cell tumor of the tendon sheath arising in hand finger / Source: Wikimedia Commons and KGH

"TGCT can be a very difficult disease to manage, with treatment options largely limited to surgery to remove as much of the tumor as possible.

Despite the best surgical intervention, recurrence of diffuse TGCT is high and the disease may advance to the point where surgery is no longer an option," said William D. Tap, M.D., lead author of the study and chief of the Sarcoma Medical Oncology Service at Memorial Sloan Kettering Cancer Center, in the July 29, 2015 news release. "These preliminary results demonstrate that by targeting CSF-1R, PLX3397 may inhibit tumor growth in some patients with TGCT, potentially offering those patients an alternative non-surgical treatment option."

Dr. Tap told *OTW,* "I was surprised to find how dramatically the drug helped patients. The results of the Phase I trial are opening up the door for a huge research collaboration surrounding TGCT. There are still numerous questions regarding the use of the drug and how to best serve this patient population. There is also a new basic science component to this work that is trying to better understand TGCT, why it develops and how to prevent it. One amazing aspect of this project is the close collaborative effort between multiple medical disciplines, especially medical and orthopedic oncology."

John H. Healey, M.D., chief of Memorial Sloan Kettering's Orthopaedic Service, told *OTW*, "PLX 3397 is transforming the way we approach what has been a very discouraging disease where we had limited treatment options, and surgery had an unacceptably high recurrence rate. Rapid dramatic responses were commonly seen, and any necessary surgery was less extensive. This drug gives new hope to patients and their doctors."

Daiichi Sankyo, Inc. Plexxikon, members of the Daiichi Sankyo Group, are the developers of PLX3397. — *EH*

SPORTS MEDICINE

Startups Test Freezing Therapy

Can freezing the body—making it very, very cold for a short period of time—promote healing? It may not be surprising that Minneapolis, Minnesota, where enthusiasts jump into lakes through holes in the ice, is the home of a trend called: "whole-body cryotherapy." Though the treatment has advocates, Ben Bartenstein, a writer for *Pioneer Press Health* called it "more commercial than charitable."

The therapy dates back to the 1800s in Japan. In 1978, Dr. Toshima Yamauchi created a whole-body cryosauna which a Polish company developed into a commercial product. It became popular in Poland where doctors believed that the cryosauna relieved pain and boosted the performance of Olympic athletes.

Brandon Johnson, a former pro-basketball player, is the owner of The Locker, a cryotherapy spa in Minneapolis. He acquired his equipment from Juka, a Polish company that sells the machine to health clubs. Johnson told Bartenstein, "The biggest thing is its natural. It forces the body into a healing state that you cannot go into in any other place without a downside."

Many in the medical community say the therapy's purported health benefits are inconclusive. Polish researchers have suggested that whole-body cryotherapy could be useful as a short-term treatment for anxiety disorders and a French team found the therapy to be effective in reducing muscle inflammation.

A well-known supporter of the treatment is famed sports medicine doctor James Andrews, M.D., who operated on Michael Jordan, Brett Favre and Adrian Peterson. Andrews is presently chairman of an Atlanta-based cryotherapy startup and plans to research the efficacy of cryosaunas compared with traditional rehab. — *BY*

Wikimedia Commons and Dori

Could Simple Protein Reduce Head Injuries?

Potential good news for football players comes from researchers at Harvard Medical School who have found a link between head trauma and the development of the degenerative brain condition called chronic traumatic encephalopathy (CTE). The finding leads to the hope that players who might develop CTE can be identified and helped before cognitive issues arise.

Funded by the National Institutes of Health, the Alzheimer's Association and the NFL Players Association, the study identified an abnormal protein that appears in the brains of mice shortly after they experience head trauma. That protein proved to be a precursor to neurofibrillary tangles which are clumps of tau protein found in the brains of deceased patients with CTE.

Not all football players get CTE. Researchers believe that the new protein might be a start in sorting out which players may be more susceptible to the ailment. At present these neurofibrillary tangles can only be found after an athlete dies.

David Geier, M.D., who wrote about the discovery for the *Post & Courier,* reports that lead researcher Kun Ping Lu, M.D., Ph.D. and his team have created antibodies to the protein. They gave those antibodies to half of their experimental traumatized mice and gave none to the other half.

They found that the mice who suffered the brain trauma but were not given antibodies showed progressive risk-taking behaviors, similar to that of athletes who have advanced-stage CTE. The mice that received the antibodies did not develop that abnormal behavior.

According Geier, Lu and his team plan to make a form of the antibody for humans. Football players, who test positive for that protein after a head injury, could take that medication and possibly prevent brain damage.

Geier warned about getting hopes too high too soon. He wrote, "Maybe a medication based on tau antibodies will prove to be a breakthrough for future football players, and maybe it won't. It has at least given football a glimpse of hope." — *BY*

Wikimedia Commons and Thivierr

PEOPLE

Catherine H. MacLean, M.D., Ph.D.: HSS' First-Ever Chief Value Medical Officer

Hospital for Special Surgery (HSS) is appointing its first-ever Chief Value Medical Officer, acclaimed specialist in healthcare quality measurement and improvement, Catherine H. MacLean, M.D., Ph.D.

Hospital for Special Surgery

Dr. MacLean will be co-leading the Value Management Office, an established group focused on improving the way HSS defines, measures, and achieves value. Dr. MacLean will also help lead efforts to improve external quality transparency, giving consumers and other key stakeholders the information they need to make informed care decisions.

Dr. MacLean, a rheumatologist, earned a Bachelor of Science in Pharmacology from University of California; a Medical Degree from Washington University

School of Medicine; and a Doctorate in Health Services from UCLA School of Public Health. Prior to joining HSS, she served as the staff vice president at WellPoint's Center for Quality Measures and Improvement.

Dr. MacLean told *OTW*, "First of all, I will work with the experts at HSS and engage with the broader orthopedic community to concretely define how to best measure 'value' in terms of both quality and cost. A key part of this work will be to define the outcomes that matter to our patients and then work backwards to ensure the care processes needed to achieve these outcomes are executed in the most effective and efficient way."

Asked what initiatives she would like to put in place in order to increase external quality transparency, Dr. MacLean added, "Transparency should extend, in its next phase, beyond the current public measures to measuring the outcomes that matter most to patients and communicating these in a way that patients can understand for decision-making. I would like to see the collection and reporting of these measures incorporated into clinical practice and reported to each of our patients, the same way we would share lab results, so that our patients know how well we did for them in terms of achieving those outcomes. The next step would be to make available to current and prospective patients, policymakers and payers, reports on how we do on a population basis. We are exploring the best way to communicate this information and look forward to working with others to develop normative standards and methods to report quality in a manner that is valid, fair and reliable." — *EH*

Orthopedics This Week I RRY Publications LLC

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

Sophie Bodek
Writer
sophiebodek@yahoo.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