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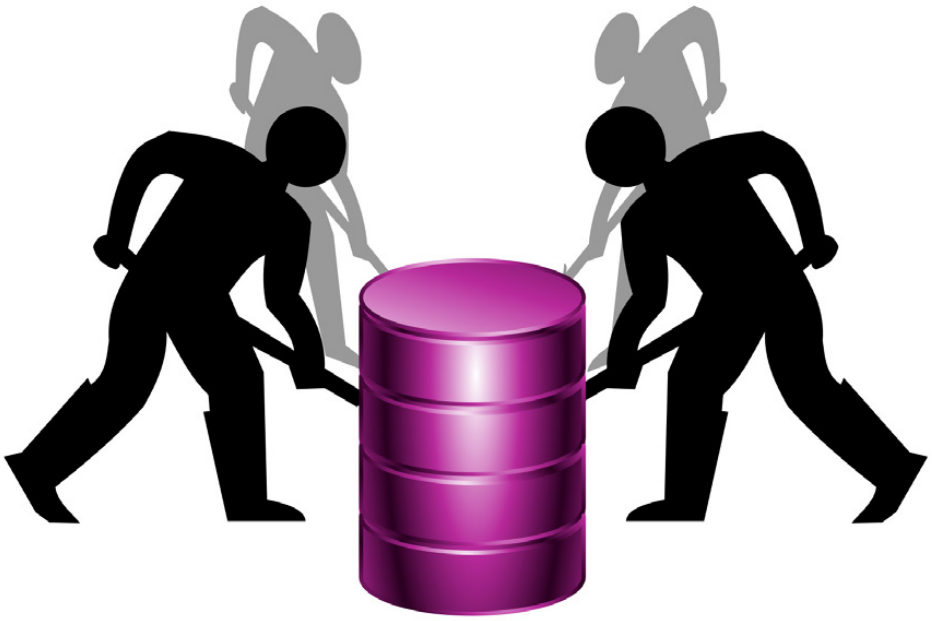
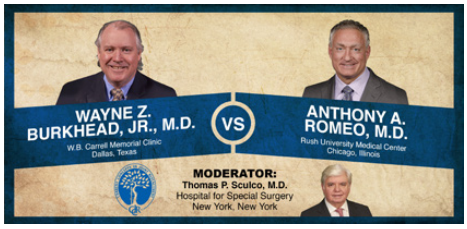
Orthopedics This Week

WEEK IN REVIEW





BREAKING NEWS

For all news that is ortho, read on.

Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

THIS WEEK: DePuy Synthes did not wow investors with their mid-year sales report. Focusing only on operational results (ignore those pesky currency swings) the largest orthopedic company in the world increased its business by just 0.9% year-over-year. While hip and knee implant sales rose nicely, trauma and spine need work.

RANK	LAST WEEK	COMPANY	TTM OP MARGIN	30-DAY PRICE CHANGE	COMMENT
1	1	Stryker	22.78%	3.27%	Acquires a leading supplier of hospital beds, stretchers, etc. in Turkey, Latin America and other corners of the Globe.
2	2	ConMed	10.41	5.48	Institutional buyers keep buying ConMed. This has been one of the most consistently rising equities in ortho. And it is still comparatively cheap.
3	3	Integra LifeSciences	13.74	4.49	Wrapped up its acquisition of TEI Biosciences. Should accelerate IART's entry into diabetic foot ulcer market.
4	5	Smith & Nephew	20.19	5.89	A surge of new buying came into SNN last week. One possible cause was the upgrade from Berenberg.
5	6	Zimmer Biomet	30.35	5.82	EPS estimates for Zimmer Biomet rose from $6.34 per share to $6.69 in the last month. Valuation-wise, ZBH is second least expensive equity in ortho.
6	8	Medtronic	27.92	1.59	MDT buys company which tracks surgical items. Like surgical sponges. So no unwanted items left in patients. This is the new face of innovation.
7	4	Johnson & Johnson	28.44	1.37	Analysts are focusing on sales growth rates (or lack thereof). But hip and knee numbers were decent and the second half should be stronger.
8	7	RTI Biologics	7.50	(2.14)	Most buyers waiting for Q2 report. We note, however, that RTI has beat estimates each of the last four quarters.
9	9	Globus Medical	30.87	5.04	Second quarter results due July 30. Consensus of analysts is that Globus will report an 11-12% rate of sales growth.
10	NR	Exactech	10.44	1.49	Fourth best value in orthopedics. Generating $250 million in annual sales, EXAC is the smallest of the diversified ortho companies.

Robin Young's Orthopedic Universe

TOP PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	MiMedx Group	MDXG	$12.97	$1,409	24.23%
2	Smith & Nephew	SNN	$35.93	$16,069	5.89%
3	ConMed	CNMD	$60.02	$1,656	5.48%
4	CryoLife	CRY	$11.68	$331	5.42%
5	Globus Medical	GMED	$26.87	$2,550	5.04%
6	Integra LifeSciences	IART	$63.12	$2,079	4.49%
7	TiGenix	TIG.BR	$0.83	$133	3.30%
8	Stryker	SYK	$98.21	$37,164	3.27%
9	LDR Holding Corp.	LDRH	$45.50	$1,209	2.41%
10	Medtronic	MDT	$76.91	$108,932	1.59%

WORST PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	Aurora Spine	ASG	$0.41	$8	-40.88%
2	MicroPort Scientific	853	$0.43	$614	-13.89%
3	Zimmer Biomet	ZBH	$107.50	$21,852	-4.44%
4	RTI Biologics Inc	RTIX	$6.40	$367	-2.14%
5	Tornier N.V.	TRNX	$25.81	$1,265	-0.96%
6	Wright Medical	WMGI	$26.72	$1,373	-0.71%
7	Alphatec Holdings	ATEC	$1.41	$141	-0.70%
8	Orthofix	OFIX	$33.37	$626	-0.36%
9	K2M Group Holdings	KTWO	$24.17	$975	-0.29%
10	Bacterin Intl Holdings	BONE	$3.35	$24	0.00%

LOWEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Johnson & Johnson	JNJ	$100.08	$277,526	17.01
2	Exactech	EXAC	$21.18	$296	18.26
3	Zimmer Biomet	ZBH	$107.50	$21,852	18.48
4	Globus Medical	GMED	$26.87	$2,550	19.88
5	Stryker	SYK	$98.21	$37,164	22.44

HIGHEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	MiMedx Group	MDXG	$12.97	$1,409	129.70
2	NuVasive	NUVA	$49.48	$2,393	102.05
3	CryoLife	CRY	$11.68	$331	62.17
4	RTI Biologics Inc	RTIX	$6.40	$367	41.89
5	ConMed	CNMD	$60.02	$1,656	32.44

LOWEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Globus Medical	GMED	$26.87	$2,550	1.63
2	Zimmer Biomet	ZBH	$107.50	$21,852	1.85
3	Exactech	EXAC	$21.18	$296	2.05
4	CryoLife	CRY	$11.68	$331	2.07
5	ConMed	CNMD	$60.02	$1,656	2.28

HIGHEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	MiMedx Group	MDXG	$12.97	$1,409	8.65
2	NuVasive	NUVA	$49.48	$2,393	6.68
3	Smith & Nephew	SNN	$35.93	$16,069	5.01
4	Medtronic	MDT	$76.91	$108,932	3.49
5	Johnson & Johnson	JNJ	$100.08	$277,526	3.30

LOWEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	Bacterin Intl Holdings	BONE	$3.35	$24	0.66
2	Alphatec Holdings	ATEC	$1.41	$141	0.68
3	Exactech	EXAC	$21.18	$296	1.20
4	RTI Biologics Inc	RTIX	$6.40	$367	1.36
5	Orthofix	OFIX	$33.37	$626	1.60

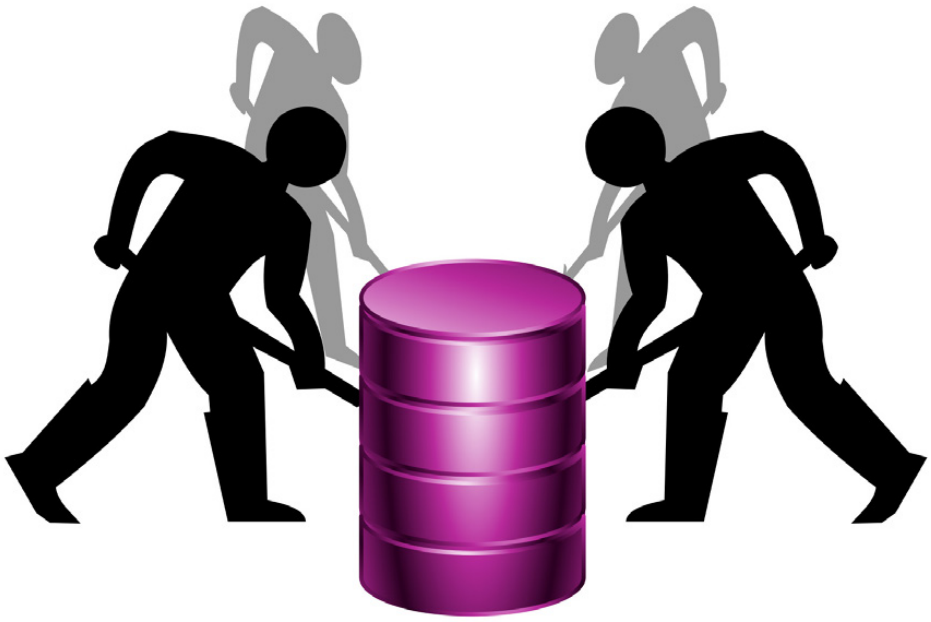
HIGHEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	TiGenix	TIG.BR	$0.83	$133	15.88
2	MiMedx Group	MDXG	$12.97	$1,409	10.10
3	LDR Holding Corp.	LDRH	$45.50	$1,209	8.10
4	Medtronic	MDT	$76.91	$108,932	5.38
5	Globus Medical	GMED	$26.87	$2,550	5.19

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

The Clinical Study Disconnect

BY ROBIN YOUNG



Wikimedia Commons and Arbeck

Two new studies caught our attention last week:

1. A May 2015 poster from the OARSI (Osteoarthritis Research Society International) annual meeting in Seattle says that the time between diagnosis of knee osteoarthritis (OA) and total knee replacement (TKR) is, on average, 114 days IF there are no intervening treatments like HA (hyaluronic acid) injections. When there is a single HA course of treatment the time to surgery extends 238% to 386 days. Two courses of HA treatment stretches the time to TKR to 648 days. And so forth. One interpretation of this data would be that HA injections work. Another, also valid interpretation is that ANY intervention of even minimal clinical efficacy would also extend the time to TKR.

Why aren't the payers all over this study?

2. And then this March 2015 study from the *International Journal of Spine Surgery* compared surgical to non-surgical treatment for chronic sacroiliac joint pain. The Level 1 study randomized 148 patients with SI joint dysfunction and very high pain scores to either SI fusion with an implant or to non-surgical treatments (steroid shots and the like). Turns out, says the study, surgery to stabilize the SI joint reduced pain from 82.3 (VAS Pain Reduction, SF-36 and EQ-5D) to 29.8 at six months versus from 82.2 to 70.4 for the same period for the non-surgical approach.

Did the payer's notice?

Payers, it is probably fair to say, do not regard clinical studies the same way as physicians.

Accepting the flaws inherent in clinical studies generally—sponsored or not—protocol-driven, Institutional Review Board (IRB) controlled testing of products or procedures on human patients—i.e., clinical studies—remain the most reliable source of information that physicians, nurses and other healthcare providers use to inform their daily practice and improve quality of care.

Right?

Well. Payers may disagree. In fact, payers seem to think that physicians (and providers in general) don't understand clinical data as well as they do.

Really.

Payers and Providers: Two Ships Passing in the Night?

We noted with interest a recent article published on the Healthcare Information and Management Systems Society (HIMSS) website which made the point that payers were more adept at analyzing "clinical data" than hospitals or clinics.

What the author (and this is endemic in all payer discussion of "clinical data")

meant was claims data mining. That, in their lexicon, is "clinical data." And that data does, indeed, provide a lot of information about outcomes, cost of care, post-operative complications, pain medicine usage and so forth.

In other words, in the payer's world, "clinical data" refers to data that arises from a clinical interaction with patients. "Clinical data" in the payer's world is not like clinical data in the surgeon's world.

Payer clinical data is about analyzing clinical costs and differences between surgeons, hospitals or clinics.

According to a 2011 HIMSS Analytics (Chicago) whitepaper study of payers' and providers' use of clinical data (sponsored by the San Diego, California-based Anvita Health) the main purpose of clinical data analytics was to frame clinical claims data within the context of meaningful use.

And here, said Marc Holland, vice president of market research at HIMSS Analytics, payers are more sophisticated in how they use clinical data than providers are.

As quoted on the HIMSS website, "[Payers] have a vested interest in insuring that the care is delivered with a minimum of cost and a maximum of quality. I think providers [physicians and hospitals] are not necessarily ignoring that, but haven't had the data to do that effectively as the payers have. The payers have a leg up and a lead on the providers, but that gap is closing."

Correlation vs. Causation

Data mining is about uncovering correlations between what appear to be independent variables. Conducting a clinical study is about uncovering the causes of an outcome by controlling variables.

Payer data mining is correlative. Protocol-driven, IRB controlled studies try to debunk correlations in the service of medical knowledge. Ideally anyway.

And therein lies the greatest source of frustration with payer reimbursement decisions.

Correlation versus causation.

PearlDiver Technologies, Inc.'s "Zombie Study" illustrates this problem well.

The data guys at PearlDiver have a study which they perform for clients called the "Zombie Study."

When you see it, it is impressive. Even a little disturbing.

PearlDiver has about 4 billion patient records from the payers—Medicare, Humana, UnitedHealthcare and so forth.

PearlDiver's data and the software program that drives it is the kind of data mining Marc Holland is referring to. Companies use PearlDiver data to do cost of care studies and market studies right down to the hospital level. Since PearlDiver's data can go back up to 10 years, it also offers data for terrific longitudinal studies. Like the Zombie study.

A couple years ago the data guys at PearlDiver looked up the code for deaths in a hospital. Yes, there is a code for that. They then asked a simple question: did any of these "dead" patients ever return for a new procedure? Like three months after they "died"?

And the answer is, of course, "yes." Turns out literally hundreds of thousands of patients are declared "dead" per the Medicare rolls yet somehow return for more treatment.

We're talking hip and knee replacements, dialysis treatments, chronic wound care and so forth

Hence the name "Zombie Study."

There are many reasons to explain such an illogical outcome—coding error, fraud and, of course, the preferred explanation—Zombies!

But this illustrates the point that claims data can only describe correlations—not causes. So there is a danger of false positives. Only protocol-driven, IRB controlled, honest-to-God in-clinic studies can debunk correlations.

Then, if, as part of a protocol-driven, IRB controlled study a "dead" patient returns for a hip replacement then we can honestly say that Zombies exist.

For more information about the Zombie study and other uses for PearlDiver's massive data, email Scott at scott@pearldiverinc.com

The Rooster Crows for Data

The classic illustration of the dangers of relying on correlational data is the one about the Rooster crowing. The fact that the Rooster crows at dawn does not mean that the Rooster causes the sun to rise. The two actions simply correlate.

What if there was a way to connect data mining techniques with protocol-driven clinical studies?

Several large integrated health systems like Oakland, California-based Kaiser Permanente or the Intermountain Healthcare in Salt Lake City, Utah, are thinking creatively about this very subject. These systems are, in effect, payers who own hospitals.

Integrated systems like this can't shift patient risk to the payer or the provider since they are both. So, they should be in an excellent position to combine clinical and claims data for population health analytics.

But so far it's more promise than actuality.

Says Keith Figlioli, senior vice president of healthcare informatics for the Charlotte, North Carolina-based Premier Healthcare Alliance on the HIMSS website, "The data the payers have is a mile wide but an inch deep."

The Fitbit Link

But maybe there is a way to link protocol-driven patient data with data mining techniques.

According to data from the HIMSS Analytics database, only 30% of U.S. hospitals presently use a clinical data warehouse/mining techniques.

There are several reasons for this:

1. Professionally and scientifically, physicians are tuned into protocol-driven clinical studies, not data mining and therefore correlational data.
2. Putting data, which can be anything from clinical notes to manually entered data, into the system is cumbersome and error prone.
3. Mapping the data. This is hard to do.
4. Errors or incomplete data.
5. Different databases.
6. And then translating the data into information useful both at the clinic level and at the payer level.

Into this world is coming the Internet of things.

Like Fitbit, the Apple watch, and the recent Spine Technology Award winner, Smart Strap.

The Internet of things refers to the ability of wearable sensors to collect real time patient data and send that over the Internet to other smart devices or "things."

Here's an illustration.

Instead of requiring patients to return at 30-days, 60-days, 90-days or whenever as part of a protocol-driven study, attach a wearable sensor which would collect the data constantly, real time and send it over the Internet.

That would pull traditional clinical studies into a data mining future. It

would create the opportunity for near universal post-market studies.

Another example is illustrated by the award winning Smart Strap from 109 Design. Smart Strap is a wearable strap that replaces the existing straps of a scoliosis back brace. These straps contain sensors and wireless communication ability.

As most parents and physicians of adolescents with scoliosis know, compliance, defined as the brace wear time, is a big issue. Researchers who've studied this report that increased compliance leads to better outcomes, in other words lower curve progressions.

The Smart Strap is like a Fitbit for scoliosis patients. It communicates with a smartphone app and sends data to the app via the Internet. It compares actual brace time and tightness to the doctor's prescriptions.

Parents, patients and doctors can see the data by using that app. Doctors, of course, can use the information to fine tune the treatment prescriptions in real time.

Wearable sensors now track all kinds of activities, blood pressure, heart rate, body temperature as well as data related to diet and psychology. And inventors are now linking this data stream to such diseases as spine deformities, joint osteoarthritis, heart diseases, non-small cell lung cancer, diabetes, obesity and various mental health disorders.

Data: a New Four Letter Word

The data disconnect between payers and providers is a big deal. And a payer's overreliance on correlation based decision models clearly has the potential to hurt patient quality of care. Data in this context is rapidly becoming a pejorative.

The Internet of things phenomenon, however, could transform clinical data collection in ways that would bridge the gaps between payers and providers.

The key will be how quickly protocol-driven studies incorporate these innovations in data collection and allow for both data mining and data sharing. ♦

DePuy Synthes: From Storm to Norm

BY WALTER EISNER

The echoes of the integration storm at DePuy Synthes were still evident in the mid-2015 sales and earnings report BUT it also clear that the company has begun to settle in and settle down into a period of routine business operations.

From Storm to Norm

Merging two large, global organizations into the largest orthopedic company the in the world is a monumental effort. By definition it is disruptive. By definition people will be let go, projects will end, new assignments will be off-base. While integration may we well planned, it can feel a bit like a mash-up. And by definition – there will be surprises (the most recent one that comes to mind is the Orsinger resignation from a few weeks ago).

To get to a stage where DePuy Synthes can start to perform again – it needs to settle in and settle down. It needs to get to normal.

With this quarter's report, DePuy Synthes appears to be there (although spine and trauma need more work).

Second quarter sales of $2.33 billion were up 0.9% from the same quarter in 2014. Because the company sells so many products overseas, currency translation dropped reported revenue down to minus 5.6%.

Operational sales change (before currency effects) for knee, hip, trauma and spine products were +4%, +2%, -1% and -1%, respectively.

Wikimedia Commons and Leo Za1

From Norm to Perform

Johnson & Johnson (DePuy Synthes' parent) CEO Alex Gorsky told analysts on July 14, 2015, that while the spine and trauma businesses have lagged market growth to date, he is "absolutely committed to turning them around. We have new products launching this year that will help us do just that."

For example, he cited the recent launch of the transfemoral nail in trauma which he thinks will be an "important addition to the bags of the portfolio of that part of the business. In the U.S., we were encouraged by the performance that we saw in knees and hips at 5% and 4% growth, respectively, for the quarter."

DePuySynthes 2Q2015	Sales ($ in millions)	% Change
Total Reported Sales	**$2,330**	**+0.9%**
Knees		+4.0%
Hips		+2.0%
Spine		-1.0%
Trauma		-1.0%

Source: Johnson & Johnson

"Accelerating Growth"

He also said "accelerating growth" will happen due to a productive research and development program. More than half of 30 major FDA filings previously announced have already been filed and their partnership with Google to revolutionize the operating room and the future with robotic surgical tools will help surgeons with precision, reduce patient trauma and reduce costs.

Pricing and Utilization

Gorsky also addressed the issue of device pricing and utilization. He said ongoing consolidation among health systems and within the insurance industry is continuing to create pressure on pricing. He said he's been encouraged by data showing that healthcare utilization trends in

the U.S. have continued to improve for the fourth consecutive quarter with growth in both hospital admissions and hospital surgical procedures. "We remain optimistic about increased global healthcare utilization as well."

New Leadership at DePuy Synthes

While not mentioning former President Michel Orsinger by name or the disruptive integration with Synthes, Gorsky noted the recently integrated J&J's global orthopedics and global surgery businesses under Gary Pruden, "will enable us to have a much more holistic approach to the way we do business." Pruden was promised to analysts for the third quarter call in October to describe his new approach to partnering with hospitals to improve outcomes.

But analysts wanted to know more and prodded Gorsky to talk about the Synthes acquisition.

"Look, overall, we absolutely believe it was the right move to bring Synthes in and create the largest and most diversified orthopaedics company. When we reflect back, there had been changes that had taken place in the market. One is, just the market growth across all these segments. If you remember back in 2008, 2009, 2010, we saw high single-digit growth really for hips, knees, trauma, as well as spine. That has changed significantly. We're now seeing that in the 3% to 4% range. I am pleased with the performance overall that we've seen through the integration."

He added that there are always a lot of moving pieces when two big organizations merge. "If you take a look at the overall disruption and the way that we've been able to manage it, I think the team has done a very good job. Now we're really focused on what do we do to ensure that we're best positioned for the future. Frankly, we're doing it at a time when a lot of our competitors are just getting ready to go through a significant amount of integration and transition."

Analysts Forecast

While the second quarter's operational growth was a nearly flat at just a 0.9% rate of year-over-year growth, most analysts are forecasting faster sales growth rates for the second half of this year. Now that DePuy Synthes' organization appears to be settling in and settling down, the base is in place to move from the storm of integration to the norm of day-to-day customer service to performing with better value propositions for patients, doctors and hospitals. ♦

Golfers Play Better After Spine Fusion // Arthroscopy Safe, Effective for MDI of the Shoulder // Emerging Leader in Spine Research is…ISSG!

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

Golfers Play Same or BETTER After Spinal Fusion While you won't want to undergo surgery just to improve your golf swing, new research from Midwest Orthopaedics at Rush (MOR) has filled a void in the golf-related spine literature. Dr. Frank Phillips, Section Head of Minimally Invasive Spine Surgery and Professor of Orthopaedic Surgery at Rush, tells *OTW* about the first study examining outcomes of lumbar fusion in golfers. "There is no data in the literature that discusses golf and spine fusion surgery; there is no clinical data at all regarding return to play. And yet patients commonly ask their surgeon, 'When am I going to be back on the golf course?'

Wikimedia Commons and Philippe Guérindon

"My colleagues and I examined data from one and two-level lumbar fusions I performed over a two year period. Our goals were to determine the ability of golfers to return to play and to find out what factors might predict their return to golf. Patients completed questionnaires asking if they had played golf before or after surgery, and inquiring about the factors that led them to decide to undergo the procedure, what limited them in terms of swing before surgery, when they returned to practice, etc."

"A full 75% of golfers will be able to play the same amount or more following fusion surgery. Within a year after surgery, 65% of patients had returned to practice and 52% had resumed on course play. Of those who did not return to the sport, 31% attributed it to ongoing back or leg pain. Pre-operatively, 80% of participants said that lumbar pain affected them while playing golf; 50% said that their inability to play golf was a reason they considered surgery."

"We found that 80% of golfers maintained or *improved* their handicap postoperatively. After surgery, 50% of golfers stated their distance was negatively affected; 23% indicated that their consistency decreased; only 9% said that their accuracy diminished. It is great to have this data because much of the public believes that if you have a lumbar fusion then you will not be able to move well or have the same swing as you did before surgery."

"The real question for me is, 'How minimally invasive spine (MIS) fusion will affect these outcomes?' At this point, 95% of my one- and two-level fusion surgeries are MIS. I plan to undertake a prospective study to study how quickly and effectively golfers return to play after MIS fusion surgery. My suspicion is that the reduced collateral tissue damage with MIS surgery would expedite return to golf.

Multidirectional Instability of the Shoulder: OK to Consider Surgery Peter J. Millett, M.D., M.Sc., director of Shoulder Surgery at The Steadman Clinic in Vail, Colorado, was seeing an influx of athletes who had developed multidirectional instability (MDI) of the shoulder. Recognizing the need to find options for patients, Dr. Millett and his research team got to work. He told

OTW, "This is a relatively uncommon condition but it is quite debilitating. Modern arthroscopic techniques give us an advantage over older open surgical techniques in that we can address the static stabilizers in both the front and back of the shoulder, the top of the shoulder, and in the rotator interval region all with a minimally-invasive approach."

"In our study, using arthroscopic surgery for (MDI) showed excellent results with low revision rates and improved patient-derived outcome scores. Modern surgical techniques that use minimally-invasive arthroscopic surgery result in better outcomes than non-surgical treatment and older surgical treatments. Improvement in outcomes was more predictable and more reliable for those who had a traumatic onset to their instability as opposed to an atraumatic onset, but those with an atraumatic onset (i.e., no injury—just occurred) still had significant improvement from surgery. In addition, return to play was high in all subjects but was more likely in athletes whose MDI was traumatic in onset versus atraumatic in onset.

"While the first-line treatment of MDI is typically non-operative with a course of supervised physical therapy, sometimes this is unsuccessful and patients remain disabled from their shoulder instability. From this study, we now know that arthroscopic surgery can be an effective and safe treatment method for these patients, decreasing pain, restoring function, and getting them back to sports and other important activities of life."

"We were surprised by the efficacy of the procedure and the reliability of the results. We expected those with an atraumatic onset to do a little worse and that is what the data showed, although the vast majority still had very significant functional improvements."

Asked about the challenges involved with the study, Dr. Millett told *OTW*, "Getting a pure group to study. We see many patients with complex instability problems but most have other confounding variables such as prior surgery or different type of instability patterns. So getting a 'pure' group of patients with MDI, with strict inclusion criteria and minimum of two years' follow up, with high enough numbers to actually study, and only including subjects who had not had prior surgery was challenging."

"From this study we have learned that surgery for MDI of the shoulder, which historically has been more difficult to treat, is safe and effective when performed using modern arthroscopic techniques. We hope that in the near future with better patient selection and continued improvements in surgical techniques that we can get even better outcomes and shorten recovery times further for athletes and other patients who suffer from multidirectional instability of the shoulder."

"I would like to acknowledge the other members of the research team: M. Brett

Raynor, M.D., Marilee Horan, Susan Sabido, and Kristin Mapstone."

ISSG: The Growing Leader in Spine Research With 14 sites in the U.S. and roughly 90 projects per year, the International Spine Study Group (ISSG) is doing much to advance the treatment of spinal deformity. Shay Bess, M.D. is an orthopedic surgeon with Rocky Mountain Scoliosis and Spine and president of the ISSG foundation, a multicenter nonprofit research foundation. He told *OTW*, "We focus on conducting multicenter research on outcomes and methodologies to improve surgical care, non-operative treatment, and the evaluation of patients with adult spinal deformities. And while we are proud of the 580 abstracts presented since 2007, what has made our group exceptional is the tremendous camaraderie that allows for productive research synergies. I am continually impressed with not only how smart our members are, but how willing they are to share knowledge and collaborate on projects."

"We are seeing a gradual shift in terms of integrating what we learn in the research arena. Instead of focusing solely on generating research, we want to know how practice patterns are changing. We are examining specific deformities and tracking how current treatments differ from what was being done five years ago. And while there are always surgeon-related factors as to how patients are treated, we want to discover how our research influences patient treatment to maximize our impact and improve outcomes."

"For example, we are meticulous about tracking complications and proximal junctional kyphosis (PJK) is a common, and potentially devastating post-operative complication. Our research on PJK has led us to discover that patients don't need quite as much correction in the sagittal plane as was previously thought. Actually, each patient needs individualized correction based on age, bone quality, and physiology. We are learning that if the patient is rather frail then they will not tolerate much correction and the risk benefit ratio resides on the side of great risk with limited benefit beyond a certain amount of correction. In the past we 'aimed high,' but often the patient could not maintain the correction. You must have a balance between what is 'optimal alignment' and what is tolerable for the patient."

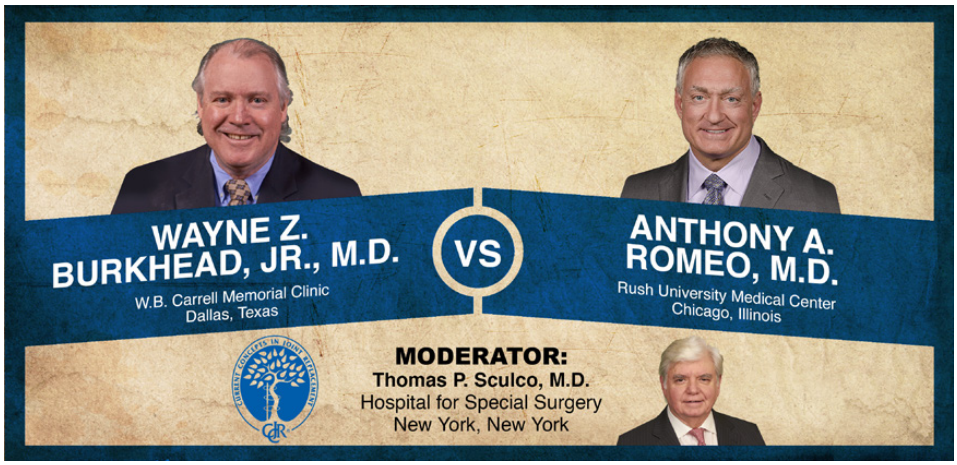
"The ISSG is also improving upon the collection of health-related quality of life measures by asking increasingly smarter questions. We are working to integrate patient evaluation metrics that are interactive, such as computer adaptive testing to increase accuracy. Our goal is to discover how to better capture patient desires and patient reported outcomes. We are also investigating how we can partner with other research entities to develop predictive algorithms to determine which patients will have good outcomes."

"We want to not only provide parameters to guide treatment, but also develop metrics that most accurately evaluate patients. A patient comes to a physician with the primary reason of why he or she is in pain; much of our research on causes of pain in adult spinal deformity has helped physicians provide answers for patients as to why they are likely in pain. We hope to continue to provide resources to health care providers and researcher to improve the evaluation and outcomes for patients with adult spinal deformity." ◆

Burkhead vs. Romeo Over Hill-Sachs Lesion for Shoulder Repair

BY OTW STAFF

Says Wayne Burkhead, M.D.: "Why consider arthroplasty for large Hill-Sachs lesions? I don't do surface replacements that often, but when I do, I do them for Hill-Sachs lesions." Au contraire, argues Anthony Romeo, M.D.: "The Hill-Sachs lesion is a lesion that occurs with instability and to jump right to some sort of surface replacement seems to be overaggressive even in individuals that have a large Hill-Sachs lesion." Despite Buz's bad cold, this was a spirited strong debate. We hope you enjoy it as much as we did.



Current Concepts in Joint Replacement/RRY Photo Creation

This week's Orthopaedic Crossfire® debate was part of the 16th Annual CCJR – Spring meeting, which took place in Las Vegas this past May. This week's topic is "A Hill-Sachs Lesion: It Is Best Treated With a Surface Replacement." For the proposition is Wayne Z. Burkhead, Jr., M.D., of the W.B. Carrell Memorial Clinic in Dallas, Texas. Anthony A. Romeo, M.D. of Rush University Medical Center is in opposition. Moderating is Thomas P. Sculco, M.D., from the Hospital for Special Surgery.

Dr. Burkhead: My first disclosure… I've never lost a debate here at CCJR. My second disclosure is I have a pretty bad cold right now. I'm feeling a little bit weak and I'm not sure the vitamin C and Zithromax will help me beat this guy that I'm talking against because he is quite a smart guy.

So I changed the title a little bit, a large 40%-45% Hill-Sachs lesion is best treated with a surface replacement and I'm affirming that. Hill-Sachs lesions, as we know, come in all shapes and sizes. They come in regular Hill-Sachs lesions, reverse Hill-Sachs lesions, they can be of various depths and this whole new concept of glenoid track is an important method of understanding the importance of the Hill-Sachs lesion in regard to recurrent instability.

Why would you consider arthroplasty as an initial option, or in this patient, in the face of previously failed surgery? Glenohumeral arthritis, for example, may already be present in this individual and that has recurrent instabilities. In further instability surgery, with its obligate decrease in range of motion, it's therefore increasing the joint reaction force posteriorly. That can do little more than make the arthritis worse in an effort to control the stability of the shoulder.

So therefore I think presenting a spherical surface to the glenoid—much like you do with avascular necrosis—can prolong the need for a polyethylene glenoid component which we know in the shoulder is problematic. We also know that the sooner you pull the trigger and do a shoulder replacement on a patient, the better. The more operations patients have prior to index arthroplasty, the worse those patients do, as is pretty well established in the literature.

So what are the options? These are the order of frequency that I use these devices in my practice.

One is a hemi-capper; we call it the "Junior Mint" replacement. That just replaces the defect alone. The other is a conventional hemiarthroplasty. The final is a surface replacement of the humeral head.

Each option may require some form of anterior stabilization procedure, possibly including a bone block, so you need to be well versed with all the different types of surgery.

When I use humeral head replacement, a conventional stemmed hemiarthroplasty, I do that when I need to change the version of the humerus. Why? Because version of the humerus…in a lot of studies, especially Swiss in old osteotomy days…shows the patients who have anteverted humeri are more

likely to dislocate. So if you have an opportunity on the CT scan…I always get some cuts through the elbow…to really see what that patient's own native humeral version is. And if they are not retroverted to 35 or 45 degrees then I put them in that amount when I do a hemiarthroplasty.

So why consider arthroplasty for large Hill-Sachs lesions? I'm undoubtedly the second most interesting man in the world. I gave these most expensive cortisone shots two years ago in Saudi Arabia. If everyone on Earth downloads one of my songs from iTunes, I will be worth $144 billion. I don't do surface replacements like the most interesting man who does the Dos Equis commercials, does. I don't do surface replacements that often, but when I do, I do them for Hill-Sachs lesions.

Dr. Romeo: Buz always has a very interesting perspective on things and great experience with managing these patients so he gives you a lot of really important clinical pearls to pay attention to. The Hill-Sachs lesion is a lesion that occurs with instability very frequently and to jump right to some sort of surface replacement seems to be overaggressive even in individuals that have a large Hill-Sachs lesion. So we try to start with something that's more biologic, more anatomic in terms of trying to resolve the problem before we go over to a metal implant. How do these things occur? The mechanism of injury is abduction external rotation with a lot of force. The shoulder goes out the front and there's a big dent in the back of the humeral head. We've written a nice paper on this, it's a good review article in the Journal of the American Academy of Orthopaedic Surgeons, which goes over the diagnosis classification and management of these lesions (2012).

We understand the Hill-Sachs lesion was described by two radiologists quite some time ago in 1940 and the key feature is that the lesion is in the back of the humeral head and away from the bare area. Again, it is related to the dislocation. It could be in different parts of the humerus depending on whether the humerus went directly anteriorly or more inferiorly. It happens very commonly and in 95% of recurrent dislocations you're going to see some bone loss in the back of humeral head.

From your exam under anesthesia you will see where you can engage that Hill-Sachs, or catch on the front of the shoulder, and you understand that soft tissue operations to resolve all of these are not likely to solve every problem related to the bone. And that's really where we get into the discussion of how to manage this.

Really, when you look at which ones need to be treated, other than the glenoid side, it's less than 10% and the vast majority of surgeon practices focus on the glenoid side, but occasionally the humeral side. The glenoid side is really critical and if you fail on the glenoid side you definitely are not going to be successful on the humeral side.

So remember that these lesions from 15-25% on the glenoid side require some consideration of bone and anything over 25% needs to be resolved with a bone operation. You can't fix these bony lesions with a soft tissue repair. No matter how tight you make the shoulder, you will not solve this problem. And if you make them so tight that you solve this problem, you've created a separate problem. We thought about the humeral bone loss in a very similar way and when it's a small lesion, as it happens in many of our patients, we just manage the glenoid side. They do very well. We've learned that we can arthroscopically assist our surgical repairs with a Remplissage and anything about 25% or more we have to consider surgical management.

How do we decide if it's 25%? We use advanced imaging. CT scan is very helpful, better than MRI. We use the concept of the glenoid track, which is a relatively new idea, but the idea is that if the pothole on the humeral side gets larger than the width of the remaining glenoid, the glenoid is going to fall into that pothole and you're going to have problems with this lesion.

Now in larger defects, we do have to engage the articular surface…and Buz showed you a technique using metal… but there are ways you can do that without metal. You can use allograft and plugs, or some soft tissue or partial resurfacing, but this is what we do.

Through an anterior approach, we can take a fresh osteochondral graft… we like this because it's bone and cartilage that we're transplanting into the shoulder. We can fill that graft so that it has a nice articular surface and won't engage. We could also do this arthroscopically…in other words we can manage our anterior glenoid instability with an arthroscopic anterior stabilization and then through a posterior approach in the lateral position we can see the defect and fill it in with a matched allograft. I think this works particularly well for those lesions from 25% to 40%. Fills in very nicely. The articular surface has now been recreated. They're not going to engage in a Hill-Sachs lesion.

The best study to date to look at this from a biomechanical view in the lab is the one by George Athwal and the group up in Western Ontario. They looked at Remplissage versus osteochondral allograft versus partial resurfacing. I'm telling you I would prefer a biological solution because many of these patients who come to us are actually under the age of 40. They've had a singular event and I can't see putting metal in them at this time.

Moderator Sculco: Wayne, I'd like to start with you. Maybe you can elaborate a little bit. Who are the ideal candidates for the surface replacement because anterior instability with the shoulder where the defects occur is usually a young person's kind of problem although it can also occur in the older patients? Tell us a little bit more about your indications, your age distribution for who you are using this in.

Dr. Burkhead: You have to take age into consideration, size of defect, as Tony elaborated, and this whole concept of glenoid tracks. This is a rare operation in my practice. I don't want anyone leaving here thinking that this is something I do routinely for small Hill-Sachs lesions. I treat them just exactly like Tony does. When you get into these 45%, 50% humeral head lesions, patients who have had previous surgery, their humeral surface oftentimes have significant chondromalacia. The seizure patients are the ones who have the worst because every time their shoulder goes out, the forces that are placed across the articular surface are just huge. Oftentimes those patients are arthritic even if they're index procedure…that being said, I don't always do that unless their defect would be 45%. It's a real unusual operation. If you compare the costs it's probably a lot cheaper to put a piece of metal in there than an osteochondral allograft.

Moderator Sculco: Anthony, let me turn to you now. You heard Wayne's argument for the use of this in large defects. What's your feeling? You showed use of allografts and dealing more on the glenoid side. Do you do surface replacements of the humeral head?

Dr. Romeo: Very rarely do I do surface replacements of the humeral head. In this diagnosis, if I'm going on to do an arthroplasty, typically it's going to be along the lines of replacing the entire humeral head -- not trying to put a circular graft into an orange slice type wedge to try and see if I can fill that in correctly. So I'd rather just take off the entire head and put in a proper sized head in the proper position. If I am going to go on to do an arthroplasty (and those arthroplasties are typically in patients who are just a little bit older or have **really** a joint that is under distress and both the glenoid and humeral side are showing signs of arthritis and it's a very large lesion) then in that situation an osteochondral allograft may, in fact, not be enough for the treatment of the patients. But that's an extremely rare situation.

Moderator Sculco: So why then, in that situation, would you do a surface replacement of the humeral head and not go to a total shoulder replacement? Maybe you could educate us about that. Your patient that has some arthritis.

Dr. Romeo: It's more along the line of Buz's talk. The idea of a surface replacement is a nice idea but we've learned that some of our surface replacements don't match the normal anatomy of the humerus very well. For people that have done this operation they'll find it sometimes very hard for the surgeon to identify exactly where that center point of the articular arc is and, therefore it can be challenging to get the surface replacement in the right spot. So when they're done, the replacement is sitting a little high or a little bit in varus. If you just take off the head at the anatomic neck and replace the head with a normal head that's in the systems and available now…an anatomic system… then I think many surgeons are more consistent with the quality of the results when they're done.

Moderator Sculco: You would agree with that Wayne?

Dr. Burkhead: I would. I don't do very many...like I said in my slide…I don't do very many surface replacements, but when I do I usually use them for this particular indication or for AVN [avascular necrosis] and it's critically important that you understand the geometry and I use a device that **is** more anatomically normal for patients.

Moderator Sculco: I think the takeaway message here is that surface replacement is an option probably very infrequently needed. Other options are available as Anthony has outlined. But certainly a serious problem in the older patient with developing arthritis, replacement, particularly in that patient population, is probably indicated. I want to thank both of our speakers. ♦

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

COMPANY

FDA Clears joimax's Endoscopic-Assisted Fusion Cage

German-based minimally invasive endoscopic spine surgery technology developer joimax GmbH has been cleared by the FDA to market the company's Endoscopic Lumbar Interbody Fusion, or EndoLIF On-Cage: 3D-printed implant.

Enabling Fusion

In a July 13, 2015 press release, the company stated the new implant allows surgeons to use an inter-muscular approach, "similar to a mini transforaminal lumbar interbody fusion (TLIF), into the intervertebral disc, enabling endoscopic-assisted fusion."

EndoLIF Implant

The implant consists of titanium alloy, produced with Electron Beam Melt (EBM) technology. The cage has a porous surface with diamond cell structure, providing an "optimal base for cell proliferation and bone growth." Two large openings can be filled with autogenous bone to support the creation of a straight column for fusion.

EndoLIF On-Cage Implant/joimax GmbH

The cage is designed to be used with supplemental posterior fixation, such as the joimax Percusys percutaneous pedicle screw-rod system. According to the company, cage implantation can be performed with a posterior or posterolateral approach, either using an open or endoscopic-assisted method.

Surgical Site Access

Access to the surgical site is one the main challenges when using endoscopic surgical methods.

Two German spine specialists, Ralf Wagner, M.D. of the LIGAMENTA Spine Center in Frankfurt and Bernd Illerhaus, M.D., at Datteln/Recklinghausen, have performed more than 200 out of 600 EndoLIF procedures in Europe, according to the company. "The access is dura and nerve-gentle, preserves the dorsal bony structures and we can avoid scar tissue because of the stepwise tissue dilation," said Dr. Illerhaus.

Yeung: "Elevate Interest"

Anthony Yeung, M.D., one of the most well-known proponents and teachers of endoscopic spine procedures, has made no secret of his caution of fusing the spine. But Dr. Yeung told *OTW* that he congratulates joimax for this implant, which he says "will elevate the interest in transforaminal endoscopic surgery, including stabilization as part of a least invasive and most effective technique."

"This is another iteration of the transforaminal endoscopic approach to augment the least invasive T-Lif approaches already on the market, specifically iO-Lif implants by Amendia, Globus, and others. There are differences in cage structure and design offered by different companies. It comes with the desirable knowledge and training for transforaminalplasty, a partial decompression of the lateral facet to make room for cage implantation without sacrificing the whole facet and destabilizing the spine, thus necessitating posterior stabilization. The transforaminal fusion approach will continue to evolve using smaller expandable cages with larger footprints that will create enough anterior stability to eliminate the need for posterior instrumentation."

Ultimately, he says a significant number of fusions can be decreased by "endoscopic decompression, ablation, dynamic stabilization and even nucleus augmentation before fusion."

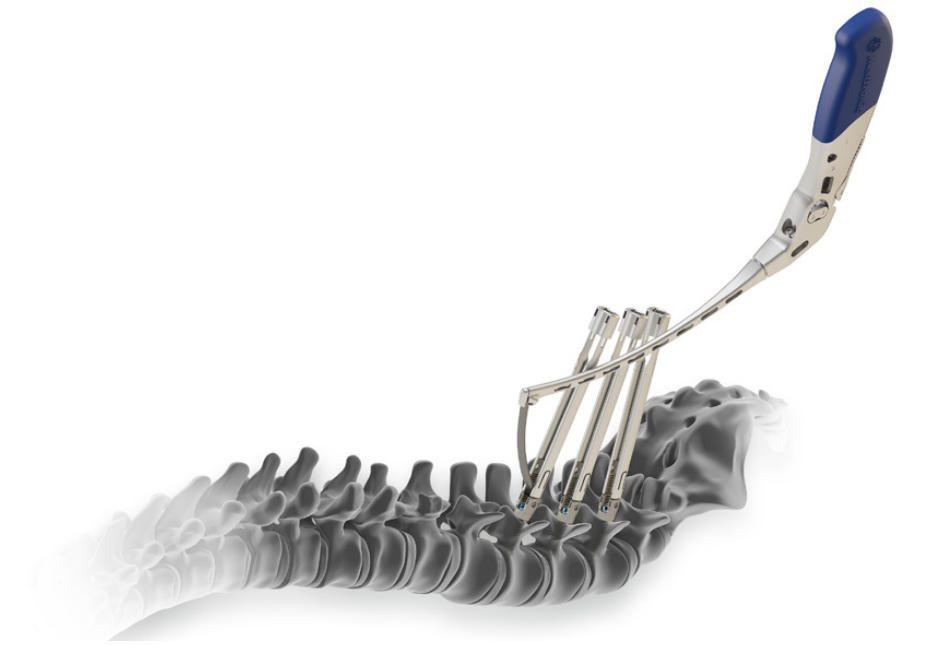
However, he adds that there are pitfalls and complication risks to the transforaminal approach consisting of anatomic nerve variations and patho-anatomy that increase complication risk, "but can be overcome with proper training."

More Gentle Techniques to Follow

"With the EndoLIF program, joimax offers a complete endoscopic-assisted solution for spinal stabilization and fusion. In the future, we will be able to treat patients with even more gentle techniques," said Wolfgang Ries, CEO and founder of joimax. "Our next development will be an EndoLIF Cage on the basis of our iLESSYS Delta system for posterior lumbar inter-body fusion (PLIF)." — *WE*

Medtronic Expands TLIF Procedure and Buys RF Surgical

Medtronic plc used the recent IMAST meeting (International Meeting on Advance Spine Techniques) in Kuala Lumpur, Malaysia, to launch its CD Horizon Solera Voyager Spinal System for Minimally Invasive Spine procedures.



CD Horizon Solera Voyager/Medtronic plc

Multiple Rod Insertion Options

According to a July 8, 2015 company announcement, the Solera Voyager "expands upon the transforaminal lumbar interbody fusion (TLIF) procedure by offering multiple, minimally invasive rod insertion options and enabling a seamless 3D-navigated surgical experience."

Percutaneous or Wiltse Approach

The system features low profile, extended tabs screw with inner threading. The company says the features "ease rod insertion and facilitates rod reduction" and gives surgeons the flexibility to use either a percutaneous or Wiltse minimally invasive approach for rod insertion.

The system is part of the company's Surgical Synergy platform, an integrated portfolio of navigated surgical technologies.

Doug King, president of Medtronic's spine business and senior vice president of Medtronic, said the Solera Voyager represents the company's "commitment to take minimally invasive techniques and 3D navigated surgery even further and develop solutions with clinical and economic value."

Agreement to Acquire RF Surgical

In an unrelated July 13, 2015 announcement, the company said it signed a definitive letter of agreement to acquire RF Surgical Systems, Inc. RF Surgical focuses on the detection and prevention of retained surgical items (sponge, gauze or towel) for approximately $235 million. The system is used as an adjunct to manual counting methods and uses a low radio frequency signal to track the surgical items. — *WE*

ChoiceSpine Launches Posterior Cervical System

Knoxville, Tennessee based, privately held, ChoiceSpine, LP launched its Blackbird Posterior Cervical System for commercial markets on July 13, 2015. The system was cleared by the FDA in June 2014.

Company Vice President of Research and Development Steve Ainsworth, Ph.D., said the system has had over 150 successful surgeries. Director of Business Development Anderson Collins said this system, and other products in the company's product pipeline, "will continue to fuel the double digit growth" the company has experienced over the last couple of years.

A company announcement stated the Blackbird is a "comprehensive system for posterior fixation of the cervical and upper thoracic spine," and offers a number of screws, hooks, & rods. The Blackbird is the first of three commercial products the company plans to launch in 2015.

Features

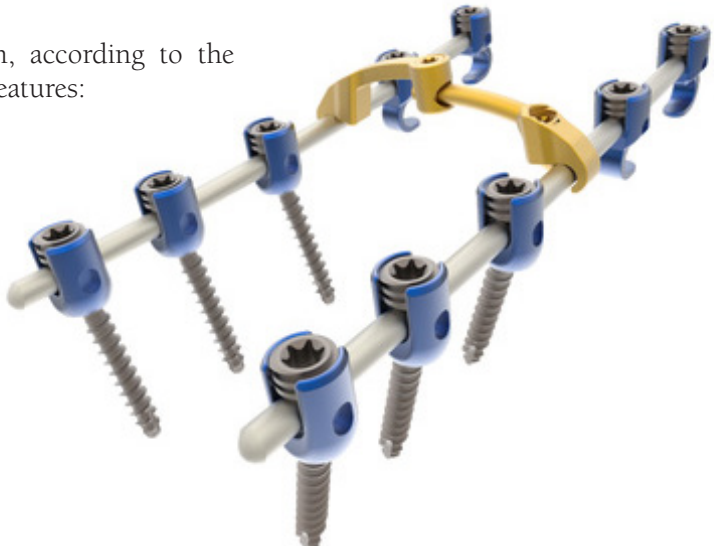
The system, according to the company, features:

- Polyaxial head that offers non-biased 70°of conical angulation
- Fully threaded and smooth shank screws in multiple diameters
- Dovetail set screw that minimizes head splaying and cross-threading
- Variety of connectors allows for diverse variation in anatomy and surgical technique

ChoiceSpine

ChoiceSpine acquired Baxano Surgical Inc.'s Veo Lateral Access & Interbody Fusion System in early February 2015. Ainsworth was TranS1's third employee and served as the company's vice president of research and development throughout Baxano's acquisition of TranS1.

Rick Henson and Marty Altshuler started the company in December 2006 in Knoxville and acquired Orthotec, then a $40 million dollar company. Orthotec is the company Alphatec, Inc. agreed to pay $49 million to settle a lawsuit filed by Orthotec alleging fraudulent transfers of assets of a company that Alphatec had previously acquired. — *WE*



Blackbird Posterior Cervical System/ChoiceSpine, LP

Outlook Improves for Amedica's Novel Spinal Implant

Could FDA clearance be in the works later this year for Amedica Corporation's composite silicon nitride spinal interbody device?

Courtesy Amedica Corporation

Amedica's Chairman and CEO Sonny Bal, M.D., J.D., MBA said: "After successfully completing an important surveillance audit with no non-conformities being identified, we've submitted responses to the FDA questions regarding our composite silicon nitride device." "Our submission starts the clock once again with the FDA, and we remain hopeful for a final response during the third quarter of this year. As sales momentum of this unique device continues to build in Europe, we look forward to beginning domestic shipments as soon as we achieve clearance."

Silicon nitride, the material from which both Amedica's spinal implants and large joints are made, is purported to be the toughest, most fracture resistant, chemically stable bioceramic currently on the market. Silicon nitride's surface texture and hydrophilic nature attract

both osteoblasts and physiologic proteins to ensure reliable osteointegration, while its surface biochemistry inhibits bacterial biofilm adhesion.

The material is manufactured through a partnership with Kyocera, one of the world's largest ceramic manufacturers. Amedica's spine products are FDA-cleared, CE-marked, and are currently marketed in the U.S. and select markets in Europe and South America through its distributor network and its growing OEM partnerships. — *BY*

LEGAL

Osteoporosis Drug Sale Manager Guilty of Fraud

Apparently no healthcare crime is too small to pursue for U.S. Attorney Carmen Ortiz of Massachusetts.

A recent guilty plea by a former bisphosphonate drug sales manager is exhibit one.

In 2010, Jeffrey Podolsky of New York, a former Warner Chilcott Sales U.S., LLC district manager, hatched a scheme to defraud payers to pay for his company's non-generic bisphosphonate drugs, Actonel and Atelvia. The drugs are used for the prevention and treatment of osteoporosis.

Clinical Justification Fraud

From 2010 through 2011, Podolsky directed his sales reps to fill out prior authorizations for physicians using false clinical justifications as to why Actonel and Atelvia were necessary for their patients. His reps reviewed patients' medical charts in violation of HIPAA (Health Insurance Portability and Accountability Act) and utilized a website to submit prior authorizations to payers that allowed them to disguise their identities as drug reps.

The sales reps needed to cook the clinical books because most bisphosphonates on the market have very little clinical difference between them. Because the drugs had become generic (risedronate), many payers had removed the drugs from their pharmaceutical formularies and moved to generics. The only way to get a prescription for Actonel or Atelvia paid for by an insurance company required a prescribing physician to explain to the payer why the non-formulary drug was medically necessary over generic versions of the drug.

$200,000 Fraud

Podolsky's scheme worked well enough that payers and Medicare paid at least $200,000 for Actonel and Atelvia prescriptions that were not medically necessary and would not have been paid but for the false information submitted by the Warner Chilcott sales reps.

On July 7, 2015, Podolsky pled guilty to conspiracy to commit health care fraud. Ortiz announced the guilty plea without comment about any physicians that may have been involved in the scheme, company culpability or how the fraud came to attention of the Justice Department.

Potential Company Investigation Resolution

According to a May 14, 2015 *Reuters* story, the company said in a regulatory filing that it held talks with the Justice Department to discuss a potential resolution of an investigation into the company's sales activities. The company and several employees received subpoenas in 2012 from Ortiz's office.

"The subpoenas," according to *Reuters*, "demanded information about sales and marketing activities, payments to people who are in a position to recommend drugs, medical education and employee training, including physician remuneration."

The investigation was "related to two lawsuits filed by former Warner Chilcott sales representatives that accuse the company of promoting several of its products by making improper claims about the products and providing kickbacks to physicians."

Prison and Fines Possible

According to the U.S. Sentencing Guidelines, Podolsky could get up to 10 years in prison, 3 years of supervised release, a fine of $250,000 or twice the gross loss to the Medicare program or twice the gross gain to Podolsky (whichever is greater), forfeiture of any proceeds of the offense, and exclusion from the Medicare program. Actual sentences for federal crimes are typically less than the maximum penalties. — *WE*

Morguefile and taysm

BIOLOGICS

Silicon for Tissue Regeneration?

In what may be a unique approach to wound healing, researchers have developed a new approach for better integrating medical devices with biological systems. The researchers, led by Bozhi Tian, Ph.D., assistant professor in chemistry at the University of Chicago, have created a world's first: skeleton-like silicon spicules prepared via chemical processes.

"Using bone formation as a guide, the Tian group has developed a synthetic material from silicon that shows potential for improving interaction between soft tissue and hard materials," said Joe Akkara in the July 8, 2015 news release. Akkara is a program director in the National Science Foundation materials research division, which funds this research. "This is the power of basic scientific research. The Tian group has created a material that preliminarily seems to enhance soft tissue function."

According to the news release, Dr. Tian and his colleagues from Northwestern University "achieved three advances in the development of semiconductor and biological materials. One advance was the demonstration, by strictly chemical means, of three-dimensional lithography. Existing lithographic techniques create features over flat surfaces. The laboratory system mimics the natural reaction-diffusion process that leads to symmetry-breaking forms in nature: the grooved and notched form of a bee stinger, for example. Tian's team developed a pressure modulation synthesis, to promote the growth of silicon nanowires and to induce gold-based patterns in the silicon. Gold acts as silicon's growth catalyst. By repeatedly increasing and decreasing the pressure on their samples, the researchers were able to control the gold's precipitation and diffusion along the silicon's faceted surfaces."

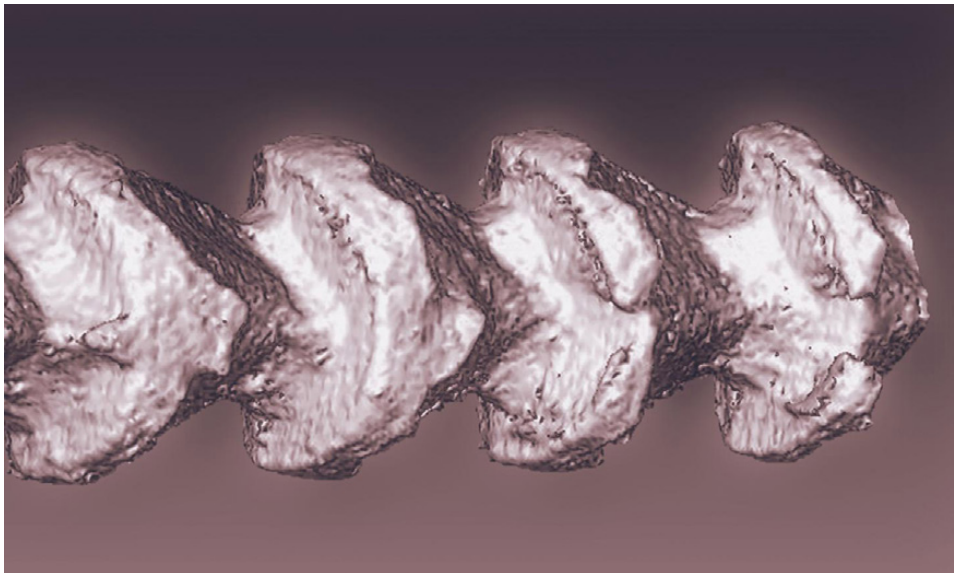
"One of the major hurdles in the area of bioelectronics or implants is that the interface between the electronic device and the tissue or organ is not robust," noted Dr. Tian.

The team indicated that these new spicules may circumvent this issue because they penetrate the collagen and then become deeply rooted.

Tian told *OTW,* "We developed a new 3D lithography method for preparing complex semiconductor materials. This 3D lithography involves reaction-diffusion cycles which we typically see in the formation of naturally occurring biominerals. The silicon materials we showed in our *Science* paper exhibit strongest mechanical interactions with extracellular matrix materials-collagen, as compared to other available silicon materials. This property is certainly nice for potential implant applications."

"The anisotropic, skeleton-like silicon provide a biomimetic mechanism for enhanced interaction with tissues and cells, suggesting their potential as element for bioelectronics (either sensing or stimulation). In particular, we are interested in electroceuticals (i.e., stimulation), in which electrical impulses are delivered through devices to target the neural circuits that regulate the body's organ functions. Any bioelectronic device works through electrical signal transduction at the bio-interfaces, and the efficacy of such transduction is closely related to the device-bio junction tightness. Our skeleton-like silicon has shown significantly stronger attachment to extracellular matrix materials. We are planning to use these 'sticky' silicon as building blocks for making flexible and macroscopic devices capable of peripheral nerve stimulation and wound healing, where electric current/field can be used for controlling cellular physiology and motility."

"Our skeleton-like materials are made of silicon, which is electrically conductive. One possibility is to use these materials for electrical stimulation to promote tissue regeneration." — *EH*



Bozhi Tian Group

Ground Breaking Nerve Transplant Study Underway

Alachua, Florida-based AxoGen, Inc. announced that the first patient has been treated as part of its ground breaking study of its Avance Nerve Graft.

Avance is an off-the-shelf processed human nerve allograft. It has the potential to significantly change the practice of nerve repair in trauma cases.

The study, called "RECON," seeks to compare Avance with nerve tubes for bridging gaps in peripheral nerve tissue. This is a Phase 3 clinical trial.

If successful, Avance will be the first FDA licensed biologic implant for peripheral nerve repair.

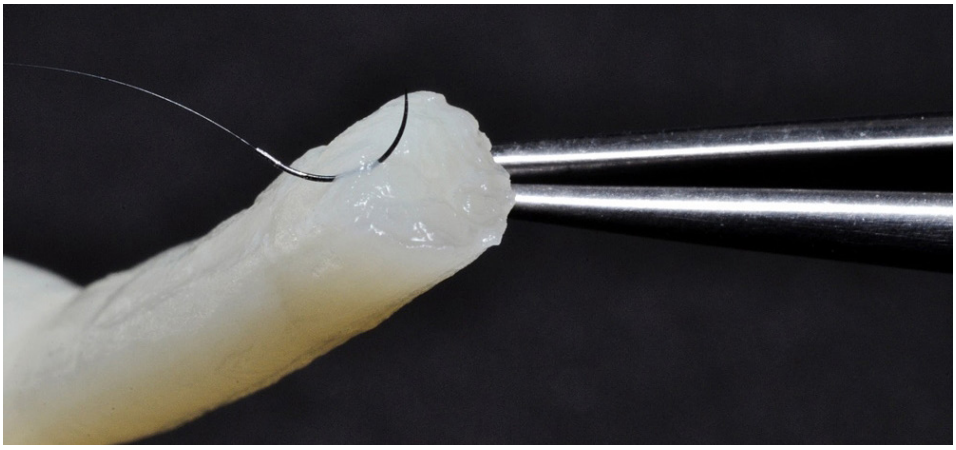
Since Avance is an allograft, it is currently commercially available in the United States and several other countries. This study, however, will allow Axogen to market Avance and make claims regarding the efficacy of Avance for peripheral nerve repair.

In May, Axogen announced that the FDA had provided clearance for AxoGen to proceed with the RECON Study after conducting a review of the Study protocols and characterization of Avance Nerve Graft.

"The commencement of the RECON Study is an important milestone in moving Avance Nerve Graft to be the first FDA licensed biologic implant for peripheral nerve repair," said Karen Zaderej, President and CEO of AxoGen. "The rigor of the BLA transition process offers an opportunity for AxoGen to develop a significant amount of data on a biological implant for nerve repair while simultaneously allowing us to continue to advance the commercial adoption of Avance Nerve Graft."

The RECON Study is a multicenter, prospective, randomized study to evaluate recovery outcomes of surgical repairs of peripheral nerve discontinuities. Enrollment of 150 subjects is expected to take 2 years with subjects being followed for 12 months after surgery.

The first patient was enrolled at Virginia Commonwealth University Medical Center by Principal Investigator Jonathan Isaacs, M.D. A second clinical study location, Hospital of the University of Pennsylvania with Principal Investigator L. Scott Levin M.D., FACS has also started recruiting for potential subjects. — *BY*



Courtesy of Axogen, Inc.

Bacterin Beats Wall Street's Expectations for Q2

Bacterin International Holdings, Inc., the Belgrade, Montana-based biologics and allograft company, surprised its analysts by pre-reporting and exceptional sales report for the June quarter. According to management, Bacterin will report sales of around $10 million for the three months ended June 30, up 12-15% from last year.

Wikimedia Commons and Fae

To put that in perspective, Bacterin had reported essentially zero growth in 2013, 6.8% sales growth in 2014 and now this year appears to be on track to post up 12-15%.

That's an outstanding turnaround and is no doubt due to both a reorganization put in place by CEO Dan Goldberger and President Robert Di Silvio and a series of new products. The most recent new product introduction was ArthroFuse.

ArthroFuse is an allograft implant specifically designed for the treatment of hammertoe deformities.

According to a June 3 press release, hammertoe deformity affects the proximal interphalangeal joint of the lesser metatarsals and often resulting in debilitating joint pain and disability. There are approximately 550,000 surgical hammertoe procedures are performed each year in the United States. But an

astonishing 60 million affected adults go undiagnosed.

What is most interesting about ArthroFuse is that it eliminates the need for externally communicating pins or permanent implants. ArthroFuse remodels over time into the patient's own bone.

So, better organization and a growing stream of innovative products and… sales are jumping.

In fact, the sequential sales growth is a very impressive 5-7% when compared to $9.5 million for the first quarter of 2015.

Bacterin supplies allograft and biologic products for a wide variety of orthopedic applications including enhancing fusion in spine surgery, relief of back pain, promotion of bone growth in foot and ankle surgery, promotion of cranial healing following neurosurgery and subchondral repair in knee and other joint surgeries. — *BY*

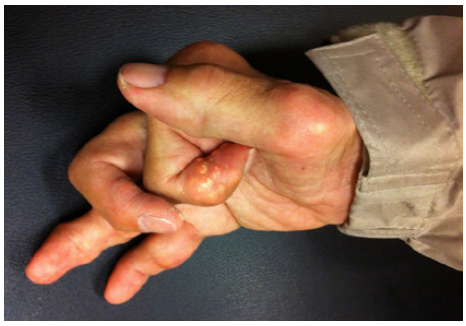
LARGE JOINTS

Arthritis Drug Could Treat Blood Cancer

Scientists at the University of Sheffield and Royal Hallamshire Hospital in the UK have found that an existing arthritis drug—methotrexate—might also come to the aid of patients with blood cancers.

According to the July 7, 2015 news release, treatment for myeloproliferative neoplasms (MPN) is limited to aspirin, removal of excess blood and mild chemotherapy. The UK team found that methotrexate (MTX) might work well in treating these patients.

Dr. Martin Zeidler of the biomedical science department at the University of Sheffield said in the news release, "Given that a year's course of low-dose



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MTX costs around £30 [about $46.90 USD], the potential to repurpose MTX could provide thousands of patients with a much needed treatment option and also generate substantial savings for health care systems. Because MTX is a World Health Organisation 'Essential Medicine,' this also means that this well understood drug could be used throughout the developing world."

"In this study scientists used cells from the fruit fly *Drosophila* to screen for small molecules that suppress the signalling pathway central to the development of MPNs in humans. Further testing confirmed this in human cells, even those carrying the mutated gene responsible for MPNs in patients."

Dr. Zeidler told *OTW*, "I think there are two things that surprised me about this finding. Firstly that the mechanisms of action of methotrexate in rheumatoid arthritis wasn't known and that our finding could explain how this drug works and second, that nobody else had found it before."

"We are currently in the process of undertaking further patient and mouse in vivo experiments. We are also preparing an application to launch Phase II clinical trials in polycythemia vera patients to examine the possibility of repurposing MTX for the treatment of MPNs. It will probably be another 12-18months before this trial starts. However, given that MTX is so well

understood in RA patients there is nothing to stop haematologists prescribing MTX off-label right now [not that we are recommending this approach!]. As such it COULD be available right now…but undertaking proper Phase II and III trials would be required before it could be formally repurposed." — *EH*

EXTREMITIES

Too Many Childhood Antibiotics Affects Bone Growth

Researchers from New York University's Langone Medical Center have further evidence that multiple courses of antibiotics in childhood may significantly impact bone development. The study was led by Martin Blaser, M.D., the Muriel G. and George W. Singer Professor of Translational Medicine, director of the NYU Human Microbiome Program at NYU School of Medicine.

According to the June 30, 2015 news release, female mice that were administered two classes of childhood antibiotics gained more weight and developed larger bones than untreated mice. Both of the antibiotics also disrupted the gut microbiome.

"The mice received three short courses of amoxicillin, tylosin (not used in children but represents another common antibiotic class called the macrolides, which is increasingly popular in pediatrics), or a mixture of both drugs. To mimic the effects of pediatric antibiotic use, the researchers gave the animals the same number of prescriptions and the same therapeutic dose that the average child receives in the first two years of life. A control group of mice received no drugs at all."

Although Dr. Blaser cautioned that the study was limited to mice, he said that it's important to note that the results are in line with results from multiple other studies pointing toward significant effects on children exposed to antibiotics early in life. "We have been using antibiotics as if there was no biological cost."

The study supports Dr. Blaser's prior work showing that "antibiotic exposure during a critical window of early development disrupts the bacterial landscape of the gut and permanently reprograms the body's metabolism, setting up a predisposition for obesity. The new study found that short, high-dose pulses of tylosin had the most pronounced and long-lasting effect on weight gain, while amoxicillin had the biggest effect on bone growth—a prerequisite for increased height."

The research team found that tylosin had a larger impact on the maturity of the microbiome compared with amoxicillin. "We also see that the effect is cumulative," said lead co-author Laura M. Cox, Ph.D., an adjunct instructor in the Department of Medicine at NYU School of Medicine. "So the number of courses of antibiotics matters."

Dr. Blaser told *OTW*, "This was the third study that we have conducted in mice comparing receipt of early life antibiotics or not. In all three studies, we have seen evidence for accelerated bone growth. So there was no surprise from this study, but rather consistency with the other study results, regardless of variation in study protocol."

"These studies provide evidence that such issues as bone maturation and length are not fixed in early childhood, but that microbes are playing a role in choreographing development. This may lead to new approaches to issues on the quantity, quality and location of new bone growth in infants." — *EH*

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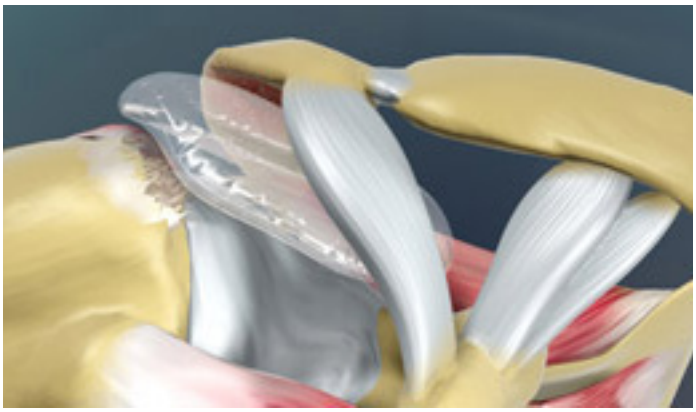
Trial Begins for Novel, Balloon MIS Rotator Cuff Repair System

OrthoSpace, Ltd, a privately held medical device company located in Caesarea, Israel, has enrolled the first three patients in a U.S. investigational device exemption (IDE) pivotal study. The study is of the company's balloon system, called InSpace, which is used to repair massive rotator cuff tears.

InSpace has been implanted in more than 5,000 patients in 15 countries but this is the first time it has been used in the United States. Edwin J. Rogusky, M.D. and Paul R. Sensiba, M.D. performed the procedures at University Orthopedics Center in State College, Pennsylvania. Following the surgeries they said, "We are honored to be a part of this study and to initiate clinical study enrollment. The data to date has demonstrated InSpace's safety and efficacy, and we look forward to contributing to the U.S. dataset to facilitate InSpace's entry into the U.S. market."

Nikhil N. Verma, M.D., of Rush University Medical Center, primary investigator of the study, commented, "Having heard about promising results with the use of this technology from our colleagues abroad and having seen the procedure in Europe, I am looking forward to leading this talented group of U.S. surgeons in completing this pivotal study. InSpace addresses a current unmet medical need for my patient population: a simple, minimally invasive way to treat massive rotator cuff pathology, with limited recovery time for the patient."

OrthoSpace company officials say that enrollment in the study is ongoing and that patients are being recruited at multiple sites across the country. — *BY*



Courtesy of OrthoSpace, Ltd

SPINE

FDA Clears Captiva Spine's MIS Pedicle Screw System Enhancements

Captiva Spine, Inc. which modestly describes itself in its press release as "creating and maintaining sincere, honest, collaborative relationships to deliver smart, elegant, and intuitive spinal solutions" has received 510 (k) clearance, from the FDA to market its enhanced TowerLOX MIS Pedicle Screw System.

The enhancements include what the firm calls its PivoQuik Rod-Inserter and Tower Guide to allow for rapid rod alignment and the Modular Open Tower locking mechanisms that allow for rod insertion and visualization through the central shaft of the tower.

Company President and Founder Dale Mitchell said, "We've obsessively invested time collaborating with leading MIS spine surgeons, discovered new resources through our vendor partners, and delivered coordinated enthusiasm through all aspects of this project."

Minimally invasive instruments for lumbar spine surgery has become the most innovative sector in spine surgery. Over the past four years, more MIS innovations have been submitted for the annual *Orthopedics This Week* Spine Technology Awards than any other category – including biologics and motion preservation implants.

Captiva Spine is a privately owned medical device organization founded in Jupiter, Florida, in 2007. For more information go to: www.captivaspine.com — *BY*

Courtesy of Captiva Spine, Inc.

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