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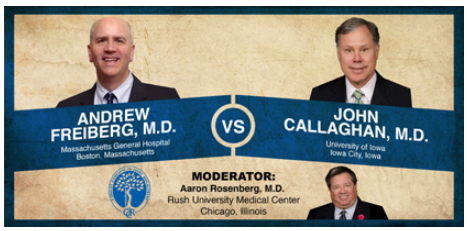
Orthopedics This Week

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: Q3's reports are just about all in and, as we and others have signaled, sales growth rates are up yet again and across the board. We're talking tail wind. Strong and steady. Year-over-year sales growth, especially in large joint recon, accelerated sequentially each quarter this year. Why? Higher employment rates in the U.S. economy. More insurance coverage. An aging population. In short, rising demand. And, at least in the case of Zimmer, even stable pricing.

RANK	LAST WEEK	COMPANY	TTM OP MARGIN	30-DAY PRICE CHANGE	COMMENT
1	4	ConMed	10.51%	9.79%	Higher profits on lower sales. That might give some investors pause, but savvy analysts see efficiencies leading to wealth creation.
2	5	MicroPort	16.53	8.16	The 7th least expensive ortho equity and, finally, buyers are taking notice of the strategic value in this company.
3	1	Symmetry Medical	6.55	0.71	SMA will report at the end of this week. Consensus says they will post up a near doubling of earnings—on down recon sales.
4	2	Stryker	11.52	2.54	Very nice quarter—courtesy of trauma and extremities. Large joint recon had pricing issues and the recent M&A splurge is still digesting.
5	3	Zimmer	29.12	1.60	On the eve of merging with Biomet, Big Blue beats Wall Street consensus. Great quarter. But investors are looking beyond Q3 to the big merger.
6	9	Medtronic	28.84	4.38	Two new spine products announced—a new anterior cervical fusion system and a new titanium plus PEEK interbody device. NASS must be around the corner.
7	7	NuVasive	8.01	1.00	The key for NUVA this quarter is more profits from each sales dollar. At current prices, NUVA is the 9th least expensive ortho equity.
8	8	Globus Medical	29.68	4.56	Speaking of expensive, GMED is the most expensive stock on the Power Rankings. Why? Because it's a little money machine.
9	6	Integra LifeSciences	12.57	(1.17)	IART wraps up the purchase of MicroFrance and Xomed's Manual ENT instrument lines. But investors are not impressed.
10	10	Exactech	10.26	(7.57)	Uff Da! Modest sales growth (only 4%) and earnings drop 6% due to currency issues. Still, doesn't justify this kind of sell off.

Robin Young's Orthopedic Universe

TOP PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	MiMedx Group	MDXG	$9.13	$965	26.10%
2	ConMed	CNMD	$41.03	$1,130	9.79%
3	MicroPort Scientific	853	$0.53	$748	8.16%
4	LDR Holding Corp	LDRH	$33.43	$868	7.08%
5	Globus Medical	GMED	$20.63	$1,950	4.56%
6	Medtronic	MDT	$66.56	$65,200	4.38%
7	CryoLife	CRY	$10.55	$295	2.93%
8	Stryker	SYK	$84.22	$31,860	2.54%
9	K2M Group Holdings	KTWO	$13.84	$514	2.52%
10	Zimmer Holdings	ZMH	$105.29	$17,830	1.60%

WORST PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	RTI Biologics Inc	RTIX	$4.11	$234	-20.50%
2	Aurora Spine	ASG	$1.34	$21	-19.76%
3	Alphatec Holdings	ATEC	$1.46	$143	-16.57%
4	TiGenix	TIG.BR	$0.64	$103	-13.51%
5	Bacterin Intl Holdings	BONE	$4.11	$27	-13.47%
6	Baxano Surgical Inc	BAXS	$0.13	$7	-13.33%
7	Exactech	EXAC	$21.36	$294	-7.57%
8	Orthofix	OFIX	$28.82	$531	-7.21%
9	Smith & Nephew	SNN	$31.84	$14,230	-6.05%
10	Johnson & Johnson	JNJ	$103.13	$290,860	-5.07%

LOWEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Medtronic	MDT	$66.56	$65,200	17.11
2	Johnson & Johnson	JNJ	$103.13	$290,860	17.19
3	Globus Medical	GMED	$20.63	$1,950	17.50
4	Zimmer Holdings	ZMH	$105.29	$17,830	18.38
5	Exactech	EXAC	$21.36	$294	18.74

HIGHEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Orthofix	OFIX	$28.82	$531	180.13
2	NuVasive	NUVA	$36.30	$1,710	69.81
3	Symmetry Medical	SMA	$9.92	$373	52.21
4	CryoLife	CRY	$10.55	$295	31.97
5	Integra LifeSciences	IART	$49.72	$1,620	27.93

LOWEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	CryoLife	CRY	$10.55	$295	1.07
2	Exactech	EXAC	$21.36	$294	1.25
3	Globus Medical	GMED	$20.63	$1,950	1.31
4	ConMed	CNMD	$41.03	$1,130	1.78
5	Stryker	SYK	$84.22	$31,860	1.98

HIGHEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Orthofix	OFIX	$28.82	$531	9.79
2	NuVasive	NUVA	$36.30	$1,710	6.24
3	Symmetry Medical	SMA	$9.92	$373	4.35
4	Smith & Nephew	SNN	$31.84	$14,230	2.69
5	Johnson & Johnson	JNJ	$103.13	$290,860	2.62

LOWEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	Baxano Surgical Inc	BAXS	$0.13	$7	0.32
2	Alphatec Holdings	ATEC	$1.46	$143	0.70
3	Bacterin Intl Holdings	BONE	$4.11	$27	0.81
4	Symmetry Medical	SMA	$9.92	$373	0.93
5	RTI Biologics Inc	RTIX	$4.11	$234	0.96

HIGHEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	TiGenix	TIG.BR	$0.64	$103	18.11
2	MiMedx Group	MDXG	$9.13	$965	12.18
3	LDR Holding Corp	LDRH	$33.43	$868	7.78
4	Wright Medical	WMGI	$31.86	$1,610	5.99
5	Globus Medical	GMED	$20.63	$1,950	4.33

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

Do Sunshine Act Disclosures Hurt Ortho Innovation? // "Holy Grail" of Registries Ramping Up // International Consortium of Orthopedic Registries Will Make Your Life Easier

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

CMS's Sunshine Act Disclosures Put Innovation at Risk With the brouhaha in full swing over the Sunshine Act, several orthopedic surgeons are hoping to set the record straight. Brian Cole, M.D. is Professor in the Departments of Orthopaedic Surgery and Anatomy & Cell Biology at Rush University Medical Center. He told *OTW*, "The benefits of the Sunshine Act are that we have greater transparency related to relationships that physicians have with industry. Notably, disclosure is not synonymous with conflict. For example, licensing and royalty agreements have specific language eliminating the potential for a surgeon to have direct financial gain from implants used by the developing surgeon or when used at institutions where he operates and where colleagues may use those same implants or devices. Thus, surgeons choose implants and devices that maximally benefit their patients independent of any financial relationship."

Pixabay and Nemo

"Surgeons are in the best position to identify knowledge and procedural gaps, to innovate and to perform basic and clinical research related to the development of new implants and devices. Finally, consulting rates are generally far below market value or physician opportunity cost essentially leading to a physician-consultant underwriting the process on behalf of industry." When asked why would a physician take time away from his family and practice to consult for below-market-rates, Dr. Cole indicated, "Those of us interested in furthering our field and improving patient outcomes do so in part because of the intangibles associated with the process. These activities provide a balance to our day-to-day clinical practice."

Neal S. ElAttrache, M.D. is a sports medicine specialist with the Kerlan-Jobe Orthopaedic Clinic in Los Angeles, California. Dr. ElAttrache, the team physician for the LA Dodgers, tells *OTW*, "I don't know if it's by design, or misunderstanding, but the manner in which the government is presenting this data is difficult for the public to understand and has the possible result of damaging the public trust in the medical community. There seems to be an implication and a general air of impropriety on the part of physicians and the medical industry surrounding the government's presentation of this data. In many cases, the media has sensationalized this data."

"The data, especially that posted under the category of 'General Non-research Related Payments,' is especially misleading if presented without context as

it currently is. For example, I am not paid to USE any products on patients. I hold U.S. patents on some very popular implant technologies and products which have been assigned to Arthrex Corporation, a quality company with which I am proud to work. I am also proud of the success of these implants in helping surgeons treat thousands of patients every year. I am compensated on that assignment of rights to my patents, however, I have no financial incentive to use my products. The royalty calculation absolutely excludes the use of these implants on my patients or patients operated upon at a facility where I am on staff."

"Innovation is as important to the advancement of medicine as it is in any other endeavor. The participation of physician-scientists and innovators in this process is beneficial, if not crucial, to the development and advancement of medical technologies that help millions of people around the world. Companies such as Arthrex make it possible for surgeons to work with their engineers to develop and perfect their ideas resulting in more rapid advancement of new surgical techniques. It is normally far too costly and time consuming for a physician to develop, produce and distribute innovative medical and surgical products independently. Therefore, the relationship between the medical community and the device manufacturers is critical to innovation."

"I truly believe that there is great societal benefit to transparency with regard to potential conflicts of interest with regard to physician relationships to industry, just as there would be regarding such conflicts in relationships between politicians and businesses that sell to the public or tax payers. I would only hope that the data provided to the public for this transparency, is given with informative context. This would then strengthen the public trust in the medical community and raise appreciation appropriately for medical innovators."

Stephen S. Burkhart, M.D. is an orthopedic surgeon with the San Antonio Orthopaedic Group. His recent cameo in the press was less than pleasant. Dr. Burkhart told *OTW*, "A recent *Wall Street Journal* article listed a number of surgeons who have received top payments for consulting fees and royalties, and my name was at the top of the list. The gist of the articles was, 'Why are they paid so much?' and 'Are these doctors getting paid to implant their inventions in their patients or in their partners' patients?' So the people reading this did so without truly understanding how the process works."

"I have consulting and royalty contracts with Arthrex, and the royalty agreement language indicates that I will not

be paid any royalties for products that I have invented when they are used in my patients, or in my partners' patients, or even in a facility where I have privileges. I have assigned the intellectual property rights from my patents to the company; probably 95% of the items that I get royalties on are patented products. I have 28 U.S. patents on which approximately 350 Arthrex products are based. We have agreed on royalty percentages for each product, and the total royalty payment is based upon worldwide sales."

"The innuendo in the press is that there is a dark side to the doctor that makes him or her do things to line their pockets. But the fact is that there is a subset of orthopedic surgeons who are inventors and they are in the best position to identify and fill a need in the market, specifically medical devices that improve patient care. And when you think about it, these inventions reduce costs to the system and reduce morbidity. For example, when rotator cuff surgeries were done through open incisions there was an infection rate of approximately 2%; now that they are done arthroscopically the infection rate is .01%. That means that the technology and medical devices that enable surgeons to do arthroscopic rotator cuff repair have reduced the infection rate to 1/200th of what it was with open repairs; so this technological advancement has resulted in dramatic reductions in costs, and even more dramatic reductions in human misery."

"Holy Grail" of Registries Ramping Up It's an unprecedented "first" in the field of device research. "Blessed" by the FDA and guided by some of the finest minds in the field, the world's most comprehensive gathering of orthopedic registries has taken shape. Art Sedrakyan, M.D., Ph.D., Sc.D. is the principal investigator of the FDA's International Consortium of Orthopedic Registries (ICOR). He told *OTW*, "This consortium came together in response to a growing need for accurate data…particularly after all of the metal-metal problems and the numerous reports on device failures. We began working with clinicians and registry leaders worldwide; we then received a grant from the FDA to create an international registry network. It started in May 2011 when we brought all stakeholders together at the FDA."

"The FDA recognized the importance of this effort, not only from a post market surveillance perspective, but because of the implementation of unique product identifiers. They could see that the ability to uniquely identify products within registries or electronic data sources

would enable the creation of learning networks. After we launched the consortium we started an aggregate level assessment and published our first ICOR book on methodology, issues related to safety, patient reported outcomes, etc. At this point we have completed eight multinational investigations that will be published as another *Journal of Bone and Joint Surgery* book next month."

"We have demonstrated the value of different data sources for device surveillance and research…not just focusing on registries but showing the value of other data sources like published literature. This is an initial demonstration of what 21st century surveillance will look like, namely, literature reviews, primary data collection, and working with clinician leaders worldwide."

"ICOR investigations provide the highest quality of evidence that has ever been generated in orthopedics because they are based on international data, they include major data owners, and the methodology is robust. Traditionally, in order to get evidence on safety and effectiveness you would do a systematic review of randomized clinical trials (RCTs). You summarize the information from all of the RCTs that address a particular research question and you synthesize that information to get an overall estimate. But there may only be, say, several RCTs. Even worse, in orthopedics we don't have many clinical trials and the ones that exist are often small and have many biases (including inventor bias)."

"The only other robust data is that coming from registries. In the past you would review all the data in the annual reports of different countries and try to synthesize it without contacting the owner of the data. This method has even more limitations than the RCT route because you don't know the follow-up issues, average age, cement used, etc. ICOR has created an algorithm by which all the factors that doctors think are important (for outcomes like revision surgery) would be part of the data collected. That is summary level information obtained from each party in a harmonized fashion…data such as age, distribution of cement use, head sizes, etc. You can combine this information in a similar way from each participating registry."

"About 80% of evidence in orthopedics comes from registries; only 20% emanates from published research. In ten years 98% of all data will come from published literature, meaning that registry data will be the Holy Grail of research."

New Osteoporosis Drug Showing Promise A fracture trial involving over 16,000 post-menopausal women with osteoporosis has shown that odanacatib, an investigational drug by Merck, significantly reduced the risk of fractures in hip, spine, and non-vertebral sites. Keith D. Kaufman, M.D. is vice president of Clinical Research at Merck. He tells *OTW*, "This work is part of the Long Term Odanacatib Fracture Trial (LOFT) that included over 16,000 post-menopausal women at 387 centers in 40 countries who were diagnosed with osteoporosis. Odanacatib works by inhibiting cathepsin K, an enzyme involved in bone resorption and remodeling."

"We found a 47% relative risk reduction of hip fracture with odanacatib compared to placebo. When we looked at the radiographic determination of vertebral fracture there was a 54% relative risk reduction compared to placebo. We also found a 23% relative risk reduction for nonvertebral fractures. For clinical vertebral fractures we observed a 72% relative risk reduction."

"The trial was designed as 'event driven' such that once a certain number of events accrued you could look at the data. The data monitoring committee for the trial sees unblinded data and can decide whether the trial met the primary objectives; Merck doesn't see the data at that point. In osteoporosis most trials are time delimited, meaning that the trial could be stopped earlier if the number of events accrues earlier than in a time-delimited trial. Our research was powered statistically such that we could stop the study once we had 237 women with incident hip fracture. The protocol was written such that the data monitoring committee could look at the data once we had 70% of the 237 patients with hip fracture and then again when we had 85% of 237. If the primary measures were met at one of those points then the trial could be stopped before we reached 237 patients with hip fracture. That did happen and we ended up with about 190 patients with hip fracture by the time the study was finished."

"Adverse events overall were balanced between the two groups. The overall mortality was 3.4% with odanacatib and 3.0% with the placebo. Adjudicated strokes were more frequent with odanacatib than with placebo but investigator-reported stroke events didn't track consistently with the adjudicated stroke events; we are planning an independent re-adjudication of major adverse cardiovascular events from the trial. Looking forward, we enrolled roughly 8,200 people in the blinded extension study; some of those individuals will be continuing in the study in a second extension in which all patients receive odanacatib for the next five years." ◆

Lobo's Big Bets Deliver in Stryker's 1st Billion $ Recon Quarter

BY WALTER EISNER

Stryker Corporation reached over $1 billion in reconstructive sales, opened a European headquarters in Amsterdam, repatriated billions in foreign profits without an inversion deal and completed the acquisition of Small Bone Innovations, Inc. (SBi) in the third quarter of 2014. They even ended the quarter with $4.7 billion in cash.

Sales of implants for large joint reconstruction rose a solid 8.5% for the third quarter. Acquisitions accounted for 3.7% of that rise. Knee sales rose 6.4%, hips were up 4.1%, trauma and extremities continued their double-digit tear climbing 11.5%. Spine, however, just limped along, rising 1.9%.

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U.S. Sales

Sales in the U.S. were even better with total recon sales up 11.9%. Trauma and extremities were up 15.3%, with Stryker's U.S. foot and ankle business soaring 30%, excluding the impact from the acquisition of SBi.

U.S. hips and knees grew 8.1% and 6.8%. Sales outside the U.S. were down nearly a percentage point in hips against a 9% comp last year in the quarter, but up 5.3% in knees on a constant currency basis.

Stryker Corporation 3Q14	Sales $ in million	% Change
Reported Reconstructive Sales	**$1,016**	**8.5%**
Knees	$335	6.4%
Hips	$316	4.1%
Trauma/Extremities	$309	11.5%
Spine	$186	1.9%

Source: Stryker Corporation

POD Spine Challenges

PODs (physician-owned-distributorships) continue to put a drag on Stryker Spine sales. Analysts asked company Chairman and CEO Kevin Lobo if he is seeing any signs of POD activity slowing.

"No, it really hasn't changed," said Lobo. "For every POD that goes away new PODs seem to pop up. It seems to be pretty stable overall." He said he hopes the prosecution [of Reliance Medical] will turn that tide. He added that their spine business has obviously had some challenges in the first quarter, highlighted around some sales force disruptions. He said they are focused on upgrading their portfolio to have "much more" MIS products. They have also made some new leadership changes at spine, and have an "exciting" portfolio of products that customers will start to see at the beginning of next year, which will hopefully make them less immune to the kind of price pressures he says the company has had on their core spinal endpoint.

A Year of Acquisitions

Lobo and his team, including VP of Strategy and Investor Relations, Katherine Owen, have had a busy 12 months, completing acquisitions of China ortho company Trauson Holdings Company Limited, robot maker MAKO Surgical Corp., Patient Safety Technologies, Inc., Pivotal Medical, Inc., Berthold Holding, AG and Small Bone Innovations.

Kevin Lobo, Chairman and CEO/ Stryker Corporation

Katherine Owen, Vice President Strategy and Investor Relations/ Stryker Corporation

But the main Stryker story for 2014 (other than the absence of a Smith & Nephew acquisition) is the transformation of Stryker orthopedic implant business to a mix of traditional procedural approach and the MAKO Surgical robotic platform. Furthermore, Stryker doubled its foot and ankle market share in the hot extremities market.

MAKO Surgical

MAKO's sales have been less than expected but Owen said they are encouraged by the pipeline development and clinical progress.

She told Wall Street analysts on October 16, 2014, that the company has made progress each quarter with a total of eight robots sold during the past quarter. "We are confident that the market for robots is improving as we have a strong pipeline of deals we are working on closing." She also said they expect robotics to eventually become the standard of care.

Owen cited several reasons for their optimism about the fourth quarter and 2015.

Integrating Sales and Financing

First, the company is in the final stages of the integration of the MAKO selling organization into the recon sales force and is developing a sales coordination system between the MAKO capital sales reps and Stryker's very large recon implant salesforce.

The first stage of this integration was completed in April as the company moved the MAKO selling and service organization into their recon division and management. Owen commented, "We continue to work toward full integration into a single implant and selling organization. Gaining near-term sales synergies has proven to be more challenging than we anticipated, but we are encouraged by the recent momentum."

"It's just integrating a capital salesforce alongside a very large implant salesforce, and going through the necessary training and coordination that has to take place in existing accounts. So it's nothing truly unique, it's a big job," said Owen.

Lobo added that there were certain parts of the country where some Stryker customers wanted better use of their robots. There was an HMA (Health Management Associates, Inc.) bulk buy. He said CHS (Community Health Systems), which bought HMA as a big chain, wasn't really pleased with the performance of some of their robots. "So we went through a big process to actually transfer and move about six or seven robots to high performing locations. That took a lot of effort on the capital sales team that's normally focused on selling. That will pay dividends for us going forward, but it's obviously tied up a lot of activity."

Flexible Hospital Financing

Second, Owen said they have developed and expanded a flexible financing offering that she believes a number of hospitals will find attractive. On the clinical side they have completed enrollment in their total knee trial and continue to target FDA approval in 2015.

Explaining the financing offering, Owen said the financing was offered because of the capital components that exist within many of the company's MedSurg businesses. "We have been in that financing area for a number of years. What we are doing is expanding that and leveraging that expertise over to the recon side, where the MAKO capital fits, and really helping them work with some of the budget limitations that exists between capital and operating budgets within a hospital… It's something that MAKO couldn't offer to customers."

MAKO Hips for 2016

Stryker is also moving hips to the robotic platform.

Owen said they are seeing an "increasing interest" on the hips side where there is an indication for clinical use. The company expects to get approval with Triathlon on the robot in 2015.

She told analysts to think about 2016 as the year when the company is really going to be on a trajectory "where it's indicative of us taking meaningful market share gains."

Lobo said "surgeons for the most part are pretty happy with our hips, so this requires really a change management with surgeons, to really get to try it and have a good experience." But he still sees the total knee as a much bigger opportunity. "There is less overall satisfaction with patients and the perception of improvement we think is far greater than total knee. The knee still for us is the biggest opportunity."

SBi (Small Bone Innovations)

Regarding SBi, Owen said they were very pleased with the early integration and sales have been better than expected. "We have trained over 100 Stryker reps on the STAR Ankle and various products. By the time the training is complete, we will have over 200 reps trained and selling the STAR Ankle and over 400 reps trained and selling SBi's various upper extremity products."

She said most of the growth is coming from expanding the market. "We are calling on new surgeons that weren't putting in implants before. That has been really the engine of growth. The STAR ankle really fills a very important gap in the product portfolio."

Recon Market

Asked about the overall recon market, Owen and Lobo said clearly the momentum they are seeing in Europe continues, and that's helping growth outside the U.S. Owen reminded analysts that the company had some very difficult comps, particularly on the hip side. "Japan, with the price cuts have been challenging...But overall, [we] feel pretty good about the environment.

And on the U.S side?

She said it was a little tough to tell yet, because not all companies have yet reported their quarterly sales. "But in terms of hips, we feel pretty comfortable that we are growing ahead of the market, even after adjusting for MAKO. For the past eight quarters, we have kept pace with the market. We may be a little trailing in that this quarter. It does seem like overall, this is a year where the hip market is stronger than the knee market."

Regarding seasonality, she said analysts will see a similar dynamic recognizing that [the market] was exceptionally strong in the fourth quarter last year.

"Clearly, Q4 is going to see the benefit of that seasonality."

In the U.S., hip and knee pricing was consistent with what they saw in the second quarter of this year—approximately in the mid-single-digit range.

"Dramatic" Medical Acceleration

Lobo said the company clearly saw a "nice performance" in medical last quarter and that has accelerated "very dramatically" in the third quarter. "We can see conditions in the market improving." He said they will have a better sense on how much of Stryker's growth is a growing market, versus taking market share. "My sense is, we are probably growing a little faster, but I can't dimensionalize that for you just yet."

The story on hips is not a new story, said Lobo. Somewhat like trauma, where the company has continued to sustain double-digit performance, "Hips, if you go back 12 quarters, we have been growing faster than the market, at a pretty steady rate." He attributed that to a combination of some new products like Accolade II, as well as really strong execution in the field.

With the knee business, Lobo said they have just been performing with the market, "Which is a very good performance, given that we had two large competitive launches."

Lobo on "Consolidation Disruption"

Analysts indirectly asked Lobo if Stryker would benefit from any sales force disruption from the pending Zimmer/Biomet deal.

"We are not really seeing much in the way of disruption yet. As we saw with the previous big acquisition [DePuy/Synthes], the disruption really didn't occur sort of post-implementation. Once implementation begins and people really understand 'what does this mean to me?' that's when we really start to see disruption. So I would say it's sort of business as usual right now, and we are seeing a pretty stable marketplace, at least at this point. Once the companies integrate, that's usually when we tend to see more turmoil."

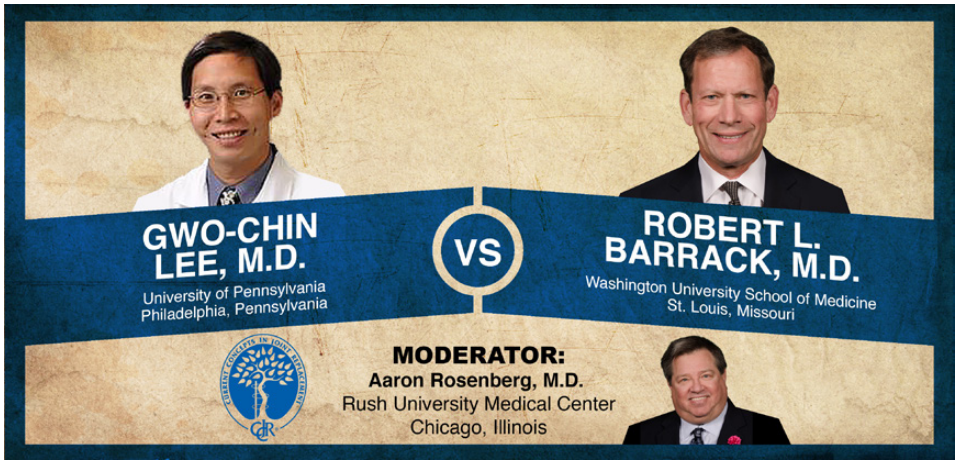
Stay Tuned

Lobo, Owen and company continue to maneuver around the existing and in-the-making ortho superpowers, DePuy Synthes and Zimmer/Biomet with big bets on robots and extremities. With a new beachhead in Amsterdam, the ortho world waits to see if Stryker has London and Smith & Nephew in their sites. Stay tuned. ♦

Lee Debates Barrack: Ceramic-Ceramic THA

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

This week's Orthopaedic Crossfire® debate is "Ceramic on Ceramic Total Hip Arthroplasty: A New Standard." For the proposition is Gwo-Chin Lee, M.D. of the University of Pennsylvania. Against the proposition is Robert L. Barrack, M.D. of the Washington University School of Medicine. Moderating is Aaron Rosenberg, M.D. from Rush University Medical Center.



Current Concepts in Joint Replacement/RRY Photo Creation

Dr. Lee: "I use polyethylene in most of my total hip arthroplasty (THA) patients, but I think there is a role for alternative bearings. Work by Kevin Bozic et al. found that the most common reasons for revision in the U.S. are: instability/dislocation (22.5%), mechanical loosening (19.7%), and infection (14.8%). Because of instability we have seen a trend towards larger heads."

"If you stick to 28/32mm heads then highly crosslinked polys will wear well in the long run, but that's not what we are seeing clinically. We are seeing 36mm heads on small cups such as 50/52mm. As for volumetric wear, I don't know if we can measure that accurately and I question whether we have the tools to measure wear sensitively."

"There has been a recent resurgence of ceramics, primarily driven by the appetite for larger heads. There have been an increased number of head size options, and the reliability of ceramics in terms of fracture rate continues to improve. And the issue of trunionosis is driving the use of ceramic ball heads because there have been some reports showing that these heads may be more trunion friendly on these modern hip designs."

"Ceramics are ideal because: they have the lowest in vitro wear rates, they are hydrophilic and wettable. And unlike metal on metal, it's inert and biocompatible…meaning that there aren't issues associated with soft tissue toxicity and local tissue reactions."

"If we look at the clinical results of ceramic in THA we see favorable numbers (from 92-100% survivorship) with relatively low complication rates. A study by Kim et al. in patients 30 years old and younger found a 99% survivorship at a mean follow-up of 14.6 years. Our institution has had similar results with young, active patients, namely, high survivorship and low complication rates. When we discuss survivorship it's important to stress clinically relevant durability. These patients will continue to be very active despite having THA."

"In some studies where ceramic-ceramic has gone head to head against metal-polyethylene, the former have shown less osteolysis and less measurable wear. So why not ceramics for everyone? There have been fewer options (until recently), risk of fracture, risk of squeaking, it's less forgiving, and in some instances cost is an issue."

"The clinical fracture rate is actually relatively low. Taking into account 13 studies from 2008-2012, the fracture rate is low (0.6%). As for squeaking, a 2014 meta analysis by D.H. Owen et al. showed a 4.25% squeaking rate with only a 0.2% revision rate for squeaking."

"Our group participated in a retrieval study looking at fretting and taper corrosion—using a matched control study with ceramic ball heads and metal ball heads. Ceramic ball heads showed less taper fretting and corrosion compared to matched metal ball heads."

"I'm not advocating ceramic-ceramic arthroplasties on everybody…not everybody should be allowed to drive a Ferrari. Just ask Adolph Lombardi what happened last time he allowed me to drive one of his cars."

"If the definition of 'standard' is that it's a level of quality or achievement that is

desirable, then I propose that ceramics are today's standard. They show better wear, they are more reliable, and there are more options (particularly in the larger heads)."

Dr. Barrack: "There is a role for ceramic heads, and some of the advantages just mentioned are particular to the head; the head helps protect the trunion. But the debate is on ceramic-ceramic, not ceramic-poly; I frequently use the latter, but I never use the former. What we just heard was that it was not a standard…that it may be occasionally indicated. But I would even take issue with that."

"Hard-hard bearings became popular in the first decade of this century. Since that time there's been a major decline in enthusiasm for hard-hard bearings. There has been a renewed enthusiasm for ceramic-ceramic because of improvements in manufacturing, taper tolerances, higher strength, and a lower wear risk."

"In spite of these major improvements, concerns were expressed with the new generation of ceramics. In 2004 I published a paper on this topic in *Clinical Orthopaedics and Related Research* with Dr. Corey Burak and Dr. Harry Skinner. Dr. Skinner actually has a Ph.D. in ceramic engineering and was one of my mentors. The concerns included the fact that even with these improvements we continue to see problems with modularity, fracture, taper limitations, stripe wear, limited surgical options… and squeaking and impingement in particular."

"The conclusion [from our study] was: 'Although ceramics show promise as a lower wear articulation, manufacturing and design modifications and improvements will continue in an attempt to address the substantial concerns that persist.'"

"The proposed solution was to alter the ceramic, particularly a hybrid material called Delta ceramic, a composite material made of alumina and zirconia. The purported advantages were higher strength, fewer fractures, a lower wear rate, and more options for heads (not liners). As for squeaking, we thought it would go away; lower wear and the disappearance of squeaking have not come true."

"In the current healthcare environment payers will not expend more for these expensive technologies without proof of added value. Also, we must account for variability in surgeon performance. You need more of a margin of error, which we don't have with hard-hard bearings. The current legal environment, espe-

cially in the U.S., is unforgiving of failures of new, unproven options."

"Michael Porter is a leading healthcare economist and is the architect of value based purchasing (i.e., that you have to either improve the outcome or decrease the cost in order to add value). I believe that ceramic-ceramic does neither. It doesn't improve outcomes and it increases the cost. In the investigational device exemption (IDE) study from Johnson & Johnson they state definitively that they have ceramic liner fractures."

"There is not a problem clinically with metal-poly (even in young patients). Metal-poly outperforms ceramic-ceramic. The problems are impingement, malposition, wear, squeaking, breakage, and mal-seating. A 2011 study by Lee et al. in the *Journal of Orthopedic Research* found that if the component is malpositioned then the wear rate goes up dramatically…even leading to cracking and liner damage. The problem is that there are a lot of outliers in hip replacement these days."

"Massachusetts General found that half of their total hips are outside the ideal zone, many by 10-20 degrees. Metal-crosslinked poly is very forgiving of this; hard-hard bearings are very *unforgiving*. A very high percentage of these liners are mal-seated. Work from Hospital for Special Surgery and two other centers showed that mal-seating is a problem. And squeaking was shown as an issue in work by Andy Shimmin et al (*Bone and Joint Journal*, 2013), who found that 11% of patients experienced 'noises' and 13% experienced reproducible squeaking."

"New generation ceramics are better, but the standard metal-crosslinked poly has improved even more. And the 10-15 year results cannot be improved upon. Sadly, ceramic-ceramic isn't ready for prime time."

Moderator Rosenberg: "Gwo-Chin, two minutes to respond."

Dr. Lee: "I believe the main difference in our positions is that ceramic-ceramic accounts for about 20-25% of my hip practice. I offer it primarily to patients under the age of 50. The literature shows that when you're comparing conventional bearings to ceramic-ceramic it is difficult to find that one is superior to another. But when you look at the issue of survivorship in the literature it is dealing with things retrospectively… our patient population is changing. The patients undergoing THA are under the age of 65 with perhaps another 30 years of life in them. They want to be active, so their usage rate of that material is

going to be different than what we've previously seen. This does fall into the 'theoretical advantages' category, but we shouldn't throw the baby out with the bath water."

Moderator Rosenberg: "So you're saying that with regard to ceramic liners you're practice is about 20%? And are those predominantly patients in whom you don't feel comfortable using a larger head because the plastic is too thin?"

Dr. Lee: "Correct."

Moderator Rosenberg: "Bob, at what size plastic—if you want to use a larger head—would you be tempted to use a ceramic liner?"

Dr. Barrack: "The wear data show that if you have a properly positioned component then you can go down to 4mm of polyethylene. I do that in older, less active patients, but in younger, active patients I would probably do a dual mobility hip. The assumption is that in young, active patients crosslinked poly might have a problem, but there is no evidence of that. At our center we looked at patients under 50 with CT scans and with Martell software and we have virtually no measurable wear at 10 years plus in patients under 50."

Moderator Rosenberg: "One thing that concerns me is that everyone is trying to do less invasive surgery and there is more tension on the soft tissues. I've seen that the hardest part of the case is getting the head on the trunion through a tiny incision. Gwo-Chin?"

Dr. Lee: "Proper implantation of ceramics is crucial and increases their reliability. My advice is to do the smallest incision possible without compromising your surgical technique."

Moderator Rosenberg: "Bob?"

Dr. Barrack: "It's a teaching point. If you're bound to using a ceramic liner then it's almost impossible to get concentric seating and impaction. It's dangerous to have a cocked component at the time you seat it because there are many more intraoperative chips and fractures than postoperative chips and fractures. And if you make a small incision you may not even realize that you have chipped or cracked a component in the ceramic liner. So we've introduced a new failure mechanism, yet we've not demonstrated the benefit."

Moderator Rosenberg: "Thank you, gentlemen." ♦

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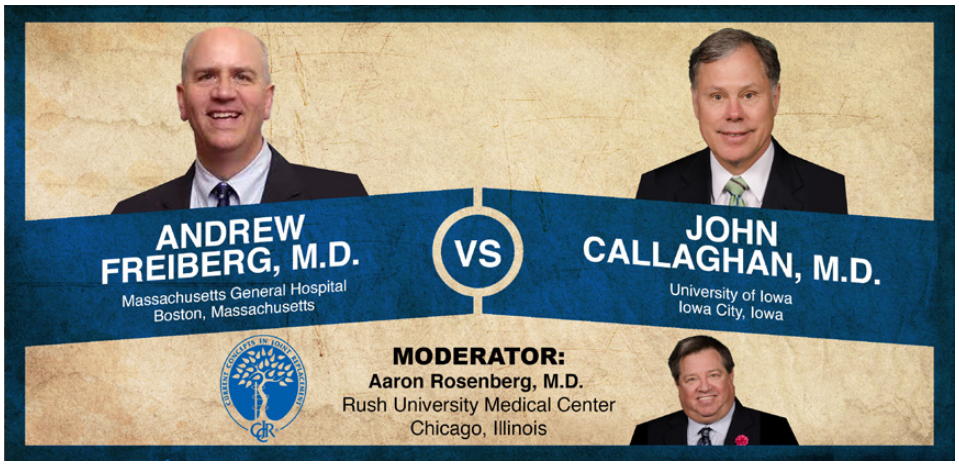
Freiberg v. Callaghan: Three Rounds Over Hip Bearing Alternatives

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

This week's Orthopaedic Crossfire® debate is "Contemporary UHMWPE's: All Our Burdens Now Over." For the proposition is Andrew Freiberg, M.D. of Massachusetts General Hospital (MGH). Against the proposition is John Callaghan, M.D. of the University of Iowa. Moderating is Aaron Rosenberg, M.D. from Rush University Medical Center.



Current Concepts in Joint Replacement/RRY Photo Creation

Dr. Freiberg: "I'll open by saying that I think highly crosslinked polyethylenes (HXLPEs) are the most significant advance in arthroplasty this decade. They have dramatically decreased revision rates, allowed younger, more active patients to have surgery, dramatically altered the revision for osteolysis and wear, and eliminated liner exchanges. And it's given perhaps millions of patients lifetime procedures."

"It was only about a decade ago that we would see retrievals such as hips with adhesive and abrasive wear with early failure, with adhesive and abrasive delamination wear in the knee…with the common problems being osteolysis, implant loosening, and failure. Poly wear in a patient with conventional polyethylene limited patients' activity and caused early failure with bone loss and osteolysis."

"By studying retrievals we came to understand how hip and knee replacements wear. The concept of crosslinking came from using this type of scanning micrograph that shows surface changes where there are these fibrils of material that could be pulled off the surface. So the idea was to make the surface more resistant to this type of wear and debris generation. Crosslinking binds the amorphous regions to the sort of 'spaghetti' parts between the ladders of the lamellae to make the material more resistant to wear as well as durable enough to handle third body debris."

"I'm guessing that Dr. Callaghan will tell you that HXLPE is new, and that the long term results are not known. (not true) He will say that crosslinked polyethylenes have inferior properties and that this can lead to failure. (that is extremely rare) And I think that John needs something other to do in retirement than garden."

"One study looking at the long term success of crosslinked bearing surfaces—a randomized level 1 clinical trial—found that at seven years the mean steady state wear rate was .005mm/year. (Thomas EG, et al, *JBJS*[Am], 2011) The early bedding in/creep of the material was a bit higher in crosslinked surfaces; the wear rate, however, was extremely low."

"Regarding RSA (radiostereometric analysis) techniques, when using the Longevity (36mm heads), out to 10 years we had very low wear rates. In our patients with a vitamin E type liner (32mm heads), out to five years, we found that the early bedding in is a bit lower, but the wear rate is the same as other melt-irradiated bearings—extremely low in the long term. At MGH there has not been a single revision for wear or osteolysis using crosslinked bearing surfaces."

"The Australian registry shows that there is a difference (in matched patients) between those with metal and crosslinked bearings or metal and non-crosslinked, with the crosslinked patients having a much lower revision rate. This is because the conventional polyethylene patients have a much higher rate of wear and loosening as a cause of revision surgery; it begins at around four or five years postop."

"If we look at the traditional pathways for crosslinked polyethylene market

introduction, we see that these materials have usually been first introduced to the hip. This is because it's easier to measure wear, because RSA can show if there is any effect on fixation, and because the wear environment is less harsh than in a total knee arthroplasty (TKA). When introducing these into TKA we are more dependent on wear simulators and registry data."

"If you examine total knee data from the Australian registry in a single knee system—the only difference being the bearing surface—there is a dramatic difference in long term revision rate between the crosslinked and conventional bearings. The reason for revision in the conventional bearings is aseptic lysis from poly debris."

"As for fatigue and fracture toughness; depending on how the material is tested (and what material is used), some of the crosslinked bearings can have decreased strength compared to conventional materials. These liner fractures are due to component malposition and are quite rare."

Dr. Callaghan: "I'm not here to debate that HXLPEs have not provided a tremendous improvement in bearing surface wear of total hip arthroplasty (THA) constructs, especially in the first decade. But, with good THA and TKA design and gamma irradiated in air polyethylene, the first decade is not where we see problems related to wear. We did a 35-year study of the hip and a 20-year study of the knee; with both it was in the second decade that problems started to occur."

"Our own data is very good for HXLPE; 5 Mrad re-melt, somewhere around 0.04mm/year with 28mm heads and a steady state wear rate of 0.04mm/year. And in those first two years there is a lot of creep. In our under 50 patients it was exactly the same as our older patients."

"So there have been great improvements over what we had, but they're not perfect. My concerns about the future are that the second decade is when wear issues become clinical issues. These issues are fracture; wear with larger heads, frictional torque, and use of polyethylene in knees (where we don't have much data). McKellop

pointed out years ago that you should keep wear rates below 0.1mm, and that if you do that, you'll have a good chance of avoiding osteolysis."

"There's no question that the more you radiate that polyethylene, the lower the wear rate. But as Andy indicated, even with just a 5 Mrad re-melt you decrease the initial strength of that material. Dr. Seth Greenwald has pointed out that it's not really the dome in the wear area, it's that these capturing mechanisms on the edges have high stresses…and if you have a material that is at all weak, then that's where you'll see the problems."

"As Andy has pointed out, some of it is related to technique. Roy Crowninshield and Bill Maloney found that the more vertical the cup you put in, the higher the stresses. But indeed they occur, and components that are malpositioned can have the same problems as the hard bearings."

"Regarding the head size issue, in wear simulator studies there is still a higher wear rate with HXLPE when compared to the controls. And that's just the tribology of sliding distance…it's going to happen. Lachiewicz has just shown with a 10 Mrad polyethylene and larger head sizes he saw more wear. And just as of September 2014 Lachiewicz found that he had 14% small osteolytic lesions associated with larger heads."

"We know that there's re-melt and annealing; the problem with the latter is that you reduce the free radicals, but you still leave some. And because some remain there may be oxidation. There is data to support this. However, you're also seeing this occur with re-melted polyethylene, which takes out the free radicals. Andy's own group has shown that lipids can diffuse into those regions, however, cyclic loading can also cause oxidation; we are seeing some oxidation in retrievals. With vitamin E there's no question that you can keep the strength while still getting the crosslinking."

"The one thing that's raised its head with crosslinking is that you might have increased frictional torque, which may be related to the trunion issues we are seeing. Recently, Menenghini has shown that with vitamin E there is substantial increase in torque. In the knee we have only one study, and that's where the capturing mechanisms might be the biggest problem."

Dr. Freiberg: "The two pictures you showed on strength and risk of liner fracture, well, John, I've seen everywhere in the world. I think the incidence of that is really at the case report level. Then there is lipid absorption and changes in crosslinked density that may occur on the surface of some of the crosslinked bearing surfaces. I think that's a real phenomenon; the question is, 'Does it affect wear rate?' You might have lipid or squalene absorption, oxidation, or changes in crosslinked density. But in our RSA studies we haven't seen any increase in wear rate at the midterm."

"As for frictional torque, I'll take issue with what you said about a 'dramatic' difference in frictional rotation because it's my understanding that the data show 8.5 or 9.5 rotations versus 11 on a pendulum comparator."

Moderator Rosenberg: "Dr. Callaghan?"

Dr. Callaghan: "Fracture remains a concern, and I agree that we don't even know how much frictional torque would have an effect on the trunion… and then there is the oxidation issue."

Moderator Rosenberg: "There is still concern about bigger head sizes showing variation in the results in terms of the amount of wear. Andy?"

Dr. Freiberg: "If you step back and look at head size there are two issues. One is wear and the other is the effect on the trunion. If I go to a 36mm head I use a ceramic head. For a 32mm head I do it by age."

Moderator Rosenberg: "What are your age cutoffs?"

Dr. Freiberg: "John's age."

Moderator Rosenberg: "John?"

Dr. Callaghan: "I try to stay 32mm and below; the older the patient the more I will go up. As you go to 36mm, some of the manufacturers will let you use very thin poly out at the edge, which concerns me. And the larger heads are going to wear a bit more than the smaller heads."

Moderator Rosenberg: "The recent claim that vitamin E increases the frictional torque makes me nervous because that wasn't on anyone's radar screen. So I wonder how much of a clinical track record would you hope to have before you can recommend switching from a HXLPE that's working well to a new poly that MAY be better?"

Dr. Freiberg: "It's our duty to study these materials, so I think it depends on what the clinician is comfortable with."

Moderator Rosenberg: "Thank you, gentlemen." ♦

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COMPANY

NovaBone Ups the BioGlass Ante With Two New Products

NovaBone Products, LLC, a biomaterials company located in Jacksonville, Florida, is expanding its portfolio of bioactive bone void fills with two new products based on the combination of bioactive glass and bovine collagen. The products are called MacroFORM Packable Graft and MacroFORM Composite.

The first combines 85% bioactive ingredient with collagen in a mixing cup while the second combines 90% bioactive ingredient with collagen in a preformed strip. Company officials claim that MacroFORM's highly bioactive collagen scaffold is engineered to have an open porous structure to enhance the absorption of bone marrow aspirate and facilitate bone growth. Both products can be manipulated into a putty format after mixing.

"Since its inception, our company has developed numerous formulations and delivery systems that accelerated bone growth," said NovaBone's President Arthur Wotiz. "We are especially proud of this collagen-based product and will continue to pioneer collagen grafting options," he added.

In 2005 the Food and Drug Administration authorized use of the term "osteostimulation," to describe how bioactive products signal genetic pathways to accelerate the regeneration of bone. Officials of NovaBone claim that their product was the first bioactive synthetic bone graft product to be offered to the orthopedic community. — *BY*

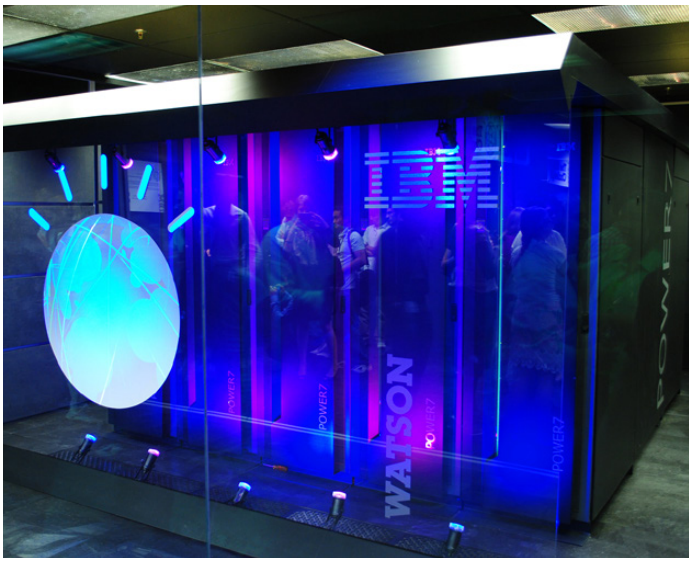
Courtesy of NovaBone Products, LLC

IBM's Watson Supercomputer Improves Clinical Studies at Mayo

At any given time, patients at the Mayo Clinic, headquartered in Rochester, Minnesota, are participating in 8,000 clinical trials. Beginning next year the process of matching patients to appropriate trials—currently done manually—will be taken over by Watson, IBM.s supercomputer. The plan is for Watson to take over much of the work of comparing a patient's characteristics to the inclusion/exclusion criteria for recruiting participants in clinical trials.

Mayo Clinic's goal is to double the proportion of patients that take part in clinical research and bring the number up to 10%, according to Nick Paul Taylor, writing in *FierceBiotechIT*. "Using Watson's cognitive computing capabilities, Mayo Clinic can consistently offer more cutting-edge medical options to patients and conclude trials faster," IBM SVP Mike Rhodin said in a statement.

Taylor wrote that IBM is designing a version of Watson specifically for the needs of Mayo Clinic. The process involves adding details of all the clinical trials underway at Mayo Clinic—plus those on ClinicalTrials.gov—to Watson's library. Watson is also being trained to find matches between the trials in these resources and health records of patients at Mayo Clinic. — *BY*



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BIOLOGICS

Infection Progress From TJU, NIH

Infections and their treatment are on the mind of every orthopedic surgeon. New work from scientists at Thomas Jefferson University and the National Institutes of Health (NIH) is giving insight into the why infections tend to be so difficult to get under control.

"Biofilm formation has been suspected to play a key role during septic arthritis and prosthetic joint infection." said Noreen Hickok, Ph.D., associate professor in the Department of Orthopedic Surgery in the Sidney Kimmel Medical College at Thomas Jefferson University, in the October 2, 2014 news release.

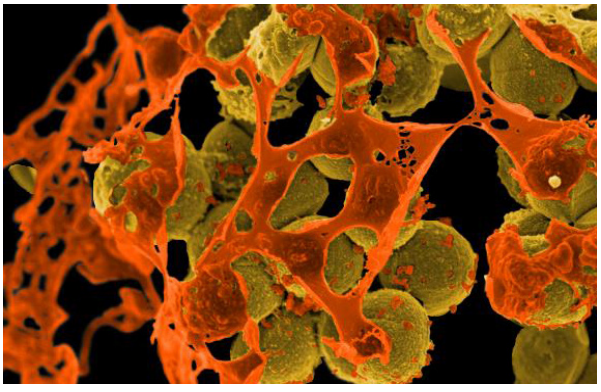
The team, also led by co-investigator is Michael Otto, Ph.D., a senior investigator with the Laboratory of Human Bacterial Pathogenesis National Institute for Allergies and Infectious Diseases, National Institutes of Health, set out to determine whether the bacteria behaved differently in the synovial fluid. After growing several strains of methicillin-resistant Staphylococcus aureus (MRSA) the team found that the "bacteria begin to grow as clumps in the synovial fluid, and that these clumps share many of the same properties as biofilms. They also found that the bacteria slow their growth, making them even less susceptible to antibiotics, which are designed to target rapidly growing cells like bacteria."

The study, published in *Journal of Infectious Diseases*, indicates that the biofilm clumps could be prevented by "pre-treating the synovial fluid with a plasmin enzyme that degraded the protein matrix. With this pre-treatment, the research team reduced the formation of bio-floater clumps and increased the bacterial susceptibility to antibiotics."

"The study also helps explain why joint infections are so difficult to diagnose, even when there are overt signs of infection," said Dr. Hickok.

Dr. Hickok told *OTW*, "The important message is that MRSA and methicillin-susceptible Staphylococcus aureus become biofilm-like as soon as they enter the synovial environment. Thus, we would expect large numbers of bacteria within these floating biofilms to survive addition of many different types of antibiotics. These results suggest reasons for the difficulty in eradicating established joint infections. They also suggest that the choice of antibiotics for peri/post-operative prophylaxis may need to be re-examined."

"These floating biofilms can be induced to be antibiotic susceptible if they can be dispersed…conversely, if the aggregation can be inhibited, the bacteria in the synovial environment would regain some degree of antibiotic susceptibility. Our future research on this topic is aimed at creating new therapies that can aid in the disruption of these aggregates to restore full antimicrobial susceptibility." — *EH*



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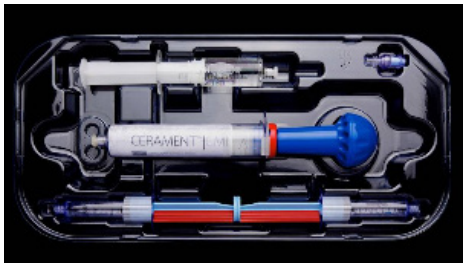
Bonesupport

Aces Twelve-Month Trial

Bonesupport, a maker of injectable bone substitutes for orthopedic trauma, has reached the 12-month point for follow-up data on a clinical trial investigating the safety and efficacy of Cerament|G—used to treat chronic bone infection.



Courtesy of Bonesupport

The data reported on a series of 41 patients with chronic osteomyelitis present for a mean of 10.4 years. Thirty-two of the patients had undergone previous surgery. The mean follow-up time was 13.2 months. Cerament|G is the first injectable antibiotic eluting bone substitute that is indicated to promote and protect bone healing that is being jeopardized by infection, according to the release.

The results were positive. Results showed complete wound healing in all patients treated with Cerament|G, and full bone remodeling of the void in 75%

of patients at six months with evidence of ongoing bone remodeling in 80% of the remaining patients.

"These clinical trial results provide important evidence and confidence for surgeons that Cerament|G provides a safe and effective delivery of antibiotics into bone defects and is an important advance in the management of chronic bone infection," said Martin McNally, M.D., presenter and lead surgeon of the Bone Infection Unit at the Nuffield Orthopaedic Centre in Oxford, United Kingdom.

He added, "Moreover, Cerament|G was administered in a one-stage procedure and demonstrated concomitant in-growth of new bone in many cases, with significantly low rates of infection recurrence (2.4%), wound complications and fracture rates as compared to previous published series using other absorbable carriers."

Lloyd Diamond, CEO of Bonesupport, expressed pleasure at the 12-month study reports. "This evidence reinforces our belief that Cerament|G has the potential to impact the surgical strategy for managing osteomyelitis, by providing a more effective delivery of antibiotics with concomitant full bone healing in a one-stage procedure, thereby reducing treatment time, minimizing surgical interventions and lowering healthcare costs."

Osteomyelitis is a $1.7 billion market where prolonged, long-term antibiotic therapy, repeated surgical interventions and the threat of amputation are the current standard of care. Rates of osteomyelitis are rising, due to infections, diabetic ulcers, war and sports injuries and antibiotic resistance. — *BY*

New Cautions for Metal Implant Allergies

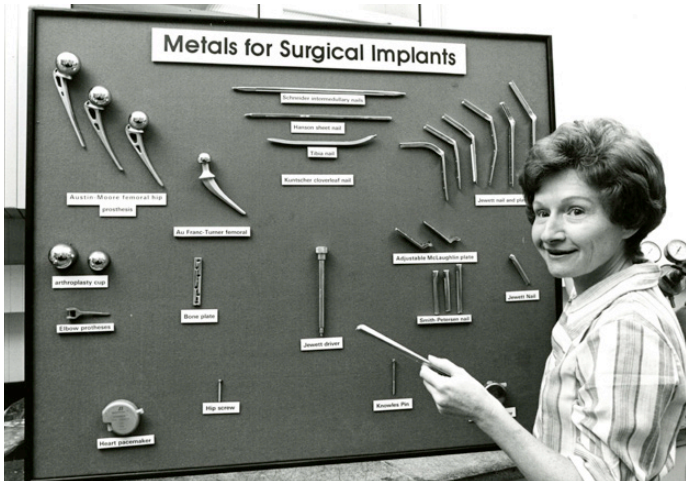
A patient who developed a skin rash after having a metal rod implanted to repair her fractured ankle alerted researchers to a skin cancer that is linked to a patient's allergy to a metal orthopedic implant. Some people are allergic to metals such as nickel, cobalt and chromium—the same metals used to make orthopedic implants stronger and more durable. Research, reported by Michael C. Purdy, senior medical sciences writer at Washington University School of Medicine, suggests that patients with allergies to metals may develop skin rashes from their implants. And these inflammations have the potential to turn into an unusual and aggressive form of skin cancer known as Marjolin's ulcer.

Researchers at Washington University School of Medicine and Barnes-Jewish Hospital in St. Louis published their findings about metal allergies and implants in the *Journal of Clinical Investigation.*

Purdy reports that the patient's diagnosis with Marjolin's ulcer, an invasive and potentially deadly squamous cell cancer, surprised physicians. To find out if inflammation from the metal rod in her ankle could have caused the cancer they turned to mouse models. "This model supported cancer development so strongly that some mice developed invasive squamous cell skin cancers similar to the patient's tumor," said lead author Shadmehr Demehri, M.D., Ph.D., a dermatologist and postdoctoral fellow.

Purdy quoted Wayne M. Yokoyama, M.D., a Howard Hughes Medical Institute investigator at the School of Medicine, "A contact allergy is a different kind of reaction from allergies to pollen, pet dander or food. A contact allergy usually develops when an allergen touches the skin or is close to it. Skin rash in response to nickel and poison ivy are two common examples of contact allergies."

The investigators demonstrated that contact allergies attract inflammatory cells to the site of the reaction. If the contact continues, other cells arrive at the site forming a mix that can lead to the development of skin tumors. The case raises the question whether allergic reactions to metal implants should be determined in advance by patients planning to have an implant installed. "Allergen-free versions of some implants are available," Demehri said to Purdy. "These versions may cost more or be less durable, but for some patients with sensitivity to metals, they may be the best option." — *BY*



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LARGE JOINTS

RA Higher Readmission Rate Than OA

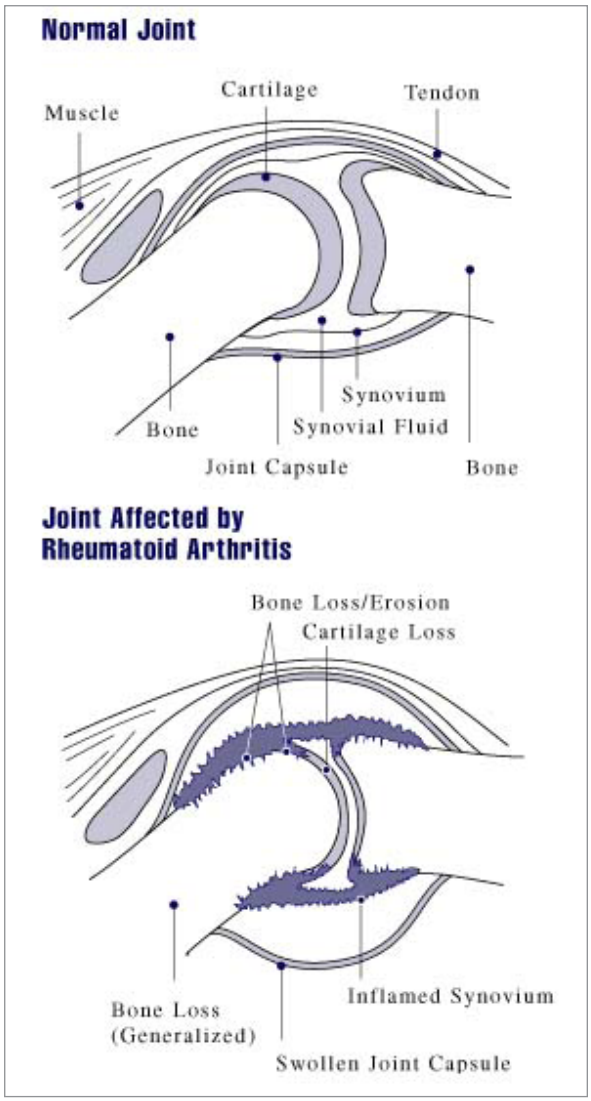
Patients with rheumatoid arthritis (RA) who have undergone a joint replacement are more likely to be readmitted to a hospital within 90 days than are patients who have osteoarthritis (OA). That is the result of a study in which investigators analyzed 34,311 joint replacement procedures performed during the three-year period from 2009 to 2011. Of the surgeries, there were 33,815 performed on OA patients and 496 performed on patients with RA.

As reported by Nicola Garrett in *Family Practice News* over the three-year period of the study, 42 RA patients were readmitted. The most common reasons for readmission were joint prosthesis infection (10.2%) and septicemia (10.2%). Of the 33,815 surgeries performed on patients with OA, 2,277 patients were readmitted. The most common reason for the readmission was joint prosthesis infection (5.7%).

The study authors noted that a 90-day readmission rate of 6.8% translates to more than 70,000 admissions annually in the United States. Garrett noted that the analysis "revealed an increasing trend in the incidence of 90-day readmissions in rheumatoid arthritis patients by year; at 5.8% for 2009, 8.9% for 2010 and 10.6% for 2011."

"We considered several patient, procedure, surgeon, and hospital variables as important covariates and adjusted for those that were significant in our multivariable-adjusted model, indicating that the increasing readmission rate in RA patients is not explained by these variables," they wrote.

Garrett noted that "the effects of medications and pre- and postoperative rehabilitation programs could have played a role in readmission rates in RA patients, but the authors did not have the information to analyze the impact of these factors." — *BY*



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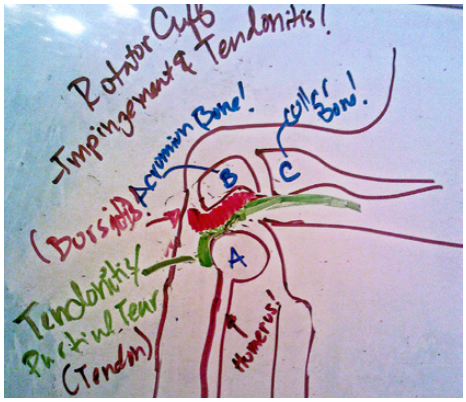
EXTREMITIES

Rotation Medical Initiates Rotator Cuff Study

Touting a bevvy of orthopedic luminaries, Rotation Medical has begun a multi-center post-market clinical study evaluating the use of its rotator cuff system in treating supraspinatus rotator cuff tendon tears. Some of the orthopedic surgeons leading the effort are Ted Schlegel, M.D., from Steadman Hawkins Clinic, Jeffrey Abrams, M.D., from Princeton Orthopaedic Associates and Timothy Codd, M.D., from Towson Orthopaedic Associates/University of Maryland Medical System, among others.



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"We are pleased to conduct this important research with these well respected and accomplished thought leaders," said Martha Shadan, CEO and president of Rotation Medical, in the September 15, 2014 news release. "The information that we gain from this post-market clinical trial will expand the body of evidence documenting the value of the Rotation Medical technology and advance our mission to provide relief for patients by reversing rotator cuff disease progression and restoring long-term shoulder function."

Patients will be implanted with a Rotation Medical bioinductive implant (used as either a standalone treatment for tendon tears or as an adjunct to surgical repair). MRIs will be used to assess post-operative changes in tendon thickness, tendon quality, and tear size; each participant will be followed for two years postop. Shoulder function will be evaluated with the American Shoulder & Elbow Surgeons' (ASES) Survey and Constant Shoulder Score.

"There are many limitations associated with the current standard of care for treating rotator cuff diseases and until this point, there has been no proven reproducible therapy to induce tendinous tissue and that has the potential to prevent the disease from progressing. As a consequence, many patients delay treatments, face lengthy rehabilitation or experience a high rate of re-tears," said Dr. Schlegel, lead investigator for the study. "This trial will add to the growing body of pre-clinical and clinical data evaluating the use of this bioinductive implant technology to improve healing at the tendon and bone interface with the goal of addressing these challenges."

Dr. Schlegel told *OTW*, "With this post market study, we seek to build on the body of clinical evidence evaluating the use of the Rotation Medical rotator cuff system in humans. Studies have shown the ability of this technology to induce the growth of new tendinous tissue. This clinical study will enable us to further explore this and better understand the clinical outcomes implications associated with this technology."

He added, "Within a year, we hope to have enrollment completed and plan to submit study results for publication. In addition, I expect that we will have significant experience using this technology in clinical practice to help patients suffering from rotator cuff disease." — *EH*

REIMBURSEMENT

Bundled Payments a Growing Practice

Bundled payments for joint replacement have come to North Carolina. According to the publication *Pharmacy Choice* doctors at Charlotte's OrthoCarolina, one of the region's largest physicians groups, have adopted a single bill with a "bundled payment" that covers pre-operative care, surgery, and follow-up appointments, 90 days of physical therapy and the services of a "patient navigator" who guides patients through the process.

OrthoCarolina is an orthopedics practice with 144 physicians working in 33 locations. The practice began working four years ago to build the system for the bundled payment plan. The practice contracted with Blue Cross and Blue Shield of North Carolina to provide joint replacement surgery for a single price for patients who agree to have their surgeries at specified medical centers.

"We get paid one price no matter how much work we do," said Daniel Murrey, M.D. and CEO of OrthoCarolina. "I'm projecting that by 2020, all of orthopedics will be paid this way. It aligns everybody's incentives to be focused on the right thing," he said.

Blue Cross, which has several similar contracts, told the writer for *Pharmacy Choice* that the bundled payments range from $22,000 to $30,000 in North Carolina. Traditional "unbundled" prices range from $27,500 to $47,300 across the state, they said.

Critics have called bundled payments "just price controls by another name." Murrey admits that complications can and still do occur, but he says that standardization leads to fewer mistakes. Doctors, he said, "get really good at it because they're (all) doing it the same way every time. We've had our best patient satisfaction and our best quality outcomes that we've ever had."

In addition to OrthoCarolina, Blue Cross has negotiated all-in-one prices for joint replacement with Duke University Health System and Triangle Orthopaedic Associates in Durham. About 1,000 members have used the plans. Because of bundled payment contracts, Blue Cross reports that it has seen a decrease of about 20% in the average cost per joint replacement, said Elaine Daniels, senior contract consultant for the insurer.

"We're seeing member satisfaction scores right out the roof. Everyone is so happy," she said. "They're getting a higher quality of care at a lower cost." — *BY*

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SPINE

Expanding Orthopedics Expands Patent Line

Expanding Orthopedics (EOI) has just has been granted its 13th U.S. patent, thus expanding its corporate footprint.

Mark Levy, M.D. an orthopedic surgeon and founder of Expanding Orthopedics, said in the October 22, 2014 news release, "My vision, since I founded the company, was to develop a unique family of expandable devices covering spine and trauma applications, creating a new standard of care. This 13th granted U.S. patent covers innovative technologies in the area of expandable interbody cages and VCF [vertebral compression fractures] solutions. This confirms our ability to develop together, with our advising surgeons, state-of-the-art devices which, ultimately, provide patients with improved clinical outcome."

Ofer Bokobza, EOI's CEO, commented, "This new patent demonstrates our continuous commitment to innovation and reinforces our position as a leading innovator in the area of expandable devices. While our Sales & Marketing team is currently focused on bringing the FDA cleared FLXfit 3D expandable cage to the U.S. market, our engineering team continues to work on the next generation of expandable devices to meet surgeons' evolving needs. We are dedicated to a continuous pursuit of raising the bar in providing a new standard of care in spine surgery."

Bokobza told *OTW,* "This patent covers several claims and devices among them are expandable cage and expandable VCF device. The company is now focused on the commercializing stage of the FLXfit, our unique 3D expandable cage, in the U.S. We have signed our first distribution agreement in the U.S. and are now in the process of signing additional distributors in the U.S." — *EH*

Expanding Orthopedics

First Surgery Using Biomet's Hyperlordotic Lateral Fusion System

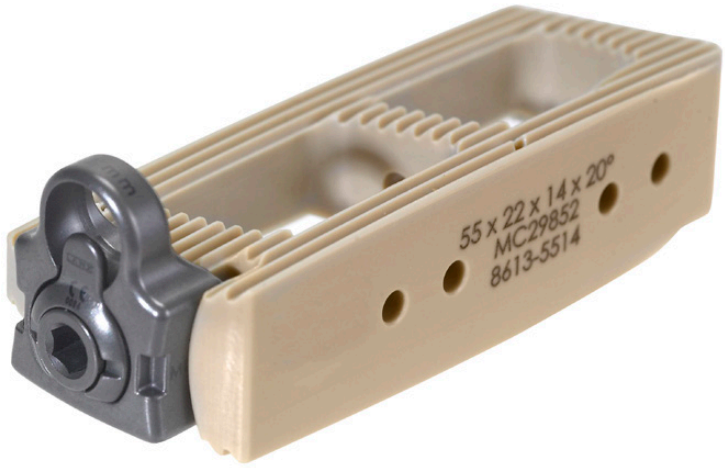
Biomet, Inc., through its 2013 acquisition of Lanx, Inc., received the first FDA 510(k) clearance for a modular plating and hyperlordotic spacer system designed to help facilitate acute sagittal correction via the lateral approach when used in conjunction with supplemental fixation.

On October 21, 2014, the company announced that the first surgery using the system.

Paul Holman, M.D., used Biomet's Timberline Modular Plate Fixation (MPF) Hyperlordotic Lateral Fusion System on a patient at the Houston Methodist Spine Center.

Dr. Holman said the system is a "fantastic addition to Biomet's Modular Plate Fixation System, allowing surgeons to achieve excellent sagittal balance restoration via a minimally invasive approach in adult deformity applications. Biomet's new system also provides instrumentation to release the anterior longitudinal ligament, which facilitates increased segmental lordosis."

Biomet's General Manager of Global Spine Jim Cloar said lateral access surgery is changing the landscape of deformity treatment options. He added that the system "has the potential to allow



Timberline MPF Hyperlordotic System/Biomet Spine

more surgeons to treat difficult pathology in a less invasive manner and to offer a more cost effective solution. The ability for a surgeon to make intraoperative decisions regarding spacer and fixation needs, and assemble the construct in situ when needed, is a distinct advantage over other available solutions."

According to the company announcement, the Timberline system features three different screw plate solutions that can be attached to a variety of lateral intervertebral spacers, including the newly cleared hyperlordotic spacer. The system also features 20° & 30° lordotic spacers in a 22mm wide footprint. — *WE*

Medtronic Claims Better Anterior Cervical Fusion System

Medtronic, Inc. has launched a new anterior fusion system that the company says makes the ACDF (anterior cervical discectomy with fusion) procedure more efficient for the surgeon and less invasive for the patient.

The Divergence system had its U.S. launch on October 21, 2014 at the Congress of Neurological Surgeons (CNS) Annual Meeting in Boston.

Traditional one-level ACDF procedures use a four-hour plate and interbody fusion cage. With the Divergence system, the company says the plate and interbody cage can be inserted simultaneously using a common set of instrumentation and one surgical technique. Traditional cervical fusion surgery requires a two-step insertion technique for the plate and interbody cage, and each implant requires its own set of instruments and its own surgical technique.

The system, according to the company, also incorporates a laterally-divergent screw insertion technique, which requires less retraction compared to the traditional medially-convergent screw insertion techniques used with other anterior cervical plating systems.

The company cited a 2013 issue of *The Spine Journal*, where Dong-Ho Lee, M.D., and colleagues published an article entitled "Anterior Cervical Plating Technique to Prevent Adjacent-Level Ossification Development." The study, says the company, concluded that ACDF patients with plates placed less than 5mm from the adjacent level disc have statistically significant increases in the frequency and severity of adjacent-level ossification disease (ALOD), a condition in which osteophytes (bone spurs) develop at the adjacent level and may become symptomatic. "The article also demonstrated that short plates allow for increased screw angulation, longer screw placement, reduced incision size, minimized dissection of the anterior longitudinal ligament (ALL) and limited encroachment by the plate on adjacent-level discs," added the company announcement.

The new system's plates are offered in relatively short lengths of 15.5mm to 20.5mm, and are designed for use with hyper-angulated screw insertion techniques.

According to the company announcement, the system's plate and bone screw components are intended for anterior interbody screw fixation from C2-T1. "The components are indicated for use in the temporary stabilization of the anterior spine during the development of spinal fusions in patients with:

1) degenerative disc disease (as defined by neck pain of discogenic origin with degeneration of the disc confirmed by patient history and radiographic studies)
2) trauma (including fractures)
3) tumors
4) deformity (defined as kyphosis, lordosis, or scoliosis)
5) pseudoarthrosis
6) failed previous fusions." — *WE*

Divergence Anterior Cervical Fusion System/Medtronic, Inc.

PEOPLE

Orthopedic World Loses Frank Cook, M.D.

Frank F. Cook, M.D., an orthopedic surgeon known for his sense of humor, left this world too soon. Dr. Cook, only 59 years of age, passed away on October 2, 2014, in Jupiter, Florida. For nearly 25 years, Dr. Cook was an orthopedic surgeon at Jupiter Medical Center (JMC). He is survived by his wife, Julie Shrewsbury; his son Skylar Cook; his mother, Dorothy Cook; two brothers, Eric Cook (Rebecca) and Andrew Cook; godchildren Michelle Williams, Mallory Rogers, Sydney Rogers, Tess Hanemann, Cole Hanemann, and Courteney Zboyen; and an extended family of in-laws, nieces and nephews. He was predeceased by his father, Donald F. Cook, a brother, Stephen Cook; and his baby sister, Nancy Cook Brocke. A memorial service was held on October 9th in Jupiter.

Frank Cook completed his orthopedic surgery residency at University Hospital (Shands) in Jacksonville, Florida. In 1985, Frank and Julie moved to Los Angeles where he completed a fellowship in Sports Medicine at the Kerlan-Jobe Clinic. In 1986 Dr. Cook relocated to Jupiter, Florida, where he entered into private practice specializing in sports medicine. Four years later he co-founded Palm Beach Orthopedics Institute, serving as its president for 10 years. In 2009, Dr. Cook opened a private practice limited to sports injuries and arthroscopic surgery of the shoulder, elbow, knee and ankle. During his career, he was orthopedic consultant to the Florida Marlins, Montreal Expos, St. Louis Cardinals, and LA Dodgers professional baseball teams.

Richard K. Ryu M.D., a longtime friend of Dr. Cook, said, "For nearly 30 years, Frank Cook was an outstanding orthopedic contributor and intellect, sharing his surgical talents and insights with many of us who shared an interest in the throwing athlete. As co-fellows at the Kerlan-Jobe Orthopaedic Clinic, I recall Dr. Cook as not only a gifted surgeon, but as one of the genuinely funniest and most irreverent people I have had the pleasure of knowing. His sartorial splendor, best described as 'Miami Vice visits Los Angeles,' was a constant source of both wonder and amusement. Always armed with a kind word for those he worked with, and quick with a quip or smile, collaborating and training with Frank was nothing short of delightful. Orthopedic surgery has lost one of its brightest lights, and his family is in our thoughts and prayers."

James E. Tibone, M.D. spoke warmly of his friend: "Frank was one of our best sports fellows and was very smart. He was a great surgeon and clinician with good hands. He was always loved by all the staff (especially the secretaries because of his Hollywood good looks). We at Kerlan-Jobe will all miss him."

Dr. Cook's obituary tells us, "Frank attended the University of Florida where he majored in Biochemistry and minored, with his best friend Ray Christian, in Rush Week Party Crashing, coursework he continued into medical school before receiving his M.D in 1980. His devotion to medicine was inspired by a singular incident at Blue Springs, Florida, when, as an undergraduate, he rescued and resuscitated a diver. Frank knew then that he would devote his life to helping others through medicine."

"His passion for physical fitness training as well as multiple sports—running, biking, swimming, baseball—made Frank ideally suited for orthopedic medicine. An athlete himself, Frank understood his patients' frustration with the recovery process and their impatience to return to the arena. Dressed in one of his trademark Hawaiian shirts for office visits, he was at one with the passion that drove his patients to push themselves. Everyone who knew him recognized that Frank's first love was medicine, but it was closely followed by his love for the ocean, and primarily surfing. Always in search of the perfect wave and the perfect rum, he traveled to many exotic locales including Mexico, Barbados, Hawaii, Nicaragua, Indonesia, the Maldives, Tobago and Australia."

"His love of the outrageous, especially in costume, was well known. At this year's black-tie JMC gala, he surprised the elegantly clad guests, including his wife, when he chose for his ensemble an authentic French Legionnaire uniform complete with epaulets, medals and braids."

John D. Couris, president and chief executive officer of Jupiter Medical Center, said, "Jupiter Medical Center has lost an incredible surgeon and wonderful friend in the passing of Frank Cook, M.D. For nearly 25 years, Dr. Cook was an integral part of the Medical Center and his death leaves a significant hole in our staff and in our community. He was an immensely talented surgeon who was deeply respected by his patients and his peers. His dedication and leadership helped transform Jupiter Medical Center into the world-class facility that it is today. He will be greatly missed. On behalf of the entire Jupiter Medical Center, I extend my deepest condolences to his family, friends and to all those who were the recipients of his expert care." — *EH*

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