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Orthopedics • This Week

week in review

4 Inside Dr. Einhorn's Hip Regeneration ◆ Media buzz is swirling around Dr. Thomas Einhorn for his successes with adult stem cells. What's the fuss all about and what does it mean for the future of biologics…and device manufacturers for that matter?

8 Europe's Spine Stem Cell Meeting ◆ Every couple years these European scientists call a meeting to compare BMP and stem cell studies for the spine. Last meeting was 2007 in Leipzig. Their work is qualitatively quite different from the U.S. meetings. Now they are meeting again. In three weeks. In Amsterdam. You should go.

11 BMPs: To Pay or Not to Pay ◆ CMS's Coverage Advisory Committee will meet on September 22 to consider and vote on the on- and off-label evidence for paying for BMPs. Read what Steve Phurrough, M.D., the former coverage director at CMS, predicts will happen.

15 Of Mice and Men in Orthopedics ◆ Drs. Charles Fisher and Christopher Bono discuss the orthopedic researcher's "Plan B"—systematic reviews of the literature. What is the purpose? The process? What obstacles do researchers encounter? Hint: the study question is key.

picture of success

28 Dr. William Martin, III ◆ Character, critical thinking, and devotion to serving others…all have led Dr. William Martin, III to his new position as Medical Director of AAOS. Dr. Martin was also Chair of the Arizona Medical Board and a "serial" entrepreneur.

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: Lessons from earnings season: Pricing pressures across the board. BUT demand continues to rise for orthopedic procedures and services. Patients get older no matter what. Healthcare reform. Oil spills. War. The joints still hurt and patients still need shots, pills, advice, rehab, and surgery—in increasing numbers.

Rank	Last Week	Company	TTM Op Margin	30-Day Price Change	Comment
1	1	Orthofix	13.51%	(5.35%)	Earnings jump 63% from last year, operating profit margin up 220 basis points, raises guidance for the year. #1 in Ortho.
2	2	Kensey Nash	38.72	(0.88)	KNSY makes 39 cents profit on every sales dollar. Cash is now nearly as high as annual sales. But growth is slow.
3	3	Medtronic	32.48	5.09	Best performer on the Power Rankings in the last 30 days. Also lowest P/E among all companies in Power Rankings universe.
4	4	Zimmer	27.69	(1.93)	Zimmer beat sales expectations for first half 2010. Ship of state is stable at Big Blue so these next 6 months should be strong.
5	7	Johnson & Johnson	27.10	1.49	Maybe last year's re-org made a different. Maybe not. Still we detect a slight uptick in operating performance.
6	8	Smith & Nephew	22.83	2.21	Narrowly beats expectations—but hits a home run in raising profitability. Huge numbers there.
7	5	Stryker	24.71	(4.86)	Ve-e-ry slow orthopedic sales growth. SYK's Med-Surg is rebounding and that saved the quarter. Down 2 places this week.
8	10	Integra LifeSciences	15.37	2.89	Whoa!—32% pop in earnings which was enough to beat consensus by about a nickel per share. Up two places.
9	9	Exactech	12.72	(7.89)	Sales rose 10% and earnings increased 14%. Decent for a small producer in an increasingly price competitive market.
10	6	Symmetry	11.48	(8.13)	As expected, 2Q sales were down but bottom line was ever so slightly better than expected. Outlook is essentially unchanged for 2010.

Robin Young's Orthopedic Universe

Top Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	Capstone Therapeutics	CAPS	$0.90	$37	32.4%
2	TiGenix	TIG.BR	$2.63	$81	27.4%
3	Osteotech	OSTE	$3.64	$66	25.5%
4	CONMED	CNMD	$19.60	$570	12.0%
5	CryoLife	CRY	$5.81	$164	8.8%
6	Medtronic	MDT	$37.81	$40,950	5.1%
7	Integra LifeSciences	IART	$37.32	$1,090	2.9%
8	Smith & Nephew	SNN	$45.37	$8,060	2.2%
9	Synthes	SYST.VX	$119.05	$14,128	2.2%
10	Johnson & Johnson	JNJ	$59.96	165,370	1.5%

Worst Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	Alphatec Holdings	ATEC	$2.39	$209	-46.3%
2	Mako Surgical	MAKO	$10.75	$363	-11.2%
3	Wright Medical	WMGI	$14.96	$587	-8.6%
4	Symmetry Medical	SMA	$9.27	$333	-8.1%
5	Exactech	EXAC	$15.76	$203	-7.9%
6	TranS1	TSON	$2.39	$49	-5.5%
7	Orthofix	OFIX	$30.05	$530	-5.4%
8	RTI Biologics Inc	RTIX	$2.66	$146	-5.3%
9	Stryker	SYK	$47.97	$19,040	-4.9%
10	NuVasive	NUVA	$32.50	$1,280	-3.6%

Lowest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Medtronic	MDT	$37.81	$40,950	11.41
2	Johnson & Johnson	JNJ	$59.96	165,370	12.71
3	Exactech	EXAC	$15.76	$203	12.74
4	Zimmer Holdings	ZMH	$53.98	$10,900	12.85
5	Kensey Nash	KNSY	$23.73	$231	12.88

Highest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Smith & Nephew	SNN	$45.37	$8,060	62.48
2	RTI Biologics Inc	RTIX	$2.66	$146	34.79
3	Synthes	SYST.VX	$119.05	$14,128	33.27
4	NuVasive	NUVA	$32.50	$1,280	26.70
5	Symmetry Medical	SMA	$9.27	$333	24.21

Lowest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	Alphatec Holdings	ATEC	$2.39	$209	0.33
2	Orthofix	OFIX	$30.05	$530	0.60
3	CryoLife	CRY	$5.81	$164	0.66
4	NuVasive	NUVA	$32.50	$1,280	0.72
5	Exactech	EXAC	$15.76	$203	0.77

Highest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	CONMED	CNMD	$19.60	$570	15.38
2	Johnson & Johnson	JNJ	$59.96	165,370	1.98
3	Symmetry Medical	SMA	$9.27	$333	1.76
4	*Average*			*$11,054*	*1.73*
5	RTI Biologics Inc	RTIX	$2.66	$146	1.51

Lowest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	Osteotech	OSTE	$3.64	$66	0.71
2	CONMED	CNMD	$19.60	$570	0.80
3	RTI Biologics Inc	RTIX	$2.66	$146	0.87
4	Orthofix	OFIX	$30.05	$530	0.97
5	Symmetry Medical	SMA	$9.27	$333	0.98

Highest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	TiGenix	TIG.BR	$2.63	$81	78.79
2	Mako Surgical	MAKO	$10.75	$363	11.58
3	Synthes	SYST.VX	$119.05	$14,128	7.83
4	NuVasive	NUVA	$32.50	$1,280	2.96
5	Kensey Nash	KNSY	$23.73	$231	2.90

Inside Dr. Einhorn's Hip Regeneration

By Jacqueline Rupp

Stem Cell/Creative Commons

In recent weeks, Thomas Einhorn, M.D., has become a stem cell savior, a doctor who is showing there's no need to go down the embryonic stem cell road full of political landmines. In fact, he's being touted as a reason why debate on the issue is not even needed since adult stem cells appear to be working just fine for his patients, thank you very much.

"Adult stem cell studies far ahead of embryonic research" and "Adult stem cell research leaving embryos behind" are just a few of the headlines to hit the street this month in relation to Einhorn's work. But behind the sound bites are some exciting prospects and progress from Einhorn's work.

For his part, Einhorn is a rather down-to-earth researcher who makes no claims of solving any stem cell dilemmas. Instead he offers up his experience as another step in a process that he has learned from his predecessors and emphasizes the need for proper patient selection in order to obtain the best results.

The Man Behind the Headlines

Thomas Einhorn, M,D., is the Chairman of the Department of Orthopaedic Surgery at Boston University and Professor of Orthopaedic Surgery, Biochemistry and Biomedical Engineering there as well. He's a graduate of Rutgers and Cornell Medical and completed his internship at UPenn before an orthopedic residency at St. Luke's-Roosevelt Hospital in New York City.

Besides bone and cartilage regeneration, Einhorn also focuses his efforts on reconstructive surgery of hips and knees and treating metabolic bone disease.

He is the past Chairman of the Orthopaedics and Musculoskeletal Study Section of the National Institutes of Health, President of the Orthopaedic Research Society, President of the International Society for Fracture Repair and Chairman for two American Academy of Orthopaedic Surgeons committees: Examinations and the Council on Research and Scientific Affairs. Today, he is on the Board of Trustees of the Orthopaedic

"The specialty that is getting Einhorn press these days is his orthopedic adult stem cell surgery for avascular necrosis (AVN) of the hip."

Research and Education Foundation and the National Osteoporosis Foundation.

Einhorn's career distinctions include publishing over 200 peer-reviewed articles and being presented with numerous awards including the Marshall R. Urist Award and the Alfred R. Shands, Jr. Award from the Orthopaedic Research Society.

Avascular Necrosis of the Hip

The specialty that is getting Einhorn press these days is his orthopedic adult stem cell surgery for avascular necrosis (AVN) of the hip.

Unlike other hip conditions, AVN's demographic is both significantly younger and broader. Most AVN patients are between 20 years to 60 years old. For these and other reasons, these patients are simply not the best candidates for hip replacements. Patients under 50 are far more active than their older counterparts and total hip replacement surgery both limits physical activity and also poses the need for revisions should the hip replacement wore out of many years of high use—as, of course, most do. Enter Dr. Einhorn's autologous stem cell therapy and the makings for a new and potentially more age-appropriate solution may be emerging.

Stem Cells to the Rescue

Einhorn has been working on this process for more than two years.

Thomas Einhorn, M.D./Boston University School of Medicine

His initial goal was to slow down the progression of AVN but as he conducted his experiments he found that the procedure appeared to regenerate bone in the femoral head. Of course, many researchers have documented the ability of autologous bone marrow stem cells to regenerate bone in several animal and some human models. But there is no substitute for seeing it yourself.

Einhorn's technique is to draw bone marrow from a patient's pelvis, concentrate it (8 ounces of bone marrow become 20 cc) and then re-inject the marrow concentrate with approximately 20 mm cells (using a specially designed drill Einhorn himself invented) into the dying bone in the hip.

Several aspects of Einhorn's autologous process and approach stand out. "In particular I was drawn to work I heard about what was going on in Paris and Brussels where they were taking patients' bone marrow, concentrating it, and re-injecting it. So I traveled to Paris and learned from Dr. Philippe Hernigou [of the Hôpital Henri Mondor]. He took a patient with avascular necrosis and that is where it all began for me," explains Einhorn.

"Bone marrow contains many different types of cells, and they interact with each other under normal conditions. So the concept of concentration with these cells accompanied by their friends so to speak that they work with all the time, means the creation of super bone marrow. This type of graft makes more sense to me than harvesting bone marrow and isolating the MSCs [mesenchymal stem cells]. You might also have endothelial cells. So I decided I was going to adopt the technique I learned in Paris."

The working theory is that concentrated cells and "their friends" will interact with each other and the surrounding environment in the avascular femoral head and stimulate new capillary and blood vessel growth while also recruiting and differentiating into new bone tissue. So in theory and perhaps (to be studied further) in fact, the therapy solves the two most critical problems associated with AVN—specifically, restoration of blood flow which led to the necrosis in the first place and restoration if not regeneration of lost bone. Einhorn adds that the necrosed tissue is actually useful as a scaffold for new osteoclasts and osteoblasts. He says the patients he's treated have been able to experience swift recoveries of about a week for full weight bearing and six months to return to vigorous physical activity.

Einhorn's patients are extolling their recoveries and some have gone from being wheelchair bound to playing soccer and bike riding.

Patient Selection

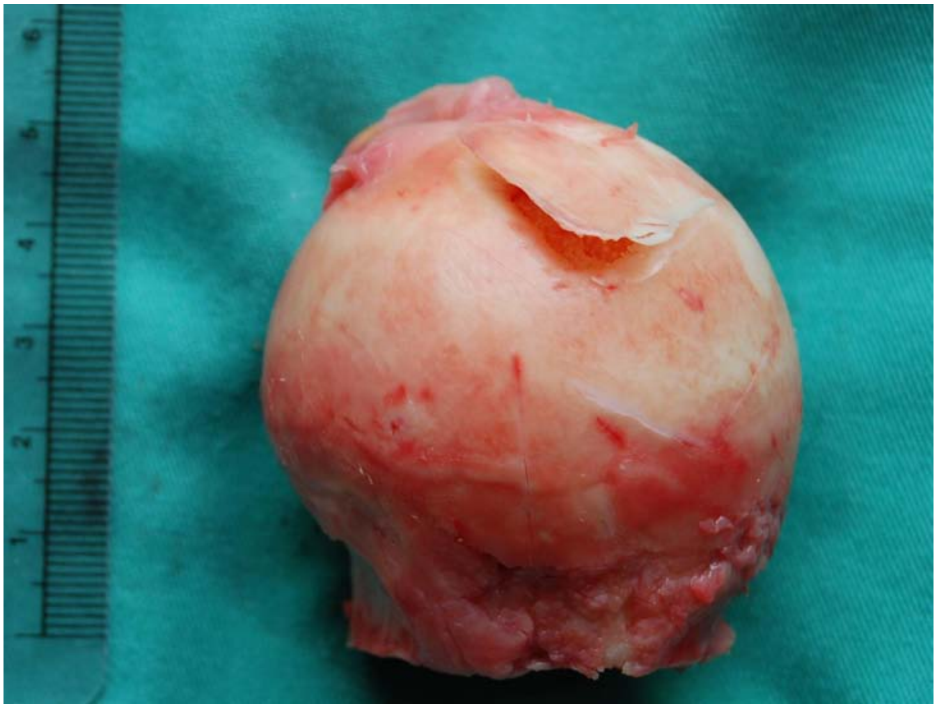
Very few physicians have attempted this type of approach to treating AVN. But Einhorn and Hernigou, two very well respected researcher/scientists/surgeons lend important credibility to this approach. Since Einhorn started treating AVN patients, the word has circulated in the patient community and he has received a barrage of patient requests. According to Dr. Einhorn, patient selectivity is so important. Specifically, success rates for this procedure are highest during the earliest stages of the disease.

"I have used the technique on 60 patients. With the Internet, people can be very resourceful about their health care and they will come to you. I believe in carefully selected patients and that is why I have an 85% success rate," explains Einhorn. "After two years we have gotten very efficient with our assessment process. Our protocol is to use assessment tools that are quantitative, such as MRIs. We use a radiographically based scale that has five categories that describe the condition of the femoral head."

Patients with categories 1 (has no symptoms, nothing on X-ray, but MRI shows damage) and 2 (femoral head not collapsed, some symptoms and MRI consistent with AVN) make for the best candidates.

"Once the hip has seen some collapse it will probably not work, so we have a very automated system of just looking at X-rays and MRIs to determine if someone is a good candidate," adds Einhorn.

He is also currently working with two knee patients, but he tells *OTW* it is too



Femoral head with avascular necrosis/Creative Commons early to tell whether this same concept will apply to the knee joint as well.

Looking Ahead

Soon the orthopedic community will have some hard numbers to digest from Einhorn. He is currently working on a four-year prospective case series study that began enrolling patients last year. The study is designed to provide organized and peer-reviewed clinical results of those patients who have received concentrated bone marrow aspirate to treat AVN.

As far as what the success of this procedure means for the device market, Einhorn believes regenerative medicine is the natural evolution. He says stem cell therapy could eventually eliminate the need for joint replacement. He says the orthopedic community is embracing this concept more every day.

Einhorn's technique, known as Bone Marrow Aspirate Concentration (BMAC), is to draw bone marrow from a patient's pelvis, concentrate it (eight ounces of bone marrow become 20 cc) and then re-inject the marrow concentrate with approximately 20mm cells (using a specially designed drill Einhorn himself invented) into the dying bone in the hip.

"I haven't done a lot to promote non-union fractures," says Einhorn. "I did one case referred to me by the Massachusetts General Hospital of this badly fractured ankle that only partially healed. After being asked if I could try treating the patient, we did and three months later it was completely healed."

NeoStem

Industry is taking notice of Einhorn's success. Last week, international biopharmaceutical company, NeoStem, Inc. (NYSE Amex: NBS) named him to its Medical Advisory Board. The plan appears to utilize Einhorn's stem cell knowledge in the development of applications of adult stem cells for orthopedic injuries. That's in addition to working on applications for NeoStem's VSEL Technology for the orthopedic community. VSEL Technology uses tiny adult stem cells that appear to mimic the beneficial properties of embryonic stem cells. And NeoStem just happens to be the worldwide license holder for this technology.

There's little doubt with so much on the stem cell horizon that we will get to revisit Dr. Einhorn's progress and enjoy some hard data from his lab in the hopefully near future. ◆

Europe's Spine Stem Cell Meeting

By Robin Young

Every two or three years a group of EU scientists and surgeons gather to compare their work with stem cells in the spine. The last meeting, in 2007 in Leipzig, presented a range and quality of work regarding mesenchymal stem cells (MSCs), embryonic stem cells, and other trophic, cellular implants that was qualitatively quite different from the kind of studies we typically see at U.S. meetings. And you are invited to join them for this year's event.

MorgueFile

BioSpine 3 convenes three weeks from now (September 1-3) in Amsterdam. Leading the way is Barend J. van Royen of the Skeletal Tissue Engineering Group of Vrije Universiteit (VU) University Medical Center in Amsterdam and joining him as co-chair is Hans Jorg Meisel of the Berufsgenossenschaftliche Kliniken Bergmannstrost (Department of Neurosurgery) in Halle, Germany. The other organizers are Marco N. Helder, also with VU Medical Center, and Theo H. Smit, from the Departments of Physics and Medical Technology at VU.

The rest of this itinerant group of regenerative medicine researchers include:

- The very eminent Frank Emmrich who heads up the Translational Center for Regenerative Medicine in Leipzig
- Robert Gunzburg who is in private practice in Antwerp but conducts some of the most interesting research in spinal regenerative medicine in Europe
- Professor of Tissue Repair and Translational Research at UMC Utrecht Wouter Dhert
- Cody Bunger who is Chairman of the Orthopaedic Research Group in Aarhus
- Dietmar Hutmacher who co-founded the Tissue Engineering Group in Queensland and was one of the leading researchers in the Singapore cellular institute and,
- Finally, one U.S. researcher, Timothy Ganey, Director of the Orthopaedic Research and Technology Development at the Atlanta Medical Center.

Having attended dozens of stem cell and regenerative technology meetings, we can say with confidence that this is one of the best. The studies are current and they cover elements of MSCs and other regenerative implants that you won't find at comparative U.S. meetings. Over the past decade, the EU was able to conduct research without many of the restrictions that U.S. researchers struggled with. The result is really, really interesting.

If you are active or interested in cellular therapies and can possibly go, you should. Here is the link to register: www.biospine.org.

Here's what we expect will be presented at the meeting (we will be there):

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1. New studies regarding embryonic, pluripotent and adult stem cells. Dr. Emmrich, for example, recently conducted a key study of allogenic bone marrow cells which showed that they can trigger endogenous hematopoiesis and faster recovery in the treatment of hematological malignancies (blood-based cancers). Dr. Emmrich is also the author of several key studies on the role of x-chromosome genes TIMP1 and IL9R in the development of rheumatoid arthritis

2. New studies regarding the treatment of stenosis using novel mechanical means to decompress. How the clinician may employ cellular therapies to treat the elderly spine patient is of great importance here. Dr. Gunzburg has written extensively about such topics as conservative and biological treatments of lumbar spinal stenosis in the elderly, treatment of vertebral fractures, and the use of interspinous implants.

Morguefile

3. New studies that dive even deeper into bone morphogenic proteins (BMPs), platelet-leukocyte gels, and various cellular implant materials and their effect on bone mineral density. We expect to see quite a bit of new information about the progression of bone mineral disease and what the clinician might consider to slow its progression. Certainly, one presentation we're looking forward to will discuss techniques of inducing BMP-2s in the patient by using <u>other</u> biomaterials and trophic implants. (It's the idea of inducing the patient's own BMP that attracts us.)

4. Of course, what self-respecting biomaterials meeting would be complete without a section on smart scaffolds? Watch for papers regarding carboxymethylcellulose collagen, or other novel materials with cellular and other trophic implants.

5. Regeneration of the disc is the new hot topic among regenerative technology researchers. Several recent studies have shown that degenerated discs can be regenerated with cellular and protein therapies. We would certainly expect to see the latest and greatest from European researchers on this subject.

6. Related to disc regeneration, we would also expect to hear more about cartilage repair studies with hydrogels, polycaprolactone collagen membrane, and other tissue engineering materials.

7. Finally, we are looking forward to papers regarding:

   a. The use of adipose-derived precursor cells in the spine

   b. Spinal cord repair strategies and technologies

   c. The use of nano particles for visualization

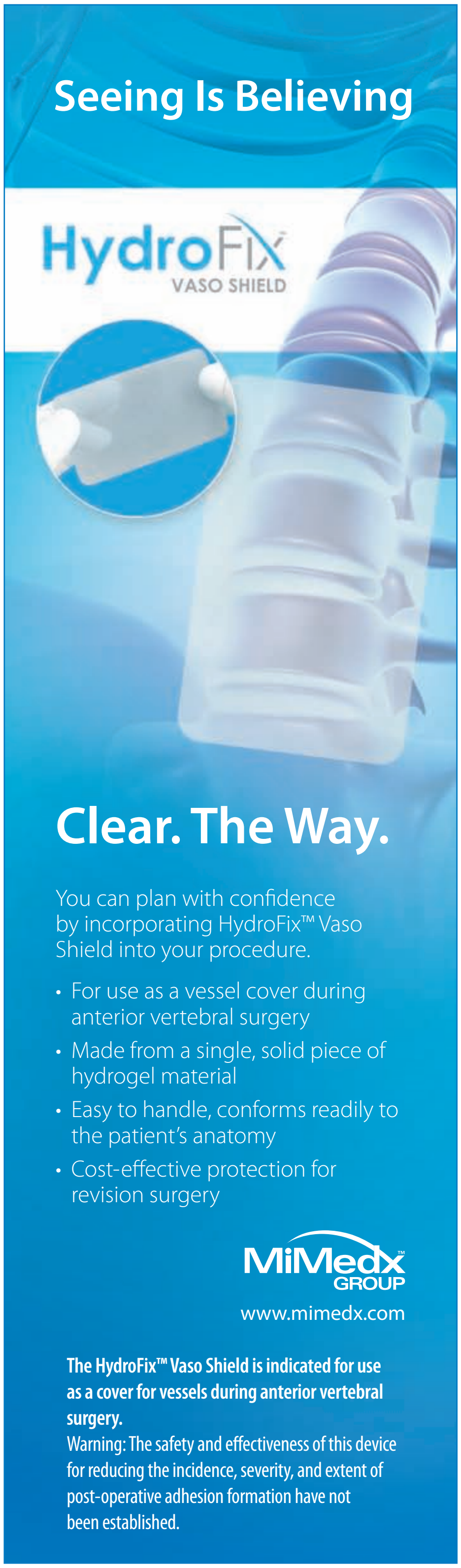
   d. New insights into minimally invasive surgical procedures

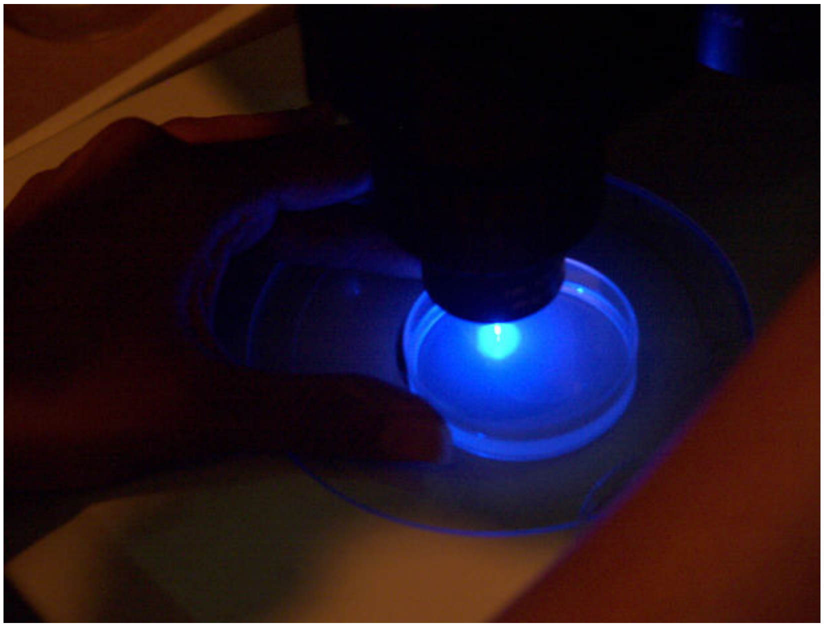
   e. Understanding and creating a risk profile for modern therapies/decision making

   f. Global regulatory issues and ethical problems

   g. Pre-validation of the patient and creating a balance of therapeutically important approaches

The entire subject of biomaterials, cellular products, and trophic implants





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has become one of the most intriguing and potentially disruptive areas in orthopedics and spine medicine. Meetings like this, which address cellular therapies, applications for growth factors, regeneration and degeneration of musculoskeletal structures are immensely valuable during this period of early adopter usage and peer-to-peer discussions.

All leading orthopedic and spinal surgeons and researchers should use these opportunities to meet directly with the researchers and scientists who are conducting these studies and discuss embryonic, pluripotent and adult stem cells, skeletal application of polymers, spinal cord repair and cellular repair strategies. Coming rapidly on the horizon are other technologies, such as nano particles for visualization, smart scaffolds and new, more conservative therapies, also tied to these trophic and regenerative technologies.

Meetings like these are absolutely essential right now and BioSpine 3, in particular, promises to bring a new and valuable perspective to U.S. surgeons and researchers. ◆

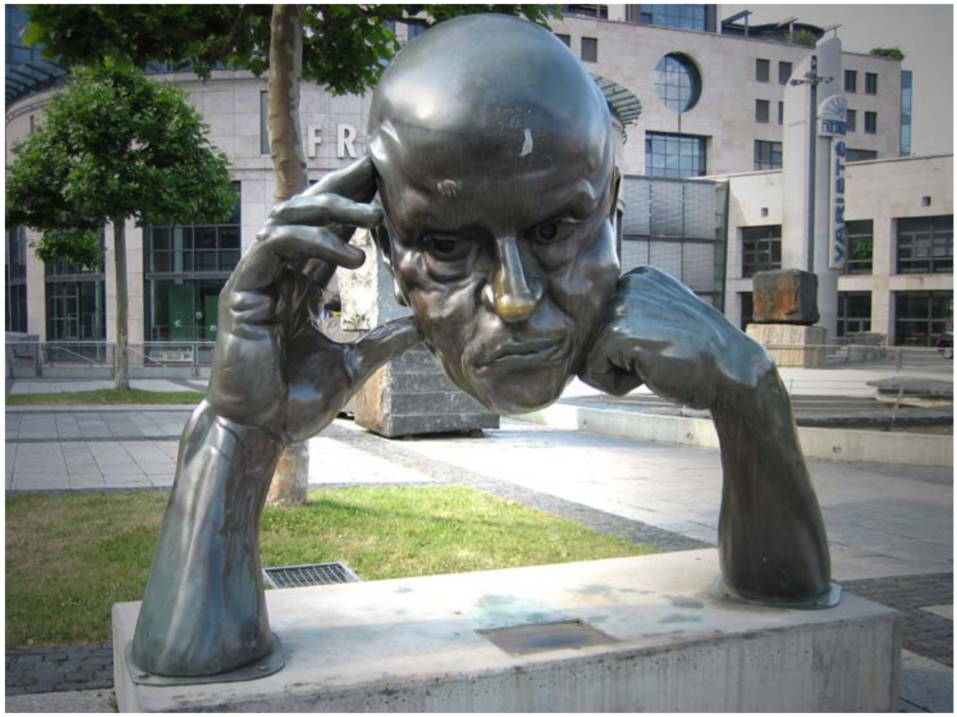
BMPs to Pay or Not to Pay

By Walter Eisner

The long and winding road for bone morphogenic proteins (BMPs) is about to reach its next destination: the Medicare Evidence Development & Coverage Advisory Committee (MEDCAC). Most recently the journey has led BMPs through the FDA's orthopedic panel, which resulted in a recommendation of approval for Medtronic's Amplify.

MEDCAC Consideration

The MEDCAC committee is meeting in Baltimore on September 22 to consider whether or not adequate evidence exists to determine the clinical benefits and harms of on- and off-label uses of BMPs. This marks the committee's first meeting to consider an orthopedic device since 2006.



Wikimedia Commons

Infuse/Medtronic

OP-1/Stryker

Specifically, the committee will look at Medtronic's Infuse [rhBMP-2] and Stryker's OP-1 [rhBMP-7], the only BMPs the FDA has approved as being safe and effective. Now CMS wants to determine if enough evidence exists to decide if the materials are reasonable and necessary.

More than 20 BMPs have been identified, but, says CMS (Centers for Medicare and Medicaid Services), only BMPs -2, -4, -6 and -7 have been shown to offer significant osteogenic properties. The main physiologic role of BMP is to promote differentiation of mesenchymal cells into chrondrocytes and osteoblasts, to promote differentiation of osteoprogenitors into osteoblasts, and to influence skeletal pattern formation.

Human BMPs are currently produced using recombinant DNA technology. CMS says the on- and off-label use of BMPs has rapidly grown since becoming clinically available in 2001. There are reports stating that up to 85% of BMP use is for off-label indications, mostly in the spine. However, a number of reports of adverse events associated with the use of BMPs have been reported.

Steven Phurrough, M.D. / U.S. Government

Phurrough's Prognostication

Steven Phurrough, M.D., is the former director of the agency's Coverage and Analysis Group (CAG). It was under his watch that a list of potential topics for coverage determinations, including BMPs, was announced in 2008. Phurrough told *OTW* that his group had met with other parts of CMS for several years discussing BMP and recognized the limited amount of information on them.

"That led to its selection for inclusion on this list," said Phurrough.

Phurrough said CAG usually announces potential topics that are being considered from internally generated requests on a quarterly basis, and allows interested stakeholders to comment on these topics. The purpose of these announcements, he added, provides advance notice regarding potential topics that CMS is considering. The agency wanted to "create a more transparent and predictable NCD [National Coverage Determination] process," added Phurrough.

Why Now?

Why are BMPs on the radar now? Phurrough said, "CMS schedules MEDCACs for two major reasons: One, to support an NCD or two, to bring to the public's attention areas where evidence is weak. CMS obviously believes that the level of evidence for use of BMP needs to be publically addressed."

Medtronic and Stryker took their opportunity in 2008 to notify Phurrough that neither company wanted the agency to consider a NCD. There are usually only three outcomes after a MEDCAC meeting. One, the agency does nothing and continues to let local carriers decide on coverage. Two, the agency issues a negative NCD, as it did for lumbar artificial discs, then reimbursement dries up. Or three, the agency issues an NCD that requires local carriers to pay for treatments and procedures, as is the case for fusion.

What does Phurrough think will happen this time? He says he believes this MEDCAC meeting falls into the category of weak evidence and CMS is "attempting to bring to full light the state of evidence for BMP."

"I don't believe that this will result in an NCD," concluded Phurrough.

Phurrough, now COO/Senior Clinical Director for the Center for Medical Technology Policy in Baltimore, advises companies to "keep the reimbursement agency's needs in mind as you design trials for regulatory approval. Don't assume that access to the market for a limited indication will always result in access for all indications."

Evidence of Improvements and Harm

Here is what CMS had to say about BMPs, as the agency detailed the specific questions it will ask committee members to answer on September 22.

"Members of the BMP family are potentially useful as therapeutics in areas such as spinal fusion. [Infuse] and [OP-1] have been shown in clinical studies to be beneficial in the treatment of a variety of bone-related conditions including delayed union and non-union...Certain off-label uses in cervical spine fusion may be associated with life-threatening complications. Is the evidence adequate to demonstrate health improvements in the Medicare population?"

Off-Label Warnings

In July 2008, the FDA issued a warning that it had received at least 38 reports of complications in the last four years, relating to the use of Infuse in cervical spine fusion.

Mike McCormack, Senior Manager, Reimbursement Planning for Medtronic's Spinal and Biologics division, addressed the use of Infuse in the cervical spine in September 2008 in a public comment to Phurrough and his coverage group.

McCormack wrote that the first warning to doctors about the off-label use of Infuse was in 2004.

"As you know, because the FDA does not regulate the practice of medicine, physicians may use an FDA-approved product for off-label indications if they believe it is in the best interest of their patients."

He noted that the majority of safety problems linked to Infuse use in the cervical spine may be due to inappropriate dosing and that using the exact volume concentration of Infuse used in lumbar interbody spine fusion may be too high of a dose for the cervical spine.

McCormack wrote that prospective studies are ongoing and designed to ensure appropriate dosage. He added that as Medtronic identifies appropriate dosages, the company believes it is important that CMS "not restrict access to rhBMP-2 for those patients that may derive benefit from it. At this time, we believe that it would be premature to initiate the NCD process on this issue."

Stryker also notified Phurrough's coverage group that the company wanted to "help CMS appreciate" that OP-1 need not proceed to an NCD.

Medical Society Conclusions

But perhaps the most detailed response to the Coverage Group's request for input on NCD topics came from the Professional Society Coalition Task Force made up of the American Association of Neurological Surgeons (AANS), Congress of Neurological Surgeons (CNS), North American Spine Society (NASS), Scoliosis Research Society (SRS), and Spine Arthroplasty Society (SAS).

The task force noted in 2008 that data suggest that routine BMP use for elective anterior cervical spine surgery does not seem to be warranted. "While appropriate dosage has been proposed as a primary factor to ensure safety, the current literature is conflicted regarding this issue...There is an overwhelming paucity of data evaluating the use of BMP in the posterior cervical spine, making any recommendation regarding its routine use difficult."

However, the task force wrote, "While the indications for the use of BMPs in spinal surgery in the Medicare population are not fully defined, substantial evidence exists supporting the efficacy and cost effectiveness of BMP in the anterior lumbar interbody fusion. Moderate and increasing evidence is being developed for its use in posterolateral fusions compared to ICBG [Iliac Crest Bone Graft]. Posterolateral fusion, in conjunction with decompression for stenosis or deformity correction, in spondylolisthesis, or degenerative scoliosis, is the most common spinal fusion technique performed in the Medicare population."

The task force believes that BMPs are, "a reasonable and safe alternative to ICBG in anterior interbody lumbar fusion. For posterior spinal fusion, there is moderate and increasing evidence that BMP is also beneficial. We also believe that ongoing additional investigation will contribute to refinements in dose, carriers and site specific applications for these valuable biologic technologies."

In the anterior cervical spine, the group said the evidence is limited and there remain unanswered safety concerns and the group "does not support its [BMPs] broad use except in ongoing research trials."

Coverage Advice

In a somewhat surprising set of conclusions, since CMS only asked about the available medical evidence, the task force offered the following unsolicited coverage advice to the Phurrough coverage group.

- Anterior Lumbar Fusions—Recommend coverage in Medicare and non-Medicare patients without severe osteoporosis.
- Posterior/Lateral Lumbar Fusion—Delay decision pending publication of upcoming literature.
- Posterior Interbody Fusion—Literature is insufficient to make recommendation. Further study should be encouraged.
- Anterior Cervical Spine—The use of BMP should not be covered/approved for routine use in the cervical spine. The use of BMP for complex, revision, or salvage situations may be appropriate in certain cases. Such cases should be considered on an individual basis. Further study should be encouraged.
- Posterior Cervical/Thoracic Spine—Literature is insufficient to make recommendation. Further study should be encouraged.

We hear from sources that this same coalition is developing another joint response. NASS Council Director William Mitchell, M.D., told *OTW* that NASS was "in the process of reviewing the BMP literature and will be preparing our findings to present to MEDCAC."

MEDCAC Voting

The testimony before MEDCAC will be followed by a vote. Committee members will show their confidence on a scale from 1 to 5 as to whether or not there is adequate evidence to determine whether the use of BMPs for a list of indications "improves at least one of the clinically meaningful health outcomes." To answer whether there are clinically meaningful health outcomes, CMS will center their focus on the criteria of: pain, patient function and adverse events.

The long and winding road for BMPs may lead to a homecoming. We'll be there and leave the light on for you. ◆

Of Mice and Men in Orthopedics

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

Deutsches Bundesarchiv:Eric Zühlsdorf/Wikimedia Commons

"So if you participate in our study, you may or may not undergo surgery. Are you interested?"

The patient—living in pain, mind you—would likely wonder if indeed this surgeon had all of his marbles.

Dr. Charles Fisher, a spine surgeon at the University of British Columbia, states, "In a perfect universe, orthopedic researchers would be able to assess the effectiveness of a given procedure by comparing those undergoing surgery and those not taken to the OR. We are dealing with humans beings, however, who quite naturally are reluctant to play roulette with their health."

The most highly regarded form of research is the meta analysis, an "animal" rarely seen in orthopedics. Dr. Fisher, who also holds a Masters Degree in Health Care Epidemiology, explains, "In performing a meta analysis you take a number of studies with similar methodology and data, and combine them to obtain more study power. This could result in a very high quality effort if in fact you have a number of Level I, randomized controlled trials (RCT) on the same subject. In most surgical disciplines, however, there isn't that degree of quantitative data that would make this possible."

Christopher Bono, Chief of the Orthopedic Spine Service at Brigham and Women's Hospital, concurs, and discusses the orthopedic researcher's "Plan B." "Because it is extremely difficult to pursue a true meta analysis in orthopedics—the exception being drug studies—the growing trend is to perform systematic reviews of the literature."

Such reviews, says Dr. Fisher, are increasingly popular because they are objective and are evidence based. "In the past, key thought leaders would be asked to write a review article and they would go perform a literature search and write the article. When it's just one person doing this, though, bias naturally comes into play, starting with the fact that they are reviewing literature *they* want to include. Times have changed, however, such that there is now a transparent methodology with at least two reviewers, and standardized inclusion and exclusion criteria for the papers that will be reviewed. It will not give you the same power/numbers of a meta analysis, but it is much more objective and powerful than our research of the past."

Breaking down the systematic review process, Dr. Bono says, "You (and at least one other researcher) first define the study question, i.e., 'Does the operative treatment of hip fracture result in lower mortality?' Then you do a literature review, preferably with the restriction that you will only include RCTs. While this usually limits you to a small number of articles, these are the highest quality studies. I recommend engaging the help of a medical librarian so that you can be confident that you have accessed all of the

"Because it is extremely difficult to pursue a true meta analysis in orthopedics—the exception being drug studies—the growing trend is to perform systematic reviews of the literature."

Dr. Marcus Gossler

relevant databases and used all of the appropriate search terms. To the latter point, for example, if I am interested in lumbar fusion and perform a search only on the term 'fusion,' then I would miss the articles that would be revealed by another search term, such as 'arthrodesis.'"

He continues, "Then you review the articles in detail, along the way distilling the information from the articles into a tabular format and assigning levels of evidence. Note that while each article already has a level of evidence, as part of this process you can downgrade them based on your review. For example, Journal X may say that a certain article is a Level 1 study, but because there was less than 80% follow up you determine that it is a Level 2. Afterwards, the team critiques the methodology, then looks at all of the articles and tries to answer the initial study question. Finally, you draw conclusions based on conflicting and/or supporting evidence."

As for Dr. Fisher, he puts a fine point on the fine art of study selection. "When you are determining your inclusion and exclusion criteria, you should think about whether you want to include only studies with similar outcomes. For example, if you want to combine the data of two studies looking at the outcome of operations to reduce pain then you should ensure that both studies used the same outcome tool, i.e., the Visual Analog Pain Scale. Additionally, the patient populations should not be too dissimilar…it is not a good idea, for example, to combine 25 year olds with 80 year olds."

And where can researchers go astray? Dr. Bono notes, "In defining the study question investigators may propose an unanswerable question, something that leads to misleading conclusions that can, for example, result in an insurer denying coverage for a procedure. For example, if I did a systematic review of the operative treatment of clavicle fracture nonunions, I would likely find no comparisons of operative and nonoperative treatment. The conclusion of this review would likely be that there is insufficient evidence to support operative treatment for clavicle nonunions. However, if you go back to the original question, namely, 'Does operative treatment of clavicle nonunions result in better outcomes than nonoperative treatment?,' then you see that by definition it is *already* unsuccessful because it is a nonunion. This type of scenario highlights the importance of asking the right, and clinically meaningful, question."

Sounds like something your average clinician wouldn't be aware of? So true, says Dr. Bono. "While some clinicians are knowledgeable in this area, most need to partner with biostatisticians and/epidemiologists—people who are well versed in the methodology of systematic reviews. The clinician's role is to keep everyone on track with regard to the definition and adherence to the study question. If the study question is defined by non clinicians then it can be quite off base. For example, I was recently on a conference call with representatives from multiple centers who want to do a systematic review about low back pain. Prior to obtaining any clinician input they said, 'Let's compare outcomes for disc herniation for a variety of treatments.' They wanted to look at intradiscal electrothermal therapy and facet rhizotomy, both of which are not treatments for disc herniation. If they had proceeded with that route, then they would have of course found a lack of evidence—and they would have spent resources on something that was not clinically meaningful."

Dr. Fisher sheds light on an organization that has spearheaded the move towards systematic reviews. "The UK-based Cochrane Collaboration, leaders in evidence-based medicine, are the ones who came up with the standard format for systematic reviews whereby you go through the literature and develop specialized research questions. By the end of 2009, there were 4,027 published Cochrane Reviews on the Cochrane Database of Systematic Reviews in The Cochrane Library; and their method is very thorough. For example, the literature search is so exhaustive that it is not uncommon to begin with 3,000 articles and end up with 60."

In the end, it is important to remember the beginning. Dr. Fisher: "Everything always comes down to the research question. If it is too precise/narrow then you can't easily generalize it to the entire population, meaning that it is not especially meaningful from a clinical standpoint. Obtaining external validity is really difficult in the surgical disciplines. You are comparing two surgical techniques, which, on the face of it may seem uncomplicated. Dig deeper, however, and you see other things that must be taken into account, namely, 'What are the experience levels of surgeons? Fifteen years or two years?' and 'What is the pathway of care at one institution versus another (a lot of one-on-one attention, excellent rehabilitation facilities, etc.).'"

He adds, "Many people think that a systematic review is the final verdict on a study issue/question, but that is not true if the review was not performed properly. It is similar to how when people see that something was a randomized controlled trial they tend to think, 'Oh, this was an RCT…the results *must* be valid.'"

"When looking at systematic reviews," advises Dr. Bono, "remember that they are just like other studies…there are good and bad ones out there. Examining the methodology that was used before you take away any conclusions will help you avoid heading off in the wrong direction." ◆

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company

Solstice Medical: Company to Watch

Get out the binoculars…Solstice Medical, LLC has been recognized by the Indiana Economic Development Corporation, its Small Business Development Center network, Purdue University and the Edward Lowe Foundation as an Indiana "Company to Watch" for 2010. The award recognizes privately held small businesses with under 150 employees and between $750,000 and $100,000,000 in annual revenues.

"Firms like these named 'Companies to Watch' continue to be the catalyst that is fueling Indiana's emergence from a turbulent national economy," said Mitch Roob, Secretary of Commerce and CEO of the Indiana Economic Development Corporation, in the news release. "Congratulations to this exemplary group of Indiana businesses that continue to invest in their communities and create new jobs in all corners of our state."

"We are extremely pleased to be honored by with this prestigious award," added Dan Sands, CEO of Solstice Medical. "Solstice Medical will continue to bring jobs to Indiana by staying true to our core objective of utilizing cutting edge technology to reduce the overall cost of healthcare while improving patient care."

Elaborating on their technologies, Sands told *OTW*, "Solstice Medical is proud to provide cutting edge inventory and workflow automation technologies to a growing list of customers in the healthcare industry. Dock-to-Doc is our flexible software platform designed specifically to solve the many challenges of managing and tracking medical products inventory. The automated functionality of the system and the information it provides helps orthopaedic companies reduce their field inventory, decreases auditing and shipping costs and meets regulatory requirements for inventory traceability. We also offer MD^3, the world's smallest and autoclavable RFID tags that help streamline the process of managing the large orthopaedic instrument and implant sets at the OEM and within the hospital. These two products, used in conjunction with advanced reader technology, provide assurance that the right product will be at the right location at the right time for the right patient."

Morguefile

He also commented to *OTW*, "The best is yet to come for Solstice Medical. We have exciting new technologies that provide 24/7 secure inventory tracking at any location, wireless (GPS type) inventory tracking for mobile field inventory, radical new 'read-thru' metal RFID to automatically scan the contents of an instrument set WITHOUT visual inspection. The sun continues to shine on Solstice because of our talented staff and our unique information technology solutions that meet the specific needs of the orthopaedic manufacturers and distribution network. Our future is bright as we continue to save our customers millions of dollars and address the challenge of improving the delivery healthcare to patients worldwide."

—EH (August 6, 2010) ◆

Alphatec in Transition

Alphatec Spine's 10% revenue increase to $45 million in the second quarter of 2010 didn't meet Wall Street's or the company's CEO's own expectations. As a result, the company's stock price dropped over 40% the day after revising its sales growth forecast for 2010 to 10%-13%, with anticipated revenue of $188 million to $193 million.

Dirk Kuyper, Alphatec's President and CEO, didn't sugar coat it when he told analysts on August 5, "While we are pleased with the long-term business prospects and fundamentals at Alphatec Spine, and our current growth rate continues to exceed that of most of our competitors and the broader spine market, our growth rate was below our expectations."

Sales Growth Factors

Kuyper cited several factors that the company believed contributed to the lower-than-expected sales result.

National Park Service/Wikimedia Commons

First, U.S. price pressure on the company's core products, which Kuyper believes to be in the mid single digits.

Alphatec Spine	2Q10	
	Sales ($ in millions)	% Change
Total Sales	$45.4	up 10%
U.S.	$29.3	up 1%
Europe	$8.9	up 75%
Asia	$5.2	up 16%
Other	$2.0	

Source: *Alphatec Spine.*

Second, the unpredictability of the FDA, which, he said makes the timing of market releases of key technologies uncertain. Canaccord analyst Bill Plovanic said that Alphatec had previously announced that while the company's OsseoScrew will be submitted via a 510(k), a clinical study will be required. He noted the company is currently finalizing the clinical protocol required for the 510(k) application and is meeting with the FDA in the fall.

Third, Kuyper spoke of the complexity of integrating Scient'x into the company's operations. Alphatec completed the Scient'x acquisition this past March.

Good News and Perspective

There was some good news and a little perspective for the quarter however. The company netted $43.1 million from an equity offering and received European approval for its OsseoScrew product.

Even while dropping the target price for the company's stock, Plovanic wrote, "We feel the company is going through a transition phase that prevents it from adapting to these environmental changes. Given the solid results [outside the U.S.]... we are encouraged about the long-term benefits of the [Scient'x] merger."

Plovanic added, "We continue to believe that once the company gets its distribution channel running at full speed again, and a new product cadence is established, that it will be able to take these pricing pressures in stride and grow at least in-line if not a bit above market growth rates."

Kuyper ended with an upbeat note:

"We continue to be enthusiastic that with the addition of Scient'x, and as a result of the transaction, we believe that Alphatec Spine is the leading pure-play spine company that is truly global, with scale to address opportunities in the U.S., Asia, Europe, Middle East and Latin America. We continue to experience strong growth in the volume of surgical procedures performed in the U.S., and have addressed the current market challenges to ensure sustainable long-term revenue growth and a drive to profitability. We look forward to leveraging our broad-based international distribution network towards those goals."

—WE (August 6, 2010) ◆

Indiana Orthopaedic Hospital and InVivoLink

A real-time win for evidence based medicine…InVivoLink, LLC (IVL) is partnering with Indiana Orthopaedic Hospital (IOH) to have the latter party use the IVL platform to collect clinical, financial and operational data directly from the operating room at the point of service. The information includes details on joint implants, patient characteristics, physician utilization, and more.

InVivoLink's iPhone / iPad app

Ryan Wells, InVivoLink CEO, said in the news release, "Ranked in the top 5% in the nation for joint replacement surgery, IOH is widely recognized as a best-in-class orthopaedic center. As an industry-leading facility, it makes sense that IOH is seeking to further streamline and improve the process for its patients and physicians. The InVivoLink team is honored to partner with IOH and its surgeons to enhance outcomes-related data collection, redefine the standard of care, and focus even more on value to the patient."

David Fisher, M.D., Director of the Total Joint Center of Excellence at IOH, said in the news release, "With IVL, I can rest assured that the right device for the right patient will be waiting for me when I walk into the O.R. In addition to streamlining the process, InVivoLink collects the clinical data that is critical to ensuring patient safety, allowing us to provide highly efficient and effective care. With the continuing surge in joint replacement procedures, we must have actionable, evidence-based data to make the best decisions for our patients."

The information IVL collects before, during and after joint implant procedures goes into a national registry. IVL's technology allows physicians and hospitals to collect deep data and even to tailor the information they capture, creating a customized registry specific to their practice.

Company Chief Operating Officer John Bass, told *OTW*, "Above all, IOH recognizes that they win when the patient wins. The value InVivoLink provides for IOH is both clinical and operational. Clinically, IOH understands the power of capturing data at the point of use for outcomes and performance analysis, ultimately enhancing patient safety. Operationally, IOH recognizes the importance of taking a collaborative approach with vendors. The InVivoLink platform allows case scheduling data to be managed collaboratively for operational and additional patient safety benefits."

He also commented to *OTW*, "As a base service, InVivoLink collects a standard set of clinical and supply chain data that will meet the needs of a registry initiative. Note that even this base set is a big advance for the majority of the market. But needs evolve, and InVivoLink is able to capture additional clinical and operational data that hospitals and doctors feel would be valuable to their specific practices and patient care."

—EH (August 4, 2010) ◆

Pre-Marketing Activies for ATR

Seeking a partner in growth (factors)...curasan AG is announcing the commencement of its pre-marketing activities for the launch of its new product ATR (Advanced Tissue Regeneration), a standardized system for extracting growth factors to support wound healing and tissue regeneration. As indicated by the company, the ATR system contains everything that is needed to extract the concentrate either in the doctor's practice or in the operating room.

curasan AG

The areas of application include severe skin damage such as ulcers, large-area burns, skin transplantations, cartilage and cell culture, or chronic wounds. Furthermore, the product can have a favourable impact on the wound healing process for the optimized regeneration of bones and mucous membranes in plastic surgery, in oral and maxillofacial surgery and implantology.

"ATR is an attractive proposition for various specialiszd enterprises on account of its wide range of applications. Since a marketable product is now available, we can actively pursue negotiations with potential sales partners with immediate effect," explained Hans Dieter Rössler, CEO of curasan AG, in the news release.

With the help of ATR, autologous platelet-mediator-concentrate (PMC) is extracted from the patient's own blood, thus ensuring a high degree of compatibility. PMC supplies the important growth factors for wound healing and tissue regeneration, which can then be brought directly in the wound area. ATR is a single use device that requires neither machines nor external laboratories. As such, there are no investment costs and no costs incurred in the services provided by third parties.

Providing details on the process, Rössler told OTW, "PMC is isolated from the patient's own blood by a filtration system. During this process an aqueous solution of growth factors is prepared. It can be applied directly into the wound, where the growth factors immediately act in the healing process."

Initially, the activities are aimed at Germany and the European market. However, in the medium term curasan AG anticipates enormous potential for ATR, above all, in the U.S. market.

As for details regarding expanding into the U.S., Rössler told OTW, "Right now we are looking for an adequate partner in the U.S. to support us with the FDA approval as a first step, and then to take over all necessary sales and marketing activities for ATR."

—EH (August 4, 2010) ◆

MAKO Goes 3 for 3

The story with MAKO Surgical Corp. every quarter is about how many RIO systems were sold, how many MAKOplasty procedures were performed, and how have utilization rates grown.

With that, MAKO batted three for three during the second quarter of 2010.

New Systems	7	up 233%
New Procedures	793	up 122%
Utilization	6.3	up 14%

Revenue Up 151%

On August 3, the company reported a 151% increase in revenue during the second quarter of 2010 compared to the second quarter in 2009.

Sales of $10.3 million came from $5.7 million in revenue from the sale of seven RIO systems, $4.2 million in revenue from the sale of implants and disposables used in 780 domestic MAKOplasty procedures performed in the quarter, and a $0.3 million stocking order for implants and disposables associated with a clinical research site.

The placement of seven new systems brings to 46 the total number of domestic commercial installed systems, while the 793 new procedures brings to 3,908 the total number of procedures that had been performed through June 30,2010, since June 2006.

"We are pleased with the addition of six new commercial sites, across multiple geographies, including three states that previously did not

RRY Publications LLC modified/Wikimedia Commons have systems installed. We are also encouraged by our first international sale of a RIO system and the 793 MAKOplasty procedures performed worldwide in the second quarter," said Maurice R. Ferré, M.D., President and Chief Executive Officer of MAKO. "Additionally, we are enthusiastic about the prospective, randomized clinical study being conducted in Scotland and the continued flow of clinical evidence supporting our procedure."

New Randomized Controlled Trial

Wells Fargo Senior Analyst Mike Matson reported that there are 40 clinical trials underway on MAKOplasty. "Most significant, in our view," added Matson, "is a new randomized controlled trial that MAKO is going to be conducting in Scotland. This trial is going to be a three-year head-to-head comparison of MAKOplasty with standard unicompartmental knee replacement. While this isn't without risk, we think it speaks to MAKO's confidence in its technology."

Given the quarter's results, Matson raised his revenue projections for the company from $41 million to $45 million for 2010 and, from $75 million to $79 million for 2011.

Challenge for Profitability

While revenue and growth metrics for the company ballooned in the second quarter, the company is still not profitable.

The company reported that operating expenses were $15.2 million in the second quarter of 2010 compared to $11.2 million in the second quarter of 2009. According to the company, the increase in operating expenses was primarily attributable to continued expansion of the direct sales force and commercialization of the RIO system and RESTORIS implant systems; an increase in research and development activities and the development of potential future products, including the RIO-enabled hip application; and an increase in general and administrative costs as MAKO continued to build infrastructure to support growth.

—WE (August 4, 2010) ◆

Wright Sales Rise 7%

Wright Medical Group reported a 7% increase in sales for the second quarter of 2010. Total sales reached $127.7 million.

President and Chief Executive Officer Gary D. Henley commented, "We are very pleased with the performance of the business this quarter, led by strong revenue growth in our global extremities and international hip and knee businesses. Additionally, we continued to execute well operationally, evidenced by 100 basis points of operating margin expansion and $7.2 million of free cash flow for the quarter."

Wright Medical Group	2Q10	
	Sales ($ in millions)	% Change
Total Sales	$127.7	up 7%
Knees	$31.8	up 5.1%
Hips	$44.2	up 7.6%
Extremities	$29.5	up 15.1%
Biologics	$19.8	up 1.9%
Other	$2.4	Down 4.4%

Source: Wright Medical Group.

The market seemed unimpressed with the results as the company's stock dropped by over 3% the following day.

Analysts Like 2011

Some analysts, however, took a different view. Wells Fargo's senior analyst Mike Matson wrote that he expected Wright's extremities sales force expansion and new Evolution knee launch to push revenue growth into the double digits in 2011.

He noted that the company had previously announced that it had increased its extremities sales force by approximately 50% from 100 reps at the beginning of 2010 to around 150 by mid-year. "While it's likely to take 6+ months for these new reps to become productive, we think that Wright could exit 2011 at over a $160 million annual run rate for its extremities business (vs. its current $120 million run rate)."

Wright's hip and knee implants account for 60% of revenue; its metal-on-metal and ceramic hip implants anchor a broad hip product line, its strongest implant franchise. Extremity implants account for 19% of revenue and orthobiologics another 28%.

Profemur Hip Focus

The company addressed recent case studies of the Profemur Modular Hip System, that claim the necks used in the original product design (launched 2001) suffered a high rate of revision.

Joanne Wuensch, BMO's Capital Markets analyst, reported that although the device had an 11% revision rate in one Australian registry, the registry includes only 200 patients with the Modular hip (compared to the over 200,000 devices implanted during the product's lifetime) and the cause of revisions were not specified.

"The company was able to locate 18 of the 20 revisions and found no modular neck fractures. In fact, with a success rate of over 90% after ten years, management backed the quality of the product," wrote Wuensch. The company also noted that the majority of the revisions were in overweight patients with an active lifestyle who had a long neck stem implant.

Wright is now selling a new model of the Profemur Modular Hip System, and of the 200,000 devices it has implanted, roughly 0.1% of the products have failed in total, and less than 0.2% of the long necks have failed. For some time, the new system has also included a warning that long-stemmed necks should not be used in overweight, obese or active patients.

Image created by RRY Publications LLC

Not all analysts were sold however, Raj Denhoy of Jeffries wrote that the very low rate "does call into question the robustness of the company's data collection as it is far below what would be expected."

Maintaining Guidance

While Wright's second quarter results received some mixed reviews, the company maintained its 2010 guidance for revenue of $515 million to $530 million.

—*WE (August 3, 2010)* ◆

legal

Grassley Goes Zimmer Fishin'

Ahh, it's summertime along the Mississippi in Iowa and Senator Chuck Grassley is going fishing. This time he's not casting a wide net, but fishing specifically for Zimmer Holdings.

On July 29, the Senator sent a letter to Zimmer saying he was "troubled" by a recent New York Times account of the company's response to allegations of safety concerns raised by two of the company's consultants, Larry Dorr, M.D., and Rich Berger, M.D.

In both cases, the Durom Cup hip and the NexGen CR-Flex knee, the company addressed complaints from the surgeons by citing evidence that the implants were safe and pointed to surgical techniques for any failures of the devices.

Questions for Zimmer

Grassley is asking Zimmer to provide him with answers to the following

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questions by no later than August 12, 2010.

1) What processes are in place to respond to concerns regarding the safety of a product?
2) How many consultants (since January 2008) have raised problems regarding products? For each problem reported, include the following:
    - The name and affiliation of the consultant and whether or not s/he is still a consultant
    - The name of the product
    - The specific problem(s) reported to Zimmer
    - Whether or not the reports of problems led to product changes/modifications
    - Whether or not the reports of problems led to product discontinuation.
3) Of the problems identified, how many were refuted by Zimmer?
4) Does Zimmer voluntarily collect data on the performance of its devices? If so, how is that data collected? If not, has Zimmer considered putting in place a process for tracking and reviewing the performance of its devices?

Why Just Zimmer?

It is not new or surprising that Senator Grassley is asking questions about the business practices of orthopedic companies, surgeons, educational institutions, and medical societies. What is new is that in the past these requests have been cast with a wide net. This time the Senator is fishing with just one line.

Zimmer Responds

Zimmer issued a statement saying the company welcomed the opportunity to discuss how it responded to surgeon complaints. "This feedback [with surgeons] can lead to modifications and improvements to products, their labeling and the manner in which we train and educate surgeons about our products,"

The company said it monitors the performance of products through a post-market surveillance program which is similar to programs for other device manufacturers. The company also noted that the clinical performance of implant products is subject to review by independently run national patient registries in many countries.

"We have long supported the creation of the American Joint Replacement Registry (AJRR) and are working with the American Academy of Orthopaedic Surgeons (AAOS) to help develop guidelines to optimize the registry's value to healthcare providers, patients and payers."

The Senator may only be fishing for Zimmer here, but don't be surprised if he's getting his nets ready.

—*WE (August 3, 2010)* ◆

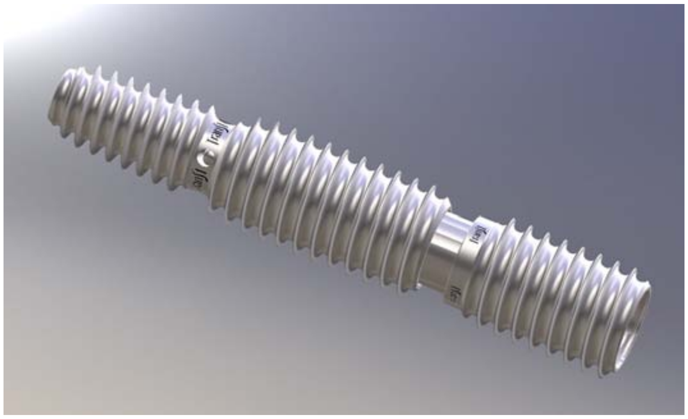
spine

Trans1's Next Generation AxialLIF

Trans1, Inc. has launched the AxiaLIF 2L+ product line, an instrumentation and implant system for L4-S1 lumbar fusion.

The Wilmington, North Carolina, company, which pioneers a proprietary access approach to the lower lumbar region, made the announcement on July 27.

According to the company, the 2L+ represents the next generation of its original system first launched in 2008. The 2L+ has been available under a limited market release since January, when the device received FDA 510(k) clearance.



Trans1 AxiaLIF 2L+/Trans1

Surgeon Acceptance/Payer Coverage

Recognizing the issues that have been raised by some payers on the novel approach to the lower spine, Atiq Durrani, M.D., an orthopedic surgeon at the Center for Advanced Spine Technologies in Cincinnati, Ohio, said:

"The lumbosacral junction can be tricky. 2L+ represents a valuable step forward for surgeons dealing with this region of the spine. I like the controlled distraction 2L+ provides, and the improved instrumentation makes the procedure more efficient. The internal fixation rod gives me total confidence in the solid, final construct."

Dr. Durrani, according to the company, is not under contract as a TranS1 consultant and has not received TranS1 stock from the company.

Reimbursement

Regarding reimbursement for the new system, the company informed *OTW* that, "AxiaLIF 2L+ is used to treat patients where the need for a fusion procedure is very clear-such as spondylolisthesis; as such, AxiaLIF 2L+ has been viewed favorably by the payer community. When the indication for fusion clearly meets the guidelines for medical necessity, payers are viewing AxiaLIF 2L+ as an appropriate minimally invasive spinal fusion technique for this patient population."

Ken Reali, Trans1's President and COO told *OTW*, "The launch of AxiaLIF 2L+ represents a major advancement in the options available to surgeons for treating the biomechanically challenging lumbosacral junction. All other techniques, including the newest lateral approaches, have significant drawbacks when used from L4-S1."

Added Reali, "Our two-level products represent the only technology that can treat L4-S1 from one small incision, avoiding major vascular structures and nerves. Furthermore, our new 2L+ system now gives surgeons the precision control to 'dial' in the desired amount of disc height restoration."

—WE (July 30, 2010) ◆

Reducing Cervical Spine X-rays

Wasted days and wasted…X-rays? Researchers from the University of Rochester Medical Center have determined that an imaging algorithm produced by a radiology department and distributed through the medical director's office, in a top-down fashion, enabled a large, academic medical center to significantly reduce the number of unnecessary cervical spine radiographs (X-rays) in the emergency department.

The study, published in the July issue of the *Journal of the American College of Radiology*, found that many routine trauma X-rays of the cervical spine were requested after a CT scan of the cervical spine had demonstrated no significant findings.

Mark J. Adams, M.D., MBA, FACR, lead author of the study, said in the news release: "With the assistance of our medical director, a clear algorithm for the X-ray evaluation of post CT cervical spines was developed and distributed from the top down to care providers through their respective departments, not directly from the imaging department. One year after the implementation of the policy, data demonstrated a significant decrease in the number of unnecessary or inappropriate studies being performed. The number of unnecessary X-ray exams performed was reduced by 83 percent between January 2008 and January 2009."

"Not only are these X-ray exams unwarranted, they consume valuable resources, add an additional burden to emergency department and radiology staff, and subject patients to unnecessary radiation," added Adams.

"It is hoped that this simple approach can also be used to address other improper use of imaging resources, thereby reducing radiation exposure and improving the efficiency of care in the emergency department and acute care setting."

Dr. Adams told *OTW*, "The algorithm is a simple one. If a CT of the cervical spine is interpreted as normal, no more routine radiographic cervical spine imaging is deemed necessary. An emphasis must be placed on routine, as if there is concern for ligamentous injury or instability, lateral radiographs in flexion and extension may be

Cervical spine MRI showing degenerative changes/ Wikimedia Commons

indicated, of if there is concern for cord trauma, an MR may be indicated. The Algorithm is: Normal CT cervical spine— routine radiographs not indicated; Normal CT cervical spine—concern for instability—lateral radiographs in flexion and extension should be considered; Normal CT cervical spine—concern for cord trauma—MRI should be considered; Abnormal CT cervical spine—radiographs may be indicated for treatment and/or follow-up."

As for what led to the top-down idea, Dr. Adams commented to *OTW*, "At onset, we tried directly communicating with the emergency department providers. This resulted in marginal improvements in reducing the number of unnecessary exams. I had the opportunity to present the project to the Medical Center's Clinical Council, which was well received by our Medical Director and Chief of Quality and Safety. Upon my request, they agreed to discuss the matter with the Chiefs and divisional leaders of the emergency department, orthopedics, neurosurgery and spine teams. This top-down approach achieved the results we sought."

—EH (August 2, 2010) ◆

biologics

Biomaterials Symposium Promises Cutting-Edge Discussions

The 10th NJ Symposium on Biomaterials Science is slated for this October. Stem cells, biomimetic and tissue engineering presentations will abound!

The 10th New Jersey Symposium on Biomaterials Science and Regenerative Medicine, titled From Materials Design to Scaffolds to Tissue Regeneration is set to run this autumn, Wednesday and Thursday, October 27 and 28 at the Hyatt Regency Hotel in New Brunswick, New Jersey.

Hosted by the New Jersey Center for Biomaterials, this symposium is especially interesting because it's going to bring together a wide variety of scientific newsmakers and researchers. Few conferences, in fact, can boast such multidisciplinary speakers and guests, including chemists, biologists, surgeons and pharmacologists.

And what would a biomaterials conference be without a hearty dose of debate!? This two-day meeting will be organized with debates bookending the presentation. First it's a look at the comparative merits of natural and synthetic scaffolds for tissue engineering and things come to a close with a discussion on the role of embryonic and fetal stem cells in regenerative medicine. Who doesn't love some controversy?

NJ Symposium Exhibitors/NJ Center for Biomaterials

Ready for some name dropping? Here are some of the key figures in biologics that will be presenting at the symposium:

- Joachim Kohn, Ph.D., Rutgers University (Combinatorial Biomaterials Design and Modeling)
- Stephen Badylak, D.V.M, Ph.D., M.D., McGowan Institute for Regenerative Medicine (Panel discussion on Decellularized Tissue vs Engineered Scaffolds)
- David Kaplan, Ph.D., Tufts University (Tissue Engineering of the Musculoskeletal System)
- Julia Babensee, Ph.D., Georgia Tech (Polymeric Biomaterials Technologies)
- Arnold Caplan, Ph.D. Case Western Reserve University (Debate and discussion on the use of Embryonic and Fetal Stem Cells in Human Medicine)

And Wednesday evening's dinner should give attendees a lot to digest with Deputy Assistant Secretary of Defense for Force Health Protection and Readiness Ellen Embrey providing a presentation on Restorative Medicine with a speech entitled: The Role of Science and Technology in Restoring Function and Quality of Life.

This biennial series typically draws several hundred professionals from academia, government, military and private industry. Those interested in attending this year should take special note of the "Early Bird" discounts for registration, listed in the event's program.

—JR (July 30, 2010) ◆

THE PICTURE OF SUCCESS

Dr. William Martin, III

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

Dr. William Martin, III

The shortest distance between two points? In Dr. William Martin's case it was not a straight line—it was actually one of life's curve balls. "After college, both of my parents became ill, so I took two years off to care for them. Along the way I did research at Loyola University in Chicago and maintained a course for medical school." That side trip laid the principled foundation that once informed his duties as Chair of the Arizona Medical Board and in his current position as Medical Director of the American Academy of Orthopaedic Surgeons (AAOS). His decision to delay his medical education in order to care for his parents is emblematic of Dr. Martin's strong character and ethical compass.

Opportunities are wonderful. But doing the right thing is everything.

Dr. Martin spent his youth in the suburbs of Chicago, where his mother owned a chain of dry cleaners and his father worked as a podiatrist. "My uncle was the first black orthopedic surgeon in the Chicago suburbs and was so very influential to me in my early life. Although he died when I was seven, the early impressions of his work have remained with me."

Bill Martin's attraction to orthopedics started early and found concrete expression while he was still in high school. "I spent my high school summers working at the University of Chicago doing research in orthopedics with the Chair, who was a family friend. This, combined with working as a cast technician, resulted in an early 'love affair' with orthopedics; I reveled in the fact that you could get tangible results. I recall the case of an elderly woman who came into the ER with a broken hip. It was quite something to be with her as she was treated there, underwent surgery, and then did rehabilitation. There are not many professions in or out of medicine that give you such an experience."

Bill Martin started his post high school educational career at Harvard but finished his undergraduate degree at Tufts University. "I had an opportunity to enroll in an accelerated program at Tufts, so I took my scholarship and transferred there. While I spent most of my time in the microbiology lab so as to boost my medical school application, I did make time for my minor, religion."

Despite their illness, Dr. Martin's parents continued to support, even drive Dr. Martin to complete his post-graduate education. "My parents pushed me to continue with my plans, and thus I entered medical school at Loyola and began doing research with Dr. Terry Light. Terry knew that I had a lot of things going on in my home life, and he had empathy for me; one day I told him that I couldn't get an assignment done. In his straightforward manner, he turned to me and said, 'Bill, if this is important to you, you will get it done.' That one line was incredibly helpful to me."

"I spent my high school summers working at the University of Chicago doing research in orthopedics with the Chair, who was a family friend."

Armed with a renewed focus, now-Dr. Martin entered the Phoenix Orthopedic Residency Program. "I wanted a program that was associated with a county hospital because I believe in the mission of helping the underserved. We saw a broad spectrum of pathology and because the patients were poor and tended to neglect problems, when they had something—arthritis, for example—it was particularly bad. The greatest thing about this period in my life was that I met my future wife and got married."

He then got wedded to a subspecialty. "With my dad having been a podiatrist and my uncle an orthopedic surgeon, I felt a certain affinity for foot and ankle. While in California I met the famed Dr. Roger Mann, who invited me to become his apprentice. Over the years I have found that some people are the best technical orthopedists in the world, but are not Mr. or Mrs. Personality. Others are the opposite. When I think of Roger, however, it is always as a scholar and a gentleman."

"I spent my fellowship with Dr. Mann, during which time I treated a lady who hadn't walked in several years…and whose favorite thing was to amble through gardens. After a successful surgery her son was able to take her to a local botanical garden for a stroll…she said it was the best day of her life."

But there would be no strolling for Dr. Martin…it was more like a sprint. "I completed my fellowship on the last day of 1998 and began my first day in practice on January 2, 1999. I joined a practice comprised of folks from my residency, meaning that it was a supportive environment. After five years I launched a solo practice, in part because I wanted to have more time to devote to entrepreneurship, as well as to AAOS activities."

For the next several years it was as if he was earning an on-the-job MBA. "I thought I knew the business of medicine but it wasn't until I started having to do it on my own that I was forced to learn it. One thing I was concerned about was that my employees didn't have enough to do if I was away from the office. My solution was to purchase a medical building and establish an urgent care center and a data management/document scanning company. As for the latter business, it emerged after a new Arizona law was implemented mandating that documents had to be kept for seven years. Storing paper charts is expensive, however; there were even some doctors who, when closing their practices, were leaving their patient charts in alleys. Having multiple businesses enabled me to put employees on different projects depending on the needs of businesses. These were creative things I could do to help the businesses survive and continue to employ people."

"It seems that diversity is a bit of a hard sell to some of our members because their time is so taken up by multiple competing interests. We hope that changes, though, as more women and minorities enter the profession."

And what of the roundabout trip to becoming Chair of the Arizona Medical Board? "I was concerned about the state of high school education in our district, and approached the superintendant and said, 'Help me do something to get grades 9-12 up to par by the time my children are ready for high school.' His response: 'Nine years is not enough time. The only way to effect change is to get on the state board of education.' I completed the online application, but was actually selected for the medical board instead. I eventually became chair, and learned how important the role of regulators is, i.e., weeding out the bad apples so as not to let them take away from the profession. Fortunately, I can say that orthopedics was not one of the professions where there were egregious abuses."

As the new Medical Director for AAOS, Dr. Martin hopes to help keep it that way. "I have three primary roles, the first of which is medical affairs, an area that largely involves issues such as coding and reimbursement. I am also in charge of supervising research and scientific affairs efforts. At present we are conducting member surveys on topics such as whether we will have enough orthopedists as the population ages, where the shortages will be, and what solutions there might be. We are also establishing orthopedic treatment guidelines; in the future, it is likely that we'll move into other areas of the 'quality arena' like appropriate use criteria. Another substantial portion of my time is devoted to government relations. The issue of doctors' decreasing Medicare reimbursement is not going away. The AAOS position is that we should have a permanent fix to the Sustainable Growth Rate formula so that we don't have to go through the, 'Are we going to have it or not?' every couple of months."

Ethics and equality are two major points on Dr. Martin's moral compass. "I am drawn to the issue of diversity, and am pleased that the AAOS presidential line has elevated its importance within the organization. It seems that diversity is a bit of a hard sell to some of our members because their time is so taken up by multiple competing interests. We hope that changes, though, as more women and minorities enter the profession. At present, the trends are flat for minorities going into orthopedics, but AAOS is taking active steps to help to change that. It has been suggested that medical schools sometimes steer minorities into primary care as opposed to the surgical subspecialties. It may also be that minorities look around and say, 'There are not many people like me in this field so why should I go into it?'"

Dr. Martin wants these—and any avenues—to be open for what he calls "God's greatest gifts." "My wife and I have four little ones…there is not a day that goes by that I don't thank God for all I have. We participate in the children's sports activities, and also volunteer as a family to help those who are less fortunate than we are. I think that you can't just say that you are concerned about people—you must act on it."

Dr. William Martin, III…a good apple who found his way to the top. ◆

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