VOLUME 6, ISSUE 33 | OCTOBER 19, 2010

Orthopedics This Week

week in review

picture of success

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: Alphatec hires the former VP and Chief Financial Officer for JNJ's worldwide information technology unit. As we saw with OFIX, great CFOs can dramatically improve a company's cash flows and, yes, earnings (OFIX's new capital plan added $0.05 to earnings). This CFO is a solid gain. ATEC is the best value in orthopedics this week.

Rank	Last Week	Company	TTM Op Margin	30-Day Price Change	Comment
1	4	Alphatec	1.59%	21.36%	In addition to the new CFO, we are impressed with their ELA stem cell product. Or, rather, the data that is supporting it.
2	1	Kensey Nash	38.72	(3.40)	Most analysts expect KNSY to report flat earnings on down sales later this week. Stock is drifting down in anticipation.
3	3	Stryker	24.71	1.03	Buyers starting to wake up the fact that SYK's numbers may be better than expected.
4	2	Orthofix	13.51	(3.26)	Despite great financial reports, OFIX is still viewed as a conglomeration of dissimilar orthopedic products.
5	5	CONMED	8.76	15.05	CNMD has significantly beat Street estimates four quarters in a row. Can't last forever. Regression to the mean is a law of nature.
6	6	Integra LifeSciences	15.37	0.89	We should see an upside surprise, albeit modest, this quarter.
7	7	Johnson & Johnson	27.10	4.13	The Street's dalliance with JNJ may be reaching a crescendo. Two more weeks? Or until November 2nd?
8	9	Zimmer	27.69	1.29	Fourth least expensive ortho stock. Finally getting some sustained buying from institutional investors.
9	8	Smith & Nephew	22.83	(0.98)	Key to SNN is this quarter's report. Can SNN beat last year's numbers? Doubtful.
10	10	Exactech	11.81	(4.74)	Not much news, like new products, coming from EXAC these days. Stock is cheap.

Robin Young's Orthopedic Universe

Top Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	TiGenix	TIG.BR	$2.91	$90	49.3%
2	Alphatec Holdings	ATEC	$2.50	$218	21.4%
3	Orthovita	VITA	$2.05	$157	16.5%
4	RTI Biologics Inc	RTIX	$2.74	$150	15.1%
5	CONMED	CNMD	$23.08	$665	15.1%
6	CryoLife	CRY	$6.59	$186	9.3%
7	NuVasive	NUVA	$34.04	$1,340	5.0%
8	Bacterin International	BIHI.OB	$7.50	$267	4.2%
9	Johnson & Johnson	JNJ	$63.57	175,100	4.1%
10	Synthes	SYST.VX	$123.54	$14,662	4.0%

Worst Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	Exactech	EXAC	$14.87	$192	-4.7%
2	Kensey Nash	KNSY	$28.66	$255	-3.4%
3	Orthofix	OFIX	$29.71	$524	-3.3%
4	Symmetry Medical	SMA	$9.44	$339	-2.4%
5	Mako Surgical	MAKO	$10.72	$362	-2.0%
6	TranS1	TSON	$2.47	$51	-1.2%
7	Smith & Nephew	SNN	$43.45	$7,720	-1.0%
8	Medtronic	MDT	$33.29	35,950	-0.2%
9	Osteotech	OSTE	$6.48	$117	0.3%
10	Wright Medical	WMGI	$14.67	$575	0.7%

Lowest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Medtronic	MDT	$33.29	$35,950	9.94
2	Exactech	EXAC	$14.87	$192	12.02
3	Zimmer Holdings	ZMH	$51.22	$10,290	12.19
4	Kensey Nash	KNSY	$28.66	$255	12.76
5	Wright Medical	WMGI	$14.67	$575	12.91

Highest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Smith & Nephew	SNN	$43.45	$7,720	59.84
2	RTI Biologics Inc	RTIX	$2.74	$150	35.84
3	Synthes	SYST.VX	$123.54	$14,662	34.53
4	NuVasive	NUVA	$34.04	$1,340	27.97
5	Symmetry Medical	SMA	$9.44	$339	24.65

Lowest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	Orthofix	OFIX	$29.71	$524	0.79
2	Wright Medical	WMGI	$14.67	$575	0.79
3	NuVasive	NUVA	$34.04	$1,340	1.09
4	Zimmer Holdings	ZMH	$51.22	$10,290	1.24
5	Stryker	SYK	$49.04	$19,470	1.48

Highest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	CONMED	CNMD	$23.08	$665	18.43
2	Smith & Nephew	SNN	$43.45	$7,720	5.00
3	Kensey Nash	KNSY	$28.66	$255	2.55
4	Symmetry Medical	SMA	$9.44	$339	2.24
5	*Average*			*$11,274*	*2.17*

Lowest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	RTI Biologics Inc	RTIX	$2.74	$150	0.92
2	CONMED	CNMD	$23.08	$665	0.92
3	Orthofix	OFIX	$29.71	$524	0.93
4	Symmetry Medical	SMA	$9.44	$339	1.01
5	Exactech	EXAC	$14.87	$192	1.02

Highest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	TiGenix	TIG.BR	$2.91	$90	321.16
2	Bacterin International	BIHI.OB	$7.50	$267	28.04
3	Mako Surgical	MAKO	$10.72	$362	10.95
4	Synthes	SYST.VX	$123.54	$14,662	8.13
5	Kensey Nash	KNSY	$28.66	$255	3.16

A Hospital of His Own

By Biloine W. Young

Dr. Gil Tepper / Courtesy Miracle Mile Medical Center

The woman, whose name means "light' in the Ethiopian language, spotted her Saudi passport on the hall table of the suite of the luxury Beverly Hills hotel where she was staying. Years before, she had been sold into virtual slavery by her Ethiopian husband to members of the Saudi royal family to care for a handicapped child. She had carried the now adolescent boy, who was unable to bear his own weight, everywhere and, as the years passed, developed back problems.

The Saudi family had been vacationing in California for a month when, two days before they were to return to Arabia, their passports were removed from the hotel safe in preparation for their departure. When the woman recognized her passport lying untended in the foyer she stood transfixed. Then she grabbed it and, fleeing for her life, left the hotel and hid the entire night and next day in the shrubbery on the hotel grounds. When darkness fell the second night she walked a half-block down a street to a market.

It happened that the market she entered was in Dr. Gil Tepper's neighborhood and several of the Ethiopian employees of the market had been his patients. The woman, who knew not a word of English, spoke to two of them. They took her to an Ethiopian shelter adjacent to Tepper's Miracle Mile Medical Center. Later, through the auspices of the LA Free Clinic, she became Tepper's patient.

"She had severe stenosis and a foot drop," he remembers. "We did a decompression, she regained muscle strength, function and got rid of a good deal of pain. In the course of her rehabilitation I used other patients as attorneys and we got her a green card. She moved out of the shelter to a community home, enrolled in English classes and now walks a mile or two each day to class and a mile or two to church."

As he tells the story Tepper leans across his desk, his voice excited, his face animated, his thinning hair hanging in Shirley Temple curls to his shoulders. "She is getting back on her feet," he exclaims. "She has been a blessing to take care of."

Dr. Gil Tepper, F.A.C.S., a Fellow of the American Academy of Orthopaedic Surgeons and a Diplomat of the American Board of Orthopedic Surgery, could take care of the woman from Ethiopia because he has done something many

orthopedists dream about but few accomplish—build their very own orthopedic hospital. The Miracle Mile Medical Center (named for its location) is a full blown general hospital with every department except an emergency room. He has the same license as do neighboring university and community hospitals and is licensed for 17 acute care general hospital beds. The Center operates as a limited liability corporation. Tepper is the general and managing partner. Other physicians are limited partners and have a financial interest in the hospital. Ultimately," he says," if you are running it efficiently and frugally, it is an economic opportunity."

Standing in the parking lot of the hospital Tepper notes the tracks from the electric gate and the poles of the twelve foot high chain-link fence (topped with rolls of barbed wire) that was there when the building served as the largest, most productive abortion clinic in the United States. The owner, Dr. Edward Allred, headed up a network of family planning clinics up and down the coast that performed out-patient abortions while doctors at this building handled the more complicated and late-term abortions.

According to Tepper, Allred was doing hundreds of abortions a week and made so much money he was able to buy the Los Alamitos race track.

Tepper spent one year in planning and two years convincing Allred to sell him the premises. He bought the building in 2004, pulled down the fence and got rid of the electronic gate. Along with the building he got the hospital license, and a commitment to transfer all of the regulatory hospital paperwork to his name. Procedures changed overnight. Abortions stopped. Tepper's application

Dr. Gil Tepper / Courtesy Miracle Mile Medical Center

for a different use of the facilities was approved. Though he is Jewish, Tepper is touched that elderly ladies with rosaries in their hands still approach his parking lot to bless the hospital because of the change that was made.

Why did a spine surgeon who was doing more and more complex spine surgery take on the administrative and financial headaches of owning and running a hospital? Tepper says it began with frustration over the calls in the middle of the night that a patient is sitting around waiting for a nurse for an hour and the nurse is busy with 16 others—one of whom might be very sick.

"I would promise to call the nursing supervisor and I would tell my patients that I would do what I could. But at the end of the day I would have to say 'I am sorry, it is out of my control. I did what I could but we are at the mercy of the hospital, the hospital administrator, the nursing ratios, the regulations, etc. And I am just a surgeon who is doing the best he can.'"

Other scenarios that got to Tepper were when a surgery would be delayed because of an emergency or when a surgeon would be bumped because an older surgeon with a little more political clout would be moved ahead in the schedule. "And my patient would suffer in the process," Tepper remembers. "It was just the day-to-day stuff you deal with as surgeons. Miracle Mile was an opportunity to take care of the patient in a way that eliminates a lot of the headaches and a lot of the sources of grief in the system. You could buffer patients from that."

"I wanted to create a place that practices medicine differently from other places. The idea was to have ultimate control of patient care, to be able to deliver the care to patients the way you want to do it—and how you want it delivered to yourself. I knew some of it and I figured

Dr. Gil Tepper / Courtesy Miracle Mile Medical Center

I would learn as I go." Tepper readily admits that he is "living the dream."

The Miracle Mile Medical Center is 35,000 square feet, three stories tall and takes up an entire block at 6000 San Vicente Avenue. On the Ogden Street side of the building, entered through a separate entrance, is the Ogden Wing of the Spine Institute. Tepper describes it as a low volume, private patient setting where, twice a week, he sees from four to eight patients who want a singular, unique, upscale experience. The décor of the Ogden Clinic could be called "quiet contemporary" with polished wood floors and original paintings on the lilac and cream walls.

Entrance to the Medical Center and Hospital portion of the building is though the parking lot where an attendant directs the parking of cars, arranges for complimentary valet parking when the lot is full, and opens the Center door for patients. After checking in patients sink into overstuffed chairs and couches. No hard straight-backed chairs here. The vertebra from a whale leans into the corner under a flat-screen TV mounted on the wall.

On the second floor, where treatment rooms are located, patients are invited to help themselves from carts laden with healthy snacks and cans of fruit and vegetable juices. In the hospital section the nursing ratio is rarely less than two patients to one nurse. The hospital chef prepares personal menus for each patient and there is a dietician on staff. A Lincoln town car, carrying a cooler with beverages, is available to take patients home when discharged. If family members arrive for a patient at the dinner hour they are not sent away hungry. The staff arranges to serve them as well.

Tepper estimates that with his associate and physician assistant, he sees approximately 150 patients a week and does from four to eight surgeries. "We have about 50 to 60 doctors on staff here," he explains," and a group of twelve or so are the busy regulars. They like practicing here because the hospital is custom tailored to meet the needs of their patients."

Tepper attributes much of his success with patients to patient selection. "Ninety percent of our headaches come from five percent of our patients," he says. "We try every trick in the book to treat them without surgery, teach them to stay fit, exercise, participate in the active aspects of rehabilitation before surgery to try to avoid it. If we carefully select patients, good results come with it."

Besides the Miracle Mile Medical Center, Tepper is also the proprietor of the Sherman Oaks Valley Spine Center that he founded in 1998. This facility is 17,000 square feet of leased space with 14 examining rooms, compared to the eight at Miracle Mile. He spends two

days a week at the Sherman Oaks facility and the remainder at Miracle Mile.

Both Sherman Oaks and Miracle Mile Medical Center take Medicare, workman's compensation, all varieties of private insurance and private payers. The costs to the patient are the same as at other hospitals. Staff member Liz Cheever attributes the Center's success to the fact employees are aware of the necessity for cost containment and efficiency and are able to assume many roles. "I am the HR director, quality and risk manager, the associate administrator, am involved in medical records and billing of patients," she explains. "But I also go down to the admitting department if we are short staffed and answer phones. We are all cross trained."

To his staff, Tepper is a "rock star." Staffer Nate Hart says, "He has a heart this big, is a dedicated family man, loves the Lakers. Patients light up when he comes in. His personality fills the room. He is a captivating speaker and an excellent teacher." Tepper is an active participant in regional and national medical societies. Hart notes, "He likes to be in the forefront of any new procedure, anything that can have better outcomes for a patient's life. He was among the first surgeons in the country to perform an outpatient artificial disc replacement in 2003."

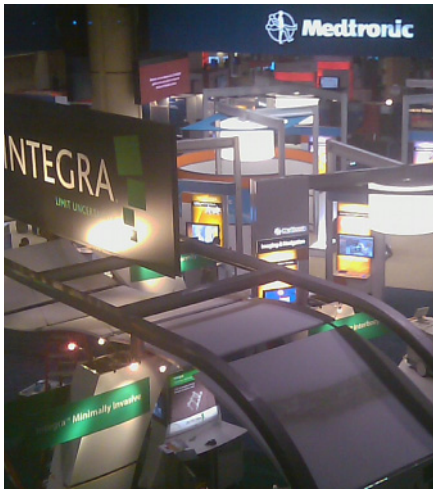
The son of two immigrants—Tepper's mother is a Holocaust survivor from Poland and his father is an Israeli—he completed his last two years of secondary schooling at Beverly Hills High School. He believes that being the child of a survivor has given him an enhanced sense of the importance of each day and a strong desire to share his skills.

Tepper is the founder of Los Angeles Free Spine Care (LAFS). In conjunction with the Saban Clinic (formerly the Los Angeles Free Clinic) Tepper accepts referrals for orthopedic care and he and his staff treat the patients without charge. The Center currently treats about 40 LAFS patients, of whom approximately eight have had surgery.

As Tepper looks ahead he finds it hard to predict what changes the new health care legislation will bring about. "For someone like us that already have a charity arm and see all kinds of patients I think the new system may help us in some ways. Young physicians should look to create this kind of opportunity. I think it would be good for entrepreneurial physicians to assemble a group around them and do something like this. At the end of the day it improves our life styles as physicians, increases our control over our choices with the patients' best interests in mind. And it enables physicians to control some of the unknowns and some of the areas in patient care that—only after many years of experience—can you know enough to help a patient through." ◆

Missing Link at NASS' 25th Birthday Party

By Walter Eisner



Photos: Orthopedics This Week

The North American Spine Society (NASS) just held its 25th birthday party in Orlando.

The biggest, smallest and newest players from the spine community were all there. Medtronic, DePuy, Synthes... wait, where was Synthes? The third largest kid on the spine block was nowhere to be found in the exhibit hall.

Coming on the heels of Medtronic Chairman Bill Hawkins' announcement that spine surgeons' influence is waning, we wondered if Synthes' conspicuous absence was a sign of the times and a wake up call for NASS.

Synthes' Conspicuous Absence

"Why weren't you at the meeting?" we asked, via email, Synthes' spokesperson Gilgian Eisner (no relation to this writer).

Eisner told us that the company's products do not really sell at the conference exhibition but are sold through the sales force in hospitals and operating rooms. "After conferring with society leadership on the best way to support NASS, we decided to opt out of the exhibit hall for 2010, and to provide a substantial increase in society managed financial support."

Synthes continues to discuss the company's role in future meetings with medical societies. Eisner said the general consensus is that the societies preferred to

"So beginning in 2011, we will return to the exhibit hall, but with a renewed focus on improving the exhibit hall experience for each meeting attendee," added Eisner.

NASS' Eric Muehlbauer/Courtesy NASS, Levar Cooper

Bill Plovanic/ courtesy of CANACCORD/Genuity

receive less financial support, and to keep Synthes as an exhibitor. He said many of the societies feel strongly that the exhibit hall is a vital component of the overall conference experience for each attendee.

"So beginning in 2011, we will return to the exhibit hall, but with a renewed focus on improving the exhibit hall experience for each meeting attendee," added Eisner.

Eric Muehlbauer, NASS' Executive Director agrees. Muehlbauer told *OTW* that he gives Synthes credit for trying something new and looks forward to seeing the company back on the exhibit floor in Chicago.

Muehlbauer told us that NASS provides a forum and marketplace for device companies at the annual meeting and the marketplace takes its own course. In Orlando over 3,500 attendees showed up, with an additional 3,700 industry representatives. "We had more exhibitors than ever," said Muehlbauer.

Not everyone at the birthday party was singing Happy Birthday.

Wall Street: "Macro Pressures & Desperate Measures"

Canaccord Genuity's device analyst Bill Plovanic* summarized the meeting for his clients with the headline: "*Macro Pressures & Desperate Measures.*" He said the impact of macro pressures was "glaringly noticeable at the meeting."

"Over the next few years, we expect to see a decreasing number of company exhibitors and surgeons in attendance as several surgeons we spoke with found very little value-add in the meeting and appear to be looking at alternative spine conferences for the future."

"Overall, the meeting presented a range of emotions associated with grief, including denial, anger, bargaining and depression (but no acceptance). We expect Darwin's theory to play out for both implant manufacturers and surgeons, as sweeping change will provide both opportunities and challenges in the dynamic spine industry."

NASS Defends Meeting

Besides noting a record number of exhibitors, Muehlbauer reminded us that there is a waiting list of companies that want to be on the exhibit floor. "If we wanted to, we could have an even larger trade show," added Muehlbauer, "but that's not our goal. Our goal is to try to keep the attendee to exhibitor ratio as close to 1 to 1 as we can."

It's also worth noting that since the last NASS meeting, the society added a record number of nearly 700 new members to the ranks.

Being a specialized society is an advantage during difficult economic times, according to Muehlbauer. As marketing budgets tighten for manufacturers, the ability to "rifle-shot" their message to a highly specialized audience is more cost effective than a "shotgun" approach.

But back to the meeting.

Plovanic cited several key take ways from the meeting, including:

- The increased offering of lateral access fusion approaches and an improved outlook for cervical discs.
- Clarity from surgeons on the payer pushback that is making it more

Ray Baker, M.D./Photo Courtesy NASS, Levar Cooper

arduous to prove medical necessity for spinal procedures.

- Surgeons' conversations are becoming more financially weighted as it relates to pricing.
- Vertebroplasty and kyphoplasty remain on the brink and he believes a blanket CMS (Centers for Medicare and Medicaid Services) non-coverage decision is possible.
- Physician-owned distributorships (PODs) are another trend proliferating in a market where some surgeons are looking to supplement declining incomes.

Baker's "State of Spine"

In his farewell speech, outgoing NASS President Ray Baker, M.D., said society policies in ethics, professionalism, and health policy are now yielding dividends. "Payers and regulators, in particular, are taking notice. Amongst spine care professionals across North America and abroad; NASS is increasingly seen as THE reasonable and credible voice for spine care."

Baker, a pain specialist, was not in denial of the changing environment.

"No one can deny that the challenges we face are very real. I know that many of us, at times, feel like Woody Allen when he said, 'One path leads to despair and utter hopelessness. The other, to total extinction. Let us hope that we have the wisdom to choose correctly.'"

"We are in the midst of the worst economic downturn this country has faced since the great depression. We have endured the glare of intense public scrutiny with heightened rhetoric leading up to passage of health care reform legislation. We now face the uncertainty of defining and implementing those unprecedented changes. Meanwhile, we watch as our reimbursements continue to spiral downward, tort reform is taken off the national agenda, and the SGR (sustainable growth rate) formula goes unaddressed."

Physician Solidarity

In perhaps a veiled reference to the apparent disagreement with AAOS (American Academy of Orthopaedic Surgeons) over vertebroplasty and kyphoplasty, Baker cautioned:

"There are many forces trying to divide us today. Coding and reimbursement remain a zero sum game—when one party wins another must lose. Scope of practice issues loom large on the horizon. Yet, as lines blur between and among specialties, we must remain united."

He noted that 11 major societies recently held their second Spine Summit at NASS.

"I'm encouraged that the coalition of societies placed working together on common coding and reimbursement issues at the top of their action item list for the coming year."

Changing Economics

In his most pointed comments about the changing economic landscape for physicians, he cited Dr. Atul Gawande's *New Yorker* article about the vastly different per capita Medicare expenditures between the Texas communities of McAllen and El Paso.

In 2006, McAllen's Medicare expenditures were twice that of El Paso's even while having lower quality ratings. In 1992, the costs per patient were identical. "What happened?" asked Baker.

He quotes Gawande:

"About fifteen years ago…something began to change in McAllen. A few leaders of local institutions took profit growth to be a legitimate ethic in the practice of medicine. Not all the doctors accepted this. But they failed to discourage those who did. **So…a medical community came to treat patients the way subprime-mort-**

"For those physicians who are happy to be employees of the hospital, have no affiliations with companies…we feel the changes will be bearable. However, for the high-volume, top recognized, seven-figure surgeon in a private practice with strong corporate ties, we feel the changes are going to be devastating."

gage lenders treated home buyers: as profit centers."

Baker urged his colleagues to take heart and look at the big picture.

"When I first entered practice, senior colleagues complained that the golden age of medicine had just passed. Medicine was going to hell in a hand basket. Now, two decades later, I hear my contemporaries saying the same thing. It appears to me that the definition of 'the golden age of medicine' is the era ending precisely when you begin practice. But in reality, medicine, like everything else, is in a continual state of change and evolution. Change is, at times, unsettling, but change is also inevitable."

Impact of Quality-Based Health Care

Plovanic's view was a bit more granular.

He said the meeting marked the beginning of the transition to a quality-based [health care] system from a volume-based one and will have "no impact for the average surgeon, but a major negative for the high volume 'engaged' surgeon."

"Compared to other surgical specialties, spine surgeons have been living like rock stars. With favorable reimbursement, hoards of sales reps available to service their every need, and consulting agreements as ubiquitous as ATM machines, doctors have been very happy."

Plovanic says he believes that this year's NASS meeting was a wake-up call for all spine surgeons.

"For those physicians who are happy to be employees of the hospital, have no affiliations with companies… we feel the changes will be bearable. However, for the high-volume, top recognized, seven-figure surgeon in a private practice with strong corporate ties, we feel the changes are going to be devastating."

Plovanic writes that the days of device companies growing their sales through consulting agreements for performing studies or designing a new product will soon change.

What will likely become the norm, predicts Plovanic, is that the development of procedures or products that improve outcomes, reduce trauma to the patient and/or hospital stays, or speed up a surgical procedure will be the main drivers for adoption of new technologies.

Birthday Party in 2011

We suspect the exhibit floor for NASS' 26th meeting will look very much like this year's, with the addition of Synthes. What will likely change, as companies execute new marketing strategies, will be how attendees are engaged by the exhibitors and by their society.

Birthday parties grow up.

** Canaccord Genuity asks OTW to include a conflict of interest disclosure document as it relates to their role as a broker/dealer. Click here.* ◆

Editorial: Dr. Christopher Centeno's FDA Critique

By Christopher J. Centeno, M.D., and Brent Robinson

Bio: Dr. Centeno is board certified in Physical Medicine and Rehabilitation and Interventional Pain Management. He is one of a handful of practicing physicians with clinical experience in the use of culture expanded mesenchymal stem cells for the treatment of musculoskeletal disorders. He has published numerous research studies on the use of adult stem cells and diagnosis and treatment of traumatic injury.

Christopher J. Centeno, M.D.

Is Activated Platelet Rich Plasma or Bone Marrow Aspirate a Drug to be Regulated by FDA?

Cellular medicine is a growing trend in orthopedic care, with many physicians using autologous platelet rich plasma (PRP) for indications such as tendon and cartilage healing.[1-2] [3] In addition, many spine surgeons have begun using bone marrow aspirate concentrate (BMAC) to enhance spinal fusion. Physicians have traditionally used 510K cleared medical devices (bedside centrifuges) to prepare PRP and BMAC. However, what these same surgeons may not be aware of is that subtle changes to the federal drug code (21 CFR 1271.1) made in 2004, when applied to activated PRP and certain uses of BMAC, purport to make these autologous substances federally regulated drugs requiring an extensive and costly Biologics License Application (BLA).

The problem began in 2004, when the Food and Drug Administration (FDA) dramatically, and quietly, changed its regulatory approach with potential to upset the traditional wall between surgical care and drug regulation. Historically, the FDA has never had the power to control any aspect of the relationship between a doctor and a patient.[4-6] In 2004, the agency made changes to the 361 Public Health Service Act (PHSA) act to classify certain autologous cells as biologic drugs requiring pre-market, federal approval before interstate distribution.[7] Before these changes in 2004, the FDA only had authority over allogeneic tissue transplants. This portion of the 1271 regulation serves the important function of preventing communicable disease transmission from donor to recipient. However, after these 2004 changes, the tissue transplant regulations were altered by the agency to also apply to all human tissue, with caveats for certain autologous tissues being regulated the same as mass pro-

Photo manipulation by RRY Publications. Source: Creative Commons

duced drugs. For the first time, this gave the FDA the authority over certain aspects of surgical procedures.

21 CFR 1271.1-1271.3 defines two categories of cells to be regulated, which the agency call Human Cells Tissues or Products (HCT/P's). The HCT/P's can be either more than or less than "minimally manipulated." If they are more than minimally manipulated, they must first have premarket drug approval, just like a new antibiotic. If they are less than minimally manipulated, they can be treated as the practice of medicine. The dividing line between HCT/P's treated like drugs and those left largely unregulated is if the "processing" of the autologous cells changes their "relevant biologic characteristics." While PRP that is simply used "as is" from a 510K cleared device is less than minimally manipulated and left unregulated, PRP that is coagulant activated with calcium and/or thrombin falls into a different category. This is because recent research demonstrates that even slight alterations in the dose of these activation agents can produce wide variations in platelet growth factor release and kinetics.[8] This means activation significantly alters the relevant biologic characteristics of the platelets (growth factor release) and thus qualifies PRP as "more than minimally manipulated", hence making activated PRP a new drug requiring a BLA new drug application per 21 CFR 1271. In addition, in its own documents, the FDA clearly refers to the term "activation" as constituting more than minimal manipulation.[9]

BMAC suffers from the same premarket drug approval problems when it's mixed with other substances that would alter the biologic characteristics of the key cells in the mix, namely mesenchymal stem cells (MSC's) that promote bony fusion.[10] Take for example a surgeon's use of a bedside centrifuge to process a bone marrow aspirate commonly utilized to promote spinal fusion. Many manufacturers recommend activating the BMAC with coagulant agents such as thrombin before surgical use. However, coagulant activation makes the BMAC a drug based on data showing that it changes the biologic characteristics of MSC's within the mix.[11-13] In addition, from multiple publications, it's clear that many of the biologic characteristics of MSC's are altered by the commercially available BMP's that many surgeons also use simultaneously with BMAC to promote bone growth.[14-15]

Are these autologous cells drugs? We believe there are significant problems with this regulatory paradigm. For example, consider a recent publication showing that a routine MRI magnetic field changes the biologic characteristics of stem cells.[16] This paper shows that a common MRI techniques dramatically change the gene expression and bone forming ability of MSC's, making them "more than minimally manipulated" cells per 21 CFR 1271.3(f)(2). If a surgeon creates BMAC using a bone marrow aspirate and a bedside centrifuge, places these into a patient's spine during surgery to promote fusion (not mixing them with another agent), and then orders an MRI for another reason, do the stem cells used in the patient become federally regulated drugs after a routine MRI?

Are activated PRP or BMAC + Coagulants +/- BMP's new federally regulated drugs? Will federal agents be knocking on your O.R. door anytime soon or requiring a one million dollar upgrade to your operating room to make it follow current Good Manufacturing Practices

(drug factory guidelines)? In summary, the problem with 21 CFR 1271 is the assertion by FDA that certain processing steps for autologous cells makes those cells federally regulated drugs and that it's rules apply to physicians practicing medicine. Any surgical or medical procedure by definition is the practice of medicine representing a one-on-one risk to the patient, not a one-on-many, drug mass production risk, something the agency has traditionally regulated. Turning autologous PRP or BMAC into drugs is not supported by any common sense argument. Furthermore, the agency's decision to insert itself into the practice of medicine by creating these regulations, sets a dangerous precedent. Where does this line get moved to in the future? Do certain compounded drugs get assigned a drug manufacture risk? Certain high risk surgeries? Certain high risk surgeries involving cells or drugs? Perhaps the judge in U.S. v. Evers (United States v. Evers, 453 F. Supp. 1141 (M.D. Ala. 1978)) put it best when he opined "Congress did not intend the Food and Drug Administration to interfere with medical practice as between the physician and the patient." Surgeons and their patients have a great interest in keeping it that way.

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The Latest in Limb Salvage

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

Orthopedist to fracture patient in the ER: "Your tibia will just have to be a bit disfigured…oh, and there's some dead bone in there, but it shouldn't cause any problems. There may be a plastic surgeon available at another local hospital, but it's just too complicated to try and find one."

An orthopedist would surely never utter such words to a patient. But the reality "on the ground," say our experts, is that orthopedic patients whose limbs are in danger haven't always had the full complement of care they need—including appropriate plastic surgery services. In some areas of the country, however, things are improving.

Final Results. Photo courtesy The Penn Extremity Reconstructive Cente

Dr. L. Scott Levin, Chairman of the Department of Orthopaedic Surgery at the University of Pennsylvania and Professor of Plastic Surgery, is both an orthopedist and a plastic surgeon. When Dr. Levin joined "Penn" in 2009 he brought with him a vision of a seamless, multidisciplinary center for limb salvage and reconstruction. Now, the plans for The Penn Extremity Reconstructive Center (PERC) are complete and the doors are set to open soon.

Dr. Levin states, "Traditionally, there have been stand-alone wound centers, trauma centers, and the occasional limb salvage center. In most cases they are run by a single service like hyperbaric medicine or vascular surgery. Our center will be jointly administered by the Department of Orthopaedic Surgery and the Division of Plastic Surgery. What we are creating is a true multidisciplinary center built on the marriage of orthopedics and plastic surgery—"orthoplastic." It has been my dream to create this type of entity within an academic institution so that we can offer patients immediate access to orthopedics, vascular care, pain management, hyperbaric care, infection control, oncology, and imaging. I am proud to say it is the first such entity in the Northeastern United States."

PERC will focus on the treatment of acquired and congenital deformities of the upper and lower extremity, debilitating conditions that may result in loss of work, limb function, and chronic pain. Dr. Levin: "The sequelae of prior extremity injuries including nonunion and malunion also remains a formida-

"What we are creating is a true multidisciplinary center built on the marriage of orthopedics and plastic surgery—"orthoplastic." It has been my dream to create this type of entity within an academic institution so that we can offer patients immediate access to orthopedics, vascular care, pain management, hyperbaric care, infection control, oncology, and imaging. I am proud to say it is the first such entity in the Northeastern United States."

Final Results. Photo courtesy The Penn Extremity Reconstructive Cente

ble problem for many patients. These patients are best served in a multidisciplinary setting where they would benefit from staged reconstruction. Infections of the musculoskeletal system including osteomyelitis require aggressive treatment and ultimately many patients require bony and soft tissue reconstruction for optimal outcome."

So how will they ensure that there is a certain specialist available when needed? Dr. Levin notes, "The upside is that patients won't have to wait for hours, and can see multiple specialists at the same visit (or two visits if it is a particularly complex case). We will take care to have enough open 'PERC' slots in each of the specialists' schedules. For example, a patient with chronic osteomyelitis who needs imaging, an arteriogram, an orthopedic surgery consult, and an infectious disease specialist, can see all these people in one day, and have a coordinated treatment plan developed along the way."

When creating a symphony, however, there are sometimes discordant notes. "This effort requires mature individuals who know what they don't know. An orthopedist has to be able to say, 'I don't know what antibiotics to give this person,' and then call in a specialist. Tamping down the ego is always necessary in order to do the best for one's patient. In effect, these multidisciplinary centers should be run by people who are doing this type of work all the time. And like any team, as long as you don't care who gets the credit then the work will get done."

A Multidisciplinary Approach Saves the Day

With regard to the delicate issue of limb salvage versus amputation, says Dr. Levin, a multidisciplinary approach can save the day. "The joint decision may be that instead of salvaging the limb, we need to amputate because it has been functioning so poorly for so long. While the consensus is fairly uniform, there are times when one physician says, 'This limb can't be saved'—but then they don't know what I have in my toolbox as a plastic surgeon. We take care to continually educate our team as to what each person/department has to offer this type of patient."

The most complex cases require a particularly methodical approach, says Dr. Levin. "In someone with polytrauma,

"While the consensus is fairly uniform, there are times when one physician says, 'This limb can't be saved'—but then they don't know what I have in my toolbox as a plastic surgeon."

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a staged reconstruction is the most appropriate treatment. For example, a multiply injured patient comes in who requires vascular reconstruction to get blood flowing into his leg. This would be followed by a microvascular tissue transfer procedure that may or may not be done at the same time. So if the vascular repair is done well, then that sets the stage for the remainder of the efforts to save the limb."

And how will this novel program be evaluated? "We will be performing outcome studies with some patients as historic controls (those who have not had a multidisciplinary approach). Then we will look at the incidence of amputation. We will use quality of life indicators and outcome research methodology to continually evaluate the success and failure of limb salvage and drill down on whether salvage or amputation improves quality of life under multiple conditions (oncologic reconstruction/acute trauma/chronic infection)."

Dr. Stephen Kovach, Co-Director of The Penn Extremity Reconstructive Center, is a plastic surgeon. He adds, "Our typical patient is a younger person with acute lower extremity trauma; we can offer these individuals exceptional orthopedic care, along with plastic surgery treatment for the soft tissue defect in a timely manner. We also see patients whose fractures have been treated elsewhere and have recalcitrant nonunions…in those cases we can offer these patients advanced microsurgical techniques for limb salvage. These techniques are also useful when it comes to salvaging limb length. Many of our patients with extremity injuries require the integrated care of multiple services to afford them the best care and chance of salvage of the function and appearance of the traumatized limb. The Center would offer them that chance. Overall, our hope is that in five years The Penn Extremity Reconstructive Center will be treating patients from all over the world."

Final Results. Photo courtesy The Penn Extremity Reconstructive Cente

Dr. Randy Sherman, Vice Chair of the Department of Surgery at Cedars-Sinai Medical Center, is a plastic surgeon who is a past president of the American Society of Reconstructive Microsurgery. He states, "Cedars-Sinai is a level one trauma center in which the plastic surgery unit is integrated for early response, stabilization, and early reconstruction. When someone comes in we immediately perform a complete evaluation of the extremity, including imaging, neurological testing, and vascular imaging—all so that we can assess how best to stabilize someone and get him or her ambulating as quickly as possible. This process also helps us gain a realistic understanding as to whether the patient is capable of undergoing a reconstruction."

"For example, take someone with a multiple segmental fracture whose knee and ankle are destroyed; this person also has neurological damage to the extremity. Together, these things mean that the patient may never actually be ambulatory again; in that case it is not in the best interest of the patient to put them through 12 months of complex reconstructive surgeries. If we select patients correctly then we can move them rapidly toward fixation and wound cover at the same time. The unique thing that we bring to the table as a plastic surgery service is the ability to not have orthopedic reconstruction be comprised by a marginal or inadequate soft tissue envelope. If an orthopedic surgeon performs a sophisticated operation but the plates get infected then the result will be osteomylitis or a nonunion. But if a free tissue transfer was done as well then the patient may be able to go on to healing without infection, with an earlier discharge, and with earlier bone healing. To achieve this streamlined approach, however, means that plastic surgeons must be dedicated to responding quickly to orthopedic surgeons."

"The need for plastic surgery expertise in orthopedics has appeared in the literature for many years. And the issue is not that my orthopedic colleagues don't want to do the right thing; often, however, the logistics and the availability of plastic surgeons have gotten in the way."

Convinced that plastic surgery is no longer just a pretty face, Dr. Sherman says, "My message to orthopedists is, 'Recognize tissue deficiency early and don't be afraid to involve a plastic surgeon from day one.' If I'm delivering this message to an audience of orthopedists, this is the point when three-fourths of them say, 'But I can't find a plastic surgeon who will do this work.' Things are changing, though, and I am pleased to see that plastic surgery is evolving towards a greater commitment to orthopedics. Previously, the economics of plastic surgery were such that there were enormous advantages to performing cosmetic surgery. Conversely, there were numerous disadvantages to performing reconstructive surgery, including poor reimbursement, sick patients, etc."

Sometimes the drumbeat of progress takes awhile to hear. In this case, says Dr. Sherman, it's been about 40 decades. "The need for plastic surgery expertise in orthopedics has appeared in the literature for many years. And the issue is not that my orthopedic colleagues don't want to do the right thing; often, however, the logistics and the availability of plastic surgeons have gotten in the way."

And then there are just times when the orthopedist isn't aware of what a plastic surgeon can offer. "The classic example—and the one that causes the most problems—is that of open tibial fractures, the most common type of fracture in the lower extremity. The problem with the lower leg is that the front side is thin skin over bone and the back is a lot of muscle. With a fracture, the bone protrudes and there is a significant amount of soft tissue damage. The orthopedist fixes the fracture, recloses the skin and puts plates in (which adds volume). You are also stripping the blood supply, and, because the skin is open, microbes have gotten in. The solution is to add soft tissue to that area using a muscle flap, a piece of muscle that has been rotated around from the back to the front or set free from abdomen and reapplied using a microvascular procedure."

When saving a limb is at issue, time is of the essence. In such cases, an all-out approach with in-house expertise is the best we can offer patients. ◆

company

Pioneer Goes Irish

Pioneer Surgical is planning to open a manufacturing and distribution facility in Ireland by the end of 2011.

The company announced on October 11 that discussions have been initiated with the Ireland Development Authority (IDA) to evaluate potential sites for the European expansion.

morguefile.com

According to a company press release, Pioneer is experiencing continued growth in Europe and the new facility will allow for the manufacturing of devices intended for sale outside the U.S. and allow for more responsive delivery of products in the European market.

Expresses Commitment to Marquette

The company was quick to try and ease local fears in Michigan's Upper Peninsula of the loss of jobs.

"Pioneer's commitment to the local and regional economy remains strong. The company continues to support local educational programs that benefit the company's high-quality, cost-effective manufacturing operations. In 2007, Pioneer expanded its facility in Marquette to more than 110,000 square feet to support continued growth in spinal and orthopedic operations," stated the announcement.

Pioneer's global headquarters in Marquette, Michigan, currently coordinates activity at physical properties located in Raleigh and Greenville, North Carolina; Woburn, Massachusetts; and the Netherlands. According to Pioneer's Vice President of Operations, Brian Motter, "While our present manufacturing facility in Marquette will continue to grow, the ability to provide products from a European facility is an essential part of our worldwide growth initiative. Having established a European presence with the opening of our offices in the Netherlands in 2006, we will continue to grow in Europe and the rest of the world. This facility will enable us to be more responsive to customers outside of the United States."

Earlier this year, Pioneer opened a facility in Austin, Texas. The facility houses the company's spine development division.

—WE (October 15, 2010) ◆

Biomet Stumbles, Binder Optimistic

Wikimedia Commons / Biomet

Despite having to report the worst quarterly financial result since taking over Biomet, Jeff Binder was in a good mood, joking with analysts during his conference call with Wall Street analysts on October 12.

Biomet did not have a good quarter. In fact it was an unexpectedly slow quarter.

The company's first quarter for 2011 showed a total sales increase of only 2%. The news was better in the U.S., where sales increased 5%. Europe was down 11%.

Biomet 1Q11	Sales $mm	% Change	% Change U.S.
Net Sales	$640.7	2%	5%
Reconstructive	$478.4	2%	7%
Knees		4%	6%
Hips		0	4%
Extremities		25%	40%
Spine	$56.1	0	2%
Fixation	$59.4	(3.00%)	0

Source: Biomet

Below Expectations

Binder, Biomet's President and CEO said the growth was "lower than our expectations." He attributed the slow growth to a "deceleration of procedural growth in the market."

Binder said he continues to be "very optimistic about the long-term growth potential of the markets in which

we compete and, as our first quarter results show, we have increased our research and development investments to address unmet clinical needs. During the first quarter, we reported strong cash flow generation, which provides us with additional opportunities to further strengthen our growing business."

The company reported an increase of $5 million in R&D expenses for the quarter. It was also announced during the quarter that the company would be expanding its production facilities in Warsaw, Indiana.

The increase in knee sales was primarily driven by demand for the Vanguard Complete Knee System and E1 antioxidant infused tibial bearings. Key products for extremities included the Comprehensive Primary and Reverse Shoulder Systems.

Spinal stimulation sales growth was positive during the quarter, while sales were flat for the spine hardware and orthobiologics product category.

For the quarter, the company narrowed its reported net loss of $17.8 million from $22.8 million in the first quarter of 2010. As of August 31, the company had a net debt of $5.65 billion with $274 million in cash on hand. Biomet's war chest is significantly smaller than competitors. However, the large debt is to a group of Wall Street investment firms, led by the Blackstone Group, and if the company needs cash for a strategic initiative, it's likely the money could be found on Wall Street.

Market Ripe for Differentiation

Binder declined to predict when market growth in orthopedics will return to previous growth levels, admitting to not having seen the persistent slowdown in procedures after June. "My predictive powers have been called into question," quipped Binder with analysts. He was in a good mood.

However, he remains optimistic. He said "Boomers" will not sit on the sideline with pain forever and with considerable unmet needs still remaining, the market is "ripe for differentiation" for new products.

Biomet's competitors will report quarterly results over the next few weeks.

—WE (October 13, 2010) ◆

Honors for Aesculap

The OrthoPilot Navigation System from Aesculap recently received the Best Practice Award for 2010 from the global market research company Frost & Sullivan.

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One of the first CT-free navigation systems, OrthoPilot is a computer-aided, image-free navigation system that was first developed in 1997 with the goal of improving surgical workflow and achieving optimal implant alignment. Over the past decade-plus, the system has been used for over 140,000 procedures. The system can be customized with software packages for the hip, knee or sports suite and there are applicatons for total knee arthoplasty, total hip arthoplasty, anterior cruciate ligament, high tibial osteotomy and unicompartmental knee arthoplasty.

The award is part of the 2010 Growth Excellence Awards which was created to acknowledge companies that make a difference with their innovations in the current economy. OrthoPilot was awarded the "European Image Guided Surgery Vertical Market Penetration Leadership Award." The distinction is for a company that quickly adds to its vertical penetration in a market.

Dr. Dirk Friedrich, Director R&D Portfolio Management & New Technologies accepted the award. He said in his acceptance speech that he was thankful to all of Aesculap's customers and employees of B. Braun Aesculap, while

expressing gratitude to Frost & Sullivan for the award, stating that the hosts created a great incentive for driving orthopedic navigation and have thus encouraged further innovation. "We are firmly convinced that computer-guided surgery will play an essential role by furthering quality assurance," finished Friedrich.

About Aesculap, Frost & Sullivan said at the ceremony, "Aesculap's European market share within the image-guided surgery market for orthopaedic applications has increased significantly during the past couple of years. While the company held about 20 percent of the image guided surgery market for orthopaedic applications in 2006, its market share in 2008 is estimated to be 27.5 percent; this represents a 37.5 percent growth in market share within two years. In addition, the number of procedures in which Aesculap's OrthoPilot navigation system is used, including total hip and knee arthroplasty, anterior cruciate ligament and high tibial osteotomy, also increased during this period."

—JR (October 10, 2010) ◆

legal

Photo manipulation by RRY Publications. Source: Wikimedia Commons and FDA

FDA Issues Bisphosphonates Warning

The FDA issued a warning to patients taking bisphosphonates, such as Boniva and Reclast, to treat osteoporosis. The October 13 warning alerted patients and their physicians of possible increased risk of thigh bone fractures.

> **According to the warning, atypical femur fractures have been predominantly reported in patients taking bisphosphonates. Atypical subtrochanteric femur fractures are fractures in the bone just below the hip joint. Diaphyseal femur fractures occur in the long part of the thigh bone. These fractures are very uncommon and appear to account for less than 1% of all hip and femur fractures overall.**

Bisphosphonates Reduce Osteoporotic Fractures

Bisphosphonates inhibit the loss of bone mass in people with osteoporosis and have been shown to reduce the rate of osteoporotic fractures in people with osteoporosis.

This information will be added to the Warnings and Precautions section of the labels approved to treat osteoporosis, including **Fosamax, Fosamax Plus D, Actonel, Actonel with Calcium, Boniva, Atelvia, and Reclast (and their generic products).** A Medication Guide will also be required to be given to patients when they pick up their bisphosphonate prescription.

Patient and Physician Guidance

Patients should continue to take their medication unless told to stop by their provider. FDA recommends that healthcare professionals should discontinue potent antiresorptive medications (including bisphosphonates) in patients who have evidence of a femoral shaft fractures.

"The FDA is continuing to evaluate data about the safety and effectiveness of bisphosphonates when used long-term for osteoporosis treatment," said RADM Sandra Kweder, M.D., Deputy Director, Office of New Drugs in the FDA's Center for Drug Evaluation and Research.

Physicians should be aware of the possible risk in patients taking these drugs for longer than five years and consider periodic reevaluation of the need for continued use of the drugs.

Report Side Effects

> **Patients taking the drugs should report any new thigh or groin pain to their health care provider and be evaluated for a possible femur fracture. Patients and their physicians should report side effects with the use of bisphosphonates to the FDA's MedWatch Adverse Event Reporting program at www.fda.gov/MedWatch or by calling (800) 332-1088.**

—WE (October 13, 2010) ◆

FDA Clearance for NovaBone Putty

This is a very busy putty…NovaBone Products has announced that the FDA has given 510k clearance of the NovaBone Putty MIS Delivery System designed for use in minimally invasive orthopedic procedures. According to the company, the NovaBone Putty MIS Delivery System delivers an osteocon-

biologics

Wikiemedia Commons/RRY Publications

ductive matrix while signaling and stimulating osteoblastic activity to the orthopedic surgical site.

The NovaBone MIS Delivery System includes a syringe pre-loaded with ready-to-use NovaBone Putty and 6mm diameter cannulas at varying lengths. The system was developed for surgeons who require controlled and precise delivery of bone grafting material to the surgical site. The product is approved for use in orthopedic surgeries of the extremities, the pelvis and posterolateral spine.

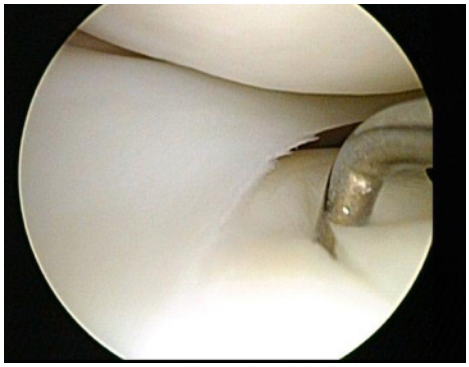
"The launch of the MIS Delivery System will be just the beginning of products our company will be offering to spine surgeons, neurosurgeons and orthopedic surgeons," said Art Wotiz, President of NovaBone Products, in the news release. "As a growing medical device company, we will introduce a number of new products this year and through 2011 that are based on advancements in bioengineered medical technology."

NovaBone representative Dennis McBride told *OTW*, "The NovaBone MIS system transforms how bone grafting material is delivered during minimally invasive surgery. The 6mm cannula, available at varying lengths, allows for the controlled and precise delivery of this unique bioactive bone graft. The bioactive material is capable of signaling and recruiting osteoprogenitor cells to the site while controlling the cell cycle to favor proliferation and differentiation of bone forming cells."

—*EH (October 15, 2010)* ◆

Study: BioCart System Shows Promise

Cartilage cells that do a great job of organizing themselves? Perhaps! ProChon Biotech has announced that results of a retrospective follow-up analysis of commercial patients who received the BioCart Autologous Cartilage System were recently presented at the 9th World Congress of the International Cartilage Repair Society (ICRS) in Barcelona. As indicated by the company, BioCart is a safe, minimally invasive, high-quality implant for long-term articular cartilage regeneration stemming from joint cartilage defects and injuries.



Lateral meniscus damaged tibial cartilage. Source: Arthroscopist/Wikimedia Commons

The study, led by Iris Eshed, M.D., at the Sheba Medical Center in Tel Hashomer, Israel, involved 31 patients who had been diagnosed with a single full-thickness cartilage defect, including those with previous knee operations. They were followed for up to four years after treatment with the BioCart System.

Dr. Eshed told *OTW*, "Significant improvement was seen in the International Knee Documentation Committee scores, reflecting clinical and functional improvement. Also, the significant change in the T2 Mapping values imply that remodeling can occur in the implanted cartilage repair tissue, resulting in re-organization of the implanted cartilage cells into the different layers typical of the native hyaline cartilage."

Also at the ICRS meeting, ProChon presented a case study involving a 24-year old male police officer who was implanted with a BioCart implant due

to severe damage to his medial patellar facet and lateral trochlea portions of his knee. Eight months post-surgery, an MRI showed almost normal appearance of the affected cartilage. The patient is back to full service as a police officer, including sports activities two years after implantation of two opposing but overlapping BioCart implants in the patella and trochlea. The physical examination of the knee is normal with 10 degrees of reduction in knee flexion and very mild reduction in quadriceps muscle tone.

"The ICRS World Congress is the premier venue for international collaboration in cartilaginous tissue research and we are pleased to introduce these compelling data sets to leading surgeons, scientists and clinical researchers," said Patrick O'Donnell, CEO of ProChon, in the news release. "Our Phase II clinical study of the BioCart System in the United States and Israel is entering the final stages of patient enrollment, which we anticipate completing early in the 2010 fourth quarter."

The BioCart System is commercially available in Israel and ProChon has established a cell processing facility in Italy. The System is undergoing an FDA Phase II multicenter clinical study in the U.S. and Israel. To date, over 95 BioCart surgical procedures in both clinical and commercial settings have been completed with some procedures over five years post-implantation.

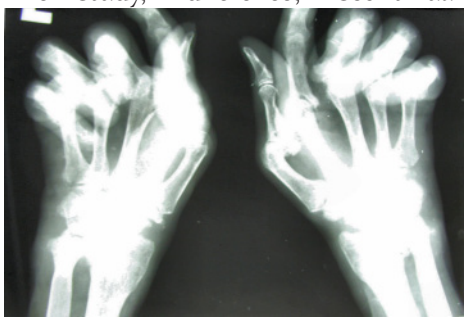
—EH (October 15, 2010) ◆

Medicaid Patients and Biologic RA Therapies

Biological treatments have shown promise for rheumatoid arthritis (RA) patients, and have been associated with significant improvement in outcomes including reduction in pain, joint swelling, serologic inflammatory indices, and rates of radiologic damage. Researchers from the University of Pennsylvania have recently determined that adherence to biologic treatment of rheumatoid arthritis (RA) among Medicaid patients is less than optimal.

The team reasoned that since the Medicaid population comprises a large part of the public payer health system, and is often underrepresented in clinical trials, that they should examine adherence to and discontinuation of RA biologics in such patients.

Their study, "Adherence, Discontinuation, and Switching of Biologic Therapies in Medicaid Enrollees with Rheumatoid Arthritis" published in ***Value in Health***, examined adherence, discontinuation, and switching of RA biologics (etanercept, anakinra, or infliximab) over a one year period following initiation of the biologic treatment in Medicaid patients with RA in California, Florida and New York. The study was co-authored by Pengxiang Li, Marissa A. Blum, Joan Von Feldt, Sean Hennessy, and Jalpa A. Doshi of the University of Pennsylvania.



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In the news release, Dr. Li stated, "This study provides valuable insights on the patterns of use of newly initiated RA biologics in routine clinical practice in three large state Medicaid programs whose combined enrollment represents approximately one-third of the total Medicaid enrollment in the U.S. Our findings of poor adherence to and premature discontinuation without concurrent switching of RA biologics among patients newly initiating these highly effective but expensive agents should raise concern for clinicians as well as payers."

The implication of the study findings will be discussed in ***Value in Health,*** the official journal of the International Society for Pharmacoeconomics and Outcomes Research.

—EH (October 15, 2010) ◆

UMass To Establish TJR Registry

How successful and effective is total joint replacement (TJR) surgery in younger patients?

The University of Massachusetts Medical School (UMMS) announced last month that it will establish a nationwide registry of 33,000 patients who have had TJR surgery to find out. The purpose of the registry is to establish tools with which to assess the success and failure of the surgery and conduct research to guide clinical care and public policy.

The school is getting $12 million in comparative effectiveness dollars from the Agency for Healthcare Research and Quality (AHRQ), where much of the $1.1 billion from the stimulus bill for comparative effectiveness and $500 plus million appropriated annually for such efforts in this year's healthcare reform legislation is housed.

large joints

The proposed database of patients treated by 130 orthopedic surgeons representing all regions of the country and varied practice settings (urban and rural, low and high volume, community clinic and academic medical center) will be the basis of the study. UMMS will lead six high volume sites across the United States and one community practice network in recruiting patients into the registry. Participating high volume centers are:

- UMass Memorial Medical Center, Worcester, Massachusetts
- University of Rochester Medical Center, Rochester, New York
- University of Maryland Medical Center, Baltimore, Maryland
- Baylor College of Medicine, Houston, Texas
- Connecticut Joint Replacement Institute at St. Francis, Hartford, Connecticut
- Kaiser Permanente Georgia

In addition, a community practice network of 26 orthopedic offices with more than 100 surgeons will also participate.

The registry will provide information for key research areas such as joint replacement failure and technical or mechanical issues, as well as the impact of the replacement on the patient's mobility, function, pain and quality of life. In addition, data will be compiled regarding disparities in TJR use among certain ethnic, socioeconomic or demographic groups, and the value of TJR in younger patients.

Patricia D. Franklin, M.D., MBA, MPH, professor of orthopedics and physical rehabilitation and family medicine and community health, and principal investigator of the study, said, "Research data currently available is limited to the Medicare population and focuses on joint replacement failure: whether an implant has to be removed or revised with further surgery.

> **"We consider the surgery a failure if it doesn't provide pain relief or improved mobility or function for the patient. We want to do a better job of measuring the real human outcome of joint replacement for those patients that are active, working adults under 65."**

Vertex Select Reconstruction System Posted Screw Module/Source: Medtronic

Franklin expects the number of total joint replacements to increase by 600% in the next 20 years as the population ages and the prevalence of obesity increases. "As it does, more and more people under the age of 65 are opting for total knee or total hip replacements in order to maintain their active lifestyle, their ability to work and their long-term health."

—*WE (October 15, 2010)* ◆

Viviant Launched in Japan, Spain

Could it be "Sayonara" and "hasta luego" to postmenopausal osteoporosis? Ligand Pharmaceuticals Inc. is announcing that its partner Pfizer, Inc. has launched Viviant (Bazedoxifene)—a selective estrogen receptor modulator—in Japan for the treatment of postmenopausal osteoporosis. The company is also making progress in Spain, where it is sold under the brand name Conbriza, and marketed through a co-promotion with Almirall. Pfizer received manufacturing and marketing approval for the product in Japan

in July 2010. Viviant was approved in April 2009 by the European Commission (under the trade name Conbriza) for the treatment of postmenopausal osteoporosis in women at increased risk of fracture.

Viviant was born of a research collaboration between Wyeth (now Pfizer) and Ligand that began in 1994. Pfizer is handling the registration and worldwide marketing of bazedoxifene, a synthetic

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drug specifically designed to reduce the risk of osteoporotic fractures while also protecting uterine tissue.

"We are excited to see the progress of Viviant as it provides a new osteoporosis treatment option to postmenopausal women. This is now the third product that Ligand will earn royalties from out of a large portfolio of partnered, royalty bearing programs," said John L. Higgins, President and Chief Executive Officer of Ligand Pharmaceuticals, in the news release. "Viviant's commercial introduction in Japan and Spain reflects the quality of Ligand's collaborations and the expertise of its partners in business, product development and international regulatory affairs."

In a pivotal Phase III study involving more than 7,600 women worldwide, Viviant achieved a significant 42% reduction in the incidence of new vertebral fractures. In addition, a post-hoc analysis showed the incidence of non-vertebral fractures in a high-risk population was reduced by 50% and 44% compared to placebo and raloxifene, respectively.

—EH (October 13, 2010) ◆

spine

Medtronic Adds Posted Screw Module

Vertex Select Reconstruction System Posted Screw Module/Source: Medtronic

At the recent NASS meeting in Orlando, Medtronic launched a posted screw module to supplement the company's Vertex Select reconstruction system.

The U.S. launch was announced by Doug King, Medtronic Spine's VP and General Manager. King said the addition of the module, "further differentiates the Vertex System by enabling surgeons to choose between multiple fixation options to better accommodate patient anatomy and pathology." The system treats patients requiring fixation of the vertebrae in the upper-thoracic spine.

According to the company announcement, the reconstruction system consists of implants and general instruments that can be used to surgically treat patients with a variety of conditions that can contribute to spinal instability, including degenerative disc disease, spinal stenosis, fracture, tumors, and/or spondylolisthesis.

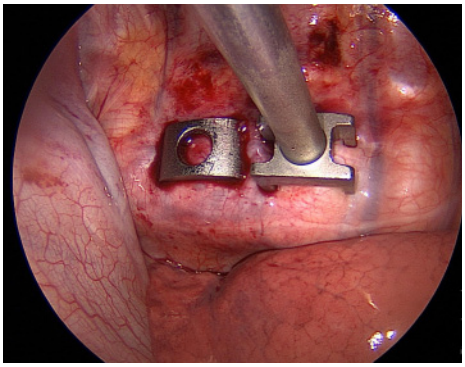
Specifically, the posted screw module provides surgeons the option of using a system that includes headless, posted screws and adjustable connectors for procedures requiring fixation in the upper-thoracic spine. These components allow for and enable connection from any direction, angle, and/or height. The connectors allow for variable rod and screw angles, and also rotate around the rod.

King added that the Vertex system has over nine years of clinical history.

—WE (October 13, 2010) ◆

New MIS Surgery for Scoliosis

Perhaps some good news for little ones suffering from scoliosis…A novel minimally invasive surgery for young children living with a difficult-to-treat progressive form of scoliosis, known as juvenile idiopathic scoliosis, may eliminate the need for spinal fusion later in adolescence, according to new research by surgeons from Children's



Courtesy: Children's Mercy Hospitals and Clinics

Mercy Hospitals and Clinics in Kansas City, Missouri. The procedure, known as vertebral body stapling (VBS), is a minimally invasive technique during which a series of metal connectors are placed to slow growth on one side of the spine.

"Scoliosis can be a challenge to treat, and can cause significant emotional distress to the child who must wear a body brace or be subjected to multiple surgeries," said George W. Holcomb, III, M.D., MBA, in the news release. Dr. Holcomb, surgeon-in-chief at Children's Mercy, added, "Our study demonstrates this relatively straight-forward procedure may be the answer for especially serious cases in young children with significant scoliosis."

Dr. Holcomb told *OTW*, "This VBS operation is designed to obviate the need for a more complex operation in adolescence for management of severe scoliosis. Thus, if the scoliosis found in the younger patients does not progress (or improves) as a result of either this operation or bracing, then the more complicated operation will not be needed. Some children will not wear the brace or if they do wear it, the scoliosis worsens. These are the two groups that might benefit from this VBS operation. Scoliosis is known to cause some lung and heart problems if left untreated. However, in this day and age, most children would not develop these problems if they underwent the more complicated operation later in adolescence. Therefore, if the children did not undergo the VBS operation (or if the scoliosis was treated successfully by bracing), then they probably would undergo the more complicated operation later in adolescence."

He also commented to *OTW*, "Right now, we are seeing more and more children that might be good candidates for this operation. We've done a total of eight more of these operations since the abstract was submitted and have continued to see the same good results so we remain hopeful that this may be a long-term solution to severe scoliosis in the younger child. We plan to continue to record our results and follow our patients closely to be sure these good early results remain good and that the scoliosis does not progress. It may be several years before we know for sure these good results will last."

—EH (October 12, 2010) ◆

THE PICTURE OF SUCCESS

Dr. Anthony Romeo

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

Dr. Anthony Romeo

Future Hall of Fame athlete Curt Schilling is the only pitcher in major league history to complete a World Series game as a 20 year old, a 30 year old and a 40 year old. Brett Favre, another future Hall of Fame athlete, has the most career victories as a starting quarterback in the history of the NFL and at age 40 took the Minnesota Vikings to an NFC championship game. What do these two remarkable athletes have in common? Astonishing shoulder durability…and Dr. Anthony Romeo.

Or perhaps more specifically, Dr. Romeo's innovative approach to tears of the labrum, which includes sewing down the tear in the superior labrum and taking the biceps tendon out of the shoulder joint. When Dr. Romeo first tried this approach many years ago it represented a direct challenge to the conventional wisdom that all superior labral lesions needed to be fixed. Curt Schilling and Brett Favre are just two notable examples of the thousands of people who've benefited from Dr. Romeo's brilliant, focused and persistent mind.

Today, as a full Professor of Orthopaedics at Rush University Medical Center, a team physician for the Chicago Bulls and the Chicago White Sox, as well as design surgeon for two widely used shoulder replacement systems, Dr. Anthony Romeo is recognized for the profound effect he has had on U.S. professional athletics and on the standard of care for shoulder repair. As a result, Dr. Romeo is this week's Picture of Success.

Dr. Romeo's training began by tagging along behind his dad on many 2AM trips to the ER when his father was a physician in the U.S. Navy, then later as a family physician in a small Idaho community.

"I spent most of my youth in a small town Idaho, where my five siblings and I often trailed along behind my dad. My mom kept us all moving forward in the right direction; I was born when my parents were seniors in college, so my mother had to give up her educational dreams for me and her family; she was especially focused on our education. I didn't disappoint her, as I was the valedictorian (in addition to being captain of the football team)."

While Anthony Romeo was inspired by those "field trips" to the ER, and his mother's devotion to education, his early interests were broad. "My parents have said that I was always determined to exceed whatever boundaries stood in front of me, and that I wanted to explore everything (choir, art, etc.). Nothing drew me in like medicine, however. It sounds cliché, but I could see that giving of myself to patients would be a rewarding way to spend my life."

After completing his undergraduate studies at Notre Dame, Anthony Romeo entered his father's alma mater for medical school: St. Louis University (SLU). "Because I played football at Notre Dame my grades suffered a bit. I was one of the last students accepted to SLU, but I worked hard and graduated in the top 5% of the class."

Then he heard the voices…the naysayers, that is. "You want to go to Cleveland Clinic for residency? Students from SLU can't get into their program." Dr. Romeo: "I tuned these people out, pressed on, and was accepted into the Cleveland Clinic program. There I encountered a few other cynics who said, 'Rick Matsen's fellowship in Seattle? Good luck. No one from here has ever been accepted into his program.'"

So when he arrived on Dr. Matsen's Seattle doorstep, the unrelenting Dr. Romeo had accomplished something indeed. "I was thrilled to be acquiring such high level training in shoulder, which had become my passion. I had injured my shoulder while playing football at Notre Dame and was struck by the real lack of knowledge about shoul-

"I have the uncanny ability to focus on the surgical procedure at hand while also talking about what I am doing. For example, I recently performed a surgery in Vienna that was broadcast to 700 surgeons, along with a moderator. All the while I was answering questions about what I was doing."

der. The treating orthopedist just said, 'Put some ice on it.' I had found something that merited further investigation! By the time I reached my fellowship, I was thoroughly consumed with discovering all I could about the shoulder."

A trailblazer, Dr. Romeo took his knowledge and improved upon current practices. "Dr. Matsen and his partner, the late Dr. Harryman, taught me the principles of shoulder surgery, namely, the unchanging rules of how the shoulder works and how to treat it with current open or developing arthroscopic techniques (when most shoulder surgeons were doing open procedures). When I went into practice most surgeons were just beginning to attempt surgeries with an arthroscope, which has its limitations. They were actually changing the way they were treating the shoulder just so they could do the surgery arthroscopically. My approach was to alter the existing tools and instruments to match the principles of shoulder surgery. This principle-based approach turned out so well that I am routinely approached by U.S. and foreign training facilities to teach my methods."

And when he does have an audience, jaws often drop. "I have the uncanny ability to focus on the surgical procedure at hand while also talking about what I am doing. For example, I recently performed a surgery in Vienna that was broadcast to 700 surgeons, along with a moderator. All the while I was answering questions about what I was doing. I've had people say to me, 'It's like you have two brains, one for lecturing and one for the procedure.' I tell them, 'It's just like with a professional athlete… they don't know how to explain it—it just happens.'"

While he cannot teach residents and fellows that particular talent, he can offer them extraordinary knowledge, coupled with some hard won life lessons. "I really emphasize to my trainees the importance of listening to patients, saying, 'The patients themselves will tell you what is wrong with their shoulders.' I focus on a thorough history and physical exam and tell them that as they learn their specialty they will be able to understand 90% of what comes in the door with just the history and examination, supported by plain radiographs. The goal is not to manage what you see but to take care of the problem the patient came in for. If you are staring at a problematic rotator cuff, but the patient is complaining of shoulder slippage, then you must investigate further."

"On a more personal level, I try to get trainees to understand the necessity of living a balanced life. In this profession we have many wonderful opportunities to help people, as well as, frankly, opportunities to feed our egos. The problem is often that we forget about the other parts of our lives. In the long run our ability to sustain that which gives us these rewards is what we do outside of our practice. If you fail to work on your personal life then your professional life will suffer and you won't reach the heights you desire. I have five daughters and was married at 22 years old. While I worked hard to be a good surgeon and dad, and thought I was being a good partner, I was often busy and for a variety of reasons the marriage didn't last. For seven years now I have been raising my five teenage daughters by myself. This is a wonderful blessing, but the challenges can be overwhelming without the support of family and friends. 'Remember,' I tell young surgeons, 'the bright lights and patient admiration is seductive, but we must balance this out with our personal lives.'"

When it is work time, however, Dr. Romeo is exceptionally focused. And if Mrs. Jones has a problem he can't solve…he takes it to the lab. "Whenever I have a patient with a problem that I don't understand, I 'sit with it.' Then, after awhile, in come a few more people

with the same problem…then we go to the lab, study it, and then apply the findings to clinical practice."

"For example, almost twenty years ago I learned how to treat superior labral tears from the people who first described them in the literature. I found that even though I could perform the operation as well as they could, I couldn't get the same results. My colleagues and I found that there are groups of patients that don't do well with what is considered the standard of care—and that many of them had postop problems with their biceps tendon. We secured a grant from Major League Baseball and investigated our way of repairing the labrum that involved sewing it down and taking the biceps tendon out of the shoulder joint. Interestingly, we learned that little if anything happened to the shoulder. We are overturning the traditional wisdom that all superior labral lesions needed to be fixed."

Industry took note of Dr. Romeo's unconventional methods, and extended its hand. "Right out of fellowship I was on the design team for a DePuy shoulder replacement system; I went on to work on a shoulder replacement system with Tornier. I developed their first press fit stem, and I was the first surgeon in the United States to implant their shoulder in 1997. Now, I design and develop shoulder replacement systems and techniques, including advanced arthroscopic techniques, with Arthrex. We are changing the instrumentation such that shoulder replacement can be done minimally invasively, without injuring the rotator cuff. This is going to change rehabilitation and will be easier on the tissues around the shoulder… it also may improve the longevity of shoulder replacements."

Now a far cry from the soda shop in Idaho, Dr. Romeo muses about his journey, "Growing up in a small town in Idaho didn't exactly lend me confidence that I could compete on a bigger stage. I have been pleasantly surprised that I could succeed against some of the brightest people I have ever met. One of my greatest assets has been my determination. Whenever someone threw up a roadblock, I just went over or around it. When I made it known that I was going to begin focusing my practice solely on shoulder and elbow, my partners had a meeting to discuss how this was going to affect our practice since this was less than half of my patients at the time. I pursued my plan and within six months my practice was twice as busy. Another thing that drives me is that I find tremendous personal value in helping others, something which makes me 'dig' until I find the answer to their problem. It's very rewarding to hear, 'If anyone can figure it out, it's Dr. Romeo.'"

Dr. Romeo has brought his sense of purpose and big heart to his most important 'operation'—raising his five daughters. "On the weekend, usually Sunday lunch, we gather around and talk for a couple of hours about what is going on in their lives. We also take trips together, attend various sporting and cultural events, and periodically head to the mountains for snowboarding or to the beach to relax. As for my personal time, I get up each day at 4:00AM to work out—whether I feel like it or not. In the overall scheme of things it's what keeps me healthy so I that can enjoy life to its fullest. It also gives me the ability to manage and overcome stress and life's challenges."

Dr. Anthony Romeo...extending and building the quality of life. ◆

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