VOLUME 5, ISSUE 11 | APRIL 7, 2009

Orthopedics This Week

week in review

05 Abuse of the Alpha: Stryker's OP-1 Shot Down ♦ In one of the most dramatic FDA Ortho Panel meetings in years, Stryker's OP-1 was found safe but not effective. The Panel said Stryker "Abused the Alpha." Read all about what they meant and what it means for Stryker.

10 The Orphan of Orthopedics ♦ The orthopedic needs of children have long taken a back seat to those of adults. Now, with their own set of superheroes, the kids may have a chance to catch up with the big folks.

15 Seriously, Should JNJ Break Up? ♦ With 238 subsidiaries and 118,700 employees, JNJ is one of the most complex enterprises in the world. If JNJ were a country it would be the 60th largest. Has the time come for radical decentralization? Could be. Read on.

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For all the news that is Ortho, read on.

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Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

This Week: Get ready for down sales reports this quarter. Procedure volumes in the first quarter hit an air pocket and they will be down year-over-year and quarter-over-quarter. Will probably push orthopedic stock prices down in April. Q2 and Q3 will be recovery quarters amidst a generally upbeat stock market.

Rank	Last Week	Company	TTM Op Margin	30-Day Price Change	Comment
1	1	Zimmer	29.96%	7.87%	Deferred prosecution agreements over. All charges were dropped. Focus is now 110% on products, surgeons, and revenues.
2	5	Stryker	23.13	(0.09)	What do you do with OP-1? Move on. How many more dollars and careers need to crash on these rocks?
3	4	ArthroCare	16.87	86.44	New CFO. Maybe we get numbers? Bottom line, buyers now betting that the intrinsic value of ARTC is higher than 0.44 PSR.
4	3	Symmetry	9.92	32.07	This quarter's drop in procedure volumes will have to affect SMA. Consensus of analysts is a **f** at YOY and a $101 million revenue quarter.
5	2	Medtronic	31.68	11.68	Sure, OP-1 loses at the FDA. This has no impact on INFUSE. The #1 issue is declining spine procedures overall in Q1.
6	9	Johnson & Johnson	25.36	9.47	Breaking up JNJ would be like setting baby raptors loose in the jungle—more aggressive companies that eat what they kill.
7	10	Integra LifeSciences	12.37	10.74	Specializing in neurosurgery has its advantages in this kind of challenging procedure market.
8	7	Osteotech	2.48	19.30	Consensus sales estimate for 2009 is for a 9% sales decline. They need new products, new technologies. It's time for a revolution!
9	8	Orthofix	6.70	30.50	Ramius loses, but does OFIX win? Will the lessons of this fight result in better sales growth?
10	6	Synthes	33.70	(2.79)	Lofty profit margins is a two edge sword. Yes, plenty of cash, but miserable returns. What to buy? Tough fiduciary duty.

Robin Young's Orthopedic Universe

Top Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	ArthroCare	ARTC	$5.50	$146	86.4%
2	I Flow Corp	IFLO	$4.03	$99	67.2%
3	Regen Biologics	RGBO.OB	$3.00	$29	44.9%
4	Symmetry Medical	SMA	$6.26	$224	32.1%
5	Orthofix	OFIX	$19.17	$328	30.5%
6	Capstone T erapeutics	CAPS	$0.58	$24	28.9%
7	CryoLife	CRY	$5.26	$148	24.9%
8	NuVasive	NUVA	$30.49	$1,110	22.4%
9	CONMED	CNMD	$14.91	$433	21.7%
10	RTI Biologics Inc	RTIX	$3.11	$169	19.6%

Worst Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	Exactech	EXAC	$12.48	$159	-4.0%
2	Synthes	SYST.VX	$108.72	$12,907	-2.8%
3	Smith & Nephew	SNN	$32.30	$5,700	-0.4%
4	Stryker	SYK	$33.29	$13,200	-0.1%
5	Orthovita	VITA	$2.84	$216	2.5%
6	Mako Surgical	MAKO	$7.80	$195	4.0%
7	Wright Medical	WMGI	$13.21	$502	5.3%
8	Zimmer Holdings	ZMH	$36.85	$8,210	7.9%
9	**Average**			**$8,565**	**8.2%**
10	Alphatec Holdings	ATEC	$1.84	$87	8.2%

Lowest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Symmetry Medical	SMA	$6.26	$224	5.52
2	Orthofix	OFIX	$19.17	$328	8.18
3	Zimmer Holdings	ZMH	$36.85	$8,210	8.80
4	CONMED	CNMD	$14.91	$433	9.69
5	Medtronic	MDT	$29.83	$33,390	10.28

Highest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	I Flow Corp	IFLO	$4.03	$99	44.69
2	NuVasive	NUVA	$30.49	$1,110	41.66
3	RTI Biologics Inc	RTIX	$3.11	$169	25.23
4	Osteotech	OSTE	$3.40	$61	19.35
5	Synthes	SYST.VX	$108.72	$12,907	17.56

Lowest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	Symmetry Medical	SMA	$6.26	$224	0.62
2	Integra LifeSciences	IART	$23.20	$653	0.68
3	Stryker	SYK	$33.29	$13,200	0.73
4	Smith & Nephew	SNN	$32.30	$5,700	0.84
5	CryoLife	CRY	$5.26	$148	0.87

Highest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	NuVasive	NUVA	$30.49	$1,110	23.55
2	RTI Biologics Inc	RTIX	$3.11	$169	1.66
3	Johnson & Johnson	JNJ	$52.15	$144,240	1.46
4	**Average**			**$8,565**	**1.40**
5	Orthofix	OFIX	$19.17	$328	1.17

Lowest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	Symmetry Medical	SMA	$6.26	$224	0.53
2	Osteotech	OSTE	$3.40	$61	0.59
3	CONMED	CNMD	$14.91	$433	0.59
4	Orthofix	OFIX	$19.17	$328	0.64
5	I Flow Corp	IFLO	$4.03	$99	0.78

Highest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	TiGenix	TIG.BR	$4.00	$97	220.88
2	Mako Surgical	MAKO	$7.80	$195	64.67
3	Regen Biologics	RGBO.OB	$3.00	$29	19.55
4	TranS1	TSON	$6.45	$133	5.22
5	NuVasive	NUVA	$30.49	$1,110	4.63

Abuse of the Alpha: Stryker's OP-1 Shot Down

By Walter Eisner

Blame the "Abuse of the Alpha" for the defeat of Stryker's OP-1 Putty at the FDA's Orthopaedic and Rehabilitative Devices Panel meeting on March 31. The panel voted 6–1 on Dr. Brent Blumenstein's motion not to recommend approval of Stryker's PMA application to the FDA.

The panel found OP-1 to be safe, but due to f aws in Stryker's methodology of measuring success, the panel could not find credible evidence that OP-1 was effective.

OP-1

Before we get into the dramatic FDA meeting, here's a quick primer on sthe product.

OP-1 is a combination product containing device and drug components consisting of a bovine

Stryker's OP-1

Type I collagen derived from demineralized bone, a recombinant human bone morphogenetic protein (rhBMP-7) – Osteogenic Protein (OP), and carboxymethylcellulose (CMC).

OP-1 Putty attempts to make a new posterolateral spinal fusion in patients who have had a failed posterolateral spinal fusion. The product is mixed with a sterile saline solution and a thickening agent to form a putty-like material. During surgery, the Putty is placed on each side of the spinal levels that need to be fused.

The protein then initiates bone formation.

The trial under consideration at the meeting has been running since 1999 and is the second trial for the material in the U.S. The first occurred in 1998 when OP-1 in tibial fracture non-unions failed to show radiographic proof of fusion.

The FDA approved this device under the Humanitarian Device Exemption (HDE) program in 2004. Since that time 15,000 patients have been treated with the device in the U.S., and 25,000 patients have been treated worldwide since 2001.

On February 19, 2009, the European Medicines Agency (EMEA) granted authorization for Stryker to market OP-1 Putty (known as Opgenra) in

certain spinal fusion applications in 28 European nations.

Stryker said the primary benefit of the device is that the putty eliminates the need for autograft harvesting. This is no small matter to a patient who avoids a secondary surgery and the associated complications. The patient also benefits from decreased operative time and anesthesia exposure and decreased blood loss.

Abuse of the Alpha

Prior to the meeting, FDA staff issued their concerns that OP-1 missed its pivotal trial primary endpoint and that Stryker changed the endpoint four times but still did not hit statistical efficacy.

By the time Stryker finished its presentation at 10:00 in the morning, and before FDA staff began their attack, the handwriting was on the wall. When panel member Brent Blumenstein, Ph.D., told the company that by going beyond the original endpoints of the trial it was biasing the data against the control group and was "doing something not quite right," it was apparent the company had hit a deal breaker with at least one panel member.

Blumenstein elaborated on that in the afternoon when answering FDA questions about effectiveness. He called Stryker's trial the "abuse of the alpha," where the "p" values were not interpretable.

What he meant was that by changing the parameters of what defines success, the company had abused the notion of a statistical set of facts based on assumptions going into the trial, and therefore the declared outcome no longer could be counted on with confidence.

That was it. Game over.

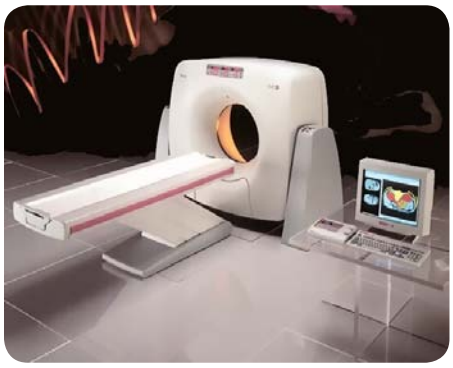
Statisticians Rule

This time the statisticians on the panel convinced their physician colleagues that statistical flaws outweighed any possible clinical benefits that might come from the product. Only Paul McCormick, M.D., M.P.H., from Columbia University voted to recommend approval. He believed that for the right patient, the demonstrated ability of OP-1 to induce bone growth was a tool he wanted in his arsenal.

Bridge Over Troubled Waters

One of the endpoints of Stryker's definition of success shifted from demonstrating "bridging bone" to "bone formation." One of the orthopedic surgeons on the panel, John Kirkpatrick, M.D., was not sure that bone formation created fusion.

This prompted statistician Kathleen Propert, Sc.D., to ask the orthopods, "What is bridging?"



CT Scanner

Kirkpatrick told her to imagine a bunch of bricks put together to span a river, creating something that is able to hold up your car. That's bridging. He said that forming bone was more like throwing the bricks into the river to create a dam, which is not bridging.

Stryker's inability to show "bridging" through X-rays prompted it to go back and take post hoc CT (computed tomography) scans, which demonstrated bone formation. The company said it didn't consider the use of the CT technology originally for measuring bone growth because the CT technology was not sophisticated enough. Since the start of the trial, however, it said that CT technology had made advancements.

Stryker determined that the use of plain films was inappropriate for the

evaluation of its product and that the initial radiographic reviewers had been looking in the wrong location for the fusion mass. The company based that determination on its observation that the OP-1 implant had migrated laterally.

Stryker then designed and conducted an extension study to collect a single CT scan image from any available study subjects.

Because the company had completed the follow-up several years previously, the new CT scan data represented a time period ranging from 36 months post-op to almost 72 months post-op.

The FDA said the resulting dataset was not representative of any single post-op time point and did not include data from all treated subjects.

Using the additional CT scan data, Stryker proposed a fourth definition of overall success. The company's analysis showed that the investigational treatment was statistically non-inferior to the control treatment.

But the FDA, and ultimately the panel, didn't buy it. They said that a statistical non-inferiority could not be claimed because of the post hoc changes.

Stryker's Cost

It's been a long road for Stryker and OP-1. Company CEO and President Stephen MacMillan has spent the last few years explaining to Wall Street analysts during quarterly earnings calls that progress was being made in getting the product ready for FDA consideration. The revenues from the product aren't significant in the scheme of things, but the cost of time, effort, attention, and credibility has been significant.

The Massachusetts plant that makes the putty received a warning letter from the FDA in May 2008 regarding quality and compliance issues, and a federal grand jury has been impaneled by the U.S. Attorney in Boston to investigate whether or not the company violated criminal laws in how it marketed the product. Two former Stryker employees have already pled guilty to charges regarding that marketing.

The FDA meeting room at the Hilton in Gaithersburg was filled with Stryker employees, consultants and family members. Even Stryker's skipper, MacMillan, was in attendance.

MacMillan sat alone for a moment on the side as the long torturous road of OP-1 appeared to come to a screeching halt with the vote of the panel. Then he slowly gathered himself up and waded into the throng of Stryker employees, consultants and family members. The group included some kids to whom MacMillan said something about how proud they should be of their Dad and the great work he'd done on the OP-1 project.

It was too early to intrude into the loss with questions about what's next. But he graciously promised *OTW* readers an answer to that question in the near future.

No ReGen Hangover

The dynamics of this meeting were dramatic.

First, Stryker had a lot riding on this meeting because of the high profile OP-1 had reached with analysts over the years.

Second, this was the first panel meeting since the ReGen Biologics Ortho Panel meeting in November. That was the meeting after which Panel Chair Jay Mabrey, M.D., publicly accused the agency of stacking the panel with members to give the agency the result it wanted. That charge prompted us to ask Chairman Mabrey if he had lost confidence in the FDA and whether or not he would resign from the Ortho Panel. "Not at this time," was his answer.

We asked the FDA if this meeting's credibility was undermined by Dr. Mabrey's comments. The agency's spokesperson, Siobhan DeLancey, told us that the FDA didn't stack the panel at the last meeting and didn't stack this one either. She acknowledged that Dr. Mabrey's comments did not add to the credibility of the process.

After the ReGen Biologics panel meeting, Dr. Mabrey also said that had he known how the FDA would eventually rule on the ReGen clearance request, he would have spoken up at the meeting. DeLancey noted that as Chair, Dr. Mabrey could speak up as he deems necessary.

Our sense was that the FDA and Dr. Mabrey were not "feeling the love" for each other at the moment.

Panel members and other FDA staff told us they had the highest confidence in Dr. Mabrey.

We asked a Stryker spokesperson whether or not the company had any concerns about the credibility of the panel or the meeting. He said the company had no comments on that subject.

We also asked the representative of the Medical Device Manufacturers Association, Pam Adams, if that association had any concerns about the credibility of the panel. Adams, a former Ortho Panel member, told us the association had not discussed this issue.

Several of the veteran attendees at the meeting told us off the record that some people were wondering about the whole value of the panel process. They said the process was unclear, confusing and inconsistent in approving some products and not others.

Meeting Lessons

We agree with the Wachovia Capital analysts, who wrote in an investor note after the meeting:

- The FDA almost never "approves" a change in trial endpoint; the FDA representative at the OP-1 [meeting] stated rather clearly that the FDA will acknowledge a sponsor's ability and/or need to pursue a different endpoint (particularly when a change in the standard of care is present) and will allow them to defend the position accordingly, but they do not "approve" changes in endpoint once a trial has enrolled its first patient.
- Humanitarian Device Exemptions and Orphan Drug Indications do not circumvent a company's need to demonstrate safety in the regulatory package (PMA/BLA/NDA). The application must stand on its own merits.
- There is no such thing as real-time data; if you look at the dataset and do a retrospective analysis you must take a statistical penalty.

Or as Dr. Blumenstein might say, "Respect the Alpha."

Back to the Drawing Board

The panel found OP-1 to be safe, but any future approvals for the device would likely require Stryker to start over with a new clinical trial. Since the company demonstrated that OP-1 was effective in promoting

FDA Official Summary

The sponsor and FDA presentations focused on pre-clinical testing relating to manufacturing and immunogenicity of the protein, and the clinical results comparing OP-1 Putty to an autograft control.

The sponsor presented clinical results using the original and modified endpoints, while FDA presented their analysis based upon the endpoint approved in the original approved IDE protocol, as well as their concerns with the subsequent analyses of modified endpoints. Except for an analysis of a modified endpoint using data collected at least three years after the initial surgery, all other analyses showed that OP-1 Putty did not achieve non-inferiority compared to the control treatment.

[There was] a significant difference between the endpoints used for the radiographic evaluation related to the use of the presence of bridging bone (radiographic definition originally approved in the IDE) versus any bone (radiographic definition contained in the modified endpoints).

The Panel voted (6-1-0) to recommend that the PMA application for OP-1 Putty be found "Not Approvable."

While acknowledging that OP-1 Putty generally appeared to be safe and potentially held promise in the future, the Panel was concerned

about the changes in the study protocol, not convinced that the study results based on presence of bone instead of bridging bone demonstrated effectiveness, and had outstanding concerns relating to the immunogenicity of the product.

The Panel recommended that future consideration be given to understanding the immunological response of OP-1 Putty, as well as to design of a future study, including issues of contemporary study design to incorporate instrumented fusions, expanding the study population, including CT scans from the start, and characterizing the amount of product in the bloodstream.

bone growth, it might find uses for the product in other indications of bone disease.

Thomas Weisel Partners analyst Raj Denhoy wrote in an April 1 investor note that Stryker recently completed enrollment in a pilot study for OP-1 in transforaminal lumbar interbody fusions.

"With over 15 years and tens of millions of dollars invested in OP-1 and only two humanitarian device exemptions to show for it (long bone non-unions and failed spinal fusion surgeries), Stryker faces difficult choices on whether to continue investing in developing the material," wrote Denhoy.

Members of the panel said that they may accept a shorter duration study (less than one year) focused on "bridging the bone" versus "presence of bone" with better CT scan technology.

Analyst Joanne Wuensch of BMO Capital Markets wrote in her investor note after the meeting that she believes OP-1 continues to represent a significant market opportunity for Stryker and doubts that the company will drop its efforts in leveraging this technology opportunity.

Stryker spokesperson Aaron Kwittken told us after the meeting that the company was very disappointed by the FDA Ortho Panel's vote. "We believe the clinical evidence that we submitted and the long history of OP-1's use demonstrate OP-1's proven safety record," said Kwittken.

The FDA panel's recommendations bring to mind strategic decisions made many years ago as Medtronic chose the INFUSE route, while Stryker bet on OP-1. Now it's back to the drawing board for Stryker.

The Orphan of Orthopedics

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

They can't drive, serve on committees, or testify on "the Hill" about market conditions. And let's face it…the baby lobby in Washington isn't that strong. But the orthopedic needs of children, which have long taken a back seat to those of adults, are beginning to get more attention. And they now have their own set of superheroes.

Nick Deeter, Chairman, President and CEO of OrthoPediatrics, explains: "As opposed to the adult implant world where things are very scientific and systematic, implants going into children are largely modified adult implants. For years, the approach has been, 'Let's just downsize it and hope it works.' But such an approach misses a fundamental understanding of the anatomy and science behind the skeletal system of the growing child."

In the last few years, however, those with the most power to act have

Laser scanning system collecting topographical data from the Hamann-Todd Osteological Collection

begun to bring law and order to what has historically been somewhat arbitrary. Says Dr. Robert Campbell, a pediatric orthopedist at Children's Hospital of Philadelphia, "While pediatric orthopedics has forever been the orphan of orthopedics, there is a new emphasis on innovation in our specialty, dating back to the passage of the Pediatric Medical Device Safety and Improvement Act of 2007. I was pleased to be invited by the bill's sponsors, Senators Christopher Dodd and Hillary Clinton, to testify to the Senate Committee on Health, Education, Labor, and Pensions in support of the bill. Fortunately for all of us involved in this specialty, the bill mandated that the National Institutes of Health (NIH) and the FDA focus on getting pediatric devices to market in a more efficient manner. Since passage of the Act, there has been a significant shift in attitude toward pediatric devices with more small manufacturers getting involved because of the new profit incentive for humanitarian use devices. The FDA has also taken a more proactive stance by assisting developers in design of protocols for regulatory approval. In addition, the NIH had a meeting last summer to define the gaps in pediatric device research and is currently working on a translational research infrastructure for pediatric therapies, including devices."

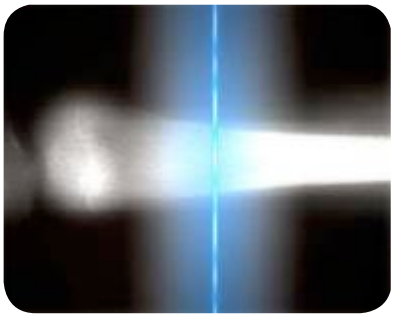
So out with the random, in with the randomized. The challenge seems obvious, namely, "How do you make products for a growing body?" Greg Downey: "OrthoPediatrics took an approach that no one in industry had ever done—to become experts at understanding the science behind the growing pediatric skeleton. In addition to consulting with many of the top pediatric orthopedic surgeons in the United States, OrthoPediatrics sought to capture as much historical clinical data as possible regarding topographical and intramedullary information. The first step was gathering data from the world famous Hamann-Todd Osteological Collection, which has more than 3,100 human skeletons that were assembled in the early 1900s, and is the largest human skeletal collection in existence. Not only does OrthoPediatrics have exclusive rights to the pediatric specimens, but it has also obtained the rights to the Bolton-Brush Growth Study, which contains yearly full-body X-rays of more than 4000 healthy children. The Bolton-Brush collection represents the world's most comprehensive source of longitudinal human growth data ever recorded. These collections are just one of several tools that we use to develop

anatomically appropriate implants for children."

Downey continues, "Several trauma products that the company expects to launch in 2009 incorporate this information. It is important that products accommodate the bow that is often found in young bones and minimize any potential trauma that can be done to growth plates. In pediatrics, there really is a difference with gender and age, things which must be taken into consideration throughout the development process. One of the products, currently awaiting FDA approval, is an intermedullary (IM) nail designed for longbones that goes into the canal of the femur. Developed with Dr. Eric Gordon, a St. Louis pediatric orthopedic surgeon, the IM nail or 'PediNail' will be offered in a broad array of anatomical sizes and is designed for lateral entry. It also helps the surgeon avoid the growth plate and the sensitive vascular area found in the greater trochanteric region of children…great progress indeed."

Detailing the evolution of their work with these impressive collections, Downey states, "We have been working with a Fortune 100 computer software firm to pull the collections together. They have taken these very large image files and cataloged them for optimal search. From there, we are able to overlay multiple images, take 3D measurements, as well as import additional X-ray or CT files for cross analysis, such as subjects with rare bone diseases. These powerful tools are allowing us to design anatomically appropriate implants that truly take into account the size, gender and age differences found in the pediatric population."

Downey continues, "We are also working with Dr. Tracy Ballock, the head of pediatric orthopedics at the Cleveland Clinic, who has discovered a way of using autologous stem cells to regenerate growth plates in children. Over 17,000 children a year suffer from some sort of a traumatic injury where the growth plate can be ruptured, at which time a bony band can form in the gap. This stress or tether can actually arrest the growth plate or cause the limb to grow irregularly. OrthoPediatrics and Dr. Ballock are currently in a Phase I study; The Indiana Economic Development Corporation has provided matching funds and grant assistance that recently resulted in a submission to the National Institutes of Health."



Laser collecting radiographical data from the Bolton-Brush Growth Study

Loud scary noises and burning heat are not things you want anywhere near your child. To this end, OrthoPediatrics has developed a quiet cast removal system that will put children more at ease than the current high decibel, high temperature system. Nick Deeter, co-founder of OrthoPediatrics, explains, "Over the course of meeting with hundreds of pediatric orthopedic surgeons from across the country and around the world, we've gained incredible insight into this underserved niche and what these special surgeons really need. One suggestion was consistent: 'You need to build a quiet cast removal device.'"

Greg Downey: "It's very stressful for kids to see these large oscillating blades with high rpms tethered to a shop vac…and hear the 90 to 100 decibels associated with it, which is comparable to the sound of a chainsaw or lawnmower. And the temperature is really a problem. The saw plunges through the casting material and that friction causes the blade to reach 180 degrees, something that can cause serious burns. We have pictures of children with horrible burns on their

legs. Our device is the size of a small hand drill that is exceptionally quiet… about the decibel level of a whisper. It creates no debris, there is no frightening high speed blade, and the system crushes and shears all of the material in one shot, as opposed to a traditional cast saw that requires some prying open."

Dr. Scott Kozin

Dr. Scott Kozin, a pediatric upper extremity surgeon at the Shriners Hospital for Children in Philadelphia, is among those keeping an eye on new developments in the field. Dr. Kozin: "I recently attended a conference on bridging the gap between developmental embryologists and surgeons. We are seeing kids born with congenital anomalies or differences of the hands, arms, and legs. In animal models using chicks and salamanders we can recreate what we see clinically by manipulating limb development, either by mechanical means or by affecting the genes. Even more amazing, a salamander can regenerate a limb and hand. As you might imagine, the Department of Defense is particularly interested in this work and in fact has funded much of it. Another area of intense growth and interest is genetic analysis of families affected by limb differences. We are seeing more kids with problems that have been linked to a genetic origin. Now we can, for example, look at a family's recessive trait and see that there is a one in four chance that a child will be affected. If the diagnosis is bad, such as cancer, an option is pre-implantation genetic diagnosis or PGD. This technique requires in vitro fertilization and growing the embryo until it is eight cells. The next step is to take a single cell out of the embryo and test that cell for the genetic defect that leads to the disease. If the cell has it, then you don't put it back in the uterus. Only the unaffected embryos are implanted. Conferences that combine clinicians and researchers are an important opportunity for surgeons and researchers to exchange ideas."

Those people are also experimenting with axons…Dr. Kozin explains, "The concept of nerve regeneration is now on the horizon. Researchers can affect the rate and success of nerve regeneration by genetically manipulating cells in a certain area. Most people doing this work are in labs, thus it is hard for basic orthopedic surgeons to have contact with them. This 'cross-fertilization' conference was so important that the *Journal of Bone and Joint Surgery* published a supplement on it and agreed to send it to their readership."

Those having experienced traumatic or congenital limb loss have new reason to hope. "There are now more advances in prosthetics, which, although they are being funded by the military, are becoming available to children," says Dr. Kozin. "There are new, very realistic looking prosthetic hands that function similarly to a normal hand providing pinch and grasp. Advances in lower extremity prostheses are making walking, running, and jumping more efficient. The innovations include prosthetic design and the development of new materials that conserve energy. The biggest stumbling blocks are funding and reimbursement. Generally speaking when you make things smaller they become more expensive. But, if we can show that such advances impact children's ability to function and saves resources for those treating them, that will help motivate the insurance companies to step up to the plate. We have had some success in the past demonstrating that new technology, such as functional electrical stimulation, decreases the amount of time that a patient needs caregivers, and increases independence."

"Imaging modalities are also improving," states Dr. Kozin. "Higher quality MRIs and improved MRI coils, which should be commercially available in about two years, are giving us the

ability to visualize small structures. Such technology will allow us to make better and earlier diagnoses for children. For example, if you have a patient with a cut tendon, given current imaging, it is easy to visualize that in an adult, but hard to do so in a child."

He continues, "Also new is the fetal treatment of amniotic band syndrome, a condition where the band goes around a limb. Fetal surgeons are now able to diagnose this on an ultrasound and release/cut those bands (we think they are pieces of the chorion). As far as instrumentation we have a limb lengthening device that sits inside the bone and results in growth of 1mm a day. This new product means less chance of infection, not to mention the fact that it is less off putting because it is not visible from the exterior."

Frustrated with watching children with congenital conditions suffer, Dr. Robert Campbell, an orthopedic surgeon at the Children's Hospital of Philadelphia, invented the VEPTR (the Vertical Expandable Prosthetic Titanium Rib), and with Dr. Melvin Smith, a pediatric general surgeon,

Pediatric Orthopaedic Surgeon Robert Campbell, MD (left) and Pediatric General Surgen Melvin Smith, MD, founders of the Titanium Rib Project

VEPTR (the Vertical Expandable Prosthetic Titanium Rib)

went on to develop five new surgical procedures made possible by the device. "Meant to treat thoracic insufficiency syndrome and rare forms of scoliosis, the device is placed vertically between the ribs, thus enlarging the chest and allowing room for the child's lungs to grow," explains Dr. Campbell. "For kids, this is an obvious improvement over spinal fusion, especially if it provides additional lung growth which may help pulmonary capacity by the point of skeletal maturity. To date it is estimated that nearly a thousand children with thoracic insufficiency syndrome have been treated by the VEPTR device in the U.S. with VEPTR surgeries also being done in another 27 countries. It has been gratifying to watch these children, who were given no hope at birth, grow into teenagers with their titanium rib cages."

A more recent development on the scoliosis front involves looking inside the double strands of DNA. "It is kind of a brave new world in pediatric orthopedics," says Dr. Campbell, "because of a new genetic test for progressive scoliosis available from Axial Biotech in Salt Lake. Scheduled for release later this year, the test will give results with greater than 90% accuracy indicating which patients' scoliosis will progress to surgical levels. I believe this work will spur efforts to develop minimally invasive growth modulation treatment of scoliosis based on genetic testing."

The indefatigable Dr. Campbell adds, "The reality is that there are few companies or individuals going to bat for kids. Until children's devices are valued as much as those for adults, to a large extent we pediatric orthopedists are stuck with off label use of adult devices. My hope is that more orthopedists will be proactive in developing devices for kids. Fortunately, we now have an ally in the U.S. government that should, over time, result in the development of more child-centered devices."

With a view from the top, Dr. Peter Armstrong, Chief Medical Officer of Shriners worldwide, is poised to see the trends and treatments as they evolve. "We have started to see a movement toward trying to identify disease early and prevent it. In addition to the scoliosis work at Axial, researchers at our Portland, Oregon hospital are looking into dwarfism to identify the genetic defect involved. Work continues to try to identify the genetic defect in club feet. Other pediatric orthopedic conditions being studied include enchondromatosis

and multiple hereditary exostosis. Pioneering work is being done in the area of fetal surgery for spina bifida, efforts which are underway at several children's hospitals as part of a randomized trial that began in 2003. The rationale is to see if achieving closure of the defect as early as possible will improve the ultimate outcome. Additionally, there are a number of orthopedic researchers, including those at Case Western Reserve, working with mesenchymal stem cells on a variety of orthopedic problems. Possibilities include articular cartilage repair, bone healing, ligament healing, etc. While it will probably be several years until such work comes to fruition, the idea is that there are various sources of these cells and that it is likely possible to direct their differentiation into one kind of tissue instead of another. For example, if you have a particular need and want the cells to evolve into articular cartilage, you must ask, 'What are the inf uences that I must put on those cells to get them to do that consistently?' This work will of course benefit adults as well."

Dr. Armstrong continues, "Dr. Randall Betz at Shriners Hospital in Philadelphia is doing intervertebral stapling of the outer side of the anterior spine, thus slowing down its growth in order to let the other side of the spine catch up. The child essentially grows out of the deformity; then when deformity corrects itself, you can remove the staples. There are other surgeons looking at variations on that theme to modulate the growth of the spine to correct deformity as mentioned by Dr. Campbell. As for what is new in the fracture arena, there is a new femoral plate from OrthoPediatrics that is set to be released in a couple of months. It is designed with an anterior bow to accommodate the bow in the femur. In the past we would take a straight plate and bend it for kids. The problem, however, is that when you bend it the holes in the plate direct the screws toward the growth plate. With this femoral plate, the holes in the part that accommodate to the f are aren't perpendicular to that part of plate… they are oblique, so the screw goes parallel to the growth plate instead of toward it. The same company will shortly release a new, anatomically correct intramedullary rod which, hopefully, helps reduce the incidence of avascular necrosis of the femoral head."

For some children, movement itself involves real pain and disability. Oddly enough, this exists alongside a world where there is only the illusion of movement. Dr. Armstrong explains: "The work being done in gait labs has to a large extent evolved from the world of animation. You take the patient and place highly ref ective balls at key areas on the body (at the joints), then cameras pick up in 3d where these balls are when a patient runs and walks. Computers take that information and create stick models of the patient to show how he or she is walking. Animators have developed the software that adds f esh and bones to the stick figures. This technology is frequently used with children who have cerebral palsy, with the idea being that you can evaluate the muscle function and timing using electrodes in order to determine what muscles are firing at any given moment during the gait cycle. Other equipment can help determine what the joint reaction forces are on the feet. This process is not without controversy, however. Some researchers are asking, 'Will doing this actually help determine what the best surgical procedure is for that person?' Many believe that such work is invaluable, however, because when you do an operation and the child has recovered, you can redo the gait lab assessment and have a wealth of 'before and after' data.

For those attempting to shine a light on the needs of children, these developments are long overdue. But the momentum is there, and, with the right level of persistence, focus on scientific inquiry, and government interest, the children may one day catch up with the adults.

Seriously, Should JNJ Break Up?

By Robin Young

With 238 subsidiaries and 118,700 employees, JNJ is one of the most complex enterprises in the world. Its $64 billion in annual sales is larger, for example, than the gross domestic product of 117 countries. If JNJ were a country it would be the 60th largest in the world.

Managing this complex of an enterprise is hard. The science of management has, over the years, developed good strategies for directing complexity, and two of them that JNJ mentions in its annual report are *decentralization* and *convergence*.

Decentralization is a strategy to push decision-making down to the lowest level of the organization. Convergence is, we think, a buzz word. It is supposed to mean the practical meshing of technologies to deliver better consumer care. Like drugs + biologics + surgical tools + surgical implants = higher market shares, better pricing and better consumer service all around.

So, how's JNJ doing – decentralizing and converging?

Actually, things were looking pretty good until 2005.

Then operating efficiencies, we think, began to slip. It may be a temporary aberration. It may, however, be a sign that this elephant isn't as quick of step as it could be or, more importantly, ***should be*** to remain at the top of the medical game.

The ultimate form of decentralization is a breakup. Kick a few of these baby JNJs out of the nest. Force them to eat what they kill. Some will starve, but some will feast very well—like a herd of baby JNJ raptors set loose in the jungle.

Anyone remember the breakup of Ma Bell? That was a transformational event that marked an upswing in innovation and wealth creation in the communications industry. Could that happen for JNJ? We think it could. Would it benefit the medical technology industry? Much as Ma Bell's breakup benefited the communications technology industry, Pa JNJ's breakup could deliver a jolt of entrepreneurism to the medical technology industry.

Changing Employee Productivity

JNJ's operating numbers are interesting, and there are clear signs of really outstanding management. There is also evidence that the complexity of this enterprise has begun to gum up the works.

JNJ has roughly 119,000 employees working all over the world. As a group, they generate about $537,000 of sales each. That's good. By comparison, the average McDonald's employee generates about $59,000 of sales. But, then again, the average General Motors (GM) employee generates $613,000 in sales. McDonald's, like JNJ, is part of the Dow 30 and is one of the most solid corporations in the world. GM, however, is essentially bankrupt.

The key is employee productivity. Each GM employee costs the company roughly $637,210 in terms of compensation, health costs, deferred pension, and the level of plant, machinery and other assets required to produce a car.

So, how much does each JNJ employee cost?

Here are the numbers from 1995 to 2005. The record is impressive.

In the decade from 1995 to 2005, JNJ's sales per employee almost doubled. In 1995, the average employee generated about $229,000 of sales. By 2005 that number had risen to almost $437,000. Impressively, the profit earned on those sales rose as well, from about $62,000 (27% of sales) to approximately $170,000 (39% of sales)!

Finally, as a measure of employee productivity, the return on assets per employee rose from 28.8% in 1995 to 33.9% in 2005!

Year	Number of Employees	Sales per Employee	Cost of Goods per Employee	Operating Profit per Employee	Return on Assets per Employee
1995	82,300	$228,943	$166,428	$62,515 27.3%	28.8%
2000	98,500	$295,827	$200,365	$95,462 32.3%	30.0%
2005	115,600	$436,972	$266,704	$170,268 39.0%	33.9%

Year	Number of Employees	Sales per Employee	Cost of Goods per Employee	Operating Profit per Employee	Return on Assets per Employee
2006	122,200	436,367	265,876	170,491 39.1%	29.5%
2007	119,200	512,542	320,487	192,055 37.5%	28.3%
2008	118,700	537,043	336,992	200,051 37.3%	28.0%

Source: SEC filings

Then things began to change.

In 2006, 2007 and 2008 the numbers turned the other way.

Employee productivity is now less than it was in 1995—if we look at each employee's return on assets employed. Each JNJ employee in 2009 is supported by $715,000 in assets—up almost 4x from 1995 when it took $217,000 in assets to support each employee. That, we think, is the core of the issue.

The number of employees actually declined between 2006 and 2008, which we interpret as management's attempt to keep productivity levels from slipping. In 2006, JNJ's return on assets per employee fell to 29.5% and it has continued to decline through 2008. The operating profit per employee rose in these last three years (to $200,000, up from $170,000) but as a percentage of sales per employee, it is down (37% vs. 39%).

The Baby JNJs

In 1984, when AT&T divided into eight "baby bells," its asset base was **$125 billion, about 50% larger than JNJ's today. Its employee base, at one million** people, was about nine times larger than JNJ's.

The market value of AT&T in 1983 was about $50 billion. One hundred shares of AT&T were worth about $6,000. Fifteen years later (October 1999), Motley Fool estimated that the value of 100 shares of pre-breakup AT&T had increased to $12,444.27, up 107%. Last year, the combined market value of AT&T, Verizon, Qwest, Lucent, and Avaya (the remains of the 1984 "Baby Bells") was $211 billion, an increase of 322% from 1984.

Source: Wikipedia

Like AT&T in 1984, JNJ is not a collection of interchangeable, modular pieces. Because of that, convergence of the various technologies within JNJ hasn't delivered higher growth or profits. For example, where is the convergence between DePuy and Cordis? Or Oral Care and Ethicon? Or Neutrogena and LifeScan? It's hard to see the synergism, for example, between Listerine and JNJ's Prescription Pharmaceuticals.

A breakup of those business segments could well, as it did with AT&T, unleash higher growth and innovation.

Johnson & Johnson

6 Consumer Products *Baby JNJs*					
OTC Pharma	**Skin Care**	**Baby Care**	**Women's Health**	**Oral Care**	**Wound Care/ Other**
Extra Strength TYLENOL	Neutrogena		Stayfree		BAND-AID

6 Professional Products *Baby JNJs*					
Prescription Pharma	**DePuy**	**Ethicon**	**Cordis**	**Diabetes**	**Vision Care**
Johnson & Johnson Pharmaceutical Research & Development, L.L.C.	DePuy	ETHICON	Cordis	LIFESCAN	ORIGINAL Visine

Source: www.jnj.com

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Are the Parts Worth More Than the Whole?

Each "Baby" JNJ would be a substantial company reporting between ***$1 billion and $24 billion in annual sales*** and trade, we Year 37.3% 28.0% expect, on all the major global stock exchanges. That's right, Vision Care, Skin Care, Oral Care, Cordis, LifeScan…each of the business segments that we identified above as a "Baby JNJ' is generating more than $1 billion in annual sales.

Analysts have pondered the hypothetical value of JNJ's parts from time to time. Usually they conclude that the sum of the parts is not much different from the whole—at least as currently valued on the New York Stock Exchange.

Using Wachovia's Larry Biegelsen's estimates (and he's probably the most knowledgeable JNJ analyst on the Street right now), here is what a hypothetical sum-of-the-parts JNJ valuation might look like.

Segment	Share of 2010 Operating Profit	Operating Margin	Est 2008-2013 Earnings CAGR	2010 Est EPS	Comp Multiple on 2009E EPS 4	Implied 12-Month Forward Share Value	JNJ Sales Growth 2008-2013
Consumer (including Pfizer consumer) [1]	18.3%	19.7%	10.2%	$0.89	12.1x [1]	$11 - $11	5.1%
Pharmaceutical [2]	32.8%	28.0%	0.9%	$1.61	9.2x [2]	$14 - $15	1.5%
Medical Device & Diagnostics [3]	48.9%	35.9%	9.1%	$2.39	10.9x [3]	$26 - $26	6.1%
Multiple and Projection Using Est EPS			**7.4%**	**$4.89**	**10.5x**	**$51 - $53**	**4.2%**

[1] Average of PG, CL

[2] Average of BMY, LLY, MRK, PFE, SGP, WYE

[3] Average of BSX, ACL, AGN, SNN, SYK, ZMH, BAX, BD, BCR, MDT, COV, BEC, HOSP

[4] Estimate From First Call

Current Operating Profit Estimates ($MM)	2010
JNJ Consumer	3,405
Pharma	6,112
MD&D	9,904
ProForma Total Operating Profit	18,611

Additional Assumptions	
One-Sided Spread in Range	$1.00
Conglomerate Discount	2%

Sources: Factset and Wachovia Capital Markets, LLC estimates

So, in Wachovia's analysis JNJ's parts combined would be worth between $51 and $53 per share. JNJ's stock is trading at around $52.60 per share right now. So, the difference between the sum of JNJ's parts and the intact company is not much of a difference at all.

Of course Wachovia is assuming, conservatively so, that there'd be no substantial change in growth or operating profit assumptions if the Baby JNJs were spun off.

We recall that one observer of the AT&T breakup noted it created a "near-chaos of opportunity which has made the total communications marketplace one of the most exciting ever to exist in this nation of opportunity."

We don't know that that would exactly occur if a dozen Baby JNJs were unleashed, but we do think that JNJ shareholders have had to pay a price for JNJ's size. Baby JNJs, we think, could reach out in new directions and apply their core technologies, experience and expertise in new ways and in new markets.

Would JNJ actually break up? No…we're making a hypothetical case. But still, we think, a good one.

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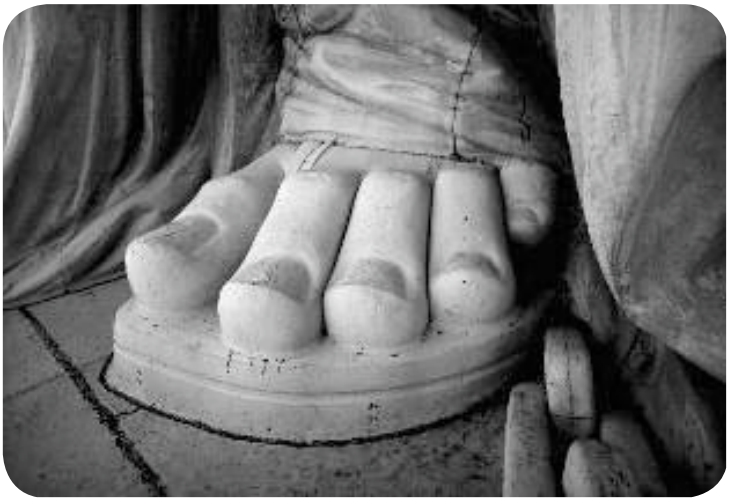
Little Toes, Big Pains

By Dev Joshi



Statue of Liberty's Healthy Foot

Toe deformities are among the most common disorders in foot and ankle orthopedics. Toes contain some of the smallest bone structures found in the body but the pain they can generate is anything but small. Bunions, hallux valgus and hammer toes are three of the most common toe deformities. How are they interrelated and how are these conditions treated?

Hammer toe is a bending of one or both joints in any one of the four small toes caused by a muscle or tendon imbalance. It may occur due to previous trauma, such as a broken toe, or it may be hereditary. Hallux valgus, is a condition that affects the joint at the base of the big toe (the word "hallux" refers to the big toe and "valgus" refers to the deformity that moves the toe out of line and toward the lesser toes). The bump that grows on the side of the first metatarsophalangeal (MTP) joint is referred to as a bunion. Bunions, however, are more than just bumps on the big toe. Even though "bunion" is often used as the common term for hallux valgus, bunions are actually a separate, progressive disorder in which the big toe leans toward the second toe which throws the bones out of alignment, producing the bump.

According to the PearlDiver Patient Record Database, these toe deformities are differentiated into 10 different sectors shown below. (The PearlDiver database consists of over 136 million orthopedic patient records of patients up to 65 years of age collected by United Healthcare). Over four million patients experience toe deformities every year and the number is rising.

Table 1 shows the toe deformities and their annual number of occurrences in the PearlDiver database. Hallux valgus is the number one deformity followed closely by hammer toe. Bunion is a distant third.

To help explain the data, Dr. Steven L. Haddad, Associate Professor of Clinical Orthopedic Surgery at Northwestern University, is one physician who

Table 1: Deformities of Toes Diagnoses (2004-2007)

Description	ICD # Code	2004	2005	2006	2007	Total
Hallux Valgus	***ICD-9-D-735.0***	***50,506***	***57,191***	***60,653***	***62,149***	***197,613***
Hallux Varus	ICD-9-D-735.1	525	503	666	588	2,146
Hallux Rigidus	ICD-9-D-735.2	6,607	7,808	8,747	9,229	29,447
Hallux Malleus	ICD-9-D-735.3	299	304	313	324	1,167
Hammer Toe	***ICD-9-D-735.4***	***48,449***	***54,758***	***56,448***	***55,978***	***182,535***
Claw Toe	ICD-9-D-735.5	1,762	1,866	1,889	1,913	6,667
Other Acquired Deformities	ICD-9-D-735.8	2,729	2,783	3,428	3,559	11,739
Unspecified Deformities	ICD-9-D-735.9	958	951	1,062	1,039	3,770
Flat Foot	ICD-9-D-734	3,785	4,288	4,646	4,585	16,365
Bunion	***ICD-9-D-727.1***	***28,579***	***31,018***	***32,504***	***32,664***	***112,591***

Source: PearlDiver Patient Record Database 2004-2007

certainly knows toes. Dr. Haddad is the lead surgeon of a design team creating a new total ankle replacement in conjunction with Wright Medical Technologies, Inc. He has given over 200 national and international lectures on foot and ankle surgery and is currently practicing at Illinois Bone and Joint Institute, Glenview, Illinois.

OTW: Hallux valgus is often termed bunion, but these two conditions have separate diagnostic codes. What is the difference?

Dr. Haddad: *Hallux valgus is a deformity of the great toe—it drifts towards the lesser toes. That may or may not occur with a bunion which is an isolated bump on the medial border of the foot at the first metatarsal head. Bunion is the Latin word for turnip, as it appears as a red prominence on the inside of the foot. You can have hallux valgus without a bunion and a bunion without hallux valgus.*

Even though these conditions have separate diagnostic codes, they still appear to be interrelated. Table 2 illustrates the number of patients who were diagnosed with other toe deformities after the primary diagnoses. Out of the 112,591 patients diagnosed with bunions, 18,179 were later diagnosed with hammer toe and 43,971 patients were later diagnosed with hallux valgus. A similar analysis appears for hallux valgus and hammer toe in the table below.

Table 2: Patients Follow-Up Deformities AFTER (2004-2007)

Description		Total	Patients After
Bunion		**112,591**	
	Hallux Valgus After		43,971
	Hammer Toe After		18,179
	% After		**55.2%**
Hallux Valgus		**197,613**	
	Bunion After		42,381
	Hammer Toe After		32,175
	% After		**37.7%**
Hammer Toe		**182,535**	
	Hallux Valgus After		31,343
	Bunion After		17,797
	% After		**26.9%**

Source: PearlDiver Patient Record Database 2004-2007

OTW: A good number of the patients who have had one of these deformities go on to be diagnosed with one or both of the other two as well. What do you see and is this common?

Dr. Haddad: *I agree that you often see all three together, but that is not always the case. They are separate deformities. A hammer toe may occur when the great toe pushes on the second toe (from hallux valgus). Over time, this chronic pressure may cause the second toe to contract at the proximal interphalangeal joint, creating a hammer toe. A hammer toe may also occur due to the lack of push-off power from the great toe suffering from hallux valgus. The lesser toes may absorb that stress, creating increased pressure across the joints and a subsequent hammer toe.*

Surgeons and doctors use numerous procedures to correct these deformities. Appropriate shoes and foot pads are generally recommended. Table 3 shows the number of corrective treatments performed for each diagnoses. Metatarsal osteotomy (a surgical operation of dividing the metatarsal bone or cutting out a piece of the metatarsal bone) is generally performed for bunion and hallux valgus while a corrective procedure like interphalangeal fusion is performed for hammer toe. These deformities are treated primarily in an outpatient setting. Less than 1% of patients are treated as inpatients.

From PearlDiver data, one can estimate that, nationally, over one million surgical procedures are performed annually for toe deformities. Almost 99% of the patients are treated in a physician's office while fewer than 10,000 procedures are performed in an inpatient setting.

OTW: What are the most common procedures related to these deformities and what surgical corrections have been the most successful in correcting

Table 3: Procedures Following These Toe Deformities (2004-2007)

Outpatient Procedures	CPT Codes	Hallux Valgus	Hammer Toe	Bunion
Correction, hallux valgus (bunion), with/without sesamoidectomy; metatarsal osteotomy	28296	33,969	10,563	17,875
Correction, hammer toe (e.g., Interphalangeal fusion, partial/total phalangectomy)	28285	14,688	31,820	8,137
Injection(s); single tendon sheath, or ligament, aponeurosis (e.g., plantar "fascia")	20550	9,090	8,479	4,730
Osteotomy, with/without lengthening, shortening/ angular correction, metatarsal	28308	4,922	4,180	4,493
Correction, hallux valgus (bunion), with/without sesamoidectomy; double osteotomy	28299	7,246	2,499	4,078
Correction, hallux valgus (bunion), with/without sesamoidectomy; Keller, McBride	28292	6,861	2,464	3,986
Capsulotomy; metatarsophalangeal joint, with/ without tenorrhaphy, each joint	28270	3,785	5,682	2,113
Correction, hallux valgus (bunion), with/without sesamoidectomy; simple exostectomy	28290	2,461	898	1,919
Correction, hallux valgus (bunion), with/without sesamoidectomy; phalanx osteotomy	28298	2,558	1,289	1,413
Correction, hallux valgus (bunion), with/without sesamoidectomy; Lapidus-type	28297	1,522	558	933
Correction, hallux valgus (bunion), with/without sesamoidectomy; resection with implant	28293	827	441	525
Correction, hallux valgus (bunion), with/without sesamoidectomy; tendon transplants	28294	196	62	104
Inpatient Procedures	**ICD-9-P Codes**	**Hallux Valgus**	**Hammer Toe**	**Bunion**
Excision and Repair of toe deformities	77.51-77.59	243	148	153

Source: PearlDiver Patient Record Database 2004-2007

them? Do these deformities come back again?

Dr. Haddad: *There are over one hundred procedures described to correct bunions. The most common procedures are distal osteotomies (i.e., Chevron osteotomy) for smaller bunion deformities, and proximal procedures (i.e., crescentic osteotomies, opening wedge osteotomies) for greater deformity. For an unstable first metatarsocuneiform joint due to gross ligament laxity, fusion of the first MTC joint is performed (a Lapidus procedure). Most bunion procedures work to correct the deformity. The key is in selecting the appropriate procedure based on the magnitude of the deformity and the pathophysiology of the bunion for that individual patient. Hammer toe deformities are corrected in a more standard fashion: resecting the proximal interphalangeal joint and pinning it straight with a removable pin. If there is a contracture about the metatarsophalangeal joint, then lengthening the lesser toe extensor tendons and cutting the dorsal capsule are performed simultaneously.*

OTW: Nationally, we are looking at over three million patients experiencing toe deformities while just over one million are surgically corrected. Do you think these deformities have been overlooked and not much has been written about them?

Dr. Haddad: *No, I don't think this deformity has been overlooked. It is simply the case that many patients with lesser toe or great toe deformities do not require surgery for they are not symptomatic. The only reason to operate on a person with these deformities is pain or difficulty with shoe wear.*

OTW: Are there controversies related to treatments for these deformities? What about innovation and new techniques for better treatment? Are the current treatments being well received?

Dr. Haddad: *There are plenty of controversies. For bunion deformities there are those who think the first MTC joint is always lax and needs to be fused. Others think that it is never hyper mobile and that proximal procedures work as well as fusions. There has been much testing in this area to determine if bunions are created by lax joints, primarily the first MTC joint. Hammer toes are not terribly controversial but if the second toe has synovitis at the MTP joint, and the joint dislocates or crosses over the great toe, there is controversy on how to reduce and stabilize that joint. Most favor tendon transfers to hold the second toe in position. Some favor cutting the bone of the second metatarsal head and shortening it to decompress the joint. There is no good answer as to which works better, though it seems that tendon transfers make the toe stiffer, and osteotomies cause the toe to be elevated and not touch the ground. The StayFuse by Tornier is one such product that is used as a new method for correcting hammer toes. The OrthoHelix plates and the Wright Medical plates are also new technologies for securing bunion osteotomies.*

OTW: Which companies and products do you use and who is the largest distributor of toe deformities products?

Dr. Haddad: *Mostly screw products. Some are beginning to use plates. Synthes makes cannulated screws that many surgeons use. Wright Medical also makes very good plates for bunion corrections. Tornier makes a component to stabilize lesser toe PIP joints called the StayFuse. It works well to hold the toe straight, and avoids pin fixation. OrthoHelix has some innovative plates as well.*

How much does it cost to treat these conditions? Table 4 below shows the surgical correction treatments for the three main toe deformities. Except for the injection procedure, represented by CPT-20550, every other surgical procedure cost is in the range of $1,200 to $2,700. Inpatient charges are a different story. Fewer than 1,000 patients in the PearlDiver database were treated as inpatients over the four years of this data. The average charges for these patients were

Foot With Painful Bunion

between $20,000 and $25,000 and they had hospital stays ranging from a day and a half to two days.

Temporary relief from toe deformities can be obtained by wearing proper shoes or shoe pads but surgical correction is often necessary and has been well received by both surgeons and patients. It is common for patients to get diagnosed with second toe deformities, as illustrated by PearlDiver data and Dr. Haddad's personal experience, so patients with toe deformities should keep a careful watch on their feet after initial treatments. With more than one million surgical corrections performed annually, companies such as Wright Medical, Tornier, and Synthes have established themselves as pioneers within the toe deformity market. As they continue research on better devices and treatments, little toes will hopefully become less of a big pain.

Table 4: Average Charges for Toe Deformities

CPT Codes	Hallux Valgus	Hammer Toe	Bunion
CPT-28296	$2,552	$2,502	$2,564
CPT-28285	$1,614	$1,674	$1,574
CPT-20550	$136	$138	$138
CPT-28308	$1,426	$1,474	$1,455
CPT-28299	$2,744	$2,747	$2,726
CPT-28292	$2,048	$1,976	$2,053
CPT-28270	$1,233	$1,251	$1,176
CPT-28290	$1,907	$1,986	$1,920
CPT-28298	$2,181	$2,095	$2,227
CPT-28297	$2,611	$2,362	$2,460
CPT-28293	$2,435	$2,178	$2,360
CPT-28294	$2,649	$2,234	$2,500

Source: PearlDiver Patient Record Database 2004-2007

company news

NuVasive and Osiris Accelerate Deal

NuVasive, Inc. announced on March 30 that it had accelerated the transfer of the processing of Osteocel Plus from Osiris Therapeutics, Inc. to its own exclusive supply chain.

The company stated that since the May 2008 announcement of the original transaction, the companies have successfully worked to increase production and transfer the technical know-how and related intellectual property to NuVasive. Due to NuVasive's confidence in its ability to supply product to support its planned sales growth of Osteocel Plus, the companies have decided to eliminate the performance contingencies applicable to $30 million of the $45 million in remaining milestones.

The terms applicable to the remaining $15 million milestone payment, which is due upon NuVasive achieving $35 million in cumulative sales of Osteocel, remain unchanged. To date, NuVasive has made a total of $40 million in up-front and milestone payments. The total potential consideration of $85 million remains unchanged.

Under the new terms, NuVasive immediately assumes control of production. NuVasive has selected AlloSource as its exclusive supplier of Osteocel Plus. AlloSource is one of the nation's largest tissue providers and has already started supplying Osteocel Plus. AlloSource has been working to scale up its production since last summer and NuVasive expects the AlloSource supply relationship to provide an efficient and consistent stream of supply. NuVasive will not assume ownership of the Osiris tissue processing facility.

NuVasive reiterates its previous guidance of $28 million in Osteocel Plus revenue in 2009 with no change in profitability targets. The company noted that the transfer of processing will support its ability to meet or exceed 2009 Osteocel Plus sales goals and fuel anticipated revenue growth to $100 million and beyond.

—WE (April 2, 2009)

legal & regulatory

Docs Oppose Industry

Medical device manufacturers breathed a huge sigh of relief last year in the Riegel case. Now they're holding their breaths.

Basically the Supreme Court said that Congress intended devices blessed by the FDA to be protected from lawsuits in state courts.

Stryker subsequently had a case thrown out in Colorado citing Riegel and thousands of other lawsuits have been tossed out of court by judges citing the decision.

As we wrote at the time of the Riegel decision, device manufacturers may have won the battle, but might lose the war.

Now Congress wants to make it clear that their intent has changed. Representatives Frank Pallone and Henry Waxman, both Democrats, introduced a bill last month to say that no such exemption will exist any longer and devices makers will have the same exposure to lawsuits as pharmaceutical manufacturers. A companion bill was introduced in the Senate by Democrat Senators Edward Kennedy and Patrick Leahy.

Rep. Henry Waxman

Medtronic, the victor in the Riegel case opposes the legislation. They say the proposed law is not in the best interest of patients.

A company spokesman reportedly said, "Patients ultimately would be the losers as they wait for new therapies

legal & regulatory

to come to market. Companies may in fact no longer want to take the risk because of the threat of litigation."

What is in the best interest of patients and who speaks for them?

How about their docs?

An editorial published in this month's issue of the *New England Journal of Medicine* disagrees with Medtronic.

"Unfortunately," says the editorial, "one major stakeholder, the medical device industry, has been shielded from the potential consequences of failing to adequately disclose risk."

"As the law now stands, failure-to-warn and design-defect lawsuits are preempted for medical devices but not for drugs. This perplexing state of affairs defies all logic," continues the editorial.

The editorial, written by Gregory D. Curfman, M.D., Stephen Morrissey, Ph.D., and Jeffrey M. Drazen, M.D., concludes:

> "Patients and physicians deserve to be fully informed about the benefits and risks of medical devices, and the companies making the devices should be held accountable if they fail to achieve this standard. We urge Congress to swiftly pass this legislation and to allow lawsuits by injured patients, which have been an important part of the regulatory framework and very effective in keeping medical devices safe, to proceed in the courts. The critical issue of preemption, which directly affects the disclosure of risks and thus the safety of the nation's supply of medical devices and drugs, should properly be decided by officials elected by the people, with whom the responsibility for the health of the public rightfully resides."

With docs and patients lined up on one side against device manufacturers and the FDA on the other, it doesn't take Machiavelli to predict that outcome.

—*WE (April 1, 2009)*

Liberation Day in Orthopedics

Monday March 30 was liberation day in the Village of Orthopedics.

On that day the U.S. Department of Justice said it had dropped criminal charges against four orthopedic device makers (Zimmer, Biomet, DePuy, and Smith & Nephew) accused of making improper payments to surgeons who used their products. The complaint against the companies was filed in September 2007, alleging criminal violations of the federal anti-kickback statute.

U.S. Magistrate Judge Madeline Cox Arleo in Newark dismissed the cases against the four companies. A fifth company, Stryker, also agreed to changes after negotiating a non-prosecution agreement.

In return for a promise of eventual dismissal of the charges against them, the companies entered into Deferred-Prosecution Agreements (DPA) with the government, mended their ways, hired federal monitors and agreed to participate in a Corporate Integrity Agreement with the Department of Health and Human Services that will run to September 2012.

legal & regulatory


John Ashcroft

With the dismissal of the complaint, former Attorney General John Ashcroft and the other federal monitors will have to pack up their $900 per hour legal fees and bid adieu to their 18-month monitoring contract that cost device manufacturers tens of millions of dollars. The hourly price tag for the lawyers doing the monitoring was not lost on physician consultants who saw their hourly "market" rate pegged at approximately $500 per hour.

The announcement was made by the Acting U.S. Attorney in New Jersey because the prosecutor who filed the original charges, Christopher Christie, resigned his position in January and is busy rounding up the Republican nomination to run for Governor of New Jersey. No doubt, he'll get some nice campaign contributions from the law firms that did the monitoring.

We don't know if any victory parades were held at the orthopedic headquarters, but the post-deferred prosecution era has already had an impact on the companies' relationships with their surgeon consultants.

According to the Justice Department, consulting payments to surgeons by the companies declined to $105 million in 2008 from $272 million in 2007, while the total number of physicians receiving payments from the companies declined to 628 in 2008 from 1,693 in 2007.

If the decline in physician payments holds out into future years, that $150+ million savings per year will allow the companies to make up their $311 million penalty payment to the feds in short order. One might even say that the physicians paid the penalty. It's unlikely those consulting payments will stay at that reduced level, but the long-term costs to the companies is likely to stay below pre-DPA levels.

"While the expiration of the DPA is an important milestone, the company remains committed to operating ethically and transparently on a global basis to preserve the trust required for productive, professional collaboration that ultimately benefits patients," said David Dvorak, Zimmer's President and Chief executive, in a statement.

DePuy said in a statement that dismissal of the deferred prosecution agreement signifies it has "fully complied" with its obligations under the pact.

"DePuy Orthopaedics has established, and will maintain, a robust health care compliance program to guide its interactions with health care professionals and entities," the company said.

"We are pleased to have successfully collaborated with the [U.S. Attorney's office] and our monitor during these last 18 months to create a more robust compliance program," said Joseph DeVivo, President of Smith &

legal & regulatory

Nephew Orthopaedics, in a statement. "Our substantial investment in and commitment to this program will help us continue our work as the leading innovator in orthopaedic technology for active, informed patients."

A spokesman from Stryker reportedly declined comment.

"Biomet remains committed to upholding the highest standards of ethical and legal conduct and plans to continue the enhancement of its compliance programs throughout its global operations," said Jeff Binder, Biomet's President and CEO, in a statement.

The full weight of the impact of the new surgeon/industry relationships has yet to be felt in determining the winners and losers in market share. Zimmer has experienced the biggest loss in market share for hips and knees, losing approximately .05% to their rivals, but the game is not over.

For now, liberation has come and the future for the Village of Orthopedics looks bright.

—WE (April 1, 2009)

Medical Societies, Just Say "No"

A proposal published in the most recent *Journal of the American Medical Association* (JAMA. 2009; 301(13):1367-1372), calls on professional medical associations (PMAs) to limit the funding they receive from drug and device companies.

The proposal calls for associations to refuse general budget support from industry, but would allow the groups to continue to accept industry advertising in medical journals and payments for industry-sponsored booths at association conference.

Funding for continued medical education would be allowed only if the contributions go into a general pool and is then parceled out by physicians who themselves have no ties to industry.

In addition they call for leaders of the specialty societies to be "conf ict-free" during their tenure with "no personal income and no research support derived from industry." They suggest similar restrictions on physicians who serve on the committees that create the specialty society guidelines.

The North American Spine Society (NASS) recently passed tough disclosure rules similar to this proposal and the American Academy of Orthopaedic Surgeons has done something similar as it relates to continued medical education funding from industry. We have heard lots of rumbling from some NASS members about the disclosure requirements. A former NASS president told us recently that the primary concern by members was not disclosure per se, but the difficulty of the mechanics of disclosing the financial relationships between physicians and companies.

The American Psychiatric Association decided last month to phase out industry-funded symposia at its conferences.

The authors of the *JAMA* article are: David Rothman, Ph.D.; Walter McDonald, M.D.; Carol Berkowitz, M.D., Susan Chimonas, Ph.D.; Catherine DeAngelis, M.D.; Ralph Hale, M.D.; Steven Nissen, M.D.; June

legal & regulatory

Osborn, M.D.; James Scully Jr, M.D.; Gerald Thomson, M.D. and David Wofsky, M.D. The writers say that current PMA policies are not uniform and often lack stringency. They identify and analyze the conflicts of interest that may affect the activities, leadership and members of the PMAs. They then formulated the recommendations to prevent the appearance of undue industry influence.

The group is made up of past presidents of the American College of Cardiology, the American Academy of Pediatrics, the American College of Physicians and the current editor in chief of *JAMA*. The article reflected the authors' views as individuals, not the positions of their organizations.

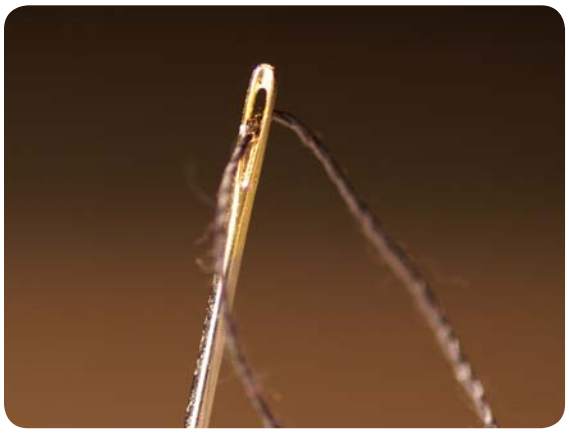
Rothman, a professor at the College of Physicians and Surgeons at Columbia University in New York, reportedly said, "You can read the ads, skip the ads, but there's nothing hidden. What I don't like is when I can't tell if what I'm hearing is science, or marketing in the guise of science."

—*WE (April 2, 2009)*

biologics

Knitting Cartilage with Stem Cells

In Scotland, one might guess that "advanced knitting techniques" refers to kilt making, but the Scottish Stem Cell Network (SSCN)



thinks otherwise. At the recent SSCN conference in Edinburgh on March 24, Professor Anthony Hollander described a new method of stitching cartilage together by using bone marrow stem cells as needle and thread. This novel procedure could be the first ever treatment to successfully heal torn meniscal cartilage in human knees.

Anthony Hollander, Arthritis Research Campaign (ARC) Professor of Rheumatology & Tissue Engineering at the University of Bristol, is no stranger to stem cell research. Four years ago, his research team successfully grew cartilage in vitro from bone marrow stem cells. It took them just over a month to grow a half-inch of cartilage, and since then, Professor Hollander has been looking forward to the day when his research could move out of the laboratory and into the hands of physicians and their patients.

According to *The Scotsman* ("Need new cartilage? Grow your own" March 25, 2009), Professor Hollander's new discovery involves lining a membrane with stem cells and implanting this "bandage" over the meniscal tear. He told The Scotsman, "'It is designed in a way that the cells will migrate across the lesion and literally knit it together. So, instead of growing new tissue, it's healing the lesion itself.'"

There is no current method for long-term, successful treatment of a damaged meniscus, an ailment common to athletes. Doctors can temporarily relieve a patient's pain by stitching together meniscal tears, but the pain often returns. Surgeons can also treat patients by removing the damaged section of the meniscus, but, according to *The Bulletin* ("Adult Stem Cell Technique May Help Injury" March 30, 2009), in at least 50% of cases where the meniscus is partially removed, "patients go on to develop premature osteoarthritis in the damaged knee—often at an age when they are too young to have joint replacement." Professor

Meniscus tear shown during knee arthroscopy

Hollander's team is working on a preclinical model of the treatment, and they hope to start human clinical trials

biologics

in one year. The researchers are also considering how this technique could be used to repair tendons, ligaments, muscles, and bone fractures. If Professor Hollander's model works, bone marrow stem cells could be nature's own stitching. But before this research team can sew anything, they'll have to show that their technique passes the initial trials and successfully threads the needle.

—DK (April 1, 2009)

people

Phelps and Cerveny Join ConforMIS Team

Knees, hips, and other important body parts are getting a leg up. The masters of osteoarthritis and joint damage at ConforMIS, Inc. have announced that Robert (Bob) Phelps has been appointed as Senior Vice President of Sales and David Cerveny, JD, has been appointed Vice President of Intellectual Property & General Counsel.

"With the introduction of the iUni unicompartmental and iDuo bicompartmental knee resurfacing implants, we have seen a strong and accelerating interest in our technologies with over 250 active surgeons," said Dr. Philipp Lang, CEO of ConforMIS, Inc., in the news release "Bob Phelps and David Cerveny enable us to strengthen our unique position within the orthopedic industry as the only company offering an entirely patient-specificapproach to the knee replacement market."

For more than 25 years, Bob Phelps has honed his expertise in medical device sales, distribution, marketing and business development experience. Phelps most recently held the position of VP of Corporate Distribution at Biomet focusing on commercial execution strategies across the strategic business units. Prior to this role, he was Senior VP of Sales for Biomet's BTBS (EBI) division involved with spine, trauma, osteo-biologics and sports medicine products. Phelps also served as Area VP for the Northeast and Mid-Atlantic regions in the joint reconstruction franchise. Prior to his Biomet days, Phelps was the VP of Sales & Marketing at Biosphere Medical, an early stage company, where he helped establish the use of microsphere technology with interventional radiologists and neuroradiologists. At Johnson & Johnson, the launching pad for his career, Phelps held various senior executive roles including VP of Group Contracting and VP of Sales for the orthopedic business (now DePuy).

When asked what he learned at Biomet that will contribute to his new role, Phelps told *OTW,* "Being with a seasoned management team at Biomet I understand the impact great execution can have for the customer. Superior customer interactions create significant value in the orthopedic business, and that, combined with the best products and services will keep the top line growing."

He added, "My start-up success with Biosphere Medical came from recruiting a great sales force, training them well, implementing excellent motivation as well as incentive programs and staying focused on dominating a market niche. The introduction of a new technology unseated an entrenched product sold by market leaders with broader sales forces and complementary products. The Biosphere professional sales team focused on the physician, their staff and the patient on a daily basis which built this business into a market leader in a short period of time."

people

For more than ten years David Cerveny has worked on legal issues related to medical devices and intellectual property. Cerveny will be assuming the responsibility of managing ConforMIS' legal affairs as well as expanding the company's intellectual property portfolio and patent strategy. Prior to joining ConforMIS, he was the Chief Intellectual Property Counsel for Palomar Medical Technologies, where he managed a patent portfolio widely regarded as the strongest in that industry. Before Palomar, Cerveny was a senior attorney in the intellectual property practice at Proskauer Rose LLP and a partner at Wilmer Cutler Pickering Hale and Dorr LLP. He earned a J.D. from Boston College Law School, and was twice named a Massachusetts Super Lawyers rising star.

Cerveny told *OTW,* "Among our first steps will be to ensure that ConforMIS has fully developed the wealth of intellectual property already in place and also to determine where we can add to the IP portfolio in ways that compliment ConforMIS' business."

When asked what interesting challenge he may face, Cerveny told *OTW,* "The greatest challenge I have experienced since joining has been keeping pace with the continual stream of innovative ideas being generated at ConforMIS."

—EH (March 30, 2009)

Vertos: New Training Center, Talent

Those with shrinking spinal canals have new assurance that their surgeons will have the latest information to treat them properly. Vertos Medical, Inc., developer of the mild (Minimally Invasive Lumbar Decompression) procedure to treat patients with lumbar spinal stenosis (LSS), has swung open the doors of its new physician training facility and headquarters in Aliso Viejo, California. The San Jose operations have been converted to the Vertos Technology Center where research and development and manufacturing will remain.

"Numerous physicians are trained and now doing the mild procedure, and there is a growing interest in training from the physician community. To support this effort, we've opened a new release. "This better enables Vertos to train large groups of doctors efficiently and effectively."

Spinal stenosis

Additionally, there are now two more talented individuals at the helm to aid the company with its national commercial rollout of mild. Michael Enxing has been appointed Vice President of U.S. Sales, and Charlene Myers has been appointed Director of Clinical Research. Mild, says the company, is the least invasive surgical procedure for LSS, with no implants left behind. It is FDA market cleared for treating central canal stenosis of the lumbar spine.

"Another significant milestone for Vertos is the addition of Michael Enxing and Charlene Myers to our senior management team. Both are experienced in bringing innovative new technologies to market," continued Corbett.

Corbett told *OTW,* "Michael Enxing's experience in building teams and recruiting top talent will help move us closer to a national commercial rollout. Charlene Myers has years of experience in PMA and post market studies, and she is well-equipped to help Vertos reach our aggressive research goals."

Enxing has worked with a variety of medical device companies, including Stryker, Advanced Neuromodulation Systems (now integrated into St. Jude Medical), Tecnol Medical Products, and Cardiovascular Systems Inc. He brings to Vertos more than 18 years of sales and sales management experience, including launching and growing new commercial products. Enxing also has extensive knowledge of the spine market.

Myers' experience encompasses a wide range of medical specialties and leadership roles at PowerVision, Genyx Medical, Johnson & Johnson's Ethicon Endo-Surgery and Alcon Laboratories. With more than 20 years of clinical research background in

legal & regulatory

IDE/PMA processes and regulations, post-approval market support data collection and technical writing, she is well prepared for her new role. As the director of clinical research for Vertos, Myers will oversee the Institutional Review Board-controlled clinical trial called the Vertos mild Preliminary Patient Evaluation Study, which is designed to gather additional post-market data on the procedure. The study is being conducted at approximately 30 centers across the U.S.

—EH (March 31, 2009)

spine

DePuy Begins rhGDF-5 Study

The day after the FDA Ortho Panel recommended against approval of Stryker's OP-1 putty, DePuy Spine announced the start of testing of its own genetically engineered human protein in patients with moderate to severe low back pain.

DePuySpine™
a Johnson&Johnson company

The protein product, intradiscal rhGDF-5 (recombinant human growth and differentiation factor-5), is investigational only within the United States.

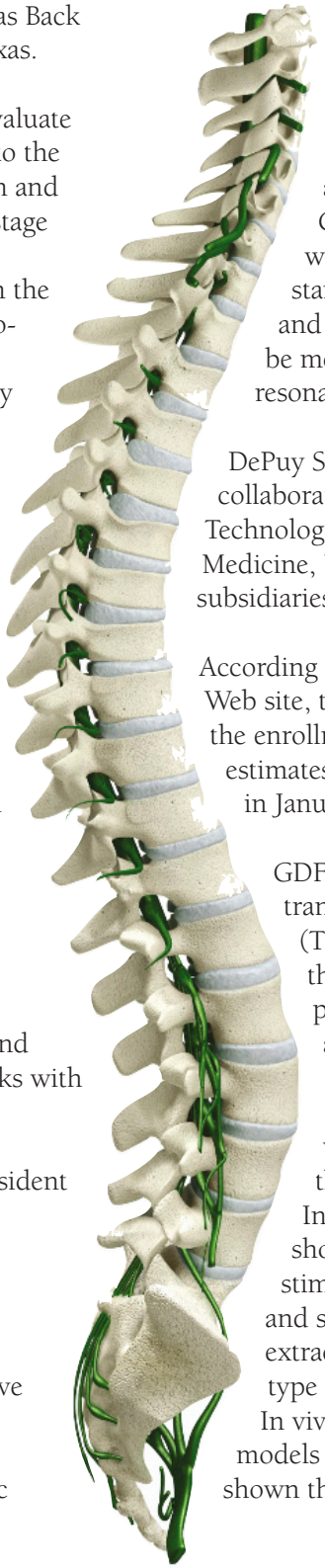
The first in a series of clinical studies evaluating the safety and effectiveness of the protein began at Texas Back Institute (TBI) in Plano, Texas.

The study outcomes will evaluate if injections of rhGDF-5 into the lower spine can relieve pain and slow or even reverse early stage degenerative disc disease. Researchers at 10 centers in the U.S. are part of this placebo-controlled, double-blind, randomized Phase I-II study that will follow patients for up to three years.

Richard Guyer, M.D., a clinical investigator and spine surgeon at TBI said, "In animal studies, the injection of rhGDF-5 inf uenced the growth and differentiation of numerous tissues including the intervertebral disc but these studies are limited in their ability to assess discogenic pain. For the first time, in a carefully controlled study, we will see how this recombinant version of human growth and differentiation factor-5 works with actual patients."

Dr. Guyer is also a past president of the North American Spine Society.

The study, announced by DePuy Spine on April 1, consists of patients who have had persistent discogenic back pain for at least three months at one symptomatic lumbar level from L3/L4 to L5/S1 and who have not responded to conservative medical treatment such as physical therapy. Clinical outcomes will be measured using standard validated tools and lumbar disc changes will be measured using magnetic resonance imaging data.



DePuy Spine is working in collaboration with Advanced Technologies and Regenerative Medicine, LLC. Both companies are subsidiaries of Johnson & Johnson.

According to the clinicaltrials.gov Web site, the study anticipates the enrollment of 16 patients and estimates study completion date in January 2012.

GDF-5 is a member of the transforming growth factor-b (TGF-b) superfamily and the bone morphogenetic protein (BMP) subfamily, and is known to inf uence the growth and differentiation of various tissues, including the intervertebral disc. In vitro experiments have shown that rhGDF-5 can stimulate gene expression and synthesis of the extracellular matrix proteins type II collagen and aggrecan. In vivo experiments in rabbit models of disc degeneration have shown that intradiscal injections

spine

of rhGDF-5 can stimulate an increase in disc height and hydration.

Principal Investigators (all MDs) are:

- James Rathmell
  Massachusetts General Hospital
- Richard Guyer
  Texas Back Institute
- Orlando Florete
  Florida Institute of Medical Research
- Greg Anderson
  Rothman Institute
- Tim Yoon
  Emory University
- Howard An
  Rush University Medical Center
- Marvin Tark
  Drug Study America
- Jim Youssef
  Durango Orthopedic Associates/
  Spine Colorado
- Norman Harden
  Rehabilitation Institute of Chicago
- Jonathan Borden
  Riverhills Healthcare, Inc.

—*WE (April 2, 2009)*

AOI: 30 Enrollees for Ascendx

If bones collapse in a spine, does anyone hear? AOI Medical does. This spine and trauma company is announcing the successful completion of surgical procedures on 30 patients in a clinical trial with Ascendx Vertebral Compression Fracture ("VCF") Reduction System ("Ascendx") at six sites across the U.S.

Single pedicle access and single cavity creation

Single pedicle access and single cavity creation

In the news release, William J. Christy, CEO of AOI Medical, said: "The clinical program has gained momentum and we are pleased with our progress to date. The Ascendx system is designed to provide notable improvements in the way physicians traditionally treat VCFs. While all currently existing VCF procedures offer immediate pain relief to the patient, the Ascendx technology is specifically designed to provide a mechanical, repeatable cutting of cancellous bone and to deliver an even distribution of the bone cement."

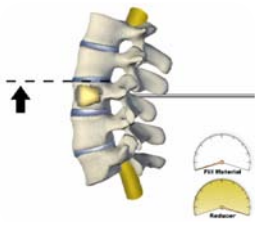
Cuts to access cortical end plates

On March 12, 2008, AOI received final FDA approval to begin the Ascendx clinical trial, which will ultimately involve 60 subjects in eight centers. The primary end point of the single arm trial is acute procedural success defined as successful device deployment, cement delivery, and device withdrawal. The data from the trial will be used to support the company's 510(k) submission to the FDA in relation to Ascendx. The clinical trial is on track to finish patient enrollment and make its 510(k) submission to the FDA in mid-2009. The company is planning for a market launch of Ascendx in the U.S. towards the end of 2009.

Cutter articulates

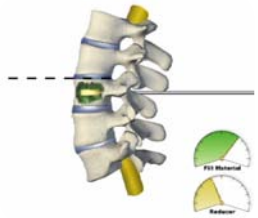
Ascendx, an investigational device, is meant for the treatment of painful pathological fractures of the vertebral body that may result from osteoporosis, benign lesions and/or malignant lesions such as metastatic cancers and myeloma. Ascendx will comprise two main instruments: a cutting device that creates a cavity in cancellous bone, and a reduction device that is used to restore the height of the fractured vertebra and which can deliver and contain the bio-material (bonding agent) in the cavity. AOI indicates that this new product is designed to offer a potential enhancement over current techniques.

As for what are physicians saying about Ascendx, William Christy told *OTW*, "While evaluation of clinical outcomes is still ongoing, initial feedback has been encouraging. Physicians who have worked Ascendx are pleased with its features including the single pedicle access and the ability to disburse bone cement uniformly. Many of our clinicians perform a large number of vertebroplasty and Kyphoplasty procedures. They have also worked on, or been involved



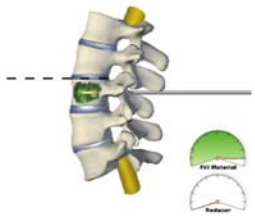
Reduction of Fracture

spine



Fill with PMMA

with, some of the other technologies that are pursuing the VCF market and they are pleased with the performance and promise of Ascendx."



Fill with PMMA

Regarding the enrollment process, Christy said to *OTW*, "As with any clinical trial, one of the primary challenges is enrollment and the Ascendx clinical trial has been no different. The clinical trial protocol requires the vertebral compression fracture to be at least four weeks old. Because of increased awareness of the success of VCF therapy, primary care physicians now frequently refer patients experiencing VCF pain directly to surgery, in lieu of other specialists (e.g., pulmonary physicians, Rheumatology physicians, etc.). With many VCFs repaired within four weeks, this trend has resulted in more patients being excluded from our clinical trial than anticipated. However, we are pleased with the clinical evidence we have seen to-date knowing that older fractures can be more difficult to treat."

Final result – even distribution of PMMA

—*EH (March 31, 2009)*

trauma

Study: Arzoxifene Trumps Raloxifene

Want those bone minerals tightly packed? You may want to consider Eli Lilly and Company's offering, arzoxifene, an investigational selective estrogen receptor modulator. Lilly is announcing new data indicating that arzoxifene was superior to raloxifene at increasing bone mineral density (BMD) in the lumbar spine, total hip and femoral neck, and at suppressing bone turnover as assessed by serum markers of bone metabolism. Arzoxifene is being studied for the prevention and treatment of osteoporosis in postmenopausal women and the reduction of risk of invasive breast cancer in postmenopausal women with osteoporosis or low bone mass.

This Phase III trial included 320 patients (postmenopausal women; mean age of 63) and was a double-blind, active comparator, controlled, 12-month study. Women were randomized to get arzoxifene 20 mg/day or raloxifene hydrochloride 60 mg/day. Calcium and Vitamin D supplements were also provided. The mean lumbar spine BMD in participants was a T-score of -2.9.

The study revealed that arzoxifene significantly increased BMD at all sites to a greater extent than raloxifene, respectively: lumbar spine BMD (2.8% vs. 1.7%); femoral neck BMD (1.5% vs. 0.5%); total hip BMD (1.5% vs. 0.8%). For lumbar spine and femoral neck, this effect was statistically significant as early as six months. Other findings include that arzoxifene suppressed bone turnover to a greater extent than raloxifene as early as three months. New or worsening hot flushes were reported less frequently with arzoxifene versus raloxifene. There were not any between-group or within-group differences in change of percentage of breast density. The proportion of women reporting one or more adverse events, including vaginal bleeding, did not differ between treatment groups. No cases of endometrial polyps, hyperplasia or cancer were reported. Nasopharyngitis and bronchitis were reported more frequently with arzoxifene versus raloxifene. Additionally, more women reported bronchitis and nasopharyngitis in the arzoxifene group versus the raloxifene group, whereas significantly fewer women reported new or worsening hot flushes in the arzoxifene group.

"The significant increases in BMD and suppression of markers of bone turnover seen in these data show the potential benefits of arzoxifene for the treatment of osteoporosis in postmenopausal women," said investigator Jose Zanchetta, M.D., specialist in osteology and mineral metabolism, Metabolic Research Institute, Buenos Aires, Argentina.

trauma

"I'm encouraged by these results and interested in seeing the next Phase III data for arzoxifene."

"We are pleased with the results of the 'NEXT' Study and its implications for arzoxifene as a potential treatment option for postmenopausal women with osteoporosis," said Adrien Sipos, M.D., Ph.D., in the news release. Dr. Sipos, the Medical Director for Eli Lilly and Company, added, "We are committed to research that will help bring innovative prevention and treatment options to patients suffering from this devastating disease, which affects one in three women over 50."[1]

There are a total of three Phase III trials for arzoxifene, with these data being from the second study, known as the "NEXT" Study. In September 2008, results from the "FOUNDATIONS" Phase III prevention study were first presented at the American Society for Bone and Mineral Research (ASBMR) Annual Meeting in Montréal.

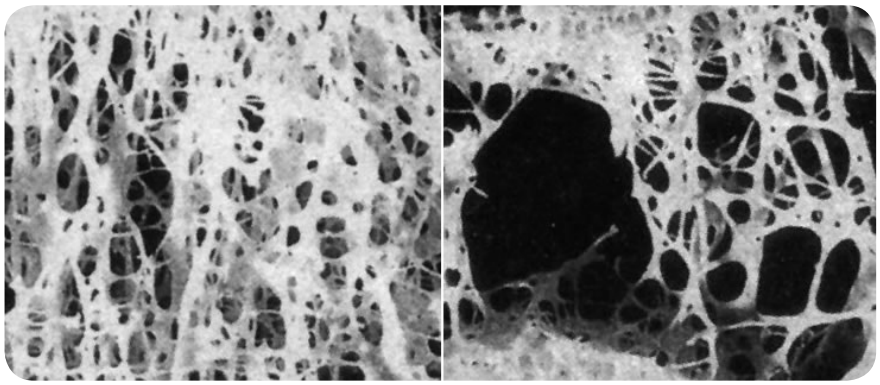
Regarding the next Phase III work, Teresa Shewman, Lilly spokesperson, told *OTW,* "The third Phase III trial, The "GENERATIONS" Study, is a five-year, randomized, double-blind, placebo-controlled study assessing the effects of arzoxifene on vertebral fracture incidence and on invasive breast cancer incidence in postmenopausal women with osteoporosis or with low bone density. Interim results from that trial are anticipated in late 2009."

[1] International Osteoporosis Foundation. Facts and Statistics About Osteoporosis and its Impact. Click here to access report.

—EH (March 24, 2009)

Attention: Spongy Bone Afficionados

Coordinate your calendars… osteoporosis treatment will get a big boost next May when the International Osteoporosis Foundation and the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis will hold a joint global congress in Florence, Italy.



Normal (left) and Osteoporotic (right) Bone Source: International Osteoporosis Foundation

The event, from May 5-8, 2010, will include "meet-the-expert" sessions on 20 key topics such as:

- Practical approach of glucocorticoid-treated patients
- Bone disease in primary hyperparathyroidism
- Pharmaco-genomics
- Developmental origins of osteoporotic fracture
- Bone mass/structure measurements during growth
- Issues in designing and conducting clinical trials

A potpourri of researchers and clinicians, as well as specialists from allied health fields, will be in attendance at the conference. Participants will find an overview of the most recent developments and cutting-edge research in the pathophysiology, diagnosis, prevention and treatment of osteoporosis and osteoarthritis, as well as policy related issues such as health economics.

The scientific program will provide a mix of stimulating plenary lectures on cutting edge topics in the field and the more clinically-oriented meet-the-expert sessions, to be led by world experts. There will also be poster presentations, late breaking news, satellite symposia, and a large exhibition area.

Please visit www.iofwco-ecceo10.org for a full list of programs, online registration, and abstract submission.

—EH (March 30, 2009)

trauma

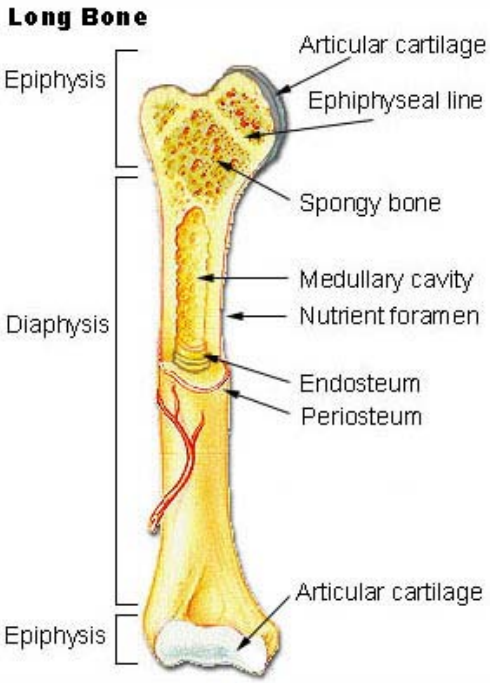
NovaLign Cleared for Fixation System

In the long bone zone…NovaLign Orthopaedics, Inc., formerly known as OsteoLign, Inc., is announcing receipt of its first 510(k) clearance from the U.S. Food and Drug Administration to market its Intramedullary Fixation System, a new system of implants and instruments for the treatment of long bone fractures (including the humerus, tibia and femur). The company now has the green light to enter the intramedullary fracture fixation market, which, according to the news release, is estimated to be $700 million in the United States for 2009.

"Attainment of this key milestone enables the company to move forward with its plans to commercialize new products that provide innovative treatment options for long bone fracture repair," said Jeffrey G. Roberts, President and CEO of NovaLign, in the news release.

NovaLign, which has filed multiple U.S. and foreign patent applications related to its technology, has reportedly engaged in extensive preclinical testing in accordance with internationally recognized testing standards and applicable FDA guidances. The company is on track to begin clinical studies in Europe and the U.S. later this year.

Roberts, commenting to *OTW*, noted, "We're looking at potential clinical trial sites right now and over the next few months. We hope to start implantations by mid-year. We're also planning to start raising money for our Series C financing later this year. And we're continuing to expand our team here in Memphis."



As for how the product functions, according to the company, trauma surgeons insert rigid intramedullary nails through the nearest joint. By entering the medullary canal from outside of the joint, NovaLign's goal is to avoid damage to the surrounding tissue thus minimizing the complications that sometimes result from traditional surgical techniques.

"The NovaLign extra-capsular intramedullary device allows a surgeon to repair a long bone fracture without violating the nearby joint space," said James P. Stannard, M.D., professor of surgery at the University of Alabama at Birmingham, in the news release.

—EH (March 25, 2009)

The Picture of Success: Dr. Thomas P. Vail

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

Stay in your own little corner of the world and your life stays little. Venture beyond its confines and new doors open. Dr. Thomas P. Vail, Professor and Chairman of the Department of Orthopaedic Surgery at the University of California, San Francisco, knows that such expansive thinking enlivens his field, his patients, and his life.

While the lay public probably wouldn't view science as a creative endeavor, Thomas Vail has always seen it that way. "Growing up in Chicago, my life path was heavily inf uenced by my father and grandfather, both of whom were engineers. I saw my early interest in science and engineering as a creative outlet. It wasn't exactly the math that got my attention, but that you could create something or learn how to put things together to build something novel. Particularly interesting to me was how that new idea may lead to a useful product or business."

In line with his propensity for broad thinking, Thomas Vail enrolled in Duke University for his undergraduate studies, in part because of the program's f exibility. "I liked the school's curriculum because I could take engineering classes but was given enough latitude to explore other things such as history and English, areas that I thought would help develop my communication skills. Mechanical engineering was a perfect major for me because it offered the most hands-on approach in terms of design and why things work the way they do. It became clear that the aspects of engineering that interested me most were the ones with human applications."

Indeed, during his undergraduate years Thomas Vail would find vast differences between asking, "What's wrong with this elbow screw?" and "What's wrong with this nuclear power plant system?" Dr. Vail: "In one engineering class we did a failure analysis on a screw used to repair an elbow fracture. The screw broke and we set about trying to determine why, asking, 'Was there some shortcoming in the design or how it was being applied?' We looked at where the threads were located relative to the fracture and found that there was insufficient material to withstand the repetitive loading. It was a confirmation to me that you could apply science, design and engineering to predict whether an implant would work."

Dr. Vail continues: "At that time I did a summer internship with a power company where I worked on nuclear plant design. It was a junior and mundane role, but I got exposed to what it was like to be an engineer on a large project…and knew that it would definitely not be as interesting to me as applying scientific knowledge to the human realm."

The idea of medical school thus began to travel from the back of Thomas Vail's mind to the front. "There were no physicians in my family, but I was captivated by biomedical engineering, a new field at the time. I envisioned numerous potential applications of engineering to medicine and wanted to use such knowledge to impact people's lives. From the time I began medical school at Loyola University of Chicago Stritch School of Medicine in 1981, I was attracted by certain aspects of cardiology, such as f uid mechanics and electrophysiology. But orthopedic surgery got my attention because of the focus on the movement of joints, how people walk, and the interaction between muscles and joints. The idea that you could intervene in the disease process, change its course, and make people walk again was very compelling."

Despite the obvious rewards of a wide breadth of knowledge, Dr. Vail would soon awaken to the beauty of getting

"lost" in one area. "In 1986 I began an orthopedic residency at Duke, selecting my alma mater because I was impressed that the program was producing leaders in surgery. Senior surgeons were telling me that Duke was a place I could go for excellent training—and that it wouldn't be a problem that I had not yet selected a specialty because of the breadth of opportunity. Between 1985 and 1991 a movement grew that shifted the field from 'renaissance' orthopedics to subspecialization. Dr. James Urbaniak, who had just become Chair of Orthopedic Surgery at Duke, was the embodiment of someone who could successfully make that transition. While he was trained in all aspects of orthopedics, he evolved into a world leader in hand and microvascular surgery who embraced subspecialization. He thus encouraged my interest in joint replacement and lower extremity reconstruction, realizing that there was a coming explosion of knowledge in the subspecialties. "Dr. Urbaniak understood the value of becoming proficient in a certain area and was someone who could push the envelope in this regard."

Dr. Vail continues, Another mentor during this time was Dr. David Sabiston, Chair of the surgery department at Duke, who positively impacted residents from a wide variety of subspecialties. An extremely focused thinker, Dr. Sabiston was a disciplined educator who pushed students to be their best. He was a supreme innovator, and the first surgeon to perform coronary artery bypass surgery. His leadership approach is particularly relevant now that I am Chair. If I'm in a case these days, I do as he did, namely insisting that residents understand not only exactly what happens in the OR but also why it is happening."

A traveling fellowship would then give Dr. Vail an in-depth appetizer of adult reconstructive surgery approaches around the world. "My fellowship, sponsored by Duke, allowed me to travel to a number of centers around the U.S. and the world doing hip and knee surgery and learning a variety of techniques and philosophies. One interesting project I worked on involved looking at how to use other living tissues like the iliotibial band to replace a damaged or absent meniscus. This meshed well with my concept/hope of eventually seeing the field of joint replacement (metal and polyethylene) merge with tissue engineering. This work, replacing joints with living tissue rather than bio inert materials, remains the Holy Grail of orthopedics."

Dr. Vail, who organized the fellowship, was guided by two notable orthopedists of the day, Colonel John Feagin, M.D. and Dr. Donald McCollum. Dr. Vail: "Dr. Feagin, who had been a fellow with Sir John Charnley, emphasized that I should select centers that would help me learn in-depth knee and hip anatomy. Dr. McCollum taught me the fundamentals of hip and knee arthroplasty, having been one of the first surgeons to perform hip replacement in the United States. One of the biggest 'takeaways' from the fellowship was the relationship between anatomy and joint mechanics. I learned, for example, that if the deficient anatomy can be replaced, then the structures that remain can resume functioning."

"This concept continues to evolve with minimally invasive surgery (MIS)," adds Dr. Vail. "On the surface, the appeal of MIS is that you're making a smaller incision. But it turns out that the length of the incision is not as important as sparing tissue and determining what is critical as far as recovery and function…and trying to protect those structures during surgery. Sometimes the importance of the interplay, the anatomy and the goal of replacing part or all of a joint gets obscured by marketing efforts. The focus on tissue preserving surgery will continue, however, because it does have a solid basis in science and anatomy."

Dr. Vail's longstanding research interest in cartilage repair could be summed up with, "Go forth, multiply, and integrate."

"In one of my early studies I examined the relationship between the meniscus and the cartilage surface and how sparing more of the meniscus helps protect cartilage. Repairing the meniscus if it's not functioning normally doesn't necessarily protect cartilage. The implication is that there is a more sophisticated understanding of cartilage tissue required to have success in doing these repairs. We now understand that just because you put a stitch in the meniscus or other soft tissue doesn't mean the tissue will function normally."

On the integration front, Dr. Vail notes, "I am also looking at how to load bone in a more normal way after replacing the hip. I see a lot of younger people in my practice with degenerative conditions of the hip, such as early arthritis. The question regarding these patients is, 'Can we make them more functional, i.e., do a replacement that would mesh more with the remaining anatomy?' In past studies I have examined a new material for a hip stem, a carbon fiber composite that I worked on with an orthopedic company. We looked at different stiffnesses of carbon fiber composite hip stems, and measured how bone around the hips was loaded. We found that by changing either the stiffness or the cross sectional area of the stem it was possible to load the bone in a more physiologic way."

"More recently we have asked, 'Is there a way to more conservatively replace or resurface the hip?' So now I am looking at how the bone in the neck of the femur is loaded in hip resurfacing in contrast to where you remove the ball of the hip. This role of hip resurfacing is being tested through experience in the clinical realm. The question remains, 'What should the role of hip resurfacing be, and who is the most appropriate patient?'"

If given free rein and resources, Dr. Vail would design a fellowship that "reaches across the aisle." "We are now at a crossroads," says Dr. Vail. "Technology has reached the point where we can do groundbreaking work in replacing parts of joints with living tissue. Ideally, fellows would be taught how to approach the hip or knee using the most conservative techniques, and set the stage so that the surface we are treating could be prepared and replaced with living tissues. This would require a focus not just on traditional joint replacement, but on tissue engineering, and perhaps computer navigation with the robotic sculpting of the joint to prepare the surface for living tissue. To our detriment, we are siloed now, teaching fellows how to use metal and plastic, but not instructing them on the biological end of things."

Lest Dr. Vail work too hard, there is someone to keep him balanced. "My wonderful family begins with my wife Lisa, who I met in medical school. An internist who focuses on health, fitness and preventative medicine, she has always brought balance to our family life. We have a freshman in college and a junior in high school, both exceedingly talented and wonderful. We enjoy simply relaxing and spending quiet time together. Family life just keeps getting better."

Dr. Thomas Vail…reconstructing joints and engineering an intriguing life.

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