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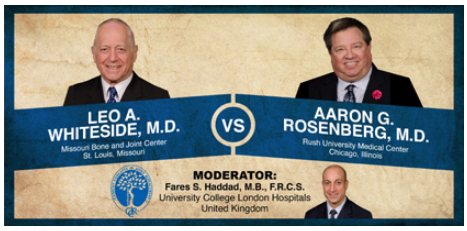
Orthopedics This Week

WEEK IN REVIEW



BREAKING NEWS

For all news that is ortho, read on.

Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

THIS WEEK: Despite a notably upbeat JP Morgan's healthcare meeting in San Francisco, probably the largest of all Wall Street sponsored medical technology and company showcases, institutional investors are taking profits in their orthopedic investments and rotating somewhere else. About the only two companies with a bounce after JPM were Integra and ConMed.

RANK	LAST WEEK	COMPANY	TTM OP MARGIN	30-DAY PRICE CHANGE	COMMENT
1	1	Integra LifeSciences	12.57%	2.75%	Integra continues to transform itself. Recent SEC filling details three top level departures. Still the least expensive equity in ortho.
2	3	ConMed	10.51	5.96	Investors liked CNMD's presentation at JP Morgan. New management has Wall Street believing. Buyers are adding to their portfolios.
3	5	Zimmer	29.12	(1.16)	ZMH's numbers were flattish for 4Q2014 and the strong dollar pulled down sales growth rates. But at these prices...ZMH is one cheap equity.
4	2	Stryker	11.52	(3.48)	Is Wall Street disappointed that SYK didn't announce a deal with SNN at JP Morgan?
5	6	Medtronic	28.84	(1.11)	What does the Medtronic merger with Covidien mean for spine? More bureaucracy? Hopefully not.
6	8	NuVasive	8.01	(1.78)	Sorry to see Keith Valentine, one of the most talented managers in orthopedics, leave. But NUVA's bench is deep.
7	9	Globus Medical	29.68	(0.80)	Purchased Texas-based biologics company and is growing sales at double-digit rates. Smart guys.
8	10	Smith & Nephew	19.92	(2.56)	If investors start to give up on the idea of SYK buying SNN, the stock might get cheap enough to trigger a deal.
9	4	Exactech	10.44	(11.78)	Exactech lost nearly 12% of its value in the last month. Clearly oversold.
10	7	Johnson & Johnson	28.44	(4.24)	Currency headwinds are setting the stage for down revenues for next three quarters—say a consensus of Wall Street analysts.

Robin Young's Orthopedic Universe

TOP PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	TiGenix	TIG.BR	$0.82	$132	30.96%
2	Bacterin Intl Holdings	BONE	$3.30	$22	8.91%
3	ConMed	CNMD	$47.64	$1,311	5.96%
4	MicroPort Scientific	853	$0.43	$616	2.77%
5	Integra LifeSciences	IART	$55.72	$1,827	2.75%
6	LDR Holding Corp.	LDRH	$33.47	$872	2.10%
7	Orthofix	OFIX	$30.50	$562	1.46%
8	CryoLife	CRY	$11.26	$315	-0.62%
9	Globus Medical	GMED	$23.58	$2,310	-0.80%
10	Medtronic	MDT	$71.40	$101,304	-1.11%

WORST PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	MiMedx Group	MDXG	$8.15	$872	-29.27%
2	RTI Biologics Inc	RTIX	$4.46	$254	-14.23%
3	Exactech	EXAC	$20.79	$287	-11.79%
4	K2M Group Holdings	KTWO	$18.90	$702	-9.44%
5	Aurora Spine	ASG	$1.17	$19	-9.32%
6	Alphatec Holdings	ATEC	$1.28	$127	-9.22%
7	Wright Medical	WMGI	$24.41	$1,247	-9.16%
8	Tornier N.V.	TRNX	$24.17	$1,182	-5.22%
9	Johnson & Johnson	JNJ	$100.14	$280,303	-4.24%
10	Stryker	SYK	$91.05	$34,446	-3.48%

LOWEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Johnson & Johnson	JNJ	$100.14	$280,303	16.74
2	Medtronic	MDT	$71.40	$101,304	17.88
3	Exactech	EXAC	$20.79	$287	18.24
4	Zimmer Holdings	ZMH	$112.10	$18,985	19.33
5	Globus Medical	GMED	$23.58	$2,310	19.39

HIGHEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	MiMedx Group	MDXG	$8.15	$872	813.14
2	RTI Biologics Inc	RTIX	$4.46	$254	373.44
3	Orthofix	OFIX	$30.50	$562	194.85
4	NuVasive	NUVA	$46.32	$2,179	119.56
5	CryoLife	CRY	$11.26	$315	38.56

LOWEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Exactech	EXAC	$20.79	$287	1.22
2	CryoLife	CRY	$11.26	$315	1.29
3	Globus Medical	GMED	$23.58	$2,310	1.46
4	Medtronic	MDT	$71.40	$101,304	1.58
5	ConMed	CNMD	$47.64	$1,311	2.00

HIGHEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	MiMedx Group	MDXG	$8.15	$872	54.21
2	RTI Biologics Inc	RTIX	$4.46	$254	24.90
3	Orthofix	OFIX	$30.50	$562	10.59
4	NuVasive	NUVA	$46.32	$2,179	10.46
5	Smith & Nephew	SNN	$35.80	$16,002	3.57

LOWEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	Alphatec Holdings	ATEC	$1.28	$127	0.62
2	Bacterin Intl Holdings	BONE	$3.30	$22	0.64
3	RTI Biologics Inc	RTIX	$4.46	$254	1.01
4	Exactech	EXAC	$20.79	$287	1.16
5	Orthofix	OFIX	$30.50	$562	1.41

HIGHEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	TiGenix	TIG.BR	$0.82	$132	23.15
2	MiMedx Group	MDXG	$8.15	$872	9.02
3	LDR Holding Corp.	LDRH	$33.47	$872	7.81
4	Medtronic	MDT	$71.40	$101,304	5.83
5	Globus Medical	GMED	$23.58	$2,310	5.01

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

510(k) FDA *Moneyball*

BY WALTER EISNER

The FDA has crowed long and hard about its improved statistics for pushing new products through its 510(k) clearance program.

The device industry's largest trade association, AdvaMed, which should be front and center at holding the agency's feet to the fire, has praised the agency for improving its performance. Alex Gorsky, chairman and CEO of Johnson & Johnson even got into the FDA lovefest on January 20, 2015 telling Wall Street analysts that "governments are…taking steps to reward innovation through FDA designations that are helping to speed product review times."

Image created by RRY Publications, LLC

Declining Review Times

FDA Commissioner Margaret Hamburg, M.D. told attendees at a recent AdvaMed meeting that review times for 510(k) clearances have declined, with the average review time for a clearance dropping from a high of 154 days in 2010 to 144 days in 2012.

"Apart from the highest risk devices, we are I think at par with comparable other countries in terms of review times. We do ask for more clinical data often on the higher risk devices. But, I think there's some urban mythology about where we stand in comparison to review times and leadership," said Hamburg.

Margaret Hamburg, M.D./Food and Drug Administration

Faster review times and a greater likelihood of success. By those measures the agency seems to be improving and making life a little easier for device companies.

But what should you be measuring to determine the likely success of getting your product through the 510(k) clearance program?

The 510(k) pathway is the most common way for companies to get their products to market. Simply put, if the company management can convince the FDA that its device is "substantially equivalent" to another product already approved by the agency through the PMA (premarket application) approval process, they are cleared to market their product.

In 2013, FDA cleared approximately 140 510(k)s for every original PMA application approved.

A recent study by Jeffrey Gibbs and Allyson Mullen of Hyman, Phelps & McNamara, and Melissa Walker, the president and chief technology officer of Graematter, Inc., applied *Moneyball*-style statistical analysis of FDA performance to yield some new insights into FDA performance.

The Mask of Averages

The authors were able to get high-level data on key metrics because Congress

Jeffrey Gibbs, J.D.
Hyman Phelps & McNamara

Allyson Mullen, J.D.
Hyman Phelps & McNamara

Melissa Walker, M.S.
LinkedIn

requires the FDA to calculate and publish statistics to help companies gauge their likelihood of success in getting through the 510(k) process. But, say the authors, a major limitation is that the calculation of averages will mask product-specific or classification-specific variations. However, the agency has also released databases that enable more probing analyses than were previously available.

They used SOFIE, Graematter Inc.'s Regulatory Intelligence System to analyze various 510(k) metrics from the agency's public database for a five-year period from 2008 to 2012.

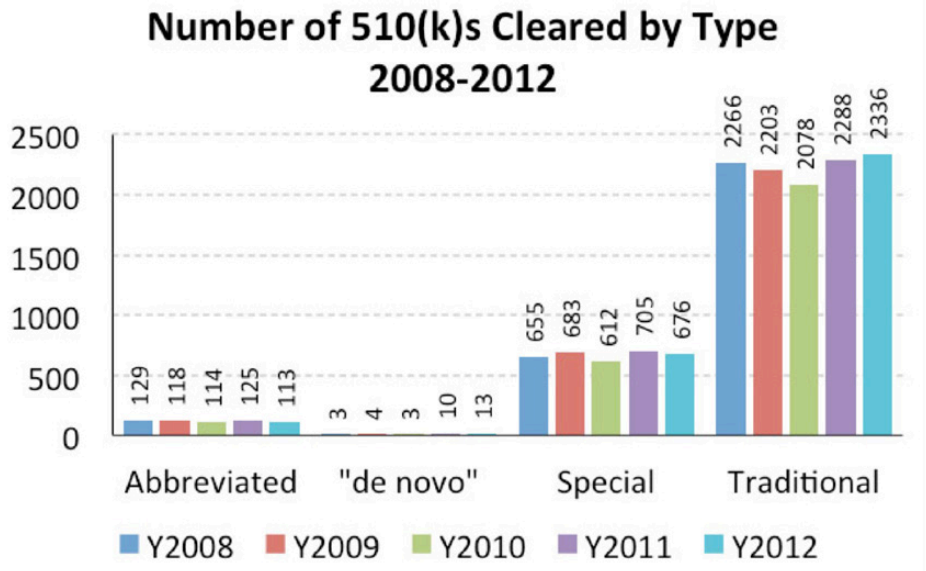
Here's what they found.

During that time period, the FDA cleared approximately 3,027 devices per year. The total number and type of clearance remained generally consistent over that period. About 74% of all submissions were done through the traditional route as opposed to De Novo, Special or Abbreviated routes. *(See chart on page 6.)*

Third-Party Reviews Dying on the Vine

The vast majority of submissions were directly submitted to the FDA instead of through an accredited third party reviewer. The FDA began accepting reviews from "accredited persons" in 1998. But that program, say the authors, had limited use because only select devices are eligible, "and companies have reported mixed experiences with their accredited persons."

They also say recent data show that the effective rate for the third-party 510(k) review process has steadily



Source: Gibbs, Mullen and Walker

declined (from 16% in 2008 to 9% in 2012). "There have not been any recent changes to this program, so this decrease appears to be attributable to industry's disuse—perhaps due to lack of interest, dissatisfaction with the program, and added expense—rather than agency policy."

Third-party-reviewed 510(k)s also took longer to get through the FDA. They found the average review times all appear to be in excess of the 30 days FDA is allowed to make its decision after receiving the third party's recommendation.

Average 510(k) Review Times

The overall average review time for a 510(k) between 2008 and 2012 was 137 calendar days. (Lower than the 144 days reported by Commissioner Hamburg). There was an increase in the average review time beginning in 2010, which leveled out between 2010 and 2012. This increase also took place across each of the four 510(k) types.

The average number of review days for traditional submissions climbed from 128 days in 2008 to 160 days in 2012. The number of review days also climbed for Abbreviated, De Novo and Special Applications in that period.

Failure of Abbreviated Pathway

The authors say this data is particularly curious because when the abbreviated 510(k) was introduced in 1998, the goal was, in part, "to streamlin[e] the review of 510(k)s through reliance on a 'summary report' outlining adherence to relevant guidance documents." While abbreviated 510(k)s may offer advantages in terms of cost and time to prepare, the projected advantage in review times didn't happen in this five-year period.

Medical Specialty Patterns

There are no apparent patterns in terms of the number of submissions cleared within and the number of device types (or product codes) assigned to a medical specialty. "But there is a strong pattern" in the medical specialties with the highest average number of review days—many of them relate to in vitro diagnostic devices (IVDs). The four medical specialties with the longest average 510(k) review times between 2008 and 2012 were pathology, physical medicine, immunology, and hematology (in decreasing order).

Ortho's 121 Day Reviews

There is some good news for orthopedics. The average number of review days for a clearance by the orthopedic review committee was 121 days. Only radiology at 92 days and cardiovascular at 108 days did better. The other 17 review committees took longer with pathology and physical medicine topping out at 273 and 256 days, respectively.

Overall, the average review time for IVD 510(k)s between 2008 and 2012 was significantly higher than non-IVD 510(k) review times (183 days versus 127 days) and had increased dramatically since 2003 when it was 82 days.

Device Type Reviews by Product Code

Average review times for devices change over time, said the authors. Review times can change more quickly and dramatically for individual types of devices than across the device program or by reviewing committee, even those that are required most often.

Orthopedic related devices accounted for three of the top six device product codes cleared most frequently. Those codes included:

- HRS – Plate, Fixation, Bone (233 clearances, 112 days in 2008 to 137 days in 2012)

- NKB – Orthosis, Spinal Pedicle Fixation, For Degenerative Disc Disease (225 clearances, 88 days in 2008 to 104 days in 2012)
- MAX – Intervertebral Fusion Device With Bone Graft, Lumbar (214 clearances, 87 days in 2008 to 99 days in 2012)

Three of the top 10 product codes saw an increase in their average review times by more than 30 days (the overall 510(k) average), with two product codes, GEI (cutting and coagulation) and DZE (endoscopic implants), seeing increases in excess of 60 days (63 and 79 days, respectively). The authors say this pattern is troubling and puzzling. There is no obvious explanation for this trend with the one exception that there were no device-specific guidance documents issued for these devices between 2008 and 2012

In another analysis looking at which product codes took either longer or shorter to be reviewed between 2005 and 2012, the authors found that of 82 product codes, only six required less time for a 510(k) between 2005 and 2012 (approximately 7%). The remaining 76 product codes took longer to review and the increased amount of time ranged from two days to 157 days. Thirteen product codes saw an increase in their average review times of more than 100 days.

The biggest increase in overall review times between 2005 and 2012 was product code NBW (over-the-counter blood glucose test systems); with a 157 day average review time increase.

Safety Concern Drives Review Times

This increase, say the authors, highlights an important point in their analysis:

> "When there is a safety concern with a particular device type, the review time for the 510(k)s is likely to increase—and in this case, increase significantly. Beginning in early 2010, FDA began considering industry-wide actions to address concerns around the accuracy of blood glucose monitors. FDA clearly changed the requirements for these 510(k)s around that same time when it withdrew the 2006 guidance documents for insulin pump 510(k)s in 2011. This conclusion is reflected in the average review time for an NBW 510(k), which increased by 126 days between 2010 and 2011."

The 510(k) Winner: Wound Dressing

On the other hand, the biggest winner in their 510(k) analysis was product code FRO (wound dressing). This product type required 32 fewer review days between 2005 and 2012; nearly all of that decrease was observed between 2005 and 2008. After 2008, wound dressings engaged the FDA two more days than before. "This variability again reminds us that patterns and trends can change significantly."

Conclusion – Write a Good 510(k)

There are many ways of predicting how long a 510(k) review will take, say the authors. Both the overall 510(k) program data and understanding how quickly particular types of 510(k)s have been cleared provide useful insight. Companies will want to draw upon multiple, complementary resources.

"In the end, the single most important variable is the 510(k) itself. A well-written, well-supported 510(k) is the sine qua non. Yet, even well-written, well-supported 510(k)s are subject to other forces and trends that can influence the speed with which a 510(k) is cleared, whether relating to the 510(k) program or the specific device," conclude the authors. ◆

It's Always Sunny in Orthopedics

BY ROBIN YOUNG

Older patients. Mega suppliers. More insured patients. A growing economy. More jobs. Some give on prices.

In the words of top gun orthopedic industry analyst Bill Plovanic of Cannacord Genuity, the signs are in place for better growth rates and, for investors, "long term opportunities within orthopedics…and [we] believe the industry will continue to evolve and offer investors ample opportunities for capital gains…"

On January 24, Plovanic issued an important new report where, among other conclusions, he revised his expected sales growth rates in two of the largest orthopedic sectors upward and suggested that the industry will grow at rates unseen since before the Great Recession of 2008.

But he isn't so sure that last year's torrid M&A activity can stay hot. "Given the mega mergers and small cap valuations trading near record highs, we believe M&A activity may cool off a bit in the near term."

The Outlook for Large Joints

For large joints, Plovanic is raising his growth expectations to levels not seen since, well, before 2008.

In many respects, this uptick in growth expectations reflects the experience of the 2008-2010 recession. U.S. unemployment peaked at 10% in October 2009 and the very next year hip and knee replacement shipments fell approximately 4% and 5%, respectively, industry wide.

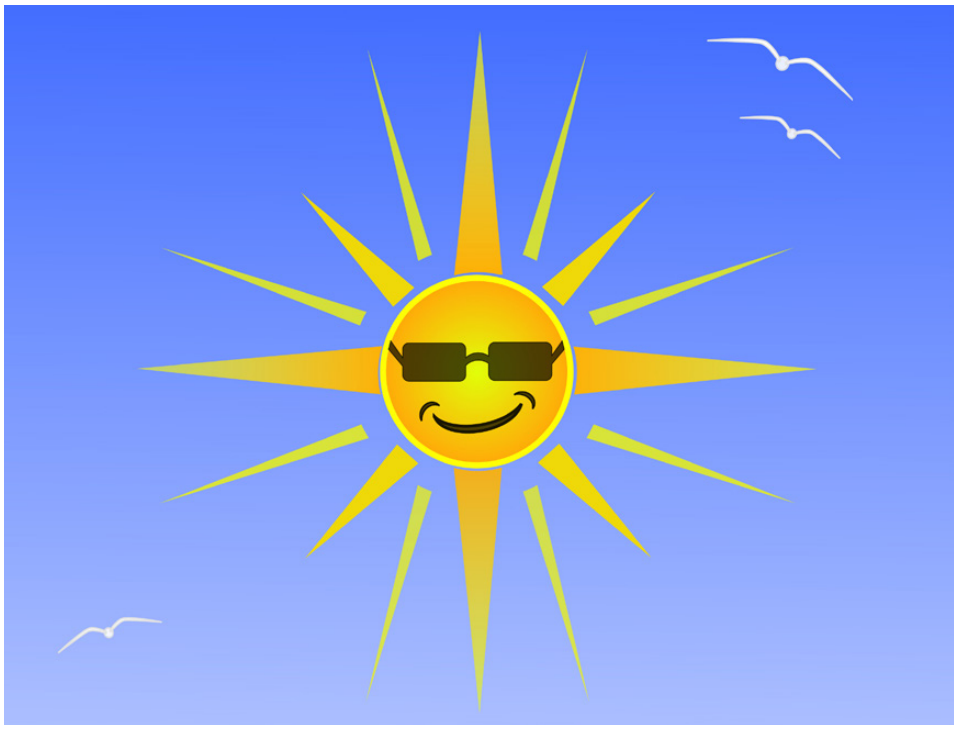


Photo creation by RRY Publications, LLC / Source: OpenClips and pixabay

The extent to which employment rates and large joint procedures are linked was driven home between 2008 and 2010. And why not? No job. No insurance. No surgery.

This year every economic analyst of note is predicting a strong job market for the U.S. According to David Payne in this month's *Kiplinger Report*, the job market will continue to be strong in 2015 and beyond. Payne is expecting that monthly job gains in 2015 will average 250,000—about 3.0 million for the year, slightly above 2014's addition of 2.95 million jobs and that those gains will keep incomes and consumption fueling a healthy economy. And trips to the doctor.

Payne wrote earlier this year that unemployment will likely finish 2015 at about 5.3%—or roughly half the rate of October 2009.

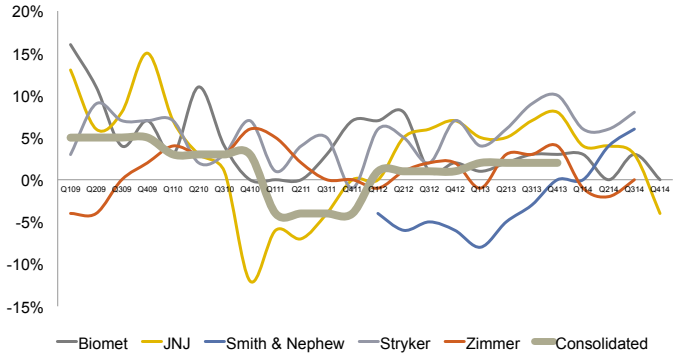
Plovanic is now "modeling for a continued 'rebound' for large joint procedure volumes through year end 2014and into 2015…"

Here is how Plovanic modeled recent history: *(See charts on page 9.)*

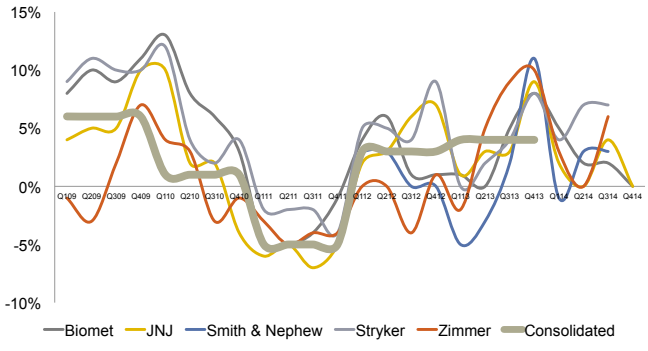
Will Consolidation in Large Joints Continue?

It's been a very busy couple of years with six high profile corporate deals in 2013 and two more earlier in 2014. Large, integrated orthopedic companies have been sitting on billions of dollars of cash which, if not deployed in ways that generate a return better than, say, money market rates, can

HIP IMPLANT REVENUE YEAR OVER YEAR GROWTH RATES 2009-2014



KNEE IMPLANT REVENUE YEAR OVER YEAR GROWTH RATES 2009-2014



Bill Plovanic

actually drag down overall assert and equity returns.

Instead of buying new technologies these buyers went for companies that had already been through the regulatory gauntlet, had distribution—preferably in China—scale and in one instance, a proven new market with robots.

Here's a chart which summarizes all the major transactions since 2011. *(See table and graph below.)*

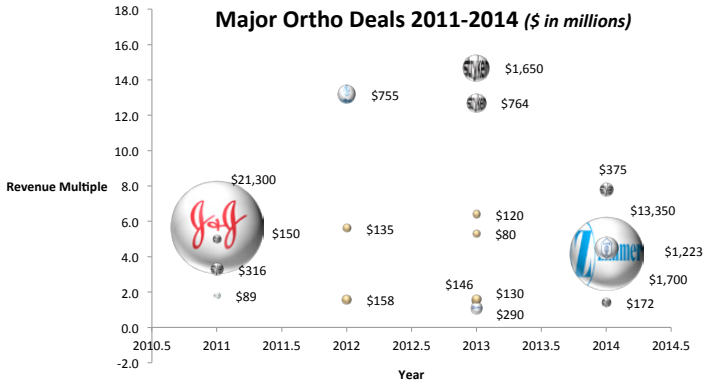
Acquiring Company	Year	Revenue Multiple	Purchase Price (millions)
JNJ	2011	5.7	$21,300
Stryker	2011	3.3	$316
Integra	2011	1.8	$89
Stryker	2011	5.0	$150
Private Equity	2012	1.6	$158
Tornier	2012	5.6	$135
Medtronic	2012	13.2	$755
Wright Medical	2012		$191
Stryker	2013	12.7	$764
RTI Surgical	2013	1.5	$130
Microport	2013	1.1	$290
Stryker	2013	14.7	$1,650
Biomet	2013	1.6	$146
Wright Medical	2013	5.3	$80
Stryker	2013	6.4	$120
Smith & Nephew	2014	4.3	$1,700
Stryker	2014	1.4	$172
Zimmer	2014	4.2	$13,350
Stryker	2014	7.8	$375
Tornier	2014	4.5	$1,223

In Plovanic's view, the urge to merge will likely slow down in 2015. As he stated in his report:"Given the mega mergers and small cap valuations trading near record highs, we believe M&A activity may cool off a bit in the near term."

Spine, Growing Again?

No sector was hit as hard by a multiple of factors nor fell from such lofty heights as spine did in the period of 2009 to 2012. As Plovanic illustrates so well in his report, spinal implant companies were rolling along at solid double-digit growth rates from 2000-2009 and innovation was the name of the game. Then the four horsemen in the form of FDA, CMS, GDP (gross domestic product) and IPO (as in no capital market) hit.

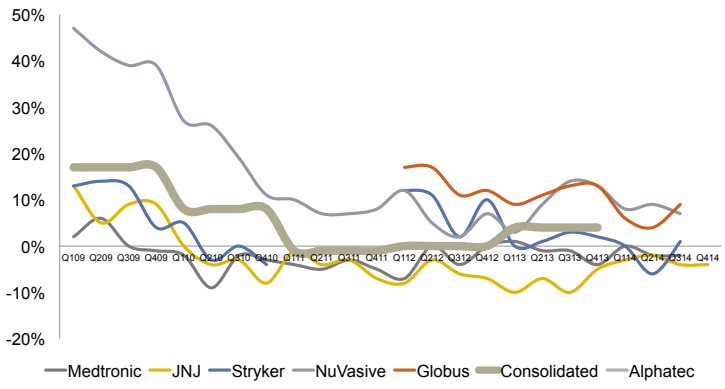
From a consolidated public spine company growth rate of 17% year-over-year growth rate in 2009 to a negative 1% in 2011, it was a rocky road for many companies. *(See graph on page 10.)*



Bill Plovanic

In Plovanic's view, "The worst of the storm has passed with several headwinds having dissipated and starting to become tailwinds. Specifically we believe Physician Owned Distributorships (POD) market share growth has stalled, if not started to shift back to the vertically integrated manufacturer/distributors, providing some growth over 2013 and 2014. We would expect this trend to continue as hospitals put rules in place to block POD business."

SPINAL IMPLANT REVENUE YEAR OVER YEAR GROWTH RATES 2009-2014



Bill Plovanic

The Key Takeaways

Wall Street analysts, who are some of our favorite straw men largely because they are forced to be so public and so specific about their opinions and forecasts (and I used to be one), operate in a kind of no-man's land between industry and the capital markets. All parties, managements, institutional investors and hacks like those of us at *OTW*, lob criticisms into this no-man's land—particularly when they blow a forecast.

But enduring the grueling quarterly round of spreadsheet calibrations and conference calls creates in most surviving analysts an especially sensitive trend antennae. Plovanic belongs to that small tribe of such analysts (there are roughly a dozen members) who can read trends and can spot inflection points very well.

His report of January 26 was, we think, a great example of this. His antennae are telling him that something fundamental has shifted and new, more favorable factors are driving company results. It is time to raise growth rate assumption. How much have conditions improved? Plovanic isn't putting a number on it. But he sure is pointing at the direction.

To close, Plovanic took his macro insights and applied them to specific companies—always an act of courage, but one for which he earns the big bucks.

Here are his summary comments by selected company (not an all-inclusive list): *(See table below.)* ♦

Company	Plovanic's Comment -- Excerpted
Alphatec	Company is transforming itself. Positioned well for new product introductions in 2015. Margin expansion possible. But Wall Street wants to see a string of positive quarters.
Exactech	Gaining share in extremity/shoulder markets. With extremity business now larger than knee business, EXAC also an attractive takeout candidate.
Globus Medical	Globus's ability to rebound from the turnover of a large distributor is encouraging. Management took a conservative tone on 2015 guidance and is therefore positioned to outperform. Long term buyer.
NuVasive	NUVA may be headed to a less robust year in terms of top line growth, but still a BUY. From an acquisition standpoint, NuVasive remains an attractive take-out candidate.
Smith & Nephew	For many reason, SNN is an attractive acquisition target and most of Wall Street expects a deal to happen – most likely with Stryker. But…there are many reasons to like SNN without being a takeout company.
Stryker	Stryker to continue to be an active acquirer for the foreseeable future. The bolus of recent acquisitions will likely cloud earnings moving forward. Recent purchases impressive. Attractive holding.
Zimmer	Even without Biomet, Zimmer is attractive. With Biomet, even more so although near term integration issues and musical chairs with sales reps and distributors may result in mixed earnings results.

The Problem With Spine Surgeons // Todd Albert, M.D. Tweaking Things at HSS // First-Ever Pediatric Elective Hand Transplant Planned!

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

Photo creation by RRY Publications, LLC / Sources: Kapa65 and pixabay

The Problem With Spine Surgeons

It's an issue in every profession. Attorneys. Physicians. Engineers. When you're trained to use only a hammer, every problem looks like a nail. And when it comes to spine care, says one of the most insightful scientist-surgeons in America, spine surgeons are too often treating back problems as if the only solution was metal. When it comes to spine care, a Florida surgeon and entrepreneur bangs the drum loudly, but most often goes unheard…or ignored. Gaetano Scuderi, M.D., an orthopedic spine surgeon in Jupiter Florida and founder of Cytonics Corporation, says that his fellow spine surgeons are focused on implant surgery and have yet to take advantage of novel new diagnostics and biologic therapies. He tells *OTW*, "Whereas physicians have been extremely successful in achieving spine fusion, we all know that patient outcomes rates aren't improving. Similarly, the industry is well aware that with epidural steroid injections (ESI) only about half of the patients experience any relief." Dr. Scuderi's strong belief is that the single biggest cause of the dismal outcome rates is related to the lack of diagnostic tools to assist physicians in making the correct diagnosis. "It's not necessarily their fault because MRIs are terribly unreliable in pinpointing the source of pain. "

Dr. Scuderi indicates that he and those in his lab have discovered a diagnostic test that can dramatically improve patient outcomes. But, says Dr. Scuderi, even after extensive promotion and publication on his science few physicians have started use it. "We have published 14 articles indicating that a unique 'pain protein' the fibronectin–aggrecan complex (FAC), is a reliable biomarker for pain. Patients who are found to have FAC in the disc space or in their joints are more likely to improve following epidural steroidal injections. The FAC test is reported to have ~95% sensitivity and specificity for pinpointing the source of orthopedic related pain."

"We took patients with back pain and bad-looking MRIs and aspirated their disc space. Following ESI treatment, we found that close to 100% of patients with the FAC inflammatory protein got better, whereas nearly none of the patients without FAC improved. The group that has the protein is the cohort that we can treat successfully; the other patients most likely have a different source of pain. Despite our unprecedented success in unraveling the biochemistry mystery of cartilage injuries and our development of a highly effective diagnostic, there has been very lit-

tle interest using our diagnostic among physicians."

Following Scuderi's discovery of the FAC and $9.5 million later, Scuderi and company have made major progress on a biologic therapeutic. "We received a major cash investment from one of the top orthopedic implant companies that helped us develop a 'theranostic,' i.e., a diagnostic tool with a corresponding treatment based on a blood based protein called A2M (alpha-2 macroglobulin) which was proven by our lab and others to inhibit all known causes of cartilage degradation and resulting pain. Recent work from Brown University showing that A2M slows the progression of osteoarthritis has validated our years of work. Unfortunately, surgeons haven't take advantage of the FACT diagnostic or the A2M therapeutic yet because they either haven't heard of it or don't have a deep enough understanding of the biologics underlying orthopedic pain to trial the system. Some are just too busy putting in pedicle screws and just haven't taken the time to fully understand the complicated inflammatory process."

But Dr. Scuderi knows he and his fellow researchers are on the right path. "We have new data that we will be submitting at the NASS meeting in October that shows A2M is a highly effective treatment. This new biologic has already been shown to be successful with intradiscal injections when used in conjunction with the FAC diagnostic. The reality is that if we find a non-surgical solution that really works, like I know A2M does, then all of a sudden the number of fusion surgeries in this country will decrease. I can think of more than a few people who wouldn't be interested in *that*. Ideally, the North American Spine Society [NASS] with all its resources will one day do a study of a larger magnitude. So far, however, I'm still waiting by the phone."

Tweaking HSS: Todd Albert Takes on OR Efficiency It's pretty hard to improve on perfection, but Todd Albert, M.D. is finding a way. Dr. Albert, surgeon-in-chief and medical director at Hospital for Special Surgery (HSS), began his post in July 2014 after serving as president of the Rothman Insti-

tute. He tells *OTW*, "I am determined to make our operating rooms as efficient as possible. When I arrived here last summer I noticed that our ORs were at capacity and that the young surgeons—who are trying to grow their practices were having to operate on weekends or late at night. So, with the option of adding space being pretty much out of the question, I decided that we would find ways to improve on OR efficiency. HSS is known for its amazing quality, however, so we are moving forward cautiously."

"We are evaluating everything, including start times and turnover times. When you examine start time you must dig into what exactly goes into that, namely sign in, healthcare compliance steps, the anesthesiology check, getting the room ready, etc. It is no mistake that we have taken a checklist approach from the airlines and applied it to hospitals…it works."

"In the next six months we will likely move our surgical start times forward. We now start at 8/8:30, but we will be incrementally moving to 7:30 for three of the days and 8:00 for one other day. We are also taking steps to ensure that the time we SAY we will be in OR is the actual time that we are in the room. Each preop element will contain a time stamp and quality metrics to ensure accountability. We also have to protect our rich educational environment at HSS with education occurring every morning."

"The other big push nationally is for 100% safety. I want it to be completely understood that people can speak up at any time if they see something that does not appear safe. We take a time out at the beginning of the operation as mandated, introduce ourselves, ensure that we have consent and that the site is properly marked. I want to know the necessary studies are available, if the side is correct, have the antiobiotics been given…and I always end with, 'Before we proceed, is everybody comfortable?' There is a lot of data on the dangers of an intimidating environment (we saw this with the Korean airliner that went down in part because the co-pilot was afraid to speak up). Unfortunately, most of us have a slavish adherence to autonomy and we don't like it if someone says, 'I have a better way.'"

"To further ensure a safe environment, I always review my notes and studies at least a day to a week before the surgery. If there are any questions then I review things with a fellow or attending; I then re-review things the morning of the surgery. When I arrive that day I go sign the patient in and make sure that we are in agreement as far as the location of the pain. I ask them if anything has changed and I make sure that they understand what I'm going to do to them. I also explain what they are going to feel like when they wake up."

First-Ever Pediatric Elective Hand Transplant "Failure is absolutely not an option," says L. Scott Levin M.D., FACS, chair of Orthopaedic Surgery at the University of Pennsylvania. Dr. Levin, professor of surgery (plastic surgery), has worked with his team for 15 months in order to prepare for the world's first pediatric elective hand transplant. Dr. Levin tells OTW, "We are building on our experience with adults and working with our pediatric colleagues and the United Network for Organ Sharing (UNOS). They are the group that allocates hands and faces for surgery, and they require many details on the capabilities of the institution and the personnel involved in the surgery."

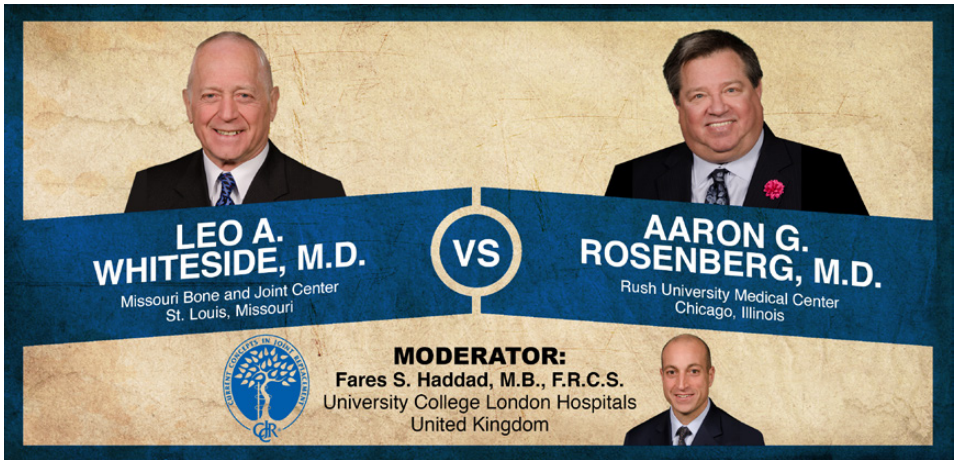
"The preparation process has been extensive, including a thorough case and personnel review by the hospital's ethics committee. We have held several surgical rehearsals during which time we learned which structures should be repaired first. We found that the bone should be addressed first, then we will vascularize the extremity, then address the remaining tendons and nerves. In addition, we will be using custom made 3D cutting guides and bone cutting jigs in order to improve accuracy. To facilitate osteosynthesis once the donor is identified, we will be making use of 3D printers."

"This effort is completely interdisciplinary and requires total preparation in order to give this young child a chance at a normal life. We have already identified another pediatric candidate (about five years old) who is a quadruple amputee. The issue is that it takes time to find donors. There are only maybe 15 kids in the U.S. per year that could be considered candidates based on size and racial features." ♦

Whiteside, Rosenberg Debate Cementless, Cemented Revision

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

"With cemented TKA, if you have the right skill level, instruments, design, fixation, and the correct implant, then you can guarantee your patients a well fixed TKA," says Leo Whiteside. Aaron Rosenberg isn't so sure about that guarantee. "The registries show a significantly higher rate of revision amongst uncemented knees. Besides, the data is trending towards cementless TKA."



Current Concepts in Joint Replacement/RRY Photo Creation

This week's Orthopaedic Crossfire® debate was part of a landmark event, the first Brazilian CCJR meeting. The event, which took place in September 2014, was held in Iguassu Falls. This week's Orthopaedic Crossfire® debate is "The Cementless TKA: Lifetime Guarantee on Parts & Labor." For the proposition is Leo A. Whiteside, M.D. of the Missouri Bone and Joint Center in St. Louis. Against the proposition is Aaron G. Rosenberg, M.D. of Rush University Medical Center in Chicago. Moderating is Fares S. Haddad, M.B., F.R.C.S. from University College London Hospitals in the UK.

Dr. Whiteside: "It's perfectly reasonable to guarantee total knee replacements (TKR) if they are cementless. Most of what I will discuss today is about the PROFIX knee, something I designed for Smith & Nephew many years ago. If you use intramedullary instruments and the AP axis—and do it well—then you're going to get them straight pretty much every time. Nothing has replaced intramedullary alignment for fixation; if you use it in the tibia and the femur both then you're going to get them straight. You use the AP axis…put the femoral head, the patellar groove, and the intercondylar notch in the same plane, then balance the ligaments of the tibia, that's a winner virtually every time in terms of patellar tracking and ligament balancing."

"Use the center of the intercondylar notch, the deepest part of the patellar groove. The femoral cutting guides and tibial guides can be made almost failsafe except for cutting ligaments, etc. Tibial intramedullary alignment is helpful and I can pretty much be sure that I have a straight tibial cut. In a study where we looked at all the X-rays, we found 2-7 degrees (and that's a Pagnano straight knee of +/-3 degrees) from the mechanical axis."

"The basic design criteria are simple and complex. They need to be wear resistant, have good fixation, and be patella-friendly. And you must be able to get the knee into deep flexion easily and safely. Wear resistant means a large surface contact area, peripheral capture of the polyethylene, and compression molded, gas sterilized material. A short posterior radius is helpful because it puts a large radius of curvature on the posterior aspect of the knee and it avoids edge loading. Also, the shorter radius puts the surface on the back of the knee in a functioning posterior cruciate ligament without rolling off the back."

"You need a broad surface in the back of the knee to keep it from being damaged. Deep flexion—past 140 degrees—must be accommodated in TKA [total knee arthroplasty]. You need peripheral capture of the metal component and robust polyethylene capture and the correct type of polyethylene. This should be somewhat difficult to get in, press fit, and then get stronger, tougher, more tight fixation as time passes and swelling occurs. You want effective press fixation, full porous coating on the femur and tibia, and then stems and screws if you need them."

"Without a stem on the tibia you're going to have to be very careful and

limit your cases to only those with hard bone. A stem allows you to broaden your criteria…this will give you fixation in almost any type of bone. Rigid fixation of the femur should require hard driving and be somewhat difficult."

"We recently published a large clinical series (1,556 knees) where two of my colleagues and I were operating. We now have 20 year follow up that started with 212 patients and ended up with 13. Patients ranged from 88-101 years of age. That's one of the reasons why you can guarantee your knees, i.e., because most patients in that age group aren't that active."

"The UK registry included 2,302 patients with cementless PROFIX knees needing revision at 10 years was 1.75%. That outperformed every other knee in the registry, including the cemented PROFIX knee by a significant margin. So if you have the right skill level, instruments, design, fixation, and the correct implant, then you can guarantee your patients a well fixed TKA."

Dr. Rosenberg: "The data is trending towards more cementless TKA. A study by Merrill Ritter and Michael Meneghini several years ago looked at a large cohort of 20 year survivors using the AGC knee. At 20 years they lost no patients, and had 15 failures (many of them were metal backed)…but two tibia were loose at 1 and 2 years. Their 20 year survivorship with aseptic loosening of any component for revision was only 75%."

"In a study of patients with contralateral knees—one cemented, one cementless—they had a relatively young mean age of 58 and 14 year mean follow up. They found no significant difference in the clinical scores in either group. Femoral survival was 100% in both groups at 14 years. But again we see a small number of cementless tibias didn't survive and required early revision. In our experience in the 1980s using cementless total knees there was a 2-3% incidence of tibial components not getting bone ingrowth."

"Recent work by Michael Meneghini is also concerning. They involved 106 consecutive posterior stabilized cementless porous tantalum tibias. In some registries these tibias have done extremely well, but here was a cohort with nine failures at a mean of 18 months. The characteristic failure mode was medial tibial collapse. If you look at the failed implants versus the well functioning ones, the former were taller, weighed

more, and had more, earlier failures in tall, heavy males."

"In a recent review for the Cochran database the authors looked at five randomized controlled clinical trials with 297 patients. There was almost no difference between groups in terms of the knee scores, but radiostereometric analysis studies showed that cemented tibias had smaller displacements. And Swedish registry data shows a significant difference between the cemented and cementless total knees. They did a Cox regression model adjusting for age, gender, year of operation and patellar component; the revision risk for the uncemented tibia was about 1.5x greater than it was for cement."

"The New Zealand registry shows about a 50% increase in component revision per 100 years of implantation (uncemented versus cemented). The UK registry shows a significantly higher rate of revision amongst uncemented knees at five years; the Australian registry shows a significantly higher revision rate per 100 years. Finally, the cumulative revision rate at 10 years is higher. So over the short to intermediate term there is a small advantage. The younger the patient the more incentive there might be for cementless fixation…but in registry studies younger patients are at a higher risk for revision (for either fixation)."

"As the polyethylene improves and wear issues diminish the advantage of removing cement from the construct may increase. Leo, let's compromise. Let's agree to respect each others' views…no matter how wrong yours may be."

Moderator Haddad: "If you look at what's happened what with hip replacement you see that the world has gone cementless. Yet in North America cementless knees still aren't the standard of care."

Dr. Whiteside: "It took Ignaz Semmelweis about 100 year to convince obstetricians to wash their hands between deliveries and they finally drove him into an insane asylum. I figure that's where I'll end up…with your help."

Dr. Rosenberg: "I'll go with you. Look, at the end of the day I think there is some merit to the concept of eliminating cement. Two things that concern me: Is cement protective of the interface in the situation when you get particulate debris? Our evidence says that it is…and that when you use cemented components you're less likely to get the infected joint space attacking the implant interface. Also, the fact that it's

biologic and requires a time period in which fixation occurs means that when you first place the implants they're not securely fixed. You must securely fix them with an interference fit. And until they get ingrowth there is a possibility that they won't get biologic fixation."

Dr. Whiteside: "I was sad to see Meneghini's article on failure fixation of the tibial component. The biomechanical data are so clear. Going back to Insall and Burstein we knew that you can't get by without good fixation. Then there's Merrill Ritter's study showing that a flexible tibial tray will sink into the tibial bone. If you're going to use cementless fixation you had better have good biomechanics."

Dr. Rosenberg: "The question in my mind is, 'Will there come a time when we add some biologic component to the underlying physiology of knee replacement without cement?' About 10 years ago when it became more popular to do surface cementing of the tibial components only and no cementing of the tibial keel, for example, I encountered a lot of patients who were referred to me for persistent pain. Also, a number of patients who have ingrowth of cementless components, but have persistent pain, we revise them to cemented components and they get dramatically better. Retrieval studies show that the amount of fixation interface that actually occurs is quite variable. And particularly on the tibial side the amounts are rarely beyond more than 20% of the interface that are fixed. And there may be variability in the degree to which people feel that this interface is comfortable."

"The beauty of cementless is that ideally you get remodeling of the bone over time. The problem is that the cementless application narrows the window of performance, so to speak, so that it may make it more difficult for a larger community of surgeons to get acceptable results."

Moderator Haddad: "The mark of two fantastic surgeons is that the moderator had to do absolutely nothing during the debate. Thank you, gentlemen." ◆

Please visit www.CCJR.com to register for the 2015 CCJR Spring Meeting, May 17 - 20 in Las Vegas, Nevada.

COMPANY

Stryker Treading Water – Going Shopping

Stryker Corporation's 2014 fourth quarter orthopedic sales of $1.11 billion were roughly in line with Wall Street expectation and rose 4.5% on a constant currency basis from the previous year's quarter.

On a reported basis, hips, knees and spine dropped 3%, 2.2% and 2.5%, respectively. Trauma saved overall sales by climbing 9.2%. There was some good news as 20 MAKO robotic knee systems were placed during the quarter, compared to eight sold in the third quarter. In addition, company management hopes for FDA approval of the MAKO total knee is expected sometime in 2015. BMO Capital Markets analyst Joanne Wuensch said excluding the benefit of MAKO in knees, "The segment saw its sales decline slightly, likely resulting from not having a brand new knee on the market."

Wuensch also said the compatible-product launches with the MAKO system "is a positive step to help sway the hospital purchasing groups to purchase the system, but at the same time, these products are not new, and are likely to see the same pricing pressures as other implant devices. Looking forward, we do expect management to sell more MAKO robots, but sales should likely ebb-and-flow (and we don't expect 20 robots every quarter)."

The company has submitted a 510(k) application for the Triathlon Total Knee, but Wuensch does not anticipate clearance contributing to sales until 2016. Management also anticipates launching, though on a limited basis, its cementless unicompartmental knee in the second quarter of 2015. On the hip side, Wuensch anticipates management to add its Accolade Hip and X3 Poly Bearing on the MAKO in 2015.

Stryker Corporation 3Q14	Sales $ in million	% Change
Reported Orthoedics Sales	**$1,111**	**1.7%**
Knees	$363	down 2.2
Hips	$331	down 3.0
Trauma/Extremities	$335	9.2%
Spine	$192	down 2.5

Source: Stryker Corporation

Image created by RRY Publications, LLC/ Sources: Stryker and sd.keepcalm-o-matic.co.uk

On a conference call with analysts on January 27, 2015, company officials blamed the weak sales on operational issues in Japan associated with the ERP (enterprise resource planning) rollout, implant pricing pressure and tough year-over-year comparisons. They do not believe the company lost any market share on a volume basis.

4th Quarter Recon Market

Glenn Novarro of RBC Capital Markets estimates the recon market grew 2.0 to 2.5% during the quarter on a constant currency basis. That's a big change from last year's fourth quarter growth when there was a big push to get procedures done before the Affordable Care Act took full effect and patients used up their health savings accounts before year's end. Mike Matson of Needham & Company also estimates that the recon market grew by 2% during the quarter versus 4% in the third quarter. Matson estimates that, on a constant currency basis, global knee growth was 2% and global hip growth was 2%. He attributes the slower growth due to the big sales growth seen in last year's fourth quarter, making this year's fourth quarter a tough comparison.

Stryker: Going Shopping

But analysts on the January 27 conference call were mostly interested in what Stryker is going to do with all its cash. The company ended 2014 with $1.79 billion in cash, up from $1.33 billion a year earlier. Company CEO Kevin Lobo the worked analysts into a lather by emphasizing that acquisitions are the priority use of cash. Jefferies analyst Raj Denhoy wrote

that merger and acquisition is likely, but remained cautious on the merits and likelihood of a Smith & Nephew acquisition.

To fatten the war chest even more, the company plans to repatriate some $2 billion in cash held overseas in the second half of 2015.

According to *Reuters*, Lobo speaking at the JP Morgan healthcare conference in San Francisco on January 13, 2015, said the company was in a very strong cash position that would allow it to make acquisitions that are "small, medium or even large…. We need to be market leaders in the areas that we choose to play in…. We'll look at deals of all different sizes…to strengthen our position."

Stryker currently has about two-thirds of its total sales in the U.S., with about a quarter coming from other developed markets and 8% from emerging markets.

Lobo told attendees at the JP Morgan conference that he sees Europe as a critical area with room for improving the company's performance, and said he believes the capital spending climate there is improving. "Our market shares are dramatically lower in Europe than in the U.S., Canada or Japan," he said. "Our products should be garnering higher market share there."

2015 Guidance

Finally, company management told analysts it expects 2015 constant currency sales growth in the range of 5.5% to 7.0%, including organic sales growth in the range of 4.5% to 6.0%. — *WE*

"State of Orthopedics" Sounding Good at DePuy Synthes

Alex Gorsky, the chairman of Johnson & Johnson sounded like a happy man when he reported fourth quarter results on January 20, 2015.

His subsidiary, DePuy Synthes, showed 3% operational growth over the prior year and healthcare utilization rates in the U.S. increased for the second quarter in a row and are expected to keep rising. Gorsky told analysts that "governments are increasingly recognizing the need to continue to address healthcare needs and are taking steps to reward innovation through FDA and EMEA [European Medicines Agency] designations that are helping to speed product review times."

In the U.S., Gorsky said there is probably the "clearest and the most tangible data" about utilization rates that he finds encouraging. "We think we've got about three quarters now in the positive, when I say in the positive I mean somewhere between 2% and 3% when we're looking at hospital admissions [and] surgical procedures. Physician office visits still appear to be negative. So I think it's too early to declare complete victory yet."

He added that, in particular for medical devices, his company's emphasis has been on "growth acceleration from innovation" and transforming their sales models to "better reflect the reality" that purchasing decisions are increasingly being made at the healthcare system level.

The "big focus" over the past year, he said, has been to make sure they've made the most of the significant investment made in Synthes. "And I think we made a lot of headway…. In fact I think we were one of the first companies to really look hard at spaces like orthopedics and recognize that consolidation was very likely to occur and so we were able to do that in a way where we feel

DePuySynthes 4Q2014	Sales ($ in millions)	% Change
Total Reported Sales	**2,441**	**down 0.6%**
Knees		0.0%
Hips		1.0%
Spine		0.0%
Trauma		down 2.0%

Source: Johnson & Johnson

Image created by RRY Publications, LLC
Sources: DePuySynthes and RRY Publications

we got a very good portfolio fit…. We feel that we're in a very good position now particularly as many of our competitors are just starting to go through some of those consolidation initiatives."

For the quarter, orthopedic sales of $2.441 billion declined slightly by 0.6%. A strong dollar cut 3.4% from reported sales.

Orthopedics sales growth, according to management, was driven by sports medicine, hips, spine and knees. "The successful launch of MONOVISC coupled with the continued strong growth for ORTHOVISC drove results for sports medicine." On a constant currency basis, hip growth of 5% worldwide was driven by strong volume growth partially offset by continued pricing pressure. Primary stem platform sales were a major contributor to the results. Spine grew 3% with solid market volume growth and new product launches partially offset by continued pricing pressure. Knees worldwide increased 3% due to the "successful launch of ATTUNE," with pricing pressure offset by positive mix.

Yes, the State of Johnson & Johnson and orthopedics looks good from where Chairman Gorsky sits. — *WE*

K2M Want $40 Million More

K2M Group Holdings, Inc. wants more money.

On January 20, 2015, the company announced it has filed documents with the SEC "relating to a proposed follow-on public offering of its common stock." According to the company announcement, it hopes the offering of 4.9 million shares will raise around $40 million.

Most of the proceeds, according to the announcement, "will be used by the company for working capital and general corporate purposes, which is expected to include the expansion of the company's global distribution network through the hiring or contractual engagement of qualified individuals and purchasing of inventory to support their sales efforts and which may also include the acquisition of or investment in complementary products, technologies or businesses."

The 11-year-old company netted around $120 million last May in an initial public offering (IPO). After the offering, the company's market cap shot up to $427 million. Today its market cap stands at about $735 million.

K2M COMPLEX SPINE INNOVATIONS™

K2M Group Holdings, Inc.

On January 12, 2015, the company announced preliminary fourth quarter sales results. Total revenue of $49.3 million was up 16% over the previous year's quarter. Full year revenue of $186.7 million climbed 18% over the previous year. The company is still looking to be profitable. In the third quarter of 2014, the loss from operations was $12.9 million, compared to $9.6 million for the third quarter of 2013.

President and Chief Executive Officer Eric Major said, "Specifically, sales increased approximately 20% year-over-year in both our Complex Spine and MIS businesses, and we saw degenerative sales increase by almost 30% this quarter. These results represent a continuation of our strong performance in fiscal year 2014—our first as a public company—a year in which we executed on our goal of increasing market penetration and on expansion of our innovative products. We remain focused on increasing our share of the $2.6 billion global complex spine and minimally invasive surgery markets and on driving shareholder value creation going forward."

The company was co-founded by company Chairman and Chief Medical Officer John Kostuik, M.D., and Major. — *WE*

LEGAL

90% of Patients Happy to Share Medical Records

There has been far too much kerfuffle about privacy of medical records, according to a study carried out by NPR (National Public Radio) and reported by Scott Hensley. Over half of Americans are willing to share their health data so long as it is going to be used for research. When it comes down to it, they are just not all that worried about what happens with the information in their medical records.

NPR interviewed 3,010 people and learned that 65% were comfortable sharing their information anonymously with health care researchers. Hensley reported that responders did not give a fig for who might be using the data, whether they were government researchers, university professors, independent laboratories or drug companies. Between 81% and 92% of the respondents were comfortable sharing information with these groups. However university professors received the highest approval rating—95% of people under age 35 were willing to share with academics.

Among people willing to share medical data, the topic of research did not matter very much. Hensley noted that "every category—ranging from safety issues to reining in health costs—scored support from at least 90% of the potential sharers." — *BY*

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BIOLOGICS

FDA Issue "Safety Communication" Over Certain Bone Graft Substitutes

Food and Drug Administration

Stop the routine use of bone graft substitutes containing recombinant proteins or synthetic peptides high-risk (Class III) medical devices in patients under 18 years of age, warns the Food and Drug Administration (FDA).

On January 21, 2015, the agency issued a "Safety Communication - Reports of Serious Injury," because reports of serious injuries, "such as excess bone growth, fluid accumulation, inhibited bone healing, and swelling," have increased the agency's concern.

Younger Patients – Added Risks

These reports of injuries, says the agency, are of special concern because patients under 18 are typically smaller and their bones are still growing. "Any product that affects bone growth could have the potential to negatively impact skeletal development by altering normal bone formation and growth, especially if implanted near open growth plates." The agency also said that before marketing such products, companies need to submit a premarket approval application (PMA) with clinical data.

The agency says certain recombinant proteins and synthetic peptides "mimic bone growth substances normally found in the body and may be added to a carrier or scaffold to be used as bone graft substitutes. Once combined, these products are surgically implanted in a patient with a bone defect to promote new bone growth or to replace or heal existing bone."

The products have been approved for orthopedic and dental use only in patients over the age of 18 who are done growing (skeletal mature). The labeling for each product provides the specific indications for use.

According to the agency, because younger patient's bodies are still growing, vital organs and tissues are closer together than in a body that is done

growing. "This could potentially allow small changes from one organ/tissue to have serious effects on another. For example, there is less space between the spinal cord and the bones surrounding it. If one of these products is used in the spine of a patient under age 18, who then experiences the same amount of excess bone growth or fluid accumulation as a patient over age 18; it may more easily lead to spinal nerve injury, pain, or weakness."

Recommendations

The FDA offers four recommendations:

- NO "routine use of these products in patients under age 18 because their safety and effectiveness has not been reviewed or approved for use in this population."
- "Consider alternatives such as autograft bone, allograft bone, and bone graft substitutes that do not contain recombinant proteins or synthetic peptides before using bone graft substitutes containing recombinant proteins and synthetic peptides in patients under age 18."
- "Carefully consider the benefits and risks before using these products in any patient. If considered the best or only option, inform parents/guardians and patients about the risks and benefits of using the product when discussing surgical options."
- "Closely monitor patients under age 18 for adverse events and if necessary, refer them to the appropriate healthcare provider for corrective treatment. Adverse events may include problems with skeletal development, excess growth of other tissues, and tissue swelling or fluid accumulation that could put pressure on adjacent organs or tissues."

Report Adverse Events

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report Online: www.fda.gov/MedWatch/report.htm
- Download form or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

Read the MedWatch safety alert, including a link to the FDA Safety Communication, at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm431001.htm — *WE*

LARGE JOINTS

Injectable Peptide to Treat OA?

While it's not ready for prime time in human patients, a protein molecule called C-type natriuretic peptide (CNP), which occurs naturally in the body, may eventually be used to treat osteoarthritis (OA). This protein, known to reduce inflammation and aid in the repair of damaged tissue, may one day be injected by general practitioners. The researchers, who hail from the Queen Mary University of London (QMUL), say that CNP can't yet be used in humans because it cannot target the damaged area, is easily broken down, and cannot reach the diseased site.

According to the January 21, 2014 news release, the researchers were led by Dr. Tina Chowdhury from QMUL's School of Engineering and Materials Science. The team used an animal model and constructed tiny microcapsules, just two microns in diameter, with individual layers containing CNP that could release the protein slowly. One day, say the researchers, injections of microcapsules could in the future be used to heal damaged cartilage in people with osteoarthritis.

Dr. Chowdhury stated, "If this method can be transferred to patients it could drastically slow the progression of osteoarthritis and even begin to repair damaged tissue. CNP is currently available to treat other conditions such as skeletal diseases and cardiovascular repair. If we could design simple injections using the microcapsules, this means the technology has the potential to be an effective and relatively cheap treatment that could be delivered in the clinic or at home."

Dr. Stephen Simpson, Director of Research at Arthritis Research UK said: "Current treatment options for osteoar-

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thritis are limited, and therefore developing new ways to treat this painful and debilitating condition is currently a major area of research. The focus is not only about identifying promising new targets, as delivery of a drug to the appropriate site can often be as challenging as developing the treatment itself, and can hinder getting otherwise effective medicines to patients. This work represents a good example of how researchers are developing innovative new approaches to get around this problem." — *EH*

New Pain Killer for Joint Replacement

More than half of all adults in the U.S. who are diagnosed with knee osteoarthritis will undergo knee replacement surgery, according to a Workers Compensation estimate. While the surgical techniques have continued to improve, pain control has not.

A study at Henry Ford Hospital, Detroit, Michigan, found that if doctors injected a newer, long-acting medicine called liposomal bupivacaine into the tissue surrounding the knee during surgery patients felt dramatically less pain. Jason Davis, M.D., a Henry Ford West Bloomfield Hospital joint replacement surgeon and the study's senior author said, "Patients had pain relief for up to two days after surgery and better knee function compared with the traditional method."

In the Henry Ford study, researchers evaluated 216 patients for pain control during the first two days after joint replacement surgery. Researchers gave half of the patients the traditional pain control which involves a continuous femoral nerve blockade. Doctors injected numbing medicine into the groin area which blunts the main nerve down the front of the knee. This caused some patients leg weakness. "Pain control came at the price of weakness and made patients somewhat tentative when walking during their hospital stay," Davis said.

Researchers gave the other half of the patient group an injection of liposomal bupivacaine at the site of the surgery. Davis reports that many of these patients were able to walk comfortably within hours after surgery. He observed that, "function-wise, it was a lot easier for patients to move around more confidently. This option is a promising, viable one for our patients," he concluded. — *BY*

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EXTREMITIES

Add Sugar, Protect Joints

It's not a license to eat bonbons all day, but there IS new evidence that sugar can be a good thing—at least if it's in saline. Researchers from Edinburgh University's Centre for Integrative Physiology have found that adding sugar to saline solution could reduce the risk of osteoarthritis (OA).

Wikimedia Commons and U.S. Army Africa

To counteract the possible cartilage cell damage caused by surgery, the Edinburgh team (working with a rat model) added sugar to the saline solution used to wash out joints during orthopedic surgery. They found that it not only protects the cartilage, but that it may even improve cartilage repair. The researchers, who were funded by Arthritis Research UK, have also shown that there is better cartilage repair when the chondroprotective solution is used, compared to the usual saline currently used in orthopedic surgery.

Dr. Andrew Hall, principal investigator and reader in cell physiology said in the January 27, 2915 news release, "Our findings could have major implications for tens of thousands of people who undergo arthroscopic surgery, such as footballers or other sportspeople who've damaged their cartilage. Or in fact anyone who's had exploratory surgery for a sore or painful knee."

"There is a worry that all these people are at risk of developing osteoarthritis from their surgery. But if surgeons can be persuaded to use this chondroprotective solution as standard that risk could be substantially reduced. It's a cheap, simple solution that can protect the cartilage in the joint during arthroscopy and surgery."

Dr. Stephen Simpson, director of research at Arthritis Research UK commented, "It's extraordinary that something as simple as a sugar solution can have such a beneficial, protective effect on the joints during surgery and can actually help repair cartilage damage. It seems a simple yet potentially valuable step that surgeons around the country could be persuaded to include in their procedures." — *EH*

Johns Hopkins Study Details How to Improve Patient Safety

A new Johns Hopkins study has found that when it comes to keeping patients safe, a health system must have clear goals, strong leadership and infrastructure, staff engagement, and transparent reporting methods. The study, led by Peter Pronovost, was published in *Academic Medicine* in December 2014.

Pronovost, senior vice president for patient safety and quality at Johns Hopkins Medicine and director of the Armstrong Institute for Patient Safety and Quality, worked with colleagues to review the model used by the Johns Hopkins Health System to improve the use of core measures. According to the January 5, 2014 news release these are, "recommended, well-researched processes for treating patients who require surgery or suffer heart attacks, heart failure, pneumonia or serious conditions."

The researchers found that while the goal of the health system was to achieve 96% compliance on seven best practice measures at five of its member hospitals, after two years these hospitals had obtained 96% compliance on six of the seven targeted measures.

Pronovost and his colleagues found that a critical part of meeting a patient safety improvement goal is ensuring that an organization first has a "commitment from leadership to invest in organizational structures and governance to hold member institutions accountable. Leaders from Johns Hopkins Medicine formed the Armstrong Institute to coordinate research, training and operations for quality improvement efforts across the organization. Clinical work groups responsible for target measures reported progress to the Johns Hopkins Medicine Patient Safety and Quality Board Committee. Better communications and identification of specific opportunities for improvement, according to the study, were also critical for success."

The other critical element to succeeding with a patient safety goal is establishing a transparent reporting system, said the authors. Hospitals that did not meet the goal of 96% compliance in one or more of the safety targets had to undergo a four-level review process. Hospitals that repeatedly missed the goal were referred to higher levels of leadership for review and possible auditing.

Regarding the biggest challenge involved with the work groups, Pronovost told *OTW*, "The clinical communities are peer-driven networks, with members from across the institution. Identifying a collaborative leader to help the network establish safety and quality priorities, set goals and achieve results is critical for success."

Asked what advice he might have for smaller institutions with limited resources, Pronovost added, "The clinical communities framework works best when you take the key principles—collaboration, social connections and active engagement—and apply them in a manner that aligns with your institution's goals and culture." — *EH*

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SPINE

First Disposable Spine Implant Fixation Kit Cleared by FDA

ECA Medical Instruments, Inc. claims to have developed a "game changer" with the "potential to transform healthcare economics."

The claim is based on FDA clearance of the company's disposable spine implant fixation kit announced on January 16, 2015.

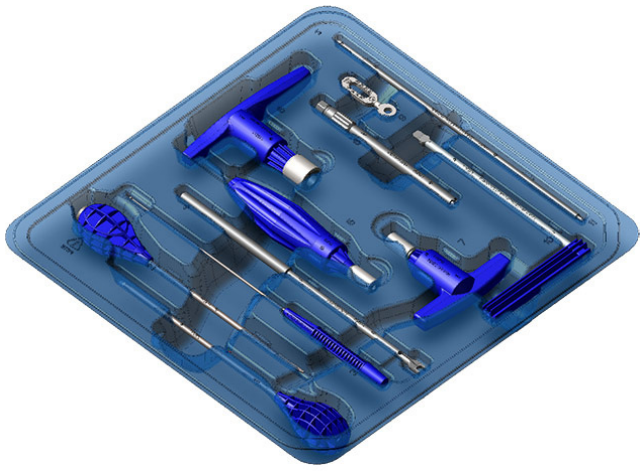
Calling it the first such sterile-packed kit to gain FDA clearance, the product "features a full complement of fixation instruments in a single sterile packed tray including proprietary and industry first cannulated torque-limiters, ratchets and fixed drivers." All the kits and instruments are disposable, biodegradable or recyclable. These specialized instruments are needed by surgeons to perform both open and minimally invasive surgeries (MIS) in both inpatient and outpatient facilities."

"This single tray of instruments is game changing for our industry and FDA approval [FDA clearance] signals a new era is taking hold with potential to transform healthcare economics," said John Nino, president and CEO of ECA Medical Instruments. "Surgeons, hospitals, ambulatory surgical centers (ASCs) and patients all benefit from cost savings, increased safety and superb outcomes." The focus will be on serving ASCs.

The instruments are to be used with the Intelligent Implant Systems, LLC's (IIS) Revolution Spinal System and will be available in the U.S. starting second quarter 2015. The announcement stated the ISS system offers a "simplified design for posterior spinal fixation implant of single or two-level constructs."

"By providing sterile state-of-the-art implants combined with a single sterile tray of disposable instruments by ECA, we are leading the way to a better approach for spinal surgery," said Marc Richelsoph, president and CEO of Intelligent Implant Systems.

Nino's bold prediction may not be idle. According to the company, "every 20 seconds of every day" an ECA torque instrument is used to secure a medical implant in a patient. The company says it has manufactured and delivered over 25 million precision torque instruments to the world's leading producers of cardiac rhythm management, neuromodulation, cardiovascular and orthopedic and spine implants "resulting in over 500 million surgical actuations." — *WE*



Revolution Spinal System/ Intelligent Implant Systems, LLC

PEOPLE

Christie Readies Presidential Campaign

The man who claims to have singlehandedly saved the U.S. orthopedics industry is taking steps to be our next president.

Reuters reported on January 26, 2015 that New Jersey Governor Chris Christie has formed a political-action committee (PAC) called "Leadership Matters for America." The *Wall Street Journal* said the formation of the PAC is the "clearest sign yet" that Christie is running for the White House.

Gov. Chris Christie/State of New Jersey

Governor Christie needs no introduction to orthopedic device makers and surgeons. When he was the U.S. Attorney in New Jersey in 2007, he hauled in all the major device companies and told them he had evidence that they had offered illegal incentives to surgeons to use their devices. In

exchange for a few hundred million in fines and temporary oversight, he offered the companies deferred prosecution agreements (DPAs). One of the "overseers," Christie's previous boss, former U.S. Attorney General John Ashcroft, was reportedly paid over $50 million for 18 months of work to straighten out one device company's surgeon/company consulting and patent agreements.

Saved Ortho From Medicare "Death Penalty"

After Christie left the U.S. Attorney office, he testified in front of a congressional committee about the agreements. He told lawmakers that had he not entered into DPAs with the companies, the overwhelming evidence of wrongdoing would have resulted in the Medicare "Death Penalty" for the companies, effectively destroying the U.S. orthopedic medical device industry.

Christie is not yet an officially declared candidate. But he has spent a lot of time in Iowa and New Hampshire and has been attending Republican activist meetings to make his pitch about what Republicans need to do to win back the White House. Seen as a "moderate" by many in the Republican Party, he may have a hard time winning over the conservative delegates and primary activists who turn out heavily in early primaries. He also has some problems at home in New Jersey, where a poll released last week said that nearly three in five registered New Jersey voters don't think he'd make a good president. He got into hot water after it was revealed that his underlings ordered the closure of the George Washington Bridge in 2013 for alleged political reasons.

Forming this PAC shortly after former Florida Governor Jeb Bush's December PAC formation, lets Christie begin to hire staff, build a campaign operation and travel around the country building support among Republican activists. He's not expected to make any announcements until next spring.

Staff Hired

According to an *AP* report, the PAC has already hired fundraisers and consultants with Republican primary election campaign experience, including Ray Washburne, the former finance chair of the Republican National Committee. Other senior advisers include Phil Cox, who was executive director of the Republican Governors Association (RGA) while Christie was chair in 2014 and Christie's long-time political adviser, Mike DuHaime. Cam Henderson, who worked on the state's Superstorm Sandy rebuilding effort, will serve as finance director, while James Garcia, Mitt Romney's national field director in 2012, will be political director. Paige Hahn, the RGA's outgoing finance director, will play a role on the finance team.

Another former Christie aide, Matt Mowers, is reportedly resigning as executive director of the New Hampshire Republican Party at the end of the month, to work in that early-voting state, while Phil Valenziano, who served as political director for Iowa Governor Terry Branstad's re-election campaign, will help lead Christie's Iowa staff.

The Governor might be good for orthopedic device makers. After all, as we learned from the old *Kung Fu* television series, there is an old Chinese proverb that says if you save someone's life, you are responsible for that person's welfare. — *WE*

Rick Simmons: New VP Sales and Marketing at Benvenue

Rick Simmons is the new person in charge of presenting the "face" of Benvenue Medical, Inc. The company has recently announced that Simmons has joined the company as vice president of sales and marketing. Simmons will use his 30+ years of experience in medical devices and spine to grow the Luna product line.

Simmons will work with the Luna 360 Interbody Fusion System, a minimally invasive lumbar interbody fusion device for degenerative disc disease (DDD) that received clearance from the FDA in November 2014.

Benvenue Medical, Inc.

"Rick brings a unique blend of sales and marketing leadership, combined with a technical and analytic mindset," said Robert Weigle, Benvenue CEO in the January 7, 2015 news release. "His wealth of spine expertise and his leadership skills will no doubt help us excel as we introduce the Luna 360 System to the U.S. market."

"Previously, Simmons served as president of g2m MedTech Advisors, a corporate consulting firm specializing in emerging technology platforms with a specialization in spine, surgical sports medicine and orthobiologic devices. There, Simmons led strategic planning, guidance go-to-market and commercialization strategies for both Fortune 100 and early stage venture funded companies. Prior to founding g2m MedTech Advisors, Simmons was vice president and general manager of Advanced Technologies, including leading marketing and sales of TranS1, Inc., from its founding through its IPO. He also held commercial leadership roles at NuVasive and Innovasive Devices. Earlier in his career, Simmons served as director of marketing, managed care and business development at Genzyme Tissue Repair, Inc., and held various U.S. and International sales and marketing management positions with Acufex Microsurgical, Inc. He holds a bachelor of arts in kinesiology from California State University, Northridge."

Simmons told *OTW*, "My primary focus is making the Luna 360 Expandable Interbody Fusion System, which was cleared by the FDA in November, available to patients and surgeons. This includes building a presence and awareness for a feature-rich Luna 360 implant that addresses the current limitations of expandable devices used in MIS posterior approaches, including a staged commercialization and ramp up in the second half of the year." — *EH*

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