05 Stem Cell Summit Preview ♦ Five years ago, few people realized that stem cell commercialization was imminent. Today five stem cell branded products are on the market and several more are coming fast. What a difference five years makes. Here’s our preview of the New York Stem Cell Summit on February 16th.

09 Learning the Lab: Research Mentorship – Part One ♦ We follow Dr. Jonathan Barnwell, an orthopedic resident at Wake Forest University, as he works with a research mentor. Dr. Barnwell is the recipient of a 2009 Resident Clinician Scientist Training Grant from OREF.

13 NASS Defends XLIF ♦ NASS jumped into the XLIF reimbursement fray by telling insurance carriers that the procedure was not experimental or investigational. As in the vertebroplasty situation, the Society defended its position as the authoritative voice for defining high quality, evidence-based spine care. Read their rationale here.

28 Dr. Thomas Grogan ♦ A “country doctor” who provides approximately 15% of his care at no cost, Dr. Thomas Grogan, a pediatric orthopedist in Santa Monica and a member of the clinical faculty at UCLA, is also a practice management expert.
Don’t Waste Your Money on Market Forecasts. Buy what you need – not what you don’t!

Is that anterior cervical fusion procedure forecast buried in a massive $6,000 spine market report? When all you need is a cruciate ligament repair market analysis or a rotator cuff repair procedure forecast—why pay 6 times more than you have to?

For $950 you get what you need—not what you don’t. Get complete and detailed forecast and analysis of the specific surgical indications. No other market intelligence company has more detailed or accurate market forecasts. PearlDiver’s data guys have built the largest database of patient records (private payer and Medicare) in the United States.

Each report details the U.S. procedure volumes and forecasts to 2013, reimbursement rates, associated procedures, private payer AND Medicare data, patient demographics, regional charging data, state charging data, associated diagnosis, state reimbursement data and comorbidities for each of the following specific surgical indications. Get what you want—not what you don’t. Just $950.

Call Heather at 260-469-4161 or email one of the data guys at www.pearldiverinc.com.
Orthopedic Power Rankings
Robin Young’s Entirely Subjective Ordering of Public Orthopedic Companies

This Week: The Golden January Effect is ending. Small cap companies like Exactech, CONMED and Wright Medical had a most excellent 30-day run. Now check out Symmetry! Up six spots to #4. SMA starts the new year with a restructuring and cost reduction program. At barely $8/share, this is a positive development.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Last Week</th>
<th>Company</th>
<th>TTM Op Margin</th>
<th>30-Day Price Change</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>Integra LifeSciences</td>
<td>15.37%</td>
<td>14.50%</td>
<td>JP Morgan upgrades IART and puts a $46 price target—18% above today’s prices.</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>Medtronic</td>
<td>31.09</td>
<td>7.98</td>
<td>3rd lowest P/E. 2nd lowest future P/E. 31% operating margin belies Wall Street’s consensus of declining sales growth rates.</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>Stryker</td>
<td>23.50</td>
<td>8.07</td>
<td>Large cap ortho benefiting from rising sales growth expectations in 2010. SYK also upgraded by analysts.</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>Exactech</td>
<td>12.61</td>
<td>16.09</td>
<td>Small cap January Effect certainly lifted EXAC. Valuation is low, but attention will, we think, be moving to large cap.</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td>CONMED</td>
<td>6.92</td>
<td>7.83</td>
<td>CNMD has significant operating leverage. If sales rebound, profit margins pop. Equity buyers looking for signs of upswing.</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>Wright Medical</td>
<td>6.61</td>
<td>8.26</td>
<td>Lowest operating margin on the power rankings. Downgraded by JP Morgan. Still, a phenomenal niche products.</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>Smith &amp; Nephew</td>
<td>22.42</td>
<td>4.08</td>
<td>Downgraded by Piper. Key for SNN is to get operating margins up 200-300 basis points.</td>
</tr>
<tr>
<td>10</td>
<td>8</td>
<td>Johnson &amp; Johnson</td>
<td>26.94</td>
<td>(0.06)</td>
<td>JNJ’s being characterized as the defensive stock to own should the “double dip” recession materialize. Yawn.</td>
</tr>
</tbody>
</table>
# Robin Young’s Orthopedic Universe

## Top Performers Last 30 Days

<table>
<thead>
<tr>
<th>Company</th>
<th>Symbol</th>
<th>Price</th>
<th>Mkt Cap</th>
<th>30-Day Chg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capstone Therapeutics</td>
<td>CAPS</td>
<td>$0.90</td>
<td>$37</td>
<td>45.2%</td>
</tr>
<tr>
<td>Mako Surgical</td>
<td>MAKO</td>
<td>$12.67</td>
<td>$421</td>
<td>27.6%</td>
</tr>
<tr>
<td>Symmetry Medical</td>
<td>SMA</td>
<td>$8.85</td>
<td>$317</td>
<td>19.6%</td>
</tr>
<tr>
<td>Exatech</td>
<td>EXAC</td>
<td>$18.47</td>
<td>$236</td>
<td>16.1%</td>
</tr>
<tr>
<td>Integra LifeSciences</td>
<td>IART</td>
<td>$38.92</td>
<td>$1,110</td>
<td>14.5%</td>
</tr>
<tr>
<td>Osteotech</td>
<td>OSTE</td>
<td>$3.14</td>
<td>$57</td>
<td>11.3%</td>
</tr>
<tr>
<td>Kensey Nash</td>
<td>KNSY</td>
<td>$25.54</td>
<td>$283</td>
<td>9.8%</td>
</tr>
<tr>
<td>Wright Medical</td>
<td>WMGI</td>
<td>$19.14</td>
<td>$739</td>
<td>8.3%</td>
</tr>
<tr>
<td>Stryker</td>
<td>SYK</td>
<td>$55.42</td>
<td>$22,040</td>
<td>8.1%</td>
</tr>
<tr>
<td>Medtronic</td>
<td>MDT</td>
<td>$45.99</td>
<td>$50,800</td>
<td>8.0%</td>
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</table>

## Worst Performers Last 30 Days

<table>
<thead>
<tr>
<th>Company</th>
<th>Symbol</th>
<th>Price</th>
<th>Mkt Cap</th>
<th>30-Day Chg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regen Biologics</td>
<td>RGBO.OB</td>
<td>$0.20</td>
<td>$1</td>
<td>-35.5%</td>
</tr>
<tr>
<td>TiGenix</td>
<td>TIG.BR</td>
<td>$5.40</td>
<td>$133</td>
<td>-13.4%</td>
</tr>
<tr>
<td>Orthovita</td>
<td>VITA</td>
<td>$3.45</td>
<td>$264</td>
<td>-7.0%</td>
</tr>
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<td>RTI Biologics Inc</td>
<td>RTIX</td>
<td>$3.64</td>
<td>$198</td>
<td>-4.7%</td>
</tr>
<tr>
<td>Synthes</td>
<td>SYSTVX</td>
<td>$129.97</td>
<td>15,424</td>
<td>-2.1%</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>JNJ</td>
<td>$64.21</td>
<td>$177,160</td>
<td>-0.1%</td>
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<tr>
<td>Orthofx</td>
<td>OFIX</td>
<td>$31.46</td>
<td>$539</td>
<td>1.4%</td>
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<tr>
<td>Average</td>
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<td>$1,177,97</td>
<td>2.2%</td>
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<tr>
<td>CryoLife</td>
<td>CRY</td>
<td>$6.46</td>
<td>$184</td>
<td>3.2%</td>
</tr>
<tr>
<td>Business &amp; Smith &amp; Nephew</td>
<td>SNN</td>
<td>$50.75</td>
<td>$8,960</td>
<td>4.1%</td>
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## Lowest Price / Earnings Ratio (TTM)

<table>
<thead>
<tr>
<th>Company</th>
<th>Symbol</th>
<th>Price</th>
<th>Mkt Cap</th>
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<td>Symmetry Medical</td>
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<td>8.72</td>
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<tr>
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<td>Medtronic</td>
<td>MDT</td>
<td>$45.99</td>
<td>$50,800</td>
<td>14.44</td>
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## Lowest P/E to Growth Ratio (Earnings Estimates)

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<th>Mkt Cap</th>
<th>PEG</th>
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<td>$6.46</td>
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<td>Stryker</td>
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<td>$55.42</td>
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<td>Exactech</td>
<td>EXAC</td>
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<td>1.22</td>
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## Lowest Price to Sales Ratio (TTM)

<table>
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<th>Symbol</th>
<th>Price</th>
<th>Mkt Cap</th>
<th>PSR</th>
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<tbody>
<tr>
<td>Osteotech</td>
<td>OSTE</td>
<td>$3.14</td>
<td>$57</td>
<td>0.58</td>
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<tr>
<td>Symmetry Medical</td>
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<td>$8.85</td>
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<td>0.78</td>
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<td>1.25</td>
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## Highest Price / Earnings Ratio (TTM)

<table>
<thead>
<tr>
<th>Company</th>
<th>Symbol</th>
<th>Price</th>
<th>Mkt Cap</th>
<th>P/E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith &amp; Nephew</td>
<td>SNN</td>
<td>$50.75</td>
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<td>28.27</td>
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<tr>
<td>CONMED</td>
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## Highest P/E to Growth Ratio (Earnings Estimates)

<table>
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<th>Symbol</th>
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<th>Mkt Cap</th>
<th>PEG</th>
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<tr>
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<td>$1,180</td>
<td>2.99</td>
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<tr>
<td>Zimmer Holdings</td>
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<td>$13,200</td>
<td>1.91</td>
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<tr>
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<td>$64.21</td>
<td>$177,160</td>
<td>1.86</td>
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<tr>
<td>Average</td>
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<td>1.70</td>
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## Highest Price to Sales Ratio (TTM)

<table>
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<th>Price</th>
<th>Mkt Cap</th>
<th>PSR</th>
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<td>TiGenix</td>
<td>TIG.BR</td>
<td>$5.40</td>
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<td>$421</td>
<td>14.16</td>
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<td>NuVasive</td>
<td>NUVA</td>
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<td>$1,180</td>
<td>3.55</td>
</tr>
<tr>
<td>Kensey Nash</td>
<td>KNSY</td>
<td>$25.54</td>
<td>$283</td>
<td>3.48</td>
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Stem Cell Summit Preview
By Robin Young

Five years ago, the prevailing wisdom was that stem cell therapies were at least a decade away from commercialization. Embryonic stem cells, according to media reports, were the predominant form of stem cells. Finally, five years ago we held the first Stem Cell Summit—in a small hotel near Chicago’s O’Hare airport.

At that first meeting we said that stem cell commercialization was imminent and that sales within five years would reach $100 million. Today, five stem cell branded products are on the market, sales this year will likely exceed our estimates from five years ago and, we estimate, one in ten surgeons in the United States has started employing stem cells therapeutically. At this pace, by 2015, virtually every surgeon in the United States will be incorporating stem cells in either autologous, allograft or cultured forms into their practices.

What a difference five years makes.

RRY Publications’ Stem Cell Summit in New York has found a home in the historic South Seaport section of Manhattan. South Seaport is where Fulton Street and South Street dock and cobblestone streets take visitors back to an earlier time. For the fifth annual New York Stem Cell Summit, entrepreneurs from Europe, Israel, Latin America, Asia, and the U.S. are finalizing their PowerPoint presentations, six key scientific leaders will bring all attendees up to date on the science and as many as six NEW stem cell products will be introduced.

This year’s meeting will have more attendees, more presentations and cooler give-aways than last year (Hint: the pens are multi-functional). It is still one full, total-immersion day with, as was the case last year, outstanding networking opportunities during lunch and the breaks.

Five Preview Highlights

Having surveyed the presentations here are five preview highlights although, as we learned last year, there are still plenty of surprises expected from the podium.

• **Spine Disc Rehydration** – Rehydrating the spine nucleus with stem cells, with or without bone morphogenic proteins, has been bouncing around the periphery of stem cell science for a decade or longer. A single study in 2009 changed all that. Degradation of the spine disc from either acute or chronic disc injury and/or degeneration is the basis for most of today’s spinal implant sales. If physicians could rehydrate a degenerated disc reliably with stem cell injections it could transform the business of selling spinal fusion implants and instruments. But the nucleus is not a benign environment. Could stem cells survive the ph levels, the compressive and stress forces or avascular nature of the nucleus? Early in 2009 data emerged from a small canine study...
that adipose stem cells in a hyaluronic cocktail could rehydrate the disc to near normal levels. Then on September 10th, a stronger study was presented at the Osteoarthritis Research Society International meeting in Montreal. The sheep study used a single, direct low-dose injection of allogeneic or “off-the-shelf” adult stem cells into the degenerated disc nucleus. At the six-month follow up, discs that were initially severely damaged and degenerated had regenerated and “become indistinguishable from healthy non-degenerated discs in their histopathology, cartilage content, height, and structure” (quote from the study’s principal investigator and one of the Stem Cell Summit’s presenters). The control group of severely degenerated discs was either not injected or was injected with hyaluronic acid. The control group had significantly lower disc height ($P < 0.01$), disordered disc structure ($P < 0.01$), disrupted histopathology ($P < 0.01$), and reduced cartilage content ($P < 0.05$) at the end of six months.

**Clinical Study Set-Backs** – Not all news in 2009 was good news. In August, the company that had received the first FDA approval for an embryonic stem cell trial announced that its IND for a study of its cell therapy for sub acute spinal cord injury had been stopped. Geron announced last August that its clinical study of GRNOPC1 in patients with spinal cord injuries was placed on hold by the FDA. With respect to embryonic stem cell commercialization, the future keeps stretching out into a vaguely defined future. Osiris, which started 2009 as the market leader in both market value and FDA approved cultured stem cells in the market, reported TWO clinical study setbacks. On June 23rd, the Osiris company reported that chronic obstructive pulmonary disease patients receiving Prochymal, the company’s formulation of adult stem cells, did not have significantly improved pulmonary function. The patients DID experience decreased systemic inflammation and Prochymal was shown, again, to be safe. But… no improved pulmonary function.

Then, three months earlier, Osiris stopped enrollment in its study of Prochymal for patients with Crohn’s disease. Turns out there was a design flaw in the study. Patients were asked how they felt. If they answered a particular way, they got long-term Prochymal treatment. Even though the study was double-blinded, it administered Prochymal in two phases. So patients and their physicians who participated in the first phase of the study could figure out who had Prochymal and who did not. At the end of the first treatment phase, all of the patients were asked, “How do you feel?” By answering a certain way, the patients could ensure enrollment in the long-term Prochymal treatment arm. So, many patients in the study used the magic words to get into the long-term treatment arm. Opps. The good news is that Prochymal is safe and a powerful anti-inflammatory treatment. Slam dunk works. Ten million patients a year can use this drug. Right now. But getting this product to market is proving to be a real puzzle in the United States. Osiris CEO Randall Mill’s presentation at the New York Stem Cell Summit will certainly be one of the most anticipated presentations.

**New Allograft Stem Cell Products** – Stem cells from human allograft placental material? Pluristem, the Israeli company developing
adult stem cell products from placental material is one of the most innovative new stem cell companies in years. Bill Prather, VP Corporate Development will make the presentation on behalf of Pluristem. Then two of the leading allograft processing companies—MTF Foundation and AlloSource—earlier announced innovative new allograft based stem cell products and we will hear about at least one of those from the podium at the Summit. Through its distribution partner

Orthofix, MTF announced that it had developed a second generation allograft stem cell product called Trinity Evolution (TE). Like the original Trinity, TE is an allograft bone matrix with concentrated progenitor MSCs derived from cadaveric donors. AlloSource, the rapidly growing and large allograft processor based in Colorado, has formed a distribution partnership with NuVasive for the original allograft stem cell product, Osteocel. We expect to hear many comments regarding the coming evolution of allograft stem cell products.

• Cosmetic Stem Cell Applications – Five companies representing a wide range of cosmetic applications of stem cells will be presenting. Where will commercialization of stem cells likely go next? The really big markets and, therefore, development capital may well be in plastic surgery and cosmetic applications. One of the highlights will certainly be Dr. Angela Christiano’s review of her work with hair follicle stem cells. Dr. Christiano, who is Professor of Dermatology and Director of Research at Columbia University, gave one of the most compelling presentations NOT heard at last year’s New York Stem Cell Summit. Her presentation regarding the rich stem cell environment in hair follicles came the day after the Summit at the Columbia University stem cell symposia we attended. But leaders in the race to commercialization are among the following strong presenters. For dermal regenerative therapies the leaders are Garnet BioTherapeutics and Histogen. For breast reconstruction and aesthetic body contouring Cytori Therapeutics will present both a facilitating technology and the science of using adipose tissues with their rich stem cell component to address these very, very large markets.

• Cardiovascular Stem Cell Wins – It may not receive quite as much attention, but the gains
in cardiovascular stem cells keep piling up. For years, literally, we have been collecting patient stories regarding the use of autologous stem cells to treat various forms of heart disease. Typically, these are patients who are nearing the end stages of their disease and the heart muscle is progressively deteriorating. Several strong studies have been released over the years that describe exactly why the anecdotal information is what it is. In 2009, the Proceedings of the National Academy of Sciences waded in and published a study from Brigham and Women’s Hospital that stated unequivocally that mesenchymal stem cells (MSCs) exhibit vascular smooth muscle and endothelial cell differentiation, contribute to large and small vessel formation, reduce infarct size and increase ejection fraction. To quote directly from the study’s conclusions; “Importantly, MSC engraftment correlated with functional recovery in contractility (R = 0.85, P < 0.05) and MBF (R = 0.76, P < 0.01). Together these findings demonstrate long-term MSC survival, engraftment, and trilineage differentiation following transplantation into chronically scarred myocardium.” From the podium at this year’s New York Stem Cell Summit, we will hear from five companies about their latest successes treating heart disease with autologous, cultured and, perhaps, allograft stem cells.

The New York Stem Cell Summit will start promptly at 8:00am on February 16th at the Bridgewater’s facility at the South Seaport. We hope to see you all there.
Learning the Lab: Research Mentorship – Part One
By Elizabeth Hofheinz, M.P.H., M.Ed.

The scientific method is clear-cut and the path of a researcher is well established...as is the path to becoming a physician. But for most orthopedists, those trails don't converge. For the aspiring clinician scientist, finding his or her way onto the research path—while retaining the life of a clinician—can be daunting. Fortunately, there is help.

Finding the Right Mentor

One physician entering the world of the clinician scientist is Dr. Jonathan Barnwell, an orthopedic resident at Wake Forest University School of Medicine. A recipient of a 2009 Resident Clinician Scientist Training Grant from the Orthopaedic Research and Education Foundation, Dr. Barnwell is pursuing research on nerve regeneration under the mentorship of Zhongyu Li, M.D., Ph.D., Assistant Professor of Orthopaedic Surgery at Wake Forest University School of Medicine.

Dr. Barnwell: “When I arrived at Wake Forest in 2008, I was rather green in the research arena. Like many orthopedists, I had done a summer research project in which I was given a task, completed it, and that was it. There was no follow-up or real understanding of how it fit into the larger picture. I was dissatisfied with only having this ‘snapshot,’ and was seeking detailed knowledge about how to take a project from design to analysis to manuscript preparation.”

Enter Dr. Li, a recipient of an OREF Career Development Award in 2006. Dr. Barnwell says, “From the outset Dr. Li’s inquisitiveness and enthusiasm made it clear that he was committed to my development as a physician scientist. He had mentored people in the past, and knew that the process required ongoing communication on both sides. At his suggestion, we meet once a week to discuss the status of grants and manuscripts, something that encourages me to stay organized as there is always an upcoming progress report or submission deadline.”

You want a mentor, says Dr. Barnwell, who is inherently excited by the research process, and revels in passing on his or her skills to the next generation of clinician scientists.

“It is clear that Dr. Li is engaged in research for reasons more than accumulating grants and scientific articles; he has a persistent energy surrounding research questions, emails me related materials throughout the week, and is always open to my ideas. He loves the process.”

Tycho Brahe in his laboratory/commons.wikimedia

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This is a case where “been there, done that” is a positive thing. Dr. Barnwell advises, “You should select a mentor who has gone through the research study process many times—you’ll feel much more comfortable taking his or her advice. Additionally, ensure that your mentor is not just interested in the hot topic of the moment, and that this person will pursue the project in a disciplined, methodical manner. The last thing you want is someone who will throw up their hands in frustration if you’re encountering obstacles. Lastly, look for a mentor who understands not just the big picture, but who has solid knowledge of all of the key components, reads the literature and will go to the mat with you if there is a problem.”

**Building a Two-Person Team**

A mentor can sort of be a backboard with a brain. “Dr. Li lets me bounce ideas off of him, and then gives advice along the lines of, ‘This is a good idea, but go this route instead to capture what you want to look at.’ He helps me veer away from dead ends. For example, I wanted to test the use of a keratin-based biomaterial derived from hair as a treatment for peripheral nerve injury. However, I was having a dilemma with narrowing down the most appropriate measures to assess the true effect of this material on nerve regeneration. Dr. Li said that while it may be valuable to examine the spinal cord as well, it had already been shown that motor neuron survival did not play a major role in what we were studying. Instead, he helped me hone in on the outcome measures that were most indicative of successful regeneration.”

“His input made me confront and reformulate my hypothesis. It’s one thing to say, ‘This growth factor promotes nerve regeneration,’ and another to be forced to think about how the process is going to occur.”

Providing a bit of background, Dr. Barnwell notes, “We had three goals in our animal study: first, examine nerve regeneration using a growth factor (glial derived neurotrophic factor in combination with the keratin based hydrogel). Specifically, we set out to learn if the factor stayed in or released in the first couple of days. Secondly, we wanted to know how the growth factor and biomaterial cause individual cells to behave (do they migrate more, grow more, etc.). Lastly, we wanted to look at how the animal recovered, and what kind of functional regeneration it would have.”

Dr. Barnwell had ideas... Dr. Li had other ideas. “I was headed in the direction of counting axons and taking histologic measures, but Dr. Li pushed me to do something more functional. He wanted me to pinpoint exactly how what we were doing was affecting the animal, i.e., ‘Is it making a difference?’ and ‘Is the animal able to recover?’ He sent me in a more practical direction, and had me think about the concrete details of the end result I was trying to achieve.”

And if their paths diverge greatly? “Our opinions are not always in sync, of course. For example, when we were looking at ways to analyze cells in culture, we initially didn’t see eye to eye. But Dr. Li understood that I had more recent experience with cell cultures, and let me take the lead in this area. In the end, the science wins. If I approach him with an idea and he is hesitant, that’s one thing; it is much better if I come prepared with evidence, and say, ‘This is what I think and why.’”

**Moving Beyond the Textbook**

In the formal world of research, animal participation injects a few quirks into the equation. “There are many idiosyncrasies to animal work,” states Dr. Barnwell. “From getting animal protocol approval to the actual behavior of the animal, it can be unusual sometimes. Dr. Li was has been especially helpful in directing me towards techniques with maximum clinical relevance. Although one of the advantages of working with animal models is standardization and reproducibility, there is still room for variability if one proceeds solely from the scientific literature. Having an expert in the field of peripheral...
nerve repair as my scientific mentor has allowed me to quickly address seemingly minor methodologic questions such as how many segments of nerve are clinically appropriate for a proper cable repair, and enabled me to focus on the larger scientific picture.”

That big picture can get quite cloudy if you do not approach it with diligence. “At one point Dr. Li helped me with complicated brachial plexus repairs; it was invaluable to have someone able to come into the lab and work one-on-one with me on the operative microscope. I don’t want to go six months into a study and then realize that I didn’t understand the technical nuances involved (putting too much tension on the nerve, not putting the sutures close enough, etc.). There is no way you can get this type of information from reading a manuscript or a textbook.”

Sometimes the best use of the textbook is to prop up a cage… freeing one to think. “Dr. Li’s dedication extends beyond technical consultations—he is a hands-on mentor whose advanced training in neuroscience means that he grasps many of the limitations of working with animal models and can easily troubleshoot problems. One recent example is a study of the glenohumeral joint deformity that follows brachial plexus birth palsy and the potential role of botulinum toxin as a therapeutic agent. The animal model, a neonatal rat, posed significant technical difficulties due to its size. Dr. Li was completely willing to get involved; he came to the lab and determined which involved muscles were accessible to address this question.”

“This active support helps to instill a sense of confidence in one’s approach and findings. This in turn frees me to think of more creative solutions to difficult problems and not be so bound by the routes others may have taken.”

And what of the freedom from politics? Dr. Barnwell: “I am fortunate to be in an environment that is, for the most part, nurturing of the clinician-scientist. I have yet to encounter a situation where I was influenced to consider certain lines of investigation over others because of reasons beyond the scientific merits. Granted, in scientific research, divergent interests may arise. However, reason most often prevails, and thus, Dr. Li has always encouraged me to make my best case for pursuing questions relevant to our central aim of understanding and enhancing peripheral nerve regeneration. On a related note, he has also been very helpful in directing me to the appropriate administrator. There is no shortage of bureaucracy in academic medical centers and if one is not familiar with the role of certain offices and the necessary protocols, productivity is easily lost.”

Advice for Aspiring Physician-Scientists

When asked about lessons learned, Dr. Barnwell sounds a bit like he’s just emerged from a meditative state. “I have learned—and accepted—that failure is inherent in research. Frankly, a project that proceeds without any surprises or setbacks is often one that did not begin with an interesting question. The critical and often most difficult part is recognizing when and how to pursue alternate routes to answer your original question. Maintaining both persistence and objectivity throughout the course of a project is a skill I will have to hone throughout my career as physician-scientist.”

Proffering a bit of advice to those a step behind him, Dr. Barnwell notes, “The first suggestion I have for next year’s grant recipients is to maintain regular communication with your mentor. When you are the one performing the experiments, there is a tendency to become consumed by managing the day-to-day activities, something that may cause you to lose perspective on where the project is going. Data which I may think is unremarkable may raise important new questions for my mentor.”
“The second tip I would offer is that no matter how enticing potential results may seem, there is a heavy price for skipping steps in the scientific process. I have a great deal of respect for my mentor, and so it is only natural for me to want to show him good work. And while characterization and optimization are not always exciting results to show, they are necessary and ultimately will save the mentor and you a great deal of time and resources.”

The road of research can be long—make sure that the person beside you is the one you want. No speed dating here…take time to find a thoughtful, experienced mentor who best fits your career interests, goals, and expectations.

Stay tuned for a second article later this year on Dr. Barnwell’s experience.
The North American Spine Society (NASS) flexed its surgeon and patient advocacy muscles when it notified five major insurance carriers on January 5 that XLIF and DLIF procedures are not “investigational” and “experimental” and should be covered by the carriers. Major carriers, such as CIGNA have characterized the procedures as investigational and said they would not pay for them.

NASS: THE Authoritative Spine Voice

The Society’s entry into an issue that has reeled the financial markets for the companies manufacturing lateral interbody fusion (LIF) devices sends a powerful message that the Society intends to be the authoritative voice for defining what constitutes high quality, evidence-based, and ethical spine care.

In letters to Aetna, BlueCross BlueShield, WellPoint, CIGNA and United Healthcare, NASS President Ray Baker, M.D., stated that NASS recently became aware that the carriers had proposed or are considering noncoverage/nonpayment of, “a technique of lumbar interbody fusion that utilizes a lateral approach with the use of specialized retractors.”

“While the concept of this technique... is not proprietary, there are two commonly used proprietary retractor systems; XLIF, manufactured by NuVasive and DLIF manufactured by Medtronic.”

NASS’ letter said the investigational and experimental terms, “do not seem to be justified.” While the retractor systems are new in recent years, the letter said “the approach is not novel.”

NuVasive Cheers

NuVasive was happy with the NASS letter.

Pat Miles, NuVasive’s President of the Americas, told OTW,

“The letter by NASS provides a clear position from the definitive authority in spine surgery that lateral interbody fusion is a longstanding technique and recent technology additions to the lateral technique are not sufficiently distinct to merit an investigational label or a new code. CMS (Centers for Medicare and Medicaid Services) has also recently included the newer...
trade names for lateral surgery within the description for anterior interbody fusion and those additions go into effect later this year. This provides clarity that there is not now, nor will there be in the future, a coding concern for lateral spine surgery.”

In a not too subtle manner, the NASS letter reminded the carriers that “in order to provide comment, it is necessary to fully comprehend the technical aspects of LIF.” In a recent conference call with Wall Street analysts, NuVasive CEO Alex Lukianov made the point that insurance carriers do not fully comprehend the procedure.

NASS Conclusions

After laying out arguments why XLIF and DLIF were not investigational and experimental, NASS offered the following conclusions regarding coverage for the procedures:

• Lateral interbody fusion (LIF), in the form of XLIF, DLIF; would be inappropriately characterized as “experimental” or “investigational”

• While additional clinical outcomes data would be helpful for any surgical procedure including LIF; these data are not needed to endorse continued use and coverage of these forms of interbody fusion

• XLIF and DLIF should be coded and reimbursed as an ALIF. The technical execution and surgical principles of LIF are sufficiently analogous to if not a variation of ALIF. It should not be coded as a percutaneous procedure (unlisted CPT code)
• XLIF and DLIF, which are anterior procedures, should not be confused with posterior procedures that have similar sounding names, such as TLIF, PLIF, and GLIF (Trademark, Alphatec)

Coverage and Patient Access

Baker told OTW that NASS entered this debate because the Society felt it was appropriate to defend its previous coding recommendations and to advocate for spine care that allows spine surgeons to offer their patients the best spine procedures and devices available.

It’s not the first time the Society has entered a coverage and payment fray. It made payment recommendations regarding vertebroplasty and kyphoplasty procedures in 2007.

Baker also told OTW that numerous NASS members had contacted the Society and asked it to get involved. “We’re looking out for our members here too,” said Baker.

NASS formed a task force of members without ties to the companies involved in the issue to draft the response to the insurance carriers. He praised Christopher Bono, M.D., Chair of the Society’s Professional Economic and Regulatory Committee for taking a leading role in the drafting of the response.

Standard Method

LIF procedures, according to the NASS letter, “utilize a portal made in the lateral flank through which serial dilators and retractors are placed through the psoas muscle to be seated on the lateral aspects of the disc space
and vertebral bodies. By utilizing a smaller incision than other open surgical techniques that often utilize a posterior or anterior approach, it is appropriately described as an open, minimally invasive operation that is performed under direct visualization (in contrast to a percutaneous procedures which are billed using unlisted CPT codes).

The letter noted, “Open lateral approaches to the upper lumbar spine and thoracic spine are considered a standard method of accessing the discs and vertebral bodies in appropriately indicated cases. Such approaches have been used for the treatment of lumbar degenerative disorders, tumors, fractures, and infections of the spine. The major anatomical distinction between open anterior and lateral approaches is, notwithstanding the size of the incision, dissection being performed anterior or through the psoas muscle. As the psoas muscle is only present in the lumbar spine (L1 to S1), this discussion is most relevant to the lumbar spine.

Variations in how exposure to the lumbar is executed are dictated by surgeon preference and are based on the location of pathology, the patient’s body habitus and the presence or absence of spinal deformity.

“The LIF procedures in question have standardized the approach to direct lateral access that utilizes dissection through the psoas muscle instead of anterior to the muscle,” noted the letter.

No New Code Needed

Prior to the introduction of XLIF and DLIF, a spinal surgeon could have chosen to perform an open procedure using a direct lateral corridor, as is performed in LIF, as part of standard customary practice, including transpsoas approaches. Anterior interbody arthrodesis (thoracic, lumbar, additional level) accurately describes these procedures and as such CPT codes 22556, 22558, and 22585 have been recommended. Regardless of the exact direction of accessing the lumbar spine from L1 to L5, the appropriate code has been that for ALIF. The technical aspects of XLIF and DLIF are not sufficiently distinct from an ALIF to justify another code. NASS has consistently held this position.”

In contrast to LIF procedures, NASS noted that the terms “investigational” or “experimental” used at the time of the introduction of lumbar artificial disc replacement (LADR) was to “the betterment of patient care.” In the case of LADR, the risks, complications, and efficacy were unknown with no analogous procedure from which one could extrapolate results. Thus, randomized trials were needed.

However, NASS’ letter states that a “major distinction must be made between a new procedure such as LADR and a modified approach for a standard, accepted procedure, such as LIF...which is a method of performing an operation that has long been considered standard practice. It is novel only in its use of a smaller incision and a different retractor system. If one were to consider LIF as experimental or investigational, then one would need to conclude that there is only one correct method of performing an anterior lumbar interbody fusion, that
all surgeons access the spine through the exact same tissue planes, and that the disc and vertebral bodies are all accessed in the exact same orientation. Not only is this technically impossible, it is not verifiable.

**Neuro Monitoring and Safety**

“While accessing the lumbar spine by dissection of the psoas muscle has attendant risk, other types of open anterior lumbar surgery also have risk.

“Because the psoas muscle and associated structures are not widely dissected, a neurological monitor is employed… If [the dilators or retractors] are too close, they are repositioned. This is analogous to neurological monitoring that is performed for any other type of spinal surgery. Cadaver studies have shown that there is a safe corridor through which the lumbar spine can be accessed by a direct lateral approach.

“The approach-related nerve complications for LIF are comparable to posterior lumbar fusion procedures.”

**Literature Results**

NASS acknowledges that there is limited data in the literature concerning LIF clinical outcomes. The data that is available primarily reports on early outcomes and approach-related complication.

“Perhaps these two parameters are most pertinent, as there are a multitude of studies regarding the outcomes of lumbar interbody fusion, whether via an anterior or posterior technique. Anand et al. (J Spinal Disord Techn. 2008; 21:459-467) published results from a prospective evaluation of 12 patients who underwent XLIF, in addition to other minimally invasive fusion techniques, for the treatment of degenerative scoliosis. At a mean follow-up of 75.5 days, the VAS pain score improved an average of 2.3 points. Knight et al. (J Spinal Disord Techn. 2009; 22:34-37) retrospectively reviewed results of 58 patients who underwent DLIF or XLIF. Though clinical outcomes were not measured, the group found that blood loss, complication rates, and operative times were comparable between the DLIF and XLIF groups.”

“These parameters were comparable to those in a historical cohort of patients who underwent posterior fusion at the same institution.”

Whether or not insurance carriers will review their coverage decisions for LIF procedures and accept NASS’ position that the procedures are common, safe and effective will be determined over the coming months. What is not in doubt is that NASS will continue to defend its position of remaining the final authoritative medical society advocating for quality spine care.

To read the entire letter from NASS, please click here:

company news

**Brady Shirley: New President, CEO at IMDS**

A management powerhouse has come on board at Innovative Medical Device Solutions (IMDS). The company has announced that Brady R. Shirley, former Senior VP of Stryker Endoscopy and President of Stryker Communications, will be its new President and Chief Executive Officer.

IMDS, which focuses on the orthopedic industry, is known for its comprehensive product development, manufacturing and supply chain management solutions for medical device companies.

Shirley, who has been at Stryker Corporation for the last 17 years in a range of general management, sales and marketing roles, has contributed directly to strong annual revenue growth and innovation in the divisions he served.

Wade Fallin, IMDS’ former President and CEO and continuing board member, said that the IMDS board unanimously selected Shirley based on his track record leading a complex organization, as well as his strong executive and personal qualities.

“Shirley came to our attention because of his strong execution skills, his proven ability to lead top performing teams and his track record in driving shareholder value, particularly through innovation,” said Fallin in the news release.

“Additionally, his straightforward style and exceptional people skills are a perfect fit with the IMDS culture that serves our employees, partners and investors so well.”

In the news release, Shirley stated, “I am excited about the IMDS of today and tomorrow based on the strategic growth of our Product Sourcing capabilities and a continued strengthening of an already best-in-market Co-Innovation business. IMDS is well positioned to be the leading source of innovation for our strategic OEM partners and we will deliver on that promise. “

Regarding the strategic growth, Shirley told OTW, “In other words, instead of simply acquiring companies to expand IMDS, we are uniquely positioned to grow by combining our world class product development capabilities with key innovative manufacturing capabilities to provide a strategic sourcing partner for our customers. We can provide turn key solutions from idea to launch in less than 12 months vs. the typical 30 month cycle. We are positioned to grow revenue 25% to 30%+ per year over the next few years based on our unique strategic sourcing capability.”

“Brady Shirley’s selection as President and CEO positions IMDS for our next phase of major growth. Brady's medical device experience, energy, and customer focus will provide both our customers and stakeholders with exceptional value,” said Harold Linville, IMDS Chairman of the Board, in the news release.

When asked about personal experiences that helped prepare him for this new role, Shirley commented to OTW, “While running Sales & Marketing for Stryker Endoscopy for the last 10 years I have had the opportunity to lead innovative product development across the orthopedic space as well as many other specialties...in doing so, I have many, many relationships with key opinion leaders as well as leaders within the orthopedic companies. From a pure leadership perspective, I helped grow one of Stryker’s largest divisions while pioneering a startup and growing it into a division. This ‘mix’ will provide experience to integrate our four service areas and lead a very good company on its way to being great.”

—EH (January 4, 2010)
Anika Regenerates with Italian Acquisition

Anika Therapeutics has acquired the Abano Terme Italian-based hyaluronic acid biopolymer firm, Fidia Advanced Biopolymers, s.r.l., (FAB) for $34 million.

FAB provides hyaluronic acid-based (HA) products for the regeneration of connective and structural tissues damaged by injuries, aging or degenerative diseases. Anika also announced that it will develop its own direct U.S. sales capability to capture “significantly higher margins, from the domestic sales of Monovisc, its single-injection osteoarthritis treatment. Direct commercialization activities will also include the portfolio of FAB orthopedic products once approvals are achieved in the United States.

Anika purchased FAB in exchange for $17.1 million in cash and 1.981 million shares of its common stock. FAB, with 50 employees, had approximately $11.1 million in annual sales last year.

Fibers, Films and Textiles

The Anika announcement on December 24 said FAB’s patented technology for modifying HA to produce fibers, films and textile biomaterials is used in a variety of medical device applications. FAB also pioneered the development of tissue engineered products for cartilage regeneration and treatment of burns and diabetic ulcers in Europe.

Anika’s President and CEO, Charles Sherwood, Ph.D., said, “FAB provides Anika with an exciting new growth platform and advances our vision to offer therapeutic products that go beyond pain relief to protect and restore damaged tissue. FAB’s complementary regenerative technology allows us to expand Anika’s commercial product portfolio and development pipeline with innovative joint health and other therapeutic products.”

FDA Approval Sought

The company filed the final module of its Monovisc PMA to the FDA on December 24, 2009, and expects to receive FDA approval in the second half of 2010.

Anika’s products include Orthovisc, a treatment for osteoarthritis of the knee available internationally and marketed in the U.S. by DePuy Mitek; Hyv visc, a treatment for equine osteoarthritis marketed in the U.S. by Boehringer Ingelheim Vetmedica, Inc.; the Elevess, Elevess Light, and Hydrelle family of aesthetic dermatology products for facial wrinkles, scar remediation and lip augmentation; Amvisc, Amvisc Plus, Staarvisc-II and Shellgel injectable viscoelastic HA products for ophthalmic surgery; Incert, an HA-based anti-adhesive for surgical applications; Orthovisc mini a treatment for osteoarthritis targeting small joints and available in Europe; and Monovisc, a single-injection osteoarthritis product based on Anika’s proprietary cross-linking technology and available in Europe, Turkey, and Canada.

—WE (January 5, 2010)
BioMimetic, Novartis Strengthen Relationship

Three more years to stimulate cellular and corporate growth… BioMimetic Therapeutics, Inc. has announced the alteration and extension of its manufacturing and supply agreement with Novartis Vaccines and Diagnostics, Inc. for the supply of bulk rhPDGF-BB (platelet derived growth factor) to BioMimetic. The agreement laid out a strengthened mutual exclusivity commitment whereby Novartis will manufacture rhPDGF-BB exclusively for BioMimetic for therapeutic applications covering bone, cartilage, tendon and ligaments.

The contract was extended by three years with successive three-year evergreen extension periods. In the event that Novartis terminates the agreement, or if BioMimetic terminates the agreement for cause, Novartis is required to support technology transfer by providing to a new manufacturer all Novartis technology and supporting documentation necessary to produce bulk rhPDGF-BB and to supply BioMimetic sufficient bulk rhPDGF-BB to fulfill its needs during the technology transfer process. In addition, the companies reduced certain minimum purchase obligations through 2011, by which time the parties anticipate that BioMimetic’s Augment will be FDA approved for orthopedic applications.

“Novartis has been an excellent partner in the supply of our bulk rhPDGF-BB, enabling the successful approval and product launch of our first regenerative product, GEM 21S, and more recently, facilitating our orthopedic development programs for Augment and Augment Injectable,” said Dr. Samuel Lynch, President and CEO of BioMimetic Therapeutics, in the news release. “The conclusion of this amended agreement reaffirms and strengthens the ongoing relationship between our two companies for the future. Our exclusive agreement covering bone, cartilage, tendon and ligaments, combined with our own patent portfolio further raises the already high barrier to entry for development and commercialization of rhPDGF-BB within the orthopedic space.”
with tissue specific matrices in all of its products and product candidates to promote tissue healing and regeneration, including Augment and Augment Injectable. Subsequently, Novartis acquired Chiron and assumed the rights and responsibilities under the original agreement. The companies amended and restated the agreement to better define their respective obligations.”

—EH (January 7, 2010)

Limits to Industry Ties in Boston

New rules of engagement between physicians and industry have kicked in at Harvard-affiliated Massachusetts General and Brigham & Women’s hospitals in Boston. The hospitals are owned by Partners HealthCare.

No More Stocks and Speaker Fees

Senior physicians will no longer be allowed to accept payment in the form of stock or stock options when they serve as directors on corporate boards of medical device or pharmaceutical companies. They may be paid up to $5,000 per day as corporate directors.

The physicians will also not be allowed to moonlight as paid speakers for companies. These so-called “speaker’s bureaus” have become a mainstay of marketing by drugmakers and device makers in recent years where the content of the talks may be scripted and controlled by the companies.

These hospitals are not the only teaching hospitals that have put in tough new rules for industry engagement. Johns Hopkins tightened its conflict-of-interest policy last year, and Stanford, Northwestern, and the Cleveland Clinic all said they’d start disclosing which of their physicians had financial ties to drug and device companies.

However, according to executives at Partners HealthCare, their new policy goes further than any other academic medical centers.

The new policy will impact roughly 25 vice presidents, clinical department heads, and other top executives. Some physicians had been receiving more than $200,000 a year as corporate board members. Stock and options were banned because they tie the director’s compensation to company profits.

Only a Start

“We’re the first to go in this deep, and we’re still into it only up to our knees,” Dr. Eugene Braunwald, a Harvard professor and former Partners chief academic officer who was chairman of the policy-writing group, told The New York Times. He said the group had “a very spirited debate” before announcing its compromise in general terms in April, much of it effective in 2010.

In April 2009, Partners HealthCare banned sales reps from its halls and barred its physicians from accepting paid speaking engagements and from receiving gifts, entertainment, or food from medical device and drug companies.
“In all fairness,” Braunwald told The Times, “what was OK three years ago is not OK now.”

—WE (January 6, 2010)

In OA...Separate Osteoclasts, Blasts

Uncoupling a bony puzzle... Researchers from Australia have set about separating bone creation and bone destruction in people with osteoporosis. Natalie Sims, Ph.D., Co-Head of the Bone Cell Biology and Disease Unit at St. Vincent’s Institute (SVI), Melbourne, along with her team, has now identified one way to do this in mice.

In the study, the molecule oncostatin M (OSM) was found to induce distinct functions in mice upon binding to two different cell surface proteins. When OSM bound OSMR it stimulated the production of cells that destroy bone. Consistent with this, mice lacking OSMR were found to have increased bone density. However, when OSM bound LIFR (the receptor for leukemia inhibitory factor) it blocked production of a protein that inhibits bone formation. Of note, say the researchers, is that OSM acting via LIFR did not stimulate the production of cells that destroy bone. These data indicate the existence of a pathway by which bone formation can be stimulated independently of bone destruction.

When asked why her team focused on OSM, Dr. Sims told OTW, “Our group has a long-standing interest in the cytokines that act through the gp130 receptor subunit. OSM is part of this family, and has been shown to have important roles in arthritic joint destruction and osteoclast formation.”

Providing details on the structure of the study, Dr. Sims commented to OTW, “We first identified that OSM and both the OSM receptor and the LIF receptor are expressed within the osteoblast lineage, including osteoclasts. This indicated a possible local regulatory role within these cells, which was intriguing. We then found that OSM regulated not only osteoclast differentiation, which has been known for many years, but also that it stimulated osteoblast differentiation and inhibited adipocyte differentiation, and identified relevant genes regulated by OSM, including the osteocyte-specific gene, sclerostin, which is a current therapeutic drug target for osteoporosis. Interestingly, the effects of OSM on these genes is regulated through different receptors—something we discovered by using OSM receptor knockout mice and a LIF receptor antagonist. This is surprising, since it’s been thought for many years that OSM, in the mouse, only acts through the OSM receptor.”

She added, “LIFR is a closely related cytokine also expressed within the osteoblast lineage and in many other cells throughout the body. The fact that mouse OSM signals through LIFR in a different manner to human OSM...”
suggestions that the design of murine OSM mimetics could be a useful therapeutic avenue. We are focusing now on the interactions between murine OSM and the two receptors, and determining the difference between this and the interaction of human OSM with the same receptors, as well as working on understanding the mechanism by which OSM stimulates bone formation.”

—EH (January 6, 2010)

**26 Days Postop? You Should Make It**

Get out the calendar…if you—the hip or knee replacement patient—can make it past the first 26 days postop, you should survive. A new study published in the January 2010 issue of *The Journal of Bone and Joint Surgery* indicates that the risk of early postoperative mortality was slightly increased for the first 26 days after the elective surgery. The risk of mortality was estimated to be 0.1%.

“Previous studies suggesting that increased mortality exists for as long as 60- or 90-days post hip or knee replacement surgery may be wrong,” said lead author of the study, Stein Atle Lie, Ph.D., MSc and professor in the Department of Surgical Sciences at the University of Bergen, Norway, in the news release. Dr. Lie led the study with colleagues from the Department of Orthopaedic Surgery, and the Norwegian Arthroplasty Register at the Haukeland University
large joints

Hospital in Bergen, Norway. He added, “We believe the risk is tied to a much shorter duration.”

Researchers looked at data on 81,856 patients with a total knee replacement and 106,254 patients with a total hip replacement from the Australian Orthopaedic Joint Replacement Registry and the Norwegian Arthroplasty Register. Only patients between 50 and 80 years of age with osteoarthritis were included. The study found the most important risk factors for increased early postoperative mortality were: male gender; and being older than 70 years old.

Regarding the difference between their findings and those of previous studies, Dr. Lie told OTW, “This study was designed to quantify the operation risk and the duration of the operation risk. Furthermore, we separated the mortality into a baseline mortality and the excess postoperative mortality, which has not been done before. The data used in the study covers more than 95% of all operations on osteoarthritis patients performed in Norway and Australia for the time period of the study. In studies based on smaller datasets (e.g., less than 1,000 patients) a small number of deaths can result in a relatively high mortality but with a low precision. Additionally, calculating mortality based on preset cut-points (like 60 or 90 days) gives a false mortality related to the operation, since we find that the operation risk only persists for the first 26 postoperative days.”

“This very low postoperative mortality after hip and knee replacements should be reassuring for patients considering these surgeries,” said co-author Lars B. Engesaeter, M.D., Ph.D. and Head of Norwegian Arthroplasty Register, Haukeland University Hospital in Bergen, Norway, in the news release.

As for what was involved in the mortality, Dr. Lie told OTW, “In this study we had no data on the causes for the mortality, but in a previous study (on a smaller sample of the Norwegian data, Lie et al., Acta Orthop Scand 2002; 73 (4): 392-399) we obtained information on the causes of death from the causes of death registry of Norway. In that study we found that ischemic heart disease and thrombo-embolic complications was most common.”

—EH (January 6, 2010)

COPD Patients Need More Osteoporosis Screening

What with the seriousness of not being able to breathe easily, osteoporosis may have gotten pushed to the back burner in some cases…Danish researchers have found that osteoporosis screening is underused in patients with chronic COPD Patients Need More Osteoporosis Screening

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obstructive pulmonary disease (COPD). Osteoporosis is a common extrapulmonary complication in patients with moderate-to-severe COPD.

The research, published recently in the *Clinical Respiratory Journal*, was undertaken by Hanne Madsen, M.D., Ph.D., of the University of Southern Denmark, Odense, along with colleagues. The team looked at osteoporosis screening, such as the use of dual-energy X-ray absorptiometry (DXA), in COPD patients, and the use of pharmacologic intervention to prevent fractures in COPD patients taking prednisolone. Data on 1909 patients with the respiratory condition who were admitted to hospital in the Danish county of Funen in 2004 were analyzed.

Dr. Madsen told OTW, “First, COPD is related to osteoporosis due to the systemic inflammation in COPD. In osteoporosis, the balance between osteoclast (bone resorption) and osteoblast (bone formation) activity is disturbed. Osteoclast function is regulated by osteoprotegerin, a receptor linked to activation of nuclear factor-κB (RANK), and its ligand (RANK-ligand). T-cells and proinflammatory cytokines, such as tumor necrosis factor (TNF)-α soluble receptor, IL-1, and IL-6, can induce expression of the RANK ligand and enhance bone resorption. Indeed, elevated levels of circulating IL-6 as well as tumor necrosis factor (TNF)-α soluble receptor types I and II have been found in patients with COPD. Thus, the systemic inflammation in COPD may cause osteoporosis, which is characterised by low bone mass and deterioration of bone architecture leading to decreased bone strength and increased risk of fractures. Moreover, many patients with COPD are treated with glucocorticoids that by itself increase the bone loss dramatically and increase the risk of fractures.”

The team found that 55% of patients had filled a prescription for prednisolone (P-COPD patients), and that those who had filled a prescription for prednisolone were more likely to receive DXA scans (17%) than those who had not (9%). COPD patients who had filled a prednisolone prescription were also more likely to be prescribed antiresorptive medicine (27%) than those who had not (16%).

Just over half of the patients in both groups met criteria for osteoporosis; the researchers also found that the groups most likely to undergo DXA scans were women, young people, and those taking high doses of systemic steroids. The researchers also found that the prescription of antiresorptive drugs in COPD patients with a bone mineral T-score of less than -1 was significantly higher in prednisolone-treated patients than in those who were not prescribed the steroid.

Dr. Madsen and her team concluded: “DXA scans are underutilized compared with the high frequency of osteoporosis or osteopenia in DXA-scanned hospitalized COPD patients, especially in the elderly. Guidelines concerning screening, prevention and treatment of osteoporosis in COPD patients with or without glucocorticoid treatment are needed.”

Dr. Madsen told OTW, “Most importantly, I think that there have been no guidelines until now due to the lack of awareness of osteoporosis among COPD patients in general. Nihilism among both prescribers and the patients may play a role. A COPD patient with very low pulmonary function and daily dyspnoea and assumingly high prednisolone prescription would be less motivated to ask for examinations (DXA) and...”
large joints

medicine with a preventive aim. They are likely to focus on the medication to relieve symptoms immediately. Also, prescribers may fail to see the point of focusing on other aspects than the respiratory problems which can be rather severe, when the patient is seeking medical assistance. The chances that guidelines will be developed are good. Currently the Danish Bone Society is working on a proposal for the Danish Medicine Agency to acknowledge that COPD is a disease associated with osteoporosis. Our future work is to spread out this knowledge, as the antiresorptive medication has to be given only for 6-18 months, before it is proven effective as measured by clinical fractures.”

—EH (January 8, 2010)

people

TranS1’s New President/COO: Ken Reali

Ken Reali, former Senior Vice President and General Manager of Smith & Nephew’s Biologics and Spine Business, is TranS1’s new President and COO.

Rick Randall, company CEO made the announcement on January 7.

Randall said Reali’s, “significant experience and proven track record in orthopedics, spine and biologics will be invaluable as we continue to advance beyond our AxiaLIF

minimally invasive approach to lumbar fusion.”

In addition to his tenure at Smith & Nephew, Reali has over 20 years of general management, sales and marketing experience with leading medical device and orthopedic companies. Prior to Smith & Nephew, Reali held positions with Stryker and Biomet.

Reali commented, “I have had a chance to observe TranS1’s products in the market and believe the minimally invasive approach provides surgeons and patients with many unique advantages relative to other lumbar fusion surgeries. I look forward to working with the Trans1 team to continue to expand its market presence in spinal implants.”

One of Realis first tasks will likely be to obtain a category 1 CPT code for the AxiaLIF procedure and working with customers on reimbursement issues.

TranS1 currently markets two single-level fusion products, the AxiaLIF and the AxiaLIF 360, and a two-level fusion product, the AxiaLIF 2L, in the U.S. and Europe. TranS1 was founded in May 2000 and is headquartered in Wilmington, North Carolina.

—WE (January 8, 2010)

Paulsen Returns to Orthopedics

Jeff Paulsen is Zimmer’s new Group President, Global Business. He is the former president of Stryker’s orthopedic reconstructive division.

He will have responsibility for Zimmer Spine, Zimmer Dental, Zimmer Trauma, and Zimmer Orthopaedic Surgical Products and will report to David Dvorak, Zimmer’s President and CEO. This appointment puts him in charge of all of Zimmer’s non-reconstructive product areas. Hips, knees, and extremities will continue to fall under Jeff McCaulley’s direction.

Paulsen was most recently the chief operating officer for MPS Group Inc., a privately held environmental services and facility management firm. He held the Stryker position from 1996 to 2006. He has also held management roles at Ford Motor Company, McDonnell Douglas Corporation, and TriMas Corporation.
A graduate of Michigan State University with a Bachelor of Arts in Marketing, Paulsen also holds an MBA from The Ohio State University.

Said Paulsen,

“There is great promise in the markets where the Global Businesses Group operates, and I look forward to working with the teams in Spine, Trauma, Dental, and OSP to maximize that potential.”

Dave Dvorak echoed Paulsen’s remarks in the announcement: “The markets that these businesses serve are expanding at attractive rates, and we have placed a strategic priority on accelerating our growth in these areas. Jeff has an outstanding record of executive leadership in medical devices, as well as in other industries, and we look forward to his contributions.”

Paulsen is also a former executive board member of Variety FAR Conservatory of Therapeutic and Performing Arts in Birmingham, Michigan. The group is a nonprofit organization that provides creative arts therapy and recreation services for children and adults with mental, physical and/or emotional impairments.

Welcome back to orthopedics Jeff.

—WE (January 8, 2010)

Lower Back Pain—Avoid TENS?

Transcutaneous electrical nerve stimulation (TENS), when used correctly, is a safe, simple and cheap treatment option for pain management. A small device, which can be purchased for under $100, sends a mild electric current through surface electrodes which can help relieve a variety of pains. However, if you are suffering from lower back pain, TENS may not bring much relief at all.

New Guidelines

This news comes from the American Academy of Neurology (AAN) which recently released new guidelines that do not recommend that patients treat their lower back pain with TENS. The new guidelines arose from a literature review of previous clinical trials. The researchers, led by Dr. Richard Dubinsky of the University of Kansas Medical Center in Kansas City and Dr. Janis Miyasaki of Toronto Western Hospital in Toronto, identified five studies that followed TENS treatment for patients with lower back pain. Two Class II studies concluded that TENS provides a modest relief from pain. However, one Class II study and two Class I studies, which all included a sham TENS control group (a mock placebo treatment), concluded that TENS treatment does not effectively manage chronic lower back pain.

The researchers found the Class I studies to be more reliable, and they formed their guidelines based on these previous findings. Although they do not recommend TENS for treating chronic lower back pain, the researchers found that TENS could still be an effective treatment for diabetic neuropathy. The group published their research online on December 30, 2009, in Neurology.

Proponents of TENS Speak Up

Despite these findings, there are still some doctors who question the finality of AAN’s conclusions. In an editorial which accompanies the guidelines, Drs. Andreas Binder and Ralf Baron, neurologists at Christian-Albrechts-Universität Kiel, in Kiel, Germany write, “[A]bsence of evidence is not evidence of absence…Taking the...
favorable benefit-risk ratio when compared with other pain relieving methods into account, TENS remains a valuable part in the armamentarium of pain therapy.”

Drs. Binder and Baron point out that TENS is much safer than opiates and pain medications which carry the risks of abuse and addiction. TENS does not conflict with other medications, and patients can end their treatment at any time.

Charles Cranny, the director of outpatient physical therapy at Rush University Medical Center in Chicago, told Health.com: “We use TENS as a last resort in people with chronic back pain who are not improving with other measures. I say, let's give it a try in these patients. We have had some who swear by it and a lot who say, 'It worked for a couple of weeks, but then I returned it to the vendor.'”

There is one point, however, on which all these doctors can agree: there needs to be more research into TENS. Even though TENS treatment has existed for decades, physicians are still not sure exactly why it works. With further study, researchers may be able to help physicians and patients understand how best to use TENS for certain types of pain. In the meantime, there is little risk in giving TENS a try for managing lower back pain, but patients may want to seek out more reliable alternatives.

—DK (January 8, 2010)
The Picture of Success: Dr. Thomas Grogan

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

Dr. Thomas Grogan, a self-described country doctor, enjoys the continuity of seeing his patients go from jungle gyms to skateboards to college athletics. As a pediatric orthopedist in Santa Monica, California and a member of the clinical faculty at the University of California, Los Angeles, this is no small feat, considering that he has seen over 34,000 new patients during his career spanning the last two decades.

Born in California, Tom Grogan watched as his father changed history. “My dad was an insurance agent during the ’70s, a time of malpractice crisis which saw numerous insurance companies leaving California. My dad developed the concept of a doctors’ co-op where physicians put money into a ‘pot’ in order to pay for malpractice claims. He organized the first physician co-op for malpractice coverage. In a sense, he saved the day for doctors.”

On the Path to Medical School

He took an educational sojourn “back East,” then found an entrée into medicine... via the role of orderly. “After my freshman year at Princeton, I returned to California and was rather directionless. My best friend got me a summer job as an orderly at Stanford, where I met a general surgeon named Bob Jamplis. This gentleman convinced me that medicine was both intellectually challenging and a great way to spend your life. I was sold, returned to Stanford each summer during college, and have always kept in touch with Dr. Jamplis.”

Tom Grogan had an uphill battle with medical school applications, followed by an uphill battle with the weather. “In the ’70s it was particularly difficult to gain entrance to medical school. I applied to 26 programs, and was admitted to three: the University of Cincinnati, Columbia, and the University of Southern California. When I visited the Cincinnati program, I really enjoyed the people and felt that it was a good fit. I had never even seen snow before, however, and was not prepared for the rough winters.”

“Toward the end of medical school I found myself interested in pediatric general surgery, and went to Boston Children’s Hospital for a rotation on this service. The Chief there told me that the best residency programs for pediatric general surgery were the University of Minnesota and the University of California, Los Angeles (UCLA). Into my mind popped visions of snowbanks versus warm beaches... UCLA was a no brainer.”

Becoming a Country Doctor

Dr. Grogan then endured medical school “Survivor” to earn his next career opportunity. “In 1980 I began a general surgery program at UCLA with 25 other interns. When the cutting was over, there were six of us left standing; much to my surprise I was named intern of the year. The Chief of orthopedics then approached me and said, ‘I have an opening for you in orthopedics.’ I jumped at the chance because while rotating through the services I had really enjoyed interacting with the orthopedic surgeons and ‘their’ residents.”

Drawn to working with children in part because of their innocence, along the way Dr. Grogan encountered what you might call the opposite of innocence: hubris. “Learning of my decision, the Chief of general surgery called me and said, ‘You are throwing your life away.’ That’s when I knew that I had made the right choice.”

The “country doctor” explains, “General surgeons must be the smartest in medicine, partially because their work is so metabolically complex. The problem is that because..."
they live in such rarified air, they don’t spend much time with people. On the other hand, pediatric orthopedics is almost like being a general practitioner—you see kids with varying problems. I’ve discovered Lyme disease in one patient, and with another youngster who had taken a fall from the monkey bars, found that he actually had a ruptured spleen. Unlike with general surgery, in orthopedics patients keep coming back—first there are the toddler falls, then the high school soccer issues, then they get their first snowboard…and you get to have a sense of continuity and community.”

Switching to orthopedics would entail flipping a switch in his head…to overdrive. “I had been planning for a certain schedule—finish my general surgery program, do a pediatric general surgery program, join an academic medical center—then all of a sudden I make this shift and must develop a new timeline. And UCLA didn’t have a place for me as a first year orthopedic resident—only as a third year. Suddenly I found myself supervising other residents for things that I didn’t know how to do. I hunkered down, however, and was eventually senior resident for two years and then chief resident for two years.”

A series of fellowships then fully launched Dr. Grogan into his specialty. “I did a sixth month fellowship at Los Angeles Shriners Hospital. That was followed by an NIH fellowship in adult reconstructive surgery at UCLA where I got to see the other side of the age spectrum. While it was interesting to work with older adults, it was tough because they can be hyper-focused on their medical problems. Children are the opposite—they don’t dwell on their problems and all they want is to get back to their lives.”

In 1986 Dr. Grogan headed to Germany for trauma training…and got an education in systems. “I went to Munich on an AO Foundation fellowship, where I experienced quite a different environment in the German trauma hospital. The professors would ponder new devices, say, ‘Eureka!’ and send off instructions to the machine shop. The device would be made promptly and put in the patient. This has its downsides, of course, but in some cases it’s wonderful.”

On his return to Los Angeles, Dr. Grogan found that all of the pieces of the orthopedic pie were in place…save one. “I joined the Shriners faculty, then became Assistant Chief of Orthopedic Surgery, a position that involved clinical research and resident education. The one thing missing was patient interaction. In 1988 I developed a part-time private practice in Santa Monica, which I took full-time in 1992. Since then the majority of my practice—80%—has been working with children. I don’t do as many surgeries as I used to, which allows me to give more time to my patients.”

“Give” being the operative word in many cases. “Six years ago I dropped all insurance plans, something that was frightening at first because I didn’t know if patients would still come. For the first two years, patients ‘fell off’ by 15 to 20%, but then things rectified themselves. At this point I provide about 15% of my care at no cost to patients.

“Orthopedists should realize that our patient base is our greatest asset because you keep seeing them as they get older. They depend on you to teach them to heal and to avoid injuries in the future. When you take care of your community, they take care of you. I have become a country doctor.”

Researching Athletes’ Anatomies

A country doctor who squires in new research. Dr. Grogan, “In one of my recent studies I found that 73%
of wrist fractures in snowboarding accidents occur in the non-dominant hand. This reflects an innate desire to protect the dominant side; it also suggests that our dominant side is slightly stronger, thus less likely to fracture.”

“I’ve been especially interested in determining which players are best suited to which sports and which positions. Athletes can be inclined toward femoral anteversion (neck of the femur leans forward) or retroversion (neck of the femur leans backward). Those in the former category tend to be suited for tennis or sports that involve speed and agility, while those in the latter group are often inclined towards power sports such as snowboarding or pitching. By understanding their natural anatomy, you can predict what sports they should play. In a study involving female soccer players, we plotted hip version against the position played. We found that soccer players tend to play those positions as defined by their natural anatomy. The bottom line is that when you try to push someone into a sport or position that their body isn’t designed for, it’s not a good thing…you can’t make a pitcher into a shortstop.”

**Advice for Fellow Orthopedists**

But you can make a country doctor into a practice management expert. Dr. Grogan, Chair of the 2010 Practice Management symposium for AAOS, notes, “While 25% of orthopedic surgeons are in solo practice, AAOS tends to be largely comprised of academicians and those in large group practices. In the past most orthopedists didn’t have many problems running their practices because we had high revenues. Now there are tremendous economic pressures, with Medicare and insurers cutting back. The typical practice has six or seven employees, and while overhead doesn’t decrease much, if you cut revenues it can dramatically affect salaries.”

Detailing his own experience, Dr. Grogan adds, “In my office every new patient generates $561 of revenue. This means that customer service is critical to our bottom line. Patients want a live person to answer the phone; they want someone to be nice to them, as well as attentive. I have an amazing, empathic woman who runs my front office. Since I’ve hired her, my new patients have increased by 300 per year.”

So they might look forward to seeing her, but whom do they really want to see? The doctor.

“Access is key…even when it is not convenient. Many of my colleagues aren’t interested in being available after hours, but I know my patients hate going to the ER, and if I can, I will be there for them. I am available on Saturday mornings for emergencies, and leave open time for such occurrences during each work day. A lot of doctors feel they are successful if their scheduler says, ‘Sorry, we don’t have any appointments for four weeks.’ But that is not success in the patient’s mind because it isn’t what they want; they want to see you.”

They also want to know how much they will have to pay to see you. “If you call most orthopedic offices, they cannot tell you how much XYZ services cost. My son is actually helping me with a ‘secret shopper’ survey where he calls different offices saying that he has a broken wrist, and inquires how much a visit and cast would cost. Out of the 22 he has called thus far, only two have been able to tell him what it costs. We must be more transparent in this field.”

Not only does he hold himself and his field to certain standards...he has done so with his children. “Along with my wife, a nurse anesthetist, I’ve raised three very responsible children, who are now ages 23, 21, and 19. The eldest graduated from Wesleyan, and...
is now considering medical school. My son is an environmental science major in Chicago, and my youngest daughter is now at Wesleyan. I am a private pilot and have owned three planes in the past—up in the clouds is a great place to clear your head.”

Dr. Thomas Grogan…practicing management excellence.
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