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EndoGastric in $5M DoJ settlement; reports favorable TIF registry data

By Omar Ford, Staff Writer

It's been a whirlwind of a week for **EndoGastric Solutions** (San Mateo, California), a company focused on the endoluminal reconstructive treatment for gastroesophageal reflux disease. On one side of the spectrum, the company reported that it has reached a $5.25 million civil settlement with the U.S. Department of Justice related to allegations that it encouraged providers to submit claims for its transoral fundoplication procedures using incorrect procedure codes, and that its co-marketing program was a potential inducement to purchase its products. On the other side of the spectrum the company reported favorable results from data from its Transoral Incisionless Fundoplication (TIF) registry.

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M&A report finds key forces shaping med-tech deals

By Amanda Pedersen, Senior Staff Writer

Changes in how healthcare is paid for and delivered is impacting the medical device industry in big ways, including M&A activity. **The Walden Group** (Tarrytown, New York), a healthcare investment banking and consulting firm, has identified 10 key forces shaping the med-tech sector in its annual healthcare M&A report. The firm analyzed several hundred transactions for 2013 to identify the 10 key forces that it says are driving healthcare innovation and deal-making.

During an interview with *Medical Device Daily* to discuss the 2013 Annual Strategic Healthcare M&A Report, Richard Cohen, president of The Walden Group, noted that the past few years have been marked by significant uncertainty concerning the

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INTERNATIONAL STROKE CONFERENCE

Ischemic stroke devices offer hope amidst more failed clinical trials

By Larry Haimovitch, Contributing Writer

SAN DIEGO — The French say that "plus ca change, plus c'est la meme chose" which translates to "the more it changes, the more it is the same." This may be the best way to characterize the seemingly unending disappointing progress that is endemic in the world of stroke.

After attending this year's International Stroke Conference, which is sponsored by the **American Stroke Association** (ASA; Dallas) this expression seems to be especially apt, with several more failed clinical trials. Indeed, this statement could have been said for each of the past several stroke meetings with failed

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WASHINGTON ROUNDUP

FDA warns Baxter for Infusor, Intermate pumps at Irvine plant

By Mark McCarty, Washington Editor

For the second time in as many weeks, FDA posted a warning letter to **Baxter Healthcare** (Deerfield, Illinois), this time for the company's operations in Irvine, California, where the firm manufactures a pair of elastomeric infusion pumps. The Dec. 19, 2013 warning letter addresses an inspection that ran from December 2012 to June 2013, the end of which roughly coincided with a recall of one of the pumps. The agency did not directly address the possibility of a recall, but FDA announced in July 2013 a recall of the Infusor and Folfusor lines of pumps for leakage associated with Luer locks.

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INSIDE

AGREEMENTS/CONTRACTS

Dentsply expands solutions with intraoral scanning for Atlantis

Staff Report

Dentsply Implants (Molndal, Sweden) says it has expanded further into the area of digital dentistry with intraoral scanning services for Atlantis abutments, the latest business development that will provide dental clinics and dental laboratories with an improved digital workflow.

This new development was made possible through an agreement with **Align Technology** (San Jose, California) paving the way for an interface where Atlantis patient-specific abutments can be ordered based upon scans from the iTero intraoral scanner. Intraoral scanning for Atlantis abutments will allow the dental laboratory to provide a complete patient-specific restorative solution to the clinician, based on a digital impression. The added value includes cost-savings, more precise impressions, increased patient well-being and expedited treatment processes. The launch is planned for the second half of 2014.

"Moving forward in this expanding area of digital dentistry, dental scanning is a strategic business opportunity. This will further strengthen Dentsply Implants and our Atlantis offer in the areas of implant dentistry and digital open solutions, respectively. More importantly, we are creating added value for our customers and their patients," says Mikael Sander, Group Vice President Atlantis Digital Implant Solutions, Dentsply Implants.

Dentsply is a maker of dental and other healthcare products.

In other agreements/contracts news:

• **TriReme Medical** (Singapore) has signed a broad distribution agreement with **Cordis** (Bridgewater, New Jersey) for the exclusive distribution of its unique Chocolate PTA Balloon Angioplasty Catheter, with an option for additional TriReme portfolio products. This agreement will expand TriReme's commercial footprint and allow the company to focus on its promising development pipeline.

"Cordis has an unparalleled track record in creating and building new and innovative product categories that have dramatically changed and improved clinical practice. We are honored to partner with Cordis and look forward to our collaboration," said Eitan Konstantino, president/CEO of TriReme.

The Chocolate PTA Balloon Catheter is a PTA balloon that is designed to allow for atraumatic dilatation in treating peripheral artery disease (PAD). The Chocolate PTA Balloon Catheter is indicated for balloon dilatation of lesions in the peripheral vasculature, including the iliac, femoral, ilio-femoral, popliteal, infra-popliteal and renal arteries.

TriReme is an emerging leader in the development and commercialization of next generation minimally invasive devices for the treatment of complex arterial disease.

• **Biolase** (Irvine, California) a manufacturer of dental lasers, including the company's proprietary WaterLase, and a maker in laser surgery in other medical specialties, as well as a distributor of digital radiography and GalaxyBioMill CAD/CAM systems for dentistry, has entered into a reseller agreement with **Stratasys** (Minneapolis).

Biolase will become a distributor of Stratasys' Objet30 OrthoDesk and a number of Design Series High End 3-D printers. The Objet30 OrthoDesk combines accurate and precise 3-D printing technology with a small footprint. It is easy to use, and includes specialized dental printing materials in convenient sealed cartridges. Dentists can fabricate stone models, orthodontic appliances, delivery and positioning trays, models

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CONTACT US

MDD.NewsDesk@medicaldevicedaily.com

Donald R. Johnston, (770) 810 3118 // Holland Johnson, (770) 810-3122 // Amanda Pedersen, (912) 660-2282 // Omar Ford, (770) 810-3125 // Robert Kimball, (770) 810-3127 // Mark McCarty, (703) 361-2519

ATLANTA NEWSROOM

Holland Johnson (Executive Editor), Mark McCarty (Editor), Omar Ford & Amanda Pedersen (Staff Writers), Robert Kimball (Senior Production Editor)

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BUSINESS OFFICE

Donald R. Johnston (Senior Director, Editorial), Sarah Cross (Marketing Director), Matt Hartzog, Paul Marino & Greg Rouse (Account Representatives)

REPORT FROM EUROPE

Cyberonics gets CE mark for AspireSR for VNS therapy

Staff Report

Cyberonics (Houston) reported that it has received CE mark approval for the AspireSR generator, the novel sixth-generation VNS therapy generator.

The AspireSR generator provides the well-established benefits of vagus nerve stimulation (VNS) therapy, coupled with a new feature – Automatic Stimulation in response to detection of a seizure. Proprietary technology enables the AspireSR generator to analyze relative heart rate changes to detect and respond to seizures. This technology is based on a growing body of evidence that seizures are often accompanied by an increase in heart rate (ictal tachycardia). With the Automatic Stimulation feature, the AspireSR generator better aligns stimulation with the clinical onset of a seizure.

Currently, patients experiencing VNS therapy can use a hand-held magnet to activate stimulation manually when they anticipate the onset of a seizure. This on-demand stimulation has been shown to stop or shorten a seizure, reduce seizure severity, and improve or shorten the postictal (post-seizure) recovery period. The Automatic Stimulation feature of the AspireSR generator may benefit patients who experience seizures accompanied by ictal tachycardia and are unable to perform on-demand stimulation with the hand-held magnet, do not have a magnet available when needed, or experience a seizure while sleeping.

Results of the E-36 clinical study, which evaluated the performance and safety of the AspireSR generator, were presented at the American Epilepsy Society meeting in December 2013. The study met its primary performance endpoint, and the safety profile for the AspireSR generator is consistent with currently available VNS Therapy systems.

"A significant number of people living with refractory epilepsy experience heart rate changes during their seizures," said Christian Elger, Head of the Department of Epileptology at the **University Hospital of Bonn, Germany**. "AspireSR builds upon the VNS therapy platform by providing a unique, innovative possible therapeutic option for these patients by automatically detecting and responding to seizures upon heart rate increase."

"European approval of the AspireSR generator represents an important milestone in Cyberonics' ongoing commitment to provide technologically-advanced, device-based solutions for people with epilepsy," said Dan Moore, president/CEO of Cyberonics. "This new generator will be particularly helpful to VNS therapy patients who are unable to use magnet-activated stimulation consistently. We believe the Automatic Stimulation feature will continue to advance VNS therapy as a foundational therapy for people with refractory epilepsy."

The VNS therapy system is FDA-approved for the treatment of refractory epilepsy and treatment-resistant depression. It uses an implanted medical device that delivers pulsed electrical signals to the vagus nerve. Cyberonics offers the system in selected markets worldwide. //

DEALS ROUNDUP

Syneron to acquire NSL for nearly $11M in cash

Staff Report

Syneron Medical (Yokneam, Israel), an aesthetic device company, reported that it has entered into an agreement to acquire **New Star Lasers** (Roseville, California), which conducts business as CoolTouch, for about $11 million in cash and earn out based on certain milestones of up to $4 million until end of 2015.

New Star Lasers develops, manufactures and markets the CoolTouch family of aesthetic devices. CoolTouch's 2013 unaudited revenues were approximately $8.9 million. Syneron anticipates the acquisition is expected to close in March.

Shimon Eckhouse, CEO of Syneron, transitioning into active chairman, said, "The acquisition of CoolTouch significantly enhances Syneron's product offerings and market opportunity while also improving the recurring revenue profile of our business. We believe CoolTouch will add value to Syneron's product offerings by expanding our reach into new markets such as the endovascular treatment of varicose veins and minimally-invasive laser assisted lipolysis. In addition, the CoolTouch business model also supports our strategy to increase sales of products with recurring revenue streams. We are very pleased to welcome the CoolTouch team to Syneron and look forward to expanding adoption of their products and technology through our global commercial infrastructure."

In other dealmaking activity; **Physicians Realty Trust** (Milwaukee), a self-managed healthcare properties REIT, said it has entered into and closed an agreement of sale and purchase with **Foundation Bariatric Real Estate** (San Antonio) to purchase a surgical hospital located in San Antonio, Texas.

The hospital totals about 46,000 square feet, is 100% occupied as of February 19, 2014 and is being acquired for approximately $18.9 million. The purchase price is payable in cash less approximately $10.8 million in assumed debt. The surgical hospital is leased to Foundation Bariatric Hospital. //

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HIT ROUNDUP

Siemens launches CareXcell for population health management

Staff Report

Siemens Healthcare (Malvern, Pennsylvania) reported the launch of CareXcell, the latest addition to its portfolio of next-generation IT solutions designed to help healthcare providers address the new care and payment requirements of value-based and accountable care models. CareXcell comprises technologies designed to help facilitate improved care management and risk stratification of individual patients and entire populations through open communication and data sharing across providers, care venues, and transitions.

Evidence-based care plans, integrated with underlying business process management technology, support the delivery of high-quality, cost-effective care across the continuum to help improve outcomes and increase patient and provider satisfaction. Siemens also reported that Inspira Health Network is the first provider to sign up for the CareXcell cloud-based service.

"The successful transition to value-based purchasing models requires new strategies and tools that shift population health management from reactive to proactive throughout the entire lifecycle of care," said John Glaser, PhD, CEO, health services, Siemens Healthcare. "CareXcell provides a collaborative framework for improving care delivery and monitoring across a community, integrating advanced workflow and event-processing technology with clinical evidence to help providers address patients' health and risk factors in a timelier, more efficient manner."

CareXcell is designed to consolidate and normalizes patient data from disparate EHRs and clinical systems into a single patient-centered repository through any health information exchange. Accessing summarized, real-time clinical data improves provider efficiency in identifying and addressing patient-specific issues and risk factors before they become more severe, costly conditions, Siemens said. For example, CareXcell can help providers initiate appropriate interventions as part of patients' personalized care plans to help improve long-term outcomes, keeping rising-risk patients from becoming high-risk, high-cost utilizers and ultimately strengthening their bottom line.

Evidence-based care plans drive CareXcell's patient-specific interventions for chronic conditions, risk reduction, and prevention. The care plans are supplied by Motive Medical Intelligence, a provider of actionable, evidence-based intelligence inside clinical workflow and point-of-care solutions. Motive's dynamic care plans, integrated within the embedded business process management technology, deliver patient-specific messages for evidence-based interventions at every point in the care workflow. An underlying workflow engine monitors the care plan activities for completion or deviations, triggering timely patient-specific interventions and event-based alerts, as well as escalating missed tasks to a specified care team member. CareXcell simplifies workflow across the care team by giving providers real-time decision support, identifying care gaps, recommending actionable interventions triggered by those gaps, and documenting problems and goals.

Throughout all these processes, CareXcell collects critical quality improvement information and analyzes patient and population data, allowing healthcare organizations to monitor clinical outcomes and performances across the continuum. This information can then be used to drive strategies for clinical, operational, and financial excellence. And because engaged patients typically have better outcomes, CareXcell incorporates tools such as a patient portal, text and secure email notifications, and evidence-based educational resources to help patients, as well as their families or personal support network, to be more active in their care and knowledgeable about their condition.

In other HIT activity, **York Hospital** (York, Maine), a 79-bed acute care hospital, reported a multi-year engagement with McKesson Managed Services (Atlanta) for full healthcare IT outsourcing services. McKesson says it provides resources and leadership to help York manage the rapid growth and complexity of its hospital IT systems, while addressing regulatory requirements and providing overall application support.

With responsibility for day-to-day management of York's IT operations, McKesson is using on-site and remote offerings to support both McKesson and third-party applications. One of the larger products to be supported includes McKesson's contemporary, Microsoft-based Paragon Hospital Information System, which consists of over 40 clinical and financial modules. Services include application build/support/management, hospital help desk, infrastructure support, data center operations, network administration, desktop operations and project management/administration. All of these offerings are designed to help hospitals and health systems manage risk and improve the operational performance of their IT investments. //

BRIEFLY NOTED

POLYMICRO IN COMPLIANCE WITH FDA REGULATION

Polymicro Technologies (Lisle, Illinois), a subsidiary of Molex, reported its recent registration and compliance with the FDA 21 CFR 820 Quality System Regulation (QSR).

Under FDA 21 CFR 820 QS regulations, medical manufacturers must establish and adhere to quality systems that ensure their products consistently meet requirements for Current Good Manufacturing Practices (CGMP). CGMP governs methods, facilities and controls used in the design, manufacture, packaging, labeling, storage, installation and servicing of finished medical devices intended for use with patients.

The Polymicro product portfolio includes silica capillary tubing, specialty optical fibers, optical and capillary assemblies, and discrete micro components, in addition to packaged and sterilized components.

EndoGastric

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The settlement resolves a whistleblower lawsuit filed in June 2012 in U.S. District Court in Montana by former employee Glenn Schmasow. The complaint alleges that the company told healthcare providers to bill for the procedure using codes that applied to a more invasive—and more expensive—procedure - when it came down to the use of the EsophyX, a less invasive way to treat gastric reflux. The government also alleged the company paid kickbacks to physicians to induce them to use the device.

In an e-mailed response to *Medical Device Daily*, Josh DeFonzo, VP of marketing for EGS noted that the cost of the settlement would not have an impact on the firm's current organizational structure.

"Monies are being accrued in relation to the details of the settlement," he said. "Payments will be made over time based on a number of factors, all of which have been considered and prepared for financially. Settlement-related costs obviously add to the company's overall operational expenditure. As a privately funded company, our investors are aware of the costs related to the settlement and have made financial plans accordingly. We do not anticipate that direct settlement related costs will have an impact on the current organizational structure."

He also noted that the settlement did not and probably would not impact the firm's product lines.

"The settlement was in no way related to product quality, or outcomes or safety-related to use of the technology," he said. "In fact, we anticipate launching two new product iterations within the next 12-18 months.

"We believe that we were able to resolve this matter on relatively quick terms due to internal corrective actions and compliance policies that were enacted prior to the launch of the investigation, when the company revamped its management team in 2011," DeFonzo said. "For us, the settlement allows us to focus the full extent of our efforts in the future. Moving forward the company is committed to seeing through high-quality clinical investigations, delivering on-going product development and innovation, as well as obtaining a level I CPT code for our technology."

Part of those future developments involve building a strong body of evidence for the EsophyX. The company took one step closer to this goal by announcing favorable results from its TIF registry. The results were published in the February 2014 issue of the journal *Surgical Laparoscopy Endoscopy and Percutaneous Techniques*. The data shows that quality-of-life scores remained the same or slightly improved over time, suggesting durability of outcomes between 6- and 12-month follow-up.

The publication reports results following TIF procedures in 100 consecutive patients enrolled in the registry and treated at 14 U.S. centers, including 13 general surgery practices and one gastroenterology practice. The study was designed to assess the impact of the TIF procedure on patients with chronic GERD at 12-month follow-up. Patient follow-up is ongoing for this registry study.

"The device enables one to perform fundoplication to a transoral approach," Adrian Lobontiu, MD, Medical Director EGS, told *MDD*. "There are no incisions on the abdominal wall. It's definitely an incisionless advantage and that's definitely a huge advantage."

Registry results show that outcomes from the procedure observed at six months remained stable across a range of evaluation methodologies at 12-month follow-up. The one-year findings showed that 78% of patients experienced elimination of troublesome heartburn symptoms and 83% stopped experiencing regurgitation. Seventy-four percent of patients completely stopped medical therapy with proton pump inhibitor medications.

"What's really interesting is that the patient after the [TIF] procedure is symptom-free for any symptoms that we've analyzed," he said. "It's very effective and the patients are free at six month follow-up and 12 month follow-up and they don't have any side effects as seen with laparoscopic procedures." //

FINANCINGS ROUNDUP

LabStyle Innovations closes private placement of $4M

Staff Report

LabStyle Innovations (Caesarea, Israel), developer of the Dario Diabetes Management Solution, has closed its previously reported $4.19 million common stock and warrant private placement financing that priced on Feb. 13, 2014.

LabStyle intends to use the aggregate net proceeds of the financing, anticipated to be around $3.79 million, primarily to continue the company's multi-market launch of Dario, the diabetes management solution that combines an all-in-one smart meter (blood glucose monitoring platform) with personalized information and community support via the users' smartphone.

Gadi Levin, chief financial officer at LabStyle, said, "Today's financing is good news for LabStyle as well as for our new and existing investors and partners, who all believe in LabStyle's strong value proposition and the importance of its present and future contribution to diabetes management. The financing, which featured the participation of new institutional investors, will help us to bring Dario to several additional markets around the world, continuing the momentum of Dario's distribution in the UK, Italy and Australia that began in December 2013."

Roth Capital Partners acted as the placement agent for the financing.

LabStyle Innovations makes technology providing consumers with laboratory-testing capabilities using smart mobile devices. //

Stroke

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trials dominating the news.

The most visible failed trial reported here was the Field Administration of Stroke Therapy—Magnesium Phase 3 Clinical Trial (FAST-MAG). This trial, which enrolled 1,700 patients between 2005 and 2012, tested whether intravenously administered magnesium, which is believed to be a neuroprotective agent, could be delivered in a timely manner (i.e., within two hours of stroke symptom onset) and could impact the neurological outcome of acute ischemic stroke (AIS) patients.

The FAST-MAG trial results revealed that administration of IV magnesium was safe but did not confer any benefit in neurological outcome, as measured by the 90 day modified Rankin Score.

The "silver lining" of this study is that it demonstrated that up to 75% of stroke patients calling emergency services early can be started on treatment in the first "golden hour" after their stroke symptoms emerge. The median time for receiving treatment in this study was 45 minutes, with 74% of the patients being treated in one hour.

At an ASA press conference, Bruce Ovbiagele, MD, **Medical University of South Carolina** (Charleston) said that "This opens up a whole new arena for us to test other promising new therapies in the pre-hospital setting. The FAST-MAG study shows it is feasible — it can be done. This is the big message from this study."

The ability to get patients treated quickly is certainly encouraging to the stroke community, where today, 18 years after its FDA approval, the thrombolytic clot-busting drug tissue plasminogen activator (tPA) is still very underutilized. A study presented here, based on 370,000 Medicare stroke claims in 2011, found that only 4% of patients receive tPA and a miniscule 0.5% had endovascular therapy. This dismal treatment rate is occurring despite the fact the number of stroke centers in the U.S. has doubled in the past five years (now approaching 1,000 in total) and that 80% of the U.S. population lives within an hour's drive of a stroke center.

With each passing year, the stroke community recognizes that "time is brain" and that reperfusion therapy has to be delivered in a timely way. Indeed, a detailed analysis of the large International Management of Stroke III (IMS III), trial, which failed to meet its primary endpoint, showed that for every 30 minutes that pass until angiographic reperfusion, the probability of good recovery after an ischemic stroke is decreased by about 10%. Moreover, there is a 5% increase in mortality for every hour that treatment is delayed.

Although acute ischemic stroke accounts for roughly 85% of all strokes and represents an enormous opportunity, the current market size of the AIS endovascular device market is paltry compared to the hemorrhagic stroke market. Specifically, the more mature hemorrhagic stroke devices market (coils, stents, flow diverters, liquid embolics and access catheters) generates approximately $1.1 billion in annual global revenue while the embryonic but faster growing AIS device market, generates global sales of only about $200-$250 million annually.

One of the key advantages of endovascular devices over tPA is that tPA's efficacy diminishes rapidly with time. In addition, its FDA label requires that it be used within 4.5 hours of stroke onset. Conversely endovascular techniques often can provide benefits far beyond that 4.5 hour window. Most devices are labeled for use of up to eight hours and some neuro-interventionalists have reported that they have achieved reperfusion in certain AIS patients for up to as much as 24 hours.

The enormous market opportunity for acute stroke therapy has not gone unnoticed, with several large device companies actively involved. **Stryker** (Kalamazoo, Michigan) has gained the number one position in the global market with three key acquisitions, the $1.5 billion purchase of the **Boston Scientific** (Natick, Massachusetts) Neurovascular division in 2010, the $135 million purchase of **Concentric Medical** (Mountain View, California) in 2011 and the $135 million acquisition of **Surpass Medical** (Tel Aviv, Israel)

Medical Device Daily estimates that the Stryker Neurovascular division currently generates annual global revenue of approximately $475 million, giving it a global market share of about 35%.

Stryker Neurovascular is actively involved in several AIS device trials and hopes to begin a large global trial dubbed DAWN by mid-year, randomizing its new Trevo XP thrombus removal device to medical management alone. DAWN is a global trial that will enroll up to 500 patients at 50 sites.

Stryker introduced the Trevo XP clot retriever at this meeting, highlighting its ease of placement and delivery and excellent visualization. It also claims to have larger clot capture area than competing clot retrievers.

The Vascular Therapies division of **Covidien** (Dublin, Ireland) is also a very active player in the neurovascular market, growing both internally and from an aggressive acquisition program. In July 2010, it acquired **ev3** for approximately $2.6 billion. Prior to that, ev3 had acquired **Chestnut Medical** (Menlo Park, California) for $150 million in June of 2009. In January 2012, Covidien purchased the distal access guide catheter product line from Reverse Medical (Irvine, California) for an estimated $35 million and in July 2012 it acquired **MindFrame Medical** (Irvine, California) for $75 million.

Medical Device Daily estimates that Covidien's global neurovascular business generates annual global revenue of about $450 million, giving it a global market share of about 33%.

Covidien is actively involved in the ischemic stroke market, with several studies underway. The company claims to be investing over $30 million annually to fund its various endovascular clinical trials. The most notable is the SWIFT PRIME study, which is a randomized multicenter prospective

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M&A

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outcome of healthcare reform and FDA changes. "There has been generally a 'wait and see' approach for the past several years except for the larger public companies," Cohen said. "I think with healthcare reform passing the Supreme Court and just generally the industry adapting to the new regime, some of the fogginess has clarified and acquisition activity has picked up."

But, Cohen added, there are a number of other drivers at play that also impact healthcare dealmaking. Some of the key influencers include: medical product offerings are becoming more standardized as budgetary cuts put pressure on reimbursements; hospitals and other providers are consolidating in large number, which will reduce the ranks of medical product suppliers; and R&D budgets are being cut as companies seek to streamline and face daunting regulatory and commercialization hurdles.

"All of this greatly impacts the med-tech sector and healthcare M&A activity. We've identified 10 key forces shaping the sector and how M&A activity is influenced by them," Cohen noted. "It is becoming harder to sustain organic growth at historic levels and M&A will increasingly be relied upon to supplement growth, but a discerning approach is now needed."

The report also uses game-changing technologies like transcatheter heart valves, intraocular lenses, and surgical robotics as examples of new technologies impacting M&A activity because larger companies like **Medtronic** (Minneapolis) will acquire the smaller innovators of such products.

On the other hand, not every new technology works out, Cohen said, using Medtronic's $800 million purchase of **Ardian** (Mountain View, California) as a prime example. Medtronic acquired Ardian for its Symplicity renal denervation technology back in 2010 (*Medical Device Daily*, Dec. 1, 2010) and until recently the industry had high expectations for renal denervation as a treatment for drug-resistant hypertension. But last month the company revealed that its U.S. pivotal trial in renal denervation, SYMPLICITY HTN-3, failed to meet its primary efficacy endpoint (*MDD*, Jan. 10, 2014).

Soon after Medtronic's SYMPLICITY HTN-3 news surfaced, **Covidien** (Dublin, Ireland) reported its exit from its OneShot renal denervation program, attributing the decision to "slower than expected" development of the renal denervation market.

Cohen suggested that a more rigorous approach to clinical data might be the lesson to come out of these investments, but that doesn't mean that larger companies shouldn't be putting money into new innovation from smaller players. "It's very important to make acquisitions of new technologies and putting them on the market," he said. "Not everything does work out and it's okay to fail, you still need to make those investments."

Medtronic CEO Omar Ishrak made a similar point during his presentation last month at the annual J.P. Morgan Healthcare Conference (*MDD*, Jan. 14, 2014). He said that at the time of the Ardian purchase a "hypothesis was made which was quite sound" but that as with any acquisition there is a risk associated with it. It was not a case of doing an acquisition without thinking, he emphasized. "We go into [deals] with our eyes wide open. It was not an execution issue, the model depended on clinical trials having certain results. This doesn't mean we're going to walk away from risk in med-tech."

During his presentation, Ishrak noted that the company's M&A policy is to ask itself, prior to an acquisition, three specific questions: Is it an attractive market? Can we win? And what value do we add?

St. Jude Medical (St. Paul, Minnesota) also has stopped its U.S. study for renal denervation due to slow trial enrollment, but the company's global renal denervation program is still ongoing. Daniel Starks, president/CEO of St. Jude, reiterated the company's commitment to the global renal denervation space during St. Jude's earnings call last month (*MDD*, Jan. 27, 2014). "We think that innovation takes patience and persistence, and we're really looking forward to learning what we can from the SYMPLICITY 3 trial data and using that to help advance our program," Starks said.

Medtronic's announcement regarding its renal denervation program does not change the fundamental reasons that St. Jude has invested in the renal denervation space, Starks said, and it doesn't change the algorithm for St. Jude's decision.

Higher healthcare insurance deductibles and co-pays is another noteworthy factor that influences M&A activity, according to the report, because more out-of-pocket expenses for patients will dampen utilization rates. This goes hand in hand with another factor mentioned in the report, reimbursement pressure.

"There is a new cost-consciousness invading the market, Cohen said. "It's very important to demonstrate not just superior outcomes" but also cost-effectiveness, which includes the cost of training that hospitals have to pay for to adopt new technologies plus the cost of maintenance. "All of that matters," Cohen added. //

PEOPLE IN PLACES

• **Icon** (Dublin, Ireland) has named Mary Pendergast as a non-executive director. Pendergast is considered an expert in the regulatory aspects of drug development and is president of Pendergast Consulting. Icon is a provider of outsourced development services to the pharmaceutical, biotechnology and medical device industries.

• **Syneron** (Yokneam, Israel) has named current president Amit Meridor to the position of CEO. He replaces Shimon Eckhouse, who will return to the position of chairman of the board. Meridor joined Syneron in July 2013 as President. David Schlachet, who served as chairman of the board during Eckhouse's tenure as CEO, will remain on the board. Syneron Medical makes aesthetic medical products.

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Washington

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FDA had posted the week of February 10 a warning letter to Baxter for the company's facility in Round Lake, Illinois, the site of the company's manufacture of HomeChoice infusion pumps (*Medical Device Daily*, Feb. 12, 2013), an inspection FDA claimed uncovered repeat violations from a previous inspection. The agency announced a recall of dual Luer lock caps as well last year due to loose particulate matter in the packaging (*MDD*, Sept. 23, 2013), an action that seems to tie in with some of the inspectional findings for the Irvine plant.

The Irvine warning letter says that Baxter had opened a corrective and preventive action (CAPA) in 2009 to address what the agency claimed was "an increasing number of complaints for leakage in the distal end of Infusor pumps. The agency noted that the leakage had occurred between the Luer body and the wing Luer cap, adding that Baxter had received additional complaints after it had closed the corrective action in 2010 despite a corrective action program that included a removal of "all suspect products" and intervention with a contract supplier.

This was one of eight CAPA citations, but FDA noted that it could not evaluate the company's response because Baxter had indicated it would "deploy a re-engineered CAPA system at [the] Irvine facility by Aug. 30, 2013." FDA did not address the lag time between the deployment of the new CAPA system and the date of the warning letter, although the agency made note of the company's "decision to [redacted] of your elastomeric infusion pumps and any associated accessories by [redacted]."

The agency reached back nearly a decade in this inspection, noting that a CAPA opened in 2005 for bladder ruptures had proven effective per a review conducted "after three months." FDA redacted many of the details of the correction for the Intermate and Infusor devices, but said that a review of the related documentation disclosed that the new protocol did not prescribe a set point for an unspecified acceptance criterion for the bladders. The warning letter also cited "inconsistencies with the production lot numbers in the protocol and final report."

FDA gave the company either failing grades for its responses to the other 10 citations or indicated the information was insufficient to allow an assessment. Among these was a citation for evaluations of suppliers, specifically a supplier of rubber presumably used in the device bladders.

Baxter's e-mailed response to *Medical Device Daily* said that the company "has already implemented a number of actions to systematically address the issues" raised in the warning letter, which the firm said "relates primarily to corrective action processes and documentation." Baxter said it will also "continue its ongoing dialog with the agency to resolve all issues noted in the warning letter."

INDUSTRY: IP A CONCERN IN MDDT DRAFT

FDA inked a draft addressing the notion of an agency-distributed set of medical device development tools (MDDTs) in November, and the proposal seems to have sparked concerns about intellectual property. Among those who commented is the **Advanced Medical Technology Association** (AdvaMed; Washington), which said in a Feb. 11 comment to the docket that anyone who offered their tools for promulgation via the agency "would seek intellectual property protection and compensation for the use of their proprietary tools."

Among the notions FDA addressed in the draft is that public health would improve with the dissemination of biomarkers and clinical outcomes measures (*Medical Device Daily*, Nov. 15, 2013), but the AdvaMed letter, along with a letter from **Boston Scientific** (Natick, Massachusetts) suggest the agency failed to reckon with industry's concerns about the cost of developing those tools. However, **Cook Medical** (Indianapolis) steered a different tack.

The AdvaMed letter, signed by Sharon Segal, PhD, the association's VP for technology and regulatory affairs, remarks that the mandate that those development tools be publicly disclosed "will likely result in few if any submissions of those tools." Segal recommended that the availability of the tools be the only public disclosure, allowing developers to "charge a reasonable fee for use."

BSX's Tamima Itani, PhD, likewise observed that the unqualified discloser of MDDTs "is a significant deterrent," suggesting as one alternative the use of venues that would allow the developer to charge a royalty payment "or other forms of recognition."

Stephen Ferguson, chairman of the board at Cook, noted that standards already serve as MDDTs, adding that ASTM is an example of an organization that has developed testing standards, including those for intravascular stents. However, Ferguson was less than enthused at the prospect that the agency's Center for Devices would act as the entity charged with qualifying an MDDT. Ferguson indicated no reservations about the IP issues addressed by Boston Scientific and AdvaMed, but recommended the agency assemble a panel of stakeholders to take up the question of what constitutes a qualified MDDT."

FDA RELENTS ON DIATHERMY

FDA reported in the Feb. 20 *Federal Register* that it has withdrawn an order that makers of short-wave diathermy devices file PMAs or product development protocols for their offerings, and in a separate *FR* entry, that these devices are deemed class II "for all other uses," apparently meaning uses other than for treatment of malignancies.

The agency reminded the reader it had issued the PMA/PDP order in July 2012, but had noticed a consensus among attendees at a July 2013 advisory hearing that "although the effectiveness data were very limited, non-thermal SWD devices did not fit the regulatory definition of a class III device" because they are not life-saving or life-sustaining.

FDA also noted that the terminology of these devices would, for regulatory purposes, be altered to "non-thermal shortwave therapy" devices. //

Stroke

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trial that will compare AIS patients with large vessel occlusions treated with either tPA alone or in combination with Covidien's Solitaire 2, Solitaire FR, and/or Solitaire RD clot retrievers. This trial will enroll up to 833 patients at up to 90 sites around the world, will assess how these two approaches affect stroke disability, mortality and functional independence.

The most notable is SWIFT PRIME, which is a randomized multicenter prospective trial that will compare AIS patients treated with either tPA alone or in combination with its second generation Solitaire 2 clot retriever. This trial will enroll 800 patients at 60 sites around the world and will assess how these two approaches affect stroke disability mortality and functional independence.

Impressive results for Solitaire FR in Covidien's STAR study were reported in the Aug. 1, 2013 issue of *Stroke*. This trial enrolled 202 patients at 14 centers in Europe, Canada and Australia and demonstrated excellent neurological outcomes. The trial was not randomized but is purported to be the largest multicenter trial of mechanical thrombectomy devices to date.

In addition to the SWIFT PRIME trial, which addresses the need for a randomized, prospective and multi-center trials for ultimate credibility, privately-owned **Penumbra** (Alameda, California) is engaged in the THERAPY trial, began enrollment about one year ago. Approximately 300 patients will be enrolled in each arm and the trial is expected to take about three years to fully enroll. This trial is designed to assess the safety and effectiveness of the Penumbra mechanical thrombectomy catheter system as an adjunctive treatment to tPA in patients with an acute ischemic stroke from a large vessel occlusion (LVO).

At last year's meeting, Pooja Khatri, MD, associate professor of neurology at the University of Cincinnati, said that tPA alone is ineffective when the stroke is caused by an LVO, specifically clots in excess of 8 millimeters long. The hypothesis of THERAPY is that the addition of a mechanical thrombectomy device in patients with a large clot burden (i.e., clot length in excess of 8 mm) can improve the clinical outcome of the patient over using tPA alone.

The trial is using Penumbra's recently introduced ACE "next generation" reperfusion catheter, which uses direct aspiration alone to extract the clot. ACE is the latest addition to Penumbra's line of mechanical thrombectomy devices and has a much larger lumen size than previous devices, which allows the interventionalist to engage the clot quickly, aspirate and remove it without the need for any other adjunctive devices.

Early clinical results for the ACE device, which achieved its success much faster than competing devices, are very promising. Blaise Baxter, MD from the **Erlanger Health System** (Chattanooga Tennessee) reported here that on a study using direct aspiration at six U.S. centers. There were 43 patients treated with ACE and adjunctive therapy, 97% of these patients achieved an impressive thrombolysis in cerebral infarction (TICI) score of 2b/3, In addition, 81% achieved TICI 2b/3 with aspiration with ACE alone and no other adjunctive products. The rate of perfect revascularization (TICI 3) in the ACE sole therapy patients was 62%. Most importantly, 55% of the ACE treated patients had a good to excellent neurological outcome (mRS 0-2) at 90 days.

As a final note, it is crucial that these aforementioned prospective randomized clinical trials are completed in a timely way and demonstrate both safety and efficacy. At a Covidien well-attended evening symposium titled "The SWIFT PRIME and Clot 3 Studies: Advancing Systems of Care and Treatment of Acute Ischemic Stroke," Hans Christian Diener MD, a noted stroke specialist from the Department of Neurology University of **Duisburg-Essen** (Essen, Germany) reviewed some of the failed stroke trials, provided his thoughts on the lessons learned and a roadmap to future success. This is summarized in the following table. //

Table 1
Lessons Learned from Recent Endovascular Stroke Trials

- Patient selection is critical – Randomize all eligible patients, confirm presence of large vessel occlusion
- Revascularization is necessary – Treat with latest generation devices (i.e., stentrievers)
- Time to reperfusion is crucial

Source: Hans Christian Diener MD

Agreements

Continued from page 2

for clear aligners, retainers and surgical guides on their desktop.

Stratasys makes 3-D printers and materials for prototyping and production.

• **Millennium HealthCare** (Garden City, New York) said its subsidiary, Millennium Medical Devices, has signed an agreement with **CDx Diagnostics** (Suffern, New York) for distribution of DermCDx, a brush biopsy test kit that is used to confirm suspected basal cell carcinoma (BCC), the most common cancer in the U.S.

DermCDx is a minimally invasive test that combines a patented brush biopsy sampling instrument with computer-assisted three dimensional laboratory analysis. It is designed to allow primary care physicians to easily confirm suspected BCC resulting in expedited referral to a dermatologist for treatment.

Millennium HealthCare provides primary care physician practices, physician groups and healthcare facilities of all sizes with cutting edge medical devices focused primarily on preventive care through early detection. //

PRODUCT BRIEFS

• **Imris** (Minneapolis) reported the initial launch of what it calls the world's first MR-safe and CT-compatible horseshoe headrest on the market for the positioning of patients ranging from neonatal to adult during neurosurgical procedures requiring intraoperative imaging in the Visius Surgical Theatre. The horseshoe headrest provides non-pinned head support in prone, lateral, and supine positions during head, neck and cervical spine surgeries where use of a head fixation device (HFD) – a clamp-like device – is not desirable because the skull is too fragile for pinning. These patients may be babies whose skulls are still soft or older patients with weakened skull bones. Inside a Visius Surgical Theatre equipped with either high-field intraoperative MRI (iMRI) or 64-slice intraoperative Computed Tomography (iCT), surgeons have on-demand access to real-time data and imaging during the procedure and from the operating room (OR) table. IMRIS also designs and manufactures proprietary head fixation devices, imaging coils, and OR tables for use in this unique and multifunctional intraoperative environment.

• **Marvao Medical** (Galway, Ireland) received FDA clearance for three additional lengths of its NexSite HD Catheter product line. These new lengths (32cm, 36cm and 40cm) complement the two previously cleared lengths (24cm and 28cm) and complete the core offering of the company's first NexSite HD catheter product line. Marvao Medical says its NexSite ESM technology is a novel technology for the management of the catheter exit site. It is based on tissue ingrowth and features the company's DISC (Dermal Ingrowth Support Collar) that enables the wound in the skin at the catheter exit site to heal.

• **RedPath Integrated Pathology** (Pittsburgh) reported the launch of a new, patent-pending, customized test to accurately measure carcinoembryonic antigen (CEA) in all pancreatic cyst fluids. Unlike routinely used, commercially available CEA assays, AccuCEA provides accurate results, even in pancreatic cyst fluid specimens with limited volume and/or high viscosity. Furthermore, AccuCEA provides physicians with more options in the diagnostic work-up of patients by preserving precious fluid and making it available for additional tests. When the amount of pancreatic cyst fluid is limited and CEA testing is prescribed, CEA can be analyzed in diluted fluid. However, dilution of cyst fluid can significantly impact the analytical accuracy of the resulting CEA measurements. RedPath has solved this problem by creating AccuCEA, which provides CEA measurements in diluted cyst fluid that are true to their corresponding neat (undiluted) cyst fluid CEA measurements. RedPath Integrated Pathology is a molecular diagnostics laboratory focused on providing novel solutions for clinicians.

• **Sonendo** (Laguna Hills, California) said its novel Multisonic Ultracleaning System was cited in the current online February issue of the *Journal of Endodontics* as having the ability to dissolve tissue at a significantly faster rate compared to current treatment methods. The study, "Tissue Dissolution by a Novel Multisonic Ultracleaning System and Sodium Hypochlorite," compared Sonendo's mechanism of action to a variety of conventional devices, and was found to dissolve tissue at least eight times faster than the other systems tested.

• **Teleflex** (Limerick, Pennsylvania) reported the launch of the Rusch DispoLED Single-Use Fiber Optic Laryngoscope Handle. The Rusch DispoLED Laryngoscope Handle is the latest addition to Teleflex's broad single-use anesthesia product portfolio – a product category that is playing an increasingly important role in clinicians' practice since the October 2011 publication of Joint Commission laryngoscope cleaning guidelines. The Rusch DispoLED Laryngoscope Handle is packaged individually in a preformed tray to protect the integrity of the light source and preloaded batteries. With a validated 3-year shelf life, the Rusch DispoLED Laryngoscope Handle can be safely stored for long periods and is ready to use out of the package.

Medtronic enrolls in trial for miniature pacemaker system

Staff Report

Medtronic (Minneapolis) reported the first U.S. implant of the world's smallest pacemaker: the Micra Transcatheter Pacing System (TPS). The device was implanted at NYU Langone Medical Center by Larry Chinitz, MD, director of the Heart Rhythm Center at NYU Langone Medical Center in New York City, as part of the Medtronic global pivotal clinical trial. The Micra TPS is an investigational device.

At one-tenth the size of a conventional pacemaker, and comparable in size to a large vitamin, the Micra TPS is delivered directly into the heart through a catheter inserted in the femoral vein. Once positioned, the pacemaker is securely attached to the heart wall and can be repositioned or retrieved if needed. The miniature device does not require the use of wires, known as "leads," to connect to the heart. Attached to the heart via small tines, the pacemaker delivers electrical impulses that pace the heart through an electrode at the end of the device.

"With its small size and minimally invasive procedure, this technology represents the future of pacing," said Chinitz. "Eliminating the need for a lead and pocket has the potential to reduce complications and recovery times compared to traditional pacemaker implants, which would be a major benefit to patients."

In contrast to current pacemaker implant procedures, the Micra TPS implant does not require a surgical incision in the chest and the creation of a "pocket" under the skin. This eliminates a potential source of device-related complications, and any visible sign of the device.

The study is a single-arm, multi-center global clinical trial that will enroll up to 780 patients at 50 centers. Initial results from the first 60 patients, followed up to three months, are expected in the second half of 2014. //

DIAGNOSTICS EXTRA

Keeping you up to date on recent developments in diagnostics

By Omar Ford, Staff Writer

Gene test developed to accurately classify brain tumors . . . Scientists at **The Wistar Institute** (Philadelphia) have developed a mathematical method for classifying forms of glioblastoma, an aggressive and deadly type of brain cancer, through variations in the way these tumor cells "read" genes. Their system was capable of predicting the subclasses of glioblastoma tumors with 92% accuracy. With further testing, this system could enable physicians to accurately predict which forms of therapy would benefit their patients the most. Their research was performed in collaboration with Donald O'Rourke, MD, a neurosurgeon at the **University of Pennsylvania Brain Tumor Center** (Philadelphia), who provided the glioblastoma samples necessary to validate the Wistar computer model. Their findings were published online in the journal *Nucleic Acids Research*. "It has become increasingly obvious that understanding the molecular makeup of each patient tumor is the key to personalizing cancer treatments for individual patients," said Ramana Davuluri, PhD, Wistar's Tobin Kestenbaum Family Professor and associate director of Wistar's Center for Systems and Computational Biology. "We have developed a computational model that will allow us to predict a patient's exact variety of glioblastoma based on the transcript variants a given tumor produces." "A gene can produce multiple variants, in the form of transcript variants and protein-isoforms. We found that when you use the gene expression information at variant/isoform-level, the statistical analyses recaptured the four known molecular subgroups but with a significant survival difference among the refined subgroups," said Davuluri. "Using patient data, we found that certain subgroups when combined with patient age, for example, could predict better outcomes using a given course of therapy." "As more targeted therapies come into use, this is exactly the sort of information clinicians will need to provide the best hope of survival for their patients," Davuluri said. "In time, we think this could form the basis of a clinical test that will help oncologists decide a patient's course of treatment." Glioblastomamultiforme is the most lethal of the malignant adult brain tumors, and accounts for over 50% of all cases of brain cancer. Even with aggressive combination therapies, the prognosis remains bleak, with median patient survival of 15 months after diagnosis. The disease is also molecularly heterogeneous, that is, composed of subtypes that are not genetically alike or produce the same array of proteins. Genetic data from the Cancer Genome Atlas (TCGA) consortium has led to the identification of four subtypes of glioblastoma, but Davuluri and his researchers sought to find a way to quickly identify which patient was which subtype. In previous studies, Davuluri and his Wistar colleagues have established how changes in the way a cell reads its own DNA can create multiple variations of a single protein. These variant proteins are called isoforms, and they are produced as cells alter how they transcribe a given gene into RNA. Slight changes in how the cellular machine reads a gene can result in protein isoforms with subtle differences in enzymatic activity or longevity. For example, their earlier research determined how human brains produce different isoforms of specific proteins throughout their lives. Developing fetal brains produce different isoforms of certain genes than adult brains. They also found that changes that trigger the production of the wrong isoform at the wrong time could lead to cancer.

Blu-ray player detects microorganisms and toxins on discs . . . In addition to storing films, optical discs can be used to detect microorganisms, toxins, allergens and tumoral biomarkers. Blu-ray technology has allowed researchers at the **Polytechnic University of Valencia** (Valencia, Spain) to develop a way to find out if a sample contains Salmonella or toxic substances. This simple and cheap analytical system may be applied to clinical diagnosis and environmental monitoring. A system devised by Chemists at the Polytechnic University of Valencia (UPV, Spain) uses Blu-ray discs and players to detect pathogenic bacteria and toxins in biological samples. The journal *Biosensors and Bioelectronics'*published the study. "We use the surface of these commercial discs as a platform for analysis to carry out the tests and then, with the laser reader of the recorder/player we can identify the bacteria and determine their concentration," Sergi Morais, one of the authors, explained. Specifically, the team has analysed the DNA of two types of pathogenic bacteria in this way: Salmonella typhimurium, which causes salmonellosis, and Cronobacter sakazakii, an intestinal parasite. "The method could be used to detect these and other microorganisms in breast milk or other foods," says Morais. The researchers also applied Blu-ray technology to determine the concentration of microcystins in water, a kind of toxin that causes gastrointestinal disorders or allergic reactions, and which are produced by cyanobacteria. "This type of test can also be used to detect tumoral biomarkers, food and drug allergens, and pesticides in water, for example," the researcher states. "The level of pollutants in water and air are regulated by directives that set a maximum residue limit, and the sensitivity of our technique allows analytes below that required by government to be detected." The samples are deposited in small quantities on the discs in the form of microarrays or two-dimensional arrays. "The hydrophobic nature of the surface of the Blu-ray disc allows the proteins to be locked in place by passive adsorption in a high-density format (64 points in each 1 mm2 drop)," one of the authors, Ángel Maquieira, points out. "On the 90 cm2

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Continued from previous page

surface of these discs it's possible to imprint 138,000 points, each one 125 µm in diameter," he adds. "Furthermore, the low sample volume used (5-10 microlitres) and the low cost of the developed hardware make this technology a very practical and economically competitive tool." According to the researchers, the accuracy and sensitivity of these electronic devices is similar to that obtained with conventional laboratory techniques, such as the quantitative polymerase chain reaction (PCR). Though it's not an "official" methodology, the process offers a very practical strategy to eliminate samples before applying more exhaustive analytical techniques. "Samples that are shown to be positive by this methodology will also be positive using the other techniques," Morais explains.

The nose knows in asthma: Nasal tissue samples may advance personalized medicine for asthma . . . It has become increasingly clear in recent years that asthma comes in several variations, with different causes, different pathologies and different responses to therapy. These subtypes of asthma can be identified by knowing which genes are expressed at higher and lower levels in patients' airways. That information can, in turn, help guide personalized treatment to more effectively manage asthma and inspire research to better understand, manage and possibly prevent asthma. The difficulty is that tissue samples necessary for this kind of genetic profiling are currently obtained from the airways, which requires bronchoscopy, an invasive procedure involving sedation. Concerns about safety, sedation, and expense limits the use of bronchoscopy, especially among children, and thus the asthmatic tissue samples needed for genetic profiling. Max Seibold, PhD, assistant professor of genetics at National Jewish Health, and his colleagues recently described a less invasive, less expensive and safer way to obtain genetic profiles of asthmatic patients. In the *Journal of Allergy and Clinical Immunology*, they recently demonstrated that genes expressed in the nasal passages can serve as accurate proxies for those expressed deeper in the airways. Tissue samples can be obtained from nasal passages with a small brush. Seibold and his colleagues showed that gene expression in the nasal passages overlaps 90% with genes expressed in the lungs. The researchers were able to distinguish asthmatic from non-asthmatic patients based on genes expressed in the nasal passages. They were also able to distinguish allergic asthma from non-allergic asthma, and associate high levels of the IL-13 gene with asthma exacerbations. If these findings are confirmed with additional research, genetic profiles of asthmatic patients could become more a more common and valuable tool to guide both therapy and research.

Impact of head movement on fMRI data shown in new study . . . Kessler Foundation (West Orange, New Jersey) researchers have shown that discarding data from subjects with multiple sclerosis (MS) who exhibit head movement during functional magnetic resonance imaging (fMRI) may bias sampling away from subjects with lower cognitive ability. The study was published in the January issue of Human Brain Mapping. Glenn Wylie, DPhil, is associate director of Neuroscience in Neuropsychology & Neuroscience Research at Kessler Foundation. He is also associate director of the Neuroimaging Center at Kessler Foundation, and an associate professor at **Rutgers -- New Jersey Medical School** (New Brunswick, New Jersey). Because head movement during fMRI degrades data quality, data associated with severe movement is frequently discarded as a source of random error. Kessler Foundation scientists tested this assumption in 34 persons with MS by examining whether head movement was related to task difficulty and cognitive status. Cognitive status was assessed by combining performance on a working memory and processing speed task. "We found an interaction between task difficulty and cognitive status," explained Wylie. "As task difficulty increased, there was a linear increase in movement that was larger among subjects with lower cognitive ability." Healthy controls showed similar, though far smaller, effects. This finding indicates that discarding data with severe movement artifact may bias MS samples such that only subjects with less-severe cognitive impairment are included in the analyses. However, even if such data are not discarded outright, subjects who move more will contribute less to the group-level results because of the poor quality of their data. It is important for researchers to be aware of this potential bias. "Some newer scanners can correct for motion," noted Dr Wylie. "Another approach is to monitor each subject's motion parameters and ensure that an adequate number of subjects with low cognition are included. Recruiting a large number of subjects may ensure inclusion of a sufficient number of people with low cognition/low movement. It is however, a costly option."