

Washington roundup

FDA seen as obstructionist on FFDM clearance question

By MARK McCARTY

Medical Device Daily Washington Editor

GAITHERSBURG, Maryland – The saying goes something like this: “If at first you don’t succeed, try, try again.” However, some who attended Tuesday’s hearing of the radiological devices advisory committee might have been inclined to tell FDA, “if you try again and you still don’t succeed, you’re fired.”

Whether that was consciously the message, it certainly was nearly the tone of some of the comments aimed at the agency in Tuesday’s hearing, which was held to address the 2008 guidance for 510(k) applications for full-field digital mammography (FFDM) systems. The agency was on the receiving end of a number of unflattering remarks during the open public hearing, including a comment that FDA’s decade-plus failure to come up with a 510(k) path for
See Washington, Page 6

Medica 2009

No sign of crisis for medtech evident as Medica turns 40

By JOHN BROSKY

Medical Device Daily European Editor

DÜSSELDORF, Germany — Celebrating its 40th birthday, Medica, the world’s largest trade fair dedicated to medical devices, showed no sign of a mid-life crisis, let alone any effect from the global financial crisis.

Begun as a modest exhibition called “Diagnostik-woche” (Diagnostic Week) with 135 German exhibitors and 4,700 participants, the three-day event that opened Wednesday has grown to 4,279 exhibitors from 65 countries and will attract an estimated 137,000 visitors, a slight increase over last year.

While the event organizers proudly promote different themes and focal points, the event defies neat categorization sprawling across 16 exhibition halls that resemble an Arab souk more than an orderly German trade fair, and
See Medica, Page 8

Report from Europe

Cardiola raises \$4 million from new and existing investors

A *Medical Device Daily* Staff Report

Cardiola (Winterthur, Switzerland) reported that it has raised an additional \$4 million from existing and new investors. Together with the \$2.3 million raised earlier this year, the total cash infusion of \$6.3 million is part of the first tranche of a \$7.9 million Series E financing round. The proceeds are being used to commercialize in Europe the company’s patented m.pulse device designed to non-surgically treat chronic heart failure (CHF) in a patient’s home.

CHF is the most frequent cause of hospitalization in persons aged 65 and older. Current treatments, including drugs, implantable defibrillators/pumps and heart transplantation, have significant risks and side effects. Cardiola’s m.pulse device, based on Muscular CounterPulsation (MCP) technology, is approved in Europe for treating CHF as a non-surgical, at-home therapy. Battery-powered m.pulse,
See Europe, Page 9

VEITHsymposium

Ekos launches ‘smarter’ blood clot dissolution device at forum

By AMANDA PEDERSEN

Medical Device Daily Staff Writer

Ekos (Bothell, Washington) launched the EkoSonic Mach4e with Rapid Pulse Modulation (RPM) for the dissolution of vascular blood clots today at the 36th annual VEITHsymposium in New York.

Last year Ekos introduced its second-generation EkoSonic endovascular system with RPM and this year the company introduced the Mach4 upgrade.

“We continue to listen to our customers in assessing how we can further improve the performance and simplicity of operation,” said Robert Hubert, president/CEO of Ekos. “The Mach4e upgrade addresses both categories.”

For performance, Hubert said Ekos has achieved even faster removal of arterial and venous clots (accelerating thrombolysis speed by up to 40%) making it even faster
See Ekos, Page 10

Don’t miss today’s MDD Extra: Orthopedics

INSIDE:

GORE TEAMS WITH QXMÉDICAL TO DISTRIBUTE STENT GRAFT BALLOON2
ABBOTT, BG, IN PACT TO DEVELOP ASSAY FOR NEW HF BIOMARKER3

AHC Media LLC

*Agreements/contracts***Gore teams with QXMédical to distribute stent graft balloon****A Medical Device Daily Staff Report**

W.L. Gore & Associates (Flagstaff, Arizona) reported it has entered into a partnership with **QXMédical** (Montreal, Quebec) a medical device development and marketing company. As part of the agreement, Gore will distribute the Q50 Stent Graft Balloon Catheter which is designed for use with aortic stent grafts that treat abdominal aortic aneurysms (AAA) and thoracic aortic aneurysms (TAA).

The FDA cleared the catheter for marketing in October 2009. This partnership allows Gore to provide customers with a balloon catheter for modeling and occlusion use with the Gore Excluder AAA Endoprosthesis and all other aortic stent grafts.

The QXMédical device is a full occlusion balloon catheter that helps aortic stent grafts to fully expand and seal in vessel diameters ranging from 10 mm – 50 mm. It offers a short, flexible tip that increases trackability through challenging anatomy, and a compliant polyurethane balloon that inflates and deflates rapidly to give physicians more control.

The Q50 Stent Graft Balloon Catheter offers the broadest inflation diameter range available on the market and is compatible with standard 0.035" guidewires and low-profile 12 Fr introducer sheaths. With 65 cm and 100 cm length pushable catheter shafts in an 8 Fr diameter, the device accommodates both abdominal and thoracic applications.

In other agreements news:

- **Mach 7 Technologies** (Schaumburg, Illinois) reported that it has formalized a product distribution agreement with **Data Distributing** (Santa Cruz, California), an international leader in providing digital image dis-

Today's MDD food for med-tech thought

"If we persist in guidances that limit new products being introduced into the U.S.," the consequences will be higher costs, triage, barriers to access in rural areas, "and limiting the ability of vendors to produce better processing algorithms."

— Margarita Zuley, PhD, speaking before an FDA panel which was held to address the 2008 guidance for 510(k) applications for full-field digital mammography systems, "FDA seen as obstructionist on FFDM clearance question," pp. 1, 6.

tribution and archiving solutions to the medical industry. Under the terms of the agreement, Data Distributing will market Mach 7 Technologies' Keystone Suite, an Enterprise Image Management Platform, in the U.S.

The agreement provides Mach 7 Technologies with expanded distribution of its flagship software product, while enabling Data Distributing to enter the fast growing PACS-neutral technology market with an innovative product solution. With Keystone Suite, Data Distributing gains a proven product to design and implement solutions for PACS-Neutral Archiving, Intelligent Image Navigation, DICOM Attribute Normalization, Open EMR Image Enablement, and monitoring of the Enterprise Image Continuum.

- **RAM Technologies** (Fort Washington, Pennsylvania) a maker of healthcare administration software, has chosen to team with IBM to bring industry-leading claims management solutions to market for small to mid-size healthcare payer organizations.

Insurance companies and health care payers are looking for new ways to simplify claims processing and take advantage of the coming wave of digital infrastructures throughout the healthcare industry that will connect doc-

See Agreements, Page 5

MEDICAL DEVICE DAILY™ (ISSN# 1541-0617) is published every business day by AHC Media LLC, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305, U.S.A. Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. MEDICAL DEVICE DAILY™ is a trademark of AHC Media LLC, a Thompson Publishing Group company. Copyright © 2009 AHC Media LLC. All Rights Reserved. No part of this publication may be reproduced without the written consent of AHC Media LLC. (GST Registration Number R128870672)

ATLANTA NEWSROOM: Managing Editor: **Holland Johnson**.
Washington Editor: **Mark McCarty**.
Staff Writers: **Omar Ford, Amanda Pedersen** and **Lynn Yoffee**.
Senior Production Editor: **Rob Kimball**.

BUSINESS OFFICE: Senior Vice President/Group Publisher: **Donald R. Johnston**.
Marketing Coordinator: **Sonia Blanco**.
Account Representatives: **Bob Sobel, Chris Wiley**.

REPRINTS: For photocopy rights or reprints, please call **Stephen Vance** at (404) 262-5511 or e-mail him at stephen.vance@ahcmedia.com.

SUBSCRIBER INFORMATION

Please call **(800) 688-2421** to subscribe or if you have fax transmission problems. Outside U.S. and Canada, call **(404) 262-5476**. Our customer service hours are 8:30 a.m. to 6:00 p.m. EST.

EDITORIAL

Holland Johnson, **(404) 262-5540**
Amanda Pedersen, **(229) 471-4212**
Omar Ford, **(404) 262-5546**
Lynn Yoffee, **(770) 361-4789**
Mark McCarty, **(703) 268-5690**

SVP/GROUP PUBLISHER

Donald R. Johnston,
(404) 262-5439

INTERNET

www.medicaldevicedaily.com



Abbott, BG, in pact to develop assay for new HF biomarker

By AMANDA PEDERSEN

Medical Device Daily Staff Writer

Abbott (Abbott Park, Illinois) and **BG Medicine** (Waltham, Massachusetts) have agreed to develop a new heart failure test for galectin-3, a new biomarker that may play a role in detecting the development and progression of heart failure.

"Abbott has a very long history of leadership in cardiac tests and biomarkers so we're always looking for new ways to diagnose and help provide early diagnosis of heart disease," Ann Fahey-Widman, an Abbott spokeswoman, told *Medical Device Daily*.

Abbott said the assay would be developed for its Architect immunochemistry instrument platform, specifically the company's i1000SR and i2000SR instruments. The agreement grants Abbott a license to BG Medicine's intellectual property related to galectin-3.

Financial terms were not disclosed. Also, Fahey-Widman said Abbott is not disclosing any specifics about the agreement.

The new test will "add to the existing very strong cardiac testing capabilities that we already have," Fahey-Widman said. She noted that heart failure is one of the most costly medical conditions in the world, and that in the U.S. alone, 37% of Medicare dollars are spent on heart conditions every year.

"Novel markers like galectin-3 have the potential to make important contributions to improving patient and economic outcomes as we work to better understand this deadly and costly disease," Michael Warmouth, senior VP of diagnostics products at Abbott, said in a company statement.

According to Abbott and BG, Galectin-3 is a protein that plays an integral role in the biological functions related to the initiation and progression of cardiac fibrosis and scarring, which is a leading cause of heart failure. Several studies have shown that galectin-3 may provide valuable insight about heart failure and its underlying disease processes, the companies said.

"This development and commercialization partnership with Abbott is an exciting opportunity to explore a promising diagnostic test with broad applicability in cardiovascular disease on a leading laboratory platform," said Pieter Muntendam, MD, president/CEO of BG Medicine. He added that BG's "strong life science discovery research program combined with Abbott's scientific and development leadership will enable us to bring important new tests to patients and laboratories."

BG says it expects to launch an optimized assay for galectin-3 measurements in plasma or serum later in 2009 subject to FDA clearance and obtaining the Euro-

pean CE mark.

According to BG, heart failure is one of the few conditions left that is described and managed on the basis of its signs and symptoms and not on the basis of the underlying disease process. Many other conditions that once were like this have advanced to the point that physicians understand the disease process and use disease-modifying therapy as opposed to therapies to manage the signs and symptoms, BG noted. Galectin-3 may help bring heart failure in the era of targeted disease-modifying therapy, the company said.

BG said that the role of galectin-3 in heart failure was a surprise finding. A group of researchers in The Netherlands studied a rat model of heart failure and found that rats with elevated activity of the galectin-3 gene went on to develop heart failure. The researchers performed a series of studies, the company said, including one in which the galectin-3 protein was administered in the space surrounding the heart. This exposure to galectin-3 induced collagen content in the left ventricle of the heart and reduced the heart's ability to pump normally, BG said.

The researchers also took biopsies from patients undergoing surgery and demonstrated elevated galectin-3 in the hearts of patients with heart failure as compared to those without it. ■

Amanda Pedersen, 229-471-4212;
amanda.pedersen@ahcmedia.com

Court report

Court affirms verdict favoring Ventas over HCP in fraud case

A Medical Device Daily Staff Report

Ventas (Chicago) reported that the U.S. District Court for the Western District of Kentucky has denied **HCP's** (Long Beach, California) post-trial motions requesting judgment in its favor and, alternatively, for a new trial in connection with the company's verdict against HCP for tortious interference with business expectation. The court also affirmed the jury's verdict in favor of Ventas for \$101,672,807 in compensatory damages. The case arose out of the company's acquisition of Sunrise Senior Living REIT in April 2007.

The court stated in its memorandum opinion that the evidence "allowed a reasonable juror to determine that [HCP's] actions constituted fraudulent misrepresentations" and permitted "the jury's conclusion that the [HCP] press release was misleading and deceitful."

Both companies are healthcare real estate investment trusts. ■

*Deals roundup***Kimberly-Clark to acquire remaining I-Flow shares****A Medical Device Daily Staff Report**

Kimberly-Clark (Dallas) reported that the initial offering period of its tender offer for all outstanding shares of common stock of **I-Flow** (Lake Forest, California) expired at midnight EST on Tuesday. The offer was conducted through Boxer Acquisition, a wholly-owned subsidiary of Kimberly-Clark.

The depositary for the tender offer has advised Kimberly-Clark that, as of the expiration of the initial offering period, a total of about 21,279,272 shares of I-Flow common stock were validly tendered and not validly withdrawn, representing about 87.1% of the outstanding shares of I-Flow common stock. All shares that were validly tendered and not validly withdrawn during the initial offering period have been accepted for payment.

The depositary has also advised Kimberly-Clark that it has received commitments to tender approximately 506,582 additional shares under the guaranteed delivery procedures described in the offer.

Kimberly-Clark also said that it is commencing through Boxer Acquisition, a subsequent offering period of its tender offer to acquire all remaining shares of I-Flow common stock. This subsequent offering period will expire at 5:00 p.m. EST on Nov. 23, unless extended.

Any shares validly tendered during this subsequent offering period will be accepted immediately for payment, and tendering stockholders will thereafter promptly be paid \$12.65 in cash for each share of I-Flow common stock tendered, without interest and less any required withholding taxes. This is the same amount per share that was offered and paid in the initial offering period.

The subsequent offering period enables holders of shares of I-Flow common stock who did not tender during the initial offering period to participate in the offer and receive the offer price on an expedited basis rather than waiting until the completion of the merger. Shares tendered during this subsequent offering period cannot be delivered by the guaranteed delivery procedure and may not be withdrawn. In addition, shares validly tendered during the initial offering period may not be withdrawn during the subsequent offering period.

Following the expiration of the subsequent offering period, Kimberly-Clark intends to complete the acquisition of all remaining shares of I-Flow through a merger. Following the completion of the merger, I-Flow will operate as part of Kimberly-Clark Health Care.

In other dealmaking news, **Expression Pathology** (Rockville, Maryland) said that **Mayo Clinic** (Rochester, Minnesota) has licensed non-exclusive rights to Expression Pathology's Liquid Tissue patent for use in diagnosis of sys-

temic amyloidosis in formalin-fixed tissue.

Liquid Tissue methodology enables solubilization of proteins for mass spectrometric analysis of formalin-fixed paraffin-embedded (FFPE) tissue, the standard form of preserved patient tissue used in clinical pathology testing worldwide. Mayo Clinic has applied the technology to develop a specific and sensitive mass spectrometry based method for diagnosis and classification of amyloidosis in routine biopsy specimens, in a format that is rapid and readily applicable in a clinical setting. This test is being offered to patients worldwide through Mayo Medical Laboratories, Mayo Clinic's reference laboratory.

With 50,000 diagnosed cases every year worldwide amyloidosis can be a localized or systemic disease, characterized by organ function impairment, sometimes as severe as cardiac and/or renal failure. Subtyping of cases is critical as management of the disease differs radically, from drug therapies to major organ transplants.

"Detailed mass spectrometry analysis of proteins related to specific disease conditions in FFPE tissue is opening huge opportunities in personalized medicine to relate those measurements to patient treatment decisions," said Casey Eitner, president/CEO of Expression Pathology. "We are delighted that Mayo Clinic has applied our Liquid Tissue methodology to solve a difficult medical problem."

Financial terms of the agreement were not disclosed. ■

*Patent watch***Aperio gains license for Image Processing tech****A Medical Device Daily Staff Report**

Aperio Technologies, (Vista, California) a global leader in digital pathology for the healthcare and life sciences industry, reported that the United States Patent and Trademark Office has issued the company patent No. 7,602,524 titled "Image Processing and Analysis Framework."

The '524 patent describes a system and method for processing and analyzing digital slide images comprised of an algorithm server that executes image analysis algorithms on digital (whole) slide images, or on sub-regions of a digital slide image.

With this patent, Aperio extends its intellectual property portfolio to image analysis processing using a client/server architecture and distribution of digital pathology information, including support for multiple servers. A client/server architecture is a key aspect of making digital pathology useful in large labs, facilitating a more efficient workflow for busy clinicians and researchers. ■

*Financings roundup***Quest prices tender offer to buy back senior notes****A Medical Device Daily Staff Report**

Quest Diagnostics (Madison, New Jersey) reported the pricing of its tender offer to buy back senior notes due 2010 and 2011.

The company said it will pay \$1,037.19 for each \$1,000 principal amount of its 5.125% notes due 2010. It will also pay \$1,099.40 for each \$1,000 principal amount of its 7.50% notes due 2011.

The tender offer will expire today, unless extended, Quest said.

BofA Merrill Lynch will serve as global coordinator and joint lead dealer manager and Morgan Stanley, RBS and Wells Fargo Securities will serve as joint lead dealer managers. Global Bondholder Services will serve as the depository and as the information agent for the tender offer.

In other financing activity:

- **Emergency Medical Services Corporation** (EMSC; Greenwood Village, Colorado) said it intends to commence a public secondary offering of 6 million shares of class A common stock.

The company said it would not receive any proceeds from the offering. The shares are being offered primarily by affiliates of Onex. The Onex entities' shares represent roughly 26% of the Onex entities' equity interests in EMSC. After giving effect to this offering, the Onex entities will own about 39% of the equity interests in EMSC and about 86% of the combined voting power.

BofA Merrill Lynch, Goldman, Sachs & Co. and J.P. Morgan Securities are acting as joint bookrunners for the offering. The underwriters will have a 30-day option to purchase up to an additional 15% of the offered amount of the class A common stock sold.

- **HealthSouth** (Birmingham, Alabama) reported the pricing of its underwritten public offering of \$290 million in aggregate principal amount of its 8.125% senior notes due Feb. 15, 2020 at a public offering price of 98.327% of the principal amount. The company will pay interest on the notes semi-annually in arrears on Feb. 15 and Aug. 15 of each year, beginning in 2010. The notes will be jointly and severally guaranteed on a senior unsecured basis by all of its existing and future subsidiaries that guarantee borrowings under the company's credit agreement and certain of its outstanding senior notes.

The company intends to use the net proceeds from this offering, together with cash on hand, to fund its tender offer for all of its outstanding floating rate senior notes due 2014, including any applicable accrued and unpaid interest on such notes, and to redeem any floating rate senior notes due 2014 that may remain outstanding following completion of the tender offer, including the payment of any appli-

cable accrued and unpaid interest on such notes. The notes offering is expected to close Dec. 1 and is conditioned upon the acceptance for purchase by the company of notes tendered in the tender offer prior to 5 p.m. EST on Nov. 30 and the satisfaction of other customary closing conditions.

The joint book-running managers for this offering are J.P. Morgan Securities, Barclays Capital, and Goldman, Sachs & Co. ■

Agreements*Continued from Page 2*

tors, administrators and payer organizations to improve customer service.

- **Novian Health** (Chicago) reported an agreement with **Tower Radiology Center** (Tampa, Florida) to provide the Novilase laser treatment to treat benign breast lumps.

Novilase is a minimally invasive procedure that uses heat from a laser to destroy benign breast tumors, (e.g., fibroadenomas).

These breast lumps appear most often in premenopausal women. Novilase, an alternative to surgical removal, is safe, effective, and less risky than surgery while providing a superior cosmetic outcome. Novilase is FDA-cleared for this indication and is not an experimental procedure.

- **iCAD**, (Nashua, New Hampshire) an industry-leading provider of advanced image analysis and workflow solutions for the early identification of cancer, reported a strategic partnership with the **AdMeTech Foundation** (Boston), a non-profit organization with a mission to end prostate cancer as a patient care crisis and socio-economic problem.

iCAD will be joining the Industrial Liaison Board of AdMeTech's International Prostate MRI Working Group, which fosters dialogue between leading physicians, prostate cancer advocacy groups and industry to facilitate important technological breakthroughs to provide men with more accurate diagnostics for early detection and treatment of prostate cancer. AdMeTech's research program was recently funded by Telemedicine and Advanced Technologies Research Center of the Department of Defense through a peer review process.

- **EraGen Biosciences** (Madison, Wisconsin) a developer of molecular reagents for the *in vitro* diagnostics (IVD) market, and **illumina** (San Diego) reported the formation of a strategic partnership and the execution of non-exclusive licensing agreements.

Under these licensing agreements, EraGen Biosciences will have access to illumina's BeadXpress platform for the continued development of molecular-based, high-throughput clinical multiplexed assays with its MultiCode PLx technology. EraGen has proven commercial success with multiplex molecular assays for the infectious disease and genetic disorder markets. illumina has licensed EraGen's MultiCode-PLx technology for the life sciences, research and clinical markets. ■

Washington

Continued from Page 1

FFDMs “is shameful.”

However, the final vote of the panel indicated that the panelists were unfazed by the views of the experts who addressed the panel despite the fact that among the speakers was the leader of the largest-ever study of digital mammography, the DMIST (Digital Mammographic Imaging Screening Trial) study.

The outcome of the meeting dovetails with the recent announcement by the U.S. Preventive Services Task Force that women between the ages of 40 and 50 should not be screened for breast cancer (see accompanying article), but both developments seem headed for a showdown with American women, who are ill-disposed to take anything for granted where breast cancer is concerned.

FDA's latest guidance on 510(k) applications for FFDM systems, a technology that has been in play for the better part of two decades, came out in May 2008 and followed by two years a previous meeting of the panel during which panelists recommended that the agency regulate FFDM systems as Class II devices with special controls (*Medical Device Daily*, May 25, 2006). Some firms took a run at the 510(k) route in the 1990s, but those efforts fell apart because studies indicated too much variance between readers of the films. All the same, the three-plus years since the 2006 panel meeting during which the panel made the recommendation helped fuel accusations that FDA is dragging its feet.

One of the agency's critics was Etta Pisano, MD, of the **University of North Carolina School of Medicine** (Chapel Hill, North Carolina), who led the parade of observers that offered a generous portion of blowback aimed squarely at FDA. Pisano's standing on the issue was especially solid inasmuch as she served as the lead investigator of the DMIST trial.

Pisano remarked that the DMIST trial was more than sufficiently exhaustive, enrolling nearly 50,000 patients to test digital mammography against its analog antecedent, film mammography. Pisano said, “these results found significantly improved sensitivity” in the study arm, and while she acknowledged early skepticism regarding digital technology, “the time for skepticism has passed,” she said.

Pisano asserted that FFDM “was specifically developed to address the problems with film” and was in part the result of a push on the part of the National Institutes of Health commencing in 1992 to improve mammography.

“FDA was there for the design of DMIST,” Pisano said, “along with many other stakeholders.” She said she earlier supported the necessity of a PMA because of concerns about spatial resolution, but remarked that “the draft guidelines of last [year] would be unethical today” because of the implicit need for double exposure to X-radiation. “It is my considered judgment as a private citizen that any study that requires double exposure . . . should not be IRB

Task force recommendation an odd backdrop to panel meeting

The timing of Tuesday's meeting of the radiology devices advisory committee fell precisely one day after the U.S. Preventive Services Task Force (USPSTF) announced its recommendation regarding breast cancer screening, an announcement that was reviewed in the *Oncology Extra* in Tuesday's edition of *Medical Device Daily*.

The announcement by USPSTF stated that breast cancer screening for women between the ages of 40 and 49 should not be universal, but rather “should be an individual one and take patient context into account, including the patient's values regarding specific benefits and harms.”

The announcement was not well received, to put it mildly, and reverses a policy announcement made by USPSTF earlier this decade that led to annual screening for this population. The oscillation on this issue seems to mirror the question of how aggressively – and even whether – to treat men for high levels of prostate-specific antigen and/or prostatic hyperplasia, another medical question that has generated enormous controversy.

According to the **Breast Imaging Commission**, part of the **American College of Radiology** (Reston, Virginia), the adoption of that recommendation could reverse “two decades of decline in breast cancer mortality” and result in “countless American women [dying] needlessly from breast cancer each year.” The BIC statement also notes that the guideline was crafted by “a federal government-funded committee with no medical imaging representation” and that the announcement comes across as “a conscious decision to ration care.”

The **American Cancer Society** (Atlanta) was no more enthusiastic than others about the move. ACS's Nov. 16 statement notes that “the most recent data show us that approximately 17% of breast cancer deaths occurred in women who were diagnosed in their 40s, and 22% occurred in women diagnosed in their 50s.” ACR acknowledged “the limitations of mammography,” adding that the association “remain[s] committed to finding better tests,” and is currently “funding a large study to improve the accuracy of mammography.” The statement, however, makes no mention of the nature of the study.

– Mark McCarty

approved.”

“Clinical studies are not only not needed but, in my mind, are unethical,” Pisano said, adding that because digital systems are widely available, “it is going to be extremely difficult to enroll” enough patients in a trial that calls for randomization to film.

See Washington, Page 7

Washington

Continued from Page 6

As is well known, the DMIST study completed enrollment of almost 50,000 women in November 2003 to test FFDM against film mammography, and resulted in essentially identical rates of detection of suspicious neoplasms. One of the long-standing arguments in favor of FFDM is that the technology cuts down on exposure to X-radiation by as much as 15%, but some estimates are that the reduction runs as high as 25%. However, the technology scored better in women between the ages of 40 and 50 and also did better in detecting abnormalities located in relatively dense breast tissue.

Margarita Zuley, PhD, spoke on behalf of the **American College of Radiology** (ACR; Reston, Virginia) and the **Society of Breast Imaging** (Reston, Virginia), argued to the panel that the approach embodied in the 2008 guidance is more burdensome than the least burdensome approach.

Zuley maintained that ACR's phantom test for mammography is more than adequate to determine whether a new product is equivalent to a predicate in clinical terms. She also asserted that FDA has available to it a raft of data from across the globe.

DMIST "was a wonderful study," Zuley said, but "there are many other studies out there" that have collectively captured data from more than 3.4 million women from across the globe. "FFDM has performed at least as well as film" in those studies, and film mammography offers "no difference in positive predictive value," she said.

"We already have all the evidence available to us" to back equivalence, Zuley continued, adding that "the safety and effectiveness" of FFDM technology has been established.

As for the differences between screening and diagnosis, Zuley observed that "if we look at all the studies I've presented . . . they all had at least one year of follow-up," which demonstrates technological equivalence beyond any reasonable doubt.

"If we persist in guidances that limit new products being introduced into the U.S.," Zuley said, the consequences will be higher costs, triage, barriers to access in rural areas, "and limiting the ability of vendors to produce better processing algorithms."

FDAer asserts clinical testing essential

Robert Smith, MD, of the radiological devices branch at CDRH, said he did not believe that the question of the day was whether a 510(k) can be cleared for an FFDM system by means of physical lab testing, with or without phantom testing. "I believe that the question is what quantity and quality of clinical performance does FDA need" to establish equivalence in both screening and diagnosis.

"Breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer-related deaths

among women in the U.S.," Smith acknowledged, but nonetheless held that "the relationship between image quality and lesion detection needs thorough analysis and further studies."

Despite the fact that DMIST employed four FFDM systems, Smith alleged that DMIST taught nothing "about how to compare two different FFDM devices." He said that more than 8,700 accredited facilities are operating more than 12,000 machines, and that "approximately 59% of the accredited machines are FFDM" units.

Smith also cited the 2001 PMA guidance for FFDM, which he noted includes the statement that "a clear correlation between design/bench parameters and clinical performance has yet to be established."

In the end, the panel concluded that clinical data are needed to demonstrate substantial equivalence unless both the software and the hardware in the predicate and tested device are identical or nearly so. The conclusion was based on the use of evaluation standards set by ACR in 2007, but a formal consensus was not reached by the panel on the number of cases needed to establish equivalence. In any event, two cases were seen as insufficient, but a couple of panelists were of the view that 30 cases are more than what would be needed in most cases.

However, the discussion included a series of remarks that suggested that if clinical data are needed, a sponsor might have to enroll as many as 4,000-5,000 subjects to sufficiently power a study of whether the study article offers a similarly reliable view of the general features of a patient's breast tissue. A multiple-reader/multiple-case study might shave these numbers down.

On the question of whether stress testing is necessary in a clinical evaluation of a system, the panel concluded that in many instances it would not be, but that when stress testing is desirable, it should include a check on detection of masses with any one of several characteristics, including microcalcifications of diameters of 300-500 microns. ■

Mark McCarty, 703-268-5690
mark.mccarty@ahcmedia.com

Sign up for our free, weekly
e-mail blog, **Perspectives**, comment-
ing on today's med-tech.

Go to **www.MedicalDeviceDaily.com** and sign up.

Medica

Continued from Page 1

effect only amplified by the cacophony of foreign languages in crowded corridors or shouted halfway around the world through portable phones.

Exhibitors cover every category in the healthcare supply chain from disposable bedpans to high-end scanners including laboratory, diagnostics, physical therapy, orthopedics, consumables, health information systems, furnishings, and textiles.

A fully equipped ambulance or integrated operating room can be bought off the showroom floor, and where medical device manufacturers rarely expect direct sales at a trade show, filling the order book is precisely the goal of executives on the stands at Medica.

Hospital administrators from Germany, Austria and German-speaking Switzerland are regulars at Medica to price out new capital acquisitions or everyday supply contracts in face-to-face negotiations.

As part of Germany's recent €4.7 billion (\$7 billion) Economic Stimulus Package, hospitals will receive up to €1 billion (\$1.5 billion) for the modernization of local institutions with an estimated 45% allocated to capital equipment purchases.

Medica remains a militantly German event, despite 40 years of international influence, and a showcase for German industry head-to-head in the massive exhibition halls with an invasion of Asian competitors, many of whom began in business less than 10 years ago thanks to technology transfers from German companies.

In a survey of 110 of its 222 members released this week during its 10th Media Seminar, the German medical device trade association **BVMed** (Berlin) reported participating companies said they grew by an average of just under 4% so far this year and are continuing to hire new staff.

In addition to the stimulus package funding, Germany enacted the Innovation Clause (NUB; Neue Untersuchungs und Behandlungsmethoden) to expedite reimbursement for the adoption of new technologies and treatments in hospitals (*Medical Device Daily*, Sept. 29, 2009).

In 2009 7,500 NUB applications were approved and 87 new treatments were included in the German DRG system, boosting the early adoption, and sales, of advanced technologies.

"The aim is a competition for the best possible medical technology provision, in order to buck the trend of cut-price medicine," according to BVMed CEO Joachim M. Schmitt, adding "The focus must lie on the quality of medical care instead of on price alone."

Fifty-eight percent of member companies said the focus on healthcare delivery quality instead of price focus has boosted demand for their products.

It is not only the Asians who compete fiercely for a share in the European, and especially German, market, the

largest on the continent for population and spending.

The large U.S. pavilion at Medica stands as a solid reminder that American companies tend to dominate key markets, such as orthopedics. (*MDD*, Oct 29, 2008)

In a survey released at Medica for the British Standards Institution (BSI; Bristol, UK) of 1,100 medical technology executives, **Emergo Group Consulting** (Austin, Texas) found a fourth of all companies targeting Europe as the single new international market they hope to enter in 2010.

Europe was the dominate target among the largest companies among the survey respondents, of whom 60% are based in the U.S.

It is not only Medica but the medical technology sector generally that continues to advance each year.

In the face of the economic crisis last year 64% of respondents to the BSI survey said they nonetheless expected sales to increase in 2009, while this year a modest but steady increase was reported among executives, of whom 70% said they were looking forward to greater sales in 2010.

Both European and U.S. companies reported positive growth from international markets during the previous three months, and a modest increase in exports from North American companies were attributed in part to the weak U.S. dollar compared to one year ago. ■

Med-Tech Notes

AET helps hospitals connect remotely

Telemedicine solution provider **American Educational Telecommunications** (AET; Omaha, Nebraska) said it completed a first of its kind, real-time remote diagnosis of a newborn baby's heart murmur between **Faith Regional Health Services** (Norfolk, Nebraska) and **Children's Hospital & Medical Center** (Omaha). The diagnosis used wireless video conferencing technology through a mobile camera device connected to an ultrasound machine.

To perform the remote diagnosis, a Phillips 5500 ultrasound machine at Faith Regional Health Services was connected to a Librestream Onsite 2000R video device through an S-video connection. The video was securely encrypted by way of AET's secured network technology system and streamed live between medical centers.

The telemedicine technology used was a result of the combined efforts of AET, their remote wireless device provider, Librestream; Phillips, and the IT support from AET and both hospitals. This was a first of its kind use of the combined technology. AET was able to set up the secure network infrastructure between Faith Regional Health Services and Children's Hospital within 30 minutes. The resultant diagnosis alleviated the fears of everyone involved, but particularly the parents of the newborn.

Europe

Continued from Page 1

the size of a cell phone that the patient attaches to his belt for about 45 minutes per treatment, is synchronized to his cardiac cycle to stimulate the muscles of the calves and thighs to make them contract counter to the heart's beating. This well-established counterpulsation action results in increased blood flow to the heart muscle while decreasing the heart's workload.

Ellipse gets CE mark for Magec system

Ellipse Technologies (Irvine, California) said it has received the CE mark for its Magec technology for the treatment of spinal deformity. The first application for this technology is for the treatment of spinal scoliosis in young children and teenagers..

Ellipse has developed the technology for minimally invasive, and ultimately, non-invasive, orthopedic deformity prevention and management. Ellipse has filed numerous patent applications for the use of the technology for a broad range of clinical applications. The company is currently concentrating on spinal and orthopedic trauma applications. The company describes the technology as a "breakthrough medical device technology capable of non-invasively adjusting implants within the human body from outside the body via remote control."

Currently, young children, pre-teenagers and teenagers with spinal scoliosis have few medical options. The standard treatment requires a series of five to ten highly invasive surgical operations with large surgical incisions and long recovery times performed over a number of years – a process so undesirable that 67% of the diagnosed patients refuse the surgical option.

With the Magec technology, a single minimally invasive surgical procedure is completed. Then, during a series of simple outpatient visits, the physician will dynamically adjust the Magec technology from outside the body via the Magec system's control unit, thus eliminating the need for multiple highly invasive surgical procedures. The system is designed to provide for spinal motion preservation, no long term permanent implant, and minimal trauma and scarring.

EDDA earns CE mark for IQQA-Liver

EDDA Technology (Princeton, New Jersey) reported that it received the CE mark for its new release of IQQA-Liver, an advanced clinical application designed to enhance efficiency and precision in liver imaging evaluation and treatment planning.

IQQA-Liver provides a comprehensive toolset for highly automated quantitative volumetric evaluation of liver, liver lobes and segments, hepatic lesions, and vascular structures including artery, portal veins and hepatic veins from CT data.

Through EDDA's proprietary IQQA PACS- and web-

enabling technology, IQQA-Liver can be readily deployed onto any existing hospital PACS workstations or via the web so that data evaluation and treatment planning results can be shared quickly anywhere anytime among authorized physicians.

EDDA is a clinical computer solution provider in diagnostic imaging and analysis. It offers a series of new generation software products to enable early detection of diseases, and enhance efficiency and precision in diagnosis and treatment. ■

Med-Tech Notes

Sanuwave Health changes stock symbol to SNWV

Sanuwave Health (Alpharetta, Georgia), an emerging medical technology company focused on the development and commercialization of non-invasive, biological response activating devices in the regenerative medicine area, has changed its stock symbol to "SNWV" effective Nov. 12. The company's name was changed to Sanuwave Health, from Rub Music Enterprises on Nov. 5. The company will continue to do business as Sanuwave.

Christopher Cashman, president/CEO of Sanuwave said, "The change in stock symbol to "SNWV" more closely aligns with our new corporate name and our branding. We believe these changes will help enhance our investor relations and business development efforts, as we further our communications as a public company, and work towards the completion of an Investigational Device Exemption wound care study for diabetic foot ulcers. We look forward to continuing to execute our business plan as we prepare to move our products through clinical development and commercialization."

NeuroStar TMS Therapy receives award

Neuronetics' (Malvern, Pennsylvania) NeuroStar Transcranial Magnetic Stimulation (TMS) Therapy has been selected by Popular Science as one of the "Best of What's New" in the health category for 2009. NeuroStar TMS Therapy is the first and only non-systemic (does not circulate in the bloodstream) and non-invasive (does not involve surgery) depression treatment cleared by the FDA. NeuroStar is effective and safe in the treatment of depression; it provides a new and unique option for the millions of depressed patients who have not benefited from prior antidepressant medications.

NeuroStar TMS Therapy was cleared by the FDA in October 2008. The TMS Therapy is specifically indicated for the treatment of Major Depressive Disorder in adult patients who have failed to achieve satisfactory improvement from one prior antidepressant medication at or above the minimal effective dose and duration in the current episode.

Ekos

Continued from Page 1

than the previous version of the device, the Mach4.

"We're always striving to improve the speed," Hubert told *Medical Device Daily*.

For simplicity, the company has eliminated user inputs, which can be safely automated without requiring operator attention, Hubert said.

"The system is much smarter. A world-class vascular innovation forum like the VEITHsymposium is the ideal event at which to launch the Mach4e."

Hubert told *MDD* that when Ekos launched the second-generation device last year the company was already thinking ahead to the next upgrade. Ekos built into the hardware the ability to upgrade, he said. So all Ekos' customers have to do, if they already have the Mach4, is upgrade to the new generation via an easy software download, he said.

"In fact, their entire inventory of devices . . . it will recognize the new upgrade so all of their inventory automatically performs to the new level," Hubert said.

The EkoSonic is FDA-cleared for controlled and selective infusion of physician-specified fluids, including thrombolytic, into the peripheral vasculature. Ekos said the device is currently used to treat patients with peripheral arterial occlusions and deep vein thrombosis and additional applications are being investigated.

So far, customer feedback has been positive, Hubert said.

"We actually had a pre-launch where we had some of our systems go out into the market to get a feel for the products actual ability and, true to form, what we saw in the lab has been what we're getting," Hubert said.

According to the company, providers can "Ekos it anywhere" in the periphery – veins, arteries, IVC filters and difficult-to-reach places such as behind valves – and the device exposes clot to a greater drug uptake.

Ekos touts several other benefits of the Mach4e, including: thrombus of any size, shape, volume and age can be treated with less lab time; uses 50% to 70% less lytic drug, no thrombus fracture or breakage reducing the risk of distal embolism; no hemolysis, no damage to valves or vascular wall; a higher level of vessel patency, removes the thrombus more completely, possibly reducing the risk of post-thrombotic syndrome.

"If you look at where thrombus occurs, it occurs on the venous side, it occurs on the arterial side, it is small, it is large . . . you can Ekos any size, any length on the venous side, on the arterial side . . . fundamentally anywhere," Hubert said. "We have no limits."

Ekos said it is currently participating in the ATTRACT trial which will evaluate the long-term benefits of using ultrasound catheter-directed thrombolysis for removal of clot.

The VEITHsymposium, now in its fourth decade, provides vascular surgeons, interventional radiologists, interventional cardiologists and other vascular specialists with

a format to learn about what is new and important in the treatment of vascular disease. The five-day event, which kicked off yesterday in New York, features presentations from vascular specialists with emphasis on the latest advances, changing concepts in diagnosis and management, pressing controversies and new techniques. ■

Amanda Pedersen, 229-471-4212;
amanda.pedersen@ahcmedia.com

Product Briefs

- **Doctors Research Group** (Southbury, Connecticut) has received FDA approval for the Kryptonite bone cement for cranioplasty applications. The company says that the cement represents a major advancement in treating cranial defects due to trauma and surgery and is the first non-toxic, low exotherm cement and bone void filler approved for cranioplasty applications that offers strong adhesive properties to organic and inorganic materials. Kryptonite bone cement polymerizes in stages, offering surgeons the option to inject it as a liquid, to secure bone-to-bone adhesion, or to shape it as a moldable putty, to create form fitting plates which eliminate the need for painful bone grafts that prolong patient recovery times.

- **GE Healthcare** (Waukesha, Wisconsin) reported results from its ongoing customer evaluation of Gemstone Spectral Imaging, a technology aiming to enhance CT's diagnostic capability. Gemstone Spectral Imaging is an available option for Discovery CT750HD systems. GE says one major clinical advantage of Spectral Imaging is to aid in the characterization of lesions. It introduces a new ability to quantify and separate materials – such as calcium, iodine and water – and helps clinicians determine whether lesions are enhancing. In cases where Spectral Imaging avoids additional diagnostic tests, healthcare costs and patient anxiety can be avoided.

- **Nanosphere** (Northbrook, Illinois) said it submitted a 510(k) application to the FDA for its cardiac troponin I test that the company believes will provide early and sensitive diagnosis of myocardial infarction and risk stratification for acute coronary syndromes. "We are pleased to submit this application and look forward to completing the regulatory process and bringing this important assay to market," said William Moffitt, Nanosphere's president/CEO. Moffitt added, "There is growing evidence that early detection of cardiac troponin using sensitive assays is a critical test to aid in the diagnosis and treatment of myocardial infarction and in the risk stratification of patients with acute coronary syndrome."

MDD'S ORTHO EXTRA

ADDITIONAL DEVELOPMENTS IN ONE OF MED-TECH'S KEY SECTORS

THURSDAY, NOVEMBER 19, 2009

PAGE 1 OF 2

Keeping you up to date on recent headlines in orthopedics.

Allograft shape does not influence clinical outcomes after ACDF . . .

Researchers have found that lordotically shaped allografts did not increase cervical/sagittal alignment or improve outcomes. Maintaining a consistent segmental sagittal alignment or increasing segmental lordosis, however, was shown to be important to improved clinical outcome scores. The findings were presented at the North American Spine Society's (Burr Ridge, Illinois) 24th Annual Meeting in San Francisco.

"Device manufacturers and tissue banks offer cervical allografts that come in various sagittal profiles, including lordotic, parallel or even convex designs that, according to indications, should restore lordosis, maximize surface area contact or allow for patient-specific needs," said Alan Villavicencio, MD, director of the Minimally Invasive Spine Surgery Program, **Boulder Neurosurgical Associates** (Boulder, Colorado). "However, these statements of long-term clinical outcomes have never been tested or proven in any prospective, randomized clinical studies [or any other kind of studies]." Villavicencio and colleagues performed the first prospective, double blind, randomized study to evaluate cervical allografts in a clinical setting. The study included 122 patients who underwent single- or multi-level anterior cervical decompression and fusion (ACDF). The primary goal was to assess quantitatively and correlate sagittal alignment with clinical outcomes when lordotic or parallel allografts were used. "These study results demonstrate that the allograft shape does not have any influence on clinical outcomes and does not improve or maintain cervical sagittal alignment," Villavicencio said. "However, when we compared the changes in segmental sagittal alignment and clinical outcomes, we noticed that the maintenance or enhancement of cervical/segmental sagittal alignment was predictive of a higher degree of improvement in clinical outcome scores. The results demonstrated that if you maintain the same — even if it is kyphotic — or increase segmental cervical lordosis, the patients had a significantly higher degree of improvement in the clinical outcomes compared to the patients who had a loss of the segmental sagittal alignment," Villavicencio said. "Maintaining sagittal alignment in ACDF surgery is a critical component of patient outcomes but is not influenced by the shape of the graft being lordotic or parallel."

Researchers report good first results using blood stem cells, HA to regenerate cartilage . . .

Scientific investigators from Malaysia reported the first evidence of hyaline cartilage regeneration using intra-articular injections of autologous peripheral blood stem cells in combination with hyaluronic acid. In their clinical trial, researchers from the **Kuala Lumpur Sports Medicine Centre** and the **University Putra Malaysia** followed 10 patients with full-thickness chondral defects treated with arthroscopic multiple subchondral drilling. The investigators followed the patients for a minimum of 2 years. After surgery, investigators placed patients' operated knees on continuous passive motion for 2 hours a day for 4 weeks, as well as on partial weight-bearing for the first 6 weeks, lead investigator Khay-Yong Saw, said at the **British Orthopaedic Association** (London) Annual Congress 2009. The researchers also harvested autologous peripheral blood stem cells (PBSCs) using apheresis after surgery. To enable harvesting, an apheresis catheter was inserted into a large vein at the top of the thigh. The catheter allows blood to be passed through a cell separator, which filters out stem cells and returns the processed blood to the body, he said. The harvested PBSCs were then divided into vials and cryopreserved for future use. One week after surgery, surgeons aspirated the affected knees and began injecting five weekly 2.5-ml intra-articular injections of PBSCs mixed with 2 ml hyaluronic acid (HA). Sequential MRI scans showed that "the subchondral bone began healing and offered evidence of chondrogenesis," Saw said. Second-look arthroscopy with biopsy on four patients also confirmed chondrogenesis as well as incorporation of the newly regenerated cartilage with the surrounding articular cartilage.

25-year review shows translumbar amputation effective in extreme cases . . .

A landmark, 25-year review of cases in which surgeons had to remove the lower portion of the body from the waist down for severe pelvic bone infections shows the therapy can add years and qual-

ity of life to survivors, say researchers at **UT Southwestern Medical Center** (Dallas). The rarely performed surgery is called a hemicorporectomy or translumbar amputation, and involves removing the entire body below the waist, including legs, pelvic bone and urinary system. "It is used as a last resort on patients with potentially fatal illnesses such as certain cancers or complications from ulcers in the pelvic region that cannot otherwise be contained," said Jeffrey Janis, MD, associate professor of plastic surgery at UT Southwestern and lead author of the study, which appears in the October issue of *Plastic and Reconstructive Surgery*. "We determined that it can be effective and a reasonable consideration in some of these extreme cases." Hemicorporectomy rarely has been performed because of the very limited indications for the procedure, said senior author Robert McClelland, MD, professor emeritus of surgery at UT Southwestern. "An increasing number of veterans of Iraq and Afghanistan conflicts are surviving very severe injuries that frequently lead to permanent paraplegia and are often complicated by severe bedsores and intractable bone infection, which is potential a source of fatal sepsis. Because of this, the frequency of indications for hemicorporectomy may soon increase significantly," McClelland said. Only 57 cases of translumbar amputations had been recorded in medical literature worldwide, although the researchers suspect more have occurred since the initial referencing in 1960. The authors added to their review nine UT Southwestern patients who had received the procedure as a result of terminal pelvic osteomyelitis, a type of bone infection. About a third of the 66 patients survived at least nine years after having a hemicorporectomy. Of those who had the procedure for the bone infection, more than half survived at least nine years. Of the nine terminal pelvic osteomyelitis-driven patients treated at UT Southwestern, four remained alive after 25 years and the average survival was 11 years. "Though it is impossible to know how the survival rate would compare had these patients not undergone the amputation, given the severe disease involved, it is reasonable to assume they survived longer than they would have without surgery. Most importantly, our survivors reported that they were satisfied with their decision to have the procedure," said Janis.

Study provides 1st clear idea of how rare bone disease progresses

• • • An international team of scientists, led by researchers at the **University of Pennsylvania School of Medicine** (Philadelphia), is taking the first step in developing a treatment for a rare genetic disorder called fibrodysplasia ossificans progressiva (FOP), in which the body's skeletal muscles and soft connective tissue turns to bone, immobilizing patients over a lifetime with a second skeleton. Reporting in the November issue of the *Journal of Clinical Investigation* senior authors Eileen Shore, PhD, Professor of Genetics and Orthopedics, and Mary Mullins, PhD, Professor of Cell and Developmental Biology, with scientists in Japan and Germany, demonstrated that the mutation that causes FOP mistakenly activates a cascade of biochemical events in soft tissues that kicks off the process of bone development. The linchpin of the cellular signaling gone awry is a receptor for a bone morphogenetic protein, or BMP. The present study provides the first clear glimpse of how FOP might develop at a cellular level in the human body. Shore and co-author Frederick Kaplan, MD, the Nassau Professor of Orthopedic Molecular Medicine, and their research team, discovered the gene for FOP in 2006. "If you think of BMP proteins as the hand that turns on a water faucet, the faucet, or receptor, should stay off if you never turn the handle," Shore says. "What our experiments show is that in FOP patients the faucet is leaky, even when it is not actively turned on." BMP receptors are protein switches that help determine the fate of stem cells in which they are expressed. "The mutation is mildly activating, and so it may take time or the right tissue environment to allow the signal to tip the balance to induce bone formation, explains Shore. "This is a very important finding, because it can help explain why the disease progresses as it does." The finding that the FOP mutation changes the BMP receptor such that it is effectively on most of the time gives Shore and colleagues a target to shoot for in potentially controlling the disease. In experiments by Qi Shen, a postdoctoral fellow in the Shore-Kaplan lab and Shawn Little, a PhD student in the Mullins lab, the team found, using both cultured cells and zebrafish, that the specific mutation modifies ACVRI in such a way that it acts as if it has been signaled by BMP, even when it hasn't. The experiments further show that the mutant ACVRI receptor alters the usual binding of an ACVRI partner protein, FKBPIA, which normally keeps the ACVRI receptor off in the absence of BMP. The result is activation of a cell-signaling cascade that culminates in changes in gene expression, and ultimately, in the formation of new bone. "FKBPIA is like the safety pin in a hand grenade," says Kaplan.

– **Compiled by Holland Johnson, MDD Managing Editor**
holland.johnson@ahcmedia.com