HEART RHYTHM SOCIETY 2014

Hopkins team forging ahead with MRI as mapping tool for ablation

By Mark McCarty, Washington Editor

SAN FRANCISCO — This year’s edition of the Heart Rhythm Society (HRS; Washington) scientific sessions included a presentation by Natalia Trayanova, PhD, of Johns Hopkins (Baltimore), who is spearheading an effort at the Hopkins computational cardiology lab to come up with a model for a virtual electrophysiology lab. She said this current effort is built around “an MRI-based modeling environment,” with the objective being the acquisition of data from the level of molecules to aid in the diagnosis and treatment of heart disease for each individual patient based on that patient’s specific features.

Cardiologists debate whether ablation overused to treat afib

By Mark McCarty, Washington Editor

SAN FRANCISCO — Physicians may believe payers tend to lose their composure over even the allegation that a device is overused, but this year’s edition of the Heart Rhythm Society (HRS; Washington) scientific sessions included a discussion of whether ablation is overused to treat atrial fibrillation. The problem with this debate is that it entails the use of quality of life (QoL) measures, which ask what it means when one “feels better.”

Brian Olshansky, MD, of Mercy Medical Center (Mason City, Iowa), took the position that ablation is overused, and said he...

Venture capitalists still skittish about medical device investments

By Omar Ford, Staff Writer

ATLANTA — It shouldn’t be shocking to anyone in the medical device industry, that venture capitalists’ interest in the space has significantly decreased throughout the last few years. Trickier regulatory pathways and longer exits have been cited as reasons why investors seem so skittish about the space.

A panel comprised of venture capital investors and med-tech executives tackled some of the changes that impacted med-tech investments at the Southeastern Medical Device Association’s (Norcross, Georgia) 2014 meeting held during the investor panel last week. Tom Hawes, MD, managing director, Bluecross

Genomic tests are blurring the line between surgeon, medical oncologist

By Diana Tucker, Contributing Writer

LAS VEGAS — The key and recurring theme throughout the 15th annual meeting of the American Society of Breast Surgeons (Columbia, Maryland), recently held here, was the dominant role that genomic testing is playing in determining appropriate treatment for each newly diagnosed breast cancer patient. No longer are all newly diagnosed breast cancer patients being treated with a “one size fits all” approach, but rather each patient’s tumor is being analyzed using gene expression to aid in the determination of which therapy will produce the best response for that specific tumor.

INSIDE

SWISS CONFERENCE HIGHLIGHTS
EUROPEAN PHOTONICS TECHNOLOGIES
MEXICAN UNIVERSITY LOOKING TO UP THE ANTE ON ISOTOPE PRODUCTION

NEUROLOGY EXTRA

Staff Writer Robert Kimball on one of med-tech’s key sectors

Read this week’s Monday Special
Swiss conference highlights European photonics technologies

By Jonathan Goldstein, Israel Editor

The MedTech Investing in Europe conference, which just took place in Lausanne, Switzerland, included a large number of early stage medical startups, mainly from Europe. Switzerland is renowned for its high precision technologies and its high-quality imaging and photonics research, especially as regards Lausanne’s Swiss Federal Institute of Technology (EPFL). A large number of the 40 companies presenting at the conference addressed the fields of optical and photonic interrogation or manipulation of tissues.

Perhaps one of the most ambitious companies presenting was GNA Biosolutions ( Martinsreid, Germany) with their PCR-like analysis to detect and identify DNA segments far more rapidly than other systems today. Their ‘Laser PCR’ technology involves the ultra-fast heating of nanoparticles linked to DNA strands which generates localized PCR on these particles. The nanosystem laser-excitation bypasses the lengthier heating-cooling cycles required by conventional PCR. GNA’s Pharos400 System adds an additional feature, by means of its sensitive proprietary endpoint detection method. These two innovations enable a GNA PCR-turnaround time of around 15 minutes, the company told Medical Device Daily, compared with standard (culture) methods of 24 hours (with the best modern methods reaching taking an hour). Given the broad base of applications and the value of more rapid PCR technologies, “we are actively seeking strategic partners that could co-develop and market our technology towards specific vertical industries,” added Federico Bursgens, PhD, co-founder and CFO.

The company’s initial product line, aimed at hospital acquired infections (HAI) and specifically, antibiotic-resistant bacteria, is planned to be available for the research laboratory market in 3Q15, with a CE-approved clinical diagnostics system available during 2016. “We see great interest and potential in this initial area of HAI, where every minute counts in early assessment of disease outbreak”, Bursgens shared with MDD. German serial entrepreneur Lars Behrend PhD, previously a consultant to the company commented, “I think that this new laser PCR technology will have a big impact on the molecular diagnostic market. It is much faster and more versatile than conventional PCR techniques. We are just beginning to understand the new options we have available using this elegant form of DNA amplification.”

Another company breaking the boundaries of modern science is Nanolive (Lausanne, Switzerland). Incorporated in late 2013, Using a modality that combines holography and rotational scanning, Nanolive has developed a disruptive proprietary nano-imaging technology, to enable the exploration of a living cell in 3-D without damaging it. While already suitable for the world of academic education, the system is being adapted to have major relevance to the pharmaceutical and cosmetic industries too.

The ability to interrogate tissues in vivo in a more effective manner was addressed by a number of presenting companies. An EPFL spinoff, Samantree Technologies (Lausanne) has developed arrays of high-resolution micro-objective lenses that substitute the lens of the standard microscope towards a sub-micron high-resolution modality. Using these micro-chip systems, the company is developing an in vivo histology solution.
LATIN AMERICA

Mexican university looking to up the ante on isotope production
By Sergio Held, Staff Writer

One of Central America’s leading research centers, the Autonomous University of Mexico (UNAM in Spanish; Mexico City), is building itself into a regional radiopharmaceutical powerhouse.

The focus on this particular segment of the industry comes at a time when demand for radioactive isotopes used in conjunction with a variety of devices such as positron emission tomography (PET) scanners is on the rise and the global supply is threatened by shortages of basic elements and limited production facilities.

In particular, concerns have emerged over the global supply of Technetium-99m, the most common medical radioisotope used in millions of diagnostic procedures around the world every year. Technetium-99m acts as a radioactive tracer, an isotope and can be detected in the body and is derived from molybdenum-99, an isotope of the metal element molybdenum.

There have been shortages of the Technetium-99m since the year 2000 but with the growth in the demand for healthcare in Latin America, the problem in the region is becoming increasingly serious.

“Next week we are going to host a conference at the Faculty of Medicine and we are going to address this issue along with officers from the federal agencies,” said Miguel Ávila, associate professor and director of cyclotron, radiopharmaceutical and microPET at UNAM.

The shortage of Technetium-99m stems from another shortage of molybdenum-99.

“Canada, The Netherlands and Africa are producing this radionuclide. Five reactors supply 90 of it, but are over 40 years (into) their lifespan and are having many problems, which will result in them shutting down in a couple of years,” he said.

“Canada’s Universal Research Reactor (NRU) is the one that faces more problems and it produces about 50% of the radioisotopes used around the world. Different countries are looking at their options and many of the solutions are going to be locally implemented,” he said.

Ávila would like to see Mexico build a plant to produce Technetium-99m and cut the country’s dependency on the international supply of molybdenum-99 but such a project would cost between $15 million and $18 million.

As it stands today, UNAM manufactures products like sodium fluoride, fluorothymidine, 11-C acetate and ammonium that are mostly used in the diagnosis of cancer, heart and neurologic diseases.

UNAM produces between 50 to 60 doses of radiopharmaceutical products every day. About 80% of the production is sold to hospitals and clinics in Mexico City. Every week about 10,000 single-photon emission computerized tomography scans and 480 PET scans are done across the country of 120 million people.

UNAM owns one of three cyclotrons in Mexico City and one of only six in existence in the country. Cyclotrons are particle accelerators used to produce radioisotopes.

The other two cyclotrons in the capital city are owned by Accesofarm and Medidores Industriales y Médicos (Miymsa in

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MDD Stock Watch

10 BIGGEST WINNERS FOR THE WEEK

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10 BIGGEST LOSERS FOR THE WEEK

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Defying a White House veto threat, the U.S. House of Representatives on Friday approved a bill making the R&D tax credit permanent. The legislation easily passed on a 274 to 131 vote Friday morning, despite strong opposition from Democrats and the White House.

The White House released a statement last Tuesday that President Barack Obama on Tuesday would veto the Republican bill because it would add $156 billion to the federal budget deficit over 10 years. The president wants to pay for a permanent R&D credit with new government revenue raised by eliminating unspecified tax loopholes, according to the White House.

The Advanced Medical Technology Association (AdvaMed; Washington) praised the passage of the bill. “AdvaMed commends the House for voting to make permanent the research and development tax credit, which will encourage R&D work here in America,” JC Scott, AdvaMed’s senior executive VP of government affairs, said in the statement. “R&D is the lifeblood for innovation and a critical element to growth and maintaining America’s leadership in the med-tech sector.”

Scott also commented on the ongoing effort to repeal the medical device tax.

“As Congress takes up additional legislation to address America’s tax code, it remains essential this effort include repeal of the medical device tax,” Scott said. “Chairman Camp (R-Michigan) included repeal of this onerous tax as an element of his fundamental tax reform plan. We encourage Congress to act now to put a stop to this job-killing policy.”

Beltsway Briefings

Defying Obama’s veto threat, House approves R&D tax credit

Staff Report

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Latin America

Continued from page 3

Spanish). The two companies along with the National Institute of Nuclear Research, which also has a nuclear reactor, share the market for Technetium-99m.

UNAM’s ambitions in this area are considerable but the steps they are taking are incremental.

For now, the university is working to obtain a Good Manufacturing Practice (GMP) and sanitary registration for its radiopharmaceutical products to secure its position as a key player in the Latin American radiopharmaceutical market.

UNAM has emerged as one of the more important producers of radiopharmaceutical products in Latin America. At a recently renovated lab, the university produces 14 radiopharmaceutical products including the fluorodeoxyglucose (FDG) used in PET scans. Mexican authorities consider FDG, the main element produced at the lab, and 13 other radiopharmaceuticals to be medical devices.

“The GMP is a certification that we have to comply with. We’ve been certified by the International Organization for Standardization in the 13485 standard, but we want to go further and we would like to obtain the GMP certificate from the Federal Commission for the Protection against Sanitary Risks (Cofepris in Spanish) and then we should register the products,” Ávila told Medical Device Daily.

Since April 2013, Mexican regulators have required medical device producers to obtain GMP certification to operate. The ISO 13485 certification is optional but it certifies a quality system for the manufacture of medical devices, in this case, radiopharmaceuticals.

But UNAM’s ambitions go beyond the local marketing. Rather, the university wants to be recognized as a reference nuclear center in the region as a whole.

“We are being catalogued as a reference center, not only in the country, but also in the region, in the field of radiopharmaceutical production”, said Ávila.

This month, delegates from Colombia’s National Institute of Oncology visited UNAM to receive training on the production of radiopharmaceuticals.

“We have an agreement with the International Atomic Energy Agency and they ask us to receive people from the region to be trained, since we’ve become a reference center for the production of diverse radiopharmaceuticals apart from FDG,” said Avila. “Cuba just installed its PET, but they don’t have a cyclotron and they are asking us now to supply them with fluor, and they may ask for FDG in the near future.”

Products

• St. Jude Medical (St. Paul, Minnesota) reported the results of the TOCCASTAR clinical trial at Heart Rhythm 2014, the Heart Rhythm Society’s 35th Annual Scientific Sessions in San Francisco. Results from the first prospective, randomized study of contact-force ablation technology for the treatment of paroxysmal atrial fibrillation (AF) met primary endpoints and supplement the growing body of evidence that supports the safety and effectiveness of contact-force ablation technology. Results demonstrated that the TactiCath Irrigated Ablation Catheter exceeded the safety and efficacy non-inferiority benchmarks set forth in the trial by 5.9% and 4.3%, respectively. The TactiCath irrigated ablation catheter is designed to give physicians a real-time, objective measure of the force applied to the heart wall during a catheter ablation procedure. Without contact-force data, physicians must estimate the amount of force applied to the heart wall during an ablation. If too little force is applied, there is a risk of incomplete lesion formation that could result in AF recurrence, potentially requiring additional treatments. If too much force is applied, there is a risk of tissue injury, which can lead to serious procedure-related complications.

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DEALS

Flatiron Health to acquire Altos Solutions, creator of OncoEMR

Staff Report

Altos Solutions (Los Altos, California), creator of OncoEMR, an oncology-specific electronic medical record, has agreed to be acquired by Flatiron Health (New York). The companies expect to finalize the transaction by the end of May. Financial details of the transaction were not disclosed.

Initially, OncoEMR was created to enable oncologists to plan cancer treatments and schedule patient visits, the company said. In an effort to create greater involvement and support for patients, SeeYourChart, a patient portal, was released in 2008.

“Altos Solutions was founded for one simple reason, to improve the lives of patients by enhancing cancer care with technology,” said Carla Wood Balch, president of Altos Solutions. “By joining forces with Flatiron Health, we’re going to accelerate that mission and deliver even stronger and more tightly integrated solutions to physicians, patients and life science companies. The cultures of the two companies are a perfect fit; every employee committed to making a difference for cancer patients.”

Altos Solutions will operate independently as a subsidiary of Flatiron Health, with Balch as president/CEO of the subsidiary.

Flatiron Health was founded in 2012 by Nat Turner and Zach Weinberg. The company’s OncologyCloud platform was designed to allow cancer centers, physicians and life science companies to gain unprecedented and actionable insights from clinical, practice management and billing data.

Flatiron and Altos expect to expand its cloud-based platform to other specialties beyond oncology starting in 2015.

In other dealmaking news:

• IPC The Hospitalist Company (North Hollywood, California), a national hospitalist physician group practice company, reported that it has acquired Total Inpatient Services (TIPS; Sugar Land, Texas). The acquisition represents an expansion in the greater Houston market, IPC said.

Mark Murray, MD, one of the TIPS co-founders and partners, will remain with the practice under IPC in a leadership position.

The TIPS acquisition is expected to bring IPC an incremental volume of about 30,000 patient encounters on an annualized basis.

• Teladoc, a telehealth provider, reported the acquisition of AmeriDoc (both Dallas), another telehealth company. This acquisition supports Teladoc’s strategy for growth into new and fast-growing market segments, the firm noted.

Through Teladoc, patients consult with a physician via phone or secure online video to receive treatment for non-emergency medical issues, such as allergies, bronchitis, pink eye and sinus problems. //

HEALTH INFORMATION TECHNOLOGY

AMC Health releases software platform for clinical trial data

Staff Report

AMC Health (New York), a provider of telehealth solutions, reported the release of a software platform designed to remotely collect clinical trial data. The mobile solution that runs on Android tablets and smartphones supports video visits and the collection of digital health and self-reported data to supplement the data collected in office visits.

“Remote site visits decrease the logistical burden clinical trials place on subjects and provide another degree of connectivity to the patient to complement the traditional, episodic site-based visits,” said Michael O’Brien, president of the Clinical Trials Division at AMC Health. “Additionally, collecting data directly from patients in their homes is an important step in enabling a more patient-centric clinical trial.”

Staff at the clinical site can remotely communicate with a subject through the application’s secure high-definition video link to observe the data collection under controlled conditions or the study participant can utilize the application independently to submit the data on a scheduled or ad-hoc basis. The site can monitor this information throughout the study to ensure protocol adherence and patient engagement, which aids in retention. //

BRIEFLY NOTED

MEDTECH INNOVATOR SPOTS, AND A CHANCE AT $100K, ARE STILL OPEN

Applications are now being accepted for the 2014 MedTech Innovator competition, which will be held during this June’s Wilson Sonsini Medical Device conference in San Francisco. The winner gets a $100,000 prize, sponsored by RCT Ventures (Tucson, Arizona). Law firm Wilson Sonsini Goodrich & Rosati are also sponsors.

Ten companies will be selected as semi-finalists by a panel of medical device VC’s, and all of the semi-finalists will get free registration to the conference. Those 10 Semi-finalists will compete to be among the four Finalists who will present on-stage during the live competition. The audience will then vote in real-time for the winner. The winner will get a $100,000 cash prize, sponsored by RCT Ventures. After the presentations, the MedTech Innovator of 2014 will be selected by an audience vote. All early-stage medical device companies are encouraged to apply, e.g. companies seeking seed, series A and series B rounds. Even university-stage technologies are welcome.

The deadline for applying is May 19th, and the application can be found at: http://www.medtechinnovator.com/wsgr2014.
Hopkins
Continued from page 1

Trayanova’s efforts have dotted the peer-review literature of late, including an article in a recent edition of Expert Review of Cardiovascular Therapy in which she and several co-authors address the question of whether optogenetics offers a means of treating electrophysiology diseases. She remarked at the HRS session that the MRI effort in her lab is aimed at development of a multi-scale modeling platform, one possible use of which is to map out the optimal targets for ablation for ventricular tachycardia with a degree of precision she suggested is not currently available in clinical practice.

Trayanova said conventional catheter-based cartography yields a 51% success rate for ventricular tachycardia ablation, but she claimed that pre-ablation MR with a dose of image processing software allows her and her colleagues to “model all the arrhythmias,” which in turn allows the user to be “able to predict the ultimate ablation target.” The use of MRI, she pointed out, allows “identification of ablation targets [that] is completely noninvasive,” and offers “smaller ablation lesions [and] improved tolerance for therapy.”

The approach at Trayanova’s lab is to assemble the two-dimensional MRI segments into a 3-D model via an unspecified set of interpolation techniques, which can aid in an exhaustive mapping of infarct segmentation. “From that, we put together a full model of the patient heart,” she said. Trayanova added that the muscle fiber orientation of the heart is part of the build of this model, which entails the overlay of fiber orientation onto an atlas of the individual patient’s heart, the accomplishment of which yields “a full geometrical model of the heart.”

Trayanova went through a study of canine and porcine subjects, offering an explanation of several scenarios for the size of a gray zone in the MR image, typically seen as an index of infarct size. She remarked that the six swine hearts included an instance each of functional and anatomical reentry, explaining how the MR data would allow an electrophysiologist to tightly target the tissue of interest, thus minimizing the volume of tissue exposed.

“Our hope is that we can provide the clinician with exact targets” with this MRI technology, Trayanova explained, adding, “we believe this would be a transformative approach.” She said that should this effort prove out, it would bring “computational modeling of individual heart dysfunction into the clinic,” a change she asserted would constitute “a paradigm shift.”

LAA DEVICE CHOICE STILL MURKY

Left atrial appendage (LAA) occlusion devices are beginning to spring up like daisies, and Shephal Koshi, MD, of the Pacific Heart Institute (Santa Monica, California), gave attendees at HRS 2014 a quick look at the current state of the art. “If all these devices close the appendage” and can do so safely, this is a promising development, Koshi said. Still, the data “do not seem to be interchangeable” at present due to an absence of head-to-head trials, he lamented.

Among the devices included in Koshi’s discussion were the Boston Scientific (Natick, Massachusetts) Watchman, the WaveCrest by Coherex Medical (Salt Lake City) and the offering from St. Jude Medical (St. Paul, Minnesota), the Amplatzer. Also on the roster were the Lifetech (Shenzhen, China) Lambre closure and the Sentreheart (Redwood City, California) Lariat, a suture-based closure device rather than the classic plug.

Koshi said the Watchman has been implanted in about 2,000 patients worldwide, with Asian studies underway that will broaden the experience. He said the WaveCrest has a fabric coating atop a frame rendering a device that is “almost like a hat,” but has only about 200 implants worldwide, a number that will be augmented by “a slow EU launch” now that the sponsor has a CE mark. “There is no metal fixation screw hub” with the WaveCrest, Koshi continued, adding that the device is covered with Gore-Tex.

Of the Lambre, Koshi said the sponsor has about 80 implants in Southeast Asia and the European Union, adding that this slimmer device “requires a smaller sheath” than most of the competition. He said FDA approved the Lariat for soft tissue approximation, and it is mostly used for LAA closure.

“They all have theoretical advantages and disadvantages,” Koshi said, making note of a “similar number in overall cases worldwide” between the Watchman and Amplatzer. He reminded attendees that these two and the WaveCrest are all CE marked, and the volume of implants is growing for all three. However, “Lambre will in the next few months have done enough cases to apply for a CE mark,” Koshi commented.

“We need to have a concept with one-size-fits-all” capability, Koshi pleaded, but he said doctors still have to make a difficult decision because of the different characteristics of the current crop of entries. “The appendage is not often round,” he said, adding that despite that some appendages are oval, “in cartoons it always seems perfect.” He mused that the next generation of LAA devices may include a device that can handle a larger percentage of cases than any that is currently on the market.

Thromboembolic risk is still at large, Koshi acknowledged, and in the case of the Amplatzer and Watchman, “thrombus typically involves these exposed stainless steel portions that in some cases just don’t endothelialize.” He said hopefully the next generation of devices deals with this problem. Koshi added that the risk of perforation “will always be there,” but he said operator experience “will decrease that risk.”

RBC Capital (New York) indicated in a recent investor memo that the problem of comparative trials for LAA closure devices might soon ease. RBC’s Glenn Novarro remarked that St. Jude’s trial for the Amplatzer “will likely be a head-to-head versus BSX’s Watchman device,” although Novarro acknowledged that this hinges on whether FDA approves the Watchman.
Ablation
Continued from page 1

found it ironic that ablation is “probably what drives this meeting, and the data are unproven” where efficacy is concerned. Despite that he obviously found a forum for his points, Olshansky remarked, “the real conflict is that you have a group of specialists who are profiting from these procedures,” and none of them is purportedly interested in hearing the procedure is overused.

Olshansky alleged that ablation is “kind of pushed down people’s throats as a curative procedure for virtually any type of afib,” remarking that the procedure appears in “over 8,000 PubMed citations,” but that “there is not one properly designed trial to support” any outcome. Olshansky said his version of a properly designed trial is one that includes a sham.

Olshansky said the number of ablations will double over the next three years and that “every study you look at shows a miserable success rates of drugs,” but pegs the success rate of ablation at 80%-90%. However, those trials “do not show optimal use of drugs,” he alleged, adding that the trials in question “do not have adequate follow-up in a carefully designed way.”

A sham study would not create any ethical quandaries, Olshansky said, adding that the Symplicity HTN-3 study was a catheter-based sham study that showed little difference in hypertension. He said a number of studies of ablation vs. drugs showed no difference, adding that the RAFFT-2 study, which compared drugs to ablation in patients with paroxysmal afib, “showed that ablation had a lower risk of recurrence.” However, he said that 55% had recurrence vs. 65% on drugs, and questioned whether that was enough difference to justify ablation given the procedural risks.

Olshansky said he is not certain that other electrophysiologists are treating asymptomatic patients, but he argued that for symptoms such as fatigue, “you don’t know that symptom is going to get better. Many of the patients are in the elderly category” and suffer from any number of comorbidities. He asserted that these patients “have no obvious benefit” and are at higher risk of complications.

A non-cardiologist should review the data from ablation trials because “there is a big conflict of interest in anyone who does a study like this,” Olshansky said. “They don’t want to show harm,” he said, adding, “if this is proven not to work, everything else falls apart.”

“I believe ablation works, but I would like to see better oversight” of the procedure in terms of data collection, “and making sure we’re not just getting a placebo benefit for a major intervention,” Olshansky remarked.

When asked about a team medicine approach, Olshansky said, “I like that idea because I think there’s a disconnect” between subspecialists and primary care physicians. Hence, he said, there is little clarity for the patient’s family “on why we’re doing ablation.” This would also relieve what he said is tunnel vision on the part of the EP, and give the EP “a more broad idea of how their therapies are actually working.”

Kalpathi Venkatachalam, MD, of the Mayo Clinic (Jacksonville, Florida) had a different view of the situation, although he agreed that ablation has not been tested against sham in trials. Still, he said shams have not been part of trials for many cardiology devices, adding, “just because we don’t have a study [with shams] doesn’t mean we sit on our hands.”

Venkatachalam quipped, “you don’t need a randomized, placebo-controlled trial to show that jumping out of a plane without a parachute is worse than jumping out with a parachute.”

The physician perspective on QoL, Venkatachalam said, is quite different from that of the patient. That discordance is “quite significant,” he said, observing “we don’t really have a way of saying you’re okay. They’re feeling miserable and we should listen to them.”

Venkatachalam said Olshansky “was making some fairly sweeping generalizations that we’re overdoing it.” Venkatachalam argued that while some patients are ablated needlessly, there are many patients in need of ablation who are untreated. On the other hand, he remarked that a number of precursor conditions could be dealt with in order to avoid the onset of afib.

“We’re not doing a good enough job” dealing with conditions such as apnea and other contributors to hypertension, Venkatachalam said. “Treat the hypertension and the apnea,” and some patients never have to deal with amiodarone and catheters, he remarked. Amiodarone and other drugs introduce “potentially serious side effects in the long run,” Venkatachalam pointed out, adding that especially when afib is diagnosed in relatively younger patients, “there’s no question that ablation is superior to anti-arrhythmic drugs.”

Venkatachalam said that thanks to the Stop AF trial, “there is no question [ablation] has been more effective” than pharmacological therapy. He added that thanks to loop recorders, “you can tell the difference in burden” even without sham studies.

“We’ve all seen patients who have been ablated and they have had a recurrence, but they don’t feel as bad as they did before,” Venkatachalam observed. Whether that is due to placebo effect is up in the air, he acknowledged, but he asked also whether the improved QoL is due to the improved rate control that often accompanies ablation.

Eight studies looking at the association between afib and dementia demonstrated “all forms of dementia are lower when you don’t have afib,” Venkatachalam said. The fact that the onset of dementia is delayed by five years in the absence of afib is “very hard to ignore,” he commented.

“There is a multi-disciplinary approach that would work for afib treatment,” Venkatachalam said, in part because “there is a psychological component to this.” He said blood pressure and sleep specialists should be involved, too, but the data on apnea and obesity suggest “we’re doing a lousy job of prevention.”
BlueShield Venture Fund/Sandbox industries; Justin Klein MD, partner, New Enterprise Associates; Timothy Patrick; president/CEO Carticept Medical (Alpharetta, Georgia); Garheng Kong, managing partner for HealthQuest Capital/Sofinnova Ventures, went into great detail to discuss the change in the relationship between device maker and venture capitalist.

Rik Vandevenne, director of capital funds, River Cities Capital Funds, served as the moderator. He started out the session by asking panelists just why are they still in the space when so many have already left.

“There’s a lot of discussion about venture capitalists bailing out of the medical device industry, and about every month or so there’s another VC firm that pretty prominently says, we’re backing out of healthcare or backing out of medical devices,” Vandevenne told the audience. “Certainly having just been on the fundraising trail myself it is challenging when talking to them and you always get that response, ‘we’re looking through your portfolio you’ve had some nice successes in medical devices, but with everything that’s going on, we don’t think that’s a good idea’.”

“As we’re being contrarian in our strategy here, or why are other people leaving and why are other people staying?” he asked the panel.

Panelists said that the space is still attractive, but investors have to change their mindset when it comes to providing funding for a company.

“We have to reset our expectations,” Kong said of investors. “The data says that medical device exits aren’t half the time as drug exits. It’s actually just as long or longer. The endpoint isn’t the device getting approved. Now it’s ramping up sales and showing that someone would buy [the device]. I think that investors would just have to think about the fact that the game is a little bit different. The value is still there, you just have to be able to get to a different part of the field…”

Prior to the panel, Kong echoed similar statements during a presentation.

“Here’s the question, where are all the med-tech investors?” Kong asked. “I think that it’s a common question that has been asked lately. Certainly medical devices have taken their fair share of pressure and contraction. But I’m here to tell you certainly from our point of view is that it [is a very good space to be in].

“One of the common comparisons is that you put the healthcare dollars in devices, diagnostics, or therapeutics. It use to be that these cousins were contrasted in a sense that devices would be a much easier way in terms of regulatory and clinical risk and drugs are of course much harder because there are all of these binary risks. I think what we’ve learned from our experience with medical devices is that the regulatory process is not quite the layup they want it to be and in fact there are binary moments as companies go through the belt line process, which of course is regulatory uncertainty.”

Panelists pointed out that uncertainty is the main culprit behind the apprehensiveness.

“We have a regulatory environment now that has changed dramatically. If I look at a previous company [I worked for in the past], I think the regulatory environment is the one thing that stands out where we have a much longer period of time and it’s much less predictable,” Patrick told the audience.

Hawes said that even though there are pressures, med-tech companies need to think beyond getting approval in hopes to successfully court investors.

“We’re looking for those medical device entrepreneurs that understand all of the implications that their device would have in the ecosystem,” Hawes said. “What’s the economic impact? Who are you displacing? Who needs to touch the device and be involved with the decision to use it? Most of these questions need to be answered before medical device companies approach a payor, or at least they need to have a sense of how to answer these questions. When we find entrepreneurs that really understand that or somebody across their team can answer each of these questions, we get really excited about being helpful. We’re seeing more and more of these companies actually think about reimbursement earlier in their development process. I think that’s really encouraging for the whole sub-sector.”

Klein noted that there were two sides to the problem of obtaining funding and a burden is often put on both parties.

“First I would acknowledge to everybody that this funding environment is terrible right now,” Klein said. “You can’t escape that. You’re a company out raising funds right now and the ability to attract multiple parties for financing is not happening. As an investor there are two sides to that coin. On the one hand you have a portfolio of 25 companies, all of whom need to advance in this window and it’s a challenge for them. At the same time when I’m inviting new investments I am seeing new opportunities where companies and programs are significantly more deemed risks for a given stage of financing and a given valuation that they would have been maybe six years ago, and I do find that compelling.”

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It has been known that about half of the estimated 230,000 newly diagnosed breast cancer patients in the U.S. can safely avoid chemotherapy, but the question has always been “which women need it?” Genomic testing has been answering that question since 2004 when Genomic Health (Redwood City, California) began testing for risk of recurrence; followed shortly by Agenda (Irvine, California).

Since then, much more evidence as to the clinical utility of genomics has been driving the adoption not only of tests that predict risk of recurrence, but also for tests that provide more information about the underlying biology driving the tumor growth. In a presentation by Pat Whitworth, MD, a surgical oncologist at Nashville Breast Center (Nashville, Tennessee), the comparison of traditional IHC/FISH vs. molecular subtyping using Agenda’s 80-gene test revealed a 22% difference between the two methods of sub classification. The additional information provided by objective measurement of gene expression over the subjective analysis performed by pathology could help in avoiding over treatment or under treatment. Whitworth said, “These tests could help define patients that would benefit from more comprehensive treatment. Our conventional subtyping does an okay job but we need to do a better job. “

This thinking crosses the traditional line between the role the surgeon plays and that of the medical oncologist, especially when the patient has a low risk of recurrence and may need surgery alone. These findings do not suggest bypassing the oncologist, but rather the criticality of collaboration since genomics brings the two roles together.

Peter Beitsch, MD, surgical oncologist at Medical City Dallas Hospital (Dallas) and out-going president of ASBS, said in his presidential address: “The future of breast [cancer] surgery is in genomics; we are no longer just removing tumors, we are now identifying the underlying biology and treating the molecular pathway that is driving that tumor’s growth; providing the right treatment for the right patient, at the right time. As breast surgeons, it is our duty to our patients to stay ahead of the curve on understanding the disease we are treating and offering the appropriate service to our patients.”

The two companies that first brought genomics into practice for breast cancer patients, Genomic Health and Agenda did so to eliminate the toxic side effects of chemotherapy for those patients who could safely avoid it. Those companies are now facing competition from newcomers such as ProSigna (Seattle), bioTheranostics (La Jolla, California) and Atossa Genetics (Seattle,) who offer additional information on top of assessing risk of recurrence. (see Table 1, bottom of page)

Atossa Genetics is developing a dynamic recurrence test that will also predict lymph node status to help select patients who can avoid the morbidity of lymph node dissection, such as lymphedema.

bioTheranostics recently launched their Breast Cancer Index test that shows not only 5 and 10 year risk of recurrence independently, but also predicts endocrine response. This will help select patients who can avoid the side effects of anti-estrogen therapy; a therapy that is not tolerated well, as evidenced by a documented 10%-40% rate of non-compliance.

ProSigna has launched a signature similar to that of Agenda’s MammaPrint that may allow for quicker results since it is an in vitro diagnostic (IVD) to be run in a local or hospital lab, avoiding the time it takes to send out the test.

The rapid explosion of utilizing genomics to direct therapy for breast cancer has outpaced many surgeons’ ability to keep up with current knowledge. To that end, a group of highly trained knowledgeable breast surgeons has formed Targeted Medical Education (TME; Allentown, Pennsylvania) that hosts a bi-annual educational meeting to train 50 breast surgeons nationwide on the latest data and practical applications of new information. Director of TME, Mark Gittleman, MD said, “Genomics has overlapped the traditional dividing line between breast surgeon and medical oncologist. In the future, the breast surgeon will become the oncologist who operates.”

Not only has genomics changed the way in which surgeons treat their patients, there has been a halo effect on new technologies to utilize genomics in designing their clinical trials. Historically, if a trial may put even a few patients at risk of a worse outcome, there has been pushback from the internal

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**Table 1: Comparison of Genomic Tests for Breast Cancer Recurrence**

<table>
<thead>
<tr>
<th>Company</th>
<th>Product</th>
<th>Methodology</th>
<th>Differentiator (in addition to rate of recurrence risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHI</td>
<td>Oncotype DX</td>
<td>RT-PCR</td>
<td>Predicts response to CMF</td>
</tr>
<tr>
<td>Agenda</td>
<td>MammaPrint/BluePrint</td>
<td>Microarray</td>
<td>Provides molecular subtyping</td>
</tr>
<tr>
<td>Atossa Genetics</td>
<td>NextCyte*</td>
<td>Microarray</td>
<td>Predicts lymph node status</td>
</tr>
<tr>
<td>BioTheranostics</td>
<td>Breast Cancer Index</td>
<td>RT-PCR</td>
<td>Predicts endocrine response</td>
</tr>
<tr>
<td>Nanostring</td>
<td>PAM 50</td>
<td>Microarray</td>
<td>Test kit to be performed by local lab or hospital</td>
</tr>
</tbody>
</table>

* in development

**Source:** Medical Device Daily, Medical Market Intelligence
that aims to transmit high-resolution histology slide images to the pathologist from the patient surgical resection. The company’s Histoscope, a surgical digital microscope, operating in real time, “will offer the pathologist an ‘inside view’ and an interactive communication channel to confirm tumor-free resection margins prior to the surgeon closing the surgical site,” CEO Davor Kosanic, PhD, told MDD. Samantree is looking to reduce the high frequency of repeat operations (claimed to be close to 40%) as a result of improved initial pathology-surgeon intra-operative communication. The company plans to complete its veterinary-based product in 2014, and to receive CE approval for its fully-functional human product in 2016. The company has already raised more than CHF 2.8 million ($3.2 million) in grants and equity finance, and plans a CHF 1.5 million ($1.75 million) raise shortly to execute its growth strategy.

Medlumics (Madrid, Spain) also presented its improved methods of working with optical coherence tomography (OCT) for therapy guidance. OCT reveals tissue morphology and - unlike visual imaging - is able to reach to a depth of up to 2mm. It is often used in retinal analysis, but has not yet advanced into other clinical areas.

By having created a miniaturized OCT component using integrated optics and micro-electronic batch fabrication methods, Medlumics is aiming to use the OCT modality in a number of novel applications. The company’s initial product is focused on skin cancer, using OCT analysis to map the relevant skin tissue for excision. This dermatological imaging CE-approved product will be entering a substantial clinical study this summer in Europe. The company’s next product line, currently in pre-clinical stages, involves a catheter-delivered OCT for improved atrial fibrillation (AF) mapping and treatment guidance. Medlumics has shown that it is able to differentiate between healthy and damaged collagen bundles in the cardiac tissue morphology ex vivo, and it aims to use this tool to optimally guide the AF ablation technique. The company has raised $3.5 million to date, and now plans to follow on with a $15 million raise to fully develop its second product line.

Fluence Therapeutics (Akron, Ohio) presented a photonic technology at the conference. Fluence is advancing a novel form of photodynamic therapy (PDT) for the treatment of psoriasis and other skin diseases. The company’s technology is based on a novel photosensitizer, Pc 4, which is inert unless stimulated by a narrow wave band of visible red light. In this excited state, Pc 4 preferentially kills activated T cells over other skin cells.

Current PDT solutions are not generally used for psoriasis, largely due to the lack of suitability of such an approach to treating large dermatological lesions simultaneously. Fluence plans to overcome this problem with its proprietary delivery platform. “A key issue with this technology,” explained CEO Warren Goldenberg, “is the uniform delivery across a broad area.”

The company is currently raising capital towards a broader European study, using its uniform dose-delivery platform, and towards applying this technology to other dermatological conditions. The company has established a subsidiary company in Tampere (Finland), due to the prevalence of psoriasis in Scandinavia, and the interest of the Finnish government and the EU in novel skin disease treatments. The company is also a member of a PDT Consortium, run by INSERM (Lyon, France), the French National Institutes of Health.

If in today’s age, a VC would consider a pan-technology approach to investing, the photonics world could be a most promising field of focus. It spans across the gamut of genomics and personalized medicine, through clinical diagnostics and to therapeutic optics. Photonics technologies continue to reach the eyes and ears of investment managers, and deservedly so. //

 review board or difficulty in enrolling patients in the study. For companies attempting to gain FDA clearance of a device or to gain clinical acceptance, randomized trials are required. By requiring a genomic test for entrance into a trial, those patients who are truly high risk and may need aggressive therapy can be excluded.

An example of this strategy is being utilized in three upcoming trials on cryoablation of cancer tumors. Rache Simmons, MD, chief of breast surgery, Weill Cornell Medical College (New York) presented amazing findings using cryoablation on breast cancer tumors. In a clinical trial, 100% ablation of tumors under the size of 1 cm was achieved using cryoablation. Sanarus (Pleasanton, California), whose cryoablation system was used in this trial, is now planning two more trials and will use a genomic test to screen out high-risk patients; as does IceCure (Memphis, Tennessee) who is also starting a trial for freezing small early stage cancer tumors. Hiding in the wings is yet a third cryoablation company CryoFem (San Diego) that is finalizing development of their system in order to enter the breast cancer treatment arena and who also plans to utilize genomics as a screening tool to enter patients into their trial.

Genomic testing of breast cancer tumors has changed not only the way we treat the disease, but also how we study and learn about it one molecule at a time. //

PEOPLE IN PLACES

• OrthoAccel Technologies (Houston) said Kelly Enos has joined the company as chief financial officer and VP of finance and administration. Most recently, Enos served as the chief financial officer for Kony. OrthoAccel makes AcceleDent, a medical device designed to speed up orthodontic treatment.

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Sleep habits associated with memory in old-age

A new research study led by Brigham and Women’s Hospital (BWH) published in The Journal of the American Geriatrics Society in May, shows an association between midlife and later life sleeping habits with memory; and links extreme sleep durations to worse memory in later life. The study suggests that extreme changes in sleep duration from middle age to older age may also worsen memory function.

“Sleep Duration In Midlife and Later Life In Relation to Cognition: The Nurses’ Health Study,” led by Elizabeth Devore, ScD, instructor in medicine in the Channing Division of Network Medicine at BWH found that women who slept 5 or fewer hours, or 9 or more hours per day, either in midlife or later life, had worse memory, equivalent to nearly 2 additional years of age, than those sleeping 7 hours per day. Women whose sleep duration changed by greater than 2 hours per day over time had worse memory than women with no change in sleep duration.

This study was the first to evaluate associations of sleep duration at midlife and later life, and change in sleep duration over time, with memory in 15,263 participants of the Nurses’ Health Study. Participants were female nurses, aged 70 or older and were free of stroke and depression at the initial cognitive assessment.

“Given the importance of preserving memory into later life, it is critical to identify modifiable factors, such as sleeping habits, that may help achieve this goal,” Devore stated. “Our findings suggest that getting an ‘average’ amount of sleep, 7 hours per day, may help maintain memory in later life and that clinical interventions based on sleep therapy should be examined for the prevention of cognitive impairment.”

Specifically, researchers report that:

• Extreme sleep durations may adversely affect memory at older ages, regardless of whether they occur at mid-life or later-life.

• Greater changes in sleep duration appear to negatively influence memory in older adults.

• Women with sleep durations that changed by 2 or more hours per day from midlife to later life performed worse on memory tests than women with no change in sleep duration, equivalent to being 1 to 2 years older in age, compared to those whose sleep duration did not change during that time period.

“These findings add to our knowledge about how sleep impacts memory,” said Devore. “More research is needed to confirm these findings and explore possible mechanisms underlying these associations.”

Does impaired sleep impact daytime functioning?

A separate study cited in the Incidence and Prevalence Database (IPD), described between-country differences in both the prevalence and type of sleep disorders seen across the globe, and gave information on how impaired sleep generally impacts daytime functioning.

The cross-sectional survey, conducted on International Sleep Well Day (March 21, 2002), used a common standardized questionnaire in all the countries (including China, Japan, Slovakia, South Africa), under the guidance of local survey managers. Subjects included in the study were adults from 10 countries representing 4 different continents with clear variations in lifestyle. The total number of questionnaires collected was 35,327, ranging from 202 in South Africa to 10,424 in Japan. The global mean age of surveyed individuals was 39.0 years. Approximately half of them (49.8%) were men and 64.1% were in the workforce. The survey was conducted with the same standardized case report form translated into local languages. All subjects also completed the Athens Insomnia Scale (AIS) and the Epworth Sleepiness Scale (ESS).

Sleep habits: The average (mode) bedtime on weekdays was 11 PM, with 32.0% of individuals reporting that they went to bed at this time. The Spanish and the Portuguese reported later bedtimes (12 PM). On weekends, the average bedtime was slightly later, at 12 PM. The average (mode) waking time during the week was 6 AM, with 35.2% of participants reporting that they awoke at this time, and 31.6% at 7 AM. On weekends, the average wake-up time was 8 AM.

The mean sleep duration during the week was 454 minutes (median 450 minutes; 7.5 hours). The shortest sleep duration was reported in Japan (413 minutes) and the longest in Portugal (504 minutes). An average of 31.4% of responders reported that they slept for 7 to 8 hours per night, and 25.7% for 6 to 7 hours. The global mean sleep latency (the time taken to fall asleep) during the week was 24.8 minutes, with a median value of 15 minutes. Approximately 40% of subjects reported that they needed between 0 and 15 minutes to fall asleep, and 20% reported a latency period of 15 to 30 minutes. At the other end of this spectrum, 39.4% of participants required more than 30 minutes to fall asleep, and 13.1% needed at least an hour.

Approximately one quarter of the overall study population (23.1%) reported that they regularly nap on weekdays. Twenty four percent answered “No” to the global question, “Overall, do you consider that you sleep well?”

Aging: The frequency of a grade 2 or 3 rating on the various Athens Insomnia Scale (AIS) items in subjects aged 18 to 65 years was compared with that of subjects older than 65 years. The frequency of four items rated as grade 2 or 3 was significantly higher in elderly than in younger subjects: delayed sleep induction (18.3% vs 11.6%); awakenings during the night (21.9% vs 13.3%); difficulty falling asleep (45.9% vs 35.8%); and non-restorative sleep (12.3% vs 6.1%).

Continues on next page
vs 11.5%); final awakening earlier than desired (15.1% vs 9.7%); and functioning during the day (10.0% vs 7.9%). In contrast, older subjects complained less frequently of insufficient total sleep duration (11.6% vs 13.6%) and sleepiness during the day (8.6% vs 10.7%).

**Daytime sleepiness:** The results of the ESS scores indicated that 11.6% of subjects could be considered very sleepy or dangerously sleepy (ESS score greater than 10). Rates ranged from 6.2% in China to 24.5% in South Africa.

**Management:** Among those who thought they did not sleep well, 30.7% (8.0% in Japan to 55.5% in Portugal) reported that they had visited a physician regarding their sleep impairment. In addition, 31.4% of them said they had taken sleep medications. The lowest rates of medication were reported in Austria (9.8%) and Japan (15.3%), and the highest rates in Portugal (45.7%) and in South Africa (52.8%).

Although there seem to be important global variations in the prevalence of impaired sleep patterns, its symptoms and their management, the present survey shows that about 1 in 4 individuals world-wide do not think they sleep well (see Article Review: “How do Individuals Sleep Around the World? Results from a Single-Day Survey in Ten Countries” as cited in the IPD).

**Study examines why we have no early memories of life**

A team of researchers working at the University of Toronto in Canada may have found the answer to the question of why we humans tend to have little to no memory of the first few years of our lives. In their paper published in the journal *Science*, the team describes several experiments they ran on mice and other small mammals that revealed the impact of neurogenesis on memory and how what they learned might be applied to memory retention in people. Lucas Mongiat and Alejandro Schinder offer a review of memory studies and how the research by the team in Toronto fits in with what has already been learned in a Perspective piece in the same journal edition.

Scientists have known for just a couple of decades that a couple parts of the human brain continue to produce and use new neurons (neurogenesis) throughout a lifetime. One of these parts is the dentate gyrus in the hippocampus – an area of the brain that has been identified with memory. Scientists have also known that while neurogenesis surges during our first years of life, it slows dramatically as we grow older. Suspecting that this might have something to do with childhood amnesia, the researchers designed some experiments in mice and other animals which have similar types of neurogenesis to learn more.

In the first experiment, both young mice and older mice were taught (via electrical shock) to fear a certain cage. Both groups were then tested to see how long they retained that memory – the young mice forgot what they’d learned in just one day, while it took the older mice up to a month to do so.

Next, the researchers installed a running wheel inside the cages of a different group of adult mice to incite exercise – prior research has shown that exercise causes a speed up of neurogenesis. They also fed another group of adult mice drugs that increase neurogenesis. They then repeated the shock experiment on both groups. In both cases, the research team found that increasing neurogenesis caused the mice to forget their fear after just one day, just as with young mice.

In analyzing their results, the researchers suggest that new neural growth that occurs before an event appears to “erase the board” a little bit, making way for new memories – something that has never been seen before. The results by the team will almost certainly lead to more studies as scientists continue to explore the mysterious mechanisms used by the brain to manage memory.

**Walking doesn’t impair thinking and multitasking**

When we’re strolling down memory lane, our brains recall just as much information while walking as while standing still – findings that contradict the popular science notion that walking hinders one’s ability to think.

**University of Michigan** (Ann Arbor) researchers at the School of Kinesiology and the College of Engineering examined how well study participants performed a very complex spatial cognitive task while walking vs standing still.

“We’re saying that at least for this task, which is fairly complicated, walking and thinking does not compromise your thinking ability at all,” said Julia Kline, a U-M doctoral candidate in biomedical engineering and first author on the study, which appears online in *Frontiers in Human Neuroscience*.

The finding surprised researchers, who expected to see decreased thinking performance with increased walking speed, Kline said. The 2011 best-selling book “Thinking Fast and Slow” suggests that because walking requires mental effort, walking may hinder our ability to think when compared to standing still.

“Past studies that have compared mental performance at a slow walking speed and standing have not found any differences, but our study is the first to show that the walking speed doesn’t matter,” said Daniel Ferris, professor of kinesiology and biomedical engineering and senior author of the paper. “Given the health benefits of walking, we should not discourage people from walking and thinking when they want.”

Ferris offered one caveat: previous research has shown that walking performance can be impaired in the elderly when they dual-task during gait.

Ferris, Kline and Katherine Poggesee of U-M’s Human Neuromechanics Laboratory measured the ability of young, healthy participants to memorize numbers and their placement on a grid, and then enter those numbers correctly with a keypad while walking different speeds and standing still.