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EUROPCR 2014

Renal denervation cautiously moves beyond HTN 3 disaster

By John Brosky, Europe Editor

PARIS — What a difference a year makes. Bold and festive a year ago when study after study reported stunning reductions in office blood pressure using any technology for ablation of nerves in the renal artery, this year the mood around renal denervation is sober, reserved and cautious among both manufacturers and clinicians.

"That party is over," laughed Mano Iyer, founder and COO for **ReCor Medical** (Menlo Park, California), one of the dozen companies lined up to enter the lucrative opportunity for renal denervation to reduce resistant hypertension.

See HTN-3, page 5

Lung cancer test shows high sensitivity, specificity, and early stage detection

By Amanda Pedersen, Senior Staff Writer

At one time a lung cancer diagnosis was considered a death sentence. That's not necessarily the case today as the field has advanced on both the screening and treatment sides of this disease. Still, the key to winning a battle with any form of cancer is early detection.

Working on the diagnostic side of lung cancer, **VisionGate** (Phoenix) has developed a test for early stage detection of lung cancer and other applications. Results from a clinical study of the company's LuCED lung test will be highlighted in a poster presentation later this month during the annual meeting of the **American Society of Clinical Oncology** (ASCO; Alexandria, Virginia) in Chicago.

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LATIN AMERICA

Bogota targets med-tech industry as key sector to attract investment

By Sergio Held, Staff Writer

Bogota, Colombia´s capital city, has classified the med-tech sector as its top priority sector to attract investment to the city.

The decision follows a study from **Invest in Bogota** (Bogota, Colombia), the city´s investment promotion agency, which classified med-tech first among 16 sectors that could bring international investment to the city.

"We do a ranking every year and the med-tech sector contained in the International Standard Industrial Classification of All Economic Activities (ISIC) ranked first. We then analyzed all the foreign direct investment coming to the Latin American region to the med-tech sector, and the medical devices sector

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INSIDE THE BELTWAY

AIPLA's Dickinson; there were 'too many moving parts' in patent reform

By Mark McCarty, Washington Editor

The latest legislative attempt to reel in patent trolls expired temporarily when the Senate Judiciary Committee failed to mark up legislation dealing with this and other problems, but one observer said that while the attempt did not lack for effort, there was a danger that S. 1720 would create as many headaches as it solved. Todd Dickinson, the executive director of the **American Intellectual Property Law Association** (Arlington, Virginia) told *Medical Device Daily* that the problems-created/problems-solved dilemma was not the only issue. He said a number of stakeholders came to the table with very different imperatives,

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HOLIDAY NOTICE

The offices of *Medical Device Daily* will be closed Monday, May 26, due to the Memorial Day holiday in the U.S., and no issue will be published that day. The next issue will be on Tuesday, May 27.

FINANCINGS

iRhythm secures $17M Series E funding round to grow ZIO market

Staff Report

iRhythm Technologies (San Francisco), a healthcare information services company, reported that it closed a $17 million Series E financing led by Novo A/S, a global life science investment firm. Norwest Venture Partners, which led the company's Series D financing, also participated in the oversubscribed round.

iRhythm's ZIO Service has been used with almost 250,000 patients at more than 800 institutions nationwide, and is covered by many public and private insurers,

The company said it will use the proceeds to further accelerate market growth for its ZIO Service, expand technology development and continue to establish clinical evidence supporting its flagship solution.

The ZIO Service enables long-term continuous monitoring using the noninvasive, small, wearable ZIO Patch, combined with proprietary algorithms and the ZIO report, to detect cardiac arrhythmias. These heart rhythm disturbances often occur infrequently and without symptoms, and may lead to serious complications if not detected and treated properly. The ZIO Patch enables continuous monitoring for up to 14 days.

iRhythm also reported that Tiba Aynechi, PhD principal at Novo Ventures, has joined the company's board. Aynechi has more than 10 years of combined research, banking, and venture capital experience in life sciences that spans various therapeutic areas and technology platforms.

In other financing news: GE Capital's Healthcare Financial Services business has agented a senior secured credit facility of up to $10 million to **Cianna Medical** (Aliso Viejo, California). The funds will be used for additional working capital as Cianna continues to expand its commercialization and product development efforts.

Cianna is a device company focused on the treatment of early-stage breast cancer. The company's brachytherapy applicator, SAVI, delivers post-lumpectomy partial breast radiation treatment to patients diagnosed with early-stage breast cancer.

"This financing strengthens our financial position for the continued commercialization of SAVI, both here in the U.S. and abroad, allowing us to fulfill our mission of making the benefits of breast brachytherapy available to more women," said Cianna's president/CEO Jill Anderson. "It also allows us to continue to selectively invest in our new product pipeline."

"GE Capital's knowledge of the healthcare industry and their support were key to successfully closing this transaction," said Cianna Medical CFO Gordon Busenbark. "They provided us with a flexible lending structure that supports our needs as we continue to ramp up our product development and commercialization efforts." **//**

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CONTACT US

medicaldevicedaily.newsdesk@medicaldevicedaily.com

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

ATLANTA NEWSROOM

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

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EUROPCR NOTEBOOK

St. Jude Medical reveals results from POST-IT study

Staff Report

St. Jude Medical (St. Paul, Minnesota) reported that results from the POST-IT Portuguese Study on the Evaluation of FFR Guided Treatment of Coronary Disease (POST-IT) registry were presented during a hotline late-breaking clinical trial session at EuroPCR 2014. Data from the registry, which was sponsored by the Portuguese Association of Cardiovascular Interventions, demonstrated that the use of St. Jude Medical PressureWire fractional flow reserve (FFR) technology changed the course of treatment for about half of the patients with coronary artery disease (CAD), ensuring patients with ischemia-producing narrowings received appropriate therapy.

POST-IT is a multi-center registry that enrolled 918 eligible patients at 19 centers in Portugal. Data from the registry highlighted the potential clinical and economic benefits of FFR measurement across a wide range of patients with both stable and unstable coronary artery disease. Results demonstrated that use of PressureWire FFR measurement systems results in improved treatment strategies for patients, with FFR changing the treatment strategy for more than 400 patients or 44.3%. Further, the registry found more patients were appropriate candidates for percutaneous coronary interventions (PCI) when assessed with FFR-guided therapy, increasing the number of patients referred for PCI from 35% to 43%. The POST-IT registry required all patients to first undergo a coronary angiogram. Based on the results of the coronary angiography, the supervising cardiologist was asked to create an initial management plan for each patient, based on all available information. Once the original treatment plan was finalized, patients underwent FFR assessment of all vessels suitable for revascularization (whether PCI or CABG), which were defined as those ≥2.25 mm. After FFR results were known, the supervising cardiologist was then asked to revise their final treatment decision. Consistency between the final and initial management plans were then evaluated.

In other conference news:

• **Medtronic** (Minneapolis) reported new data showing that patients treated with the CoreValve system experienced positive clinical outcomes in the ADVANCE Study. The transcatheter aortic valve implantation (TAVI) study revealed low rates of mortality and stroke, and showed what the company said is exceptional valve performance through two years.

Two-year follow-up was reported on 96.8% of 1,015 patients, all of whom had severe aortic stenosis and were treated with the CoreValve system. Patients experienced low rates of all-cause mortality (25.6%), cardiovascular mortality (16.8%) and major stroke (2.9%) at two years. These findings are consistent with the positive findings previously reported at one-month and one-year.

A majority of patients experienced improvement in symptoms through two years (87% improved to New York Heart Association class I or class II). Overall hemodynamic (blood flow) performance was strong and stable, with mean gradients (resistance) remaining below 10 mmHg, a threshold of exceptional blood flow, at each follow-up visit out to two years (9.8 at discharge, 9.5 at 1 year and 9.4 at 2 years).

The international ADVANCE Study was conducted at 44 centers in 12 countries, with patient receiving CoreValve implants between March 2010 and July 2011. The study calculated clinical endpoints according to Valve Academic Research Consortium standardized definitions. All data were independently monitored, all adverse events related to primary endpoints were adjudicated by an independent Clinical Events Committee (CEC) consisting of experienced cardiac surgeons and interventional cardiologists, and all cerebrovascular events (including stroke and other events) were adjudicated by an independent neurologist using neuroimaging and systematic NIH Stroke Scale assessments.

A separate analysis comparing patients 75 years and younger (n=182) with older patients (n=833) in the ADVANCE Study showed that both age groups benefitted from CoreValve treatment, demonstrating similar and low all-cause mortality rates at 30 days, 12 months, and two years (23.6% vs. 26%, p=0.448 at two years). No significant differences were observed between the two age groups for rates of cardiovascular mortality, stroke, myocardial infarction, bleeding, moderate and severe paravalvular leak, or the need for a new permanent pacemaker at either 1 or 2 years. At baseline, patients 75 years and younger had considerably higher rates of comorbidities at baseline compared to older patients. //

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Lawmakers try, try again to out the patent trolls

By Mari Serebrov, Staff Writer

Unsuccessful in its first attempt to shut down the patent trolls threatening the livelihoods of small businesses, the House is trying again.

The morning after Sen. Patrick Leahy (D-Vermont) said he was shelving the Innovation Act, the House's first effort, because of potential consequences for legitimate patent holders, a House subcommittee held a hearing on a discussion draft bill once again aimed at rooting out the trolls. The challenge is finding the proper wording that separates the trolls from the goats without running afoul of the First Amendment, lawmakers acknowledged at the hearing.

Med-tech and other small businesses all over the country are falling victim to trolls – otherwise known as patent assertion entities, which force others to license their broad, vague claims by threatening "infringers" with costly litigation. When faced with the trolls' extortion letters, small businesses are forced to pay their demands or hire attorneys. That drains resources that could have been used to help the businesses

The Innovation Act, H.R. 3309, fell victim to a lack of stakeholder agreement on "how to combat the scourge of patent trolls on our economy without burdening the companies and universities who rely on the patent system every day to protect their inventions," Leahy said after withdrawing the bill from the Senate Judiciary Committee's agenda Wednesday.

Given the growing number of trolls abusing the patent system, Leahy held out hope for a legislative solution yet this year. "If the stakeholders are able to reach a more targeted agreement that focuses on the problem of patent trolls, there will be a path for passage this year and I will bring it immediately to the committee," he said.

The House Energy & Commerce Subcommittee on Commerce, Manufacturing and Trade is intent on drafting a bill everyone can agree on. "We have heard from numerous businesses that are desperate for relief from patent trolls, and I believe there is a narrow path forward to provide that relief," Rep. Lee Terry (R-Nebraska) said in opening the hearing Thursday.

Intended to pick up where the Innovation Act left off, the subcommittee's discussion draft seeks to distinguish the deceptive demand letters of trolls from legitimate demand letters patent holders send to infringers. Throughout the hearing, lawmakers and stakeholders alike joked about locking themselves in a windowless room until they came to a consensus they all could live with.

Much of the discussion focused on the wording of the bill and concerns about treading on First Amendment speech rights. There also were concerns about preemption. In the absence of federal protection, several states already have laws in place prohibiting abusive demand letters. The draft bill includes a broad preemption clause that could override those state laws and prevent states from seeking civil penalties from bad actors, Rep. Jared Polis (D-Colorado) said.

He noted that 42 state attorneys general have said that while they want federal reform on infringement demand letters, it must be concurrent with state authority. But businesses don't want a patchwork of state laws dictating how they phrase their demand letters and enforce their patents.

While the new discussion draft primarily focuses on fraudulent demand letters and other pre-litigation issues, the Innovation Act dealt with litigation. For instance, it specified information that had to be included in an infringement suit and required courts to award the prevailing party reasonable fees and other expenses, except in certain circumstances.

The administration supported House passage of the Innovation Act last year, but it said the final version to come out of the Senate should recognize the importance of judicial discretion in balancing competing interests. The administration also had concerns about provisions on post-issuance review proceedings and wanted to see other measures added to protect innovators, including transparency of demand letters and pre-litigation patent ownership. The new discussion draft in the House would address some of those concerns.

The Innovation Act has been on the Senate Judiciary Committee agenda since the House passed it in December on a 325-91 bipartisan vote.

Leahy withdrew the bill rather than bringing it up for a vote. //

BRIEFLY NOTED

VuCOMP installs new M-VU CASD in hospital

VuCOMP (Plano, Texas) has installed M-Vu computer-aided detection (CAD) for mammography at **Mon General Hospital** (Morgantown, West Virginia). VuCOMP's CAD system is designed to provide an unprecedented level of performance to help radiologists find breast cancer earlier. Mon General will use this technology with its Fischer Giotto imaging system and Fuji CR mammography systems.

M-Vu CAD received FDA approval for digital mammography in October 2012. While mammography CAD systems have been FDA-approved since 1998, recent FDA guidelines have raised the bar for demonstrating CAD effectiveness, and now recommend comprehensive reader studies proving that radiologists are more effective when they use CAD. The VuCOMP system is the first mammography CAD product in the world to achieve FDA approval under these clinical study guidelines. VuCOMP's other flagship product, M-Vu Breast Density received FDA market clearance in December 2013.

VuCOMP specializes in CAD and automated breast density measurement.

HTN-3

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"Last year everyone was riding on the coat tails of Medtronic and now the playing field has been leveled and we all have an opportunity to differentiate with what we believe is a superior technology," he said.

The party ended in January when **Medtronic** (Minneapolis, Minnesota) announced its SYMPLICITY HTN-3 pivotal trial for renal denervation in the U.S. failed to meet its primary endpoint for efficacy against a sham-control group of patients.

One manufacturer, **Covidien** (Dublin, Ireland), immediately announced it would quit the business.

In March, 2014 at the meeting of the **American College of Cardiologists** (Washington), the trial investigators revealed details that confirmed SYMPLICITY HTN-3 was indeed the most rigorous renal denervation clinical trial conducted to date, and that the validated data did indeed show the therapy was no more effective than compliance to medications to lower blood pressure.

Sixty days later all players in the sector, who now have had a chance to digest the trial data, gathered at Europe's largest meeting of interventional cardiologists. While caution is the watchword, manufacturers who were initially taken aback have found their footing and are moving forward with their renal denervation programs.

On the third day of EuroPCR, the leaders for the newly formed Resistant Hypertension Course (RHC) issued what they called a strongly-worded statement declaring that the available evidence for catheter-based renal denervation indicates the procedure is safe and that it is "here to stay."

Course chairmen Konstantinos Tsioufis, MD, and Felix Mahfoud, MD, jointly stated, "We see the results of this trial [SYMPLICITY-HTN-3] as neutral and after a careful assessment of this study have identified various potential procedural and methodological considerations that could partly account for the study's results."

The field of renal denervation is "too interesting and too young to be written off," said Mahfoud, an interventional cardiologists at the **Saarland University Hospital** (Homburg, Germany) who has consulted with Medtronic, **St. Jude Medical** (St. Paul, Minnesota), and Recor.

Responding to questions from *Medical Device Daily*, the General Manager for Renal Denervation (RDN) at Medtronic, Nina Goodheart replied in an e-mail, "As the leader in RDN, Medtronic will continue to support our global HTN (hypertension) clinical program to better understand the potential of RDN in uncontrolled HTN. "

"We are continuing our analyses of SYMPLICITY HTN-3 and are committed to better understanding the confounding factors observed in this trial. We believe there are many factors that may have contributed to the observed efficacy results in SYMPLICITY HTN-3, including key variables that have arisen such as population differences and medication and procedural variability in SYMPLICITY HTN-3 versus other SYMPLICITY studies," she said.

"We will use these post-hoc analyses to help inform future clinical and technological efforts to bring RDN to its full therapeutic potential. We are in active discussions with our physician advisors and regulatory bodies on the future evidence needs for Symplicity and the therapy," she said.

"Medtronic is in discussions with the FDA to determine our path forward for the next IDE, which will likely be a global trial," wrote Goodheart.

"Medtronic also will continue to support its studies in other disease states, including cardiac arrhythmias, chronic kidney disease, and heart failure, among other areas," she said, adding that Symplicity remains available in countries where there is regulatory approval and Medtronic is currently expanding availability of its new multi-electrode Symplicity Spyral technology.

St. Jude Medical is just as heavily invested in renal denervation as its Twin City rival Medtronic, presenting data at EuroPCR from its EnligHTN clinical trials which, as all other RDN trials, continue to be single-arm evaluations without a control population.

"St Jude Medical is committed to this space," Rachel Ellingson, vice president for corporate relations with St. Jude, told *MDD*.

"True innovation takes time and persistence to develop," she said. "The good news is that industry, academics and regulators are interested in talking about how to develop evidence that is supportive of the therapy, and whether new trial designs might help bring this therapy to patients with severe high blood pressure."

In scientific sessions, the parade of trial results from **Boston Scientific** (Natick, Massachusetts) continued unabated while Medtronic, St. Jude, **Cordis** (Bridgewater, New Jersey) and **Terumo** (Somerset, New Jersey) sponsored special sessions or workshops for hands-on training with their latest generation of ablation technology.

The new RHC program offered a series of sessions on techniques and issues in RDN. Created by the European Association of Percutaneous Cardiovascular Interventions, which organizes EuroPCR, RHC responds to rapid growth over the past few years in association membership that is owed in part to anticipation of an interventional therapy for hypertension.

This groundswell of clinical interest and the expanding portfolio of tools and devices has now been slowed by the setback for the SYMPLICITY-HTN-3 trial. Many recalled a similar Black Tuesday for the then-emerging practice of stents for coronary revascularization with the SYNTAX at EuroPCR in Barcelona in 2006.

While the causes of SYMPLICITY-HTN-3 failure to prove efficacy may be confounding, one clear result of that study,

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ASCO

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According to VisionGate, the study demonstrates three major advantages to incorporating the LuCED lung test into the diagnostic algorithm: high sensitivity, "exceedingly high" specificity, and the ability to detect cancer cells in stages I and II. Investigators used the LuCED test with the company's Cell-CT imaging system to analyze sputum samples from patients with biopsy-confirmed, non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). The results show the Cell-CT accurately detected lung cancer in cells in three-day pooled, spontaneously produced sputum.

In the 30 cases studied, 26 were NSCLC and four were SCLC. Moderate/severe dysplasia or cancer cells were found in 28 of the 30 cases, the company reported. Half of these cases were either stage I or stage II lung cancer with 93.3% sensitivity to early lung cancer.

Among 5,146 sputum cells from 17 normal patients at high risk for lung cancer, the Cell-CT processed all cells with zero false positive indications for highly specific lung cancer screening. Based on this performance, the lower 95% confidence interval bound for cell specificity is 99.8%, VisionGate said.

Currently, cancer diagnosis is almost always done by a pathologist using a microscope and viewing the cells in a two-dimensional world, said Alan Nelson, PhD, the company's founder and CEO. "You do not have cancer until the pathologist sings," he told *Medical Device Daily*.

VisionGate's technology makes it possible to see those cells in 3-D and does not require a pathologist to confirm a diagnosis. "In essence, we've added another dimension to pathology by removing human error to overcome hurdles traditionally seen with sputum testing," Nelson said.

Also, unlike CT scans that are often used to identify suspicious lesions, the Cell-CT does not expose patients to radiation.

VisionGate's technology is designed to capture images rapidly, rendering scanned objects into 3-D images, the company said. For this particular study, VisionGate said the Cell-CT platform produced clear, detailed 3-D images of cells in sputum, which the system automatically analyzed to identify key features, or biosignatures, associated with potential malignancy. The analysis yields a high score when cancer cells are present, the company said.

"The good news and the expected news was that indeed, we can reduce the false positive rate dramatically and still get very high detection, north of 90% detection of all cancers in the lungs," Nelson said. "We were happily surprised by the fact that our false positive rate is almost zero; it's actually better than what we expected."

While this particular study did not have any false positives, Nelson acknowledged that it's not a scientific claim and that it doesn't prove the system will never yield any false positive test results.

Another "happy surprise" from this study, Nelson said, was the test's ability to detect lung cancer in its earliest stages, when the disease is most treatable. "We were absolutely celebrating" the fact that the study revealed a better than 90% sensitivity to early lung cancer.

"That points to the power of looking at cells analytically in 3-D," Nelson said.

VisionGate is in the final phases of its Clinical Laboratory Improvement Amendments certification and plans to open a clinical services laboratory in August in Phoenix.

"While CT scans are effective at identifying suspicious lesions, more invasive procedures are required to confirm malignancy and the type of lung cancer," said Bonnie Addario of the **Bonnie J. Addario Lung Foundation** (San Carlos, California). "A safe, accurate, non-invasive diagnostic test that could be used earlier in the process would be a significant game changer for the diagnosis of lung cancer. Although early stage lung cancer is typically asymptomatic, the ability to detect it sooner at stage one or two offers the patient a much improved outlook for longer-term survival."

Nelson told *MDD* that VisionGate is focused on lung cancer because that is where the company's compelling clinical evidence is. But he said the company has studied other potential indications for the test by looking at circulating tumor cells in blood, pancreatic cancer and Barrett's Esophagus. "In those cases, the data is amazingly good," he said.

Nelson compared the potential impact of VisionGate's technology to the impact the invention of the CT machines had on radiology more than 40 years ago. He pointed out that before 1970, virtually all radiology exams consisted of film chest X-rays. "And in 1972, a brilliant engineer and a mathematician got together and invented CT . . . and that completely transformed radiology," he said. "Imagine if they had, at that time, included an intelligent system that was able to read the CT images."

Another important objective of VisionGate, Nelson said, is cost effectiveness. "We want two things when we go commercial; one is high sensitivity for detection of early stage cancer without the burden of false positives and [second] we want it to be cost effective." **//**

Latin America

Continued from page 1

ranked as number one among 16 sectors that we studied," said Juan Carlos Jiménez, investment promotion manager at Invest in Bogota.

Jiménez is leading studies on the opportunities that medical devices could have in Bogota. The sector has been on Invest in Bogota's radar since 2008, when it became one of 25 sectors that the agency started prioritizing. Jiménez and his team are preparing a plan to attract more investment in the space to the city, whose GDP of between $100 billion and $140 billion is higher than that of entire countries like Ecuador, Panama, Costa Rica, Paraguay and Uruguay.

"In the med-tech sector we had not seen many aspects in a proactive way . . . but we are now studying the sector and we are conducting a market research study, which will be ready in June," said Jiménez.

Invest in Bogota officers attended February's Medical Device Design & Manufacturing Conference in Anaheim, California to understand how the med-tech industry works.

"That was the first event in which we participated trying to understand the medical devices' industry and to review the value proposal that Bogota has to offer to the medical devices' sector," said Jimenez.

Last year, the investment promotion agency organized Biolatam 2013, a Latin American biobusiness meeting attended by about 190 companies mainly from Spain, Mexico, Brazil and Ecuador that participated in more than 900 one-to-one meetings.

The agency is also looking closely at the biotechnology sector and the opportunities that could be developed with it in Colombia.

The agency is also taking concrete steps to help more companies in the sector develop strategies to be more competitive and access regional markets. One example is the work the agency has done with **B. Braun** (Melsungen, Germany).

"B. Braun contacted us. They've been producing in Colombia for more than 50 years and they were landlocked, manufacturing sutures in Chapinero, a locality in the northeast part of the city. They were looking for a new location," said Jiménez. Chapinero is an old neighborhood where long time ago many small industries boomed but the city grew and industries moved to different areas looking for more space and better infrastructure.

"They needed to understand Bogota's potential. We took them to free trade zones, showed them the logistic and regulatory possibilities that they offer, we helped them to understand where the city was growing to and how infrastructure and the closeness of these zones to the international airport presented an opportunity," said Jiménez.

B. Braun's interest in Bogota was enough reason for Otto Philipp Braun, responsible for the Iberian Peninsula and Latin America, to visit Bogota.

"For B. Braun this is the best location in the country, because 30 percent of our clients are here, and the air cargo available to export our products to Latin America is an advantage. The city offers a great level of professionals to our company," Manuel Hernández, B. Braun's operations country manager in Colombia told *Medical Device Daily*.

Bogota's El Dorado International Airport is Latin America's biggest cargo airport in terms of the tonnage it moves and is ranked 36 in the world.

"We consider that the strength of the Colombian market and the potential of the Andean market are key elements to position Bogota as an interesting hub for European, North-American and Asian medical devices companies to start looking at the city, to initially distribute and supply and then to manufacture and export to other countries," Jimenez said.

The agency helped B. Braun relocate their plant.

"The agency has been a great help since they provide updated information on the infrastructure of the city and the city's region to assess where a company should be located. They have also helped us to identify and contact local companies to start our studies and assess the offers from different sectors of the city," Hernández said.

"We are not at a level to bring plants to manufacture CAT scans and those kindds of devices, not yet. Nowadays we have to take advantage of the consumable and supplies markets. In the value proposal of Bogota, in contrast with some countries of the region, for example, the advantage lies in the human talent available. Our value proposal is not built in terms of tax incentives, but in the offer of human talent," Jiménez said. //

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Washington

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creating a bill in which "there were too many moving parts" to allow a consensus to form on the legislation.

The Patent Transparency and Improvements Act of 2014 (S. 1720) was part of a push to address some of the holes in the America Invents Act of 2012, a list that includes the post-grant review process that many observers have said encourages abusive reviews. The companion bill on the House side, H.R. 3309, seemed unlikely to garner much support in the Senate, although some expressed the view that the House would accept the Senate bill for a vote should the upper chamber affirm S. 1720 (*Medical Device Daily*, May 19, 2014).

Dickinson indicated that S. 1720 faced more obstacles than its sponsors could reasonably hurdle, however. He said there were "too many people asking for too many things," and that hence the bill "never gelled, and I think the majority said 'were not getting there."

"This was a classic case of the devil's in the details," Dickinson observed, adding, "this is a very detailed bill, and those details had real consequences." He said the bill's backers "knew if they didn't get it right, there would be very real consequences."

Dickinson made the case that the Senate bill did not die of neglect. "I've rarely seen as much hard work put in by [congressional] staff," he said, citing in particular the staff of Senate Judiciary Committee chairman Pat Leahy (D-Vermont). Dickinson said the Obama administration was not deeply involved in the effort, but in any event, "there was never a manager's amendment" available on the day of the mark-up despite a flurry of Capitol Hill rumors to the contrary.

Dickinson also indicated there was substantial GOP support for S. 1720 in the days leading up to the Judiciary Committee's markup, but that the fee shifting question kept Democrats on the sidelines as the date approached.

The bill could resurface during the lame duck session between the November elections and the swearing in of the new Congress, but Dickinson remarked, "the big question will be whether the Senate changes parties," explaining that a lame-duck vote would most likely not happen if the Senate flips to the GOP.

Dickinson said a House committee is looking into the practice of demand letters, adding that the Federal Trade Commission and state attorneys general are also examining this as an enforcement issue. He said this is a consumer fraud issue and that "I think that's what we need to deal with."

AHA pushes back on site-of-service

One of the policy ideas for constraining Medicare spending is to flatten the fees paid for a service across sites, a subject that came up again in a recent hearing in the House of Representatives. Among the legislative proposals steering this tack is a post-acute care bill, H.R. 4673, an untitled bill dealing bundled payments, but this untitled bill is not the only one taking on site of service.

Officials with the Medicare Payment Advisory Commission appeared before the House Energy and Commerce Committee health subcommittee May 21, advising Congress that Medicare spending on fee-for-service post-acute care varies considerably for a number of device-intensive services, including for major joint replacement and coronary artery bypass/catheterization.

Mark Miller, PhD, MedPAC's executive director, said in written testimony that the commission "holds that payment for the same set of services should be comparable regardless of where the services are provided," which he said would "help ensure that beneficiaries receive appropriate, high-quality care in the least costly setting consistent with their clinical conditions."

Erik Rasmussen, senior associated director for federal relations at the **American Hospital Association** (AHA; Washington), told *Medical Device Daily*, "Medicare can't pay a doctor's office rate and expect a hospital" to survive.

"MedPAC is not saying we're overpaid," Rasmussen observed, saying that Medicare margins for hospitals are in negative territory for many procedures. "They're just saying they want to pay us less" as a way of driving patients to other sites, such as ambulatory surgical centers (ASCs).

Rasmussen noted that hospitals "see 24% more acute care patients" than ASCs, adding that these patients are sicker, poorer, and often are eligible for both Medicare and Medicaid. Unlike physicians, hospitals must "take all comers regardless of ability to pay. Try calling a doctor's office" for Medicaid in an emergency situation, Rasmussen suggested.

Rasmussen said one reason hospitals have tougher cases is that "a doctor does not want to take patients with five comorbidities. We're already seeing the hardest cases," he continued, adding that the MedPAC proposal amounts to adverse selection. "Take adverse selection and pile on top the cutting of payments to ASC levels, and the hospitals just can't take it," he claimed.

Congressional reaction to these proposals "is mixed," Rasmussen observed. MedPAC has given voice to site-of-service pay equalization on several occasions, but "Congress has chosen not to take this up for three years in a row," he remarked. Congress is aware of a need to avoid blunting access, but Rasmussen said AHA believes it must stay on top of the discussion.

"In this budget environment we always have to be vigilant," Rasmussen said. He suggested that the debt ceiling debate may have driven MedPAC farther into this discussion than it otherwise might have gone. "I think MedPAC was under a lot of pressure to come up with" some financial relief for Medicare, he said, remarking that a lot of this conversation will disappear when the red ink disappears.

"Congress has not traditionally wanted to constrain where beneficiaries get care," Rasmussen observed. //

PATENT WATCH

Neuros wins U.S. patent for electrical nerve block technology for chronic pain

Staff Report

Neuros Medical (Cleveland, Ohio), a device company focused on using electrical nerve block technology for chronic pain, said it has received a new U.S. patent for its high frequency electrical nerve block technology.

The U.S. Patent No. 8,731,676 features broad claims, focusing on blocking nerve activity, in nerve sizes 3 millimeters up to 12 millimeters in diameter, for a variety of applications, including pain, spasticity, and bladder. Neuros said it now has three issued patents in its portfolio, with others pending.

The company is in the initial stages of a randomized, controlled, pivotal clinical trial to evaluate its Altius high frequency nerve block system for the management of intractable limb pain of amputees. The study consists of 130 patients at 15 medical centers in the U.S.

Neuros said it plans to use the study results to support an application for FDA approval. The pivotal study builds upon the company's long-term pilot study which reported significant pain reduction. In addition, more than half of the subjects discontinued their pain medication use during the study, Neuros said. //

PEOPLE IN PLACES

• **AMC Health** (New York) said Walter Hosp has been named to the newly created position of chief financial officer, starting on July 7. Previously, Hosp spent five years as VP and treasurer of Medco Health Solutions. AMC Health is a provider of telehealth solutions that provide customized, scalable, cost-effective programs that assist organizations serving at-risk populations and those conducting clinical trials.

• **Cielo Healthcare** (Ochre House, UK) has named Donna Boles and Michael O'Boyle to its Healthcare Advisory Board. Boles is the former senior VP, HR of BD (Becton, Dickinson and Company), O'Boyle holds more than 30 years of experience in healthcare, serving the provider, payer and service sectors. Most recently, he was a senior officer for HCA Holdings, serving as the president/CEO of Parallon Business Solutions. Cielo Heathcare is a provider of talent acquisition and management solutions.

• **Hoya** (Tokyo) said Augustine Yee has joined the Company as its executive officer, chief legal Officer and head of corporate development and affairs. Yee joined Hoya from AstraZeneca, where he was head of Asia Pacific Regional and Corporate Business Development. Hoya is a med-tech company and a supplier of high-tech and medical products.

• **Intelligent InSites** (Fargo, North Dakota) has named Shane Waslaski as president/CEO. Waslaski will also join the board. Most recently, Waslaski was president of Varistar. Intelligent InSites provides open, real-time, healthcare platforms.

HTN-3

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according to Mahfoud, is that all clinical trials in the field moving forward will require a control arm.

"Sham-control arms will be a real problem in Europe," he told *MDD* without elaborating.

Separately, Iyer explained, "If you talk to European physicians they will tell you that a sham-control may be scientifically important but not clinically relevant and that practically it is very difficult," he told *MDD*. "They are not believers here in Europe that a sham is necessary. They have real problems putting their patients through a fake procedure. They will ask how they can ethically prescribe a sham procedure if there is a procedure for a patient coming in who is suffering with no alternatives. They will tell you this patient is going to come back with a significant cardiovascular event if we don't get their blood pressure down. Meanwhile here is a technique that is proven to be safe that might help."

"What will be the FDA's position? We don't really know. This is why everyone is so reserved at the moment," he said.

Several company representatives at EuroPCR said they expected to see an "open day" organized in the U.S. to assemble companies, clinicians and the FDA for discussions around outstanding issues raised by the Symplicity trial.

"It has happened before around transcatheter aortic valves, in the carotid artery space," said one company representative who declined to be identified.

The most memorable criticism of the SYMPLICITY-HTN 3 trial at EuroPCR came from Mel Lobo, MD, the director of the Hypertension Clinic at **St Bartholomew's** and the **Royal London Hospital Trust**. A member of the audience in a Medtronic-sponsored session that invited critical comment of the trial, Lobo stood to say, "It is interesting to see you use the term heterogeneity of operator experience. To me they were homogeneously inexperienced," referring to the presented data showing 57% of SYMPLICITY-HTN 3 interventions were performed by physicians who had done two procedures or less.

By contrast, the new Medtronic Global Registry that now holds almost 1,000 of its targeted 5,000 patients, excludes patients who received the therapy from an operator with less than 10 previous interventions.

Session chairman Roland Schmieder, MD, a nephrologist specializing in hypertension at the University of Erlangen in Germany, told *MDD* that "Moving forward with renal denervation means two things. First we need to move forward with more robust study designs. It does not need to have sham-control, but it does need to be randomized with a real control group." "As for the technology, we have heard of new technologies for a more reliable delivery of the energy, such as ultrasound, or 360-degree radio-frequency. What will become important are technologies for making the procedure less operator-dependent with reproducible effects. We are not there yet." //

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DIAGNOSTICS EXTRA

Keeping you up to date on recent developments in diagnostics

By Omar Ford, Staff Writer

Urine test could point out blood clots in at risk patients

A new study by researchers from California and Canada indicates a simple urine test can indicate the presence of venous thromboembolism, a blood clot that has broken free from its point of origin and which travels through the bloodstream, eventually lodging in a vein. The test evaluates the levels of fibrinopeptide B (FPB), a small peptide that's released when a thrombosis forms and which is removed from the body through urine.

Study lead author Timothy Fernandes, MD, said the study was developed based on the results of a pilot trial that suggested that urine FPB levels could be used as a screening tool for venous thromboembolism in patients at risks for clots.

"The urine FPB test offers advantages over other screening methods because it doesn't require blood to be drawn and it can provide more accurate results than the D-dimer test," Fernandes said.

The D-dimer test looks for blood evidence of a protein fragment called D-dimer that is present in the blood after a clot begins to break down. The FPB test has the potential for greater specificity because it can reflect ongoing clot activity, while D-dimer can only be measured once a clot has already become degraded. The researchers used stored urine samples taken from 344 patients who participated in the Pulmonary Embolism Diagnosis Study, a multicenter study of 1,417 patients considered likely to have an acute pulmonary embolism. For all urine samples, the researchers measured the FPB concentration and evaluated the sensitivity and specificity of the test at various cut-off points in relation to its ability to predict the presence of venous thromboembolism.

What they found was at concentrations of 2.5 ng/ml, urine FPB demonstrated sensitivity comparable to previously published values for plasma latex and whole blood D-dimer levels, but with greater specificity.

Dogs shown to detect prostate cancer

With an accuracy rating of 98% , specially-trained dogs were able to smell volatile organic compounds (VOCs) released into urine by prostate tumors, setting the stage for a potentially new means of early prostate cancer detection, according to a new study at the 109th annual scientific meeting of the **American Urological Association** (AUA; Linthicum, Maryland).

It has long been known that dogs have a stronger sense of smell than humans. While humans have roughly five million olfactory cells in their noses, dogs have about 200 million. For years, law enforcement and the military have used dogs to them help locate bombs and drugs. It should then be no surprise that a dog's intricate sense of smell has also captured the interest of the medical world. In recent years, new findings have emerged to indicate dogs are capable of detecting the onset of epileptic seizures as well as malignancies of the breast and lung. In 2010, research emerged demonstrating a dog's ability to "sniff out" prostate cancer; however the study was relatively small with 33 patients. This study, however addresses the ability of canines to accurately detect the presence of prostate cancer in a much larger cohort.

Researchers at several institutions, including **Humanitas Research Hospital** (Milano, Italy) and **Humanitas Castellanza** (Italy), investigated the level of accuracy at which a highly-trained dog can recognize prostate-cancer-specific VOCs in urine samples.

The study consisted of 677 participants who were placed in one of two groups: prostate cancer group (n=320) and control group (n=357). The prostate cancer group included patients with prostate cancer ranging from those at a very-low risk to metastatic. The control group included a diverse cohort of healthy subjects affected by non-neoplastic disease or non-prostatic tumors. Two dogs carried out the testing in an environment free of olfactory interference.

Nose bacteria could be an indicator of skin disease

Bacteria found in the nose may be a key indicator for future development of skin and soft-tissue infections in remote areas of the body. Scientists have long known that a number of bacteria reside in the nose, and that those who carry the pathogen *Staphylococcus aureus* in their noses are at a higher risk for developing skin and soft tissue infections (SSTIs). However, until now, no one has been able to determine why some *S. aureus* carriers develop infections while others do not.

The nose is the primary *S. aureus* reservoir in humans and nearly 80% of the time, an individual's colonizing strain is the same strain that causes subsequent remote skin infections. Given this association, researchers at the F. Edward Hébert School of Medicine, **Uniformed Services University of the Health Sciences** (Bethesda, Maryland), postulated that the population of *S. aureus* in an individual's nose may harbor valuable clues regarding SSTI susceptibility that had not yet been described. This is of particular interest to the military, as it is well known that soldiers in training are at increased risk of developing an SSTI.

Using a DNA sequencing strategy, the microbial composition of each sample was determined. The biodiversity of the bacterial population in each nose was compared between individuals colonized and/or infected with Methicillin-Resistant *S. aureus* (MRSA), Methicillin-Sensitive *S. aureus (*MSSA), and

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those individuals that were culture-negative for *S. aureus*. The researchers observed a significantly higher percentage of a type of bacteria known as Proteobacteria in the noses of individuals who did not develop SSTI, suggesting that Proteobacteria may, in fact, be protective against the development of SSTIs. Furthermore, *S. aureus* carriers had a unique nasal microbiome that differed from non-carriers.

Establishing a nose "marker microbiome" associated with development of SSTI infections may pave the way for focused preventive treatments that target the microbiome, rather than *S. aureus* itself.

The scientists believe that this study will aid in the design of future prophylactic procedures that can help prevent SSTI, particularly in the setting of military training, and help influence how health care providers think about and treat these complex and diverse infections.

Most schools across the U.S. provide simple vision tests to their students – not to prescribe glasses, but to identify potential problems and recommend a trip to the optometrist. Researchers are now on the cusp of providing the same kind of service for autism.

Researchers develop Autism screening software

Researchers at **Duke University** (Durham, North Carolina) have developed software that tracks and records infants' activity during videotaped autism screening tests. Their results show that the program is as good at spotting behavioral markers of autism as experts giving the test themselves, and better than non-expert medical clinicians and students in training.

"We're not trying to replace the experts," said Jordan Hashemi, a graduate student in computer and electrical engineering at Duke. "We're trying to transfer the knowledge of the relatively few autism experts available into classrooms and homes across the country. We want to give people tools they don't currently have, because research has shown that early intervention can greatly impact the severity of the symptoms common in autism spectrum disorders."

The study focused on three behavioral tests that can help identify autism in very young children.

In one test, an infant's attention is drawn to a toy being shaken on the left side and then redirected to a toy being shaken on the right side. Clinicians count how long it takes for the child's attention to shift in response to the changing stimulus. The second test passes a toy across the infant's field of view and looks for any delay in the child tracking its motion. In the last test, a clinician rolls a ball to a child and looks for eye contact afterward – a sign of the child's engagement with their play partner.

In all of the tests, the person administering them isn't just controlling the stimulus; he or she is also counting how long it takes for the child to react – an imprecise science at best. The new program allows testers to forget about taking measurements while also providing more accuracy, recording reaction times down to tenths of a second.

"The great benefit of the video and software is for general practitioners who do not have the trained eye to look for subtle early warning signs of autism," said Amy Esler, an assistant professor of pediatrics and autism researcher at the **University of Minnesota** (Minneapolis), who participated in some of the trials highlighted in the paper.

"Th e software has the potential to automatically analyze a child's eye gaze, walking patterns or motor behaviors for signs that are distinct from typical development," Esler said. "These signs would signal to doctors that they need to refer a family to a specialist for a more detailed evaluation."

According to Hashemi and his adviser, Guillermo Sapiro, professor of electrical and computer engineering and biomedical engineering at Duke, because the program is non-invasive, it could be useful immediately in homes and clinics. Neither, however, expects it to become widely used – not because clinicians, teachers and parents aren't willing, but because the researchers are working on an even more practical solution.

Later this year, the Duke team (which includes students and faculty from engineering and psychiatry) plans to test a new tablet application that could do away with the need for a person to administer any tests at all. The program would watch for physical and facial responses to visual cues played on the screen, analyze the data and automatically report any potential red flags. Any parent, teacher or clinician would simply need to download the app and sit their child down in front of it for a few minutes.