



## Vacuum-like probe gives insight on cellular activity

By OMAR FORD

Medical Device Daily Staff Writer

A vacuum cleaner isn't really something that a person would usually identify with medical technology, but researchers from **McGill University** (Montreal, Quebec) have developed an application that is based off the principles behind those cleaning tools.

The device, known simply as the probe (at this point at least), gives researchers a greater chance at detecting the activity of cells.

The probe was developed by Mohammad Ameen Qasimeh and David Juncker from McGill's Department of Biomedical Engineering, and Thomas Gervais from the **Ecole Polytechnique of Montreal**.

Researchers say the probe is based on using quadrupoles, or paired identical objects, two "positive"  
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## *Society of Laparoendoscopic Surgeons meeting* Presenters discuss cutting edge ablation technology

By DIANA TUCKER

Medical Device Daily Contributing Writer

LOS ANGELES – At the **Society of Laparoendoscopic Surgeons (SLS)** (Miami) annual meeting, Doron Kopelman, MD, Department of Surgery, **HaEmek Medical Center** (Haifa, Israel) moderated a general session on 'Directed Energy for Tissue Ablative Therapy' that included presentations on radio frequency (RFA), interstitial laser, plasma and non-invasive high intensity focused ultrasound (HIFU). Kopelman opened the session by saying, "We live in an era of technological revolution. The rate of change is constantly increasing and surgery is no exception. We are not far from declaring "Open Surgery" as a sub-specialty mostly practiced in trauma and acute abdominal emergencies. Tissue ablation holds a very significant part in the revolution  
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### *Report from Europe*

## Sapheon gets CE mark for new varicose vein treatment

A Medical Device Daily Staff Report

**Sapheon** (Santa Rosa, California) has received CE mark approval for its new approach to the treatment of varicose veins caused by venous reflux disease. The Sapheon Closure system addresses the estimated one million procedures performed each year to close the great saphenous vein. Sapheon's technology uses a medical adhesive and single-use catheter-based delivery system to immediately and permanently achieve vein closure without thermal ablation or sclerosing chemicals. Patients treated with the Sapheon Closure system avoid significant post-procedure pain and bruising, do not need to wear compression stockings, and can immediately resume normal lifestyle activities.

Unlike current thermal ablation procedures, the  
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### *Washington roundup*

## JDRF says FDA's low-glucose guidance 'unduly burdensome'

By MARK McCARTY

Medical Device Daily Washington Editor

FDA released a draft guidance earlier this year addressing the low-glucose suspend (LGS) insulin unit (*Medical Device Daily*, June 28, 2011) shortly before the annual scientific sessions hosted by the **American Diabetes Association** (ADA; Alexandria, Virginia) in June. The guidance hints at a need for two glucose sensors, although an FDA manager said that might not be necessary, but the guidance's demands on clinical trials has caught the attention of the **Juvenile Diabetes Research Foundation** (JDRF; New York), which is still of the view that the agency is imposing needless barriers on such systems.

Aaron Kowalski, PhD, senior VP for glucose research  
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### Don't miss today's MDD Extra: Diagnostics



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*Patent watch***PLC gains two patents for RenalGuard application****A Medical Device Daily Staff Report**

**PLC Systems** (Milford, Massachusetts) said it has been granted two additional U.S. patents by the U.S. Patent Office, as well as the company's first Japanese patent, all covering aspects of PLC's new product technology, RenalGuard.

The innovative RenalGuard Therapy is designed to reduce the toxic effects that contrast media can have on the kidneys for patients undergoing imaging procedures, and prevent the occurrence of contrast-induced nephropathy (CIN) in the millions of at-risk patients around the world. This novel therapy is based on the theory that creating and maintaining a high urine output allows the body to rapidly eliminate the contrast media, reducing its toxic effects, and especially reducing the incidence of CIN, which can be costly and deadly, and for which there is currently no other effective remedy available.

The patents issued in the U.S. cover both the core methodology as well as the actual RenalGuard device, with the method patent providing broad coverage for the use of matched fluid replacement to combat CIN. The Japanese patent covers the specific RenalGuard device and operation, and represents an important step forward.

In other patent news; **Kips Bay Medical** (Minneapolis) said that USPTO has issued it the patent number 7,998,188, titled "Compliant Blood Vessel Graft," which includes eleven permitted claims covering the company's core eSVS MESH technology, and represents the first patent obtained in the U.S. covering this technology.

The USPTO also has issued a notice of allowance approving a second patent application, titled "Compliant

Venous Stent," which includes three claims related to the eSVS MESH design.

"At present, the company possesses issued patents in Japan and Canada covering the eSVS MESH. In addition, it has received a notice of allowance from the European Patent Office and is presently engaged in the grant phase to validate the European patent in eight European countries. The company is pursuing additional patent applications which are pending in the U.S. and in strategic countries world-wide. ■

**People in the News**

- **AngioDynamics** (Albany, New York) said Scott Solano, senior VP and chief technology officer, has resigned his position effective Oct. 14, to pursue other interests. Solano joined AngioDynamics in Sept. 2010. AngioDynamics makes minimally invasive medical devices for vascular access, surgery, peripheral vascular disease and oncology.

- **Maxim Healthcare Services** (Columbia, Maryland) has named Brett Barlag as chief financial officer and chief strategy officer. Previously, Barlag was a senior managing director at FTI Consulting. Maxim Healthcare Services is a provider of home healthcare, medical staffing, and wellness services.

- **Wolters Kluwer Pharma Solutions** (Phoenix) has named Jack Bush as VP, marketing for the Healthcare Analytics business. Previously, Bush held several senior management roles in Alcon, GlaxoSmithKline, Merck, Roche, and most recently Xanodyne. Wolters Kluwer Pharma Solutions makes scientific information and analytics to pharmaceutical and healthcare professionals.

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*Agreements/contracts***Massport installs Zoll AED defibrillators in airports****A Medical Device Daily Staff Report**

**Zoll Medical** (Chelmsford, Massachusetts) said the **Massachusetts Port Authority** (Massport; Boston) is installing Zoll AED Plus with Real CPR Help throughout its three airports – Boston Logan International, Hanscom Field, and Worcester Regional – and the maritime facilities it owns and operates in the Port of Boston.

The contract, awarded to Zoll distributor **Life Support Systems** (Dedham, Massachusetts), is for the installation and service of 145 AED Plus units. The installation of the Zoll AED Plus devices is part of a safety policy initiative to make automated external defibrillators (AEDs) more accessible to travelers and Massport employees when sudden cardiac arrest (SCA) occurs.

Zoll's AED Plus is unique in that its real-time CPR feedback guides all responders – including the infrequent responder and lay rescuers – to the correct depth and rate of chest compressions with audio and visual prompts, so they know how to perform this critical life-saving technique in an emergency. Fully compliant with the 2010 American Heart Association Guidelines for deeper CPR chest compressions to help responders provide high-quality CPR, the AED Plus guides rescuers through the complete chain of survival, helping all sudden cardiac arrest victims, not just those who need a shock.

Jonathan Rennert, president of Zoll, said, "We are extremely pleased that Massport recognizes the unique aspects of the AED Plus that make it able to both provide a life-saving shock when needed, as well as help rescuers perform quality CPR. The combination of features played an important role in their selection of our product."

The Massachusetts Port Authority is a public authority whose transportation facilities generate more than \$8 billion annually, and enhance and enable economic growth and vitality in New England. Zoll makes medical devices and software solutions that help advance emergency care.

In other agreements/contracts news:

- **Cardica** (Redwood City, California) has achieved the first MicroCutter milestone under its distribution agreement and loan commitment with **Century Medical** (Tokyo), allowing Cardica to draw the first \$2 million of an up to \$4 million loan commitment from Century.

"We are pleased to have achieved this milestone within two weeks after signing the original agreement, bringing us access to additional capital as we continue to work with a select group of surgeons in Europe to gain initial experience and feedback for our MicroCutter Xpress 30," said Bernard Hausen, MD, PhD, president/CEO of Cardica. "We continue to believe Century is the right distribution partner for our MicroCutter product line in Japan, and look forward to a

positive ongoing collaboration ahead."

Under the terms of the agreement, which was reported earlier this month (*Medical Device Daily*, Sept. 12, 2011), the balance of all amounts drawn by Cardica will be due in September 2016, subject to certain conditions. Cardica expects to achieve the second milestone, which would enable Cardica to access additional amounts under the loan facility with Century, within the next several months.

Cardica makes stapling and anastomotic devices for cardiac and laparoscopic surgical procedures.

- **Accelr8 Technology** (Denver) said that Accelr8 and **Schott Technical Glass Solutions** (Jena, Germany) have renewed Accelr8's license to Schott for Nexterion microarraying slides using OptiChem biocoatings. In addition to renewing the existing non-exclusive license, Accelr8 also granted to Schott the right to sell OptiChem-coated products for application in medical diagnostics. Previously, Schott's license excluded medical diagnostic applications. The new right for diagnostic products allows Schott to sell up to 20,000 units/year to any single customer. If the customer plans to exceed this volume, Schott will refer the customer to Accelr8 to negotiate a direct license from Accelr8.

In return for the license, Schott paid \$150,000 to Accelr8 for a license fee and non-recourse pre-paid royalties. After reaching cumulative sales that generate the prepaid royalty amount, Schott will pay additional cash royalties to Accelr8 for subsequent sales. The term for the renewed license continues through Nov. 24, 2014.

Accelr8 Technology specializes in applications in medical instrumentation, basic research, drug discovery, and bio-detection.

- The **Premier** (Charlotte, North Carolina) healthcare alliance reported new agreements for medication and supply automation have been awarded to **AmerisourceBergen Technology Group** (Buffalo Grove, Illinois); **CareFusion Solutions** (San Diego); **Kirby Lester** (Lake Forest, Illinois); **McKesson Automation** (Cranberry Township, Pennsylvania); **Omniceil** (Mountain View, California); **Rx Security** (Port Chester, New York); and **Swisslog Healthcare Solutions** (Denver).

Premier maintains a repository of clinical, financial and outcomes information and operates a healthcare purchasing network. ■

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*HIT roundup***IntrinsiQ gets meaningful use approval for IntelliDose 3.9****A Medical Device Daily Staff Report**

**IntrinsiQ**, a division of **ION Solutions** (Burlington, Massachusetts), said its IntelliDose version 3.9 has received the federal government's "meaningful use" stamp of approval by earning EHR Modular certification. The designation officially deems the electronic health record (EHR) software or healthcare application capable of enabling providers to qualify for funding under the American Recovery and Reinvestment Act (ARRA). Tested and certified under the Drummond Group's Electronic Health Records Office of the National Coordinator Authorized Testing and Certification Body (ONC-ATCB) program, the software is 2011/2012 compliant in accordance with the criteria adopted by the Secretary of Health and Human Services.

"With this certification, IntelliDose users can be confident our application is a key asset in helping them achieve their meaningful use targets," said Andrew Scott, director of product management for IntelliDose. IntelliDose is certified under number 09012011-1286-8 and listed on the ONC-Certified Health IT Product List.

Drummond Group's ONC-ATCB 2011/2012 certification program tests and certifies that EHRs meet the meaningful use criteria for either eligible provider or hospital technology. In turn, healthcare providers using the EHR systems of certified vendors are qualified to receive federal stimulus monies upon demonstrating meaningful use of the technology – a key component of the federal government's push to improve clinical care delivery through the adoption and effective use of EHRs by U.S. healthcare providers.

IntelliDose provides oncology-specific functionality for EHRs and health information systems. By creating a unified system to track chemotherapy treatments, IntelliDose says it helps practices become safer and more efficient, reducing the margin for human error and allowing practitioners to spend less time entering data and more time with their patients. It's installed at private and multi-specialty practices, community hospitals, and academic medical centers.

IntrinsiQ is a provider of medical oncology clinical information systems and the premier source of U.S. oncology data and analysis. ION Solutions provides technologies, resources and expertise to community-based oncologists to help improve clinical and operational management.

In other HIT news, **HealthPort** (Alpharetta, Georgia), an authority on the HIPAA-compliant exchange of protected health information through release of information services and audit management technology, reported key enhancements to its meaningful use (MU) certified EHR module, eSmartlog, for both inpatient and ambulatory use.

As HealthPort experiences an increase in customer

meaningful use participation, the Company anticipates that in the next two years, meaningful use will be the largest force driving change in release of information services, HealthPort's core-competency. Now available for customer use, the new release of eSmartlog equips HealthPort with the technological breadth to meet the security requirements of meaningful use, and to monitor, tally, and report the results for the release of information requirement of responding to patient requests for medical records in an electronic format within three business days.

This EHR Module is 2011/2012 compliant and has been certified by Drummond Group, an ONC-ATCB approved to certify any complete or modular EHR both ambulatory and inpatient, in accordance with the applicable certification criteria adopted by the Secretary of Health and Human Services. ■

**Med-Tech Notes****NeuroMetrix regains Nasdaq compliance**

**NeuroMetrix** (Waltham, Massachusetts) said it has received a letter from the Nasdaq stock market indicating that it has regained compliance with the minimum bid price requirement under Nasdaq Listing Rule 5550(a)(2) for continued listing on the Nasdaq capital market. NeuroMetrix is in compliance with all applicable listing standards and its common stock will continue to be listed on The Nasdaq Stock Market.

NeuroMetrix is a science-based healthcare company improving patient care through neurotechnology. The company makes products for the detection, diagnosis, and monitoring of peripheral nerve disorders such as those associated with diabetes and carpal tunnel syndrome.

**PPD expands clinical lab services**

**PPD** (Wilmington, North Carolina) said it has expanded its clinical microbiology laboratory at its global central laboratories worldwide, strengthening its laboratory testing services in infectious diseases, one of the largest therapeutic areas for clinical research and development.

PPD says it can now offer clients a full range of microbiology testing services such as bacteriology, mycobacteriology and testing of microbioterrorism pathogens. The laboratory also provides extensive virology testing, including real-time polymerase chain reaction, viral load, genotyping and single nucleotide polymorphism analysis. The laboratory has the capability to culture, quantitate, identify and determine antibiotic susceptibility and resistance for aerobic and anaerobic organisms. PPD is already running studies for staphylococcal and yeast infections and for the presumptive identification and quantification of microbiota.

## Vacuum

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and two “negative” arranged in a square in order to create a force field between them. Electrostatic quadrupoles are used in radio antennae, and magnetic quadrupoles serve to focus beams of charged particles in particle accelerators. Quadrupoles also exist in fluids. They have been described theoretically for decades, but this is the first time that they’ve been fabricated in a lab setting.

The concept of fluidic multipoles, in analogy to electrostatics, has long been known as a particular class of solutions of the Navier-Stokes equation in potential flows; however, experimental observations of fluidic multipoles and of their characteristics have not been reported yet. Here researchers have presented a two-dimensional microfluidic quadrupole and a theoretical analysis consistent with the experimental observations.

“We can locally probe cells in the sense of exposing them to different chemicals,” Juncker told *Medical Device Daily*. “The original start of the research [behind the device] was how to apply cues to cells. We then developed the idea of this quadrupole because we came to realize we could apply different gradients in a place where there would be no flows or the cell would be kind of sheltered in there and we could quickly vary different cues that would be applied to the cells.”

The device, which is shaped like a pen is fabricated by etching four holes in a silicon tip, which is about 1 mm square. When the device is brought close to a surface, it acts on it pretty much like a water jet vacuum cleaner would. Two apertures (the “plus” holes, or sources) emit microscopic jets of fluid, onto the surface below and the two other apertures (the “minus” holes, or drains), immediately suck them back into the device.

To take the vacuum analogy a bit further, “the probe is sitting on top of the cell and you have two ejection holes that are spitting out chemicals,” Juncker said.

The chemicals can stimulate, probe, detach or kill the cells depending on the application.

In explaining how it works more in depth, researchers say the microfluidic quadrupole was formed by simultaneously injecting and aspirating fluids from two pairs of opposing apertures in a narrow gap formed between a microfluidic probe and a substrate. A stagnation point was formed at the center of the microfluidic quadrupole, and its position could be rapidly adjusted hydrodynamically. Following the injection of a solute through one of the poles, a stationary, tunable, and movable — that is, ‘floating’ — concentration gradient was formed at the stagnation point. The results lay the foundation for future combined experimental and theoretical exploration of microfluidic planar multipoles including convective–diffusive phenomena.

Researchers also say that the probe can also create regions of smoothly varying chemical concentration called gradients. These gradients could be key to studying many cellular processes such as how bacteria and other cells

transverse the body.

The researchers hope that this new kind of device will find many applications in the *in vitro* study of a wide range of essential cellular processes.

“I think the primary application of the probe at this point is in research,” he said. “But maybe you could think of clinical applications too but more downstream. The idea could be having a single cell and seeing how it would respond to stimuli. You could take tumor cells and process them in the device and see how they would respond to different cues.”

Juncker said that there were no plans for commercialization at this time. ■

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### *Court report*

## Judge dismisses class-action suit vs. Boston Scientific

**A Medical Device Daily Staff Report**

A shareholders’ lawsuit accusing **Boston Scientific** (Natick, Massachusetts) of fraudulently concealing problems within its cardiac rhythm management division has been dismissed, according to various media reports.

Several firms sued the device maker last year after the company faced criminal charges for allegedly hiding information from the FDA regarding failures in some of its implantable cardioverter defibrillators (ICDs) (*Medical Device Daily*, Feb. 26, 2010). Shareholders’ groups claimed losses of more than \$2.8 million from buying stock at an artificially inflated price. However, U.S. District Judge Douglas Woodlock in Boston ruled this week that the complaint of at least one of those groups failed to state a “cognizable” claim for securities fraud.

“Rather than suggesting an intent to deceive investors, the facts contained in the complaint exhibit the defendants engaging in a good faith process to inform themselves and the public of the risks,” Woodlock said in a 41-page court document.

Boston Scientific reportedly failed to promptly disclose its decision to fire some sales representatives after an internal audit uncovered ethical violations in dealings with physicians, according to the complaint, filed on behalf of investors who bought the stock from Oct. 20, 2009, to Feb. 10, 2010.

The company disclosed the terminations in February 2010 after many of the sales personnel were hired by competitor **St. Jude Medical** (St. Paul, Minnesota), according to court papers. Boston Scientific reported in April 2010 that the combined criminal penalty of the actions would cost the company nearly \$300 million (*MDD*, April 14, 2010).

Woodlock ruled that the company made the disclosures in a “reasonable time.” ■

## Ablation

*Continued from Page 1*

of minimally invasiveness. Not only are we replacing open surgical procedures, but many times replacing the entire need for surgery. We are now performing ablation as an ambulatory procedure, many times under local anesthesia or as a totally non-invasive procedure.”

In addition, he noted that ablative therapies would have a profound effect on palliative therapy where many cases of brain, liver, kidney and lung cancers will be transformed from a malignant metastatic disease to a chronic illness.

The use of plasma energy for tissue ablation was discussed by Farr Nezhat, MD, Professor of OB/Gyn, **St. Luke's-Roosevelt Hospital** (New York). Nezhat described plasma energy as the 4th stage of matter after solid, liquid and gas that we are all familiar with. Plasma surgery provides an electrically neutral energy source that does not require grounding pads; and that it cuts, ablates, and coagulates many types of tissue from adhesions to bone with very minimal collateral damage. The downside for plasma energy is that it cannot seal large vessels nor can it be delivered via a flexible instrument. **Plasma Surgical** (Roswell, Georgia), an exhibitor here, is currently the only vendor for this type of surgical energy source. Nezhat presented his study of 45 patients with endometriosis on whom he performed plasma surgery and demonstrated effectiveness of removing the tissue without any complications.

Kambiz Dowlatabat, MD, **Rush University Medical Center** (Chicago) presented his study on the long-term survival of breast cancer patients whose tumors had been treated with interstitial laser ablation. He percutaneously treated 64 breast cancer patients using the interstitial laser manufactured by **Novian Health Systems** (Chicago) that utilizes a temperature probe placed parallel alongside the treatment probe in order to determine that the laser probe has reached -60 degrees Celsius, the temperature required for 100% kill accuracy.

The first 54 patients also had a lumpectomy and their tumors were sectioned for pathology while the remaining 10 patients were only monitored for 10 years. At one year out, the tumors were no longer visible upon imaging. At 10 years out, there was a 96% total ablation of the tumor with no residual scar. Dowlatabat concluded, “Ten year follow up shows that laser ablation is a viable alternative to surgery for selected breast cancer patients. These patients can be monitored using MRI to detect any recurrence.”

**InSightec** (Carmel, Israel), along with an investment from **GE Healthcare** (Chalfont, UK), has developed a non-invasive system using HIFU guided under MRI that was FDA cleared in 2004 for treatment of symptomatic uterine fibroids. They have also received the CE mark for pain palliation of bone metastases in June 2007 and for adenomyosis in June 2010.

Kopelman explained how he uses MRI to identify the target lesion then directs the focused ultrasound to

heat and destroy the targeted tissue non-invasively. The InSightec system has been used to treat adenomyosis, benign and malignant breast cancer, liver and prostate tumors. Research is ongoing to use the system for low risk prostate cancer, bone cancer, and recent investigations are looking into neurological tremors, strokes and possibly even bariatric treatments on the hypothalamus. For bone cancer, they have discovered that by zapping the bone mets there is a denervation of nerves resulting in pain palliation.

The drawback to ablation has been a slightly higher local recurrence rate at the site of the ablation and the fact that the tumor should be less than 4 cm (no advanced disease). However, unlike select other therapies and sometimes surgery, re-treatment is always an option with ablations.

One study presented here by Jeffrey Cadeddu, MD, Professor of Urology, **University of Texas Southwestern Medical Center** (Dallas), compared treatment of kidney tumors using RFA energy vs. surgery. The study demonstrated that in stage 1 tumors less than 4 cm there was a 99% cancer specific survival rate and at 5 years a 95% metastasis-free rate in kidney cancer. Cadeddu noted, “The chance of developing chronic kidney disease with surgical partial nephrectomy is relatively high but lower with RFA. If looking to preserve kidney function, RFA should be considered as primary option not a secondary one.”

Kopelman presented an innovative use of HIFU that can attain transcranial HIFU ablation. He opened by stating, “For decades, therapeutic transcranial ultrasound was assumed impossible, due to disruption of the focused acoustic beam by the skull, and the production of damaging heat by the ultrasound. Novel technology using high-power phased array transducers and multiple channel driving electronics enabled a sharp focal point in the planned target. MR images provide intraoperative anatomical data to identify the target, and real-time thermo-sensitive images allow intraoperative feedback to evaluate treatment outcome and guide the therapy.”

Potential applications for transcranial HIFU technology are essential tremor, neurogenic pain, epilepsy, and Parkinson's. Researchers at the **University of Virginia** (Charlottesville) are targeting the hypothalamus with either ablation or stimulation to cause reduced food intake for prevention of obesity. It could also be used to disrupt the blood brain barrier for enhanced delivery of therapeutic drugs, and for lysis of blood clots to treat ischemic and hemorrhagic stroke. Preclinical studies in a variety of experimental models have shown that it is safe, feasible, reproducible, and efficacious.

Although RFA, laser, and HIFU studies were presented in this plenary session, there are two other ablative energy modalities that are also being used to ablate tumors: cryoablation and Irreversible Electroporation (IRE). Cryoablation is the use of freezing temperature, below -40°C required to cause cell death in tumors of the kidney,

*See Ablation, Page 7*

## Europe

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Sapheon treatment does not require tumescent anesthesia or patient sedation.

“Treatment of incompetent great saphenous vein segments with the Sapheon technology is safe and effective,” according to Dr. Thomas Proebstle of Mannheim, Germany, a clinical investigator and early adopter of the Sapheon Closure system. “It is a welcome and exciting improvement over existing vein closure technologies.”

Distribution of the Sapheon Closure system within the EU will commence in 4Q11. The company plans to initiate a post-market study — the European Sapheon Closure System Observational Prospective (eSCOPE) Trial — in the EU starting in November 2011.

Sapheon is an early stage medical device company specializing in the treatment of vascular disease.

## Foundation Medicine to present at conference

**Foundation Medicine** (Cambridge, Massachusetts), a cancer diagnostics company that aims to bring comprehensive cancer genome analysis to routine care, will present data using its next-generation sequencing (NGS) approach to identify novel mutations with clinical use in routine cancer specimens at the 2011 European Multidisciplinary Cancer Congress in Stockholm, Sweden. These data will be presented by Gary Palmer, MD, JD, senior VP, medical affairs and commercial development, Foundation Medicine, in an oral presentation on Sunday, Sept. 25, at 9:00 a.m. during the “personalized medicine” proffered paper session, abstract number 800.

“We look forward to sharing data on our comprehensive pan-cancer diagnostic test with members of the European clinical oncology community,” said Palmer. “As additional mutations driving patients’ cancers are discovered and more targeted cancer therapies are developed to target these specific mutations, there is an even greater need for comprehensive cancer genome analysis to help inform treatment recommendations. Foundation Medicine’s test detects genomic alterations in relevant cancer genes, including many that are missed using conventional hot spot analysis, at a level of sensitivity and specificity that makes this a clinically relevant test.”

Foundation Medicine’s laboratory test is being designed to accommodate a broad landscape of cancer genome information and a growing repertoire of more targeted treatments and clinical research opportunities. Foundation Medicine’s test will assist physicians to make prompt and informed determinations about the best cancer treatments and clinical trial options for each patient, taking into account each patient’s unique cancer-associated alterations alongside publicly available scientific and medical information.

## Life Technologies, Quidel in European partnership

**Life Technologies** (Carlsbad, California) has signed an

agreement with **Quidel** (San Diego) to distribute molecular diagnostic assays for the European market.

The agreement calls for Life Technologies to sell Quidel’s current and future assays in Europe, where Life has a broad established distribution network. Beginning in October, Life Technologies will distribute the Quidel Molecular Influenza A+B Real-Time RT-PCR Assay and hMPV (human metapneumovirus) kits to European markets.

The companies say the kits offer both performance benefits and workflow benefits over currently available tests. The influenza kit was shown to be more sensitive and specific than the comparator assay in a trial with more than 600 samples. The workflow has been improved by allowing for refrigerated storage rather than freezer storage, one-step reagent setup, and fast qPCR cycling resulting in answers 75 minutes after sample preparation.

Both kits are for use with Life’s 7500 family PCR Instruments, which are installed in hundreds of clinical diagnostic labs across Europe. ■

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## Ablation

*Continued from Page 6*

liver, lung, soft tissue and the prostate. Long needles or probes are inserted percutaneously into the tumor and the ice formation is monitored under ultrasound, CT or MRI, potentially resulting in less damage to healthy tissue than heat ablation. While current cryoablation requires the use of large tanks of gas, a new approach to cryoablation has been developed by **CryoMedix** (San Diego) that eliminates the need for tanks and reduces the length of the procedure.

Another form of ablation not represented here is irreversible electroporation provided by **AngioDynamics** (Queensbury, New York). IRE has European CE mark to treat kidney and lung tumors and is being studied to treat pancreatic cancer, a disease with few and morbid options.

Pancreatic cancer is the fourth leading cause of cancer death in the U.S. and advanced disease at diagnosis correlates directly with worse overall survival. Symptoms often do not present until the tumor is inoperable at which point treatment options are limited, have extreme side effects, and often only extend life by a few months. IRE has been used to treat pancreatic cancer in 4 centers in the U.S. and some have patients surviving over 2 years when the average with standard treatment is 9-12 months. There have been more than 30 cases of IRE used to treat unresectable pancreatic tumors to date in the U.S. These have been done off protocol (off-label) in major centers located in Louisville, Stony Brook, Detroit, and recently in Tampa. All cases except one have been done open using a combination of surgical resection and IRE. Results are very preliminary; however, sudden adverse events have not been a major issue and several patients are survivors at 15-2.5 years. There is currently an approved protocol ongoing in Europe and discussions with FDA to initiate an approved clinical protocol in the U.S. ■

## Washington

*Continued from Page 1*

at JDRF told *Medical Device Daily* that the guidance's requirement to demonstrate superiority over the standard of care – as well as the demand for both in-patient and out-patient study arms – impedes access to a device that is widely available in other nations. "Are we going to withhold this product in the U.S because of this guidance?" Kowalski asked.

The guidance suggests a need for two glucose sensors, but Chip Zimliki, PhD, who supervises the artificial pancreas project at FDA, told *MDD* at the ADA gathering that this is not a concern for the agency so long as a sponsor can demonstrate that its device can do the job with just one sensor. Still, Kowalski indicated that he is concerned about the wiggle room the language of the guidance gives FDA to revert to a two-sensor requirement in the future. He said "this a major potential issue."

Another point Kowalski brought up is that FDA "has taken a systems-based approach" which requires that reviewers at the Office of Device Evaluation "review an entire package." The problem, Kowalski said, is "people with diabetes use a variety of meters, and locking these devices into" a particular meter is "really a huge problem, we think," and renders impossible any chance of "substituting equivalent components."

Kowalski described the in-patient study mandate as "an extremely burdensome requirement for in-patient studies," asking rhetorically, "what is this getting at?" He said JDRF has conversed with and "polled the entire clinical community," and that "all agree that the risk of a system that turns off insulin is very low. In fact, its difficult to find a significant risk," he said.

As for the out-patient arm of the trial, Kowalski said FDA "wants a close look at hypoglycemia. That may seem reasonable, but demonstrating a significant change in hypoglycemic exposure is a tricky problem" in part because "the person is already slightly hypoglycemic" when the device activates.

Regarding the Veo system, made by **Medtronic** (Minneapolis), Kowalski said, "we have a product that's saving lives all over the world," but "it's non-approvable in the U.S." because of FDA's demand for a trial showing superiority to conventional glucose monitoring. "Withholding a product like this because it's not showing superiority with a very difficult outcome is a huge issue," Kowalski said.

Kowalski said the requirement is a disincentive for industry to jump into the U.S. market. "We have a pathway that could cost millions of dollars and take many years, and there's a good chance it could fail," he said, adding, "this is a strange scenario. Here is a product that everybody agrees would add safety. The initial debate was whether the pump could turn off inadvertently" and cause diabetic acidosis, "but there's a lot of data to show that's not a risk," Kowalski said, a position he said was taken by a member of the FDA

staff, Patricia Beaston, MD, a medical officer at the agency.

FDA has also demonstrated an interest in seeing whether the patient will experience poor glucose control when the pump goes off due to lack of a trigger. "That's even a stretch," Kowalski remarked, adding, "we have lots of data to see what happens in the real world." He said "a patient can set a threshold" for hypoglycemia manually, but although there may be a risk of a patient failing to monitor the situation, such as when falling asleep, most pumps have a reset function. As a safety feature, the generally accepted time frame is that it turns the pump back to the pre-set level after two hours, he said.

There was a concern that the insulin would clog the pumps, but the data do not bear out that problem either, Kowalski said. "You have all of this data" from the European Union, he said, but the data from "all these thousands of people are not being utilized, which is very frustrating." Kowalski also pointed out that the artificial pancreas project became part of the agency's Critical Path Initiative five years ago.

Zimliki indicated at the ADA event that part of the agency's interest in feedback on the LGS system was due to the need to use that feedback to inform a guidance for an artificial pancreas system, but *MDD* asked whether FDA is likely to have that second guidance out by December as promised. "This is the million-dollar question," Kowalski observed. He said "the outcomes are easier to quantify" for low-glucose suspension than for a mechanism to regulate the entire range of glycemic values. "It turns out that quantification of hypoglycemia is a very difficult thing to do," Kowalski observed, adding that the issue is somewhat dependent on sensor accuracy, but "I think FDA has become too hung up on that," he said.

Regarding the mindset that reviewers at the Office of Device Evaluation have become too fixated on numerical input, a mindset seconded by biostatisticians that is experiencing push-back by clinicians of late, Kowalski said, "I call it the clinical camp and the chemistry camp" in the world of diabetes. He said one question often asked is: "Does a blood glucose perfectly match interstitial glucose?" He said FDA "want[s] a number of studies looking at paired points between" continuous glucose monitor read-outs and a standard test of blood glucose, but asserted "we should be looking at the outcomes" instead of correlations.

Kowalski said that FDA is under some stresses that make it difficult to operate rationally at times. "I think there's a conservative nature [at the agency] because they get hammered from all angles," he said, but was not willing to back off the criticism in the case of the artificial pancreas effort. "In this case it's justified because we've been working with them for years." ■

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## Product Briefs

- **Aethlon Medical** (San Diego) reported the introduction of HER2osome, a medical device strategy to inhibit the progression of HER2+ breast cancer, which is characterized by aggressive growth and poor prognosis resulting from the over-expression of HER2 protein. HER2+ breast cancer accounts for about 25% of new breast cancer diagnosis in women. The goal of HER2osome therapy is to simultaneously reduce the circulatory presence of HER2 protein and breast cancer exosomes, which have increasingly become recognized as playing pivotal role in the development and progression of breast cancer. Researchers report that breast cancer exosomes suppress the immune response, stimulate angiogenesis, contribute to the spread of metastasis, and inhibit the therapeutic benefit of Herceptin (trastuzumab), a leading monoclonal antibody treatment against the HER2+ breast cancer. As an adjunct therapeutic candidate, HER2osome offers to address an unmet medical need and enhance the benefit of Herceptin and standard of care chemotherapies without adding drug toxicity or interaction risks. The evolution of HER2osome therapy is based upon an adaptable dialysis-like affinity platform technology known as the Aethlon ADAPT system. Therapies evolved from the Aethlon ADAPT system target the selective clearance of harmful agents from the entire blood volume within clinically relevant time frames and without the loss of essential blood components.

- **Covidien** (Manningsfield, Massachusetts) reported published data demonstrating that the company's first powered surgical stapling system provides deeper access, better visibility and easier placement inside the low pelvis than a competing mechanical stapling device. The results of the pre-clinical cadaver study directly comparing Covidien's iDrive powered handle and Right Angle Linear Cutter (RALC) to the Contour Curved Cutter Stapler (Ethicon Endo-Surgery) are available online in the *Annals of Surgical Innovation and Research*. The iDrive powered handle is a battery-powered, multi-patient, reusable handheld stapler and the RALC is a single-use reload, combining stapling and cutting functionality. When fired, the system deploys 32 titanium DST Series staples in two double-staggered rows and an integrated knife bisects the underlying tissue. With the push of a single button, the handle's high-speed brushless motor delivers 4 rows of staples and cuts at an angle that is perpendicular to a curved shaft. This study shows that the stapler's geometry may help gain deeper access to, and better visibility within, the pelvis during low anterior resections. The iDrive powered handle and RALC could be placed lower in the rectum than the Ethicon Contour Curved Cutter Stapler in both the coronal and sagittal positions. The median distance of the stapler

from the pelvic floor in the coronal position for the iDrive powered handle and RALC was 1.0 cm, compared to 2.0 cm for the Contour.

- **NanoString Technologies** (Seattle) reported the availability of the nCounter miRGE assay for use on its nCounter Analysis System. The nCounter miRGE assay enables researchers to investigate expression levels of both micro RNAs (miRNAs) and the messenger RNAs (mRNAs) they potentially regulate in a single reaction, without the need for amplification. The miRGE assay provides the capacity to perform multiplexed profiling of 5-30 miRNAs and 100-200 mRNAs simultaneously, with specificity and sensitivity comparable to qPCR. The nCounter system is an automated digital detection and counting system with a very simple workflow. The assays contain all of the reagents and consumables required to conduct an experiment. The nCounter Analysis System is currently available for research use only.

- **PeriOptix** (San Clemente, California) reported the launch of its new 4.0x prismatic loupe and the Solaris LED headlight. The new prismatic loupes will be mounted on the Hogies modular and stylish sports frame system. The Hogies feature a magnetic system that attaches the optics, splash shield and nose pad to the frame. There are 10 color choices available. Dissimilar to most prismatic loupes, the PeriOptix prismatic loupes use Optilock technology that provides for a one-knob adjustment of the loupes to accurately align both loupe barrels to the user's eyes. Once adjusted, the alignment is locked and no further adjustment will be required. PeriOptix makes dental products.

- **Seegene** (Seoul, South Korea) reported the commercialization of its first real-time assay based upon its new TOCE technology. The Anyplex II STI-7 detection assay will provide clinicians with a powerful new tool to help protect health and prevent the spread of sexually transmitted infections (STIs), also known as sexually transmitted diseases (STDs). The Anyplex II STI-7 detection assay is a multiplex real-time PCR test that can simultaneously detect seven of the more common causes of STIs from a wide range of specimen types such as, urine, vaginal and urethral swabs, and liquid-based cytology specimen. The Anyplex II STI-7 assay enables clinicians to simultaneously detect the presence of: *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium*, *Mycoplasma hominis*, *Trichomonas vaginalis*, *Ureaplasma urealyticum*, and *Ureaplasma parvum*. The Anyplex II STI-7 detection assay is based on Seegene's recently introduced TOCE technology, which turns any multiple color real-time PCR instrument into a powerful multiplexing platform. TOCE enables complex multiplexing in a single fluorescence channel, provides consistent T<sub>m</sub> values regardless of the sequence variation of the target, and a level of sensitivity better than that of currently used probe-based singleplex real-time PCR assays.

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# MDD'S DIAGNOSTIC EXTRA

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

FRIDAY, SEPTEMBER 23, 2011

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*Keeping you up to date with recent developments in diagnostics*

**Imaging technique can better spot ovarian cancer . . .** Ovarian cancer is one of the most frequent forms of cancer that affect women. As tumors can initially grow unchecked in the abdomen without causing any major symptoms, patients are usually diagnosed at an advanced stage and have to undergo surgery plus chemotherapy. During the operation, surgeons attempt to remove all tumor deposits as this leads to improved patient prognosis. To do this, however, they primarily have to rely on visual inspection and palpation – an enormous challenge especially in the case of small tumor nests or remaining tumor borders after the primary tumor excision. Yet surgeons could now be getting support from a new multispectral fluorescence imaging system developed by a team of researchers in Munich, headed by Vasilis Ntziachristos, Professor of Biological Imaging. A study carried out on nine patients with ovarian cancer has shown that the new system can be used to localize cancer cells during surgery. Before the operation, the patients were injected with folic acid chemically coupled to a green fluorescent dye. Most ovarian tumors have a protein molecule on their surface that bonds with folic acid and transports it inside the cell. This protein is known as the folate receptor alpha. During abdominal surgery, the surgeon can then shine a special laser light onto the patient's ovaries, causing the green-labeled folic acid inside the cancer cells to emit light. Healthy tissue remains dark. The fluorescent cancer cells, however, cannot be detected by the naked eye. Three cameras, mounted on a pivoting support arm over the operating table, detect optical and fluorescent signals at multiple spectral bands and then correct for light variations due to illumination and tissue discolorations in order to provide truly accurate fluorescence images that can be simultaneously displayed with corresponding color images on monitors in the operating room. The surgeon can thus check whether all the cancer cells have been removed by inspecting for remnant fluorescence light. In eight of the nine patients, doctors were able to remove small clusters of tumor cells that might otherwise have gone undetected. The multispectral fluorescence imaging system has thus passed its first OR test. However, it will have to prove its value to improve clinical outcome in further operations before it can be deployed for routine surgical procedures. The researchers in Munich and Groningen also want to further develop the camera system so it can be used to detect other forms of tumors during operations. Of significant importance in future developments is the ability to offer accurate fluorescence imaging so that data collected reflect true presence of disease. "The use of advanced, real-time optical technology will allow us to standardize data collection and accuracy so that studies performed at multiple clinical centers can be accurately compared and analyzed" explains Ntziachristos. This is important for the clinical acceptance of the technology and its approval by regulatory agencies. In the future patient selection through personalized medicine approaches, for example by obtaining a molecular profile of the tumor of each patient, would further enable custom-tailored surgical treatment of improved accuracy. The team is also planning to build a version for minimally invasive operations.

## **UCSB group works to develop micro-device for studying cancer cells**

. . . A team of researchers at **UC Santa Barbara** (Santa Barbara, California) has developed a breakthrough technology that can be used to discriminate cancerous prostate cells in bodily fluids from those that are healthy. The findings are published this week in the Proceedings of the *National Academy of Sciences*. While the new technology is years away from use in a clinical setting, the researchers are nonetheless confident that it will be useful in developing a micro-device that will help in understanding when prostate cancer will metastasize, or spread to other parts of the body. "There have been studies to find the relationship between the number of cancer cells in the blood, and the outcome of the disease," said first author Alessia Pallaoro, post-doctoral fellow in UCSB's Department of Chemistry and Biochemistry. "The higher the number of cancer cells there are in the patient's blood, the worse the prognosis. "The cancer cells that are found in the blood are thought to be the initiators of metastasis," Pallaoro added. "It would be really important to be able to find them

and recognize them within blood or other bodily fluids. This could be helpful for diagnosis and follow-ups during treatment.” The researchers explained that although the primary tumor does not kill prostate cancer patients, metastasis does. “The delay is not well understood,” said Gary Braun, second author and postdoctoral fellow in the Department of Molecular, Cellular, and Developmental Biology. “There is a big focus on understanding what causes the tumor to shed cells into the blood. If you could catch them all, then you could stop metastasis. The first thing is to monitor their appearance.” The team developed a novel technique to discriminate between cancerous and non-cancerous cells using a type of laser spectroscopy called surface enhanced Raman spectroscopy (SERS) and silver nanoparticles, which are biotags. “Silver nanoparticles emit a rich set of colors when they absorb the laser light,” said Braun. “This is different than fluorescence. This new technology could be more powerful than fluorescence.” The breakthrough is in being able to include more markers in order to identify and study unique tumor cells that are different from the main tumor cells, explained Pallaoro. “These different cells must be strong enough to start a new tumor, or they must develop changes that allow them to colonize in other areas of the body,” she said. “Some changes must be on the surface, which is what we are trying to detect.” The team is working to translate the technology into a diagnostic microdevice for studying cancer cells in the blood. Cells would be mixed with nanoparticles and passed through a laser, then discriminated by the ratio of two signals. The two types of biotags used in this research have a particular affinity that is dictated by the peptide they carry on their surface. One type attaches to a cell receptor called neuropilin-1, a recently described biomarker found on the surface membrane of certain cancer cells. The other biotag binds many cell types (both cancerous and non-cancerous) and serves as a standard measure as the cells are analyzed. In this study, the team mixed the two biotags and added them to the healthy and tumor cell cultures. The average SERS signal over a given cell image yielded a ratio of the two signals consistent with the cells’ known identity. Pallaoro said she believes the most important part of the new technique is the fact that it could be expanded by adding more colors – different particles of different colors – as more biomarkers are found.

**New blood test could detect heart attacks . . . Loyola University Chicago Stritch School of Medicine** (Maywood, Illinois) researchers are reporting a possible new blood test to help diagnose heart attacks. In the *Journal of Molecular and Cellular Cardiology*, researchers report that a large protein known as cardiac myosin binding protein-C (cMyBP-C) is released to the blood following a heart attack. “This potentially could become the basis for a new test, used in conjunction with other blood tests, to help diagnose heart attacks,” said senior author Sakthivel Sadayappan, PhD. “This is the beginning. A lot of additional studies will be necessary to establish cMyBP-C as a true biomarker for heart attacks.” Sadayappan is an assistant professor in the Department of Cell and Molecular Physiology at Loyola University Chicago Stritch School of Medicine. First author is Suresh Govindan, PhD, a postdoctoral researcher in Sadayappan’s lab. Between 60% and 70% of all patients who complain of chest pain do not have heart attacks. Many of these patients are admitted to the hospital, at considerable time and expense, until a heart attack is definitively ruled out. An electrocardiogram can diagnose major heart attacks, but not minor ones. There also are blood tests for various proteins associated with heart attacks. But most of these proteins are not specific to the heart. Elevated levels could indicate a problem other than a heart attack, such as a muscle injury. Only one protein now used in blood tests, called cardiac troponin-I, is specific to the heart. But it takes at least four to six hours for this protein to show up in the blood following a heart attack. So the search is on for another heart attack protein that is specific to the heart. The Loyola study is the first to find that cMyBP-C is associated with heart attacks. The protein is specific to the heart. And it may be readily detectable in a blood test because of its large molecular size and relatively high concentration in the blood. Researchers evaluated blood samples from heart attack patients. They also evaluated rats that had experienced heart attacks. They found that in both humans and rats, cMyBP-C was elevated significantly following heart attacks. Sadayappan said cMyBP-C is a large assembly protein that stabilizes heart muscle structure and regulates cardiac function. During a heart attack, a coronary artery is blocked, and heart muscle cells begin to die due to lack of blood flow and oxygen. As heart cells die, cMyBP-C breaks into fragments and is released into the blood. “Future studies,” Sadayappan and colleagues wrote, “would determine the time course of release, peak concentrations and half life in the circulatory system.”

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