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BB&T at the Society of Laparoendoscopic Surgeons annual meeting 2011

Many paradigm shifts predicted in the near future for surgeons

By DIANA TUCKER, *BB&T* Contributing Writer

LOS ANGELES — Insights into the future of surgery were presented here at the 20th anniversary of the **Society of Laparoendoscopic Surgeons** (SLS; Miami) annual meeting. Predictions on telementoring guidance, single port surgery vs. NOTES, robotic surgery, ablative therapies, and even the elimination of general anesthesia in select cases were debated among the general, gynecological, urological, foregut surgeons and endoscopists attending this conference.

Telementoring guidance

In the opening ceremony, James "Butch" Rosser, Jr., MD, President of SLS, Chief of Minimally Invasive Surgery at **Beth Israel Medical Center** (New York) coined the term "edutainment" to describe the format for this year's meeting; as he delivered an entertaining form of education with many interactive events, town hall meeting formats for controversial issues, and his now famous "Top Gun" laparoscopic skills shoot out contest. Rosser addressed the audience of advanced laparoscopic surgeons and endoscopists by telling them that in his book SLS stands for the Society of the League of extraordinary Surgeons because members of this society are the promoters and early adopters of advanced surgery.

The Inside Story

Rosser is known internationally as a pioneer who has likened video games to laparoscopic skills and has pioneered telementoring guidance as a form of directing a surgeon from a distance. Telementoring is much like using Skype, where the experienced surgeon is watching a remote surgery being performed in real time by the less experienced surgeon who is doing the surgery in a distant place while listening to the mentor from afar walk him through the procedure.

Until now the hurdle to widespread use of telementoring has been a medical-legal one, where licensure across state boundaries along with lack of malpractice coverage has been a huge barrier. At this meeting, Rosser announced that for the first time ever "one of our members" would now be offering a medical malpractice coverage on an episodic basis for telementoring guidance. In addition, all states will provide a temporary medical license. The combination of licensure and temporary interstate malpractice coverage will now provide a higher degree of confidence for surgeons to employ telementoring guidance.

"Not only is this important to the surgeons residing in the 50 United States, but also to the over 40 countries represented at this meeting that has now become an international meeting. Representatives from Australia, Russia, Serbia, Singapore, South Africa, Spain, Switzerland, UK, Nepal and 31 other countries are in attendance here and now have telementoring available to them," said Rosser. "Traditional laparoscopy is broken. There are too many complications and not enough adopters of advanced techniques. Telementoring's time has come. The time has come where no surgeon should operate alone," he added. (*See Table 1*)

Table 1
Methodology of Telementoring

- Pre-procedural assessment and enhancement of laparoscopic surgical skills
- Computer-based instruction
- Military like two-way communication
- Establish a standardized technique algorithm
- Familiarization with teleguidance tools
- Telementoring simulation

Source: Butch Rosser, MD, Presidential address, SLS opening speech

Single port surgery vs. NOTES

"We need to stop being either a NOTES (Natural Orifice TransEndoscopic Surgery) or single port (laparoscopic surgery done through the umbilicus) purist and bring them all together to attain the next level of minimal access surgery," opened Paul Curcillo II, MD, Director, Minimally Invasive Surgical Initiatives and Development, **Fox Chase Cancer Center** (Philadelphia) in the master's class for Reduced Port Minimally Invasive Surgery (MIS) aptly titled "More than an Incision Decision." "With this new rebirth of reduced port techniques, we need to stay focused on techniques and not products; along with attention towards safety, outcomes, and cost effectiveness," Curcillo continued, "Reduced port surgical techniques will take us to the next level of minimal access surgery whether it is NOTES, single port, a combination, or something beyond. NOTES let us realize we could push our limits."

While understanding that reducing the number of holes made into the abdomen can benefit patients (*See Table 2*), Curcillo emphasized the importance of measuring the risk vs. benefit when making decisions for the procedure being done on a patient. His SPA concept is based on how multiport surgery can be mimicked into a single hole, but not at the expense of patient safety. "It is far better to add an additional hole, or use an additional NOTES entry than to risk the safety of the patient," he admonished.

Table 2
Patient Benefits of Single Port or NOTES Surgery

- Scarless
- Less pain
- Faster return to normal activities
- Possible to avoid general anesthesia in select cases
- Comparable length of stay in hospital to conventional laparscopy
- Comparable outcomes

Source: BB&T notes from SLS seminars, Industry contacts

So far, only 15% of all laparoscopic procedures are performed using a single port. It is expected that the next frontier for conversion to single port will be laparoscopic cholecystectomies since 100% of them are now being performed laparoscopically through multiple ports. According to the mentors at this meeting, residents without prior procedural habits learn very quickly and should be taught single port from the beginning of their training. However, only procedures that are routinely done laparoscopically should be converted to single port; those procedures that are currently performed as an open procedure should not be converted directly to single port laparoscopy.

To date, worldwide NOTES procedures number 7.000, with the U.S. accounting for about 275 of those procedures. NOTES procedures in the U.S. have had an uphill battle for both FDA clearance as well as reimbursement. Outside the U.S. patients pay for their own NOTES procedures.

Since the most popular NOTES approach is transvaginal, Curcillo pointed out that should NOTES hybrid procedures become more widely utilized, only 1/3 of the population would be a potential candidate if consider-

ing a transvaginal approach. Obviously men would be excluded, but additionally young women or women with prior pelvic surgeries would also be excluded, leaving about a 30% potential candidate pool for that method. To which, Michael Marohn, MD, Associate Professor of Surgery, **Johns Hopkins Medical Center** (Baltimore) quipped, "More than likely, there will never be a NOTES transvaginal prostatectomy."

Reduced port learning process

Curcillo, who has never changed his method in more than 500 single port cases using his own single port access (SPA) technique, stressed the importance of mimicking standard multi-port laparoscopic technique with the only difference being a reduced number of holes. In order to learn single port surgery, Curcillo advocates beginning with the normal five ports and then reducing one port at a time until only one or two ports are being used routinely. The exact opposite of that approach is being advocated by Sharona Ross, MD, Assistant Professor of Surgery, **University of South Florida, Tampa General Hospital** (Tampa, Florida).

In her presentation that followed his, she said that she felt single port surgery will replace conventional laparoscopy for all operations that are now using conventional multi-port laparoscopic technique.

She claimed "Single port surgery is here and now and growing fast. It involves a similar skill set as conventional laparoscopy and has a short learning curve." Ross advocates starting with a single port and adding holes as necessary. "Do not change your current surgical approach; do not change the operation. If you are changing the way you would operate using conventional laparoscopy, then something is not going well," she told the audience.

Ross also advocates using enabling devices but only as necessary to complete the procedure safely and limiting additional (unnecessary) cost. "You should develop your own toolbox with instruments that make it easier to address the challenge of single port surgery," Ross explained. (*See Table 3*)

Table 3
Enabling Devices for Single Port Surgery

- Articulated instruments
- Multi-trocar port
- Bent or curved instruments
- Needleoscopic instruments
- Internal retractors
- Magnetic retractors

Source: Curcillo, Ross, Industry contacts

Cost considerations

Since the inception of single port surgery, there has been a proliferation of devices to assist in performing single port procedures; however, simultaneously there has been increasing cost pressures placed on surgeons so that the current mantra is to use only additional cost instruments that are necessary to insure the safety of the patient. One audience member calculated that if a hospital performed 600 cholecystectomies a year and only used one additional multi-trocar port per procedure at an average cost of $325 each, the incremental cost to the hospital would be close to $200,000. One of the first categories of enabling devices designed for single port surgery was a single port device that accommodated multiple trocars. (*See Table 4*)

Table 4
Single Port, Multiple Trocar Devices

Brand name	Manufacturer
Air Seal	Surgiquest (Orange, CT)
Gelport	Applied Medical (Rancho Margarita, CA)
SILS port	Covidien (Norwalk, CT)
Single incision, multiple low profile trocars (Curcillo technique)	
SSL Access System	Ethicon Endosurgery (Cincinnati)
Triport	Olympus (Center Valley, PA)
Quadport	Olympus (Center Valley, PA)
Uni-X	Pnaval Systems (Morgansville, NJ)

Source: William E. Kelley, Jr., MD

Regardless of whether surgeons are using the reduce-one-port-at-a-time learning process advocated by Curcillo, or the start-with-one-port-and-add-as-needed learning process supported by Ross, those medical device manufacturers that have developed single port instrumentation will probably need to adjust their sales forecast downward as cost pressures are exerted and surgeon skills are increased that allow surgeons to depend more on their skills and less on enabling devices.(*See Table 5*)

Since the insurance companies pay the same per procedure whether it is multi-port, single port, or robotic; the surgeons and the hospitals are absorbing the additional costs. For cholecystectomies, Curcillo's SPA technique that does not entail any special instrumentation actually costs the hospital $190 less than multiport because they are using fewer (single vs. multi) instruments, demonstrating that single port can be performed without incremental cost.

Table 5
Cost Considerations for Robotic & Single Port Surgery

Additional costs	No additional costs
Surgeon spends more operating time	Payer pays the same
Hospital uses more OR time	No difference for patient
Hospital pays for extra device cost	

Need for standardization of new techniques

William Kelley, Jr., MD, **Richmond Surgical Associates** (Richmond, Virginia), Director of the Master's course on Reduced Port Surgery, addressed the safety, cost, and safe adoption of single port surgery and noted that at the present time there is very little standardization in any aspect of single incision surgery, including nomenclature. (*See Table 6*)

With standardization for all current procedures becoming a fait de compli; Kelley, along with many of the surgeons presenting in the master's course, emphasized the need especially for standardization of single port technique and referred to a committee meeting on this topic during the upcoming **American College of Surgeons** (Chicago) annual meeting in October.

Robotic surgery of the future

In a private interview with *BB&T*, Ross opined that in the future all operations would either be performed using single port laparoscopy or the robot. There are 10 million surgical procedures performed annually in the U.S. and 3 to 4 million of those are performed via minimally invasive surgery. Ross believes that there will be an evolution into two camps: robotic or single port. Current conventional multiport laparoscopic procedures will no longer exist, nor will open surgery. In essence, she feels that procedures that are performed frequently, do not require a high degree of special skill, and do not warrant the high cost of using the robot, will all be performed using single port surgery. Other procedures that are complex, rarely performed, often involved with cancer resection, frequently require reconstruction or anastomosis, require a high skill level and were previously performed as an open procedure will be performed robotically. (*See Table 7*)

Table 6
Nomenclature being used to describe Single Port Surgery

LESS	Laparo-Endoscopic Single-site Surgery
NOTUS	Natural Orifice Transumbilical Surgery
OPUS	One Port Umbilical Surgery
SILS	Single Incision Laparoscopic Surgery (Covidien)
SIMPL	Single Instrument Port Laparoscopic Surgery
SLAPP	Single Laparoscopic Port Procedure
SLIT	Single Laparoscopic Incision Transabdominal
SPA	Single Port Access (Curcillo)
SPLN	Single Port Laparoscopic Surgery
SSL	Single Site Laparoscopy (Ethicon Endosurgery)
TTLS	Totally Transumbilical Laparoscopic Surgery
TUES	Transumbilical Endoscopic Surgery

Source: William E. Kelley, Jr., MD

Table 7
How Procedures will be Performed in the Year 2020

Single Port Procedures	Robotic Procedures
Bread & butter operations	Complex procedures
High volume (frequently performed)	Infrequently performed Reconstructive procedures
Low cost (robot not justified)	High cost justified Requires high level of skill Previously performed open
Easy skill level	Often cancer resection

Source: Sharona Ross, MD, Assistant Professor of Surgery, University of South Florida

Currently the da Vinci robot – the only one on the market – manufactured by **Intuitive Surgical** (Sunnyvale, California) is not FDA cleared, nor is capable of, single port surgery although a single port system is in development.

However, it is estimated that 85% of all conventional multiport laparoscopic prostatectomies performed in the U.S. in 2011 will be done on the robot. Driven by patient demand and not surgical necessity, there are currently 2250 robots placed worldwide at an average price of approximately $2 million each, with gynecology motivating the current expansion. While many experienced surgeons have said that the robot is a crutch for poor surgeons, it appears that by training new surgeons on the robot, there may be no need for good surgeons who can perform difficult procedures without the robot in the future. In fact, several of the leaders at this meeting have commented on the poor surgical technique of incoming residents since they have had little surgical training other than laparoscopic. Overheard at this conference was "New residents could not possibly convert to an open surgery if a prob-

lem arose. They could, however, convert from a single port to a multi-port procedure." Surgeons who have embraced the robot may have realized their own planned obsolescence.

Potential to eliminate general anesthesia for select cases

Ross also discussed the highly controversial issue of being able to perform some single port surgeries without general anesthesia. Her first case without general anesthesia was on a surgeon who was deathly afraid of general anesthesia and requested that Ross try using an epidural, the same as is used for Caesarian sections, instead of general anesthesia. Ross and her assisting anesthetist were able to paralyze the patient almost up to her diaphragm but still keep her breathing on her own. With careful synchronization of suturing with the patient's breathing, the procedure went well and now Ross offers this to select patients routinely. The cost savings as well as patient benefits are significant. (*See Table 8*)

Table 8
Cost Savings & Patient Benefit When Eliminating General Anesthesia

Patient Benefits
- No nausea
- No grogginess
- Nominal recovery room time if any
- Go home significantly quicker
- No sore throat from intubation
- Less meds used

Cost Savings
- Significantly shorter OR time
- Epidural is done prior to going to OR
- No intubation
- No induction of anesthesia
- Nominal costly recovery room time

Source: Sharona Ross, MD, Assistant Professor of Surgery, University of South Florida

Tissue ablation therapies

Professor 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 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. (*See Table 9*)

Table 9
Directed Energy Modalities for Tissue Ablation

Energy source	Select Manufacturers
Radio frequency	Angiodynamics
Cryo therapy	CryoMedix Galil Ice Cure
HIFU Microwave	InSightec
Irreversible electroporation	Angiodynamics

Source: Industry contacts

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 Dowlat, 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 11 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. Dowlat 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. (*See Table 10*)

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. "

Table 10
Advantages of Ablation Therapies in General

- No toxicity
- OK to repeat treatments
- Can often be performed percutaneously
- Significantly less costly than surgery
- Can be performed laparoscopically
- Fewer complications
- Follow-ups can be monitored using imaging
- Studies comparing cryo, RF and surgery have shown comparable outcomes

Source: SLS seminars, Industry contacts

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, 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 1.5-2.5 years. There is currently an approved protocol ongoing in Europe and discussions with FDA to initiate an approved clinical protocol in the U.S.

If this conference reflects the future of surgery, then

Controversy spotlighted at world's largest cardiology meeting

By JOHN BROSKY
***BB&T* European Editor**

PARIS — Boasting a record participation of more than 30,000 cardiologists, the **European Society of Cardiology** (ESC; Sophie Antipolis, France) said this year's meeting is the largest cardiology meeting in the world, and Europe's largest medical meeting.

ESC 2011 is easily the most international of events with 144 countries represented, a tribute to the success of the society in gathering cardiologists from the four corners of the globe. The society today counts 53 national cardiac societies, five associations, and 35 affiliate national cardiac societies.

***BB&T* at European Society of Cardiology annual meeting**

Being held outside Paris at the Parc des Expositions near the Charles de Gaulle airport, the 30-minute train ride from the central city is a cacophonous celebration of languages, even by the standards of this cosmopolitan city. Most participants say they are drawn by the strong educational program that features 521 scientific sessions and the presentation of 4,276 accepted abstracts.

Yet many admit the chance to take a long weekend in Paris at the end of the summer vacation season was equally attractive.

The new ESC President, Michel Komajda, MD, said this is "the year of registries" at the congress with 15 presentations of data covering a broad range of treatments and conditions. He said the collection of registries is the fruit of ESC's drive to force greater study of safety and real world clinical practice.

The registry campaign is also a response to complaints by members of the heavy dependence on studies sponsored by industry that are narrowly focused, highly selective and centered on the performance of a specific device or drug.

Komajda highlighted the largest of the registries, Prospective Urban Rural Epidemiology (PURE), a large-scale study that recruited 150,000 individuals residing in 28 low-, middle-, and high-income countries around the world.

PURE is designed to examine the impact of urbanization on the development of primary risk factors for cardiovascular disease, such as obesity, hypertension, dysglycemia and dyslipidemia, and smoking.

Data collection includes medical history, lifestyle behaviors, dietary profiles, electrocardiogram, and anthro-

pometric measures as well as blood collection and storage for biochemistry and future genetic analysis.

PURE and 14 other studies will be showcased in presentations at the ESC's trademark Hotline Sessions this week.

Drugs give ground to devices

Traditionally more pharma-oriented than the device-heavy congress of the European Association of Percutaneous Cardiovascular Interventions (EAPCI) held in May, ESC has given ground to interventional cardiologists with five Hotline presentations devoted to drug-eluting-stent (DES) or PCI studies, and a further two presentations of results from implantable-cardioverter-defibrillator (ICD) studies.

The chair for the scientific program, Michael Böhm, MD, of **Saarland University Hospital** (Homburg, Germany) said highlights of the device studies will include a three-year study of new generation DES that shows reduced in-stent thrombosis, a registry comparing transfemoral versus transapical approaches for transcatheter aortic valve implantation (TAVI) and FRANCE II, the FRench Aortic National CoreValve and Edwards registry.

The Spotlight theme for ESC 2011 is "Controversial issues in Cardiology," and in the comments of both the new ESC President, Michel Komajda, MD, and Böhm, clearly place in this limelight the inroads made by interventional cardiology.

The recent scandals involving ICD implantations and the "runaway train" of rapid adoption of TAVI procedures create a friction among cardiologists.

Valves are increasingly being implanted in younger patients and the jury is still out on the effectiveness of the $6 billion annual cost worldwide for stenting of arteries compared to optimal medical treatment, or drugs.

"It's a fact that we don't have a consensus in many areas of treatment and prevention," said Komajda who leads the Cardiovascular Medical and Surgical Departments at the Pitié Salpetrière Hospital in Paris.

"There are differing opinions on many topics, and these occur anywhere from basic science and research to the most complex interventional procedures," said Böhm.

"We want the ESC Congress to be the platform for a constructive debate on these issues based on evidence and experience," he said.

Expanded indication for Mitraclip

Even as cardiologists debate the merits of drugs versus devices for effective therapy, the innovation pipeline continues to produce new, alternative treatments.

Last year **Abbott Laboratories** (Abbott Park, Illinois) presented one year results from the Endovascular Valve Edge-to-Edge Repair Study (EVEREST) II study showing the percutaneous implantation of the MitraClip was noninferior against the conventional surgery for patients with significant mitral regurgitation.

At ESC 2011 Abbott expanded the potential indications for the device with the presentation of the investigator-led PERMIT-CARE study among 51 patients considered ineligible for mitral valve surgery.

The study results showed functional mitral regurgitation reduction with MitraClip treatment, substantial improvement in New York Heart Association (NYHA) functional classification and reversed left ventricle remodeling in approximately 70 % of patients.

"This study suggests that MitraClip treatment could offer, for the first time, a solution for heart failure patients who have severe mitral regurgitation and are unresponsive to cardiac resynchronization therapt," said Angelo Auricchio, MD, the lead investigator with the **Fondazione Cardiocentro Ticino** (Lugano, Switzerland).

"Surgery is not a good option for these patients because of their advanced left ventricular dysfunction and low ejection fraction," he said, adding "We have shown that they were significantly improved following treatment with the MitraClip device."

The device is introduced by a catherter through the femoral vein to the right atrium of the heart and then punched through the septum to be passed through the mitral valve into the left ventricle.

Once the device is deployed it clips the free edge of the anterior mitral-valve leaflet to the posterior leaflet.

Electronic 'nose' smells heart failure

"Sometimes it takes something crazy to shake up our ideas," said session chairman Frank Ruschitzka, MD, with the Zurich University Hospital by way of introducing the presentation of a new device that proposes sniffing out heart failure.

The very serious Vasileios Kechagias, PhD, from the University Hospital Jena seemed far from crazy in presenting his invention, yet session participants could not supress their smiles as they heard out his proposal to attach an electronic sensor to the skin to detect odors indicative of heart failure patients.

Emphasizing that the results are from a pilot study and that the device is far from finished, Kechagias said the study succeeded in demonstrating among 126 patients that those with decompensated heart failure could be divided from compensated heart failure patients with 89% sensitivity and 88% specificity.

The "electronic nose" consists of an array of three thick-film metal oxide based gas sensors with heater elements.

Each of the sensors has a slightly different sensitivity to various odorant molecular types.

Interactions between molecules and the sensor are caused by reactions with oxygen on the heated sensor

surface leading to a change of the free charge carrier concentrations and thus to a change in conductivity in the metal oxide layer.

The odor components are divided by a statistical analysis into two principal components.

Further work is needed he said, adding the goal is to create a minimally invasive technique to rapidly screen, diagnose, and monitor chronic heart failure.

Version one seems to be something out of a 19th century laboratory with a long road to reach the 21st century.

The device is a bulky cube strapped to the forearm, and the detection session takes 30 minutes.

It also needs to be connected to a high-end gasometer and molecular analysis system at the University for Applied Sciences in Jena.

Yet the potential is intriguing with the possibility of one day seeing a miniaturized version for a skin patch that remotely transmits the readings.

Roughly 2% of the general population suffers from heart failure and present a heavy cost burden for healthcare systems. Among people older than 65, the affected population jumps five-fold to 10%.

Philips, Toshiba advance 3-D strain echography

The world of stress echography just became more stressful for the makers of two-dimension speckle tracking systems.

Suddenly this widely used assessment of heart tissue viability is so 1990s.

Or as one sales executive put it at the ESC meeting, "2-D speckle technology is from the last century." Both **Toshiba Medical Systems Europe** (Zoetermeer, the Netherlands) and **Philips Healthcare** (Eindhoven, the Netherlands) pushed the envelope to break into the third dimension for assessing deformation of heart wall motion with new ultrasound systems and software.

"Last year when we introduced 3-D speckle tracking, the theory sounded too good to be true," said Willem Gorisen, cardiac ultrasound market manager for Toshiba.

"This year we are presenting data that shows it is true and with a novel parameter for measurement that demonstrates a superiority over other 3-D data sets and visualizations," he said.

Meanwhile, Philips is promoting the built-for-purpose X5-1 transducer to break the barrier to adoption by offering a toggle choice between 2-D and 3-D scanning.

For its 3-D speckle tracking and strain analysis software Philips has partnered with **Tomtec** (Unterschliessheim, Germany) offering that company's 4-D Left Ventricle Analysis as a plug-in on its Xcelera platform to reconstruct full volume renderings from data acquire in 2-D slices or planes.

Toshiba has moved faster and further into 3-D speckle tracking by building a proprietary software for the Artida platform that is distinctive for acquisition and analysis of a full volume data set, rather than slices.

Novel volume acquisition yields new metric

Building on the new analytic approach of 3-D volume acquisitions on the Toshiba technology, Sebastiaan Kleijn, MD of the **Free University** (Amsterdam, the Netherlands) developed a novel parameter for measuring deformations in heart wall motion that he proposes can replace existing speckle tracking parameters to provide a rapid and robust evaluation for everyday clinical use.

Published in the March issue of the *Journal of the American Society of Echocardiography*, Kleijn et al. describes the Automated Area Tracking metric in "three-dimensional speckle tracking echocardiography for automatic assessment of global and regional left ventricular function based on area strain."

In their conclusion, the authors propose that area strain represents a promising novel automatic index to identify regional wall motion abnormalities that may provide an accurate and reproducible alternative to current echocardiographic standards, which rely on visual assessment by experienced echocardiographers.

The key words, Kleijns told *BB&T*, are reproducible and accurate.

"The ability to reproduce the same results each time with automated area tracking becomes very important, not only for the specific exam but for a consistency between different exams at different moments in time of the same patient," he said.

"Follow up exams and evaluations of patients are critical to know if the patient is improving as a result of treatment or is doing less well," he said. "We need to work fast and get results quickly, and this software gives very rapid analysis that is reproducible and accurate."

Toshiba's Gorisen said the Artida 4D Area Tracking provides an automated assessment without the need for high-level expertise.

"Current speckle tracking parameters require great insight into the ultrasound technology itself and are sensitive to small changes in settings or patients, either of which will affect the results of the exam," he said. "This is a robust method that makes it ideal for clinical use."

Because area tracking is performed on a volume and not calculated from points on a plane the speckles targeted and tracked for analysis over time do not move out of scan range, which can frequently be the case with plane-acquisition data.

According to Kleijn, the newly proposed parameter "provides basic information clinicians need to know, an everyday evaluation we perform on almost any patient in our clinic for interventions, for drug management or any other protocol of treatment."

"You can repeat the experience, and for physicians all over the world, this reproducibility will help them come to believe in this parameter," he said.

'It's all about the transducer'

Philips spent the first half of its presentation at ESC on 3-D speckle tracking analysis describing why the technique is not ready for routine clinical use.

According to Jan Balzer, MD from the **Duseldorf University Hospital**, there is a need for more testing, a standardization of measurements and a standardization among manufacturers.

Having made the case to go slow on adoption, the Philips symposium strangely turned to an all-out promotion for a 3-D transducer capable of feeding data into the TomTec 4D analytic software offered on the Xcelera platform.

In the following presentation titled "Is 3-D echo ready for routine use?" Jose Luis "Pepe" Zamorano Gomez, MD, the director of the Cardio Vascular **Institute at the University Hospital San Carlos** (Madrid), responded with an unqualified "yes."

The past president of the **European Association of Echocardiography** (EAE), Zamorano focused on the role of the transducer in volumetric image acquisition all the while praising the virtues of the Philips X5-1.

The all-in-one X5-1 combines Philips' xMATRIX array with PureWave crystal technology and supports 3-D, 2-D, color flow, M-mode, pulse wave Doppler, tissue Doppler imaging, and contrast-enhanced exams.

The show-stopping features are the ability to tilt and rotate the transducer scan without moving the transducer.

The scan angle can be electronically rotated in five-degree increments clockwise a full 360 degrees, he said.

Because the TomTec approach tracks and calculates speckle movements on a plane, a higher performance trandsducer becomes essential for a high quality data set and to minimize the potential of losing a targeted speckle with an out-of-plane movement during the twisting movement of the heart muscle.

"It is all about the transducer, the acquisition quality and the spatial and temporal resolution," said Ludwig, ultrasound product manager for Philips in Germany.

"You can only diagnose based on what you can see and what the system can make visible," he said.

Both Isken from Philips and Gorisen from Toshiba said their respective companies are participating in a newly formed work group with the EAE that hopes to set standard metrics and an interoperability between manufacturers platforms for 3-D speckle tracking.

As a first step the task force plans to tackle the same objectives for 2-D speckle tracking.

Doctors, not industry, drive clinical case for stents

The clinical case for revascularization using drug-eluting stents advanced modestly at this year's meeting.

The third-generation of drug-eluting stents (DES) won a green light for effectiveness, and a national strategy for rushing acute cases directly to the cath lab for immediate revascularization was shown to result in lower mortality.

Yet another study showed that for complex cases where patients have triple vessel disease, percutaneous coronary intervention (PCI) was associated with a significantly higher risk for serious adverse events.

What was especially significant is that not one of these studies was sponsored by industry, and all had large-scale patient populations reflecting real-world practice, precisely the long-awaited evidence ESC has called for.

The absence of industry's heavy footprint in stents was remarkable at ESC 2011, a stunning silence after the blaring grandstanding for DES at past congresses.

With the exception of the French manufacturer **Hexacath** (Rueil-Malmaison) that set up a counter and modest backdrop, there was no promotion of stents on the exhibition floor, nor in the distributed publications and literature.

This retreat from the floor is all the more surprising considering the worldwide market for stents is estimated to be well north of $4 billion.

Despite the overwhelming commercial success that stents have brought to medical device companies and the rapid clinical adoption, the evidence that the metal sleeves are better than optimal medical therapy or traditional bypass surgery has remained dubious.

Findings about DES were criticized as coming from underpowered studies with selective data or masked p-values, which show the significance of results.

In May, the **European Association of Percutaneous Cardiovascular Interventions** (EAPCI; Sophia Antipolis, France) went so far as to ask manufacturers to retrospectively report their data by recasting the results using criteria for patient-oriented outcomes rather than device-oriented outcomes.

New generation DES win SCAAR approval

Five years ago stent utilization was soaring and sales were cresting $5 billion.

Then came the firestorm in Barcelona when the efficacy of DES was criticized during a packed plenary session at the ESC congress.

If this was the spark, it was the report at that same congress from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) that threw gasoline on the fire by questioning the long term safety of DES due to blood clotting.

European usage of DES dipped slightly after the ESC

meeting, but sales in the U.S. crashed from over 90% usage in PCI procedures in early 2006 to around 55% before the end of that year.

At ESC 2011, SCAAR was back, this time to report that third generation DES are associated with a 38% lower risk of clinically meaningful restenosis and a 50% lower risk of stent thrombosis compared to old generation DES.

The study included 94,384 stent implantations in Sweden from November 2006 to October 2010 using a national registry where all consecutive patients undergoing coronary angiography or PCI are included.

The performance up to two years of 10,551 different types of DES considered "new" was evaluated in an unselected large real-world population – including patients with myocardial infarction, three-vessel and/or left main disease, bifurcation lesions, graft disease, restenotic lesions and chronic total occlusions.

The new stents needed to be represented by more than 500 cases to be include, according to Giovanna Sarno, MD, with the Department of Cardiology at **Uppsala University** (Sweden).

Sarno told *BB&T* the three dominant stents in the new generation analysis of the SCAAR registry were Xience V and Xience Prime from Abbott, PROMUS Element from Boston Scientific and Endeavor Resolute from **Medtronic** (Minneapolis).

Also included were 64,631 bare metal stents, as well as 19,202 DES considered to be "old," and including the Taxus line from **Boston Scientific** (Natick, Massachusetts), Cypher from the Cordis division of **Johnson & Johnson** (New Brunswick, New Jersey) and Endeavor from Medtronic.

Sarno attributed the improved performance for the new generation to stent designs with thinner struts, and especially greater biocompatibility of polymers that bind the therapeutic to the strut, which "may have an important impact on drug elution profiles, endothelial coverage, and functional recovery."

She concluded that patients treated with PCI with "new generation" DES have a considerably lower risk of restenosis and stent thrombosis at two years compared to older generation DES in a large real world population.

The most remarkable finding in the SCAAR study was the lack of any cardiac events after 15 months for patients receiving the new DES, where such adverse events continued, and even increased beyond that point for patients with older generation stents and even more so with bare metal stents.

The risk of mortality was reduced 23% with the newer stents compared to other versions.

A 'protective effect' of by-pass surgery

The SYNTAX study will not go away.

Commissioned by ESC after the Barcelona disaster, and funded by Boston Scientific, the Synergy between PCI with Taxus and cardiac surgery was a head-to-head comparison between clinical outcomes for bypass surgery and DES.

But instead of closing the door on criticisms of DES, it turned out PCI is not always as good as surgery for patients, and that among patients with severe coronary artery disease (CAD), CABG was found to have a benefit).

The legacy of SYNTAX is an objective scoring system for assessing the complexity of a patient's CAD.

Now the trial has inspired a Japanese study to retrospectively assess a 26-center registry enrolling consecutive patients having a first coronary revascularization between January 2005 and December 2007.

CREDO-Kyoto (Coronary Revascularization Demonstrating Outcome Study in Kyoto) PCI/CABG registry cohort-2 is a physician-initiated non-company sponsored study that looked at 2,981 patients with triple vessel disease where 1,825 patients underwent PCI and 1,156 patients had coronary bypass surgery.

The primary endpoint of the study was a composite of all-cause death, myocardial infarction (MI) and stroke.

Presenting the findings, investigator Hiroki Shiomi, MD, from **Kyoto University Hospital** (Japan), reported PCI was associated with significantly higher risk for serious adverse events in these patients.

PCI as compared with CABG was associated with a higher 3-year risk for this primary endpoint, though the risk for cardiac death was not found to be significantly different.

Yet the risk for all-cause death was found to be significantly higher after PCI.

"Especially remarkable was a protective effect of CABG for myocardial infarction," according to Shiomi.

Frans Van de Werf, MD, with the **University Hospitals** (Leuven, Belgium) was the discussant for the presentation of the CREDO-Kyoto during a ESC signature Hotline plenary session.

"This study confirms the overall findings of the SYNTAX trial in a large, real-world population," he said, adding it also confirms the usefulness of the SYNTAX score in clinical practice.

"A big surprise was to see there is a benefit with CABG, even among patients with a low syntax score," he said.

'Get thee to a cath lab'

Forget the door-to-balloon time, the critical measure for success in revascularization is call-to-balloon time.

"Americans are obsessed with reducing the time from door-to-balloon," said Christian Juhl Terkelsen, MD, with the **University Hospital of Aarhus** (Denmark).

"Yet when they do not see improved outcomes they wonder what they are doing wrong," he said.

Door-to-balloon time improvements have failed to produce changes to survival and long-term risk of subsequent cardiac events for patients who do survive, he said.

The answer turns out to be what he called the system delay, of the call-to-balloon time.

By reducing the critical moments between the onset of symptoms and the inflation of the angioplasty balloon to reopen the culprit artery, the informed patient and a well-trained emergency medical technician with the ambulance.

If you are having a cardiac crisis, he said, do not take a taxi.

"It's unbelievable, but that is how some of our patients arrive," he said.

Results of a registry analysis for 9,514 patients treated by a regional cath lab from 1999 to 2009 included 1,656 of the self-presenters, 4,805 patients transferred from a hospital and 3,053 who were delivered direct to the center after calling the emergency hotline.

These patients did the best, leading Terkelsen to suggest that in the event of a heart attack, patients should not go to the nearest hospital.

"Field triage by the EMT cuts out an hour of hospital processing," he said.

The exception is where the hospital is also a qualified cath lab, which Terkelsen defines as one performing PCI 24/7.

More than 50% of PCI patients in the region are today brought direct to the cath lab and the program's goal is 85%, he said.

In 2003 the western Denmark region decided on a strategy for reperfusion by PCI rather than with medical treatment.

The healthcare system covering 3 million people was realigned to assure fast response among three regional centers in coordination with EMT services. Public education was also a critical factor for success, Kristensen said.

Steen Dalby Kristensen, MD, with the **Skejby Hospital** (Aarhus, Denmark) today leads a Europe-wide program called Stent for Life that is backed by ESC and the European Association for PCI.

The goal is to expand the Denmark experience to participating countries.

Home monitoring of ICDs fails to lower mortality

Implantable cardiac defibrillators (ICDs) are routinely implanted in patients at risk of sudden cardiac death as a result of rhythm disturbances.

So much so that cardiologists' offices are overwhelmed by the required follow-up visits scheduled every 3 months.

Remote monitoring features have since proven to help reduce this burden and throughout the developed western countries, ICDs and the new monitoring technology have seen a rapid adoption.

Except in France.

Where the implantation rate is 140 ICDs per one million population in western countries, penetration in France hovers at 88 ICDs per million.

At the meting, two studies designed to yield cost-benefit and resource utilization data for remote monitoring of ICD patients in France were presented, offering new insights into the effectiveness of home monitoring.

Sponsored ICD studies consistently show that remote monitoring is safe, and that they are effective in reducing unnecessary office visits.

But the EVATEL study (EVAluation of TELe follow-up) is the first controlled trial aiming to assess the impact of remote follow up on mortality.

"An important achievement of this study is that it was investigator initiated, included multiple vendors and featured a large patient population," said Angelo Auricchio, MD, from **Rondazione Cardiocentro Ticino** (Lugano, Switzerland) who critiqued the study as a discussant during the ESC Hotline session.

Unfortunately much-anticipated financial data was withheld pending further review by the French government that commissioned the study.

The study was also limited by the caveat that it was technically underpowered, enrolling 1,501 patients rather than the required 1,600.

According to Luc Cheminot, who leads French operations for **Biotronik** (Berlin), the government funding of the study also came with a strict timeframe forcing the investigators to go forward without waiting for the last 99 patients.

The study also suffered from poor telecommunications with more than 50 patients from the remote-monitoring group converting to the control group due to an inability to transmit data remotely.

There was yet another disappointment for EVATEL investigators in missing the primary endpoint.

EVATEL hypothesized that remote monitoring would affect the rate of major cardiovascular events, defined as all cause death, hospitalization for a cardiovascular event, unsuccessful ICD therapies, and inappropriate ICD therapies.

It did not. There was no difference in survival at one year between the monitored group and the control group.

There were also no statistically significant differences between the two groups for a secondary outcome measures of the time to onset of the first major cardiovascular event and the one-year survival rate.

EVATEL did demonstrate that demonstrate across multiple vendor platforms the safety and efficacy benefits from the remote follow-up of ICD patients.

The one good piece of news was a significant reduc-

tion in inappropriate therapy in the remote monitoring group.

Thirty French centers participated in the study and the remote reporting ICDs came from Biotronik, Medtronic, **St. Jude Medical** (St. Paul, Minnesota) and Boston Scientific.

"The remote follow-up of patients implanted with an ICD seems to be a safe alternative to conventional in-office follow-up," said principal investigator Dr Philippe Mabo from the **University Hospital of Rennes** (France).

"However, for the widespread uptake of this new strategy — at least in France — reimbursement from the healthcare system will be needed," he said.

Biotronik's Cheminot said that France currently pays a supplement of €1,000 for an ICD that is capable of home monitoring, requiring in exchange a validation report that the device was actually used and not merely switched on.

Fewer shocks, longer battery life

The ECOST trial (Effectiveness and Cost of ICD Follow-Up Schedule with Telecardiology) sponsored from Biotronik investigated the safety, effectiveness, and costs of long-term follow-up over 27 months with Home Monitoring.

Once again, the cost figures have been withheld for review by the French Ministry of Health, apparently still on vacation at the end of August.

Cheminot told *BB&T* that the forthcoming results of the cost study will be worth the wait, adding that Biotronik has a unique agreement with the government that will allow the company access to the entire healthcare cost of ICDs per patient, including paramedic interventions, pharmaceutical impacts and monitoring.

A total of 433 patients were followed for 27 months in 43 centers for ECOST with all patients seen in the clinic within the first three months after implantation.

Patients were then randomized to a remote monitoring group or an in-clinic follow-up control group with the remote patients seen in the ambulatory department only once a year unless an anomalous ICD function or an event of clinical concern was reported by remote monitoring.

In the control group, the patients were followed in the ambulatory department at 6-month intervals.

ECOST principal investigator Professor Salem Kacet with the **Lille University Hospital Center** (Lille, France) reported a clear benefit for home monitoring with a 52% reduction of the number of patients with inappropriate shocks and a 72% reduction in the risk of hospitalizations related to inappropriate shocks compared to the control group.

ECOST also demonstrated a 76% reduction in the number of charged shocks with a significant impact on ICD battery longevity. ❖

International Report

Masimo's Pronto-7 wins approval in Japan and Canada

By JOHN BROSKY
***BB&T* European Editor and Staff Reports**

Masimo (Irvine, California) last month said it received both Japanese Ministry of Health Labor & Welfare (MHLW) and Health Canada regulatory clearances of the Pronto-7 – enabling clinicians tin those countries to measure total hemoglobin (SpHb), SpO_2, perfusion index, and pulse rate without removing a drop of blood.

According to the company, Masimo SpHb provides immediate real-time hemoglobin results that enable clinicians to more rapidly assess patients and detect and treat internal bleeding and low hemoglobin conditions earlier. And, although Masimo noninvasive and continuous total hemoglobin (SpHb) monitoring – commercially available in both Japan and Canada for over a year – is the preferred technology for hospitals and inpatient care centers due to its ability to provide continuous SpHb measurement, access to quick and easy spot-check hemoglobin measurements are valuable for a variety of healthcare assessment applications, including physician offices, outpatient care centers, and pre-hospital emergency settings.

The company said the palm-sized, handheld Pronto-7 offers a breakthrough solution for measuring total hemoglobin, SpO_2, perfusion index, and pulse rate in less than one minute without the needles, time-consuming laboratory analysis, risk of blood contamination, hazardous medical waste, and patient discomfort associated with traditional blood tests. With dimensions of just 13 cm x 7.2 cm x 2.5 cm (5.1" x 2.8" x 1") and weight of 296 grams (10.5 ounces), the Pronto-7 puts the power of noninvasive hemoglobin spot-check testing, along with SpO_2, perfusion index, and pulse rate into any clinician's hands in various clinical settings — including physician offices, hospitals, clinics, and on the scene of medical emergencies.

In addition to Normal Mode, Pronto-7 offers Max Sensitivity Mode that allows measurement over a broader range of patients and three noninvasive sensor sizes to accommodate the range of finger diameters. Each sensor is color-coded to make size identification easy (Small-Yellow, Medium-Red, and Large-White) and optimized

to improve performance in low ambient temperatures. And, because of the device's embedded 802.11 b/g and Bluetooth communication capability, wireless printing or emailing of test results is enabled with future upgrades that will allow for wireless transmission to electronic health record systems.

Prior to the introduction of the Pronto-7 internationally, Masimo received FDA 510(k) and CE mark clearance and first introduced the ability to noninvasively and continuously measure SpHb in 2008 using its Radical-7 bedside Pulse CO-Oximeter. In 2009, Masimo launched Pronto — its first handheld noninvasive spot-check device for total hemoglobin, SpO_2, perfusion index, and pulse rate measurements. And in 2010, Masimo established Medicare reimbursement for transcutaneous hemoglobin measurement in the U.S.

As part of Masimo's verification process, more than 11,443 Pronto-7 measurements were performed on 1,445 subjects at 14 sites and compared to hemoglobin measurements from a venous blood sample analyzed on a hematology analyzer (Coulter Counter). This testing resulted in a product specification of 1.0 g/dL for normal sensitivity mode. While not a regulatory requirement, Masimo elected to perform additional testing on Pronto-7 devices and sensors produced at a Masimo manufacturing facility. This additional testing included 474 subjects in three outpatient clinic-type environments. The hemoglobin measurements from the Pronto-7 and a point of care device using capillary blood (Hemocue) were compared to hemoglobin measurements from a venous blood sample analyzed on a Coulter Counter. The Pronto-7 showed a bias of was -0.1 g/dL and a standard deviation of 1.1 g/dL, while the Hemocue showed a bias of -0.1 g/dL and a standard deviation of 1.6 g/dL.

OptiMedica wins CE mark for Catalys

OptiMedica (Santa Clara, California) has received CE mark for its Catalys Precision Laser System for cataract surgery in Europe. The company says the system combines a femtosecond laser, integrated Optical Coherence Tomography imaging and OptiMedica's pattern scanning technology in an ergonomic, easy-to-use system designed to bring new levels of precision and accuracy to the cataract procedure.

Mark Forchette, president/CEO of OptiMedica, told *BB&T* that he was at a facility the other day that happened to be the same facility where he first saw a cataract surgery performed 27 years ago. "I don't know that in that 27 years I've seen anything like this kind of reset in the cataract procedure . . . it makes you reconsider everything," he said.

The company noted that while there have been incremental advancements in surgical tools and techniques in recent decades, the conventional procedure still requires physicians to perform several critical steps manually. This manual approach limits predictability and precision, potentially affecting refractive outcomes and complication rates.

"This is an outstanding day for patients, physicians and for OptiMedica," Forchette said. "We believe that the field of cataract surgery is in the midst of a revolutionary change, and we expect Catalys to provide leading technology that satisfies the high expectations of surgeons and their patients. Our system's CE mark approval is a huge achievement made possible by the efforts of OptiMedica's dedicated and talented team of scientists, engineers and medical advisors to develop and bring this breakthrough innovation to market. We are excited to enter this new stage in OptiMedica's history, and we look forward to introducing Catalys to markets around the world in the very near future."

With Catalys, physicians have the opportunity to perform cataract surgery with an unsurpassed level of accuracy, OptiMedica says. The system is now CE mark approved to deliver capsulotomy (a circular incision in the lens capsule) and lens fragmentation (segmenting and softening of the lens to prepare for removal), with CE mark approval for corneal incisions anticipated in the near future. A clinical study has demonstrated that Catalys delivers marked improvement over manual surgical technique, with key metrics including:

- Capsulotomy size, as measured by deviation of capsule diameter from intended target. The average deviation in capsule diameter with Catalys was only 29 microns, as compared to an average deviation in the manual technique of 337 microns;
- Capsulotomy shape, with a score of 1.0 representing perfect circularity. Capsulotomies delivered with Catalys achieved almost 95% circularity, with very little spread in outcomes across all eyes. In the manual group, only 77% circularity was achieved, with a larger spread in results;
- Capsulotomy centration. Capsulotomies performed with Catalys were within only 77 microns of perfect centration relative to the dilated pupil; and,
- Ease of lens fragmentation and disassembly. With Catalys, cumulative dissipated energy (CDE) during ultrasound phacoemulsification was reduced by nearly 40%.

OptiMedica expects to ship its first Catalys system in Europe in 4Q11.

Forchette said the biggest challenge OptiMedica is faced with right now is "managing the levers" and meeting the high demand for the product while also making sure it's right when customers get their hands on it.

"Having had a really wide footprint with PASCAL [PAttern SCAn Laser], we know what that feels like and we would like to get there – and customers want us to get there," Forchette said. "So the challenge is just making

sure that we get this product in the hands of customers – at the speed at which they want it – all over the world, and not only getting it to them quickly but we've got to get it to them right. I realize that this is a significant investment that each customer will make and we need to make sure that we treat it that way."

OptiMedica says it developed the Catalys system in close collaboration with a medical advisory board of cataract experts from around the world, with the shared objective to deliver unprecedented accuracy and an exceptional experience. Key innovations reflecting this objective include a Liquid Optics Interface that ensures stable system-patient attachment and optimizes the optical path to the patient's eye, and a proprietary Integral Guidance system that ensures the femtosecond laser pulses are delivered safely and precisely to the intended location. In addition, the system features an easy-to-use and elegant graphical user interface designed to simplify the planning process and minimize the time the patient is under the dock.

"Stuff like this doesn't happen by chance," Forchette told *BB&T*. "We have a brilliant group of engineers and technical people at OptiMedica who have been obsessing over this, but we've also had physicians and nursing staff involved through the whole process. We've had our medical advisory board deeply ingrained in the development . . . that was really important in the product being as good as it is because it made us consider all the different needs and I believe we've been able to meet or exceed those needs."

MedWaves gets KFDA certification for AveCure

MedWaves (San Diego) reported that it has received receipt of Korean Food and Drug Administration (KFDA) Certification to import and sell its AveCure microwave ablation (MVA) system and devices through its distribution partner in South Korea.

The AveCure MVA system uses microwave energy to volumetrically coagulate-ablate soft-tissue lesions. The system has successfully treated more than 1,000 patients worldwide, including lesions in bone, kidney, liver, lung and pancreas.

The company said it plans to bring its technology to treat lesions in other locations in the body. Its technology makes available treatment options for many cancer patients in either early or late stage and helps those who are running out of options.

South Korea, with 48.5 million in population, is an important market for MedWaves. Cancer is the leading cause of death in South Korea, and the company said it is pleased to receive KFDA approval to import and sell products. MedWaves said it is in close coordination with its South Korean distributor-partner in scheduling and conducting clinical evaluations for sales of its AveCure system in key South Korean hospitals.

Solta's Clear + Brilliant gets Canadian approval

Solta Medical (Hayward, California) in September reported Health Canada approval of its new Clear + Brilliant laser aesthetic treatment. This technology is now available to physicians in Canada. In May, the company received FDA 510(k) clearance and the CE mark to market and sell Clear + Brilliant. This treatment is an effective treatment based on fractional laser technology that is performed in a professional setting, the company said.

The launch of Clear + Brilliant creates and defines an entirely new category of laser aesthetic treatments designed to attract younger patients looking to take control of their aging process. The company said that Clear + Brilliant provides a new offering for physicians and skin care providers to address evolving consumer needs and expand their patient base.

Unlike other conventional lasers that utilize the stamping delivery method, Clear + Brilliant features a patented Intelligent Optical Tracking System that the company claims provides consistent coverage and insures a uniformly toned treatment area.

Angioslide launches new SFA device

Angioslide (Caesarea, Israel) has launched its new 5x300 mm Proteus device for treating the superficial femoral artery (SFA). Proteus technology combines a percutaneous transluminal angioplasty (PTA) balloon and embolic capture of particles in one device.

The new 5x300 mm size joins Angioslide's product line solutions for the lower limbs. According to the company, the new device makes it possible to treat lesions up to 300 mm with one device, while providing immediate solution for embolic capture.

Initial treatments using the new Proteus device were conducted in leading world centers, **Parkkrankenhaus Leipzig** and **Herzzentrum Bad Krozingen**, in Germany.

"Angioslide's breakthrough technology, now available also in 300 mm length as well, is a unique solution for lesions with high level of embolic material, including chronic total occlusions (CTO), in stent-restenosis, thrombus containing lesions and post atherectomy PTA," said Thomas Zeller, head of the Angiology Department at Heart Center Bad-Krozingen.

With the increase in life expectancy, diabetes prevalence, and number of high-risk patients, together with the shift toward an endovascular-first approach as a preferred procedure over surgical revascularization, there is a growing need for expanding the current interventional tool box to accommodate procedures designed specifically to treat long and diffuse lesions in a quick and effective manner, the company noted.

The device is currently released for the European market only, and is under review with the FDA. ❖

Acquisitions & Agreements

• **AmSurg** (Nashville, Tennessee) has signed a revised definitive agreement to purchase substantially all of **National Surgical Care**'s (NSC; Dallas) assets for $135 million in cash. If earnings from the purchased assets exceed specified targets for 2012, an additional payment of up to $7.5 million in cash will be made. The assets to be purchased include 17 ambulatory surgical centers, 15 of which are multi-specialty centers and two of which specialize in gastroenterology procedures. One multi-specialty center will be held for potential sale within 90 days of the completion of the transaction to the center's physicians under a change of control provision in their existing partnership agreement.

• **Bayer Healthcare** (Leverkusen, Germany) said its affiliate, **Medrad** (Warrendale, Pennsylvania) has acquired **Pathway Medical Technologies** (Kirkland, Washington) for a reported figure of $125 million. With this acquisition, Bayer said it is strengthening its Medrad Interventional business by expanding its presence in the field of vascular intervention technologies.

• **Concentric Medical** (Mountain View, California), a provider of acute ischemic stroke intervention products, said that **Stryker** (Kalamazoo, Michigan) has signed a definitive agreement to acquire it for $135 million in an all-cash transaction. The acquisition, pending customary regulatory approvals, is expected to close early 4Q11. Stryker says the acquisition of Concentric provides it with immediate entry into the fastest growing and most innovative segment of the interventional neurovascular space. Ischemic stroke represents the vast majority of all strokes, and this strategic acquisition offers Stryker immediate access into the rapidly expanding acute ischemic stroke segment.

• **Elekta** (Stockholm, Sweden) said it has successfully completed its acquisition of **Nucletron** (also, Stockholm) for €365 million. Through the combination, Elekta will offer a complete range of radiotherapy planning and delivery technologies.

• **Integra LifeSciences** (Plainsboro, New Jersey) and **Ascension Orthopedics** (Austin, Texas) reported an agreement for Integra to acquire Ascension, a provider of products for the foot, hand and shoulder markets, for about $65 million in cash, subject to adjustments. When combined with Integra's legacy business, the products will represent about 45% of Integra's orthopedics revenues. Integra says the acquisition provides it with a complementary product portfolio. Ascension will brings a strong position in upper extremity products, including shoulder. Ascension's lower extremity offerings significantly enhance Integra's leading line of foot and ankle products.

• **Kindred Healthcare** (Louisville, Kentucky) said that its subsidiary has acquired the equity of **Professional HealthCare** (Woodbridge, Virginia), a portfolio company of Mainsail Partners, for a purchase price of $51 million in cash. Professional is a provider of home health, hospice, private duty nursing services and durable medical equipment. The company used its operating cash flows and proceeds from its revolving credit facility to finance the transaction.

• **Natus Medical** (San Carlos, California) has acquired **Embla Systems** (Denver), a maker of devices used in the diagnosis of sleep apnea. Natus acquired all outstanding shares of Embla capital stock for $16.1 million in cash, exclusive of direct costs of the acquisition.

• **PerkinElmer** (Waltham, Massachusetts) has signed a definitive agreement to acquire **Caliper Life Sciences** (Hopkinton, Massachusetts), a company focused on imaging and detection solutions for life sciences research, diagnostics and environmental markets for about $10.50 a share which is a total net purchase price of $600 million in cash.

• **Solta Medical** (Hayward, California) said it has entered into a stock purchase agreement to acquire all of the outstanding shares of **Medicis Technologies** (formerly LipoSonix; Bothell, Washington), a subsidiary of **Medicis Pharmaceutical** (Scottsdale, Arizona). Solta will pay to Medicis $15 million upon closing, up to $20 million upon the achievement of a near-term FDA regulatory milestone and certain additional future contingent payments based upon, among other things, the achievement of specified year-to-year increases in the commercial performance of the LipoSonix technologies. Solta's obligation to make these additional future contingent payments expires after approximately 7 years. The transaction is expected to close during 4Q11.

• **Thermo Fisher Scientific** (Waltham, Massachusetts) reported that it has completed its previously reported $3.5 billion acquisition of **Phadia** (Uppsala, Sweden), a global developer of blood tests for the clinical diagnosis and monitoring of allergies and autoimmune diseases. Phadia has about 1,500 employees globally and had 2010 revenue of €367 million (or approximately $525 million). Phadia will become part of Thermo Fisher's Specialty Diagnostics business.

• **Urologix** (Minneapolis), the maker of minimally invasive Cooled ThermoTherapy (CTT) for the treatment of Benign Prostatic Hyperplasia (BPH), reported the signing of an exclusive worldwide license for the Prostiva RF Therapy System from **Medtronic** (also Minneapolis). Prostiva RF (Radio Frequency) Therapy is a transurethral needle ablation device that is 510(k) cleared for the treatment of BPH and is most commonly used in the urologist's office. The license agreement is for a 10-year term.

Market Developments

BioEnterprise says VC funds down, but Angels on rise

By OMAR FORD
***BB&T* Staff Writer**
and *BB&T* Staff Reports

Money invested in med-tech firms isn't as much as it once was. One can look no further than **BioEnterpise**'s (Cleveland) most recent venture investment study to see that venture capital financings aren't at the levels they used to be. The *BioEnterprise Midwest HealthCare Venture Investment Report* shows that while funding for the number of med-tech companies is high, the total dollars invested are down as compared to recent years. This is also resulting in the rise of angel funding for many of these companies.

The report covers the first half of 2011 and reveals that healthcare start-ups reported $315 million in total investments across 86 companies. "In the Midwest in particular you have a bias toward device and software companies during these economic times," Baiju Shah, President/CEO of BioEnterprise told *BB&T*. "Those companies tend to raise fewer dollars than biotech companies. And you're probably seeing more angel-led financings than venture-led financings."

Shah said that many venture capital firms are moving toward funding companies that are further along in the development path. "The number of companies and entrepreneurs remain strong," he said. "I think the sources of capital have diversified because there are fewer venture firms that have investment capital available for early stage opportunities. So these entrepreneurs are seeking capital where they can find it. Angels are increasingly stepping into that void where venture used to tread," Shah said.

Shah said also that companies in the development spectrum are turning to angels and federal grant sources to help migrate their development to the point where venture capital companies become interested. Shah's observations about angel funding don't just apply to the Midwest area. In an interview with *BB&T*, Michael Riedlinger, director of the **Rochester BioCenter** (Rochester, New York), echoed similar statements regarding the availability of venture capital for these early stage companies.

"About five or six years ago venture capital was much more prevalent if you were talking to an early stage medical device inventor," Riedlinger said. "They really thought they could capture millions of dollars through a traditional VC investment in their business." Riedlinger said companies are now singing a different tune. "They are not thinking of venture capital as the first source of funding for what they are doing," he said.

A tougher regulatory process has in some cases made it difficult for companies to rely on venture capital. Speaking specifically about the Rochester area, Riedlinger said "because the FDA process has looked less clear and there has been exactly less clarity around what is going to be required; and how long the process was going to take," new med-tech companies are having a difficult time.

"That's not to say folks don't want to go through with the process," he said. "But having clarity around it helps them build plans and helps them understand what they need to raise capital, and that's become a big challenge. There are some companies that have adopted a model and said there are other things we can do with this technology to raise funds that don't necessarily require regulatory approval."

Shah said the very structure of angel investors is changing and becoming more complex and organized. "Angels are also becoming more sophisticated in their organization," he said. "So we've seen over the last three to four years a real growth in angel capital funds – not just angel investors as individuals. They are banding together to form official funds and they are looking at deals not only as an individual fund but as syndicates."

Last year, Midwest healthcare start-ups attracted $737 million in new investments across 159 companies according to the 2010 *Midwest Health Care Venture Investment Report* from BioEnterprise. While the total numbers of investments are comparable to 2008 and 2009, the total dollars invested are down 5% from the prior year.

Since BioEnterprise began reporting on investment numbers across the region's healthcare sectors, a few years stood out as particularly good. In 2007, Shah called 2006 the "breakout year" for the Midwest as a whole as $792 million was raised across 135 companies, a 25% increase over 2005. That year was also highlighted by a number of public offerings and several significant exits through acquisitions.

But that was nothing compared the following year when Midwest healthcare start-ups attracted a record $1.2 billion in new investments in 2007, representing a 55% increase over 2006 and still outpacing the national venture industry growth. The numbers from 2008 were also pretty good for the region, but didn't quite break the previous year's record. That year Midwest healthcare companies attracted $1.1 billion in new investments across 166 companies.

"The total dollars per company are down and the total dollars invested are down relative to last year," Shah said. "When we've gone back and analyzed our data, there isn't any pattern that we can discern that would allow for us to predict where we would end up at by the end of 2011. Of course with the events of the last couple of weeks with the global financial market – that also cascades down into the venture world."

FDA looks at provider training in clinical trial draft

FDA has issued a draft guidance for diagnostic and medical device clinical trials and takes on a few bones of contention with industry along the way, including the meaning of the phrase "least burdensome." However, the agency also indicates that it is unfriendly toward a sponsor's training of doctors and other providers participating in those clinical trials unless the sponsor is willing to do the same for doctors in routine practice. This, the guidance indicates, applies even to studies engaged prior to the pivotal clinical trial.

FDA offers an interesting caveat early in the guidance, stating that "even with a well-planned design, the study may not yield the results expected or necessary to demonstrate safety and effectiveness," adding that a sponsor may have to "re-assess their goals . . . and conduct additional studies" to demonstrate safety and efficacy. Whether that's intended as a signal that the standalone pivotal trial will become a less common species is difficult to parse, but industry might be inclined to read it as such, given that even though much of the emphasis at the agency's Center for Devices and Radiological Health has been on the 510(k) channel, observers have awaited some signal about a formal toughening of the PMA mechanism.

The draft also states that a trial should account for variability in "the performance of the device when used by practitioners of varying expertise." Later in the guidance, however, FDA states that if the sponsor intends to offer no training to practitioners in real-world use, providers engaging in the trial "should not be specifically trained in the use of the device" as a means of ensuring "that the study reflects real-world conditions."

A substantial portion of the 56-page guidance deals with implantable devices, including a passage addressing exploratory studies. FDA states that it may require "continued animal testing of implanted devices at six months, two years and three years after implant" even as the pivotal trial is underway.

One of the more interesting aspects of the guidance is that it reintroduces the boilerplate pertaining to the standard of "least burdensome," a bit of phrasing that had been omitted from a number of documents issued by the agency over the past year and a half. The guidance goes into some detail about the precise meaning of the phrase, however. FDA states that the principal of "least burdensome" is described as "a successful means of addressing a pre-market issue that involves the most appropriate investment of time, effort and resources on the part of industry and the FDA."

The draft guidance notes that it applies to both therapeutic and diagnostic devices as well as those dealing with purely "aesthetic" considerations. However, the guidance does not apply to humanitarian device exemption studies or to companion diagnostics, which were the subject of a separate draft guidance published in July.

On the subject of site selection, the guidance states that a sponsor of a clinical trial should "consider diversity of sites in terms of investigator or operator experience," stating that surgeons at tertiary care sites "may have more specialized experience than those at a community hospital." FDA states that selecting only referral sites for a study "could lead to a biased assessment of device performance."

FDA took on a topic of considerable interest to industry in addressing clinical study endpoints, and although this was not the primary point to be made in this portion of the guidance, it may jump out more at device makers than other features of this section of the guidance, even though the topic is not unexplored. The draft guidance states that if a trial is underway "when the understanding of science or medicine changes . . . the relevance of particular endpoints, outcomes or measurements may change," in which case the sponsor is advised to consult with the agency as to "the best possible course of action."

In the portion of the guidance that deals specifically with diagnostics, the draft indicates a long-standing concern about the "variability in the performance of persons interacting with the device," which the agency states can create a need to conduct additional studies to remedy. Another source of bias might be the effects of sequential readings, which has been a matter of concern for reviewers at the radiological devices branch for some time. One potential fix for the sequential problem is, as might be expected, a wash-out period during which a reviewer has time to forget what he or she saw from that patient's other scans.

The draft guidance is open for comment for 90 days from the Aug. 15 date of publication.

Selective DES saves millions of healthcare dollars

Limiting the use of drug-eluting stents to a selected group of patients is cost efficient and did not increase risk of death or heart attack within a year, according to an analysis published recently in *Circulation: Journal of the American Heart Association*. The researchers said the selective use of drug-eluting stents, which began in 2007, is saving the U.S. healthcare system about $400 million a year.

In this analysis, researchers compared the use of drug-eluting stents in 2004 through 2006 to their use in 2007, using data from the Evaluation of Drug-Eluting Stents and Ischemic Events registry. This U.S.-based registry of percutaneous coronary interventions included more than 10,000 patients undergoing angioplasty at 55 medical centers. The use of drug-eluting stents decreased from 92% in 2004 through 2006 to 68% in 2007. At the same time, rates of death and heart attack remained virtually unchanged, while procedures to re-treat a blockage at the same coronary artery site increased slightly, from 4.1% to 5.1%.

"The bottom-line was that using drug-eluting stents in a relatively unselected way was only resulting in marginal improvement compared to more selective use," said David Cohen, MD, senior author and director of cardiovascular research at **Saint Luke's Mid America Heart and Vascular Institute** (Kansas City, Missouri).

In the earlier years of broader use, "we were putting a lot more drug-eluting stents in and we benefited very few additional patients," he said. Several studies in late 2006 reported a higher risk of clotting, heart attacks and deaths in patients with drug-eluting stents compared to bare-metal stents. That year, at the **World Congress of Cardiology** (WCC; Sophia, Antipolis, France) annual meeting in Barcelona, Spain, researchers issued reports indicating that drug-eluting stent (DES) devices may increase the risk of potentially fatal blood clots.

At that time, nearly 6 million patients worldwide had received a DES since the devices were first launched in 2002, creating a $5-billion-a-year business for then market leaders **Boston Scientific** (Natick, Massachusetts) and **Johnson & Johnson** (J&J; New Brunswick, New Jersey), the two companies at that time that sold the devices in the U.S.

At that meeting, Salim Yusuf, MD, of **McMaster University** (Hamilton, Ontario), called the findings disconcerting. "Now that we are having this concern, I would urge limited use," he said. "As clinicians we seem to have lost our clinical judgment, let alone our ability to view data and evidence. We therefore need a thoughtful and selective approach to PCI, complementing full medical therapy . . . the whole field of angioplasty has been led astray by a preoccupation with restenosis, for which study after study has shown has no prognostic value."

Soon after that WCC meeting, an editorial published on the website of the **American College of Cardiology** (ACC; Washington) added fuel to that fire, charging that 2,000 patients were dying needlessly each year as a result of DES use. Written by Sanjay Kaul, MD, and George Diamond, MD, of **Cedars-Sinai Medical Center** (Los Angeles), the guest editorial, "Drug-eluting stents: An Ounce of Prevention for a Pound of Flesh," said patients face a lower risk if treated with older, less costly, bare-metal stents (BMS) that might work just as well.

"I think the debate here is not the drug-eluting stent vs. the bare metal stent," Kaul told *BB&T* in 2006. "There's a bigger debate here, and that is our obsession with revascularization as the primary therapy for treating stable angina." He said that drug therapy should be the first avenue for treating chronic stable angina "and only in those who don't respond to [drug] therapy should revascularization therapy – whether stenting, angioplasty or bypass surgery – be offered." He said that in a "quick fix society," patients demand that approach, and "we are too eager to please them."

With more than one million Americans annually receiving the stents at that time, and at least 80% of them getting DES devices, this works out to an additional 2,160 deaths each year, the doctors calculated. The figure assumed that 45% of the people who suffered such clots had died.

Kaul also said during that time that DES is the proper application for many patients, but that the devices were used far too often in cases where clinical data suggested that BMS use or long-term drug therapy was safer. Only about 20% of DES devices were being inserted in patients who have the kinds of conditions studied in the clinical trials that led federal regulators to approve them, he said.

The 2006 studies led to the FDA examining the issue later that year. "These concerns led to a stair-step reduction in the use of drug-eluting stents, which had expanded rapidly since their introduction in 2003," said Cohen, also a professor of cardiovascular research at the **University of Missouri-Kansas City**. "Because of the safety concerns, we were able to verify what many of us had suspected – that using drug-eluting stents in virtually all patients is not that efficient."

While Cohen believes the FDA concern was appropriate at the time, newer evidence with longer follow-up and more data has indicated that drug-eluting stents are safe. "Our current understanding is there is no real excess risk," he said. Later risk of dangerous clots might be balanced by earlier benefits.

Researchers found that when use of drug-eluting stents declined in 2007, the stents were more likely to be placed in patients who were at highest risk of re-blockage – including younger patients with smaller vessels or with longer problem areas in the vessels being treated. "Because we were selectively targeting the highest-risk patients, we were able to use far fewer drug-eluting stents while preserving the clinical benefit," Cohen said. Researchers estimated that when compared with less selective use of drug-eluting stents in 2004-2006, more selective use in 2007 reduced healthcare costs by an average of $401 per patient. Per-patient cost is magnified into hundreds of millions of dollars each year, given the

nearly one million angioplasty procedures performed in the U.S., the authors noted.

Patent reform may prompt more filings

The U.S. Senate passed H.R. 1249, the version of the America Invents Act passed by the House of Representatives earlier this year, and the bill was signed very shortly thereafter by President Obama. However, opinions diverge as to the value of the legislation for med-tech firms in the U.S.

On the one hand, Tony Shaw, counsel at the law firm of **Arent Fox** (Washington), and an adjunct professor of law at the **Georgetown University Law Center** (Washington), told *BB&T* in an interview that once all the provisions of the law goes into effect in 18 months, inventors may conclude they "have to file preemptively even if [they] haven't quite perfected the invention" because of the imposition of the first-to-file (FTF) paradigm embodied in the bill. Shaw also remarked that inventors in other nations are more savvy about the FTF approach and hence "we sort of put ourselves at a competitive disadvantage by adopting their system."

On the other hand, JC Scott, senior executive VP for government affairs at the **Advanced Medical Technology Association** (AdvaMed; Washington), said in a statement e-mailed to *BB&T* that modernizing the patent process "is an important element of making sure that America's medical device companies continue to be the world leaders." Scott made note of the transition to FTF – or first-inventor-to-file, as some refer to it – which he said "will promote international harmonization and create efficiencies throughout the system."

Scott also made note of a provision in the bill to deal with false markings, "which discourages deceptive patent markings and would help eliminate frivolous lawsuits" as well. Scott concluded the statement by noting that the association is "glad the Congress has passed this bill and look[s] forward to the President signing it."

Not all the associations are as optimistic, however. Tom Novelli, VP for government affairs at the **Medical Device Manufacturers Association** (MDMA; Washington) said in a statement e-mailed to *BB&T* that MDMA "appreciates the progress made by Congress to improve the patent reform bill from earlier versions." He said the bill "while not perfect, is a positive step towards updating the current patent system," although Novelli expressed concern that the establishment "of a new post-grant review process may overburden PTO and provide a potential vehicle for abuse by some parties." He finished the statement by stating, "we look forward to working with the PTO as it seeks guidance on implementation of the new law."

The debate over the America Invents Act covered several amendments addressing issues such as business method patents, but the most important amendment in terms of the U.S. Patent and Trademark Office's operations was offered by Sen. Tom Coburn (R-Oklahoma). Coburn's amendment would have removed any vestige of patent fee diversion into the general treasury, but the Senate voted by the razor-thin margin of 50-48 to table the vote, which quashed any further discussion.

Sen. Pat Leahy (D-Vermont), chairman of the Senate Judiciary Committee, said "acceptance of [Coburn's] amendment will effectively kill the bill. The leadership of the House has told me" it would gain no traction in the House under such circumstances, but Coburn would hear nothing of it. He replied that such threats are "how bullies operate," adding that the way "you break a bully is you challenge the bully."

Coburn remarked at one point that such failures on Congress's part are "why we have a 12% approval rating," and he asserted further, "there are 750,000 patents pending right now, and there should be only about 100,000." Coburn also made the case that Congress "can change the amount of fees [PTO collects] if they're not doing a good job."

Shaw hinted that he did not see false marking as a huge issue, although he noted that it can prove somewhat expensive when it does arise. He also said that FTF will change minds about when and what information to file. "I think now a lot of companies take their time" about filing, waiting "until they've perfected" or further refined the invention. "They won't file when they're not sure what the commercial value is" in a first-to-invent world, either, he said. "Now you'll probably have to file preemptively even if you haven't quite perfected the invention," he said.

The switch to FTF "is probably going to result in a lot more filings for more incremental changes" as well, Shaw predicted. He also said that the bill's provision for *inter partes* review "creates a nine-month window for people to come in and try to reverse the decision to grant the patent," a feature he confirmed might push applicants to describe more of the prior art in their filings "so you can inoculate your application to some extent."

Shaw also echoed some of the widespread skepticism regarding Congress's ability to keep its hands out of PTO's cookie jar. "I don't think anyone thinks Congress will behave itself" on this score, he said. "I think everyone recognizes the need to stop fee diversion and it didn't happen," he shrugged.

Regarding the pendency/patent backlog problem, Shaw remarked, "you see articles by people who think throwing more money at PTO won't solve the problem," but he noted that the Board of Patent Appeals and Interferences at PTO is also working under a backlog. "There's nothing in this legislation that's going to address that," he said. ❖

Product Briefs

AirXpanders gets IDE to study AeroForm

By AMANDA PEDERSEN
***BB&T* Senior Staff Writer**

There has to be a better way.

That sentiment is what inspired the development of a new breast tissue expansion device for mastectomy patients undergoing breast reconstruction. The device, called AeroForm, was developed by **AirXpanders** (Palo Alto, California), which recently received an investigational device exemption from FDA to move forward with a clinical trial evaluating the technology.

The prospective, randomized, controlled, open-label pivotal study, XPAND (AirXpanders Patient Activated Controlled Tissue Expander System for Breast Reconstruction), will be conducted at multiple centers across the U.S. AirXpanders said the results will be used as the basis for its AeroForm 510(k) filing with the FDA.

Scott Dodson, president/CEO of AirXpanders, said that the current method for undergoing breast reconstruction following a mastectomy is a procedure during which the surgeon creates a space for a permanent implant. To do this, the surgeon makes a small incision into the woman's pectoral muscle and inserts a silicone bag. Then, during weekly office visits, the surgeon inserts a needle through the skin into the tissue expander's port to inject saline into the temporary implant. These weekly injections continue for upwards of four months, Dodson said.

So Daniel Jacobs, MD, a practicing plastic surgeon and one of the co-founders of AirXpanders, decided there had to be a better way.

What AirXpanders ended up coming up with was a breast tissue expansion device that would address the limitations of traditional saline expanders. The AeroForm tissue expander consists of a technologically advanced self-contained tissue expander and a small hand-held wireless remote control. Dodson said the system uses compressed carbon dioxide that is gradually released through a small internal valve, in place of invasive saline injections, to fill the expander. After a standard procedure to implant the expander, the patient is able to inflate the expander herself at home using the remote control, eliminating the need for weekly doctor visits and needle-based saline injections.

The patient can inflate the expander up to three times a day with a three-hour lock-out between doses. "We thought if we could expand the patient on a gradual daily basis we could get her there quicker," Dodson said.

The way the remote control part of the system works is that the patient waves it over the implant area to allow it to communicate with the implant.

"It's like using a stud finder on the wall to find out where a stud is," Dodson said. "This dose controller communicates when it is over the implant . . . once you're in the sweet spot you simply press the button and immediately a 10 cc dose is delivered."

He said the company recently completed its feasibility trial in Australia which showed that the implant was able to reach full expansion in about two weeks using the new device.

"This is a significant event in the fact that women want to get on to the recovery phase after they've gone through this horrible ordeal with cancer . . . we validated that we can help get them there quicker," Dodson said.

AirXpanders noted that the randomized, controlled clinical trial is designed to directly compare the outcomes of tissue expansion using the traditional saline expansion method to the investigational AeroForm, remote-controlled, needle-free tissue expander. Enrollment will continue until a total of 92 AeroForm devices have been implanted and 46 saline expanders have been implanted. Dodson said the company expects the trial to take six to eight months to complete.

Participating sites include hospitals in Atlanta, Boston, New York, St. Louis, San Diego and other cities across the U.S., the company noted.

Elsewhere in the products pipeline:

• **AB Sciex** (Framingham, Massachusetts) reported the extension of its Eksigent line of column chips for the cHiPLC-nanoflex system. Five new chips were introduced at the HUPO (Human Proteome Organization) conference, expanding the flexibility and application of the system for high-performance proteomics analysis, including biomarker discovery, validation and verification. The company says the extended offering adds higher flow micro cHiPLC columns for peptide separation at increased throughput levels, as well as new phases for the analysis of intact proteins, phosphopeptides and glycans.

• **AngioScore** (Fremont, California) reported the launch of its new 100 mm AngioSculpt PTA Scoring Balloon catheters for the treatment of peripheral artery disease (PAD). These new AngioSculpt catheters have received FDA clearance to market for the dilatation of lesions in the iliac, femoral, ilio-femoral, popliteal, infrapopliteal, and renal arteries, and for the treatment of obstructive lesions of native or synthetic arteriovenous dialysis fistulae. These new PTA catheters are not labeled for use in the coronary or neuro-vasculature. The new An-

gioSculpt catheters use longer 100 mm Scoring Balloons in diameters of 4.0, 5.0, and 6.0 mm. These catheters are expected to be particularly useful in treating lesions typically encountered in the treatment of complex PAD above the knee. The AngioSculpt Scoring Balloon's nitinol scoring elements provide circumferential scoring of plaque, leading to precise and predictable luminal enlargement across a wide range of lesion types while avoiding "geographic miss" through their unique anti-slippage properties, the company said.

• **Baxter International** (Deerfield, Illinois) said the FDA has expanded the indication of ARTISS [Fibrin Sealant (Human)] to include adhering tissue flaps during facial rhytidectomy surgery (face-lift). ARTISS is a premixed, ready-to-use fibrin sealant specifically indicated for tissue adherence in facial rhytidectomy (face-lift) and burn surgeries. It was first approved by the FDA in 2008 to adhere autologous skin grafts to surgically prepared wound beds resulting from burns in adult and pediatric populations one year of age or older.

• **Caliper Life Sciences** (Hopkinton, Massachusetts) reported the availability of the IVIS Spectrum CT, a preclinical imaging system that integrates, into a single instrument system, advanced optical imaging and low-dose microCT (micro computed tomography). Spectrum CT enables simultaneous molecular and anatomical longitudinal studies, providing researchers with vital, unparalleled insights into complex biological systems in small animal models used to develop new, clinically translatable discoveries. A broad array of applications exist for the new instrument, with musculoskeletal, vascular, oncology, phenotyping, cardiovascular and respiratory disease among those areas particularly enabled by the integration of optical and microCT imaging.

• **Carestream Molecular Imaging** (Woodbridge, Connecticut) reported the introduction of the In-Vivo Xtreme, the newest addition to its family of multimodal imaging products dedicated to preclinical research. Xtreme is powered by an innovative system architecture that provides the ultimate combination of sensitivity, speed and flexibility to meet the most demanding challenges and broadest range of applications for molecular imaging. One of the most compelling features of this new system architecture is the ability to precisely match camera choice with research needs, performance criteria and budget. Xtreme comes in two camera configurations. The front-illuminated 16MP camera is ideally suited for applications that demand high resolution, while the back-illuminated 4MP camera excels at very low light imaging experiments.

• **Concentric Medical** (Mountain View, California) reported the completion of enrollment of the TREVO study. The TREVO study is the first evaluation of Stentriever technology in a European, multicenter, prospective clinical trial. The TREVO study was designed to assess the ability of the Trevo system to remove the blood clots that cause strokes and to restore blood flow to the brain. The TREVO study used the latest generation of the Trevo retrieval system and the preliminary results are very promising. The interim revascularization rate in the first 36 patients was 96%. Thirty patients had 90-day follow up and 63% of these had a good outcome. A "good outcome" was defined as being functionally independent at 90 days. The Trevo System is a thrombus retrieval system. The main component of the Trevo system is the Trevo retriever which introduces Stentriever technology, creating a new generation of retrieval devices to remove clots in acute stroke patients. Concentric Medical makes devices for ischemic stroke intervention.

• The **Centers for Disease Control and Prevention** (Atlanta) reported a new *in-vitro* diagnostic kit to diagnose human infections with seasonal influenza viruses and novel influenza A viruses with pandemic potential. The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel utilizes a three-module design. The modules incorporate and streamline previous versions of CDC's two separate FDA-cleared diagnostic test kits. The first module is used to identify and distinguish between infection with influenza A and B viruses. The second module can further classify influenza A viruses by subtype, such as H1N1, H3N2 or 2009 H1N1. And the last module specifically detects highly pathogenic avian influenza A (H5N1) virus infection in human respiratory tract specimens, in support of ongoing global preparedness efforts against a possible H5N1 bird flu pandemic.

• **Delcath Systems** (New York) reported top-line results from the metastatic colorectal (adenocarcinoma) cohort of the phase II clinical trial of the Delcath chemosaturation system with melphalan in the treatment of patients with unresectable liver cancer. The company also confirmed plans to initiate a new Phase II single-arm study in the second half of 2012. The new study is intended to evaluate the efficacy of Delcath's chemosaturation system and its next-generation high efficiency filter in patients with colorectal cancer that is metastatic to the liver and is refractory to first line systemic chemotherapy. Delcath is a development stage specialty pharmaceutical and device company focused on oncology.

• **DSM** (Berkeley, California) reported a collaboration with vascular catheter developer and manufacturer PendraCare resulting in the launch of the Primum guiding catheters. PendraCare uses ComfortCoat hydrophilic coating, a DSM technology, in its line of Primum guiding catheters. The hydrophilic coating aids in smooth catheter introduction and positioning by lowering friction in tortuous and calcified anatomy and reducing the risk of vessel wall trauma, while significantly extending Primum guiding catheter's effectiveness over prolonged procedure times. The no slip-stick effect results in more accurate positioning in ostial lesions and reduced catheter friction results in real 1:1 torque control of the tip.

The properties and characteristics that DSM's Comfort-Coat coating provide include excellent lubricity, superior durability and adhesion as well as proven biocompatibility thereby making it an excellent material choice for catheters and guidewires in vascular, neurological, urinary and other applications.

• **Echo Therapeutics** (Philadelphia), maker of the Symphony tCGM system as a non-invasive, wireless, transdermal continuous glucose monitoring (tCGM) system and the Prelude SkinPrep system for transdermal drug delivery, said it is initiating a clinical study of its Symphony tCGM system. Echo's clinical study will enroll healthy volunteer subjects and will compare data obtained from its Symphony tCGM system with both the YSI 2300 STAT Plus Glucose Analyzer and a commercially available professional-use glucometer. The study will collect more than 900 data pairs to be used in the analyses by taking frequent reference glucose measurements for 24 hours. The study data will be blinded to study subjects and study personnel. A comparison of the data relative to the blood glucose values will determine the accuracy of Symphony.

• **EnteroMedics** (St. Paul, Minnesota) reported data from the company's VBLOC-DM2 ENABLE (DM2) trial evaluating the company's second-generation Maestro RC System in the treatment of obesity, diabetes and hypertension, was presented at the XVI World Congress of the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) in Hamburg. DM2 trial results presented at IFSO reflect statistically significant, sustained improvement in glycemic control and blood pressure, as well as clinically meaningful weight loss in obese, diabetic patients using the Maestro RC System. The Maestro RC System delivers VBLOC vagal blocking therapy via two small electrodes that are laparoscopically implanted and placed in contact with the trunks of the vagus nerve just above the junction between the esophagus and the stomach. The Maestro RC System is powered by an internal, rechargeable battery. The battery is recharged via an external mobile charger and transmit coil that the patient uses for a short time each week. EnteroMedics developed VBLOC vagal blocking therapy to offer bariatric surgeons and their patients a less invasive alternative to existing surgical weight loss procedures that may present significant risks and alter digestive system anatomy, lifestyle and food choices.

• **Iridex** (Mountain View, California) reported the introduction of its new XP Module – a high-power factory-installed option for the Iridex IQ 532 green laser system. The IQ 532 XP is a multifunctional device that can be utilized by both ear, nose and throat (ENT) surgeons and ophthalmologists – expanding overall use and making a laser investment more attractive. The optional XP module doubles the power of the standard Iridex IQ 532, facilitating the rapid and efficient treatment of tissue while limiting unwanted thermal effects and provides ENT surgeons with a portable KTP 532 nm laser system that is optimized for their clinical needs. Our IQ 532 products are small, portable, depot serviced, and solid state semiconductor-based laser systems. Some notable features include a modern touch screen user interface, wireless foot switch control, and voice confirmation.

• **Lifetime Products** (Clearfield, Utah) said it is expanding its product depth and adding a new Health and Wellness product category. Initially, the new Lifetime Health and Wellness category will feature products like the award-winning Lifetime Tru-Motion Walking Cane already on the market, and a new full line of home safety accessories including bath and towel safety grab bars.

• **Merit Medical Systems** (South Jordan, Utah) has received regulatory approvals for multiple products. Merit recently received regulatory approval in China for its Laureate guide wire, Concierge guiding catheter, and Impress

Companies and organizations in this issue

catheter. Merit also recently received FDA clearance for its EndoMaxx esophageal stent and its flow control device. The company also received approval for its Zeonex syringe, which will extend the shelf life of its Embosphere product line. Additionally, Merit received its first regulatory approval in Singapore for its EN Snare foreign body removal device. Merit makes disposable medical devices used in interventional and diagnostic procedures, particularly in cardiology, radiology and endoscopy.

• **Philips Electronics** (Amsterdam, the Netherlands) reported the introduction of ClearVue, what the company calls a family of ultrasound solutions featuring innovative technology, smart design and ease of use to make high quality imaging available to a wider range of clinicians. The system features Active Array technology, a solution that harnesses the power of larger ultrasound systems, enabling 2-D, color and Doppler image quality for increased diagnostic confidence.

• **Rexam Healthcare** (Buffalo Grove, Illinois) has received FDA approval for its passive safety device for staked prefilled syringes – Safe'n'Sound. The device is designed to protect workers in the health sector from needle injuries and contamination from blood borne pathogens. The passive Safe'n'Sound device provides protection against the risks of being pricked by a soiled needle through a protective sheath which activates automatically once the medicine has been administered, the company claims. Rexam Healthcare makes packaging for containers and closures, drug delivery devices, metering pumps and valves and medical components to improve patients' health.

• **Starkey Laboratories** (Minneapolis) has introduced a new receiver-in-canal (RIC) style with a size 13 battery to the Wi Series hearing aid line. Wi Series is a wireless hearing aid solution engineered to deliver a better listening experience. It contains a noise reduction and speech preservation system and eliminates buzzing and whistling. Additionally, Wi Series has the ability to stream stereo sound directly from a TV, radio or computer to the hearing aids – meaning that one person can listen at a comfortable level directly through his or her hearing aids like wearing head phones, while those around them can listen at the volume that is most comfortable for them. All of this is done without the need for additional hardware or pairing. Wi Series is available in two styles of RIC hearing aids featuring size 13 and 312 batteries and ranging from 40-gain to the 70-gain Absolute Power.

• **St. Jude Medical** (St. Paul, Minnesota) said the first patient in a clinical study examining the safety and effectiveness of an ST segment monitoring feature in an implantable cardioverter defibrillator (ICD) has been implanted with the investigational device in the U.S. The ST Monitoring to Detect ACS Events in ICD Patients (Analyze ST) study will evaluate effectiveness of the feature in the Fortify ST ICD by analyzing its accuracy in detecting acute coronary events, such as myocardial infarction, commonly known as a heart attack. The ST segment is a section of an electrocardiogram (ECG) that depicts electrical changes between heartbeats. Changes in ST segments have long been studied in clinical settings using external devices as indicators for an obstruction of blood flow and oxygen to the heart muscle (cardiac ischemia). However, due to several limitations, it has not been practical to study them on a continual basis. ❖

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