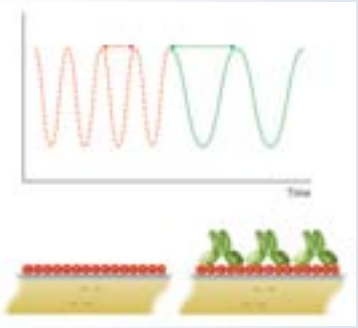
SurFACTS in Biomaterials

July-August 2011 | Volume 16 Issue 2

Biomaterials In-Situ: Nanoscale Investigation of Molecules on Surfaces using QCM-D

By Mark A. Poggi, Totta Kasemo and Bengt Kasemo

Is it possible to measure the weight and the structural properties of nanostructures and molecular films at the same time? What better way to discuss biomaterials than to talk about cooking. Imagine grabbing an empty plate with one hand at each end. Start swinging the plate back and forth rhythmically. Eventually you will find an oscillation rhythm that requires only a small effort. Suppose that you put Jello onto the plate. The rhythm needed to oscillate the plate will change, and you will find that you need to use slightly more energy to perform each oscillation. If you look at the Jello you will see that it deforms during the back and forth motion. The deformation of the Jello requires more energy than just moving the mass of Jello: energy is dissipated. Recording such changes at the molecular or nanoscale on an oscillating sensor is the basic principle of the Quartz Crystal Microbalance with Dissipation technique, QCM-D. The technique provides information about the mass change and the structural properties of a material or molecule at the same time.



The binding of proteins onto a quartz crystal microbalance changes the oscillation behavior of the crystal.

QCM-D is a real-time sensing technique used to study a variety of molecules and interactions at interfaces. The technique records changes in oscillation rhythm (frequency) and measures the energy dissipation caused by materials, and thus provides information about binding to

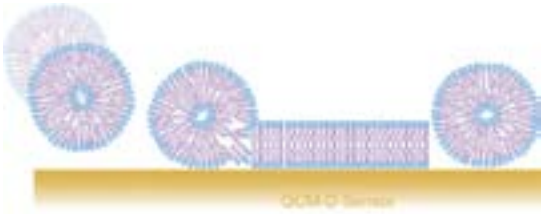
Nanoscale Investigation Continued on Page 2

Inside this Issue

Nanoscale Investigation Continued from Page 1

surfaces, along with mass and structural properties. Studies are conducted on a sensor surface, which can be coated with a wide range of materials, and instead of using Jello, the surface can be exposed to cells, bacteria, proteins or whatever substance is of interest.

In the field of biomaterials, QCM-D sensor



A common way to mimic cell membranes is to form lipid bilayers on a QCM-D sensor, and to insert molecules of interest (e.g. protein) into the bilayer.

coatings typically include hydroxyapatite, titanium, titanium oxide and biomaterial polymers. These materials are the ones commonly used in medical implants, or as catheter tubing for biological fluids (blood, urine, etc.).

Host reactions to biomaterials are to a large extent determined by the surface properties of a material, which can have a large influence on the adhesion strength of biomolecules, cells and tissue. Proteins and cells attach to a rough titanium surface differently than to a smooth titanium surface. In designing biomaterials, it is essential to understand both the topographical and chemical surface properties, along with the nature of the interactions between a surface and proteins and cells. Here are several examples where the QCM-D technique has been successfully used in the study of biomaterials.

Weber et al. (1) have investigated polymers which could typically be used for blood-containing implants and vascular tissue engineering scaffolds. Smooth muscle cell adhesion, proliferation and motility on biomaterials affect the performance of such devices, and are therefore important to understand thoroughly.

Using QCM-D, the researchers studied the adsorption behavior of serum proteins onto various polycarbonate polymers. The structure of the co-polymers were changed by varying: (A) the content of iodinated tyrosine to achieve X-ray visibility; (B) the content of poly(ethylene glycol) (PEG) to decrease protein adsorption and cell adhesivity; and (C) the content of desaminotyrosyl-tyrosine (DT), which regulates the rate of polymer degradation.

In the study, the differential serum protein adsorption was quantified as a function of the chemical structure of the polymer. With QCM-D it was found that serum protein adsorption to the copolymers decreased when the PEG content in the copolymer was increased. A complex interplay among the three components of the copolymers was discovered, and the results indicate that polycarbonate copolymers offer a range of sensitive platforms to study cell adhesion, proliferation and motility responses.

Jensen et al. (2) have reported the use of QCM-D to obtain information on the interactions of human mesenchymal stem cells with osteopontin (OPN) coated hydroxyapatite (HA) surfaces. The OPN protein belongs to a group of bone proteins, and plays an important role in bone remodeling.

In the study, the adsorption of OPN onto gold and HA surfaces was monitored in real time using the QCM-D technique combined with ellipsometry. The binding of the OPN protein was verified by subsequent binding of the OPN antibody.

Nanoscale Investigation Continued on Page 3

SurFACTS in Biomaterials is the official publication of the foundation and is dedicated to serving industrial engineers, research scientists, and academicians working in the field of biomaterials, biomedical devices, or diagnostic research.

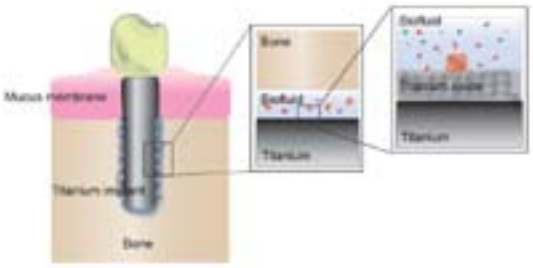
Nanoscale Investigation Continued from Page 2

The protein-antibody interactions cause an uptake in mass, which was monitored by a decrease in the oscillation frequency of the QCM-D sensor. Just like Jello on a plate, the bound proteins change the rhythm of the sensor oscillations. The binding protein and antibody also dampen the oscillations (increase energy dissipation) due to the viscoelastic properties of the bound molecules.

The interaction of human mesenchymal stem cells with the protein modified surface was then monitored. The attachment, spreading and motility of the cells differed significantly between the OPN-coated HA surface and OPN-coated gold surface, as well as between the uncoated gold and HA surfaces. The in vitro results indicate the great potential of OPN coated biomaterials to promote integration with bone, and also serve as an example of the importance of understanding the mutual interplay between specific surface properties, and biomolecules and cells.

Another common application area is in the study of dental implants. A key issue is to secure integration between the implant surface and the surrounding bone tissue, referred to as osseointegration. However, the implant also integrates with the soft mucosa above the bone. How the surface of the implant interacts with blood proteins will have a large impact on the success of the integration according to results from Kasemo and Gold (3). Another important aspect is the long-term effect of the implant surface on the mucosa, the area exposed to the oral cavity space. Here, the implant interactions with saliva and saliva proteins need to be understood and controlled.

For successful implantation, rapid integration is desired, so that the implant can be subjected to mechanical loading without a long waiting period. Scheideler et al. (4) have experimented with surfaces coated with biomolecules in order to improve the degree of tissue integration. Upon insertion of a dental implant, a macromolecular film rapidly forms on the implant surface (in the oral cavity the film is called pellicle). This film, created from macromolecules in blood and saliva, will indirectly determine subsequent cellular and bacterial interactions with the implant surface, as well as the inflammatory and immune responses of the host. The aim of current research on dental implants is not only to improve the increase of bony anchorage, but also to accelerate of the entire healing process.



Schematic of the regions of interaction between a titanium implant and surrounding tissue and bone.

The adsorption and desorption of blood and saliva macromolecules, key to understanding initial plaque formation on biomaterials, have been investigated in real-time using QCM-D (4). A titanium coated QCM-D sensor served as a model for titanium implants, and the sensors were surface modified in order to influence the saliva-surface interaction. Fibronectin, which can be found in saliva, was used as a model protein to create a biological coating on the titanium surface and the effect of Fibronectin coating on pellicle adsorption and desorption was investigated, and compared with bare titanium surfaces.

Upon exposing the sensors to saliva, the mass and the viscoelastic properties (softness/rigidity) of the resulting film, the pellicle, were studied. Perhaps more importantly, desorption processes were also studied. The results indicate that Fibronectin coated titanium surfaces substantially increase the reversibility of pellicle adhesion compared to unmodified titanium surfaces.

Bacteria in the oral cavity primarily adhere to the acquired pellicle layer and not directly to the biomaterial surface. It may therefore be hypothesized that the reversibility of bacterial adhesion in vivo also will be increased by the observed strong reversibility of pellicle formation on a titanium implant coated with Fibronectin. It is important to note that the risk for bacterial growth and unhealthy conditions around the implant, which could eventually lead to infection and loosening of the implant, are higher for an irreversibly bound plaque film than if removal of the plaque by normal oral hygiene treatment is possible.

In all these examples, QCM-D has proven useful in the study of biomaterials, both alone and in combination with other methods such as ellipsometry. The information derived in real time from the frequency

Nanoscale Investigation Continued on Page 4

Zinc-Removal Technology Prevents Biofilm Formation on Wounds, Implants

By Shana Leonard, Medical Product Manufacturing News

A testament to the belief that there's strength in numbers, biofilms can be 1000 times more resistant to antibiotics than planktonic bacteria. This level of resistance to antibiotics and host immune responses, coupled with the extreme speed at which they develop, has established biofilms as a leading contributor to hospital-acquired infections and a formidable foe. In an effort to keep these dangerous biofilms at bay, startup company 3G BioTech LLC (Boston) has developed a technology that prevents bacterial colonization on wounds, catheters, pacemakers, orthopedic implants, and other medical devices through zinc removal at the cellular level.

Building on research conducted in the lab of Andrew Herr at the University of Cincinnati (www.uc.edu), 3G BioTech's technology exploits the scientists' identification of a 'zinc zipper' during the biofilm-formation process. Biofilms form when planktonic bacteria such as Staphylococcus aureus or Staphylococcus epidermidis attach to a substrate. Once anchored to the surface of a medical device, for example, the bacteria colonize and produce an extracellular polysaccharide matrix composed of polysaccharide, protein, and other components, which provides protection.

During this study of biofilms, however, Herr's team found that a zinc-dependent adhesion module acts like a molecular Velcro or glue, promoting intercellular adhesion. Staphylococcal biofilm formation, the researchers deduced, thus requires cell surface proteins that are zinc-dependent.

In light of this revelation, the researchers tested the effects of zinc chelation, or removal, on biofilm formation. To do so, they employed DTPA, a chelating agent that is approved by FDA for treating heavy-metal poisoning. "We show in our studies that when you remove zinc at the cellular level, biofilms will not form," Gary Young, CEO and founder of 3G BioTech, said during a presentation at the 2011 BIOMEDevice Boston forum. "Bacteria thus do not have the ability to excrete the polysaccharide matrix to protect themselves, so they're left in the planktonic state." Conversely, the scientists found that when zinc was added back in, biofilm formation once again occurred.

"Our mission is clear: to be the first in class commercializing a biofilm prevention product for biolfilm-related infections, reducing healthcare costs and decreasing all of the pain and suffering that goes along with these infections caused by biofilm," Young said. "There is not an FDA-approved product available that prevents biofilm; it's all about treatment today."

3G BioTech's technology can be incorporated onto the implant or product by the medical device OEM prior to market release, or it can be sold directly to end-users for application in the clinical environment. It can be supplied in spray, gel, cream, or coating form. In addition,

Zinc-Removal Technology Continued on Page 5

Nanoscale Investigation Continued from Page 3

and dissipation factor changes of the rhythmically oscillating sensor simultaneously give information about the added or lost mass on the sensor surface, along with any variations in viscoelastic properties. The QCM-D technique indicates whether binding occurs or not (did the Jello really land on the plate?) and whether there is a rigid layer or trapped water between molecules on the sensor, which make the film more Jello-like.

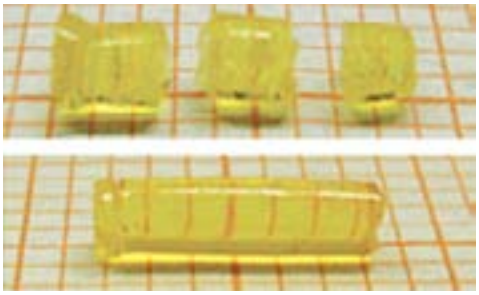
References

1. Weber N, Pesnell A, Bolikal D, Zeltinger J, Kohn J, Viscoelastic properties of fibrinogen adsorbed to the surface of biomaterials used in blood-contacting medical devices, Langmuir, 2007.
2. Jensen et al., Interaction of human mesenchymal stem cells with osteopontin coated hydroxyapatite surfaces, Colloids and Surfaces B: Biointerfaces, 2010.
3. Kasemo and Gold, Implant Surfaces and Interface Processes, Advances in Dental Research, 1999.
4. Scheideler et al., Photocoupling of fibronectin to titanium surfaces influences keratinocyte adhesion, pellicle formation and thrombogenicity, Dental Materials, 2007.

Self-Mending Polymer Could Fix Future Implants

By Bob Michaels, Medical Product Manufacturing News

Scientists' efforts to develop self-mending materials, from thermoset resins to self-healing rubbers, could have vast implications for a host of industrial, consumer, and medical applications. However, many self-repairing systems require the use of heat to reform bonds and fix cracks, making them commercially unviable. Taking a different approach, scientists at Carnegie Mellon University (CMU; Pittsburgh and Kyushu University (Fukuoka, Japan) are developing a polymer that self-heals at room temperature when exposed to UV light.



An implantable diamond-coated flexible electrode is designed to last a lifetime in the body.

"Most self-mending techniques rely either on one-time healing by using an encapsulating agent that cannot be regenerated or on weak noncovalent bonding," explains CMU chemistry professor Krzysztof Matyjaszewski. "Our concept differs from these approaches. It produces covalent bonds that can be self-mended repeatedly."

The scientists' photoinduction method relies on covalently cross-linking polymers with trithiocarbonate units using a process known as reversible addition-fragmentation chain transfer. "Our material uses a network of chemical bonds that fracture at lower energy than the remaining links in the network," Matyjaszewski comments. "This phenomenon protects the majority of the network, and since the fractured bonds can reform new bonds with adjacent complementary function groups, the complete network is reformed."

Because this noncontact polymer can mend itself under room-temperature conditions, it is also easy to acquire and handle, Matyjaszewski says. In addition, it is capable of targeting specific areas for repair and does not require the use of chemicals.

While an early iteration of this covalent-bonding technique required close contact and pressure between the two surfaces of the severed material, Matyjaszewski does not consider this to be an inherent property of the material. "We believe that the system can absorb more energy than a system without breakable and healable bonds, thus presenting a tougher structure than the parent material," he remarks. "Any bonds that break during a noncatastrophic event will be absorbed by a fraction of the breakable/healable bonds and undergo self-repair to regenerate the material." As a result, the regenerated polymer will resemble the original material rather than a material containing multiple microfractures, eliminating the need for material surfaces to remain in proximity to each other or to be subjected to high pressure.

Despite progress in developing his self-healing material, Matyjaszewski cautions that it has not yet been evaluated to determine its suitability for medical device applications—including implantable devices. "Further work is required to develop implantable materials that can withstand repeated self-repair reactions autonomously in the biological environment," he says. However, he envisions that this concept could potentially prolong the lifetime of any material that is subjected to numerous stress-related events. "In the medical field, many potential applications can be imagined, including orthopedic implants."

Zince-Removal Technology Continued from Page 4

the chelating technology can be incorporated into a biodegradable polymer to provide sustained release, according to Young.

Entirely self-funded, privately held 3G BioTech is currently seeking strategic partners for commercialization of the technology within select medical segments, including diabetic wound treatments and various medical implants. Young estimates that the zinc-removal product could go to market within 12 to 18 months of such a partnership. "We think we have an effective therapy in preventing these unmanageable infections [that] also reduces [their] economic and emotional burden," Young stated. "What we have here is a very elegant, very simple solution to a very large problem."

Depositing Drug-Release Coatings on Orthopedic Implants a Layer at a Time

By Bob Michaels, Medical Product Manufacturing News

Despite progress in technologies for combating biofilm formation, approximately 1% of hip implants, 4% of knee implants, and more than 15% of implants associated with orthopedic trauma still fail as a result of implant-induced infection, according to the Stevens Institute of Technology (Hoboken, NJ). Contributing to the effort to further reduce infection rates, researchers at the Massachusetts Institute of Technology (MIT; Cambridge, MA) have designed a coating technique that relies on a layer-by-layer deposition method and tunable drug loading. Their goal is to create a coating that will provide long-term protection against biofilm formation on orthopedic implants.

"Our layer-by-layer technique is a versatile approach to the formation of conformal thin films on surfaces with various geometries, including materials commonly used for implantable devices such as pins, sutures, and prosthetic bones," explains Jessie (Sze Yinn) Wong, a PhD candidate in the department of chemical engineering at MIT. "Using the layer-by-layer technique, films that are very thin and have tunable antibiotic or anti-inflammatory drug-loading capability can be applied onto surfaces of orthopedic implants."

The MIT team's layer-by-layer approach is based on the alternating adsorption of materials containing complementary charged or functional groups, leading to the formation of nanostructured thin films. Most often, according to Wong, this method is used to alternately deposit oppositely charged polyelectrolytes to build up a polymeric film, the composition of which can be tuned on the nanometer-length scale by changing their assembly or postassembly conditions. "Because we are building up the films a monolayer at a time, we are able to control the drug loading as well as the architecture of the film," Wong says. "In this work, we combine a permanent microbicidal film with a hydrolytically degradable top film, offering controlled and localized delivery of therapeutics."

Designed to prevent biofilm formation, the technology contains a permanent antimicrobial coating that kills bacteria on contact. Built on top of this film, a second completely degradable film incorporating a therapeutic agent is designed to slowly degrade under physiological conditions, releasing drugs into the local environment. "For example, the top degradable film can be made to load an antibiotic that will be released and take out any infection present at the implant site," Wong remarks. "When the top degradable film is completely gone, the permanent antimicrobial film is left behind for long-term prevention of biofilm formation."

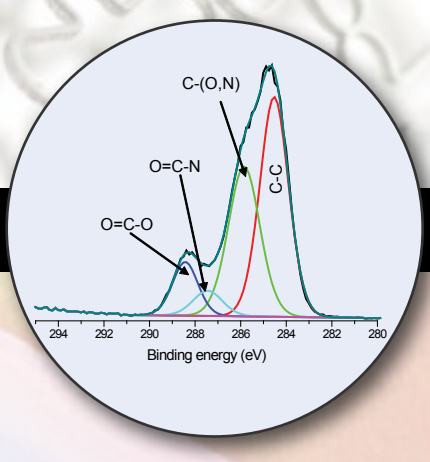
In addition to its ability to deposit a permanent antimicrobial film, the MIT researchers' layering process is cost-effective because it requires only minute quantities of polymer material, according to Wong. At the same time, the film is so thin that it does not alter the original functionality of orthopedic implants. "High drug-loading capacity is achieved," Wong states, "even though the film is very thin."

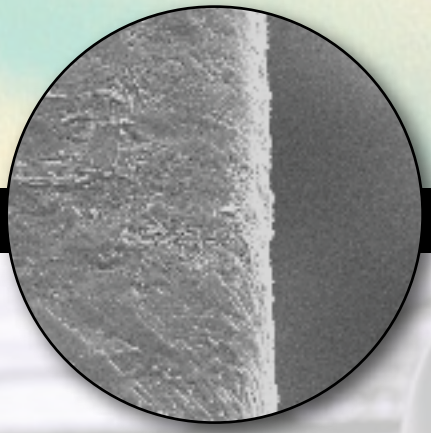
Another advantage of this layer-by-layer technology is that it can be used to tune drug loading simply by changing the number of layers that are deposited, Wong notes. The degradation rate can also be tuned by using polymers with different degradation kinetics.

An in vivo model has shown that the drug-releasing film does not raise biocompatibility issues, while in vitro studies indicate that mammalian cells adhere and proliferate well on the surface of the permanent antimicrobial film. The researchers' next step, Wong notes, is to build an in vivo model for testing both the drug-releasing and the permanent antimicrobial films.

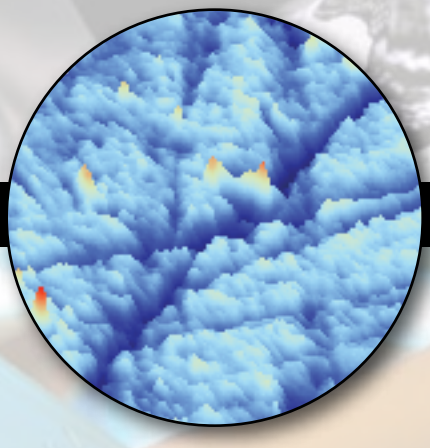
Specialists in Materials Characterization

XPS Spectrum of Hydrophilic Polymer Coating





SEM of Polymer Coated Stent



AFM of Used Contact Lens

Surface Modification

Contamination

Adhesion Issues

Corrosion

Coatings

Failure Analysis

Now with C_{60} buckyball sputtering capability for chemical state profiling of organics.

Providing state-of-the-art surface analysis on orthopedic implants, pharmaceuticals, artificial tissue, stents, surgical devices, vision care products and diagnostic equipment. We work with our customers to provide answers to problems, not just data.

bio@eaglabs.com
www.eaglabs.com
408.530.3500

EAG℠
Evans Analytical Group

Abbott Receives CE Mark Approval for World's First Drug Eluting Bioresorbable Vascular Scaffold for Treatment of Coronary Artery Disease

Abbott announced January 10 that it has received CE Mark approval for the world's first drug eluting bioresorbable vascular scaffold (BVS) for the treatment of coronary artery disease. Abbott's BVS device restores blood flow by opening a clogged vessel and providing support to the vessel until the device dissolves within approximately two years, leaving patients with a treated vessel free of a permanent metallic implant. Abbott's BVS device will be commercialized under the brand name ABSORB(TM).

"The CE Mark approval for ABSORB in Europe is a significant accomplishment that validates the impressive clinical results that have been observed with this device," said Patrick W. Serruys, M.D., Ph.D., professor of interventional cardiology at the Thoraxcentre, Erasmus University Hospital, Rotterdam, the Netherlands. "Abbott's ABSORB has the potential to change the way patients with coronary artery disease are treated, as it does what no other drug eluting coronary device has been able to do before - completely dissolve and potentially restore natural vessel function in a way not possible with permanent metallic implants."

ABSORB is made of polylactide, a proven biocompatible material that is commonly used in medical implants such as resorbable sutures. Since a permanent metallic implant is not left behind, a patient's vessel treated with ABSORB may ultimately have the ability to move, flex and pulsate similar to an untreated vessel. Restoration of these naturally occurring vessel functions, or vascular restoration therapy (VRT), is one of the features that makes ABSORB a significant innovation for patients in the treatment of coronary artery disease. In addition, continuing research indicates that the need to administer long-term dual anti-platelet therapy to patients may be reduced because the temporary scaffold is completely resorbed.

"Our ABSORB technology has the potential to revolutionize the treatment of coronary artery disease - with the prospect for positive therapeutic outcomes resulting from its unique ability to treat a blocked vessel, potentially restore natural vessel function and disappear within approximately two years after implant," said Robert B. Hance, senior vice president, vascular, Abbott. "Receiving CE Mark is a significant milestone on the path to providing patients with new treatment options for coronary artery disease. Abbott is committed to building the clinical and economic benefits of this therapy in anticipation of making it widely available in Europe by the end of 2012."

CE Mark approval for ABSORB in Europe was supported by data from the ABSORB clinical trials, which included patient follow-up out to three years. To further study the device in an expanded population, Abbott plans to initiate a randomized, controlled clinical trial in Europe later this year. The study will enroll approximately 500 patients at 40 centers throughout Europe and will compare ABSORB to Abbott's XIENCE PRIME, which, together with XIENCE V, is the market-leading drug eluting stent system in Europe. The trial will provide additional data to support European commercialization and reimbursement activities. A global trial, including the U.S. and other geographies, is planned for later this year.

In addition to clinical trial product, ABSORB will be made available in select sizes to a limited number of centers in Europe later this year and into 2012. This will enable physicians in these centers to increase their clinical experience with the technology and to continue to develop the therapy. A full-scale European commercial launch of ABSORB with a broad size matrix is planned by the end of 2012.

About the ABSORB Clinical Trials

The ABSORB trial is the world's first clinical trial evaluating a drug eluting BVS for coronary artery disease, and Abbott is the only company with long-term, four-year clinical data on a complete patient set evaluating the safety and performance of a drug eluting BVS. The ABSORB trial is a prospective, non-randomized (open label), two-phase study that enrolled 131 patients from Australia, Belgium, Denmark, France, the Netherlands, New Zealand, Poland and Switzerland. Key endpoints of the study include assessments of safety - major adverse cardiac events (MACE) and treated-site thrombosis rates - at 30 days and at six, nine, 12 and 24 months, with additional annual clinical follow-up for up to five years, as well as an assessment of the acute performance of the BVS device,

ABSORB Recognition Continued on Page 9

ABSORB Recognition Continued from Page 8

including successful deployment of the system. Other key endpoints of the study include imaging assessments by angiography, intravascular ultrasound (IVUS), optical coherence tomography (OCT), and other state-of-the-art invasive and non-invasive imaging modalities at six, 12 and 18 months and at two, three and five years.

Results from the first stage of the ABSORB trial with 30 patients demonstrated that Abbott's BVS successfully treated coronary artery disease and was resorbed into the walls of treated arteries within approximately two years. Patients in this first stage of the ABSORB trial experienced no blood clots (thrombosis) out to four years and no new MACE between six months and four years (3.4 percent at four years).

Nine-month results from the 101 patients enrolled in the second stage of the ABSORB trial showed that the MACE rate remained consistent at 5.0 percent at nine months. There were no reports of blood clots in any of the 101 patients at nine months.

The ABSORB EXTEND trial is a single-arm study that will evaluate patients at up to 100 centers in Europe, Asia Pacific, Canada and Latin America. The trial will enroll approximately 1,000 patients with more complex coronary artery disease.
Abbott's bioresorbable technology delivers everolimus, an anti-proliferative drug. Everolimus is developed by Novartis Pharma AG and is licensed to Abbott by Novartis for use on its drug eluting vascular devices. Everolimus has been shown to inhibit treated-site neointimal growth in the coronary vessels following vascular device implantations, due to its anti-proliferative properties.

About the ABSORB Bioresorbable Vascular Scaffold

ABSORB is made of polylactide, a proven biocompatible material that is commonly used in medical implants such as resorbable sutures. The device is designed to restore blood flow by opening a clogged vessel and providing support to the vessel. Once the vessel can remain open without the extra support, ABSORB is designed to slowly metabolize and eventually be resorbed by the body. Since a permanent implant is not left behind, a vessel treated with ABSORB may ultimately have the ability to move, flex and pulsate similar to an untreated vessel. Restoration of these naturally occurring vessel functions, or vascular restoration therapy (VRT), is one of the features that makes ABSORB a significant innovation for patients in the treatment of coronary artery disease. ABSORB is currently under development and is not available for sale in the United States.

Boston Scientific gets European OK for Latest Stent

March 7, 2011 - From Reuters

Boston Scientific Corp (BSX.N) on Monday said its latest bare-metal stent technology received European regulatory approval, and it remains on track to launch its Promus Element stent in the United States in mid-2012.

The bare-metal stent, called Omega, is designed to be easier to deliver and conform better to the artery.

Stents are wire-mesh tubes inserted into arteries to prop them open after they have been cleared of plaque. Drug-eluting stents are coated with medicine to help prevent re-clogging.

Boston Scientific said it expects U.S. Food and Drug Administration approval in mid-2011 for its next-generation drug-eluting Taxus Element stent and in mid-2012 for its Promus Element stent. Taxus Element will be called Ion in the United States.

Promus Element will replace the Promus stent in Boston Scientific's product line that the company now co-markets with Abbott Laboratories (ABT.N). The original Promus is Abbott's popular Xience stent sold under the Promus name, with Abbott receiving about 40 percent of the profit.

Promus Element is coated with the drug everolimus to prevent clots from reforming in the artery, while Taxus Element is coated with the drug paclitaxel. Both use an advanced design and catheter delivery system.

Bulging Market for Aortic Stents

By Janet Moore, Minneapolis Star Tribune

Gene Sandvig had no clue that a silent killer lurked within his trim 79-year-old body.

The former Olympic speed skater still considered himself to be in good shape, thanks to lifelong commitment to fitness and a fervent love of golf. But during an annual checkup last year, his doctor suggested he get screened for an abdominal aortic aneurysm, or AAA, a weakness in the wall of the aorta not uncommon in men over 60.

Good thing. The Edina grandfather had a bulge in his aorta – the body's biggest artery – that was three times its normal size. Had it burst, chances of survival were slim.

"Then that would have been the end of me," Sandvig said, matter-of-factly. "So I needed to go in and get it taken care of."

For years, these aneurysms were treated with surgery, a long hospital stay (up to two weeks) and an even-longer recovery. But, increasingly, doctors are using a minimally invasive treatment that involves inserting a stent inside the aortic bulge through an artery in the groin. A one-day hospital stay is pretty standard afterward, and recovery much swifter.

"The old-fashioned way works well, but it was quite an ordeal. The risks associated with surgery are so much higher, and the recovery dramatically longer," said Dr. Steven Santilli, a vascular surgeon with University of Minnesota Physicians.

It helps that doctors have several newfangled stents from which to choose. Last December, the Food and Drug Administration (FDA) approved the Endurant AAA Stent Graft System from Fridley-based Medtronic Inc., which the company claims is easier to use than competing devices.

Already a market leader in aortic stents, Medtronic immediately began rolling out its new product in the United States – and Sandvig was among the first recipients last week at the University of Minnesota Medical Center, Fairview.

Market Evolution

As is often the case in medical technology, the field is highly competitive. W.L. Gore & Associates said last week it began using a new aortic stent delivery system recently approved by the FDA – a technology the company claims is "game-changing." Other competitors in the market include Indiana-based Cook Medical and Endologix Inc. of Irvine, Calif.

"There's been a lot of evolution in the [aortic stent] market, " said Tim Nelson, an analyst with FAF Advisors. "It's been a great success story – here's a minimally invasive technology that turned out to be better."

Currently, the market for aortic stents is about $675 million, according to Millennium Research Group, a Toronto-based research firm. But technological advances developed by both new and veteran players in the field will expand the pool of potential patients and make it easier for doctors to use the devices, the firm said in a recent report. This will drive further market penetration and revenue growth through 2015.

This is good news for device manufacturers since sales of cardiac stents, a onetime blockbuster in med-tech, have slowed considerably in the past two years for makers Boston Scientific Corp., which employs 5,000 in Minnesota; Johnson & Johnson; Abbott Laboratories, and Medtronic. Healthier growth is expected for stents used in other parts of the body, including the legs, carotid arteries – and the aorta.

But a vexing challenge remains for makers of aortic stents. While the potential market is large – Medtronic estimates that 1.2 million Americans have abdominal aortic aneurysms – screening potential patients is challenging because they may not experience any symptoms and don't know they need a simple ultrasound screening. In fact many abdominal aortic aneurysms are found by happenstance.

But public awareness has been growing. In 2005, then-President George W. Bush signed into law provisions that call for Medicare to reimburse screenings for men with risk factors for AAA, including high blood pressure, high cholesterol, a history of smoking and heart disease. And several celebrities, including football legend Joe Theismann and Olympic hockey champion Jim Craig, have spread the word about the condition.

Aortic Stents Continued on Page 11

Aortic Stents Continued from Page 10

Theismann's campaign is sponsored by Medtronic.

Resting Comfortably

As Sandvig lay unconscious in an operating room last Monday, doctors made a small incision in his groin maybe an inch long. Nurses prepared for the procedure by removing the 4-foot-long Endurant stent system – which looked like a sophisticated fishing rod to one observer – from its packaging. Each device costs $15,000 to $20,000; two stent systems were used in Sandvig's procedure.

A wire, and then a catheter loaded with a compressed metal and fabric stent, were snaked through Sandvig's femoral artery to his aorta. Using the motor skills and steely nerve of an avid video gamer, Santilli steered the catheter inside the body by twisting an external lever while following the stent's progress on a nearby computer screen.

Once in the right spot, the thick-as-a-thumb stent was carefully released into the aorta. The deployed device created a new pathway for blood within the bulging vessel and two iliac arteries. A second stent was used on the left iliac artery.

All told, the procedure lasted a little more than an hour. Sandvig remained in the hospital Monday night and went home the next day.

"He's a little sore," his wife, Carolyn, reported. "But he's fine."

World's First Tissue-Engineered Urethras Hailed as Success

By Michelle Roberts, BBC News

The world's first tissue-engineered urinary tubes or urethras, grown in the lab using patients' own cells, have been hailed a success by medical experts.

US surgeons have used the lab-grown tubes to treat five Mexican boys with damaged urinary tracts. They told the Lancet that all of the boys are now fit and that the grafts have taken and repaired the defects. The same team has already managed to grow new bladders for patients.

Professor Anthony Atala and colleagues are currently working to engineer more than 30 different replacement tissues and organs. He is director of the Wake Forest Institute for Regenerative Medicine in Winston-Salem, North Carolina.

The first step in engineering the replacement urethras was taking a small sample of cells from the bladder of each of the boys. Aged 10 to 14, the boys had suffered injuries in accidents.

Lab grown

From these samples, the scientists isolated the cells they would need to grow the new structure that expels urine from the bladder.

These cells, needed to make the muscle, lining and supportive tissue, were nurtured and multiplied in the lab for weeks until they were plentiful enough for the job. They were then placed onto a biodegradable mesh that was shaped into a tube and sized to be a perfect fit for the patient.

After a week of incubation to allow the cells to take to the mesh, the lab-grown grafts were surgically transplanted into the patients.

Six years on the grafts are still doing well, looking and functioning exactly like a normal urethra in the five boys who are now entering their teens.

Without this revolutionary treatment the boys would have required an artificial graft that has up to a 50% chance of failure, or would have faced a life of probably incontinence and repeated urine infections.

Professor Chris Mason, an expert on regenerative medicine at University College London, said, "Totally grown in the laboratory, these urethras, living tubes which convey urine from the bladder, highlight the power of cell-based therapies."

"When an organ or tissue is irreparably damaged or traumatically destroyed, no amount of drugs or mechanical devices will restore the patient back to normal. If the goal is cure, then cell-based therapies are the answer."

"Using living cells as 'medicines' is a major step-change in clinical practice. Cell-based therapies complement drugs and devices by aiming to cure the large unmet medical needs of our generation, including blindness, diabetes, heart failure, Parkinson's disease and stroke."

Thank You to Our Members!

American Preclinical Services

Nano Surface Technologies

UNIVERSITY OF MINNESOTA

Wanted: Members

To be leaders in the surface science community

- Join a forum that fosters discussion and sharing of surface and interfacial information
- Have your voice heard and your interests represented within the surface science and biomedical community
- Help shape workshops and symposia that further the world-wide education of surface science
- Promote understanding of interfacial issues common to researchers, bio-medical engineers and material scientists.

Benefits of Membership:

- Discounted registration at BioInterface, the annual symposium of the Surfaces in Biomaterials Foundation.
- Your logo and a link to your Web site in the member directory on the official Web site of the Foundation, www.surfaces.org.
- Complimentary full page ad in surFACTS, the Foundation's newsletter and discounts on all advertising.

Join the Foundation that connects the academic, industrial, and regulatory committees within the surface science/biomedical communities!

Visit the Foundation at www.surfaces.org for a membership application or call 651-290-6267.

Surfaces in *Biomaterials* Foundation