SurFACTS in Biomaterials

September–October 2009 Volume 14 Issue 5

Join Us at BioInterface 2009

By Joe Chinn

The Surfaces in Biomaterials Foundation's annual meeting is a scientific event not to be missed! The BioInterface 2009 Symposium and Workshop will be held in San Mateo, California, at the San Mateo Marriott, Monday, October 26 through Wednesday, October 28.

Dr. Marc Hendriks of DSM Biomedical will chair this year's workshop, Advances in Thermoplastic Elastomers and Biodegradable Polymers: Analysis and Applications. In addition, the exciting Applied Technology Workshops will highlight several companies demonstrating the practical applications of their technologies. Following the BioInterface Welcome Reception, the conference Keynote Speaker, James Barry, Vice President, Corporate Research and Advanced Technology Development, Boston Scientific Corporation, will share his perspectives on Drug-eluting Stents: Past, Present and Future.

The Annual Student Poster Competition, where students will present their research and the best poster is awarded a cash prize, will kick off the technical symposium Tuesday morning, with sessions including Recent Advances in Biodegradable Systems, Next Generation Drug Eluting Stents, and Surface Interaction Designs for Controlled Biological Response to follow. This year's event also includes the Student Town Hall, where students learn from industry about potential future career paths. The popular "Point-Counterpoint" debate session, where opponents will vigorously debate the resolution, "Be it resolved that in vitro biological assays

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From the Editor

BioInterface Networking

What makes for a great meeting? High quality presentations, open discussions, and excellent networking.

This perfectly describes BioInterface. I know of no other industrially focused medical device meeting that has the quality of presentations, the extensive discussions, and the networking (Oh, the networking!) of BioInterface. As I have explained to colleagues who have never attended BioInterface, "If there is someone at the meeting who you would like to meet and you do not, there is no excuse. All you need to do is ask at the numerous networking opportunities."

But how do you find a potential collaborator, or partner, or provider, when you don't even have a clue who to ask? The answer is the Ultimate Networking session that will debut in the final session at BioInterface 2009. In this closing session, entitled, "Academic and Industrial Partnerships," all registered attendees have the chance to address attendees to find what they are seeking. For example, "Our company (or Academic Institution) is seeking partners to develop, test,

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From the Editor
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By Steven L. Goodman, Ph.D., 10H Technology Corporation

evaluate, commercialize, and/or market this widget, technology, intellectual property, or service." For information on how you can present, see the Call for Submissions below.

The Academic and Industrial Partnerships Session will begin with two invited speakers. Colin Fairman, JD, Ph.D., of Fulbright and Jaworski, LLP will present, "Turning Ideas into Reality: Creating, Protecting and Managing Patent Portfolios," and Jeanine Burmania of The Wisconsin Alumni Research Foundation (WARF is arguably the nation's premier university technology transfer office) will present, "The Role of the Technology Transfer Office in the Pathway from Collaboration to Commercialization."

Following the formal presentations, this is where the program opens up for Networking. Again, see the Call for Submissions below to learn how you can present your Networking needs.

Session Announcement – The Ultimate BioInterface Networking Session

Are you seeking partners to help you with device testing, evaluation or research? Do you have a technology or service that is likely to be of interest to BioInterface attendees? Did you ever wish you could simultaneously reach all the attendees at a meeting?

Here is your chance: "The BioInterface Networking Session."

Any registered attendees may present, "I am seeking partners…" or a similar message at the final session of BioInterface 2009 on Wednesday, October 28, at 3:30 pm. Presenters will be allotted a maximum of 5 minutes, including any questions. Submissions will be accepted on a first-come, first-served, time-available basis, at the discretion of the session chair. To enable last minute discussions, submissions may be received up until 3 pm on the day of the session. Up to 5 PowerPoint slides will be allowed, but must be received no later than noon on October 28. Send your request to session chair Steven Goodman. Include the "Seeking Partners" title, your name, institution and contact information. Send to sgoodman@10HTech.com. Include "BioInterface Networking Session" in the subject line.

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.

Abbott to Acquire Evalve, Inc., a Leader in Minimally Invasive Cardiac Valve Repair Technology

From PRNewswire

Abbott announced a definitive agreement to acquire the outstanding equity of Evalve, Inc., the global leader in the development of devices for minimally invasive repair of cardiac mitral valves. The acquisition provides Abbott with a presence in the growing area of non-surgical treatment for structural heart disease, in which physicians use catheter-based devices to repair or replace basic structural components of the heart such as mitral and aortic valves. The agreement includes an upfront payment of $320 million in cash, plus an additional payment upon completion of certain regulatory milestones, for a total of up to $410 million.

"The acquisition of Evalve will provide Abbott with leading technology in the emerging field of minimally invasive heart valve repair and further broadens Abbott's medical devices portfolio," said John M. Capek, Ph.D., executive vice president, Medical Devices, Abbott. "Evalve is on the cutting edge with its non-surgical approach to treating structural heart disease. With this breakthrough mitral valve repair technology, physicians will be able to offer their patients a minimally invasive alternative to open heart surgery—not unlike the opportunity that stents provided more than two decades ago for the treatment of coronary artery disease."

Mitral regurgitation, a condition that prevents the mitral valve from closing completely, is the most common type of heart valve insufficiency in Europe and the United States, and affects millions of people worldwide. Traditionally, mitral regurgitation is treated through open heart surgery. However, only about 20 percent of the 600,000 patients diagnosed in the U.S. and Europe each year undergo surgery. Evalve's minimally invasive catheter-based MitraClip® system, used to clip the leaflets of the mitral valve together to reduce regurgitation, is the first commercially available treatment option approved in Europe for non-surgical mitral valve repair for patients suffering from the effects of mitral regurgitation. The MitraClip system is an investigational device in the United States and is currently in clinical trials.

"Combining Evalve's first in class mitral valve repair technology with Abbott's global presence, commercial infrastructure and manufacturing expertise will help advance minimally invasive treatment options for the millions of patients with mitral regurgitation," said Robert Hance, senior vice president, vascular, Abbott. "We look forward to welcoming Evalve as a key part of Abbott's vascular business."

"Patients in Europe have benefited from having access to the MitraClip technology since it received CE Mark last year," said Ferolyn Powell, president and chief executive officer of Evalve, who will continue to lead the Evalve team and will report to Hance after the acquisition closes. "We look forward to becoming a part of Abbott and working together to accelerate our business and expand our global reach to patients around the world with our minimally invasive technologies."

Under the terms of the agreement, Abbott will acquire the remaining 90 percent of outstanding equity of Evalve, Inc. that it does not already own for an upfront payment of $320 million, plus a $90 million payment if certain regulatory milestones are met. The transaction does not impact Abbott's previously issued earnings-per-share guidance for 2009.

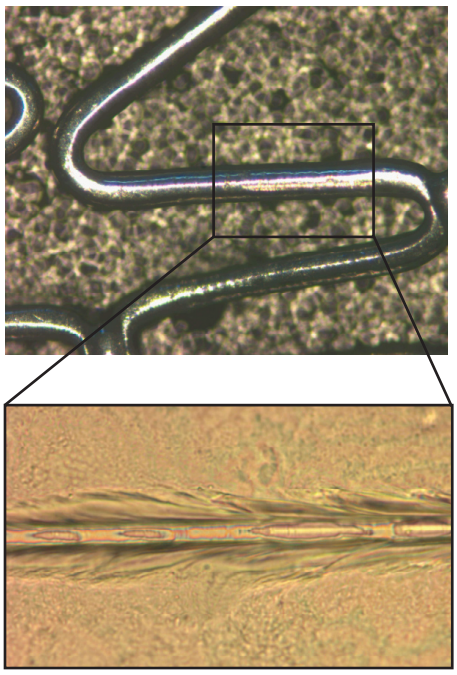
The transaction is subject to customary closing conditions, including antitrust clearances. Abbott expects the transaction to close in the fourth quarter of 2009.

CSM Instruments Develops the Scratch Test for Better Measurement of Adhesion of Drug-Eluting Stent Coatings

By Dr. Nicholas Randall, CSM Instruments

The mechanical properties of coatings on stents have long been known to affect the general device properties, especially during deployment and also during the period after permanent installation when the stent and surrounding artery are in the healing phase.

A surface coating on a stent must withstand significant pressures, both lateral and longitudinal, during preparation, insertion and deployment. If the coating is brittle and cracking occurs, then the coating may disintegrate producing unwanted debris inside the patient's body.

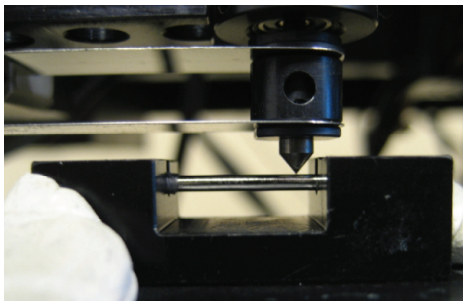


Typical scratch test made along a drug-eluting stent coating.

As stent manufacturers have been developing better surface coatings, especially drug-eluting coatings that aid healing, the challenge has been to find a reliable test method for measuring the mechanical properties of such coatings in an accurate and meaningful way. The only FDA-approved test for measuring the adhesion of a stent coating is still the tape-peel test (ASTM D3359) which is especially subjective (as it depends on tape quality, pressure of application, speed of removal and type of cross-hatched pre-scratches made). In addition, it is impossible to perform a tape adhesion test on a stent wire which may have a diameter of only a few microns. This means that a tape-peel test can only be performed on a large flat "witness" sample of material with the same substrate and coating materials. In practice, it has been found that the process used for coating a stent cannot often be used to coat a larger area. Therefore, any witness sample may not have the same properties as the coating-substrate combination on the stent.

Over the last few years, CSM Instruments has devoted significant resources to the development of a scratch test method which could be used for in-situ testing on an actual coated stent wire. The Nano Scratch Tester (NST) has become the instrument of choice for such tests because it has a load range (mN) suited to the thickness (µm) of most drug-eluting coatings.

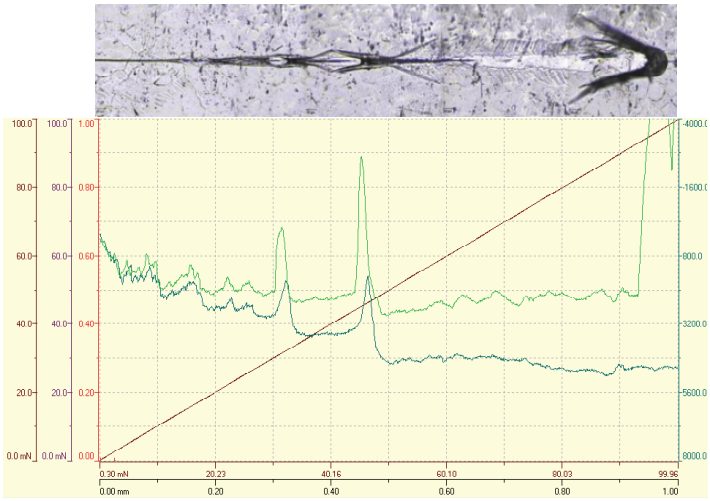
In the scratch test method, scratches are generated on the coated sample using a diamond indenter (commonly a spherical Rockwell C geometry with tip radius of 2µm) which is drawn across the surface under either constant or progressively increasing load. The sample is displaced at constant speed and at a certain load, damage occurs along the scratch path. This value of critical load, Lc, can be used to accurately characterize the adhesive strength of the coating-substrate system. The onset of coating failure can be determined by acoustic emission, optical microscopy, variation in penetration depth or variation in the tangential frictional force between tip and sample.



Nano Scratch Tester (NST) performing a scratch on a stent coating.

The indenter tip can be positioned with an accuracy of 1µm which allows the test to be made routinely along a stent wire. In addition, the system can be automated so that several scratches in different areas of the stent can be easily made. Note that the stent is threaded onto a rigid mandrel in order to support the wire during the test.

A typical example of a progressive load scratch test is shown below. In this example, the applied load has been ramped linearly from 0.1 – 100 mN with a loading rate of 100 mN/min. over a scratch length of 1 mm. There are 2 corresponding critical failure points which can clearly be seen by optical microscopy.



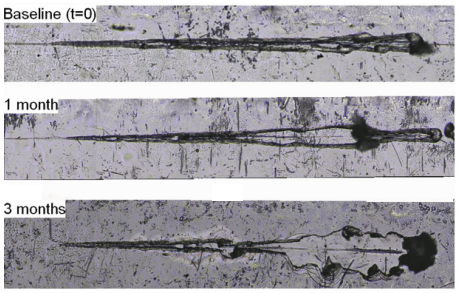
Typical scratch test result showing an optical micrograph of the entire scratch and the corresponding penetration depth data. Dotted lines show the two failure points (cracking and delamination).

The first failure point (Lc1) is where the coating starts to crack and chip from the surface. The second failure point (Lc2) corresponds to the onset of complete delamination of the coating from the substrate. In the example shown, Lc1 occurs at an applied load of 35.8 mN and Lc2 occurs at 67.5 mN.

In addition to using the scratch test as a measure of the adhesion of a coating, some recent work has also focused on using this method to evaluate the influence of storage time on coating mechanical properties.

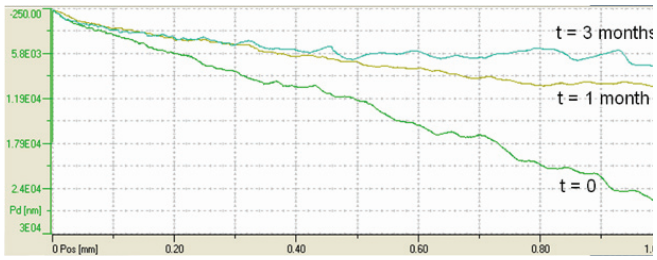
When a stent is manufactured (time = 0) the surface coating will have certain properties. Once the stent has been packaged and placed in storage, the coating may change significantly even over relatively small time periods (months). The scratch test can be used to monitor the changes in the coating by repeating the same test on the same coating at different time intervals.

The example (above right) shows 3 scratches made with identical conditions on the same coating at 3 time intervals (time = 0, 1 month and 3 months). Just optical observation of these scratches is already rather revealing: one can see that the level of damage in each case is progressively worse as time elapses. After 3 months of storage, the coating is delaminating at approximately 50% loading, whereas at time of manufacture the coating shows little delamination.



Scratch tests on a drug-eluting stent coating after 0, 1 and 3 month intervals.

The acquired data, particularly the penetration depth, shows significant differences as shown in the example below. The overall trend is that the penetration depth is decreasing for the same load range, over the 3 time intervals. This would suggest that the coating is softest at time of manufacture, after which it progressively hardens with time.



Scratch test penetration depth plots after 0, 1 and 3 month intervals.

These changes in mechanical properties are not negligible. If the coating is hardening at such a rapid rate, then it certainly questions the maximum length of time that a stent can be stored on the shelf before deployment in a patient.

Further work is planned to try and correlate the level of hardening to the risk of coating failure and debris being formed during deployment. This should provide manufacturers with a better "lifetime" test which correlates with known parameters.

It can be concluded that the scratch test is a strong contender for replacing the tape-peel test as a quality control tool for drug-eluting coatings on stents. The scratch test method is now standardized to ASTM D7187 and is in use in several major stent manufacturing corporations.

For further information, or to run some samples in the CSM Instruments Laboratory, contact Dr. Nicholas Randall at nra@csm-instruments.com.

Comparative Effectiveness Research

By Phil Triolo, Ph.D., Phil Triolo & Associates LC

The American Recovery and Reinvestment Act of 2009 (ARRA) contains $1.1 billion of funding to be spent on comparative effectiveness research. Comparative effectiveness research (CER) compares treatments and strategies to improve health.

More specifically, ARRA provides:

- $300 million for the Agency for Healthcare Research and Quality
- $400 million for the National Institutes of Health, and
- $400 million for the Office of the Secretary of Health and Human Services

These funds are to support research assessing the comparative effectiveness of health care treatments and strategies, through efforts that:

- Conduct, support, or synthesize research that compares the clinical outcomes, effectiveness, and appropriateness of items, services, and procedures that are used to prevent, diagnose, or treat diseases, disorders, and other health conditions; and/or
- Encourage the development and use of clinical registries, clinical data networks, and other forms of electronic health data that can be used to generate or obtain outcomes data.

This clinical effectiveness information is considered essential for enabling clinicians and patients to decide on the best treatment for their medical condition. http://www.hhs.gov/recovery/programs/cer/.

Background information on CER, including a description of how it is used in other nations to determine whether or not to pay for certain treatments, can be found at http://www.randcompare.org/options/mechanism/comparative_effectiveness.

Although methods used to conduct CER are not entirely new, the federal initiative will support research that is both more comprehensive and more relevant to real-world clinical decisions than the more traditional clinical research that has been typically funded. The top 100 treatment areas targeted for CER have been identified by the Institute of Medicine (See http://www.iom.edu/Object.File/Master/71/032/Stand%20Alone%20List%20of%20100%20CER%20Priorities%20-%20for%20web.pdf.) Priorities include funding of several areas that are of interest to the surfaces community. One of the top 25 (first quartile priorities), efforts is "to compare the effectiveness of strategies (e.g., bio-patches, reducing central line entry, chlorhexidine for all line entries, antibiotic impregnated catheters, treating all line entries via a sterile field) for reducing health care associated infections (HAI), including catheter-associated bloodstream infection, ventilator associated pneumonia, and surgical site infections, in children and adults."

The NIH also recently solicited proposals for:

- Clinical Research to Reduce the Risk of Antimicrobial Resistance (05-AI-103)
- Comparative Effectiveness of Medical Implants (05-EB-105)

(See http://www.iom.edu/Object.File/Master/71/032/Stand%20Alone%20List%20of%20100%20CER%20Priorities%20-%20for%20web.pdf.) So, there are opportunities to obtain funding to improve or evaluate the clinical effectiveness of different coatings and surface modification techniques using some of the recently allocated funding.

The CER initiative is controversial, and it is not clear whether or not the efforts will result in reduced healthcare costs. A RAND report http://www.rand.org/news/press/2009/09/08/ opines that "while there are benefits to having better information for doctors and patients about what works best in treating different health problems, it is uncertain that the research will lead to reductions in spending and waste or improvements in patient health.

"Under some circumstances comparative effectiveness research might reduce spending for certain diseases, but there is no clear evidence that a large new undertaking in this area would result in overall savings to the U.S. health care system…"

The RAND report points out that ARRA specifically prohibits using the results of federally funded comparative effectiveness research to guide payment policy. Consequently, the strong incentives necessary to drive changes in medical practices to reduce spending are not in place, and, without these, reductions in healthcare costs are unlikely. RAND researchers further conclude that at least in the near term, any reduction

in spending created from comparative effectiveness research would be offset by the up-front costs associated with generating, coordinating and disseminating the research findings. Visit www.randcompare.org for the RAND Corporation's analysis of the different proposals for changes in U.S. health care policies, including CER.

A recent article in the New England Journal of Medicine (Vol. 360:1925-1927 May 7, 2009) by Alan Garber and Sean Tunis discusses the potential effects of CER on personalized medicine. The authors point out that in CER, the effects of treatments on groups of patients are analyzed to compare the effectiveness of alternative medical strategies, and that "personalized medicine" is an approach to healthcare that is based on individuals rather than groups. However, the authors suggest that "far from impeding personalized medicine, CER offers a way to hasten the discovery of the best approaches to personalization, providing more and better information with which to craft a management strategy for each individual patient."

In short, there are many good reasons for conducting research to help optimize treatment options for patients with specific disease states, and opportunities exist to both evaluate current treatment modalities and practices as well as to improve treatments where the use of coatings and other surface modifying strategies could be employed.

What is unclear is how the information that is gained from CER will affect medical device manufacturers. Where the use of drugs is shown to achieve clinical results superior to those achieved using devices, there could be a change in care away from device use. But what if the drugs are significantly more expensive and their long-term side effects relatively unknown? Will the brand names of devices used in CER be identified? As significant differences in outcomes can be achieved using devices of the same generic type yet manufactured by different manufacturers, perhaps using different materials or with slightly different functional features or characteristics—how broadly can CER results be applied? Although the federal government may not use the information from CER to make reimbursement decisions, may insurance companies? Many more questions can be conjured, and depending on how they are answered, the quality of healthcare could improve or degrade.

Ultimately, additional information on the relative effectiveness of treatments can only help patients and physicians. How the information is used will affect medical device manufacturers, hopefully helping to justify the use of technology when it is shown to be clinical superior to other available medical interventions.

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provide little predictive relevance for validating human in vivo responses to implanted devices," will close the day.

The Cell and Protein Interactions with Biomaterials Podium/Poster session will kick off Wednesday morning's activities. Participants will first give a 5-minute oral presentation, then present further details of their work in an intimate poster session in which attendees engage presenters with more in-depth questions. Additional Wednesday sessions include Stability of Biomaterials in Clinical Applications and Coming Innovations in Medical Devices. The Student Poster Award and Excellence in Surface Science Award will be presented over lunch, with award winner Dr. Gabor Somorjai discussing the recent advancements in the field of surface chemistry.

The Industrial/Academic Roundtable will conclude the Symposium. Stick around to find out what the Surfaces in Biomaterials Foundation is doing to develop and promote Academic and Industrial partnerships.

All in all, this will be an enlightening three days where leading scientists from industry can meet and greet their colleagues from academia and medicine! We look forward to seeing you in San Mateo, California, October 26-28, 2009!

Call for Nominations To Board of Directors, Committees

Is there a leader in your midst who could help the Surfaces in Biomaterials Foundation move forward in its mission to explore creative solutions to technical challenges at the BioInterface? Can YOU help the foundation further its mission?

The Surfaces in Biomaterials Foundation is now accepting nominations for the Board of Directors. The positions of President-Elect, Vice President, Treasurer and Secretary will be filled at the annual meeting at the BioInterface Conference in October. Vice President, Treasurer and Secretary are one-year terms. The president-elect effectively is a three-year term. as that person becomes president and then past-president in succeeding years.

Click here to see the job description per the Foundation's by-laws.

**An officer must be from a supporting member of the foundation that is in good standing. To view a list of supporting members please visit www.surfaces.org.*

The Surfaces Foundation also is recruiting for members to be active on the Membership Committee and for an editor and writers to SurFACTS, the newsletter of the Foundation.

If you or someone you know can help move the Surfaces Foundation forward as a member of the board of directors, or through service on a committee, please forward nominations to Andy Shelp, SIBF Executive Director, at AndyS@surfaces.org.

Deadline for nominations is October 14, 2009.

BioInterface 2009

New Board Experts for DSM Biomedical

From Medical Device Link

DSM Biomedical, a global leader in biomedical materials, announced the addition of three experts to its Scientific Advisory Board. Established in July 2007, the Board supports DSM Biomedical's research and development strategy by advising on its scientific and technological quality, validity of hypotheses, and clinical relevance. The newest members of the Biomedical Scientific Advisory Board include Samuel Stupp, James Kirkpatrick and Wouter Dhert, all leaders in the field of biomedical materials science. They join existing members Tony Mikos, Ivo Buschmann, and Patrick Cahalan. Samuel Stupp is a Board of Trustees Professor of Materials Science, Chemistry, and Medicine at Northwestern University (Chicago, USA), where he also serves as the Director for the Institute for BioNanotechnology in Medicine. This year he received an honorary doctorate from Eindhoven University for his pioneering work in complex molecular systems and their biomedical applications, and is the recipient of numerous awards and honors, including the Materials Research Society Medal Award and the American Chemical Society Award in Polymer Chemistry.

James Kirkpatrick is an expert in pathology and in vitro methods for biomaterial research and has authored nearly 350 articles in peer-reviewed journals on the topic. He has taught at universities across the globe and is currently Professor of Pathology and Chairman of the Institute of Pathology at Johannes Gutenberg University (Mainz, Germany). Dr. Kirkpatrick also serves as an external reviewer for several research councils and programs throughout Europe, as well as scientific journals, and was President of the European Society for Biomaterials, 2002-2007.

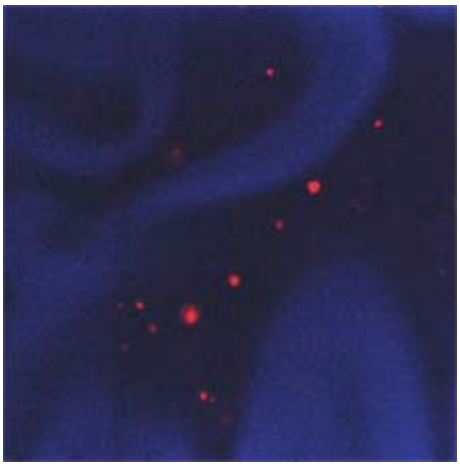
Wouter Dhert joins Dr. Stupp and Dr. Kirkpatrick, and brings almost 20 years of experience in translational orthopaedic research on biomaterials and tissue regeneration to DSM's Biomedical Scientific Advisory Board. He is Professor of Translational Musculoskeletal Research, Director of Orthopaedic Research at the University Medical Center Utrecht, and part-time professor in Tissue Repair at the Faculty of Veterinary Medicine at Utrecht University (The Netherlands).

Molecular Condom Blocks HIV

By Emily Singer, MIT Technology Review

A polymer gel that blocks viral particles could one day provide a way for women to protect themselves against HIV infection. The gel reacts with semen to form a tight mesh that blocks the movement of virus particles. The material, which is still in early development, could eventually be combined with antiviral gels currently in clinical trials to provide a dual defense against HIV.

Scientists have been working on microbicide gels for HIV for more than a decade. This type of prophylactic, which women could use without relying on their partners, is of particular interest in areas such as Sub-Saharan Africa, where HIV-infection rates are high and use of condoms is relatively low. But development has been slow—a number of products have failed clinical trials.



Viral blockade: A gel, shown here stained blue, forms tendril structures at pH 7.4. The red dots are 100 nanometer particles, about the same size as HIV, which are trapped in these structures. Credit: Kristopher Langheinrich

Most of the topical microbicides being tested for HIV prevention contain antiviral drugs designed to block replication of the virus once it infects a cell. The new gel, which is being developed by Patrick Kiser and colleagues at the University of Utah, in Salt Lake City, acts at the first stage of infection—when the virus moves from semen to the surface of vaginal tissue.

"This research stresses improvement not in the drugs but in the vehicle used to deliver the drugs," says Ian McGowan, a physician and scientist at the University of Pittsburgh Medical Center who was not involved in the research. "That's a relatively neglected area, and the technology is quite exciting."

Kiser and colleagues developed a gel from two polymers--PBA (phenylboronic acid) and SHA (salicylhydroxamic acid)—that can be spread around the vagina prior to intercourse. With the introduction of semen, the vagina reaches a higher pH level, causing molecules in the gel to bind together, creating a finer mesh that prevents HIV particles from passing through. "The idea is to use the trigger of semen to activate the gel and create a more effective barrier," says Kiser.

In research published this week in the Journal of Advanced Functional Materials, researchers showed in lab tests that the gel can block the movement of HIV particles, and that it appears safe when tested in human vaginal cells. The next step is to test the gel on human tissue collected from women who have had hysterectomies to show that it can prevent infection.

"It's a very interesting approach to take advantage of normal vaginal physiology and alter it to inhibit HIV transmission," says Craig Hoesley, an infectious-disease specialist at the University of Alabama, in Birmingham. But this might also prove troublesome. McGowan points out that the change in pH after intercourse can be variable, so researchers need to show that the gel can react under different chemical conditions.

Kiser and his team ultimately want to combine this type of gel with an antiviral drug in order to block both the movement of HIV and its replication. But extensive testing, including safety testing, remains to be done. For example, for use in Sub-Saharan Africa, the gel must be stable at different temperatures. "We will also need to see if it is compatible with antiviral drugs," says McGowan.

FDA Medical Device, Radiological Health Regulator Resigns

From Diagnostic and Invasive Cardiology

The Food and Drug Administration's (FDA) top medical-device regulator, Daniel Schultz, M.D., director of the FDA Center for Devices and Radiological Health, announced his resignation in August.

While Dr. Schultz said it was a mutual agreement with FDA Commissioner Margaret Hamburg, the decision followed internal dissent over device-approval decisions that the regulator's critics said were too friendly to industry.

Dr. Schultz has worked at the FDA's Center for Devices and Radiological Health for 15 years and led it for the past five years. However, concerns over Dr. Schultz's decisions surfaced two years ago when Sen. Chuck Grassley (R-Iowa) held hearings on Dr. Schultz's approval of a nerve stimulation device to treat depression, irrespective of objections from multiple FDA doctors. The senator again opened an investigation into a knee-surgery device made by ReGen Biologics Inc., also approved by Dr. Schultz despite numerous objections from FDA scientists and reviewers.

A year ago, the House Energy and Commerce Committee launched an investigation into allegations by at least eight FDA scientists that agency managers coerced those in the medical device division into approving products despite serious safety and effectiveness concerns.

The investigation was prompted by a letter released publicly from "a large group of scientists and physicians" within the FDA's Center for Devices and Radiological Health (CDRH), dated Oct. 14, 2008, said Committee Chair John Dingell (D-Mich.) and Oversight and Investigations Subcommittee Chair Bart Stupak (D-Mich.) According to the statement, the letter describes CDRH managers that have "corrupted and interfered with the scientific review of medical devices."

The statement went on to say that the committee has been "provided with compelling evidence to support the charges that senior managers within CDRH 'ordered, intimidated and coerced FDA experts to modify their scientific reviews, conclusions and recommendations in violation of the law.'"

The scientists claim that they were threatened with removal or negative performance reviews if they did not modify their scientific data to obscure unscientific clinical and technical data submitted by device companies and legal violations, including a lack of informed consent from study participants.

Synthes and Kensey Nash Announce Strategic Agreement for Extracellular Matrix Products

From PRNewswire

Synthes, Inc. a leading global medical device company in the orthopaedic trauma, spine, and cranio-maxillofacial markets, and Kensey Nash Corporation, a leading developer and manufacturer of innovative regenerative medicine products, have announced a strategic agreement for products developed from Kensey Nash's unique extracellular matrix (ECM) technology.

Kensey Nash Corporation has developed a proprietary technology platform for processing porcine-derived extracellular matrix tissues. Under the agreement, Kensey Nash will develop and manufacture porcine dermis-based ECM products, which Synthes will market and distribute for select reconstructive surgical applications. Specific terms of the agreement were not disclosed.

The ECM products have the benefit of rapid revascularization and are therefore quickly repopulated with cells from the host tissue, ultimately converting into functional living tissue. They are to be used in a wide range of soft tissue reinforcement procedures. Among the many possible applications being examined are abdominal repairs as well as head, neck and chest plastic reconstructions.

"We are pleased to broaden our product offering with this important biomaterials technology. We look forward to our partnership with Kensey Nash in our efforts to provide our customers with innovative and effective solutions for the benefit of their patients," commented Michel Orsinger, President and CEO of Synthes.

"This partnership represents an important milestone in our plans to build upon Kensey Nash's leadership position as a developer of innovative regenerative medicine products," commented Joseph W. Kaufmann, President and CEO of Kensey Nash. "Synthes is well respected as a global leader in the medical device industry and we look forward to building a valuable franchise with a series of ECM products," he concluded.

U.S. FDA Questions Studies of Q-Med's Durolane

From Thomson Reuters

U.S. Food and Drug Administration staff have flagged concerns over company data for Q-Med AB's Durolane injection for arthritis knee pain after two studies found no statistical benefit, according to documents released ahead of a recent advisory panel meeting to review the product.

The FDA said the methods for conducting two of the company's three studies—both done outside of the United States—were not first reviewed by the agency.

It also said that one of those studies, as well as another one conducted in the United States, "showed no observable or statistical difference" between patients who received Durolane and those who got a saline control injection.

Q-Med is seeking U.S. approval of Durolane to treat patients with arthritic knee pain who have not seen enough relief through other methods such as acetaminophen and other painkilling drugs.

The product is a transparent gel that contains high levels of hyaluronic acid that aims to cushion and lubricate the joint. Distributed and marketed by Smith & Nephew Inc, it is already approved in parts of Europe as well as in Canada and Indonesia, according to Q-Med.

Shares of Q-Med rose 2.8 percent on the Stockholm exchange, while Smith & Nephew was off 2 percent in morning New York Stock Exchange trading and down less than 1 percent in London.

The FDA planned to ask its panel of outside experts to weigh the company's data before recommending whether the agency should approve the product. The FDA usually follows the advice of its panels, but not always.

The Swedish device maker conducted three studies of Durolane. The first two—one looking at 346 patients over six months and another examining 218 over six weeks—showed no statistically significant pain reductions among patients given the company's product than those getting an injection of saline, the FDA staff said.

Q-Med then conducted a third study of 433 patients over 12 weeks to show whether Durolane worked as well as an injection of methylprednisolone, a steroid hormone anti-inflammatory product sold under a variety of brand names by several manufacturers, including Pfizer Inc.

But the way the company identified and tested patients in that study "can ... make it difficult to interpret the results of such a comparison," FDA staff wrote.

In separate documents also released by the FDA, Q-Med officials said their three studies showed Durolane was safe and effective in treating arthritis knee pain.

They also found Durolane as safe as both saline and methylprednisolone except for a higher rate of joint pain, or arthralgia, the company added.

Two-Year SYNTAX Data Show Comparable Safety Outcomes for Complex Patients Treated With TAXUS® EXPRESS® Stents and Bypass Surgery

From PRNewswire

Boston Scientific Corporation has announced two-year data from its SYNTAX clinical trial comparing percutaneous coronary intervention (PCI) using the TAXUS® Express® Paclitaxel-Eluting Coronary Stent System to coronary artery bypass graft (CABG) surgery. The overall results demonstrated no statistically significant difference between PCI and CABG in the composite safety endpoint (all-cause death, stroke and myocardial infarction [MI]). The Company made the announcement at the annual European Society of Cardiology (ESC) Congress in Barcelona.

"These results reinforce the one-year SYNTAX data and show impressive outcomes for PCI in patients with complex coronary anatomy, the majority of whom are normally treated with CABG surgery," said Keith D. Dawkins, M.D., Associate Chief Medical Officer of Boston Scientific. "Today's findings build on our prior data and provide additional support for PCI as a viable treatment option for many of these challenging patients."

The patients in the SYNTAX trial—all of whom have left main and/or three-vessel coronary disease—are a unique study group in the PCI field. In the SYNTAX trial, mean stent use was 4.6 stents/patient, with one patient having 14 stents implanted. By contrast, the average number of stents implanted in a PCI patient in everyday practice is 1.5. In addition, the study included 33 percent of patients with >100 mm stented length, 71 percent with bi/trifurcations, 27 percent with chronic total occlusions and 39 percent with left main disease.

The results showed comparable safety profiles for the two treatment groups at two years, with a combined rate of all-cause death, stroke and MI of 10.8 percent for PCI and 9.6 percent for CABG (p=0.44). The rate of stroke was 1.4 percent for PCI as compared to 2.8 percent for CABG (p=0.03), while MI was 5.9 percent for PCI and 3.3 percent for CABG (p=0.01). The rate of all-cause death was 6.2 percent for PCI and 4.9 percent for CABG (p=0.24).

Overall MACCE (Major Adverse Cardiovascular or Cerebrovascular Event rate, including all-cause death, stroke, MI and repeat revascularization) was significantly higher for PCI (23.3 percent as compared to 16.4 percent for CABG, p=0.0002), driven largely by the anticipated higher rate of revascularization in the PCI group (17.4 percent as compared to 8.6 percent for CABG, p<0.0001), with the difference narrowing in the second year of follow-up. Most patients requiring repeat revascularization in the PCI group were successfully treated with another PCI.

The trial results were also analyzed based on the SYNTAX Score, which demonstrated no statistically significant difference in MACCE for patients in the lower two terciles—those with low lesion complexity (19.4 percent for PCI and 17.4 percent for CABG, p=0.63) and moderate lesion complexity (22.8 percent for PCI and 16.4 percent for CABG, p=0.06). For patients in the upper tercile—those with the most complex disease—there was a significant increase in MACCE for PCI patients as compared to CABG (28.2 percent as compared to 15.4 percent, p=0.001).

The SYNTAX Score is a novel angiographic tool used to measure the complexity of coronary artery disease based on nine anatomic criteria, including lesion frequency, complexity and location. Higher SYNTAX Scores indicate patients with more complex disease and increased treatment challenges. A SYNTAX Score website, www.syntaxscore.com, was launched in May and allows cardiologists and cardiac surgeons to characterize a patient's anatomical complexity, which can be used in combination with a physician's clinical judgment to help determine the best revascularization option.

The SYNTAX Score and SYNTAX Score website were developed under the direction of the SYNTAX trial steering committee, chaired by Patrick Serruys, M.D., Ph.D., and F.W. Mohr, M.D., Ph.D., and were made possible by support from Boston Scientific and Cardialysis BV.

The safety and effectiveness of the TAXUS Express Stent System has not been established in patients with left main or three-vessel disease.

Boston Scientific is a worldwide developer, manufacturer and marketer of medical devices whose products are used in a broad range of interventional medical specialties. For more information, please visit: www.bostonscientific.com.

CryoLife Announces First Clinical Use of BioFoam®

From PRNewswire

CryoLife, Inc., an implantable biological medical device and cardiovascular tissue processing company, has announced the first clinical implant of its BioFoam® Surgical Matrix, which received CE mark approval in August 2009. BioFoam was used in a liver resection procedure following tumor removal as a supplemental measure to promote hemostasis (a complex process that stops bleeding) by sealing vessels.

"Despite advances in surgical technique, bleeding complications continue to be a problem in liver resection surgery and can be life-threatening," said Professor Brian Davidson, MD, FRCS, Professor of Surgery, Department of Surgery, Royal Free Hospital in London, who performed the procedure on September 9. "We are very hopeful that BioFoam will reduce the time required to achieve hemostasis during liver resection surgery and will reduce the number of complications following surgery."

CryoLife is conducting a controlled clinical launch of BioFoam at up to six centers in the United Kingdom, Germany, France and Italy. The objectives of this 45-patient controlled launch, in which BioFoam is used as a surgical hemostatic adjunct in the open repair of liver parenchyma following liver resection and/or liver transplant surgery, are to (1) collect additional clinical data supporting the safety and performance of BioFoam and (2) further refine the optimal application technique.

"The clinical availability of BioFoam is another milestone in the company's corporate objective of providing world-class surgical options for the control of intraoperative bleeding," said Steven G. Anderson, CryoLife president and chief executive officer. "We believe the unique adherence and expansion characteristics of this product make it useful for organ sealing and other future surgical applications. It is a wonderful complement to our existing hemostasis products, BioGlue® and HemoStase™."

In December 2008, CryoLife received conditional approval from the FDA to conduct the feasibility phase of the company's BioFoam IDE submission for liver parenchymal sealing. The feasibility phase will enroll a total of 20 subjects at two investigational sites in the U.S. Before beginning this phase, the Company must receive final approval of the study protocol and related documents from the FDA and an additional approval of the study from the U.S. Department of Defense. CryoLife is in the final stages of this approval process and expects to start enrollment in Q4 2009.

During the European Association of Cardio-Thoracic Surgery (EACTS) annual meeting in Vienna, Austria, Oct. 17-21, CryoLife will be soliciting input from the attendees on potential future clinical applications for the use of BioFoam in cardiothoracic surgery.

Meeting/Conference/Trade Show Calendar

Meeting/Conference/Trade Show	Dates	Place	Web Address
Orthopedic Design & Technology (2nd annual)	Oct 6-8	Fort Wayne, IN	odtexpo.com/
American Neurological Assoc (ANA)	Oct 11-14	Baltimore, MD	aneuroa.org/index.php?src=gendocs&ref=2008SLC__Home
VIVA (Vascular Interventional Advances)	Oct 19-23	Las Vegas, NV	vivapvd.com/index.cfm
Medical Device & Manufacturing Minneapolis	Oct 21-22	Minneapolis, MN	devicelink.com/expo/minn08/
BioInterface 2009	**Oct 26-28**	**San Mateo, CA**	**surfaces.org**
American Association of Pharmaceutical Scientists (AAPS)	Nov 8-12	Los Angeles, CA	aapspharmaceutica.com/meetings/futuremeetings/index.asp
American Heart Association (AHA)	Nov 14-18	Orlando, FL	scientificsessions.americanheart.org/portal/scientificsessions/ss/seeyounextyear2009
Medica	Nov 18-21	Dusseldorf, Germany	medica.de
BIOMEDevice 2009	Dec 9-10	San Jose, CA	devicelink.com/expo/biomed08/
Third International Conference on Mechanics of Biomaterials & Tissues	Dec 13-17	Clearwater Beach, FL	www.icmobt.elsevier.com/
International Symposium on Surface Science Aspects of Pharmaceutical Science, Pharmacology, Cosmetics and Bio-Technology	Apr 19-21, 2010	Danbury, CT	mstconf.com/SurfSciPharm.htm

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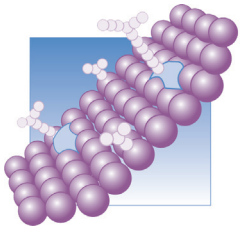

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