2015
BioInterface Workshop & Symposium
Celebrating 25 Years of Scientific Excellence

September 21–23, 2015 | Scottsdale, Arizona USA
Fairmont Scottsdale Princess
From the President

Welcome Surface Science Professionals, Colleagues and Friends,

On behalf of the Surfaces in Biomaterials Foundation (SIBF), I welcome you to BioInterface 2015. The BioInterface Symposium has been presented annually by the Foundation since 1991. This year we are proud to celebrate the 25th Symposium, which is matched by an exciting and forward-looking technical program. The Foundation was founded based on the premise that the interface between the body and a medical device is critical to the device’s performance. From another perspective, the foundation also facilitated the interface between various industries and with academia to address challenges with bringing medical devices through to the clinic. As was the case in previous Symposia, this year’s technical program provides a forum where a diverse group of scientists can openly discuss and debate recent innovations and research topics. The BioInterface Symposium has a strong applied focus and brings together engineers, scientists, clinicians, and regulatory experts from all aspects of the biomedical community. Throughout the years, this conference has been characterized by many in our industry and academia alike as a preeminent technical symposium that allows easy connection between attendees; I am confident that this year’s technical program will more than live up to this description.

I encourage you to take this opportunity to engage and interact with your fellow attendees who represent the leading corporations, start-ups and educational institutions that research and produce the innovative medical devices and products that help people to live longer, healthier and more productive lives.

Thank you for attending this year’s meeting. We hope your experience at the 2015 BioInterface Symposium stimulates your thinking and provides you with information and solutions that will be beneficial in your ensuing scientific endeavors.

Sincerely,
Aylvin A. Dias Ph.D, M.Sc., President, Surfaces in Biomaterials Foundation

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BioInterface Workshop
Hemocompatibility Technologies, Models, and Testing
Do’s and Don’ts in Hemocompatibility Testing and Current Developments Towards Better Biocompatible Devices

Speaker: Hans Peter Wendel, University Hospital Tuebingen

University Hospital Tuebingen, Dept. of Thoracic and Cardiovascular Surgery, Calwerstr. 7/1, 72076 Tuebingen, Germany

In order to evaluate the hemocompatibility of medical devices, various in vitro models with fresh human whole blood are used. In a closed system the influence of artificial surfaces on corpuscular blood components as well as the activation or inhibition of different haemostatic parameters can be displayed effectively without the autogenic regulation of the patient attempting to equalize these effects. Therefore, before clinical application, it is imperative to test the hemocompatibility of medical devices under standardized conditions. This standardization can be performed by in vitro models for dynamic hemocompatibility testing of stents, vascular prostheses, catheters, tubing etc., according to ISO 10993-4. This talk discusses the important settings of models, blood quality, and parameters chosen for quantification of the hemocompatibility rank. Results of comparative animal experiments with identical devices are shown to classify the different test systems. Additionally, the need of new surface modifications is highlighted to show new developments towards better biocompatible devices.

Biography

Academic education and professional experience:
• 1981 - 1987 Undergraduate studies in Biology / Study of Zoology, Pharmacology, Plant Physiology and Paleontology at the University of Tuebingen, Germany.
• 1987 - 1989 Diploma-thesis in the lab of Prof. Dr. W. Engels at Dept. of Zoology / Developmental Physiology in Tuebingen
• 1990 - 1994 PhD-thesis in the research lab of Prof. Dr. H.-E. Hoffmeister at the Dept. of Thoracic, Heart and Vascular Surgery at the University of Tuebingen
• 1995 - 1996 Junior-group leader in the research lab of Prof. Dr. G. Ziemer at the Dept. of Thoracic, Heart and Vascular Surgery at the University of Tuebingen
• 1997 - 2003 Group leader and head of the research lab at the Dept. of Thoracic, Heart and Vascular Surgery at the University of Tuebingen
• 2003 - 2009 Akademischer Rat / Asst. Professor, head of research, Dept. of Thoracic, Heart and Vascular Surgery at the University of Tuebingen
• 2008 Habilitation in “Experimental Cardiac Surgery”
• Since 2008 Head of GLP test laboratory for blood contacting devices according to EN DIN ISO 10993-4 at the University of Tuebingen
• Since 2009 Akademischer Oberrat / research director, Dept. of Thoracic, Heart and Vascular Surgery at the University of Tuebingen
• Since 2011 Professor Eberhard-Karls-University Tuebingen
• Since 2013 Director Steinbeis transfer center for blood contacting medical devices

Research focus
• Haemostaseology of extracorporeal circulation
• Hemocompatibility / Biomaterials in blood contact
• Biologization of medical devices / in vivo Tissue Engineering
• DNA/RNA Technologies: Aptamers, RNAi, mRNA

Publications: >150 PubMed listed original papers
Patents: > 12 patent families
ISO10993-4 Biological Evaluation of Medical Devices: Selection of Tests for Interaction with Blood. Anticipated Changes and Updates on Working Group Round Robin Study Activities

Speaker: Michael F. Wolf, Medtronic Inc.

Medtronic Inc., Core Technologies Group, Minneapolis, Minnesota

The International Standard Organization ISO10993-4 document identifies general requirements and considerations for evaluating interactions of potential concern between medical devices and blood. It describes (1) a classification of blood-contacting medical devices based upon intended use and duration of contact as defined in ISO 10993-1, (2) fundamental principles and scientific bases behind various methods of evaluating interactions of devices with blood, and (3) a structured selection of suggested tests based upon intended use and contact duration. In short, this standard is a guide for industry and regulatory agencies to assess the apparent blood compatibility of candidate devices and materials intended for human blood contact applications.

Several sources form the foundation of the ISO10993-4 standard. However, since its inception in 2002, the document has received only minor revision. Over the past several years a number of revised drafts involving review of hundreds of comments have culminated in a new Part 4 standard submitted for final review in 2015. Given the breadth and complexity of the topic, this task has not been easy. The general focus areas and some details of changes in the standard will be reviewed.

In addition to the work on improving the Part 4 standard, members of the Part 4 working group from both industry and regulatory agencies have initiated a series of multi-lab round-robin studies that are examining important tests/test areas within the standard. These test areas include: (1) hemolysis testing and the consistency of test results between various test methods, (2) in vitro alternatives for testing devices/materials for thrombogenicity, and (3) improved complement testing through identification and use of more meaningful controls and refined methods. The goal of these activities is improvement in the scientific rigor of the standard and enhancing its ability to identify safety and areas of risk involving medical devices that contact blood. An overview and update on these supplemental working group activities will be provided.

Biography
Michael F. Wolf is a Senior Principal Scientist and Technical Fellow at Medtronic Inc. Mr. Wolf received B.S. degrees in Biochemistry and Chemical Engineering from the University of Wisconsin-Madison and an M.S. degree in Biomedical Engineering from the University of Minnesota. At the UWM and UMN his studies focused on biomaterials science, pathobiology, and endothelial cell seeding. Now approaching his 27th year at Medtronic, Mr. Wolf has worked heavily in the area of characterizing and improving how blood- and vascular tissue-contacting devices/materials interact with the body, using both in vitro and in vivo models. This work has covered device areas such as CPB equipment, mechanical heart valves, vascular grafts, stents, and cardiac pacing and hemodynamic sensors. For more than a decade, Mr. Wolf has also been active in development of standards for medical devices. He has served as subject matter expert, chairperson, and convenor (presently) to the ISO TC/194 working group focused on ISO 10993 Biological evaluation of medical devices - Part 4: selection of tests for interactions with blood. Mr. Wolf is an inventor on eight patents and author or co-author on more than 20 peer-reviewed publications and four book chapters.

Blood Compatibility: Controlling Protein Interactions at the Blood-Material Interface

Speaker: John L. Brash, McMaster University

This presentation will touch on several topics related to blood compatibility and blood-material interactions. These include plasma protein adsorption, protein resistant surfaces, anticoagulant surfaces, and fibrinolytic surfaces. Much of our work in recent years has been focused on two important aspects which, we believe, have been largely ignored by the research community: (1) the role of plasma lipoproteins in blood-material interactions, and (2) fibrinolysis, as opposed to anti-thrombosis, as an approach to thromboresistant surfaces. With respect to lipoproteins we have shown that the main protein component of HDL, apolipoprotein A-I, is ubiquitous and abundant on blood contacting surfaces, suggesting that HDL itself may be ubiquitous and abundant. An interesting recent observation is that while a PEO-modified surface was found to be strongly resistant to the adsorption of apolipoproteins (apo A-I, apo A-II, apo B), it was less resistant to the "whole" lipoprotein particles (HDL, LDL and VLDL). Our work on fibrinolytic surfaces has focused on the "capture" of endogenous plasminogen and t-PA, the key players in clot lysis, by the surface in contact with blood. Some newer ideas on the possibility of triggered and controlled release of t-PA from the surface are also under consideration.


Biography

John Brash is a Distinguished University Professor of McMaster University. His research interests are in biomaterials and biocompatibility with emphasis on materials for use in blood contact. The behaviour of proteins at interfaces is an important underlying theme of his work. He is the author of over 300 publications, including books, book chapters, and papers in refereed journals. He is a Fellow of the Royal Society of Canada, and recipient of the Clemson Award for Basic Research (1994) and the Founders Award (2009) of the US Society for Biomaterials.
The assessment of device thrombosis should consider the multiple modes and components that govern this process. Blood flow is an important parameter in this assessment and in-vitro models that incorporate this factor will be discussed. Such models generally evaluate the integrated thrombotic process of protein adsorption, platelet adhesion and aggregation, and fibrin consolidation. These underlying processes will be discussed to develop the foundation of device thrombosis assessment using in-vitro blood flow models. This system represents a well-controlled and economical setting for the study of device thrombosis. The ability to compare multiple devices under the same conditions is a valuable feature of this system. In its most generic form, the in-vitro flow model incorporates anticoagulated blood flowing through a test chamber (e.g. polymer tubing) in which the device to be evaluated is deployed. The thrombus that develops on the device is generally measured after blood has circulated for a desired duration. Blood from the same subject can be divided into as many reservoirs as there are devices to facilitate simultaneous comparisons (e.g. coated versus uncoated devices). Variations of this basic construct of the model may include different species/sources of blood, methods of anticoagulation, test chamber geometries, hemodynamics (flow rates, flow inducing mechanisms, etc.), system configurations, experiment duration, and methods to assess thrombosis. These features of the model will be illustrated using several device types as examples, and the merits and limitations of such models will be discussed. Comparisons of in-vitro and in-vivo results as applied to devices with surface modifications will be presented, and the overall role of in-vitro blood flow models in the general development of devices and surface modification technologies will be identified.

**Biography**

Vice President at Thrombodyne, Inc. Faculty at University of Utah and Brigham Young University. Over 20 years of experience in studying device thrombosis and its mitigation by surface treatments, pharmacology, and mechanical design improvements. Developed unique methods and experimental models (in-vitro and ex-vivo) to assess device thrombosis in pre-clinical studies that have been widely used by the medical device industry, reviewed by academia, and recognized by the US FDA. Published over 50 scientific articles, abstracts, and patents in the area of platelets and thrombosis, and delivered several invited lectures on device thrombosis.
Comprehensive Approach for Blood Compatibility of Medical Devices and Biomaterials

Speaker: Patrick Cahalan, Ension, Inc.

Abstract
To date, blood compatibility testing of biomaterials and medical devices has not led to a consensus on what materials are non-thrombogenic — nor has it advanced understanding of what and how variables and responses can be measured in vitro to begin to predict in vivo performance. While ISO 10993-4 identifies five categories of responses that should be considered (thrombosis, coagulation, platelets, leukocyte activation, and complement), the scientific and regulatory communities continue to focus on coagulation and platelets. The other ISO categories dealing with inflammation are typically dealt with early and separately as part of biomaterial development. This approach all but guarantees missing interactions of coagulation and inflammation that are critical for predicting in vivo performance. Current testing methodologies also fail to evaluate the categorical responses under physiological limits of the key Virchow variables of blood flow, condition of the blood (e.g., coagulopathies), and the influence of the blood contacting surface. This uncertainty and the current cost of comprehensive testing stifles progress in developing new materials or surface coatings. If proven successful, ETS will enable designed experiments capable of generating quantitative analysis of variance and identify conditions for optimal performance in all five ISO categories from a single perfusion experiment.

Preliminary Data
Enston has developed the Ension Bioactive Surface (EBS) with a series of increasing bioactivities from low to essentially equivalent to intact aortic glycocalyx to minimize inherent blood activation within the system. We have published on critical interactions between the variables of blood condition (levels of anticoagulant) and bioactivity of the blood contacting surface (ATIII adsorption and FIIa deactivation), and we have demonstrated statistically significant categorical responses that identify known clinical mediators not revealed in current testing protocols.

Current Efforts
With the demonstration of statistical and quantitative correlation of EBS bioactivity to all five ISO test categories, the ETS system can now be used for the design of experiments (DOE) and analysis of variance (ANOVA) to quantitatively characterize the interactions of all three Virchow variables. This will demonstrate a heretofore unattainable and reproducible rank ordering of blood compatible materials as well as identifying how categorical responses vary within meaningful ranges of flow, blood condition, and surface properties.

Biography
My expertise in biocompatibility was initially formed as a biomedical engineer at Medtronic, starting in 1978 with the FDA GMP Regulation of 1978 that determined testing of medical devices based on location and duration of use. Since that time, I have tested numerous materials and devices through internal screening as well as GLP test facilities such as NAMSA, Toxikon, and TUV. My specific interest and expertise in blood compatibility began in 1982 with Medtronic qualifying the Carmeda Biologically Active Surface (CBAS) for oxygenators for CPB, and a significant program to expand application of CBAS to other blood contacting medical devices. This effort was followed by a comprehensive effort to identify physical and chemical methods to modify all biomaterials in order to attach bio-interactive surfaces with enhanced and stable blood and tissue compatibility. This also required development of expertise in surface analysis and biological evaluation. The combination of this expertise was instrumental in achieving ISO certification for design, surface modification, and manufacturing of medical devices in Europe in 1993. At this time we had internal GLP human blood testing capability and were performing numerous ELISA assays as well as flow cytometry on research and commercial blood compatible coatings. We produced comparative data with numerous loops systems to include pulsatile flow with valves as well as microperfusion systems, spinning discs, and ellipsometry to identify first principles in blood materials interactions. In the last three decades, I have worked with international experts and suppliers of blood compatible coatings and compared most of the approaches in human blood.
Hemocompatibility? Where Platelets Predominate, Hydrophobic Surfaces are the Way to Go

Speaker: Buddy D. Ratner, University of Washington

University of Washington, Seattle, Washington

In flow regimes associated with high wall shear rate blood flow (arterial regimes) platelets, in contrast to the intrinsic (fibrinogen) coagulation system, are the key element leading to thrombosis. This talk will advance the hypothesis that in such flow regimes, good blood compatibility will be observed with hydrophobic surfaces. Starting in the 1970s, using a quantitative baboon A-V shunt model, we demonstrated that highly hydrophobic materials (silicones, polyethylene, Teflon) had reduced platelet consumption compared to hydrophilic materials. In a study with this baboon model comparing many polyurethane compositions, those with the highest surface hydrophobic content showed the lowest platelet consumption. When hydrogels were studied with this A-V shunt model, the higher the water content (i.e., the more hydrophilic), the higher the platelet consumption. In contrast, in studies with vascular prostheses treated with a highly hydrophobic plasma-deposited fluoropolymer coating, good graft patency was observed. More recently, we have also been studying adsorbed proteins and their relationship to blood compatibility. Revisiting an old hypothesis, that increased surface-adsorbed albumin will lead to improved blood compatibility, we have updated that hypothesis to also relate albumin affinity to surface retention of albumin (tight binding). In addition, we consider the amount of fibrinogen adsorbed to surfaces (in competition with albumin). Based upon data from Horbett and his group, adsorbed fibrinogen is the most important activator of platelets. Highly hydrophobic materials that have shown low platelet reactivity demonstrate high albumin affinity, low fibrinogen adsorption levels and also tight binding of proteins.

Biography
Buddy D. Ratner is Director of the University of Washington Engineered Biomaterials (UWEB21) Engineering Research Center. He holds the Michael L. and Myrna Darland Endowed Chair in Technology Commercialization and is Professor of Bioengineering and Chemical Engineering, University of Washington. Ratner received his Ph.D. (1972) in polymer chemistry from the Polytechnic Institute of Brooklyn. He has been at the University of Washington since 1972. From 1985 to 1996, he directed the National ESCA and Surface Analysis Center for Biomedical Problems funded by the National Institutes of Health. In 1996, he assumed the directorship of UWEB (now UWEB21).

Ratner has won numerous awards. A partial list includes the Medard W. Welch Award of the American Vacuum Society (2002), Founders Award of the Society for Biomaterials (2004), C. William Hall Award from the Society for Biomaterials (2006), the BMES Pritzker Distinguished Lecturer Award (2008), the Acta Biomaterialia gold medal (2009), the University of Washington Faculty Lecture (2011), the Pierre Galletti Award from the American Institute of Medical and Biological Engineering (2011) and the George Winter Award of the European Society for Biomaterials (2012-2013). He received the 2014 Lifetime Inventor and Innovator Award from the University of Washington.

Ratner has authored over 400 scholarly works and has over 30 issued patents. He is on the advisory board of Biointerphases and serves on the editorial boards of ten other journals. He is the lead editor for Biomaterials Science: An Introduction to Materials in Medicine, a textbook that has sold over 25,000 copies. He has supervised the theses of approximately 80 graduate students.

Buddy Ratner’s interests include biomaterials, tissue engineering, polymers, biocompatibility, drug delivery, surface analysis, self-assembly, nanobiotechnology, RF-plasma thin film deposition, technology commercialization and biomaterials education. He has participated in the launch of eight companies based on technologies from his laboratory, and serves as a consultant for numerous other companies.
Monday, September 21

Applied Technology Workshops
New Directions in ISO-10993-4 Hemocompatibility Testing of Medical Devices

Speaker: Kent Grove, American Preclinical Services

Kent Grove will lead an informal discussion on new updates in both in vivo and in vitro hemocompatibility and thrombogenicity testing. Kent was an invited speaker at the FDA workshop on Methods for Thrombogenicity Testing held on April 14, 2014. Kent has also championed a new minimally heparinized in vitro blood-loop system for testing surfaces and coatings of catheters and wires. This presentation will discuss new methods and techniques from both these hemocompatibility testing systems.

Biography
Kent Grove, MS, HT, Director Biocompatibility – American Preclinical Services

Kent received his Bachelor of Science degree in Biomedical Science from Saint Cloud State University (SCSU) in 2005, and his Master’s in Science from SCSU in 2008. He worked as a technical supervisor for the SCSU Aquatic Toxicology Laboratory, conducting EPA funded research. In 2008, Kent accepted a position as a research assistant for WuXi AppTec. In May 2009, Kent moved into the role of a project manager working directly with clients to help design, quote, and implement a custom toxicology studies to meet sponsor needs. In late 2010, Kent accepted a position as a study Director at American Preclinical Services and has been instrumental in building the biocompatibility testing program at APS over the past 4 years.

About American Preclinical Services

APS is a State of the Art, AAALAC and ISO17025 accredited, USDA registered and GLP compliant Contract Research Organization (CRO) located in Minneapolis, Minnesota, specializing in medical device and pharmaceutical testing.

We are a preclinical center of excellence whose catalogue includes ISO10993, USP <87>, USP <88>, JMHLW, custom biocompatibility testing, interventional, surgical, toxicology, pharmacology, pain, physician training and bioskills, animal model development and complete pathology services.

Our state-of-the-art facilities include three Siemens catheterization labs, a 128-slice Siemens CT Imaging Suite, Intravascular Ultrasound, Optical Coherence Tomography, Endoscopy, Cardio-Pulmonary Bypass, Histopathology and much more! In addition, we have one of the largest preclinical capacities in the world, housing over 500 large and 2,000 small animals on site.

Whether your company is a startup or an established industry leader, our experienced scientific staff has the expertise to meet your research needs and timelines. Pilot and screening evaluations, feasibility and efficacy testing or ultimately GLP safety studies of the finished product, you will have industry experts to rely on every step of the way.

We strive to deliver comprehensive, yet rapid service with the understanding that in product development, the only constant is change. We’ve tailored our processes, capacity, and customer service to keep up with today’s fast paced business cycles. APS will go from a quote to a ready to implement study design with your time lines in full focus.

However, starting a project is only half the battle. APS meets and exceeds quality, accuracy and timelines for data reporting and study finalization. The study director dedicated to your project will have the full support of a team of study coordinators, technicians, quality assurance auditors, and APS management to ensure precise and complete reports, from your proof-of-concept study, all the way through to your pivotal GLP preclinical study.
Surfaces to Control Cell Attachment and Tissue Morphology in Vitro

Speaker: Eric Guire, ISurTec, Inc.

Innovative Surface Technologies, Inc.
Saint Paul, Minnesota

Introduction
Cell-based assays and therapeutics are experiencing a renaissance due to recent advances in tissue engineering. ISurTec is developing technologies useful for controlling cell interactions with surfaces and influencing cell and tissue morphologies in vitro. Nanotopography, nanotexture, and control over cellular adhesion were used in various combinations to pattern tissue morphology, improve reproducibility, and control cell or tissue harvest. In this work, we demonstrate a prototype “brain-slice-on-a-chip” for electrophysiological drug screening, validate a nanotextured 96-well plate insert for generation of spheroids for cell therapeutics research and drug screening, and provide advanced thermoresponsive solutions for cell and tissue sheet production.

Bioartificial Brain Slices for Drug Screening
Brain slice scaffolds were generated from electrospun photoreactive nanofibers. Random non-woven nanofiber mats were photopatterned with passivating and pro-adhesion polymers to generate distinct co-culture regions on the scaffold (Fig. 1, green and red areas). Aligned photoreactive nanofibers with photoimmobilized collagen were included in the scaffold for neurite guidance. The brain slice scaffolds were seeded with neonatal rat hippocampal cells and cultured for 30 days prior to electrophysiological recording.

Bioartificial brain slice electrophysiology
The neural circuits generated by the bioartificial brain slice scaffolds recapitulate in vivo-like structural connections that are normally lost in cell culture. This enables the generation and detection of field excitatory postsynaptic potentials (fEPSPs, Fig. 1). Green, presynaptic cultures. Red, postsynaptic cultures.

Tumor aggregates and embryoid body formation
Schematic diagram of a single ISurSphere® insert placed in a single well of a multi-well cell culture plate holding a drop of cell suspension in growth medium above the viewing hole. Inset: single aggregate of bovine aortic endothelial cells (BAECs).

ISurTherm® Surfaces for Cell Harvest
Thermoresponsive cell cultureware and microcarriers were produced using solutions of thermoresponsive polymers and ISurLite® photo-crosslinker. Films were deposited on polystyrene, nylon, PET, or PCL from a solution in IPA by flood or spray application prior to curing with UV light. Cells are grown under standard cell culture conditions and released from the growth surface by briefly lowering the temperature to 22°C.
Surfaces to Control Cell Attachment and Tissue Morphology in Vitro, continued

Figure 3.

Enzyme-free cell release
ISurTherm® coated surfaces have higher versatility and improved manufacturability compared to commercially available poly(N-isopropyl acrylamide) graft coatings. Coated surfaces are able to release strongly adherent cell types, such as Mesenchymal Stem Cells (MSC, above) or T47D cells, as well as efficiently release standard cell types.

Summary
Shown herein are examples of three cell and tissue culture technologies developed with a focus on cellular interactions at the surface. Bioartificial brain slices, when populated with human neurons and glia, may lead to improved circuit-level drug screening for neurological diseases and disorders, as compared to commonly used rodent brain slices. ISurSphere® inserts enable efficient and reproducible generation of cell spheroids (3D cancer drug screening) or embryoid bodies (stem cell research), by preventing cellular interactions with the surface. ISurTherm® surfaces enable release of cells or tissues from their growth surfaces, without enzymatic digestion, due to a temperature-dependent phase change of the growth surface. Preservation of cell membrane proteins during harvest produces more efficient scale-up for bioreactors, reduced aneuploidy due to repeated trypsinization, and can release tissues from their growth surfaces without disrupting tissue architecture. Continued research to develop novel or improved cell culture surfaces and scaffolds will undoubtedly lead to future advances with important applications in medicine.

Biography
Eric Guire is R&D Manager and Principal Investigator at ISurTec, Inc., and an academic staff member at the University of Minnesota. He received a B.S. in Biochemistry from the University of Minnesota and a Ph.D. in Neuroscience from Oregon Health and Science University. He joined ISurTec in 2008 after completing a postdoctoral fellowship at the Vollum Institute for Advanced Biomedical Research. His current research focuses on the interfaces of surface chemistry, biology, and neuroscience.
Characterizing Biomedical Coatings Using Nanoindentation and Nanoscratch

Speaker: Dehua Yang, Ebatco

Abstract

Biomedical coatings are often applied to improve or to modify the properties of substrate materials in order to achieve desired performances and functionalities. As is the case with bulk biomaterials, biomedical coatings need to be characterized and analyzed to meet product specifications and quality requirements, or for biocompatibility purposes as well. Furthermore, because of the nature of coatings, special measurements and analysis methods are necessary to ensure reliability and integrity of the coating-substrate system. Therefore, appropriate characterization of biomedical coatings has significance.

In this presentation, advanced nanoscale analytical techniques for characterization of coating mechanical properties will be introduced. Steps on how to obtain accurate hardness and elastic modulus data from nanometer to micron thick coatings through nanoindentation tests will be provided. In addition, interfacial adhesion evaluation of coating to substrate through nanoscratch tests will be discussed in relative detail.

Biography

Dr. Dehua Yang is the Founder and President of Ebatco, a Minnesota corporation specializing in providing high quality testing instruments and equipment, technical consulting and contract lab services. His expertise and experience spans from nanoscience and nanotechnology to product failure analysis. Prior to founding Ebatco, Dr. Yang was the Vice President, Commercialization of Hysitron Inc., a world leading manufacturer of nanomechanical testing instruments.

Dr. Yang holds a Ph.D. in Physical Chemistry and a M.S. and B.S. in Solid State Physics and Metal Physics, respectively. He is a recipient of the Chinese Academy of Science top-ranked presidential award and natural science research award. The products he designed and managed at Hysitron, namely, nanoTensile 5000 and 3D OmniProbe, won the 2007 Micro/Nano 25 Award, and the 2005 Nano 50 Award respectively. In 2009 his company, Ebatco, was selected to receive the Best of Business in Commercial Physical Research by SBCA. In addition, he has authored/coauthored more than 50 peer-reviewed publications on nanoscience and nanotechnology, tribology and surface science and engineering related topics. He is an inventor/co-inventor of 6 issued US utility patents. He is the 2010-2011 Vice Chair and 2011-2012 Chair of Minnesota Chapter of ASM International, a member of MRS and STLE. He has served many times as a US National Science Foundation grant review panelist, journal referee, and international conference organizer and session chair.

More information about Dr. Yang can be viewed at www.ebatco.com.
Keynote Presentation
Surface modification of biomaterials has resulted in new generations of medical devices with improved function. These modifications were originally relatively simple changes in surface chemistries and have evolved to include chemistries that directly alter the tissue response following device implantation. Cell-based biomaterial modifications continue to evolve and now include the technology known as 3D Bioprinting. This evolution in surface modification technology will be explored with the goal of creating a new generation of “Bioficial” devices and organs.

Biography
Dr. Stuart Williams received his Ph.D. in Cell Biology from the University of Delaware followed by postdoctoral training in Pathology at the Yale School of Medicine. During the period 1980 to 1990 he held a faculty appointment at Jefferson Medical College, where he was Director of Research in the Department of Surgery. In 1990 Dr. Williams joined the faculty at the University of Arizona and founded the University of Arizona Biomedical Engineering Program, creating a research and educational link between the Medical School and College of Engineering. He held faculty positions jointly in Biomedical Engineering, Surgery, Physiology and Materials Science and Engineering. In 2007 Dr. Williams was selected as the Scientific Director of the newly established Cardiovascular Innovation Institute, a partnership between Jewish Hospital and the University of Louisville in Louisville, Kentucky. He recently established the Bioficial Organs Program to create human tissues and organs for clinical therapeutics and in vitro toxicity testing using a patient's own cells. Central to this effort is the use of 3D bioprinting technologies. Dr. Williams' research interests have focused on medical devices and regenerative medicine. He developed and patented the first methods to use fat-derived stem and regenerative cells for therapeutic use. He has maintained continuous funding from the National Institutes of Health since 1979. Dr. Williams has authored over 300 scientific publications. His entrepreneurial spirit has resulted in 18 issued US patents with numerous patents pending. He has founded six biotechnology companies; maintained active managerial positions and has been an active consultant to the medical device, regenerative medicine and pharmaceutical community. He is a Fellow of the American Heart Association and a Fellow of the American Institute of Medical and Biological Engineering.
Tuesday, September 22

Session 1
Analytical Techniques for Surface Characterization of Biomaterial
Advances in Mass Spectrometry Imaging of Biointerfaces Using Femtosecond Lasers and Postionization

Speaker: Luke Hanley, University of Illinois at Chicago

Department of Chemistry, University of Illinois at Chicago, Chicago, Illinois

Secondary ion mass spectrometry, matrix assisted laser desorption ionization mass spectrometry (MS), electrospray-based MS and other strategies are widely used for the analysis of intact bacterial biofilms, mammalian tissue, cell cultures, and their interfaces with biomaterials [Bhardwaj & Hanley, Nat. Prod. Rev. 31 (2014) 756]. The combination of these desorption/ionization methods with high resolution MS and tandem MS capabilities permit metabolomic and proteomic imaging of such samples. Nevertheless, the use of these ion sources to detect many analyte classes within intact biological samples still often suffers from low sensitivity, selective ionization, and/or poor spatial or depth resolution. Laser desorption with femtosecond laser pulses can remove material from a solid with minimal damage to the remaining sample, potentially allowing both depth profiling and additionally, higher spatial resolution [Cui, et al., Anal. Chem 87 (2015) 367]. Furthermore, recent work has shown that ultrashort pulse laser desorption can, under the proper experimental conditions, lead to no more molecular fragmentation than other popular ion sources. Laser desorbed neutrals can undergo postionization by vacuum ultraviolet or ultrashort pulse radiation for subsequent detection by MS. Postionization has the additional advantage that proper selection of the delay time between the desorption and postionization laser can improve molecular analysis. Here, we demonstrate the small molecule imaging capability of these methods on intact biological samples and other complex organic thin films. Finally, a laser desorption-based strategy is described that should allow solid sampling with any portable MS instrument with an atmospheric pressure ion source.

Biography

Luke Hanley is Professor and Head of the Department of Chemistry at the University of Illinois at Chicago, where he has been a faculty member since 1990. He received his B.Sc. and Specialist in Chemistry from the University of Toronto in 1983 and his Ph.D. in physical chemistry from the State University of New York at Stony Brook in 1988. He was awarded a National Science Foundation Postdoctoral Research Fellowship in Chemistry at the University of Pittsburgh from 1988 to 1990, was a NSF Young Investigator in Chemistry from 1994 to 1998, and a University of Illinois Scholar during this period. In 2009, he was awarded the UIC Researcher of the Year Award and was elevated to a Fellow of the American Vacuum Society. His research focuses on the surface modification and analysis of organic, nanocomposite, and biological surfaces and films. He has developed and applied various advanced instrumental methods in MS, photoionization, and photoemission. His ~130 refereed papers cover diverse topics including laser desorption, laser photoionization, surface science, mass spectrometry, analytical chemistry, and bioengineering. His recent research projects have included the development of new methods in mass spectrometric imaging, the deposition of organic-inorganic nanocomposites for optoelectronic applications, the surface chemical modification and analysis of biomaterials, and the identification of metabolic processes in bacterial biofilms. chem.uic.edu/hanley
New Tools for Quantitative Nano-Mechanical Force Microscopy and High-Speed High-Resolution AFM

Speaker: Stefan B. Kaemmer, JPK Instruments

Dimitar Stamov, Heiko Haschke
JPK Instruments, 4189 Carpinteria Ave. Suite 1, Carpinteria, California

Atomic Force Microscopy (AFM) is well known as a multi-purpose tool for imaging a wide range of different samples with nanometer scale resolution in air and under controlled environmental conditions in liquid using forces ranging from several pN to nN. Optical tweezers extend the observable force range to the sub-pN regime enabling applications from single molecule interactions to rheological phenomena (see fig 1).

AFM can also be used to obtain mechanical properties of different kinds of samples. Nevertheless, the traditional imaging modes demonstrated well known drawbacks for challenging samples that have steep edges, as well as those that are soft, sticky, or loosely attached to the surface.

A new imaging mode: “Quantitative Imaging” (QI) combines nano-topography with the opportunity of obtaining mechanical properties simultaneously. The QI tip movement algorithm prevents lateral forces and controls the vertical forces for nondestructive imaging at each pixel. Information such as, topography, adhesion, slope and even more complex data like contact point images, Young’s moduli maps, or even recognition events can be analyzed. Furthermore challenging samples which are fragile or loosely attached, like fibers, viruses, and bacteria can be measured by QI. A comparison between QI, force spectroscopy and traditional AFM imaging modes is given.

More than half a century after the first high-resolution electron microscopy images of collagen type I banding have been reported, high-speed AFM enabled us to gain a high-resolution temporal insight into the dynamics of collagen I fibril formation and its characteristic 67nm banding hallmark as an example of studying dynamic processes in fluids. The literature still abounds with conflicting data regarding the models of its fibril formation, structural intermediates, and kinetics. AFM is the only currently available high-resolution imaging technique to offer insight into the collagen I fibrillogenesis by operating in situ. The described technique could be instrumental for future studies of the structural dynamics in biology as well as material sciences.

Biography

Dr. Stefan B. Kaemmer is the General Manager for JPK’s US operations located in Carpinteria, California. Stefan earned his doctorate degree in Physical Chemistry in 1992 from the Technical University of Braunschweig working on Scanning Probe Microscopy on crystal surfaces. Before joining the JPK team, Stefan was with Bruker/Veeco for over 20 years in various technical management and scientific roles in Europe, Japan, and the US. Stefan has over 20 years of SPM experience, has authored over 40 publications and application news, and has led several scientific collaborations as well as being an adviser on a number of Diploma and Ph.D. theses.
Nanoparticles (NPs) have been widely used in many fields of science due to their unique physical properties. While many applications of NPs such as imaging probes or drug carriers often require the conjugation of proteins or biomolecules, the surface interactions between NPs and biomolecules remains underexplored. For example, the immobilization of immunoglobulin G (IgG) onto nanoparticle surfaces is critical for the development of many immunosensors and drug delivery nanocarriers. Notably, the orientation of the immobilized IgG can have significant impact on the clinical outcomes of these carriers by impacting its biostability and efficacy.

In this work, Protein G B1, a protein that will selectively bind to the Fc tail of IgG, was immobilized onto gold NPs (AuNPs) functionalized with maleimide and oligo-(ethylene glycol)(OEG) self-assembled monolayers (SAMs). Protein G B1 was immobilized on AuNPs using either carbonyldiimidazole (CDI) chemistry or maleimide-cysteine interaction (Figure 1). We use the surface sensitive analysis techniques of X-ray photoelectron spectroscopy (XPS) and time of flight-secondary ion mass spectrometry (ToF-SIMS) to characterize the immobilization of protein G B1. Unlike conventional NP characterization techniques such as dynamic light scattering (DLS) and UV/Vis, XPS and ToF-SIMS can provide additional information on the surface elemental composition, protein coverage and orientation.

The functionalization and protein immobilization chemistry was systematically characterized using XPS (Figure 2). XPS analysis confirmed the CDI activation of the OEG-SAMs AuNPs by detecting the nitrogen containing active intermediate and the attenuation of gold signal. After incubation with protein, the immobilization of the protein was demonstrated by the increased nitrogen signal on the surface. A small increase in nitrogen was observed for samples without CDI activation, possibly due to non-specific adsorption of the protein.

ToF-SIMS analysis also confirmed the successful functionalization, CDI activation, and protein immobilization by identifying signature secondary ions from each step of the protein immobilization process. Further, by utilizing ToF-SIMS high surface sensitivity and sampling depth (2nm), it was possible to determine the orientation of immobilized protein G B1 of similar thickness (3nm) by comparing the ratio of secondary ion intensity originating from the opposite end of the protein. As expected, the non-site specific CDI chemistry did not lead to a specific protein orientation on the AuNPs. Additionally, no significant difference was observed between the amino acid peak intensity ratios of functionalized AuNPs with or without CDI activation, suggesting that CDI chemistry had limited impact on the adsorbed protein’s orientation.

In contrast to CDI chemistry, we expect to control the orientation of the immobilized protein using maleimide functionalized AuNPs and cysteine mutants of Protein G B1 through site-specific carbon-sulfur interaction. Overall, the systematic characterizations in this study will provide detailed information.

Biography
Yung-Chen Wang received his B.S. in Bioengineering from the University of California, Merced in 2012. As a NSF GRFP fellow, Yung-Chen is currently advised by Professor David Castner at the University of Washington, where he is working on his Ph.D. in Bioengineering. His research focuses on the characterization of protein conjugated nanoparticles using time of flight-secondary ion mass spectrometry (ToF-SIMS) and X-ray photoelectron spectroscopy (XPS).
Imaging of Novel Daily Disposable Contact Lenses Having Unusual Water Characteristics Before and After Wear

Speaker: Katarzyna A. Wygladacz, Bausch + Lomb


Introduction
Contact lens wearers today spend much more time using digital display devices than a decade ago. To account for reduced blink rate and increased tear film evaporation, manufacturers recently introduced two novel daily disposable contact lenses with atypically high surface water content. Bausch and Lomb launched Biotrue ONEday (nesofilcon A, 78% water content), an FDA Group II (high water, non-ionic) lens in 2012, while Ciba Vision (now Alcon, Ft Worth TX) launched Dailies Total1 (delefilcon A, ≥80% surface water content; 33% bulk water content), an FDA Group V (silicone hydrogel) lens in 2013. Previous high-water lenses are reported to dehydrate at the lens surface over the course of normal wear. Therefore, we studied changes in lens water characteristics over the first 15 minutes of wear to see if either lens remains hydrated at the surface compared with 1-Day Acuvue Moist (etafilcon A, Vistakon, Jacksonville, FL; 58% water content).

Methods
Clinical Wear
Twenty subjects wore each of the three lens types studied in a randomly determined order for 15 minutes. After each wearing, lenses were removed and the surface refractive index (RI) of each lens was immediately measured with the Metricon M-2010 Prism Coupler (Pennington, NJ) by a masked operator using sodium light (λ = 589.3). For reference, the surface RIs of ten unworn lenses of each type removed from their respective original packaging and shaken five times to remove excess fluid were measured. Published values of RIs of various materials [Millodot (2009)] ranging from pure water (RI=1.33) to HEMA (1.43) were compared with measured values to estimate water lost during early lens wear.

Lens Characterization
To confirm clinical observations, a different subject wore one delefilcon A lens and one nesofilcon A lens for 4hr, after which lenses were removed and imaged by Atomic Force Microscopy (AFM) using a Dimension ICON instrument (Bruker Corp, Billerica, MA) and compared to images of unworn lenses.

Results and Discussion
Clinical Wear
The surface RI of the delefilcon A lens before wear was 1.34, consistent with water content in excess of 80%; however, RI shifted to 1.43 after 15 minutes of wear, consistent with 33% water content. In contrast, the mean surface refractive index of the nesofilcon A lens was a constant 1.38, while that of the etafilcon A lens increased from 1.41 to 1.42 after 15 minutes of wear. This suggests that the surface of the delefilcon A lens behaves like a high water hydrogel before insertion but quickly dehydrates to behave like its low-water silicone-hydrogel bulk material with respect to surface water content during wear, while both nesofilcon A and etafilcon A lenses maintain their water during initial wear.

Lens Characterization
AFM images of the nesofilcon A lens show little change in surface morphology after wear (Figs. 1A and B). In contrast, the delefilcon A shows a “brain tissue”-like surface texture before wear (61±19nm depth, peak to valley) that collapsed after wear (Figs. 2A and B).

Fig. 1. AFM images of nesofilcon A before and after wear
Imaging of Novel Daily Disposable Contact Lenses Having Unusual Water Characteristics Before and After Wear, *continued*

Summary
The nesofilcon A lens appears unique among high water lenses in maintaining high surface water content during wear, thus preventing visual aberration that occurs with changing RI. In contrast, the high surface water of the delefilcon A lens is lost within the first 15 min. of wear when the supra-hydrophilic coating layer collapses upon itself.

Reference

Biography
Katarzyna (Kasia) Wygladacz is a Senior Research Scientist in Vision Care R&D at Bausch + Lomb, a division of Valeant Pharmaceuticals International. At B+L, she is focused on development, commercialization, and marketing activities of ophthalmic medical devices using surface chemistry and advanced microscopy technologies. She was awarded her MS in Chemical Technology/Chemical Engineering from Radom University of Technology, and her PhD in Analytical Chemistry from Warsaw University of Technology (Poland). In 2001 she obtained a EU Maria-Curie fellowship and worked at Exeter University, UK on sensor for neurotransmitters monitoring. She completed two postdoctoral fellowships implementing fluorescent micro-bead and fiber-optic technology for the analysis of mammal physiological fluids supported by Beckman Coulter, Inc at Auburn and Purdue University, U.S. She co-authored a number of peer-reviewed publications and U.S. patent applications.

Her areas of expertise are medical devices, miniaturized diagnostic platforms, surface chemistry, advanced microscopy, fluorescence spectroscopy, materials science, analytical and lipid chemistry.

Disclosures: Employee of Bausch + Lomb

Figure 2. AFM images of delefilcon A before and after wear
Session 2
Chemical and Physical Strategies to Regulate Biological Adhesion
Preventing Biological Adhesion Using Liquid-infused Materials

Invited Speaker: Caitlin Howell, Harvard University

Caitlin Howell\textsuperscript{1,2}, Joanna Aizenberg\textsuperscript{1,2,3}


Learning from and mastering nature’s concepts promises to drive a paradigm shift in modern materials science and technology. Based on this philosophy, our group has recently developed ultra-slippery, pressure stable surfaces through inspiration from the \textit{Nepenthes} pitcher plant. These Slippery Lubricant-Infused Porous Surfaces, or SLIPS, use an immobilized liquid layer to present a “moving target” for biological adhesion.\textsuperscript{1} As anti-thrombogenic surfaces, SLIPS have been shown to prevent fibrin attachment and reduce platelet adhesion and activation, preventing arteriovenous shunt occlusion in vivo for up to 8 hours without anticoagulants.\textsuperscript{2} As biofilm-resistant coatings, they have proven effective against clinically-relevant bacteria such as \textit{E. coli}, \textit{S. aureus}, \textit{S. epidermidis}, and \textit{P. aeruginosa}, significantly reducing the amount of adherent bacteria and effectively preventing the formation of stable biofilms.\textsuperscript{3,4} SLIPS can be fabricated on a range of different materials, including plastics, metals, and glass, and can be designed to use FDA-approved liquids. SLIPS can also be engineered to contain self-replenishing systems, which can significantly increase their longevity.\textsuperscript{4} We anticipate that this new approach to antifouling will prove useful in controlling biological adhesion in a wide range of applications.


Biography

Caitlin Howell is a Technology Development Fellow at the Wyss Institute for Biologically Inspired Engineering at Harvard University, working in the group of Joanna Aizenberg on bio-inspired adaptive materials technologies. Her focus lies in understanding and engineering the molecular-level interactions of cells and biological molecules with immobilized liquids and other unique interfaces to create new, high-value technologies for medicine and industry. Prior to joining the Wyss, Caitlin received her doctoral degree as an NSF Graduate Research Fellow in Physical Chemistry at the University of Heidelberg, Germany, under the direction of Michael Grunze.
Introduction
Medical device-associated infections are a significant cause of morbidity, mortality and high healthcare costs. Most hospital-acquired infections are associated with medical devices and the majority of blood stream infections stem from the use of vascular catheters. With increasing use of antimicrobial devices, the potential for inducing resistance to mainstream antibiotics is a critical concern. There is a need for improved approaches to prevent colonization and biofilm formation on devices. In particular, there is an unmet need for antimicrobial technologies that resist fouling in the presence of blood and approaches that won’t select for antibiotic resistance traits. In this work, we investigated the potential for a novel antimicrobial peptide based coating to reduce colonization and fouling of acute vascular catheters.

Methods
Polyurethane 7 Fr, triple lumen catheter tubing was coated with a hydrophilic polymer formulation containing ASP-1, a broad spectrum, engineered cationic antimicrobial peptide. After sterilization by ETO, release and stability of ASP-1 was measured by HPLC. To assess antimicrobial efficacy, samples were incubated in 50% serum for up to 36 days with weekly serum replacement followed by incubation in 3x10^4 CFU/mL Staphylococcus epidermidis (RP62A) for 24hrs. Viable bacteria remaining in the solution surrounding samples were counted by serial dilution and plating. Biofilms on surfaces were removed by sonication followed by serial dilution and plating. Resistance to fouling was evaluated by measuring fibrinogen adsorption and coated tubes were tested for hemolysis and cytotoxicity.

Results
Antimicrobial Peptide Release and Stability
Coated tubes continuously released ASP-1 out to 36 days with no substantial burst effect. Preliminary data indicate ASP-1 retained over 95% of its original purity in the coating for at least 9 months post sterilization.

Figure 1. ASP-1 release from coated tubing incubated in PBS at 37°C.

Antimicrobial Efficacy
The antimicrobial coating reduced bacteria in solution by over 4 logs relative to controls. After incubation in serum for periods up to 36 days, coated samples effectively eradicated bacteria from surrounding solutions (Fig 2).

Figure 2. Bacteria recovered from inocula incubated with catheter tubing.

Biofilm Inhibition
Biofilm formation on coated catheter tubing was significantly reduced relative to controls, even after incubation in serum for over 4 weeks (Fig 3).
The hydrophilic, antimicrobial coating reduced fibrinogen adsorption by over 65% relative to controls. Coated surfaces showed no cytotoxicity and pass the ASTM (F756) direct contact hemolysis test.

Summary
This work demonstrates the hydrophilic, ASP-1 coating is a promising technology for reducing medical device associated infections. ASP-1 is rapidly biocidal with a mechanism of action that is distinct from most mainstream antibiotics. As such, it is unlikely to promote antibiotic resistance. The coating displayed effective biofilm inhibition for more than 4 weeks, in line with the needs for acute vascular catheters. It was also found to be stable and conferred resistance to fouling. These results provide a strong foundation for applying this technology to improve the safety and function of medical devices.

Biography
Dr. Neff is the CEO of Allvivo Vascular, a company developing biomimetic coatings for medical devices and combination products. She was previously the Director of Research for Allvivo and currently serves on the board of the Southern California Biomedical Council. Jennifer graduated with honors in Materials Science Engineering and earned a Ph.D. in Bioengineering from the University of Utah.
Introduction
Surface structure is increasingly recognized for its strong effect on cell behavior. Finding the appropriate surface to elicit desired cell behavior for a whole area of medical implants offers great opportunity as it will facilitate better host-interaction performance. Current medical implants are processed through applying conventional chemical surface treatments and/or modifications but do not feature designed surface structures, limiting their functionality. In contrast, producing medical devices with an intelligently designed surface structure enhances the tissue response to the implant’s surface. For example, designing implant surfaces featuring topographies that inhibit the foreign body reaction of macrophages reduces the formation of scar tissue around the implant, thereby preventing encapsulation and implant rejection. Intelligently designed surface topographies hold great promise in improving implant performance and enable the next generation of medical devices. We present several cases showing how designed surface topographies can be applied to improve medical device functionality.

TopoChip Method
We use our high-throughput TopoChip screening platform to identify optimal surface topographies. The TopoChip holds nearly 2200 intelligently designed topographies based on parameters considered being important in cell surface-surrounding interactions. Depending on the application the appropriate biomaterial, cell type and biological assay are selected to study the effect of each topography individually. After identifying those designed topographies that elicit the desired biological response strongest, these so-called hit-topographies are verified and undergo secondary screening to ensure the efficiency of the surfaces.

Results
Based on clinical need and market opportunity, we have selected a range of clinical applications to design optimal surfaces for. We have identified surfaces that:

- promote bone formation. In vivo validation confirms improved implant integration in native bone when the implants feature these specific surface topographies. Enhanced bone-integration is critical in improving bone implant function and durability.
- are anti-thrombogenic. We designed unique topographies that lower blood platelet adherence even on commercially available biomaterials specifically developed for their good blood-contacting properties (see Figure 1). Adding the identified topographies to these materials allow for lowering the risk on e.g. IV-catheter-related thrombogenesis even more. In addition, to further improve blood compatibility of endovascular medical devices we are also screening for surface topographies that enhance endothelialization of e.g. cardiovascular stents. Optimizing endothelialization is expected to reduce e.g. in-stent thrombosis and restenosis after stent placement.
- decrease differentiation of macrophages into foreign body giant cells (FBGC), a process that is the onset of encapsulation of an foreign material. These surfaces are highly promising in preventing encapsulation of implanted biomedical devices such as blood glucose sensors.
- prolong in vitro culture of primary hepatocytes. These designed surfaces easily double the in vitro culture time of primary hepatocytes combined with high cell number and quality and without the need of a surface coating, such as collagen. Prolonged hepatocyte culture is highly interesting for setting up e.g. a functional 3D liver model for pharmacological drug testing and toxicology.
Summary
Intelligently designed surface topographies improve the functionality of medical devices and can be applied for a wide range of clinical applications.

![Figure 1: Fluorescent microscopy images comparing blood platelet adhesion to (left) a surface featuring a topography scored for high platelet attachment, (middle) a surface featuring a topography scored for low platelet attachment and (right) a non-patterned, flat surface. The blood platelets are indicated by the green and red dots due to the use of a green and red fluorescent label. Platelet adherence is less than half on the 'low attachment' topography compared to the benchmark, the non-patterned surface.](image)

Biography
Dr. Joris van Ark is scientist cell biology at Materiomics B.V. He obtained his Ph.D. from the University of Groningen, The Netherlands (2008-2013). After getting his Ph.D., Joris started working as a scientist cell biology at Materiomics B.V. His expertise is focused on cell culture protocol and assay development, high-throughput imaging, and cell-material interactions.
Alternative Approaches for Long-Term Hemocompatibility

Speaker: Melissa Reynolds, Colorado State University

Each year billions of health care dollars are spent on medical devices that fail in clinical practice. These device failures occur over various timescales of the devices and are due to multiple factors including thrombosis, inflammation, infection, and tissue overgrowth on the surface of the implanted device as well as mechanical device failures. Over the last 50 years much has been learned about these device failures and attempts have been made to prevent failures using (1) alternative systemic drug therapies, (2) surface modifications on the device, or (3) a combination of both approaches. Despite efforts to improve the efficacy of blood-contacting and implantable medical devices, the incompatibility of these materials within human blood and tissue still causes serious complications in patients. Thus, systemic or regional drug therapies such as heparin remain necessary. Synthetic polymers that can replace the function of the injured cells without activating platelets will lead to more effective devices. In this presentation, the development, characterization and applications of polymer composites capable of long-term function will be described. The new material platforms use metal organic frameworks (MOFs) that are practically manufactured into polymeric devices via extrusion or grown from the surface of polymers via simple surface treatments without loss of function. The resulting materials have maintain the mechanical performance of the polymer and eliminate the need to store anticoagulants in the polymer constructs. Finally, the devices can be sterilized using common techniques and stored at ambient conditions, making them ideal for use.

Biography
Melissa Reynolds, Ph.D., is a Boettcher Investigator and Associate Professor at Colorado State University in the Departments of Chemistry, Biomedical Engineering and Chemical and Biological Engineering. She received a B.Sc. in Chemistry from Washington State University and a Ph.D. from the University of Michigan. Her research focuses on the molecular design and fabrication of biomimetic materials for use in medical device applications, including the development of metal organic frameworks as biocatalysts. She has been recognized as an emerging investigator by the Journal of Materials Chemistry and her research has received an NSF CAREER award. In addition to her academic interests, she is co-founder of Diazamed. Her research also received a 2013 TechConnect National Innovation Award.
Session 3
Ophthalmic Drug Delivery
Challenges and Approaches for Long-Acting Delivery of Biologics to the Back of the Eye

Speaker: Karthik Rajagopal, Genentech Inc.

The emergence of new biologics for treating back of the eye diseases has spurred the development of long-acting delivery (LAD) technologies. The main goal of these technologies is to reduce treatment burden by decreasing frequency of intravitreal injections. As a result, biologics are exposed for longer period of time in the eye under physiological pH and temperature conditions which can be challenging for such molecules. Here, we present challenges and opportunities for various ocular delivery systems designed for long-term delivery of antibody therapeutics to the posterior segment of the eye.

Biography
Karthik Rajagopal received his Ph.D. in Chemistry from the University of Delaware in 2006. He joined Genentech in 2010 after completing post-doctoral fellowship at the University of Pennsylvania. Karthik’s academic research involved the development of peptide and polymer-based materials for drug delivery and tissue engineering applications. Since joining Genentech in 2010, Karthik has been leading the evaluation of several polymer-based drug delivery technologies for therapeutic proteins.

His current research interests include investigation of new drug delivery materials, polymers, antibody stability challenges and novel excipients. Karthik has thus far published more than 20 peer-review articles and holds two patents.
Developing New Ophthalmic Formulations Using PRINT

Speaker: Benjamin Yerxa, Envisia Therapeutics

Envisia Therapeutics is developing novel ocular dosage forms by leveraging the PRINT® platform for manufacturing drug particles with precise control over size, shape and composition. Envisia is developing ENV515, a long-lasting intraocular prostaglandin formulation which lasts for more than 6 months after a single administration in vivo. The other areas of focus are sustained release intravitreal formulations of drugs for treating back of the eye diseases and subconjunctival delivery for treating anterior segment diseases. The talk will focus on the formulation and preclinical data for various projects and will highlight how the PRINT process has been industrialized to create new ophthalmic pharmaceutical products.

Biography
Dr. Yerxa is President and co-founder of Envisia Therapeutics, a spin out of Liquidia Technologies. Previously, he was the CSO for both Liquidia and Envisia and joined Liquidia from Clearside Biomedical. Prior to Clearside, Dr. Yerxa was the Executive Vice President and Chief, Research & Development of Inspire Pharmaceuticals, a top ranked publicly traded biotech company acquired by Merck & Co., Inc. During his time at Inspire, Dr. Yerxa helped the company build and commercialize a portfolio of innovative new products and was part of the senior management team through multiple rounds of financing, including the company’s initial public offering (ISPH). Throughout his 25-year career in the pharmaceutical and biotechnology industry, Dr. Yerxa has been involved with the discovery and development of several investigational new drugs, phase 3 clinical programs, new drug applications and drug approvals. He is an inventor of DIQUAS™, an innovative treatment for dry eye approved in Japan. His experience spans a variety of therapeutic areas including ophthalmology, pulmonary, cardiovascular and HIV. Dr. Yerxa has more than 50 U.S. patents to his name, led a variety of licensing deals including technology transfers and manufacturing agreements, and has built several R&D and corporate functions from inception. Dr. Yerxa serves on the board of directors of the North Carolina Biotechnology Center and Sharefish.
Idea to Product in Ophthalmic Sustained Release

Speaker: Paul Ashton, pSivida

Introduction

The normal path from product concept to approval is straightforward and well known: test tube analyses, pre-clinical models, pre-clinical tox. studies, phase I, II and III clinical trials and NDA submission. In practice this path has many twists and turns; it is also expensive (estimates of development costs typically begin at $1B), time consuming (12 plus years) and is littered with failures. This need not be the case and successful development of two retinal products, each for posterior uveitis will be reviewed.

Development Plan: A Patient Focused Approach

Product development often begins with discovery of a new tool or technology followed by a search for a practical application. In the case of Retisert (FDA approved for posterior uveitis) and Medidur (now in phase III trials for the same disease), the focus was on the unmet medical need and the need to do something, almost anything. Posterior uveitis affects a relatively small number of people (175K in the US) but is responsible for over 10% of all blindness. It can be treated with oral steroids (topical drops don’t penetrate to the back of the eye) but this can have very bad systemic side effects.

It was thus a relatively simple matter to take an existing steroid and design an insert that would provide long-term release. A key to rapid development was to use polymers that had already been used in existing approved devices. Another key was the indication selection. The first patients to receive these devices (in a phase II study, no phase Is were conducted) did not have uveitis, but an even worse (and rarer) blinding disease POHP, for which surgical treatment was the only (and largely ineffective) treatment. For these patients, the risk/benefit of receiving an experimental implant (with minimal anima testing) was clear. With successful clinical data on 10 patients (it worked!) it was then possible to enter directly into phase III clinical trials in posterior uveitis. With agreement GLP tox. studies were conducted during the Phase III clinical studies and the product was approved approximately 7 years after the initial concept.

Medidur is a more recent device (using polymers in approved products), releases the same drug as Retisert and is injected via a 27 gauge needle. Relying on existing safety data from Retisert and the well known safety data from the polymers used, Phase III trials (which are ongoing) were initiated without either Phase I or Phase II studies. For the patients in these trials, there was a positive benefit/risk profile even without additional safety of pre-clinical or early stage clinical studies.

Conclusion

Many of the more restrictive rules and requirements for clinical trials are more perceived than actual. Frequent and open dialog with the FDA is vital for any development program.
Biography
Paul Ashton,
President and Chief Executive Officer, pSivida Corp.

Dr. Ashton has over 25 years experience in drug delivery. He has invented and developed (with colleagues) Vitrasert (the first intraocular drug delivery system to be approved by the FDA), Retisert (the first FDA approved product for uveitis) and Iluvien (the first FDA approved sustained release product for diabetic macular edema).

Dr. Ashton has served as President and Chief Executive Officer of NASDAQ-listed pSivida Corp. since January 2009, where he was previously the Managing Director from January 2007 and Executive Director of Strategy from December 2005 to January 2007. From 1996 to 2005, Dr. Ashton was the President and Chief Executive Officer of Control Delivery Systems, Inc., a drug delivery company that he co-founded in 1991. He has raised over $150m in funding from big pharma, public market, hedge funds and VC.

Dr. Ashton has authored over 200 peer reviewed publications, including original articles, chapters, books and abstracts. He also has over 70 issued patents. Before going into industry, Dr. Ashton was on the faculty at the New England Eye Institute and prior to that on the faculty in both the Departments of Ophthalmology and Surgery at the University of Kentucky. Earlier in his career he worked as a pharmaceutical scientist at Hoffman-LaRoche. Dr. Ashton received a Bachelor of Science degree in chemistry from Durham University, England, and a Ph.D. in pharmaceutical science from the University of Wales.
An effective treatment for ocular diseases requires that the drug delivery system is well tolerated in the eye and can release adequate amounts of drug to achieve therapeutic concentration levels in the target tissues over a desirable duration. Topical delivery is the most common route of administration for treating diseases of the front of the eye. Approximately 90% of ophthalmic drug formulations are for topical administration. However, bioavailability of topically administered drugs is very low, typically less than 5%. Anatomical and physiological barriers of the eye make it very challenging for topically administered drugs to reach the target tissues in the back of the eye.

Several long-acting polymeric drug delivery systems, such as Retisert, Iluvien, Ozurdex, etc., have been developed and marketed for local drug delivery to achieve maximum bioavailability and efficacy. A number of investigational systems are also being evaluated clinically. These systems are made of either biodegradable or non-degradable polymers and delivered via various routes of administration to overcome absorption barriers and to improve effectiveness of the treatments, including intraocular (i.e., intravitreal, intracameral), periocular (i.e., subconjunctival, sub-Tenon's), and suprachoroidal routes.

In this presentation, the influence of polymers and their properties on the performance of the delivery systems will be reviewed and discussed. The impact of anatomic barriers and the considerations in the design and selection of the delivery systems will also be briefly discussed.

Biography
Principal Scientist, Allergan
Ruiwen Shi holds a Ph.D. in Pharmaceutics from the University of British Columbia and is currently a principal scientist at Allergan. His work at Allergan is centered around developing novel long-acting polymeric drug delivery systems for treating both front and back of the eye diseases. Ruiwen has been very passionate about biomaterials and intraocular drug delivery and was the past chair of the Ocular Drug Delivery Focus Group of the Controlled Release Society.
Session 4 — Point Counterpoint
Therapies of the Future: Tissue-Based or Device-Based Revisited

Tuesday, September 22
Therapies of the Future: Tissue-Based or Device-Based Revisited

Jim Brauker, Extreme Deer Habitat LLC

Biography
Jim Brauker is a biomedical scientist with 22 years of industrial experience designing and developing implantable biomedical devices. He worked on cell transplantation for diabetes at Baxter Healthcare, and on small diameter vascular grafts at W.L. Gore and Associates. He was founding Vice President of Research and Development and Senior Technical Officer at DexCom, Inc, where he participated in all stages of development and product release of the STS and STS-7 continuous glucose sensors. He is a past President of the Surfaces in Biomaterials Foundation. He is an inventor on 189 issued U.S. patents and has over 250 pending patent applications. He is currently a biomedical consultant and CEO of Extreme Deer Habitat LLC, a company dedicated to helping landowners improve the habitat on their properties.

Gail Naughton, Histogen, Inc.

Biography
Dr. Gail Naughton founded Histogen, Inc. in 2007, and currently serves as CEO and Chairman of the Board for the Company. She has spent more than 30 years extensively researching the tissue engineering process, holds more than 100 U.S. and foreign patents, and has been extensively published in the field.

During her tenure at Advanced Tissue Sciences, where she was the company’s co-founder and co-inventor of its core technology, Dr. Naughton oversaw the design and development of the world’s first up-scaled manufacturing facility for tissue engineered products, established corporate development and marketing partnerships with companies including Smith & Nephew, Ltd., Medtronic and Inamed Corporation, was pivotal in raising over $350M from the public market and corporate partnerships, and brought four human cell-based products from concept through FDA approval and market launch.

In addition to this work, Dr. Naughton served as Dean of the College of Business Administration at San Diego State University from 2002 until 2011, where she helped to make SDSU the first campus in the nation to found a Ph.D./MBA in life sciences. In 2000, Dr. Naughton received the National Inventor of the Year award by the Intellectual Property Owners Association in honor of her pioneering work in the field of tissue engineering. She sits on the Board of Directors of CR Bard (NYSE: BCR) and the La Jolla Institute for Allergy and Immunology, as well as in the Advisory Board of Georgia Tech, the Ackerman Foundation, Perminova and the Centre for Commercialization of Regenerative Medicine.
Session 5
Integration for Tissue Repair and Regeneration
Development of Porous Space Maintainers for Craniofacial Tissue Engineering

Speaker: Antonios “Tony” Mikos, Rice University

Department of Bioengineering, Rice University, Houston, Texas

Optimization of the wound bed is critical for the reconstruction of large craniofacial defects. Previously, oral surgeons have had limited success in utilizing non-porous bone cement constructs in maintaining defect space while allowing for wound stabilization. To improve host/material interactions and create an environment primed for regeneration, we have developed a porous bone space maintainer (PBSM) for craniofacial application. In addition to promoting healthy wound healing, the PBSM can be loaded with antibiotic-containing microparticles to mitigate infection in the defect site. In animal models of large craniofacial defects, this technology has resulted in improved tissue healing as well as clearance of oral infection. In a small case series, the PBSM allowed for successful reconstruction of large craniofacial defects in humans. In this presentation, we will discuss the process of developing the PBSM and our in vitro, pre-clinical, and clinical findings.

Biography
Antonios G. Mikos is the Louis Calder Professor of Bioengineering and Chemical and Biomolecular Engineering at Rice University. His research focuses on the synthesis, processing, and evaluation of new biomaterials for use as scaffolds for tissue engineering, as carriers for controlled drug delivery, and as non-viral vectors for gene therapy. His work has led to the development of novel orthopaedic, dental, cardiovascular, neurologic, and ophthalmologic biomaterials. Mikos is a member of the National Academy of Engineering, the National Academy of Medicine, and the Academy of Medicine, Engineering and Science of Texas. He is a Fellow of the American Association for the Advancement of Science, the American Institute of Chemical Engineers, the American Institute for Medical and Biological Engineering, the Biomedical Engineering Society, the Controlled Release Society, the International Union of Societies for Biomaterials Science and Engineering, the Tissue Engineering and Regenerative Medicine International Society, and the National Academy of Inventors. He has been recognized by various awards including the Lifetime Achievement Award of the Tissue Engineering and Regenerative Medicine International Society-Americas, the Founders Award of the Society for Biomaterials, and the Robert A. Pritzker Distinguished Lecturer Award of the Biomedical Engineering Society.
Characterization of Electrospun Scaffolds

Speaker: Robert Diller, Northern Arizona University

Objective
To create electrospun scaffolds that mimic the native extracellular matrix of the dermis for wound healing applications — electrospun skin mimics (ESMs).

Background
Biomedical implants that are created with the native structural and physical characteristics of the tissue or organ being treated will elicit a favorable, biocompatible response. This is evidenced by a growing body of research focused on decellularized organs for their extracellular matrix (ECM) (Chen, Liu, 2015). Prior to in vivo studies, several types of material modifications or in vitro characterizations can be completed in efforts to provide investigators early feedback on how a biomaterial may respond in living tissues or living organisms.

Several products undergo surface modification of materials through plasma treating, protein coating, and the addition of bioactives to increase cell adhesion and proliferation (Shin et al., 2003). The structure and organization of an organ helps to facilitate its function. Therefore, it can be said that a scaffold being created to positively influence dermal wound healing should have similar mechanical and physical characteristics as the native dermis.

Methods
A variety of methods were used to assess the structural and mechanical characteristics of ESMs.

Scanning Electron Microscopy (SEM):
SEM was used in combination with MatLab and Image J to determine the percent relative porosity and fiber diameter of decellularized skin and ESMs.

Atomic Force Microscopy (AFM):
AFM was used to quantitatively determine differences in fiber morphology between ESMs.

Optical profilometry (OP):
ESM surface roughness was determined using OP.

Mechanical Characterization:
A unidirectional tensile testing device was used to evaluate the stress/strain relationship and modulus of elasticity in decellularized integument and ESMs.

Results

![Stress-Strain Relationships for Fresh and Decellularized Murine Integument](image)

Figure 1. (Left) Decellularized murine integument with a dermal % relative porosity of 58.2%. The epidermal layer is less porous, more cellular, and has less matrix than the dermal layer. (Right) Cross-section of an ESM with a % relative porosity of 57.6%. This scaffold has two different regions with various porosities, similar to the epidermal and dermal layers in the decellularized skin sample to the left.

Figure 2. Stress strain relationship between cellularized and decellularized murine integument. The decellularized integument has a greater modulus of elasticity compared to the fresh sample. The fresh sample reaches plastic deformation at lower stresses compared to decellularized samples.

Conclusions
By using different analytical tools available, scaffolds can be created that mimic the physical (demonstrated by optical
Characterization of Electrospun Scaffolds, continued

techniques), and the mechanical (demonstrated by stress strain data) characteristics of the dermis. By using SEM in combination with MatLab and Image J, the physical properties of the dermis and the scaffold can be evaluated. By knowing the characteristics of these native organs, materials can be created that will elicit an appropriate response in that environment (Williams, 1987). Therefore a working hypothesis of the current research is: biomaterials with similar physical properties to native tissues will result in improved biocompatibility.

References


Biography
Robert Diller is a Ph.D. student in biological sciences at Northern Arizona University. His research has primarily focused on using electrospun protein scaffolds to influence wound healing. His prior education includes a B.S. in Biomedical Science and an M.S. in Biology. His Master’s research focused on developing and implementing digital analysis to evaluate biocompatibility of medical devices. His previous work experience includes more than five years in biocompatibility evaluations using digital morphometric analysis and numerous medical device redesign evaluations. He is currently Associate Faculty at NAU and CCC, teaching classes in Biology and Anatomy and Physiology.
Development of a Biopolymer-Based Compliance Matched Vascular Graft

Speaker: Jonathan Vande Geest, University of Arizona

Ehab Tamimi, Cata Ardila, Marv Slepian, Robert Kellar, Tom Doetschman, Burt Ensley, Jonathan Vande Geest
University of Arizona, Tucson, Arizona
Northern Arizona University, Flagstaff, Arizona

Objective
The long-term objective of our research team is to develop a biopolymer-based tissue engineered vascular graft (TEVG) that is compliance matched to native vascular tissues.

Background
One of the most common forms of heart disease is coronary artery disease (CAD). The need for an alternative vascular substitute is warranted as autologous vessels are oftentimes unavailable due to prior use or cardiovascular disease. Providing a functional tissue engineered vascular graft (TEVG) for coronary artery bypass graft (CABG) surgeries would therefore result in drastic improvements in patient care. Despite significant progress by several research groups in the last few decades, a mechanically and biologically functional TEVG has yet to be developed. The primary goal of this research proposal is to fabricate a TEVG that is composed of non-synthetic polymers arranged in a fashion that mimics native vessel microstructure and that is compliance matched to a native porcine coronary artery.

Methods
Our TEVG constructs are electrospun from several native biopolymers including gelatin, fibrinogen, and human tropoelastin. We have assessed the biocompatibility of our constructs to both smooth muscle cells (SMCs) and endothelial cells (ECs). We have also used two photon microscopy to show that the migration, proliferation, and collagen deposition of our constructs can be fine-tuned by modulating the degree of biochemical stimulus using TGFβ2 (Figure 1, Ardila et al., Biomaterials 2015).

We have also shown that the compliance and biaxial mechanical properties of our 80/20 gelatin/fibrinogen constructs can be further modulated by varying the amount of time each is subjected to glutaraldehyde vapor fixation (Figure 2).

We have also shown that inclusion of human tropoelastin into our 80/20 gelatin/fibrinogen TEVGs results in a construct that displays the classic strain stiffening mechanical response of all soft tissues. Finally, we have utilized a computational optimization scheme where the number and thickness of gelatin/tropoelastin layers is optimized to generate a construct that is compliance matched to a native porcine coronary artery (Table 1).

Figure 1. Migration and collagen production of SMCs in gelatin/fibrinogen constructs stimulated with varying amounts of TGFβ2 (Ardila et al., Biomaterials 2015)

Figure 2. Tubular biaxial mechanical properties of our constructs as a function of crosslinking time. LDCA – porcine left descending coronary artery (in review JBME).
Development of a Biopolymer-Based Compliance Matched Vascular Graft, continued

| Results for Porcine, Compliance = 0.0007 ± 0.00027 mmHg⁻¹ |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Number of Pairs                | Thickness of Gelatin (µm) | Thickness of Tropo (µm) | Crosslinking Time (hrs) | Compliance (mmHg⁻¹) |
| 1                              | 180              | 20              | 7.52             | 0.0007          |
| 2                              | 80               | 20              | 8                | 0.00072         |
| 3                              | 46               | 20              | 8                | 0.00076         |
| 4                              | 30               | 20              | 8                | 0.00081         |
| 5                              | 20               | 20              | 8                | 0.00081         |

Table 1. Computational optimization of a representative gelatin/fibrinogen and tropoelastin construct.

Conclusions
Our laboratory has developed biopolymer-based constructs that mimic the compliance of native vascular tissue. Future work on this project will focus on endothelialization and in-vivo functional assessment of our TEVG.

References

Biography
Dr. Vande Geest is the Principal Investigator of the Soft Tissue Biomechanics Laboratory (STBL) at the University of Arizona. The goal of the STBL is to understand structure-function relationships in soft tissues and use this knowledge to better understand, diagnose, and treat human disease.

The STBL is particularly interested in how the structure and function of soft tissues develop and how mechanical forces play a role in tissue growth and remodeling. Dr. Vande Geest’s laboratory has developed state-of-the-art tools in computational and experimental biomechanics that are poised to address complex challenges in cell and tissue mechanobiology.

Dr. Vande Geest holds appointments in Aerospace and Mechanical Engineering, Biomedical Engineering, the BIO5 Institute, and the Applied Mathematics Program. He also received the Y. C. Fung Young Investigator Award, a society level award from the Bioengineering Division of the American Society of Mechanical Engineers.
Micropatterns Promote Cell Migration for Enhanced Epithelialization

Speaker: Chelsea Magin, Sharklet Technologies, Inc.

Chelsea M. Magin,a Michael C. Drinker,a Dylan B. Neale,b Bradley J. Willenberg,c,d Shravanti T. Reddy,a Gregory S. Schultz,b and Anthony B. Brennana,a

aSharklet Technologies, Inc., Aurora, Colorado, bDepartment of Obstetrics and Gynecology and Institute for Wound Research, University of Florida, Gainesville, Florida, cDepartment of Internal Medicine, University of Central Florida, Orlando, Florida and dDepartment of Materials Science and Engineering and eJ. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, Florida

Nearly 12M wounds are treated in U.S. emergency departments every year. The most costly and debilitating wounds — e.g., severe burns, traumatic lacerations or non-healing/chronic wounds — are often deep, complex, and require reconstruction using autologous skin grafts. Although skin grafting is the current “gold standard” treatment, it is not without serious limitations. While synthetic grafts do not exhibit the same complications, there are currently no treatments that address repair of dermis and epidermis concurrently. Toward the goal of reducing dependence on autologous skin grafting and overcoming the limitations of current wound dressings, we hypothesize that a full-thickness wound dressing with engineered physical guidance cues, including a Sharklet™ micropatterned apical layer, will encourage autologous epidermal healing via guided cell migration.

Smooth (SM) and Sharklet™-patterned (+1SK10x5 and +10SK50x50) samples were fabricated by casting gelatin (Type A 300 g bloom, Sigma) against negative polydimethylsiloxane (PDMS) molds and crosslinking. Circular samples were adhered to silane-treated coverslips and placed in a 12-well plate with features aligned parallel to the direction of cell migration. Samples were treated with fibronectin (15 μg/mL overnight) to enhance cell attachment. PDMS rectangles (3 mm x 20 mm) were placed along the center of the sample to create a modified scratch wound assay. Human epidermal keratinocytes (HEKs) were seeded over the entire configuration at 1x104 cells/cm2 and maintained in complete growth media. At ~70% confluence, rectangles were removed to allow cell migration across the empty patterned area. Migration was monitored until Day 4 when samples were stained with CellTracker Orange and fixed. Fluorescent microscopy images were taken of the wounded area and the average area covered by cells within this region was calculated using ImageJ software.

Results indicate that Sharklet™ micropatterns induce highly oriented migration of HEKs on gelatin surfaces that led to faster closure of a simulated wound in vitro (Figure 1). The +1SK10x5 pattern increased artificial wound coverage by 46%, p=0.045 while the larger +10SK50x50 pattern increased coverage by 64%, p=0.024 compared to SM (ANOVA, Tukey test). Sharklet™ micropatterns use contact guidance to actively orient the direction and speed of migration to accelerate wound closure. As a result, early re-epithelialization in vivo will not only reduce risk of infection and lower patient pain, but it will also initiate the remodeling of underlying granulation tissue, which reduces the possibility of hypertrophic scarring.

Collectively, these results provide a strong foundation for preclinical studies designed to show that micropatterned wound dressings will reduce reliance upon autologous skin grafting by providing a dermal-regeneration template and an improved epithelialization pathway to accelerate wound closure, reduce contracture, and minimize dressing changes.
Micropatterns Promote Cell Migration for Enhanced Epithelialization, continued

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Biography
Dr. Magin is currently the Director of Product Development at Sharklet Technologies, Inc. in Aurora, Colorado. In this role she leads the completion of research and development for medical devices that use the bio-inspired Sharklet surface texture to control biological adhesion. She is an active member of the Colorado Bioscience Association and the Charles C. Gates Center for Regenerative Medicine. Dr. Magin earned her BS with highest distinction in Materials Science and Engineering from the University of Florida in 2006. She subsequently received a Ph.D. in Biomedical Engineering from the University of Florida with Dr. Anthony Brennan 2010, where her doctoral research focused on developing biomaterials to control adhesion of both marine fouling organisms and mammalian cells. During her graduate work, Dr. Magin was both a University of Florida Alumni Fellow and a Clare Booth Luce Graduate Fellow. She recently completed an NIH Postdoctoral Fellowship at the University of Colorado at Boulder in the Anseth Research Group where she developed user-controlled, dynamically tunable biomaterials to study mesenchymal stem cell differentiation and the progression of heart disease in a valvular cell model.

Dr. Magin’s work has been published and presented in internationally recognized venues including the International Congress on Marine Corrosion and Fouling, where she received an award for best poster, and the World Biomaterials Congress. She recently edited and contributed a chapter to the first book in the Wiley-Society for Biomaterials Series entitled “Bio-inspired Materials for Biomedical Engineering.”
Session 6
3D Printing in Medical Applications
3D Printing of Medical Devices at Small Length Scales

Speaker: Roger Narayan, University of North Carolina and North Carolina State University

3D printing is a materials processing approach that is being considered for use in processing a wide variety of biomaterials. The term 3D printing is commonly used to describe processing of three-dimensional objects by selective joining of solids, liquids, or powders in a layer-by-layer manner. We have examined use of 3D printing techniques such as fused deposition modeling, stereolithography apparatus, two-photon polymerization, laser direct writing, and inkjet printing to create medical devices with features that cannot be obtained via conventional approaches. For example, two photon polymerization is a 3D printing approach that involves use of ultrashort laser pulses to selectively polymerize photosensitive materials at small length scales. Structures with well-defined geometries are prepared by polymerizing the photosensitive material along the laser trace. It should be noted that two photon polymerization can be undertaken in a conventional manufacturing environment; no cleanroom facilities or other specialized facilities are required. This approach has been used to prepare structures out of biocompatible inorganic-organic hybrid materials and polymers for medical applications. The use of biocompatible photoinitiators (e.g., a combination of riboflavin and triethanolamine) for two photon polymerization will be considered. Use of two photon polymerization to process medical devices such as microneedles for drug delivery and scaffolds for tissue engineering will be reviewed. Evaluation of two photon polymerization-processed materials using in vitro assays will be described. Several application-specific studies of two photon polymerization-processed structures will be considered. Our results indicate that 3D printing techniques provide unique benefits for processing medical devices with small-scale features.

Biography

Roger Narayan, MD, Ph.D., is a Professor in the Joint Department of Biomedical Engineering at the University of North Carolina and North Carolina State University. He is an author of over 150 publications as well as several book chapters on laser processing and 3D printing of biomedical materials. He currently serves as an editorial board member for several academic journals, including as editor-in-chief of Materials Science and Engineering C: Materials for Biological Applications and as associate editor of Applied Physics Reviews. In addition, Dr. Narayan has edited several well-known books, including the textbook Biomedical Materials (Springer) and the handbook Materials for Medical Devices (ASM International). Dr. Narayan has received several honors for his research activities, including the NCSU Alcoa Foundation Engineering Research Achievement Award, the University of North Carolina Jefferson-Pilot Fellowship in Academic Medicine, the National Science Faculty Early Career Development Award, the Office of Naval Research Young Investigator Award, the Fulbright-Brazil Scientific Mobility Award, and the American Ceramic Society Richard M. Fulrath Award.
How 3D Printing Is Changing Cardiac Care

Speaker: Janelle Schrot, Materialise

Abstract
There is a growing trend towards personalization of medical care, as evidenced by the emphasis on outcomes-based medicine, the latest developments in CT and MR imaging and personalized treatment planning in a variety of surgical disciplines. To support this trend, 3D printing is being used more readily for clinical assessment, training and education of complex and unique cases. Here we will describe the current use and history of 3D printing within the cardiovascular medical and the medical device innovation communities. Case studies performed with leading institutes will demonstrate how 3D printing is changing planning of complex congenital heart disease intervention and valve replacement planning.

Keywords
CT/MRI, image processing, 3D printing, medical devices, patient specific planning, cardiac intervention

Biography
Janelle Schrot manages a biomedical engineering team at Materialise which focuses on cardiovascular applications of Materialise’s technology. Her group particularly focuses on translating medical image data to three dimensions for research, design, testing and additive manufacturing environments. She has focused on additive manufacturing and its uses within the cardiovascular field for the last seven years. Her background is in product design engineering and she holds a degree in mechanical engineering from Grand Valley State University. Schrot serves on the advisory board for Lawrence Technological University for the Biomedical Engineering curriculum and on the advisory board for Society of Manufacturing Engineers (SME) Medical Additive Manufacturing Workgroup.
Tissue engineering has emerged as a promising solution to the limitations of current bone grafting procedures. However, it remains challenging to produce scaffold architectures that approach the complexity and function of native tissues. Emulsion templating is a relatively new method that is capable of producing porous scaffolds through polymerization of high internal phase emulsions (HIPEs) to form porous foams (polyHIPEs). We have previously demonstrated the potential of this system to generate injectable bone grafts with mechanical properties comparable to cancellous bone.\(^1\) We have expanded upon this platform to fabricate grafts with hierarchical architectures by 3D printing the polyHIPE into predefined geometries. Briefly, biodegradable, acrylate-functional macromers are combined with surfactant and photoinitiator, emulsified with water to form a viscous paste, and deposited layer-by-layer into geometric shapes using a HYREL 3D printer equipped with an EMO-25 paste extruder. Emulsions were photocrosslinked using cure-on-dispense (COD) technology to form strong, cohesive shapes. Recently, we were able to create composite scaffolds combining traditional thermoplastic extrusion of poly(lactic acid) with our COD polyHIPEs. These dual material prints mimic the native structure of bone, which is composed of dense cortical bone that confers strength and porous cancellous bone that permits cellular infiltration and remodeling. Scaffolds were evaluated for geometric accuracy and SEM to evaluate porosity and internal construct morphology. This development, as well as the emergence of affordable, open source, 3D fabrication technologies has opened the door for complex 3D scaffold designs such as cellularized and vascularized tissues.

References


Biography

Dr. Cosgriff-Hernández is an Associate Professor of Biomedical Engineering Department at Texas A&M University. Her laboratory specializes in the development of biomaterial scaffolds for tissue engineering applications.
Introduction

Historically, medical providers either relied on 2-dimensional images, virtual renderings or simply waited until the patient was sedated in the operating room for visualizing anatomies of interest. Patient-specific models provide a tool for appreciating complex geometric relationships along with the natural variance between patients. With increasing accessibility of additive manufacturing technology, the opportunity to print patient-specific anatomic models has become an economically feasible tool in clinical workflows; however wide ranges of hardware and software product cost and operations, coupled with time consuming image processing algorithms, have limited widespread implementation of these tools in the clinic.

Methods

Routinely acquired medical imaging studies for congenital malformations and tumors, abdominal aortic aneurysms and developmental or post-traumatic orthopedic abnormalities were processed and printed using a fused deposition modeler. Processing algorithms were developed for CT, CTA, MRI and MRA studies. Example models are shown in Figure 1.

Results

Anatomical models were used to appreciate complex anatomy, evaluate placement and approach for different sizes and types of medical devices, discuss treatment plans with patients and families and facilitate consults amongst providers. Models correlated well with actual anatomy and traditional methods of sizing and measuring for device placement. Additionally, physical models offered an intuitive tool for visualizing both problem and potential solutions.

Conclusions

When preparing for interventions involving complex and/or rare anatomy, physical models offer a reliable, economical and beneficial tool for planning and evaluation. Significant investments of time and resources are required to establish a feasible integration with clinical workflows after which 3D printed models become a cost effective tool for both patients and physicians.
Integration of 3D Printing into Clinical Workflows: Validated Case Studies, continued

Biography
Jennifer started her studies with natural and social sciences followed by Radiography. Based out of Children’s Hospital Colorado, Jennifer earned an A.A.S. in Radiographic Technology from the Community College Denver, followed by a B.S. in Engineering from the Colorado School of Mines (Mechanical Specialty, Bioengineering and Life Science minor). After 3 years in aerospace she transitioned back to the medical field where she currently works for the University of Colorado, Denver, Department of Bioengineering.
Session 7
Neuroendovascular Interventional Devices
Update on Flow Diversion Therapies for Intracranial Aneurysms: Recent Successes and Ongoing Challenges

Speaker: David Kallmes, Mayo Clinic

Biography
As an undergraduate, Dr. David F. Kallmes attended Virginia Polytechnic Institute & State University where he received his B.S in Chemical Engineering. Dr. Kallmes’ educational journey continued at the University of Massachusetts Medical School where he obtained his medical degree. Dr. Kallmes’ residency was carried out at Duke University and thereafter he completed his diagnostic and interventional neuroradiology fellowship at the University of Virginia.

At Mayo Clinic, Dr. Kallmes has done extensive work as a neuroradiologist. His primary area of focus is on the diagnosis and treatment of saccular intracranial aneurysms. His track records include the invention and development of the elastase-induced aneurysm model in rabbits, a model that has been used to test most, if not all, currently used endovascular aneurysm treatment devices. His research lab has also carried out preclinical evaluations for numerous endovascular devices, including the HydroCoil, the Woven Endobridge, and the Pipeline Embolic Device, that led directly to clinical implantation. He remains highly focused and involved in multiple clinical trials. Additionally, Dr. Kallmes has devoted many years to the exploration of vertebroplasty as a viable treatment for compression fractures of the spine. Dr. Kallmes’ research has contributed to the publication of over 400 peer-reviewed papers and he currently serves as a Deputy Editor for Radiology.
Thin Film Nitinol: A Unique Biomaterial for Next Generation Endovascular Devices

Speaker: Colin Kealey, NeuroSigma, Inc

Director of Advanced Development and Medical Affairs
NeuroSigma, Inc.,
Los Angeles, California

Introduction
Thin film nitinol (TFN) is a novel biomaterial fabricated in sheets ~5μm thick on micropatterned silicon wafers using techniques adapted from the microelectronics industry. TFN is distinct from the bulk form of nitinol commonly used in endovascular devices, and potential advantages of TFN include its high purity, low-profile, excellent hemocompatibility, unique mechanical properties, and the ability to produce pores of virtually any shape down to the single micron scale. NeuroSigma Inc. has developed a unique process for fabricating micropatterned three dimensional TFN constructs, such as cylinders and cones, that facilitate use of TFN in endovascular devices. Here we present an overview of NeuroSigma’s TFN technology including the fabrication process, in vitro studies of TFN’s hemocompatibility and biocompatibility, and in vivo studies of a next-generation flow diverting stent based on TFN.

Methods
TFN constructs with different micropatterns were fabricated using sputter deposition techniques. Micropatterned TFN constructs were subjected to a series of in vitro and in vivo studies to examine the hemocompatibility, biocompatibility, and mechanical properties of TFN and TFN-based endovascular devices. More recently, three dimensional TFN constructs were fabricated and used to construct a flow diverting stent for the treatment of intracranial aneurysms with a significantly higher pore density (~70 pores/mm²) and a lower percent metal coverage than current-generation devices. The TFN flow diverter was deployed over 19 model aneurysms and 17 lumbar arteries in the rabbit elastase aneurysm model.

Results
TFN constructs with various micropatterns were successfully fabricated. In vitro hemocompatibility testing in a whole blood flow loop demonstrated that TFN covered stents attracted significantly less blood product deposition than expanded polytetrafluoroethylene (ePTFE) covered stents. Studies of TFN as a cell scaffold demonstrated robust cell growth and the ability to influence cell morphology via different micropatterns. In vivo studies of the TFN flow diverter have demonstrated 75% complete or near complete aneurysm occlusion at 4 and 12 weeks. No lumbar artery occlusions were observed. En face CD31 immunostaining of the aneurysm neck region demonstrated robust endothelial cell growth and an average neck coverage of 75% after 6 weeks.

Conclusions
TFN is a unique biomaterial that with excellent hemocompatibility. Micropatterned TFN can serve as a scaffold for cell growth, where the micropatterns can influence cell morphology, and presumably, cell function. In vivo testing of a TFN-based flow diverting stent for treating intracranial aneurysms demonstrated a high rate of aneurysm occlusion at 4 and 12 weeks, as well as robust endothelialization of the aneurysm neck region. Based on these results, further development of TFN based devices and therapeutics is warranted.
Biography
Dr. Colin Kealey is NeuroSigma’s Vice President of Advanced Development and Medical Affairs and has been with the company since 2011, having previously served as NeuroSigma’s Manager of Business Development and Director of Medical Affairs. In these roles, Dr. Kealey spearheaded development of NeuroSigma’s Thin Film Nitinol (TFN) flow diverter and helped introduce NeuroSigma’s external Trigeminal Nerve Stimulation (eTNS) to major epilepsy centers throughout the EU.

In his current role Dr. Kealey oversees pre-clinical and clinical development of NeuroSigma’s product portfolio and interfaces with key opinion leaders to convey the science behind Neuro Sigma’s products and how they fit into clinical practice. Dr. Kealey has has been Principal Investigator on two National Institutes of Health (NIH) small business grants, and is a liaison to regulatory bodies in the U.S. and EU.

Dr. Kealey received his B.S. in Biochemistry and Molecular Biology from the University of Wisconsin – Madison, and his M.D. from the University of Iowa Carver College of Medicine.
Implanted medical devices such as stents, orthopedic prostheses, and heart valves need to be resistant to corrosion to avoid adverse effects after deployment in the human body. For nickel-containing alloys such as nitinol, this resistance is dependent on the surface condition of the device as well as the alloy composition and microstructure. Optimization of the surface condition is critical and can be characterized by several complementary methods such as electrochemical corrosion testing and surface analysis. Auger Electron Spectroscopy (AES) enables both measurement of the surface oxide layer thickness and investigation of the oxide layer uniformity and elemental composition of electro-polished medical devices. It can be used to provide characteristic information on the surface condition of a device, or localized to highlight differences between various areas of interest or process variations. This paper investigates the use of AES Analysis to characterize resultant surfaces from different electrochemical and chemical processing conditions, environmental exposure, and design features.

Biography
Siobhan Carroll is a principal R+D engineer at Boston Scientific located in Los Gatos, California, specializing in TAVR heart valves. Siobhan is currently leading the development of high cycle fatigue resistant nitinol through microstructural optimization and metallurgical processing. Her other areas of research include corrosion, surface characterization and biocompatibility of medical devices. Siobhan’s experience in the medical device industry over the past seven years has covered permanent implants and delivery systems for self-expandable and balloon expandable cardiovascular devices.

She has over 15 years of experience in metallurgy in industries from medical device, defense and semiconductor working on a wide variety of interesting materials and applications from military vehicles to instrumented wafers. Siobhan holds a B.E. (Mech) from University College Dublin and M.Met from the University of Sheffield.
Surface Quality of Incoming Nitinol Wire Used to Manufacture Braided Implants

Speaker: Carolyn Lahti, Boston Scientific

Boston Scientific Corporation, Maple Grove, Minnesota

The surface quality of medical implants influences the mechanical performance and biocompatibility of the product. In particular for nitinol implants, the surface quality is believed to have an impact in predicting fatigue and wear resistance. In addition, properly passivated surfaces allow for increased corrosion resistance. The incoming surface quality of nitinol wire used to manufacture braided implants must be such that allows for the wire to be etched and electropolished (EP) and still meet dimensional requirements after processing. This study will analyze the surface quality of incoming wire and EP material for Nitinol implants. Scanning electron microscopy (SEM) will be used to obtain images and surface roughness data to determine treatments to minimize surface defects that can cause premature fatigue and low corrosion resistance. This data will also be used to optimize the EP process to reduce the amount of material removed from incoming wire.

Biography
Carolyn Lahti is a R&D Materials Science Engineer at Boston Scientific in the Materials Testing, Analysis, and Characterization department. She provides metallurgical expertise to a wide variety of Boston Scientific products from the Cardiac Rhythm Management and Interventional Cardiology divisions. Her research interests include shape memory alloys for medical implant applications.
Session 8
Drug Coated Balloons
Local Drug Delivery Using Drug Coated Balloons: Insights from Bench to Bedside

Speaker: Elena Ladich, CVPath Institute

The introduction of drug-coated balloons (DCBs) represents a major breakthrough in percutaneous coronary intervention (PCI) as it helped refine pathways of local drug delivery during endovascular procedures. Despite its confirmed efficacy in specific clinical indications, understanding of the underlying biological sequences leading to this profound treatment effect remains a notable scientific gap.

Peripheral artery disease affects approximately 8.5 million Americans and has a growing incidence on a global scale. In contrast to coronary artery atherosclerosis, lesions in the superficial femoral artery (SFA) and below-the-knee are characterized by greater calcium burden, predominantly as sheet-like intimal calcification or isolated medial calcification (Moenckeberg). Any permanent endovascular device is exposed to substantial mechanical forces in the SFA segment owing to anatomical constraints during movement. DCBs combine the benefit of temporary balloon dilatation with unique drug delivery capability, and it is important to understand that there is no class effect of DCB technology. Preclinical investigation of DCBs entails assessment of mechanical balloon and pharmacological effects. Most important in this regard is the evaluation of smooth muscle cell loss, proteoglycan deposition and prolonged fibrin deposition. Investigation of drug tissue levels as well as dedicated examination of endothelial recovery and downstream emboli should accompany preclinical safety studies.

From a clinical perspective, DCB technology has proven effective in the treatment of coronary restenosis and, more importantly, for the treatment of de novo lesions in the SFA segment. While the adoption of DCBs for treating peripheral atherosclerotic lesions represents a landmark in the evolution of percutaneous interventional procedures, further studies are needed to reveal their relative merits in other circulatory territories.

Biography
Dr. Ladich currently serves as the Chief of Anatomic Pathology at CVPath Institute in Gaithersburg, Maryland. CVPath Institute is a leading medical research and education organization dedicated to improving patient health management for those suffering from cardiac and vascular diseases. The institute’s mission is to conduct basic and translational “bench to bedside” research. They provide consultation, histology, and diagnostic services to promote discoveries that advance diagnosis and treatment of cardiovascular diseases.

Dr. Ladich has been trained in both cardiovascular pathology and was a recipient Callendar-Binford Fellow in the Department of Environmental & Toxicologic pathology at the Armed Forces Institute of Pathology in Washington, DC. Dr. Ladich completed both her medical training and residency in Anatomic and Clinical Pathology at Georgetown University School of Medicine and has been board certified in both. Dr. Ladich has authored and co-authored nearly 30 scientific publications in peer-reviewed journals and more than 10 book chapters.
**Inhibiting Intimal Vessel Hyperplasia through Local Delivery of Anti-Proliferative Drug: Medtronic Drug-Coated Balloon**

*Speaker: Claudio Silvestro, Medtronic, plc*

Claudio Silvestro and Susan R. Peterson

1 Research & Development Department, Medtronic Aortic and Peripheral Vascular, Santa Rosa, California

**Introduction**

Peripheral arterial disease (PAD) is a common circulatory problem manifesting as a narrowing of peripheral arteries, (i.e., any artery not supplying the brain or the heart). The reduced blood supply due to PAD mostly affects the legs, causing claudication, skin ulcers and tissue damage that may result in amputations. In the United States alone, PAD affects nearly 20% of those aged 65 and older.

Symptomatic PAD was historically treated with surgical bypass. Less invasive endovascular treatments, however, are now the first-line option when medical therapy fails. The most widely adopted procedure is percutaneous transluminal angioplasty (PTA) with provisional stenting. A catheter is used to reach the diseased vessel and a balloon inflated to treat the stenosis; if needed, a metallic scaffold (stent) is implanted to keep the lumen patent to blood flow.

The aforementioned options only act at a mechanical level and do not interfere with the biological mechanisms responsible for lesion growth in the vessels. Medtronic was among the first to pioneer anti-proliferative drug use to block restenosis, without the need for a permanent implant. Research and development has led to the IN.PACT™ Admiral™ drug-coated balloon (DCB) catheter platform (Figure 1), with FDA approval granted in December 2014.

**Methods**

**PTA Platform**

The Admiral Xtreme balloon catheter, a proven technology for treatment of stenotic lesions in the superficial femoral artery (SFA) was selected as the basis for IN.PACT Admiral.

**Pharmaceutical Ingredient**

Paclitaxel, a potent mitotic inhibitor, is the active pharmaceutical ingredient of IN.PACT Admiral. This lipophilic drug is retained well in biological tissues and interferes with cellular DNA synthesis, eliminating smooth muscle cells responsible for restenosis. These factors make paclitaxel ideal to achieve long-term restenotic inhibition. Multiple benchtop and preclinical studies were conducted to identify the optimal drug content and concentration to be used for balloon coating.

**Excipient**

Urea was identified as the excipient to be combined with paclitaxel to facilitate drug release. Urea is a natural substance with low toxicity and hypersensitivity reactions. During inflation, the balloon unwraps and the coating is exposed to the blood stream and vessel wall. Urea’s hydrophilicity allows rapid drug transfer to the vessel.

Figure 1. A rendering of the Medtronic DCB device inside a peripheral artery to treat stenotic lesions.

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Results
Clinical studies have shown IN.PACT Admiral to have excellent in vivo safety and efficacy (Table 1), with the highest primary patency, as well as the lowest target lesion revascularization (TLR) and binary restenosis for PAD treatment (Figure 2).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>DCB (n = 220)</th>
<th>PTA (n = 111)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary efficacy – primary patency</td>
<td>82.2%</td>
<td>52.4%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Clinically driven TLR</td>
<td>2.4%</td>
<td>20.6%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Primary sustained clinical improvement</td>
<td>85.2%</td>
<td>68.9%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Target limb major amputation</td>
<td>0.0%</td>
<td>0.0%</td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>1.4%</td>
<td>3.7%</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Figure 2. Comparative data for PAD therapies.

Conclusion
IN.PACT Admiral provides physical dilation and targets the biological mechanisms at the origin of arterial stenoses. A science-based approach was used to develop each of the device components. Clinical results confirm IN.PACT Admiral to be the most effective long-term treatment option for endovascular treatment of PAD.

Biography
Claudio Silvestro is a Research & Development engineer for the Santa Rosa, California-based Aortic and Peripheral Vascular division of Medtronic, a major player in the medical device manufacturing industry. Prior to working on combination devices in the U.S., Claudio worked for Medtronic Invatec (Brescia, Italy) with different roles on several peripheral catheters R&D projects.

He earned a B.Sc. and M.Sc. in Biomedical Engineering from the Politecnico di Milano (Milan, Italy) and joined California Institute of Technology (Pasadena, U.S.) as a visiting student in 2010.
Drug Delivery to the Vessel Wall: Coated Balloons and the Role of the Excipient

Speaker: Nathan Lockwood, SurModics, Inc

Nathan Lockwood, Rick Murphy, Joram Slager
SurModics, Inc., 9924 W 74th Street, Eden Prairie, MN 55344, USA

Diseased vessels occluded with fat and calcium deposits are typically treated by angioplasty and stenting to restore blood-flow. However, in some coronary and many peripheral sites stenting may be complicated or not an option at all. Albeit an effective treatment in the short term, angioplasty alone typically fails to keep vessels open permanently. Without local drug treatment the trauma from angioplasty usually results in hyperplasia of arterial smooth muscle cells, causing restenosis. Recently, the development of new technologies has enabled the local delivery of anti-restenotic drugs such as paclitaxel or sirolimus directly from the surface of a coated angioplasty balloon (DCB). This way, lesions can be treated where placement of devices such as drug-eluting stents is less preferred [1, 2].

To effectively deliver drug from the surface of a DCB, excipients are needed to:

• minimize drug loss from the DCB during its introduction and movement to the targeted lesion in the vessel wall
• permit release of the drug particles to the intima of the lesion within the timeframe of balloon inflation against the vessel wall, and
• promote drug adhesion to the vessel wall after deflation of the balloon and restoration of the blood flow

The success of SurModics’ DCB program is based on the discovery of excipients that answer all of these requirements. To better understand the mechanism of the excipient mediated drug transfer, an in vitro assay was developed looking at differences in drug adsorption to an extracellular matrix (ECM). SurModics’ excipients were compared to iopromide, known to be used as an excipient in various commercially available DCBs. In addition, differences in adhesion were assessed as a result of seeding different cell types (such as endothelial cells or smooth muscle cells) on top of the ECM.

This talk will give an overview of the successful development of SurModics’ paclitaxel DCB platform SurVeil™ and delve into some of the mechanisms underlying excipient mediated drug transfer to arterial vessel surfaces.

References

Biography
Nathan Lockwood, Ph.D. is Director of Research & Development at SurModics, Inc. in Eden Prairie, MN. He has spent a decade at SurModics—first as a scientist and later in management—developing novel materials, processes, and technologies that enhance the performance of medical devices. Nathan can be reached at nlockwood@surmodics.com.
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