2004 Buyers' Guide Inside

BIOMATERIALS FORUM

First Quarter 2004 • Volume 26, Issue 1

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Special Interest Group

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BIOMATERIALS FORUM

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Special interest Group Reporters

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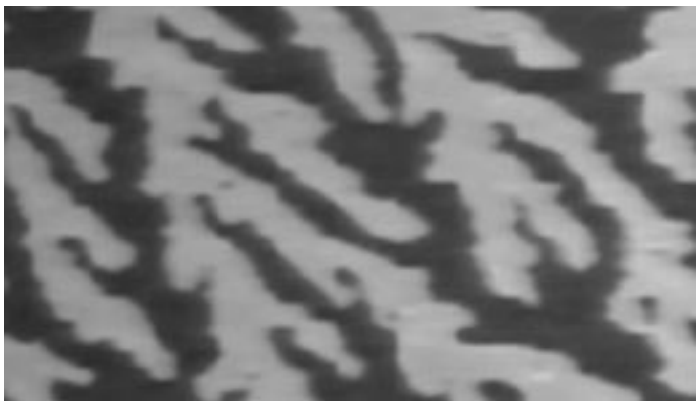
Features



AFM image of PEG crystallized on cationized SAM (HS(CH2)16COO-Na+). Image provided by NESAC/BIO (NIH Grant EB-002027), University of Washington. Courtesy of the Surface Characterization and Modification Special Interest Group.

Departments

From the Editor

By Martine LaBerge, Executive Editor

From Concept to Market: Bridging Academia and Business

Over the past years, the medical device industry has seen an explosion of possibilities for the marketing of new ideas. With the evolution of knowledge in the field of biomaterials, numerous new products and technologies have been introduced for clinical use. Competition is in an effervescent trend! During the past few years, the traditional research and development (R&D) of medical devices conducted by manufacturers has been commonly, and mainly, replaced by the development (D) of medical devices; research (R) is a combined effort with universities. This teamwork has a positive impact on the innovation and performance of devices. The First Quarter issue of *Biomaterials Forum* for 2004 highlights several successful examples resulting from teamwork between university and industry. Featured are two very active Special Interest Groups (SIGs), the Cardiovascular Biomaterials SIG and the Advances in Metal Surfaces, Characterization, and Modification SIG, that exemplify the benefits of collaboration between academia and industry to bring products from concept to market.

Since its establishment in the early 70s, the Society For Biomaterials has clearly promoted an open communication between industry, academia, government, and regulatory agencies. Workshops, town meetings, and panels have been held at annual meetings of the Society to promote exchange between these different groups. Over these years, traditional education and academic research in biomaterials has been challenged to provide innovative and integrated education programs that better answer the needs of the biomaterials industry and bridge the communication gap. Leadership and entrepreneurial skills have been emphasized as highly desirable in biomaterials graduates to better understand the industrial culture and market. Even though few biomaterials academic programs integrate business, leadership, entrepreneurship, or regulation in the training of their students, the industry leaders of tomorrow formed in universities can be made aware of the importance of communication by being involved in joint projects with industry as demonstrated in this issue. *Biomaterials Forum* invites its readers to share their experience with innovative education or research programs that fostered and integrated teamwork with industry and led to success stories as depicted in this issue; something to add to a New Year's resolution list!

The editorial staff of *Biomaterials Forum* wishes members and friends of the Society For Biomaterials a prosperous and successful year in 2004. We look forward to informing you about the latest news within the biomaterials community and the Society, and to your active participation.

Happy New Year!

Membership

By Richard Gemeinhart, Membership Committee Chair

Streamlining New Member Applications

Scientists often hear the words interdisciplinary, collaboration, and inclusiveness. The Society For Biomaterials is at the forefront of collaborative, interdisciplinary science and must update our membership admission process to allow for new and prospective members to become active members. In the last issue of *Biomaterials Forum*, the membership committee outlined some of the general topics that were identified as limiting new membership. One issue not addressed is the election of members; this is a major hurdle to overcome for many prospective members, specifically in years when a quorum is not reached during the annual meeting.

The current bylaws require that the Membership Chair present all applicants to the Society during the annual meeting, at which time the membership must approve the new members by a three-quarters majority. This means any potential member who applies in April or later (the annual meeting is typically in April or May) will not be an official member until the annual meeting the following year. There are membership applications still pending that were submitted just prior to the annual meeting in Reno in April 2003. If a quorum is not attained at the 7th World Congress in Sydney, Australia, these applicants will need to wait another year to become members! To rectify this situation, the membership committee is in the process of suggesting changes to the bylaws that will maintain the high standards of membership in the Society but also expedite the process of becoming a member. Several alternatives are being considered, all of which would shift the voting responsibilities from the membership to the membership committee. This would involve a change in the bylaws and must be approved by the membership. When the final version of the proposal is established, it will be distributed at least 30 days prior to the annual business meeting as required in the bylaws for vote. The committee will keep the members updated on this issue in future issues of *Biomaterials Forum*.

The Society For Biomaterials is at the forefront of collaborative, interdisciplinary science and must update our membership admission process to allow for new and prospective members to become active members.

In addition to the bylaws change, a subtle change in the eligibility criteria for Active Membership is being suggested to the Board of Directors. This change would add receipt of a doctoral degree in an area relevant to biomaterials as one means of demonstrating activity in the field, which is one of the criteria for active membership. Most applicants for active membership hold a PhD, MD, DDS, or DVM degree. This change in criteria would simplify the process of determining who is eligible for membership and be a benefit for potential members commencing collaborative research that does not yet have biomaterials publications or those in industry. This subtle change will allow the membership committee to nominate more members for active membership and more potential members should then apply since they will be eligible for active, not associate, member status. The membership committee believes this change, in combination with a bylaws change and the change in meeting fee structure (discussed in the last issue of *Biomaterials Forum*), will itself prompt an increase in membership.

The final suggested change to the criteria for membership is the addition of a postdoctoral associate category. This category would be similar to the student associate category, although at a slightly higher fee that has not yet been determined. Individuals would need to supply an official transcript stating the date of conferral of the doctoral degree. The postdoctoral associate member would only be eligible to maintain their status at this level for three years following the conferral of the doctoral degree. At the end of the term, the member would be asked to reapply as either associate or active member. The membership committee believes this reduced rate term will have the advantage of maintaining members early in their scientific career who may not be able to afford to belong to several societies. The expectation is that members will advance to active status and remain contributing members of the Society. The committee believes the three-year term restriction is important and only those recently graduating qualify for this category. It is also important to note that this category would apply to all doctoral degrees; employment status of the individual would not determine postdoctoral status, so industrial scientists would be given the same benefit as academic and governmental members. The membership committee believes this may prompt more participation from industrial members as well as those doing residencies and fellowships.

The membership committee strongly believes these changes will have an immediate impact upon the membership of the Society. These are only suggestions at this point, but it is believed that the membership should be kept updated on progress made since some may feel these issues are potentially controversial. None of these suggestions will weaken the Society in any way, and the changes will, in fact, strengthen the Society by increasing active membership, collaboration, and interdisciplinary participation. If any member would like more details on these suggestions, or to comment on the suggestions, please contact the membership chair, Richard A. Gemeinhart (rag@uic.edu), or another member of the membership committee.

Education and Professional Development Committee:

By Joel D. Bumgardner and Kay C. Dee

Resources for Building Your Professional Career

This is the first in a series of articles sponsored by the 2003-2004 Education and Professional Development committee reviewing books and resources for building a successful biomaterials career. An understanding of the scientific/engineering enterprise and skills necessary to succeed are rarely part of our education and training. And the skills and ability to navigate a constantly changing and evolving career are part of our continuing professional development. In particular, for young scientists/engineers just beginning their careers, issues regarding choosing career paths, giving presentations, convincing a university, governmental agency or industrial organization to hire you, and/or what is involved in promotions, teaching, and obtaining funding are obstacles often not well defined or understood. This article reviews two books, "Advice for New Faculty Members," and "Academic Scientists at Work: Navigating the Biomedical Research Career," aimed at describing how to successfully meet many of the challenges individuals may face in developing an academic career. These books also provide an excellent primer for sharpening the skills of current faculty. It is strongly suggested that students and faculty not just read the books, but include them as part of discussions in student chapter or lab meetings, and/or in special courses/seminars/workshops. Please feel free to make comments or suggest other books/resources to Joel D. Bumgardner (jbumgard@abe.msstate.edu), chair, or any of the other members of the education and professional development committee.

Academic Scientists at Work:
Navigating the Biomedical Research Career
by Jeremy M. Boss and Susan H. Eckert
Kluwer Academic/Plenum Publishers, New York, 2003

Available through Kluwer (www.kluweronline.com) for $36 or amazon.com starting at $32.32.

This book is aimed at graduate and post-doctoral students interested in planning a career in academics. Scientists and engineers interested in moving into academic positions also will find this book helpful. The book covers the full spectrum of challenges facing scientists/engineers, including preparing for the first job, business and lab management practices, teaching, mentoring, service, and promotion and tenure. What is special about this book is it provides samples of cover letters, curriculum vitae, forms for comparing job positions, lab management protocols, budgets, and outlines for preparing manuscripts and grant proposals. Blank copies of the sample forms are also provided on the accompanying CD-ROM. The book is based in part on the careers of the two authors, their colleagues, and on an extensive survey of faculty at different career stages.

The book is organized into three parts, beginning with getting a position and ending with the promotion and tenure process. Part I begins by discussing how to find positions, writing cover letters, what to expect during the interview process, negotiating your position, and how to compare multiple offers. Once you begin, issues regarding setting up your lab or office, strategies for obtaining funding, preparing budgets, and the grant review process are discussed. Forms for keeping up with and tracking supplies and equipment are well organized. Tips on hiring technicians, post-docs, and graduate students, getting along with other faculty members, as well as how to say "no" are also provided. The ability to say "no" is a particularly important skill since many assistant professors are eager to show their worth and run the risk of over-extending themselves to the detriment of their professional and personal lives.

Part II covers topics on establishing and building your career. This section begins by providing tips on how to organize your research program, discussing the importance of manuscript preparation and submission, including what is a minimal publishable unit, and handling critiques. The guideline on how to approach writing a paper and grant is particularly good for those who struggle with writing. The chapter on teaching realistically details the commitment needed for successfully preparing lectures as well as undertaking teaching evaluations and developing a teaching c.v. Additional information is provided on how to mentor students and on undertaking departmental, university, and professional service duties.

The final part of the book steps through the process for promotion from an assistant professor to an associate professor with tenure. Tips for preparing the promotion and tenure application are provided as well as information on what to do if the process does not work out for you. Detailed comments and insight are also provided from faculty at all stages of their careers.

I found this book to contain much useful information regarding the business end of academics (i.e. managing a lab and personnel, preparing budgets, etc). While it is difficult to cover all the topics in detail, and some of the information may come across as overly general, the inclusion of sample forms to be used and/or adapted makes the book a valuable resource and one that I would strongly recommend to young faculty, post-docs, and graduate students.

Advice for New Faculty Members
by Robert Boice
Allyn & Bacon, Needham Heights, MA, 2000

Available through amazon.com for $35.

This book is not just for new faculty. The book presents and illustrates practical techniques for working with constancy and moderation as a way to become more efficient and productive and therefore happier with your job performance. It will be useful to graduate students writing papers and dissertations,

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James Anderson Elected to National Academy of Sciences' Institute of Medicine

James M. Anderson, MD, PhD, was elected to membership in the Institute of Medicine of the National Academy of Sciences, effective October 1, 2003. Members are elected by the incumbent membership on the basis of professional achievement and demonstrated interest, concern, and involvement with problems and critical issues that affect the health of the public.

Dr. Anderson is an internationally recognized scientist in the area of tissue responses to biomaterials, medical devices, and prostheses. His expertise is broad-based, ranging from fundamental biomaterials research, to clinical device retrieval and evaluation, to policy development. He has made pioneering and significant advancements in the understanding of biological information, such as new biological design criteria for the development of new materials and prostheses that modulate cellular interactions at implant interfaces.

His recent studies on the surface-dependent mechanisms of foreign body giant cell formation, and the apoptosis of adherent inflammatory cells as a mechanism for the persistence of cardiovascular infections provide insight and information into the development of materials and therapies for enhancing the performance of medical devices and prostheses.

Dr. Anderson has provided significant leadership and unique contributions to the science and engineering of biomaterials and medical devices through his interactions with the National Institutes of Health (NIH), Food and Drug Administration (FDA), International Standards Organization (ISO), and the American Institute for Medical and Biological Engineering (AIMBE). As evidence of the quality of his research, he is the recipient of the only NIH/NHLBI Merit Award in biomaterials.

Dr. Anderson is a 1963 chemistry graduate of the University of Wisconsin-Eau Claire. He earned a doctorate in chemistry from Oregon State University in 1967, and a Doctor of Medicine degree in 1976 from Case Western Reserve University School of Medicine. He has authored and co-authored more than 300 publications in areas related to biomaterials. He is the Editor-in-Chief of the *Journal of Biomedical Materials Research*, an official journal of the Society For Biomaterials, current president of the Controlled Release Society, and a consultant to industry, NIH, and FDA.

The Society For Biomaterials congratulates Dr. Anderson!

Officer Nominees

The task of selecting the slate of Officer Nominees for 2004 has been completed. Following are the nominees for President-Elect and Member-at-Large. The Society encourages all members to cast their vote for the candidate of their choice. Ballots will be distributed to members shortly.

Included in this feature is a brief description of the responsibilities of each position, along with a description of the nominees' biographical background and their Society experience. Each nominee has also developed a vision statement for the Society that they would work to achieve should they be elected.

President-Elect

The President-Elect shall become familiar with the duties of the President and shall at all times cooperate and assist with the duties of that office. In the absence of the President, the President-Elect shall preside at the meetings of the Society, and the Council and the Board of Directors, and perform the duties and exercise the powers of President. The term of office is for a period of one year without succession. The President-Elect is the chairperson of the Long Range Planning Committee.

Nominees for President-Elect

Mutlu Karakelle

Mutlu Karakelle currently is Senior Director of Surgical Products Research at Alcon Research Ltd., in Forth Worth, Texas. He earned his Ph.D. in materials science and engineering from the University of Utah. His research focus area is ophthalmic implants and intraocular lenses, with an emphasis on their long-term biocompatibility and *in vivo* performance.

Mutlu has been a member of the Society For Biomaterials since 1997. He is the chairperson of the Reference Materials and Reference Data Subcommittee and a member of the Liaison Committee. He also has served on the Long Range Planning committee. His involvement in the Society For Biomaterials has also been as an invited speaker, symposia organizer/moderator, abstract reviewer, and chairperson/vice chairperson of the Ophthalmic Biomaterials Special Interest Group.

Vision Statement:

We are engaged in science and engineering in an effort to improve people's lives by discovering or innovating new and improved medical therapies. Our research activities vary from establishing scientific foundations to product design, from defining its engineering principles to developing novel test methods. A vast number of cross-disciplinary teams of scientists and engineers from biology, bioengineering, biostatistics, cell biology, chemistry, chemical engineering, clinical sciences, electrical engineering, mathematics, computer science, materials science, mechanical engineering, medicine, molecular biology, pharmacology, physics and many more other disciplines are actively pursuing academic or industrial biomedical research and development. We have been enormously successful in improving people's lives. Cardiovascular devices, intraocular lenses, orthopedic implants, and many other devices are giving patients a second chance in pursuing an active and fulfilling life. A large number of medical devices, implants, and instruments are playing important roles in saving lives every day. The Society has played a key role in bringing scientists and engineers together, facilitating sharing of information, and helping to establish a scientific foundation to guide research and innovation.

There are a number of societies that are currently working toward the same general goal using different pathways. However, the

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Michael V. Sefton

Michael Sefton is University Professor and Director of the Institute of Biomaterials and Biomedical Engineering at the University of Toronto. He is also a Professor in the Department of Chemical Engineering and Applied Chemistry, University of Toronto. His research interests include cardiovascular biomaterials, microencapsulation of cells, and tissue engineering. His research is based on the premise that a biomaterial is an agonist of a biological response, much like a drug can be. However, because the biomaterial is a solid, the interactions with the biology are more complex. Responses of current interest include thrombogenicity, inflammation and immune response, angiogenesis, and wound healing.

Michael was educated at the University of Toronto (B.A.Sc., 1971) and at M.I.T. (Sc.D., 1974). He has been at the University of Toronto since 1974. He was awarded the Clemson Award of the Society For Biomaterials for Basic Research in 1993. He is the 1992 recipient of the teaching award of the Faculty of Applied Science and Engineering. In 1988, he was awarded the Albright and Wilson Americas Award of the Canadian Society for Chemical Engineering (CSChE) in recognition of his contributions to research on the application of chemical engineering principles to medical problems, especially related to tissue engineering and biomaterials. He was one of only 20 given a Century of Achievement Award by the CSChE in 1999. He was until recently an Associate editor of the journal, Biomaterials, and is/was on the editorial board of almost every other journal in biomaterials, controlled release, and tissue engineering. He is a Fellow of the American Institute of Medical and Biological Engineering, the American Institute of Chemical Engineering, the Chemical Institute of Canada, and of Biomaterials Science and Engineering. In addition to being a member of the Society For Biomaterials and the Canadian Biomaterials Society, he is also a member of the Controlled Release Society, the Biomedical Engineering Society, the Tissue Engineering Society International (TESi), and both Canadian and American Chemical Engineering Societies. He is also a professional engineer in Ontario. He was recently a member of the Surgery and Bioengineering study section of the U.S. National Institutes of Health. He was named University Professor, an honor reserved for 1% to 2% of the faculty at the University of Toronto.

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Member-at-Large

The Member-at-Large shall serve as an unencumbered representative of the membership at meetings of both the Board of Directors and Council. The Member-at-Large shall serve for a period of one year.

Nominees for Member-at-Large

Alan S. Litsky

Alan Litsky is an associate professor of Biomedical Engineering and Orthopaedics at Ohio State University (OSU), where he also serves as Director of Orthopaedic Research. He earned his medical degree from Columbia University's College of Physicians and Surgeons and his Sc.D. in Materials Science and Engineering from M.I.T. Alan is Director of the Orthopaedic Biomaterials Laboratory at OSU. His research focus is hard-tissue biomaterials with an emphasis on new materials for orthopaedic and dental applications, including development and evaluation of a reduced-modulus acrylic bone cement and a hydroxyapatite-metal alloy composite for net-shaped manufacture of musculoskeletal implants. Continuing research projects include quantifying the micromotion between components of total hip arthroplasties, the use of shape-memory alloys for fracture fixation, and the fatigue behavior of external fixators and dental prostheses. Alan teaches three courses on biomaterials (fundamentals of biomaterials, hard-tissue biomaterials, and tissue mechanics) and a course on professional and ethical issues in biomedical research.

Alan has served on the Orthopaedic study section at the National Institutes of Health and on the American Academy of Orthopaedic Surgeons' Basic Science Evaluation subcommittee. He is currently chair of the Arthritis Foundation's Technology and Biomechanics study section and sits on the editorial boards of Technology and Health Care and the Annals of Improbable Research. He is a regular reviewer for the Society's Journal of Applied Biomaterials and for Clinical Orthopaedics and Related Research. He is an active participant in the Orthopaedic Research Society and the Society For Biomaterials.

Alan's involvement in the Society For Biomaterials includes review of abstracts for the annual meetings, service on the program committee, membership in the Orthopaedic Special Interest Group (SIG) (vice chair 1999-2000, chair 2000-2001), and the Education and Professional Development Committee (chair 2001-2003). He was a founding member of the Biomaterials Education SIG. He currently serves on the Membership Committee and the Awards, Ceremonies, and Nominating Committee, as well as continuing his participation on the Education and Professional Development Committee. Alan has been an active participant in workshops and plenary sessions at recent Society meetings.

Vision statement:
If elected Member-at-Large, I intend to serve as the voice of the membership at Council meetings, bringing the suggestions and concerns of all Society members to that forum. In particular, I hope to encourage and support increased student involvement in Society decision-making processes. One specific project I hope to accomplish, with input from all aspects of the Society, is the development of a Code of Professional Conduct to serve as a guidance document for members and for other professionals in the field of biomaterials.

Antonios G. Mikos

Antonios G. Mikos is the J.W. Cox Professor of Bioengineering and Chemical Engineering at Rice University. He is the Director of the J.W. Cox Laboratory for Biomedical Engineering and the Director of the Center for Excellence in Tissue Engineering at Rice University. He received his Dipl.Eng. (1983) from the Aristotle University of Thessaloniki, Greece, and his Ph.D. (1988) from Purdue University, both in chemical engineering. From 1990 to 1991, he was a post-doctoral fellow at the Massachusetts Institute of Technology and Harvard Medical School. He joined the Rice faculty in 1992 as the T.N. Law Assistant Professor of Bioengineering and Chemical Engineering. He was promoted to Associate Professor in 1996 and to Professor in 1999. During 1998, he was a Visiting Professor at Case Western Reserve University and the University of Utah.

Antonios' research contributions have been in the synthesis, processing, and evaluation of new biomaterials for tissue engineering, scaffolds for three-dimensional cell culture, conduits for guided tissue regeneration, substrates for targeted cell adhesion, carriers for controlled drug delivery, and non-viral vectors for gene therapy. His research has led to the development of novel orthopaedic, cardiovascular, neurologic, and ophthalmologic biomaterials. He is the author of more than 250 publications, 100 proceedings, 170 abstracts, and 17 patents. He is the editor of six books, including Frontiers in Tissue Engineering (Elsevier Science, 1998), as well as the editor of nine journal special issues. In addition, he has given more than 70 invited seminars and 350 scientific presentations.

Antonios was elected a Fellow of the International Union of Societies for Biomaterials Science and Engineering in 2000 and the American Institute for Medical and Biological Engineering in 1999. He has been recognized by various awards, including: the 2003 Huygens Lectureship of the Netherlands Organization for Scientific Research, the 2001 Clemson Award for Contributions to the Literature of the Society For Biomaterials, the 2000 Phoenix Pharmazie-Wissenschaftspreis, the 1998 Young Investigator Research Achievement Award of the Controlled Release Society, the 1996 Outstanding Young Investigator Award of the Materials Research Society, the 1994 Whitaker Young Investigator Award of the Biomedical Engineering Society, and the 1991 Victor K. LaMer Award of the American Chemical Society. He was also the recipient of a FIRST Award of the National Institutes of Health in 1996.

Antonios has supervised 15 Ph.D. and four M.S. theses, and is currently supervising the research of 15 additional Ph.D. graduate students. He has trained 17 post-doctoral fellows and supervised the research of 60 undergraduate students at Rice University. He is a founding member of the Bioengineering Department at Rice University (1997). He is the organizer of the Continuing Education Course, "Advances in Tissue Engineering," offered annually at Rice University since 1993.

Antonios is a founding editor of the journal *Tissue Engineering* and member of the editorial boards of the journals *Biomaterials* (Special

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Advances in the Development of Coronary Stents

Feature

By Joan Zeltinger, Eric Schmid and Don Brandom, REVA Medical, Inc., San Diego, and Durgadas Bolikal, Aaron Pesnell, and Joachim Kohn, New Jersey Center for Biomaterials, Rutgers University, Piscataway, N.J.

Given the high incidence of coronary artery disease and associated mortality, there is a constant effort to improve upon the stent therapies available to patients. Stents are small, wire-mesh tubes that are commonly made of stainless steel or Nitinol. These devices are tightly secured on a balloon catheter and are gently guided to an area of occlusion within the coronary arteries. Once properly placed, the balloon is pressurized, resulting in the expansion of the stent and diseased blood vessel wall. The balloon catheter is then retracted, and the stent remains in place, providing mechanical support to keep the blood vessel open for increased blood flow to the heart.

Recently, drug-eluting stents have been introduced into clinical use. These stents were shown to reduce significantly the build up of tissue (in-stent restenosis)[1] that occurs after the injurious effect of stent delivery.[2-3] Commonly, metal stents are coated with a thin, usually nonresorbable polymer that serves as the drug reservoir. In this way, a small amount of a highly potent drug can be delivered over a short period (usually 30 days).[4-5] After the drug elutes from the thin polymer coating, the metal stent and the residual polymer coating remain in place. Over time, the permanent presence of the nonresorbable device may lead to complications at the implant site.[6]

Dr. Colombo, a clinical thought leader,[7] and others recognized healing of vessel plateaus in animals and patients around six months after treatment,[8-10] indicating that a stent may only be needed temporarily. This realization is the driving force behind several attempts to develop fully resorbable polymer stents. In addition, such resorbable polymer stents can serve as a platform for the site-specific delivery of larger quantities of drugs.

Tamai and colleagues[11] were the first to show in humans that resorbable stents, prepared of poly(lactic acid), are clinically feasible. However, the stents required expansion with a heated balloon, which represented additional risks to the patient. The Tamai stent has therefore not been commercialized.

Another disadvantage of stents made of poly(L-lactic acid) and similar polymers is their lack of visibility by X-ray radiography/fluoroscopy. This is a critical disadvantage as the physician relies on X-ray images to guide the stent to the location of the diseased vessel, as well as monitoring the performance of the stent after implantation. This disadvantage has contributed to the limited clinical and commercial acceptance of resorbable polymer stents.

In principle, however, clinical leaders in stent therapy agree that resorbable stents have the potential to be superior to metallic devices.[7,12] First, resorbable stents would alleviate complications associated with re-intervention. Second, resorbable stents may enable clinicians to treat not only the injurious effect of stent delivery but also the focal disease as they afford greater freedom in the design of site-specific drug delivery. Elution of a drug from a resorbable stent, essentially a mechanical stent pill, should allow simple and versatile drug delivery schemes to resolve complex coronary atherosclerotic lesions, reoccurring lesions, or other disease states such as vulnerable plaque. The most clinically efficacious approach will likely be a stent platform that delivers therapeutics acutely and over a longer-term (>30 days) and delivers more than one agent.

To address the significant challenges associated with the development of a fully resorbable, drug eluting stent, Dr. Joan Zeltinger of REVA Medical established a collaboration with the New Jersey Center for Biomaterials under Professor Joachim Kohn to design a revolutionary new stent, referred to as "Casper."

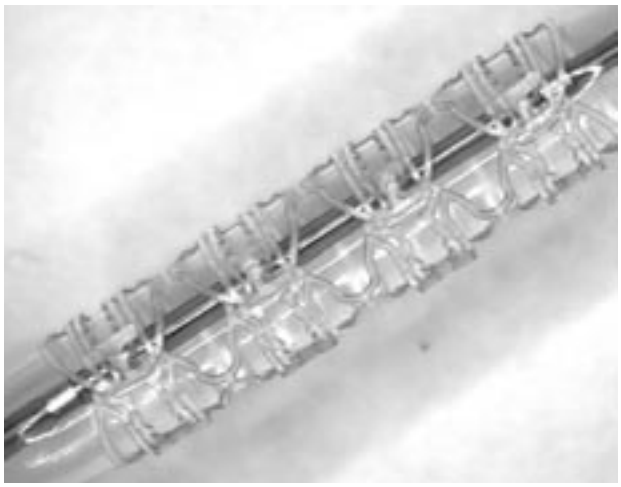

Figure 1: *A balloon-expandable, slide-and-lock CASPER stent.*

Casper stents resulted from the convergence of a new stent design (Figure 1) and a new polymer design strategy (Figure 2).

REVA Medical has developed an enabling technology for polymer stents to be comprised of any load-bearing polymer. The proprietary stent design eliminates the need for material deformation using a slide and lock ratchet mechanism. This design addresses the fact that polymers and metals have fundamentally different physico-mechanical properties. Polymers crack faster under deformation than metals, they exhibit creep under stress much more than metals, and they have significantly

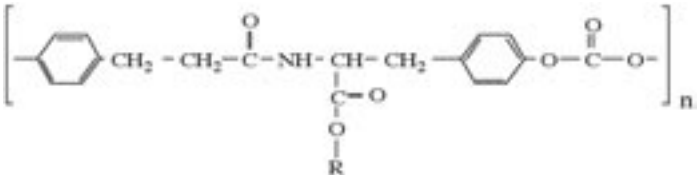

Figure 2: *General chemical structure of tyrosine-derived polycarbonates. The pendent chain "R" is usually an alkyl group such as ethyl, butyl, hexyl or octyl. In REVA's current studies, the pendent chain is ethyl. The corresponding polymer is poly(DTE carbonate). When R is a simple hydrogen, the repeat unit is desamino-tyrosyl-tyrosine, referred to as "DT." The incorporation of such DT units has a dramatic effect on the rate and mechanism of polymer resorption.*

less stiffness and strength than metals. Attempts by others to simply replace the metal by a polymer while using a balloon-expandable, metal-stent design have consistently failed in the past, even with a strong polymer such as poly(L-lactic acid).

Even though REVA's slide-and-lock stent design enables the use of polymers for stenting, the stringent performance requirements of a stent impose significant demands on the polymer properties; none of the off-the-shelf polymers appeared to fulfill the complex requirements for stents.

Dr. Kohn therefore postulated that a new materials approach was needed to provide vascular biocompatibility in addition to tunable resorption, radiopacity, and higher mechanical strength than most other degradable polymers. Using tyrosine-derived polycarbonates (Figure 2) as the material platform, Dr. Kohn has shown that this family of polymers provides considerable freedom in optimizing material properties. For example, tensile strength can be altered through modifications in the polymer pendent chains, exceptional hemocompatibility can be imparted

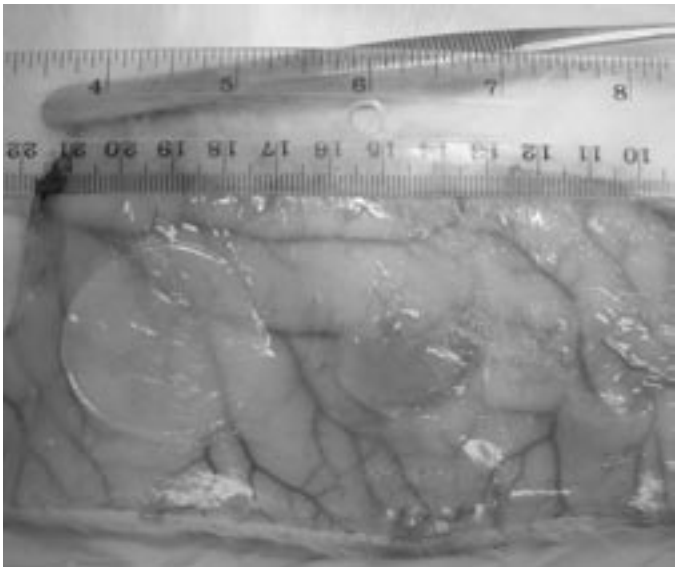

Figure 3: *Bioresorption of polymer as function of DT content in vivo in a subcutaneous implant site (rat). Three disks of poly(DTE carbonate) containing 17, 37, and 47% of "DT" units were implanted side-by-side, subcutaneously in the back of rats. After one month, the disk containing 17% DT is still intact (left side), only traces of the disk containing 37% DT are still visible (middle), and the disk containing 47% DT had completely resorbed. Noteworthy is the absence of tissue irritation or inflammation at the implantation site.*

by copolymerization with polymer blocks that deter blood cell and protein adsorption, and radiopacity can be achieved by iodination of the tyrosine ring. Notably, by incorporating desaminotyrosyl-tyrosine units (DT) into the polymer backbone,[13] one can tailor device resorption and drug elution from hours to years in a predictable fashion (Figure 3). A particular advantage of the system of tyrosine-derived polycarbonates is the incorporation of DT units has a dramatic effect on polymer degradation rate but does not significantly change the polymer's mechanical properties or reduce its hemocompatibility.

In spite of the revolutionary stent and material designs that form the basis for the Casper stent, the prototypes currently available have many handling characteristics of conventional metal stents. Most important is that the stents are deliverable by percutaneous access with standard clinical balloon delivery techniques.

The Casper stent is sufficiently radiopaque to be readily visible by X-ray fluoroscopy (Figure 4). Casper stents (3.0 mm x 15 mm) have been balloon expanded in pig coronary arteries to demonstrate *in vivo* radiopacity.

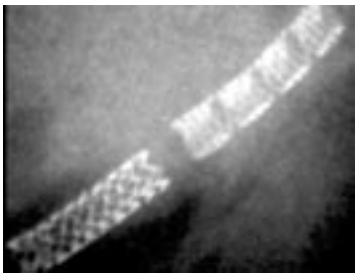

Figure 4: *The Casper stent (top, right) compared to a currently marketed steel stent (bottom, left) is visible by X-ray radiography/fluoroscopy in the excised animal heart.*

The Casper stent exhibits steel-like scaffolding for structural performance with 15 psi radial crush strength. While the Casper stent is fully load-bearing, it is also sufficiently flexible to track through a tortuous coronary path.

Casper stents currently have a crossing profile compatible with a 7F guide. The stents can be gently tacked up against the vessel wall using low-pressure deployment (<4 atm), which is clinically desirable particularly for fragile lesions.[6]

Casper stents exhibit <2 percent recoil and zero shortening. Studies with various polycarbonate formulations in animal coronary and femoral arteries show that the stents maintain proper balloon retention to the delivery site. Over a six-month experimental follow-up, no incidence of stent migration was observed.

REVA's *in vitro* IS0-10993 studies of extracts of the radiopaque monomer and polymers show the materials are non-genotoxic and non-cytotoxic. Other ISO-10993 studies for coagulation and platelet deposition showed that Casper materials and stents are comparable. Recent pig coronary artery studies of Casper stents and poly(DTE carbonate)-coated metal stents (Figure 5)

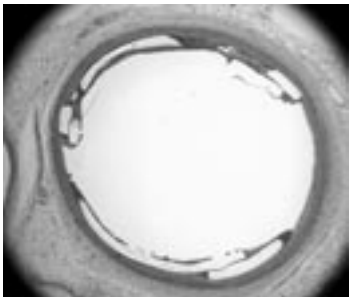

Figure 5a: *A resorbable stent comprised of a formulation of degradable poly(DTE carbonate) deployed in a pig coronary artery. The stent is well apposed to the vessel wall. Studies with such stents for up to 28 days show little to negligible inflammation and thrombosis.*

from five to 28 days showed the stents were well apposed to the vessel wall with little damage to the internal elastic lamina and negligible inflammation and thrombosis. Exploratory studies of the polymer combined with an anti-proliferative drug applied to the surface of steel stents show that the polymer can successfully elute drug of various doses with predictable dose effects on the formation of neointima. These studies demonstrated that the

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Surface Characterization and Modification Special Interest Group News

By Lara Gamble and Erika Johnston

The focus of the Surface Characterization and Modification (SCM) Special Interest Group (SIG) is to encourage the advancement of surface modification research and the development of surface analytical methods. Since the Reno meeting in April 2003, this SIG has undergone several changes, including the election of new officers. In October, Erika Johnston (Genzyme, erika.johnston@genzyme.com) was elected chair, Anna Belu (Medtronic, anna.belu@medtronic.com) was elected secretary/treasurer, and together they have appointed Lara Gamble (University of Washington, gamble@nb.engr.washington.edu) as *Biomaterials Forum* reporter. The initial focus of the new officers will be broadening student recognition and participation in the group and improving interaction across its diverse membership. The diversity of the group is quite apparent. In 2003, the SIG consisted of about 66 percent academic and 33 percent industrial members representing 11 countries and 40 institutions. Among academic members, approximately twice as many were students as were faculty.

In a November survey, members expressed an interest in improving the use of the Internet to enhance communication among members. At present, a list of web resources for surface modification and analysis is being compiled. The enhanced web page should be available early in 2004. Ultimately, the SIG leadership wants to team with the Society's new management to create an online forum for members to share information about the latest methods, funding sources, and employment opportunities. In the interim, members should keep an eye out for Surface Activation e-newsletters. This will be an informal means to disseminate information about upcoming surface related events. Members are encouraged to provide links to their surface-related sites and news of upcoming events by e-mailing one of the officers.

As was mentioned in the last issue of *Biomaterials Forum*, all SIG awards to students have been suspended, causing SIGs to rethink their options for promoting student recognition and participation. This SIG is taking the approach of contacting the student chapters directly to seek innovative ways to recognize students and enhance their Society experience.

Finally, the SIG is abuzz with news that the two Surface Characterization and Modification symposia at the 2004 7th World Biomaterials Congress in Sydney, Australia, (Biomaterials Surface Modifications and Biomaterial Surface Characterization) had the largest contribution of abstracts at ~140 abstracts for both symposia. With such a strong interest in symposia at the 2004 conference, the group looks forward to a healthy SIG member turnout. Members should keep an eye out for the Surface Activation e-newsletters for more information about informal group events in Sydney.

Surface modification can improve biocompatibility of materials, and surface sensitive analytical methods are required to provide a more detailed understanding of the chemistry, structure, and morphology of complex surfaces. These topics are relevant to most Society researchers because the interaction between the surface of an implanted biomaterial and the biological environment can dictate the ultimate (and unfortunately, often deleterious) biological response to that implanted biomaterial. For example, undesirable surface

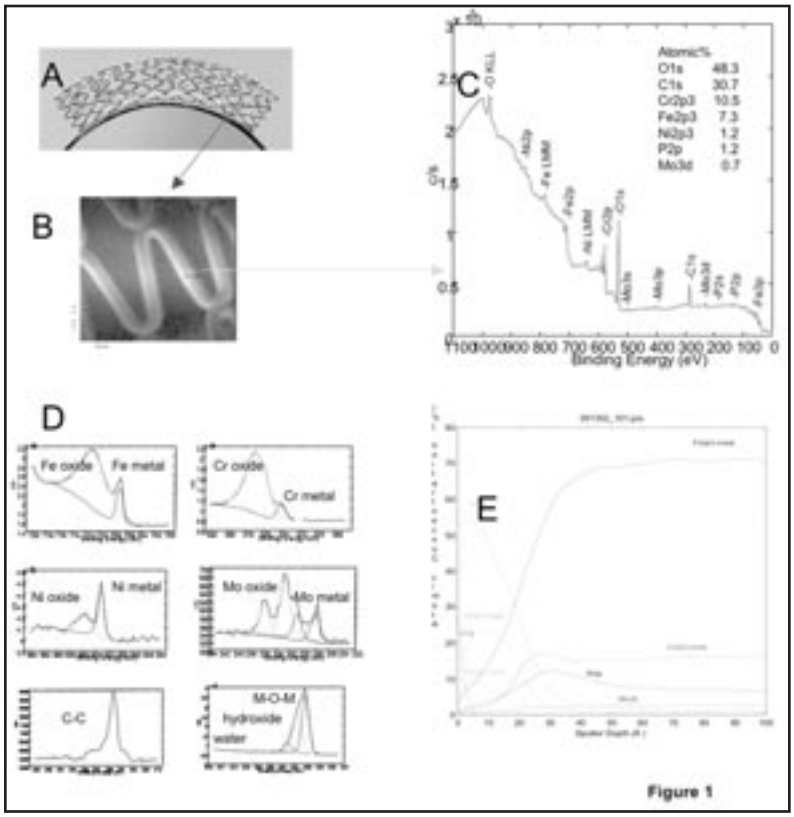

Figure 1

Figure 1: *ESCA analysis of a stent (Image A shows optical photo of stent). The surface chemical composition can be mapped by ESCA. Image B shows the x-ray induced total electron image generated by ESCA. The 100 micron area probed for spectroscopy and profiling is labeled on the image. Image C shows the elemental composition of the surface of the stent, identified through spectroscopy mode. Image D shows the high-resolution spectroscopy mode that gives information on chemical state of species. Image E shows a depth profile where the thickness of the oxide and the distribution of species within the oxide can be determined. Figure provided by Anna Belu of Medtronic, Inc.*

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Cardiovascular Special Interest Group Honors Students

By Julie Trudel

The Cardiovascular Special Interest Group (SIG) presented awards to two graduate students at the Society For Biomaterials annual meeting held in Reno, Nev., in April 2003. Each student presented exceptional work, which is summarized in the following paragraphs.

Trevor Snyder, a graduate student from the University of Pittsburgh, gave the presentation "Assessing Ventricular Assist Device Associated Leukocyte Activation in a Bovine Model." The foundation of Trevor's paper comes from the clinical observation that patients implanted with ventricular assist devices (VAD) have elevated levels of monocyte expressing tissue factor (MTF), monocyte-platelet aggregates (MPA), and granulocytes-platelet aggregates (GPA). His study was aimed at determining whether this elevated inflammatory activity is related to the device or to the underlying advanced cardiomyopathy that affects most recipients of these devices (and the inflammation associated with this medical condition). To answer this question, healthy juvenile calves were implanted with rotary VAD for 30 days and their blood was assayed for the inflammatory markers of interest pre-operatively and for several days following implantation of the device. Trevor used flow cytometry with appropriate antibodies to detect the presence of MTF, MPA, and GPA. A significant increase in each of these markers was quantified immediately following implantation of the device. MTF and MPA gradually decreased over time, without a return to pre-operative values. GPA levels were not as elevated as the other two markers and remained at its post-operative level for the time of the study. This study demonstrated that implantation of rotary VAD causes an inflammatory response. It also introduced assays that can be used to study device-related inflammatory response in a large animal model. Trevor's work was done under the direction of Dr. William Wagner.

Donna Hilton, a student who recently graduated with her master's degree from Clemson University, discussed fundamental work in the field of biomaterials in the presentation "Direct Correlation between the Change in Adsorbed Protein Structure

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Bionanotechnology for Better Tissue Engineered Materials is Alive at Purdue University

By Tom Webster

Research is alive in Purdue University's Department of Biomedical Engineering at the intersection of nanotechnology and tissue engineering. Nanotechnology can be defined as the use of materials with constituent components less than 100 nm. Numerous disciplines have already identified ways to take advantage of nanophase materials. For example, the computer industry, catalytic processes, space exploration, pharmaceutical industry, and others, all point to unprecedented improvements that can be gained through the use of nanophase materials. Now, the promises of using nanophase materials in biomaterial applications are being realized through efforts at Purdue. Nanophase materials are intriguing materials for tissue engineering applications since tissues in our body are composed of nanostructures (including proteins). Thus, cells of all tissues are accustomed to interacting with materials with nanostructured surface roughness. This is in contrast to materials used today that do not possess a high degree of nanometer surface roughness.

In collaboration with companies such as Argonide, Applied Sciences, Spire Biomedical, and Nanophase Technologies, Thomas Webster develops nanophase ceramics, metals, polymers, and composites that promote new bone growth more efficiently than currently used materials. Specifically, these materials include alumina fibers, hydroxyapatite, titania, carbon nanofibers, Ti, Ti6Al4V, CoCrMo, poly-lactic-co-gycolic acid, polycarbonate urethane, and composites thereof. Other researchers at Purdue have extended applications of nanophase materials into other organs as well. For example, Karen M. Haberstroh and co-workers have developed nanostructured poly-lactic acid, polyurethane, and polycaprolactone scaffolds that increase vascular and bladder tissue regeneration. Lastly, Riyi Shi and Webster are showing the promise of carbon nanofibers/nanotubes to serve as neural implants. They have provided evidence of increased functions of neurons and decreased glial scar tissue formation on nanometer dimensioned carbon fibers. Since all of these studies have maintained similar chemistry in respective nanophase compared to conventional material formulations, they point to the influence that a nanometer topography can have on increasing tissue regeneration for a wide range of applications. This work is funded by the NIH Bionanotechnology Initiative and the NSF Nanotechnology Initiative.

Rutgers Launches New Cross-disciplinary Program on Engineered Biointerfaces

By Linda Anthony

Rutgers University has recently initiated a new cross-disciplinary program on integratively engineered biologic interfaces, supported by a five-year $4.2 million IGERT award from the National Science Foundation (NSF) and Rutgers University. The NSF IGERT program supports integrative graduate education and research traineeships at research-intensive universities. The Rutgers IGERT is unique in its focus on integrative synthesis and analysis of the various biointerfaces that combine advances in molecular and cellular biology, complex materials, surface sciences, biomaterials, nanotechnology, tissue engineering, and regenerative medicine.

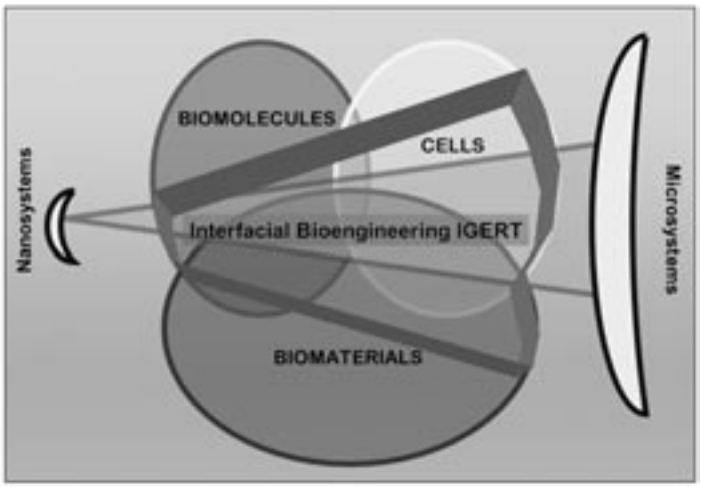

Figure 1. The research and educational efforts in the IGERT program on Integratively Engineered Biointerfaces will be organized at the confluence of three major constituents of biological substrates: cells, biomolecules, and biomaterials, and focused over a range of micro-through nanoscales (the cone embodies the scope of the IGERT research thrusts).

The program comprises three thematic thrust areas: living cell-based interfaces; micro and nanoscale engineered biointerfaces; and bioresponsive, bioactuatable, and biosensor substrates.

The goal of the program is to help educate a breed of bioscientists and bioengineers that can be multilingual in the field of biointerfaces and integrative in their perspective. Unlike classical graduate education and research, which usually occur within the confines of a specific academic department, the Rutgers IGERT program will establish a structured process to train graduate students to become cross-disciplinary in their thinking and skills, and to develop a solid appreciation for the professional context for their thesis research. This will be formally accomplished by: (a) a requirement that students' thesis research be co-advised by experts from cross-cutting disciplines; (b) new graduate coursework on biointerfacial topics that integrate across size scales (nano-micro-meso), integrate systems across biomolecules-cells-biomaterials, and review emerging synthesis and analysis approaches in biomaterials and biointerfaces; and (c) a new partnership through a COLTS (community of learners and thought shapers) program with the Rutgers School of Education.

The keystone of the program is its focus on fostering cross-disciplinary research and scholarship. "In contrast to the classical development of the materials and biology fields, which have largely occurred in isolation, the next generation of bioinspired and biointeractive materials will be systematically developed through the integration of these disciplines with strong links to classical molecular/cellular biology and structural biochemistry on the one hand, and to nano/microsystems materials sciences and engineering on the other," notes Dr. Prabhas Moghe, associate professor of biomedical engineering and chemical & biochemical engineering.

Thirty-three Rutgers faculty with a wide range of research and educational expertise have joined together in the proposed IGERT program. The foundation of the program rests on this diverse community of committed scholars and educators, who are affiliated with graduate programs in molecular biosciences, physical sciences, and engineering. The IGERT program is directed by Dr. Moghe, co-directed by Dr. Kathryn Uhrich, associate professor of chemistry and chemical biology, and managed by Dr. Linda Anthony, an analytical chemist formerly with Bell Labs. The IEB-IGERT also builds on the existing strengths at Rutgers in the areas of biomaterials. The nationally recognized New Jersey Center for Biomaterials, led by Professor Joachim Kohn, is a major research partnering center and a gateway for student internships on biointerfaces.

The first class of IGERT fellows at Rutgers was inducted January 2004. IGERT graduate awards include annual fellowship stipends ranging up to $30,500 per year, tuition-benefits allowance, and all-expense-paid travel to Europe for an academic research internship. Students must be U.S. citizens or permanent residents and must enroll in a Ph.D. granting track in a relevant Rutgers graduate program.

For more information about the Rutgers IGERT in Integratively Engineered Biointerfaces, visit the Web site, www.igert.rutgers.edu, or contact the program director at moghe@rci.rutgers.edu.

New Center for Industrial Collaboration in Biomaterials and Tissue Engineering Opened in United Kingdom

BITE CIC, a unique R&D base and center for industrial collaboration in the fields of biomaterials and tissue engineering has been created in the United Kingdom. Combining the internationally recognized, multi-disciplinary expertise and facilities from the "White Rose" Universities of Leeds, Sheffield, and York creates an industry-facing organization that supports the development of new clinical treatments and products based on biomaterials and tissue engineering.

Developments in biomaterials and tissue engineering increasingly require the involvement of multi-disciplinary teams combining biological, clinical, and materials expertise, together with many other related disciplines. The CIC offers industry access to this broad portfolio of competencies and services:

- Applied research, product design, and development of biomaterials, medical devices, biomimetic tissues and tissue engineered products.
- Pre-clinical testing and evaluation.
- Performance analysis of clinical products and devices.
- Technical marketing and support for new product developments.
- Development and evaluation of manufacturing processes for tissue engineered products.
- Technical consultancy, scientific advice, regulatory, and quality systems advice.
- Training and short courses for industry, training and supply of skilled personnel.

This range of services is made available through access to expertise and facilities from across the three collaborating universities, together with a new centralized project management function that can deliver these services to industry.

John Egan, commercial manager of the new BITE CIC, says, "The research excellence of our Universities is well recognized, and we are now using new project managers to focus this expertise and facilities to develop an essential resource to enhance the competitiveness of our industry partners. With over 100 research staff involved in projects currently valued at over £10 million, spanning the spectrum of biomaterials and tissue engineering applications, together with the active involvement of clinical collaborators in the University hospitals, the BITE CIC has a strong base from which to enable our partners to develop and successfully commercialize the latest generation medical devices."

BITE CIC, which began operating in July 2003, is supported for the first three years by a grant of over $1 million from Yorkshire Forward, the regional development agency. BITE CIC is operating from a base within the brand new University of Leeds technology transfer facility at Thorpe Park.

For further information see (www.bitecic.com) or contact John Egan, commercial manager at john.egan@bitecic.com, or John Fisher, director of BITE CIC, at j.fisher@leeds.ac.uk

Submit Your University News

The Editors of *Biomaterials Forum* would like your input for enhancing the University News section of the magazine. As a member of the Society For Biomaterials and a reader of the Forum, what do you want to see in the University News section? Do you have any information about your institution that other SFB members may find informative? Has your department/center/program recently hired in the area of biomaterials? Do you plan additions in the near future?

Although we cannot guarantee publication of the information, please submit news for consideration for inclusion in the University News section. News items can be submitted to the Executive Editor, Martine LaBerge, via e-mail at martine.laberge@ces.clemson.edu. The submission deadline for the next issue (April-June 2004) is March 8. Other deadlines for 2004 are: June 2 (July-September issue), and Sept. 1 (October-December issue).

We thank you for your help.

NIBIB Biomedical Entrepreneurial Science Working Group Releases Executive Summary

Government News
By Christine Kelley

The Executive Summary from the Biomedical Entrepreneurial Science Working Group held August 1, 2003, in Bethesda, Md., is now available on the NIBIB Web site.

The goal of this working group was to attain specific recommendations regarding the role of the NIBIB in facilitating the translation of fundamental discoveries and innovative research into biomedical applications for the benefit of public health. Despite efforts to translate scientific knowledge and discoveries into useful medical applications, researchers often encounter barriers to commercializing technology. Participants of this working group identified academic culture, researchers, funding, technology transfer offices, and government as the major hurdles. To address these barriers and improve technology transfer of important research, it was recommended that the NIBIB empower students and investigators with entrepreneurial training opportunities and incentives, offer opportunities for researchers to establish viable industrial partnerships, and improve the review of technology-driven grant applications.

More information is available in the Executive Summary, which can be accessed at www.nibib.nih.gov/events/BESWG/BESWG_ExecSumm.pdf.

ASTM Task Force Open for Development of Reference Scaffolds for Tissue Engineered Medical Products (TEMPs)

Government News
By John A. Tesk, Government News Contributing Editor

At a workshop held at the National Institute of Standards and Technology (NIST) in July 2000[1], the reference materials most needed for tissue engineering were identified as being three-dimensional reference tissue scaffolds of known porosity, interconnectivity, surface and bulk chemistry, physical and mechanical properties, and cellular reactivity. In response to this workshop, NIST has been pursuing collaborations to accomplish this objective. An ASTM task force was initiated at the November 19, 2003, meeting (Tampa, Fla.) of Committee F04.42 – Biomaterials and Biomolecules, for the development of reference scaffolds for TEMPs. The task force will conduct measurements for characterization of test scaffolds that will be supplied to its members. The development will focus on scaffolds that will consist of a regular array of cubic pores with consistent interconnections. It was decided that two test scaffolds should be characterized, having either 300 µm or 600 µm pore-edge dimensions.

Results from the characterization effort will be used by NIST in the development of reference scaffolds for distribution to researchers and developers of scaffolds for tissue engineering applications. The characterizations of the test specimens will be used to help ensure that the features needed in the reference scaffolds will be well-defined and that their measurements will produce consistent results for terms such as porosity, interconnectivity and tortuosity, and possibly others (these terms are found in a draft characterization guide that is under development in a related effort headed by Dr. Paul Tomlins of the National Physical Laboratory). The task force is headed by Dr. John Tesk (NIST), and Drs. Michael Yaszemski and Esmaiel Jabbari (Mayo Clinic). The target schedule is to have measurements of test scaffolds completed in time for the April 2004 meeting of the ASTM, all issues resolved by August 2004, and the start of fabrication of the reference scaffolds by the end of August 2004, after which scaffolds with spherical geometry will be considered for the next development. The task force planned to begin the evaluation of test scaffolds in January 2004. Enquiries as to participation should be made as soon as possible to facilitate planning and coordination of the effort. To join the task force or request further information, contact John Tesk at 301-975-6799 or john.tesk@nist.gov; or Liisa Kuhn (chair of Committee F04.42) at 860-679-3922 or lkuhn@uchc.edu.

1. J., Appl Biomaterials, 58, #5, p 463-466, 2001.

"Bone Graft Substitutes"

Book Review
By Liisa Kuhn

Edited by Cato T. Laurencin, MD, PhD
 315 pages.

This is a unique monograph exploring not only the clinical and scientific aspects of bone grafting, but also the practical issue of bringing promising new bone graft substitutes to market in a fashion that ensures their safety and efficacy. Dr. Laurencin, with help from Dr. Mohamed Attawia, assembled an accomplished multidisciplinary panel of scientists, clinicians, and members of the regulatory agencies for a workshop held at the American Society of Testing and Materials (ASTM) Fall Committee Week in 2000. This volume represents, in large part, the proceedings from that workshop on bone graft substitutes. Together the panel members have collectively authored a comprehensive and authoritative summary of this complex field.

This monograph is divided into three sections. The first section presents a summary of the clinical use of bone allografts and allograft-based bone graft substitutes. The second section addresses the use of cells and growth factors as bone graft substitutes. Representatives from academia, industry, and the regulatory communities present their perspectives on the exciting opportunities and formidable challenges involved in bringing scientific advances in the field of bone-tissue engineering to the patient-care arena. The final section addresses the use of synthetic materials, including polymers and ceramics for bone graft substitutes. All sections begin with an overview by some of the leading authorities in the field. The issues involved in standards development for bone graft substitutes are addressed in each section and provide motivation to become involved with ASTM Committee F04 on medical and surgical devices. The contributing authors can be found by going to www.astm.org/sitesearch and entering MONO6.

It is rare to find such thorough topic coverage in conference proceedings. It is reminiscent of a classic 1994 monograph on the same subject, "Bone Grafts, Derivatives and Substitutes," edited by MR Urist, BT O'Connor, and RG Burwell, published by Butterworth Heinemann, England. The main difference between that text and this one is the coverage of tissue engineering approaches that were not yet developed enough to be included in the earlier text on bone substitutes. Clinicians will find this new monograph an excellent addition to their personal library as a self-educational resource because of the thorough coverage of the topic area. This monograph is also an excellent resource for academic or corporate researchers because, in addition to containing the essential basic science components, important aspects of product development and regulatory pathways are covered that may influence research direction.

Audience
Clinical, corporate, and academic researchers working in the field of biomaterials. University libraries and biomedical engineering department libraries. Excellent resource for clinicians interested in learning about cell-based and growth factor delivery systems, and for students beginning study in this area. Researchers in this area will appreciate the focused content as background information for grant proposals.

Contents

The Newest and Trendiest Vascular Device

By Julie Trudel

"I want the new kind, the one that has drug on it and will make my artery stay open," one patient says. Since they became available this past April, patients around the United States have been requesting them ... drug-eluting stents (DES), the newest generation of coronary stents approved by the FDA. For the past several years, the standard of care for treating coronary stenosis has been the use of plain stainless steel stents. Unfortunately, about 25 percent of the patient population had to return to the cath lab within six months after their initial surgery. Diagnostic: restenosis, re-occlusion of the native vessel. Contrary to what one might think, this is not an occlusion event related to blood clotting. Rather, it is linked to a hyper-proliferative response of the vascular smooth muscle cells in reaction to the injury caused by stent deployment and migration of these cells from their original location into the vessel lumen. It is also associated with an inflammatory response at the site of the implant. The idea of drug-eluting stents seems very well justified: to reduce all these cellular events by locally delivering therapeutic agents.

For anyone belonging to the Cardiovascular Special Interest Group or the Drug Delivery Special Interst Group, the concept is not foreign: take a device, pick the right drug, and control its release by using a good polymer system. A great combination device. No that easy. Which drug to pick? What polymer? What release profile? How does one make the coating adhere to the device? How is it sterilized? These are the kind of questions that have kept engineers, scientists, technicians, and operators from most stent companies busy over the past few years. Several months of labor to come up with the right formulation. Cordis Corp., a Johnson & Johnson company, did it first. This past April, they received FDA approval to sell their Cypher™ stent in the United States. Cypher™ is their coronary stent eluting sirolimus (rapamycin, Rapamune), an immunosupressant. This drug is also a potent inhibitor of smooth muscle cell migration and proliferation. More recently, Boston Scientific also received favorable response from the FDA to sell their Taxus stent in the United States. Taxus elutes paclitaxel, a drug known to prevent normal cell division by promoting the formation of highly stable microtubules.

A Lucrative Business

The word is out and all evidence presented to the scientific community so far is pointing towards the following conclusion: these devices work! Indeed, after more than a year of patient follow-up, binary restenosis is now down to single digit. This hard labor to get these devices to work is highly compensated. While bare metal stents sell for less than $1,000, drug-eluting counterparts sell for $3,000. The worldwide stent market that was $2.4 billion in 2002 is predicted to rise to more than $7 billion by 2006 as physicians start using DES in more clinical cases.

Prior to the arrival of DES, the coronary stent market was dominated by the following four manufacturers: Guidant Corp., Boston Scientific, Cordis, and Medtronic Vascular. As expected, every stent maker wants their share of the pie. No need to mention that Guidant and Medtronic Vascular are also trying to finish the DES race by bringing to the market their version of the product. In the vascular device community, these are sometimes labeled the "me-too-limus" stents, referring to the fact that they are both using drugs that work under the same mechanism of action as sirolimus. Guidant is using everolimus, a drug they exclusively licensed from Novartis, while Medtronic is currently into clinical trial with ABT-578, a compound they licensed from Abbott Laboratories. If clinical trials demonstrate expected results, it is anticipated that Guidant and Medtronic will launch their products in the United States in late 2005 or early 2006.

An Evolving Industry

Manufacturers of DES have learned a lot over the past few years. The industry that was once dominated by mechanical engineers launching new stent designs on a yearly basis is changing to adapt to the demand of combination devices. This transition requires the common knowledge of multidisciplinary teams. The creation process is different now than it was before. For example, while finite element modeling might have been an important skill to master in the era of bare metal stent design, additional skills are now considered an asset. In a team meeting, discussion around cell cycle can be followed by a debate around polymer sterilization issues. Basic knowledge of different disciplines can be very useful.

Such A Small Surface Area

Getting the recipe "just right" to make the perfect DES can be somewhat tricky considering the multiple challenges surrounding the conception and manufacturing of these devices. One of these is the fact that a typical coronary stent measures approximately 2-cm in length, and once expanded in the vessel, covers about 25 percent of the vessel surface area (metal-to-artery ratio). This means that only a very small metal surface area is available to be loaded with therapeutic agents. In this case, better pick a very potent drug! Potent, but not toxic. Early on, stent manufacturers learned about the difference between cytostatic drugs versus cytotoxic drugs. Preventing cellular proliferation by killing cells (accomplished by using cytotoxic drugs) is not as appealing as decreasing cell growth by preventing their division using a cytostatic drug.

How About The Polymer?

Another key element to success is the selection of an adequate polymer that will not only elicit minimum local inflammatory reaction, but also allow for an adequate release rate of the drug of choice in the vessel wall. Needless to say, the polymer also needs to be non-thrombogenic; causing clotting locally might not be a desired outcome. What kinds of polymers are best suited for the application? Each manufacturer has its own preference, and in this arena, intellectual property homework has to be done diligently. Two general classes of polymers are part of the DES lingo: the "durable" polymers and the

Continued on page 28

2004 Buyers' Guide

Your guide to the latest in research and technology in the biomaterials community.

Coatings
AST Products Inc.
4th State Inc.
Surface Solutions Labs Inc.
SurModics Inc.

Contract Research & Consulting
AST Products Inc.
4th State Inc.
Hysitron Inc.
Southern Research Institute

Device Development & Manufacture
Midwest Plastic Components

Drug Delivery & Pharmaceuticals
PURAC America
Surface Solutions Labs Inc.
Southern Research Institute
SurModics Inc.

Image Analysis
Asylum Research

Materials & Materials Services
Innovatech Labs LLC
Midwest Plastic Components
NuSil Technology
PURAC America

Packaging Products & Services
Midwest Plastic Components

Recombinant Biomaterials
FibroGen Inc.

Surface Modification & Treatment
AST Products Inc.
4th State Inc.
Surface Solutions Labs Inc.
SurModics Inc.

Testing Equipment
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EnduraTEC Systems Corp.
Hysitron Inc.
MTS Systems Corp.
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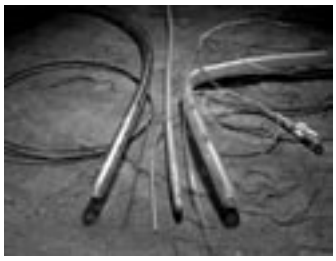
Testing Services
EnduraTEC Systems Corp.
Hysitron Inc.
Innovatech Labs LLC

AST Products Inc.



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AST Products is a world leader in medical device coatings. The company's platform technology, BioLAST, offers technically superior, environmentally friendly coatings that are easily incorporated in manufacturing processes. Coatings developed using BioLAST include lubricious, anti-microbial, non-thrombogenic, hydrophilic, and anti-encrustive treatments. An ISO 9000:2000 registered company, AST offers BioLAST on a contract manufacturing or tech-transfer basis.

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Asylum Research manufactures the MFP-3D™ Atomic Force/Scanning Probe Microscope, the next generation AFM with power and flexibility in one complete system. The MFP-3D uses the company's patent-pending Nanopositioning System (NPS™) for precise and accurate measurements, MicroAngelo™ for built-in nanolithography capabilities, and top and bottom optical access for simultaneous optical measurements such as phase contrast, epi/transmission fluorescence, etc.

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EnduraTEC manufactures the ELectroForce® (ELF®) Series of test instruments using patented BOSE® linear motors. EnduraTEC offers instruments and laboratory services for characterization of soft tissue, bones, medical devices, biomaterials, stents, endovascular grafts, cardiovascular devices, and many types of viscoelastic engineered materials. The new ITEMS BioReactor™ is a breakthrough in mechanical stimulation for tissue engineering.

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FibroGen provides highly purified, well-characterized recombinant human collagens (Types I & III) and gelatins for medical and pharmaceutical use. FibroGen's yeast fermentation process allows high-level expression in a defined, animal-free media. Potential uses include vaccine stabilization, drug delivery, cell culture, hemostats/tissue sealants, and tissue engineering.

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4th State specializes in providing plasma surface modification solutions for polymers (including fluoropolymers), elastomers, ceramics, metals and films. 4th State offers other companies the plasma advantage through process development, consulting, contract services, equipment design, and sales supported by staff with more than 25 years experience assisting the plastics industry.

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Hysitron manufactures nanoindenters designed for true nanoscale mechanical characterization with integrated *in-situ* SPM imaging. Techniques such as nanoDMA® and ScanningWear™ provide advanced capabilities for measurement of storage and loss moduli, hardness, and wear resistance. The BioIndenter™ provides a comprehensive nanoscale testing solution for characterization of biomaterials under controlled environmental conditions.

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Innovatech Labs is an independent, analytical laboratory specializing in personalized service, rapid turnaround times (typically 3 – 5 days), and innovative approaches to materials analyses. Innovatech Labs is committed to helping our customers find the answers they need. Services include: XPS, AUGER, SEM/EDS, GC/MS, FTIR, IC, LPC and more.

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IonBond is the global leader in the fields of Physical Vapor Deposition (PVD) and Chemical Vapor Deposition (CVD). IonBond has the largest selection of biocompatible coatings designed to enhance implant and instrument life and performance. The company's comprehensive range of services includes: technical consultation, application development, custom fixture design, and custom coating development.

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Midwest Plastic Components is a thermoplastic contract manufacturer specializing in implantable components and devices. Extensive experience molding sophisticated biomaterials, including bioresorbable resins. The company offers complete program management with cleanroom Manufacturing, Assembly, and Packaging coupled with Sterilization management (MAPS™). FDA registered (#2183967) contract device manufacturer with Quality Systems registered to ISO 9001, EN46002, and ISO 13488.

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MTS Systems offers systems, software, and accessories for mechanical testing of biomaterials and medical devices. MTS solutions are specifically designed for testing biomechanical components, biomaterial properties, and simulation of biological forces and displacements. The systems can be used for characterizing biomaterials, surface interfaces, and surface modified materials.

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NuSil Technology specializes in the development and manufacture of silicone materials used in the medical device industry with more than 400 custom and standard formulated products. These include: adhesives, gels, elastomers, dispersions, fluids, coatings, and primers. Consistent quality assures customers lot-to-lot reproducibility and traceability. NuSil Technology and NuSil Technology Europe are ISO-9001 certified.

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PURAC's biomaterials business unit manufactures and markets lactide and glycolide monomers and biodegradable (co) polymers worldwide under the PURASORB brand name. These polymers can be manufactured with any of the glycolide and lactide isomers (L, D, or DL) and are widely used for such applications as resorbable surgical sutures, medical implant devices, and controlled drug delivery systems.

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Surface Solutions Labs develops coating and adhesive technologies for the medical device industry. Coating customization and consulting services are available for all substrates. Water-based coating technologies include: scratch-resistant, hydrophilic anticorrosion, radiopaque, laser-markable, electrically conductive, light reflecting, light absorbing, and sustained release antibacterial, antithrombogenic, anticancer, growth promoting/inhibiting.

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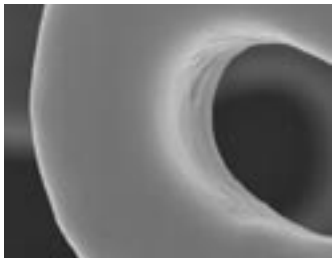
Southern Research Institute has more than 30 years in drug delivery formulation, with expertise and patented strategies for depot formulations . . . microencapsulation, implants, and gels. Product development programs include feasibility studies, preclinical development, process scale-up, and production of clinical trial supplies. Commercial manufacturing offered through a corporate partner.

SurModics Inc.



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SurModics provides surface modification solutions to the medical device industry. Their patented PhotoLink® technology provides many performance-enhancing characteristics such as lubricity, hemocompatibility, and biomolecule immobilization. The coatings are easily applied under ambient conditions. Other hydrogel-matrix coatings recently developed by SurModics enable the time-controlled elution of drugs from device surfaces.

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TestResources is a supplier of fatigue, tensile, and compression test systems, grips, fixtures, software, controllers, extensometers, and accessories. The company's new systems test sutures, catheters, tissues, bones, medical devices, hydrogels, biomaterials, wire, seals, and joints. TestResources engineers biomechanical systems and upgrades MTS and Instron frames.

Officer Nominees...

(Continued from page 7)

Mutlu Karakelle continued…

dynamic and multi-disciplinary nature of the biomedical sciences is increasingly requiring a closer communication and collaboration platform between different scientific disciplines and sister societies. A significant number of members are actively participating in more than one society. Increasing the level of cooperation between these societies will advance the biomaterial and biomedical research to the next level.

I will make expanding Society membership and achieving closer communication and collaboration with sister societies my key focus areas. I am looking forward to the opportunity to serve this great Society as President-Elect and Chair of the Long-Range Planning Committee in the coming year.

Michael V. Sefton continued…

Michael is a regular attendee at Society for Biomaterials meetings and served on the International Liaison Committee for several years and has participated from time to time on other Society committees (e.g., the Awards and Nominations Committee). He was a member of the local organising committee for the financially and scientifically successful World Congress in Toronto in 1996. He is currently chairing the organising committee for the 2004 SFB Symposium on Biomaterials in Regenerative Medicine; the Advent of Combination Products. He was on the Board of Governors and Strategic Planning Committee for the Controlled Release Society and has participated in the organisation of TESI and its new North American chapter. He is also credited with building the large tissue engineering presence at the University of Toronto.

Vision statement:
Membership value. You expect to get something for being a member of the Society For Biomaterials. You study, use, develop, manufacture, specify, or work with biomaterials and you want to share your ideas and know-how with others like yourself. You want to network at annual meetings, read papers in JBMR, or hear what people are doing in the Biomaterials Forum.

The President's job is to make sure that all of this is possible and continues to be possible.

Previous leaders of the Society have created a strong member-driven society. The Special Interest Groups, professional management, superb meetings, and journals are elements of this. A strategic planning exercise was conducted to ensure that steps are taken to keep the Society strong. As biomaterials have become more varied, more complex, and more important to more other groups, the Society for Biomaterials now has to do more: to retain and attract members and to work with other societies that are our natural collaborators. Biomaterials has moved from a course or two in materials departments to a major division in bioengineering departments. Biomaterials were used primarily in implanted prostheses and are now a key technology for tissue engineering. Biomaterial specialists have moved from a focus on the material side of the host implant interface to a focus on the interface itself—both the bio and the material. It is hard to imagine a better background for tissue engineering, controlled release, or modern bioengineering, itself. Integrating biology and engineering is our bread and butter. The FDA interest in combination products is driven largely by this combination of biomaterials with biologicals or drugs.

My objective is to build upon the Society's strong past and lead it into the future. I would:

- Ensure the Annual Meeting is a spectacular opportunity to learn from colleagues and students and to celebrate the richness and diversity of biomaterials.
- Develop working, collaborative relationships with the Biomedical Engineering Society (BMES), the Tissue Engineering Society International, and the Controlled Release Society, among others, to minimize meeting overload and so that the Society emerges as the best forum for the best work in all these areas. The Society symposium on regenerative medicine, which I am chairing, is being held immediately after the BMES meeting in October 2004 as a first step to building a relationship with that group.
- Actively recruit clinicians and others who use, study, and work with biomaterials, in the context of regenerative medicine and other areas. The best Society For Biomaterials has the best members. We must be the Society for all biomaterials.
- Listen to you through the SIGs, the Web site, and every other means. Ensure that your dues are well spent and accounted for, that the services the Society provides are the ones you want, and that the services meet the highest degree of professional standards.
- Ensure that excellence pervades everything the Society is associated with: excellent science in meetings and publications and excellent services.

I will be honored to serve you in this endeavor.

Antonios G. Mikos continued…

Issues Editor), *Cell Transplantation*, *Journal of Biomaterials Science* Polymer Edition, *Journal of Biomedical Materials Research* (Part A and B), and *Journal of Controlled Release*. He has been very active working in the Society For Biomaterials, American Institute of Chemical Engineers, Biomedical Engineering Society, Controlled Release Society, and Tissue Engineering Society International. He was chair of the Hybrid Artificial Organs Special Interest Group of the Society For Biomaterials from 1993 to 1995.

Vision Statement:
Recent advances in nanotechnology have had enormous impact on biomaterials science and engineering. Nanoparticles and nanotubes of exciting new physico-chemical characteristics are now being explored for different medical applications not only as diagnostics but also as therapeutics. Nanomaterials, including nanocomposites, are currently being investigated for potential medical use in a variety of forms ranging from permanent prostheses to degradable tissue engineering scaffolds and non-viral gene delivery vectors.

Nanobiotechnology presents many new opportunities for biomaterialists and a challenge for our Society For Biomaterials. Our Society will need to address the critical issues associated with the use of nanobiomaterials, including their safety and regulation. A Special Interest Group will need to be formed focusing on nanobiomaterials to stimulate interest within our Society and help increase its membership by attracting researchers from different disciplines working with nanomaterials. The meetings and publications of our Society and its web page will need to support the growth of this emerging field and provide new forums to realize its true potential.

The implementation of new initiatives to promote nanobiomaterials will help create a solid, diverse, dynamic, and visionary Society For Biomaterials. It will further enhance our Society's visibility and strengthen its leadership role in the community.

Industry Insights:

Midwest Plastic Components …"Implantables and More"

By Jeff Ringhofer, Marketing Communications Manager and Mark Schaefer, VP of Business Development

Midwest Plastic Components has a very successful 40-year history of serving the needs of the medical device industry in the development of implantable devices and the instruments required in the implantation of those devices. Originally focused on polyurethane and the cardiovascular marketplace, Midwest Plastic Components has expanded its material processing expertise to the many grades and formulations of bioresorbable polymers, PEEK-OPTIMA® polymer from Invibio™, and other specialized polymers to serve the orthopedic, sports medicine, dental and drug delivery system needs of the medical device industry.

Evolution from Tough Components to Finished Devices

Midwest Plastic has always been known for producing some of the toughest pieces the industry has designed. With this track record, a variety of services is provided, from producing the most complex part, to regulatory support, to providing assembly services. As the industry has expanded, so have the capability, product, and service offerings of Midwest Plastic Components. Today Midwest Plastic can mold devices or components, and in fact serve as a "manufacturing department," as it will Mold, Assemble, Package and manage the Sterilization (MAPS) of devices. Having this full-service capability available for the medical device industry allows its clients to utilize whichever portion of its total offerings that are prudent for their particular business/manufacturing strategy.

ISO 9001:2000, EN46002, ISO 13488, QSR compliance/FDA registration are all in place to give the medical device industry the "foundation of confidence" that is necessary for the outsourcing of all, or any portion of, these critical functions. As a partner, it will work together to build on that foundation by transparently becoming part of your organization's "infrastructure" so together we take safe and validated products to market. This is true whether it is a Class I or Class III device!

Client, Material and Capability focused organization

Midwest Plastic is committed to staying on top of biomaterial polymer developments and being a pioneer in the development of production processing capabilities in these polymers. This gives its clients the ability to quickly develop and test products, gain approval, and market devices utilizing these new(er) polymers. Its focus is not on basic research and/or material development, but rather on developing full scale, validated manufacturing processes for its clients. By having the infrastructure and talent available to work with all of the currently available and newly developed biomaterial polymers, as well as other engineered thermoplastics, it saves its clients from either trying to develop the capability in-house or from having to "teach" a molder. It works just this way with many of the current major medical device manufacturers, as well as early stage companies with new product ideas.

Midwest Plastic Components understands that as a contract manufacturer, success depends on its clients' success. In a well developed relationship it truly is an extension of its clients engineering and manufacturing resources, thereby allowing them to invest in research and development of additional devices and the sales and marketing of those already released and approved. Having experience with regulatory requirements and a full understanding of the issues its clients must address in the regulatory approval process, whether it be a 510K or a full PMA, we can be a valuable resource. It even helps guide these efforts for some early stage organizations to ensure they are done correctly.

In-House Bioresorbable Lab

Midwest Plastic Components has invested in an in-house wet lab so the manufacturing process can be monitored not only on a dimensional basis, but also regarding potential performance-related issues such as degradation, strength, and other items that Inherent Viscosity testing may relate to in a finished molded device. Since every bioresorbable material formulation and each

and every device geometry affects this important measure of a bioresorbable device's ultimate *in vitro* performance, the earlier in the device manufacturing process it can be monitored, and then correlated to the process, provides yet another level of security and ultimately cost control to the bioresorbable program developed. All products then undergo an independent lab verification of Inherent Viscosity that serves as a part of the ultimate product certification.

Total Client Commitment

Midwest Plastic Components strives to take care of all of its clients' needs, but also understands that its core injection molding process may not be the correct process for some of our clients. It established an aligned network of capable manufacturers within the biomaterial community that utilize compression molding techniques, CNC machining of molded rod stock or compression molded plates, and to a limited degree, extrusion capability. It is their desire to never force a product design into an incorrect manufacturing process. The ability to supply-base manage these and other potential program needs makes the company more valuable to its clients and rounds out its ability to be a full-service medical device contract manufacturer.

Midwest Plastic remains committed to working with you to meet your needs, be it new polymers, reformulations of existing polymers, or any new polymer with either a master file available, or which its clients choose to utilize and obtain approval for use. It remains committed to helping the medical device industry continue to bring new and helpful devices to market.

The **EPA** is interested in identifying commercial partners to license and bring to market its "Methods for Isolating and Using Fungal Heolysins." Some studies have suggested a link may exist between serious health problems and exposure to molds. This technology uses fungal hemolysins to create antibodies that can be used to test humans and animals for exposure to *Stachybotrys chartarum* and other indoor molds. Enviromental samples can also be tested. Contact information: technology@nttc.edu

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The first gene linked directly to heart attacks has been isolated from an extended Iowa family that has been plagued for generations with rampant coronary artery disease. The gene, called **MEF2A**, plays a role in protecting the artery walls from building up plaque that can impede blood flow and lead to heart attacks. The gene makes a protein that regulates some other genes, and it will now be analyzed to see if they can be linked generally to heart disease. It will take more study to determine if MEF2A plays a role in heart disease among people outside of families where the mutation is inherited.

Tens of thousands of activists and health workers rallied worldwide to mark **World AIDS Day** (December 1), and officials hailed new initiatives, new funding, and a new pill to fight the disease that has infected 40 million people and kills more than 8,000 every day. The World Health Organization (WHO) and UNAIDS promised cheaper drugs, simpler treatment regimens, and more money as part of a campaign launched in Nairobi to provide 3 million HIV infected people with the latest drugs available by the end of 2005 in a US$5.5 billion effort. WHO also certified an innovative, generic drug for treating HIV that combines three essential anti-retroviral drugs into one pill to be taken twice a day. UNAIDS estimates 3 million people have died this year. WHO says more than 5 million HIV patients need anti-retroviral drugs, but fewer than 400,000 have access to them. The drugs improve patient health, but they remain infected and can transmit the disease.

Neurogen Corp. (Nasdaq: NRGN), Branford, Conn., formed a partnership with pharmaceutical giant **Merck** & Co. (MRK) to develop novel small-molecule drug candidates, vanilloid receptor (or VR1) for the treatment of pain and urinary incontinence. If regulators approve the deal, Merck will make an upfront payment of $30 million to Neurogen. Merck has one of the most-developed VR1 programs in the industry.

Cook Inc., Bloomington, Ind., was allowed by the FDA to begin an IDE study of its Zenith TX2 Thoracic TAA endovascular graft for thoracic aortic aneurysms (TAA). The study involves 140 subjects at 20 U.S. medical institutions. The Zenith TX2 Thoracic TAA endovascular graft, which already is approved for commercial distribution in Australia and Asia, incorporates clinically proven technologies to treat life-threatening thoracic aortic aneurysms. Thoracic aortic aneurysms occur when a section of the aorta, the body's main circulatory vessel, weakens and bulges outward like a balloon. Should the aneurysm rupture, the patient would be at high risk for death due to internal bleeding.

Officials with the **Medical Device Manufacturers Association** (MDMA), Washington, D.C., told FDA officials during the first Medical Device User Fee and Modernization Act (MDUFMA) stakeholders meeting that small manufacturers cannot afford the significant increases in user fees. Shortfalls in FDA's MDUFMA budget—both this year and in the future—require the industry to make up the difference through increased user fees. User fees increased an average of 35 percent from FY03 to FY04. If MDUFMA fees follow the drug industry suit, the application fee for a PMA will climb to $871,000 within 12 years, and 510(k) fees will increase to $12,500.

Raymedica, Inc., Minneapolis, Minn., a medical device developer and manufacturer, has begun the enrollment of patients in a U.S. IDE study, a non-randomized, prospective clinical trial. The IDE study will evaluate the company's PDN-SOLO device in patients with chronic low back pain due to degenerative disc disease who have not responded well to non-surgical alternatives. The PDN-SOLO device is comprised of a hydrogel material designed to replace the function of a failed spinal disc nucleus. The U.S. IDE clinical trial is required in meeting FDA requirements for marketing approval. The implant has had more than seven years of clinical experience and 1,900 patient implants worldwide. Earlier this year, the company initiated the international part of this clinical study at six locations in Asia, South America, and Europe.

Australia's **CSL** Ltd. (Australian Stock Exchange: CSL) agreed to buy Aventis SA's **Aventis Behring** unit for as much as $925 million, creating the world's biggest maker of plasma products. The deal eclipses the A$1 billion CSL spent in 2000 to buy ZLB Bioplasma from the Swiss Red Cross. The combination makes great economic sense and gives CSL critical mass and competitive position. In addition to providing a stronger rival to Baxter International Inc. and Bayer AG, a combined CSL and Aventis Behring will give the company wider geographic coverage and a broader product portfolio.

Olympus has been named the recipient of the 2003 Frost & Sullivan Technology Innovation Award. In its analysis, Frost & Sullivan highlighted Olympus' distinct contribution in introducing the EndoEYE™ rigid videoscope for general surgery, urology, and gynecology laparoscopic applications. The device places the miniaturized camera chip in the distal end of the scope for advanced digital image processing and output. This one-piece design eliminates the need for fragile rod/lens assembly, making it the first, fully autoclavable design.

Medtronic of Canada Ltd. announced that it has received Health Canada approval for the new Medtronic EnPulse™ pacemaker series with advanced device features to automatically fine-tune therapy for patients whose hearts beat too slowly, a condition known as bradycardia. An estimated 20,000 Canadians receive pacemakers for bradycardia each year. The device's enhanced search method senses the patient's natural heartbeats before delivering pacing therapy, which may reduce unnecessary stimulation impulses in the ventricle. Recent clinical studies have suggested that reducing the pacing stimulation may reduce the patient's risk of developing heart failure and consequently extend the longevity of the device.

MacroPore Biosurgery Inc. (Frankfurt Stock Exchange: XMP) announced it has agreed to sell the thin film product line, which includes SurgiWrap™, CardioWrap™, and HerniaMesh™ for $12 million to privately held Medicis Ventures Management GmbH (Medicis Ventures). A syndicate of international investors led by Medicis Ventures will establish a privately held medical device company to further develop and market these products internationally and in the United States. The transaction was expected to close before January 23,

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surface chemistry of the polymer provokes little or no foreign body reaction or thrombosis as scored by standard histomorphometrics established for coronary stents[14] confirming the high degree of polymer biocompatibility.[15-19]

There is a trend among manufacturers of many types of biostable devices to replace or cloak the surfaces with body friendly

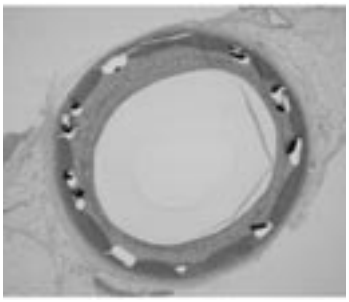

Figure 5b: *A clinically used metal stent was coated with a thin coating of poly(DTE carbonate) prior to implantation. The tissue response to a poly(DTE carbonate) surface is identical in all aspects to the tissue response seen for the corresponding bare metal stent.*

resorbable polymers and drug-eluting coatings. One can easily envision how a fully resorbable stent could integrate seamlessly and gradually with the arterial wall, potentially offering improved tissue biocompatibility[20-21] versus a metal device.

The tyrosine-derived polycarbonates are unique since they exhibit outstanding physico-mechanical properties while providing an inherent edge over other polymers for biocompatibility; they are derived from natural metabolites and

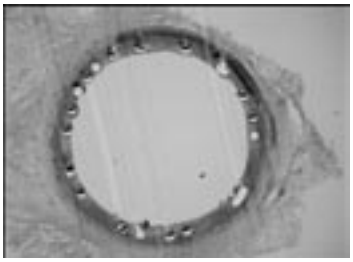

Figure 5c: *Same poly(DTE carbonate) coated metal stent as in Figure 5b, except that the poly(DTE carbonate) coating delivered an anti-proliferative drug. The drug-eluting formulation reduced neo-intimal hyperplasia.*

nutrients with known benign breakdown products (amino acids, ethanol, carbon dioxide) and have no event of acid bursting like other polymers.

For the first time, novel stent and polymer design strategies were applied in close coordination to develop a stent that fulfills simultaneously four critical design requirements: (i) clinically acceptable design, (ii) bioresorption and drug elution, (iii) X-ray visibility, and (iv) a high degree of hemocompatibility. Together these technologies will likely be of major significance in the treatment of cardiovascular disease.

Acknowledgements: REVA thanks Dr. J Anderson of Case Western Reserve University for expert histopathology and J. Early of Happy Valley Medical for her contributions to drug elution studies. Research at Rutgers was supported in part by funding from REVA Medical, by NIH research grant GM39455, and by seed funding from the New Jersey Center for Biomaterials.

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reactions can result in rejection of the device or device-related infections.

It is surprising then that the definition of a surface is not always well appreciated. Among surface scientists, the surface is the interface between the material and the surrounding environment. Typically, the surface is considered to be the outer few atomic layers of a material. Surface modification, for example to make a device surface biologically active, should not affect the properties of the bulk material. Whenever the surface is modified, it should also be characterized to ensure that the desired modification has been achieved. The characterization should also verify that there are no undesirable side reactions or surface contamination that may affect the beneficial properties of the modified surface.

Because the surface is such a small part of a material, specialized techniques must be used to specifically characterize the surface without interference from the bulk. Such surface sensitive techniques include X-ray photoelectron spectroscopy (XPS), secondary ion mass spectrometry (SIMS), atomic force microscopy (AFM), and Near Edge X-ray Adsorption Fine Structure (NEXAFS). These techniques have complementary advantages. A thoughtful combination of two or more techniques can usually provide a good understanding of the chemistry and structure of molecules at the surface.

One of the most commonly used surface analysis techniques is XPS (also known as electron spectroscopy for chemical analysis, ESCA). XPS exploits the photoelectric effect to obtain information about the chemical composition and structure of a surface. XPS analysis requires that a sample be placed in an ultrahigh vacuum (UHV) environment, then be exposed to a low-energy, monochromatic X-ray source producing photoelectrons. The resulting spectrum shows peaks from the elements present in outer surface (<100 angstroms) of the sample, giving information about the atomic composition and molecular structure of the surface. Higher resolution scans of peaks for specific elements (e.g. carbon) give information about the types of binding environments of the carbon (e.g. CH, CO, or CF). The information-rich quality of the XPS technique, combined with its ability to generate data that correlate well with observed biological interactions, makes XPS one of the most valuable surface analysis methods available for the study of biomaterials (Figure 1). XPS can also be used for chemical-state imaging giving information such as composition, structure, and spatial distribution of surface functional groups.

More detailed (and surface sensitive) information about the molecular structure of biomaterials surface can be obtained from static SIMS. The SIMS process is initiated by bombarding the surface of a solid sample with an energetic beam of ions under UHV conditions. This primary ion beam bombardment results in the ejection of atoms and molecular fragments from the surface region that, when analyzed, produce a mass spectrum of the outermost ~12 angstroms of the surface. In static mode of SIMS, the primary ion beam is maintained at a very low fluence (typically less than 1012 ions/cm2), resulting in the emission of molecular fragments from organic and biological materials and minimal damage to the surface. The structure and composition of these fragments is directly related to the surface molecular structure from which they were emitted. SIMS spectra can be used as a fingerprint to identify polymers as well as proteins. The highly sensitive nature of SIMS makes it a valuable tool for identifying small concentrations of elements (such as contaminants). Some SIMS instruments are also capable of imaging, and can be used to verify the chemical structure of patterned surfaces.

AFM is capable of atomic-level imaging of the top surface layer in a variety of environments (dry, aqueous, buffer, etc.). In scanning probe microscopies, images are derived from measurements taken at a large number of individual positions (i.e., a 200 x 200 point array) as a probe is moved across the surface. The scanning is controlled with sub-atomic precision using a piezoelectric scanner. AFM uses a microscopic sense of touch, measuring weak mechanical forces of attraction and repulsion between the atoms at the apex of the tip and those of the surface to produce topographic images of the surface. In addition, force curves (determined by the force required to push the tip into the surface and then to remove it) can give valuable information about surface interactions. By modifying the AFM tip with a biologically active molecule (e.g. biotin) it can be used to test interactions with a surface bound molecule (e.g. streptavidin).

Near Edge X-ray Absorption Fine Structure (NEXAFS) is a photo-absorption technique that utilizes a synchrotron X-ray beam. Different elements and, in detail, their different bonds adsorb a specific X-ray energy. This allows NEXAFS to be element and bond specific. NEXAFS adsorption can be monitored in different ways to emphasize bulk signal (transmitting beam or emitted fluorescence) or the surface signal (the emitted secondary electrons). By utilizing a polarized X-ray source, NEXAFS can be used to determine the orientation or order of molecules. NEXAFS requires a synchrotron for the X-ray source and is commonly done in a UHV chamber. However, it has the advantage of very good resolution along with the option of using fluorescence detection instead of detecting a photoelectron. Fluorescence detection can be done in a purged nitrogen environment or potentially in a liquid cell.

Each surface characterization technique provides a different type of information. Often, multi-technique surface analysis is usually the best way to obtain a detailed understanding about the surface structure and composition of a biomaterial. Results from these surface analysis studies can be used to determine the type and degree of changes produced by surface modification strategies and to develop correlations between surface structure and biological performance.

Education and Professional Development...

(Continued from page 4)

and to anyone who often finds themselves completing large projects (especially presentations and writing projects) at the last minute and under stress.

Instead of "self-help" feel-good advice, this book is based on 20 years of Boice's research. The ideas presented were originally gleaned from the practices of 21 exemplary new faculty out of 415 new tenure-track faculty studied by Boice through the first years of their appointments, and have been shown in subsequent research to help faculty from diverse backgrounds and institutions.

The book is divided into sections concerning teaching, writing, and socializing/service (essentially, navigating your way through the people and cultural aspects often found in academe)—three absolutely critical aspects of faculty jobs that are typically not formally addressed in graduate education. Fundamental principles discussed in the teaching and writing sections of the book are to: deliberately wait before starting a project; begin projects early; work in brief regular sessions and stop before reaching a point of diminishing returns; and value preliminary, imperfect work instead of rushing to complete a project. Moderation and patience are key underpinnings of Boice's advice, and these ideas are embodied in principles echoed throughout all three sections of the book, such as: beware of over-attachment and over-reaction; moderate negative thoughts and emotions; let others help you; and limit wasted effort.

The sections of the book associated with writing—specifically, "pre-writing" as a route to reflective and improved writing, and getting yourself writing without waiting for large uninterrupted blocks of time to appear in your schedule—will be of the most use to the widest audience. For new faculty, the sections on learning about academic culture, making time for socializing, and recognizing and avoiding what Boice calls "middle-aged, disillusioned colleagues" are critically important. Boice includes short topical quotations throughout the book that readers (depending on their personality) will either find inspiring or redundant. Similarly, Boice's discussion of working in mindful ways will probably be perceived as either fulfilling or too "far out" to be taken seriously. Maybe the time is exactly right to read a book whose main tenets are moderation and patience. This book is highly recommended for junior faculty and graduate students interested in faculty careers.

BioInk

(Continued from page 23)

2004. Under the terms of the agreement, MacroPore will receive an upfront payment of $7 million at the January closing and a $5 million payment before year-end 2004, with additional revenues from a back-up supply commitment to Medicis Ventures. Over the next three to five years, MacroPore could receive up to $13 million or more in additional milestone payments, royalties, and revenues for collaborating with Medicis Ventures on regulatory and distribution of SurgiWrap in Japan, the world's second largest market for anti-adhesion barriers. Further, MacroPore will retain an exclusive, royalty-free license for applications of the thin film technology for spinal surgeries and a non-exclusive, royalty-free license for delivery of regenerative applications.

Cardiovascular Special Interest...

(Continued from page 11)

and Platelet Adhesion." Donna's work was conducted under the supervision of Dr. Robert A. Latour, Jr. The purpose of this study was to evaluate the correlation between denaturation of adsorbed proteins and platelet adhesion. Polyethylene and polyprolylene surfaces were sulfonated using a liquid-phase sulfonation process. These surfaces were used as substrates to adsorb monolayers of porcine serum albumin and porcine fibrinogen, the model proteins used in this study. Spectroscopic ellipsometry was used to determine thickness of protein layers. Circular dichroism spectroscopy, along with deconvolution software packages, were used to determine secondary structure composition of adsorbed proteins in terms of percentage of α-helix, ß-sheet, and random coil. Structurally, native porcine serum albumin and porcine fibrinogen are mainly made of α-helix. After adsorption of these proteins onto the different chemically-modified surfaces, a loss in α-helix was measured, more importantly on surfaces that were lightly sulfonated. Platelet adhesion study was done with each surface, where the number of adherent platelets on surface-treated disks were quantified using an LDH assay. An important finding of this work is that a very strong correlation was demonstrated between the loss in α-helix structure and the number of adherent platelets (R2 value of 0.95). Results of this research imply that platelet adhesion at the surface of biomaterials could be reduced if implant materials were selected to minimize blood protein denaturation.

Congratulations to Trevor and Donna. The cardiovascular SIG is proud to encourage student participation in the Society For Biomaterials!

17th Annual Meeting of the International Society for Ceramics in Medicine

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Topics include (but not limited to)

Biological ceramics
Biomimetic ceramics/coatings
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Ceramic/surface-body fluid interactions
Bioceramics-bone interactions
Materials-cells interactions
Ceramics/surfaces in delivery system
Clinical application -fixation
Clinical application - bone replacement
Clinical application - bearing surfaces
Novel biomaterials and their synthesis
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Bioactive coatings for fixation of osteoporotic bone
Academia-Industry-Clinic forum

Deadline of abstract submission: May 15, 2004

Please send your abstract to info@bioceramics17.com and visit
www.bioceramics17.com for the guideline on abstract preparation.

The Newest...

(Continued from page 16)

"bioabsorbable" polymers. Guidant, in its ongoing Future I and Future II clinical trials, is using a bioabsorbable polymer.

Don't Forget the Stent and the Delivery System

Granted, a great drug and an excellent polymer system are wanted components for any DES manufacturer. However, the stent design itself, and the ease of deliverability of the stent to the occluded lesion are also important factors in the equation of success. A great drug and polymer combination on a lousy stent that can hardly make it to the lesion might not gain a lot of loyalty from physicians. All components of DES are important. Sales representatives certainly have an incredible job to do when visiting cath labs around the country, describing advantages of their products over the competition.

What Is To Be Expected In The Coming Months?

More talk about late response to DES

Life is good. DES restenosis rate has reached single digit, but this is not a guarantee that everything will keep going right. Reports from patient follow-up will continue to feed discussion. This is an important educating experience for the scientific community. Stents, as for the majority of medical devices, are tested in healthy animals, such as adult swine. The healing response in these animals might be very different than the one observed in individuals suffering from coronary diseases. Will stent lumen remain un-occluded for the patient lifetime? Some concerns have recently been voiced regarding the possibility of sub-acute thrombosis (SAT) several months after DES implantation. The occurrence of these events is limited, but careful monitoring of clinical events is essential.

Price war

It is anticipated that in the coming year pricing of coronary stents will fluctuate. The market has to find reasonable pricing for both DES and bare metal stents. Ultimately, this should lead to more treatment options for physicians, and better clinical outcome for patients.

Law suits

Stent manufacturers will continue to take legal action against each other for patent infringement reasons, trying to prevent the other from selling their products and gaining market shares! This has already begun between Johnson & Johnson and Boston Scientific.

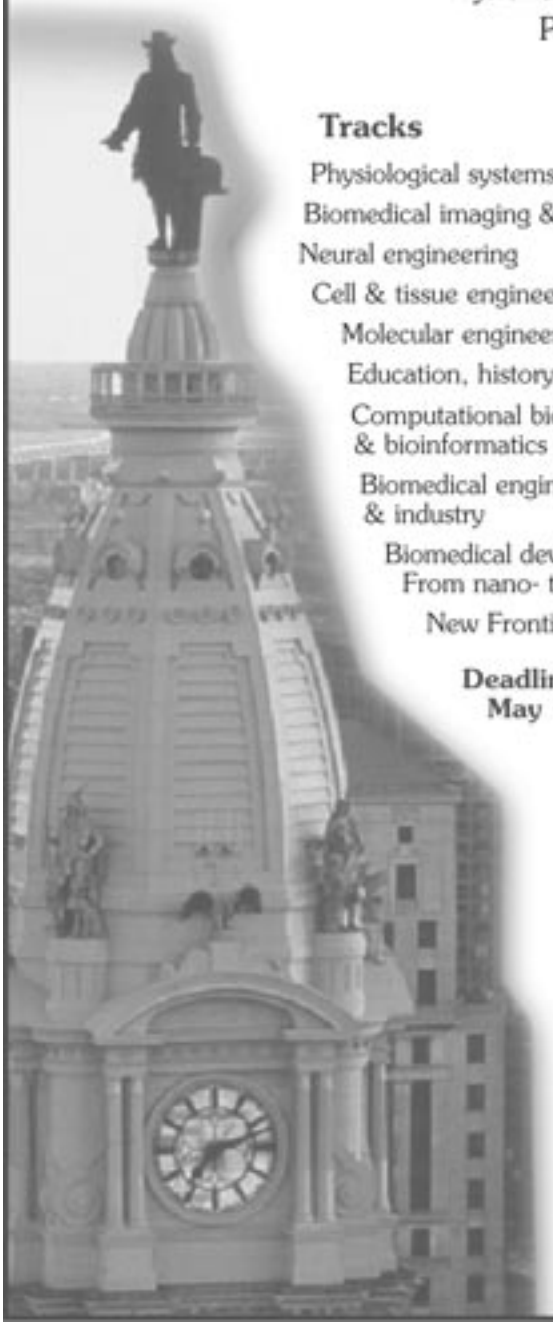
A suivre!

2004 Annual Fall Meeting

BMES

Biomedical Engineering Society

October 13-16, 2004
Wyndham Philadelphia at Franklin Plaza
Philadelphia, Pennsylvania



Tracks

Physiological systems engineering
Biomedical imaging & optics
Neural engineering
Cell & tissue engineering
Molecular engineering
Education, history & future approaches
Computational bioengineering & bioinformatics
Biomedical engineering in society & industry
Biomedical devices: From nano- to micro- scale
New Frontiers in BME

Deadline for Abstracts: May 15, 2004

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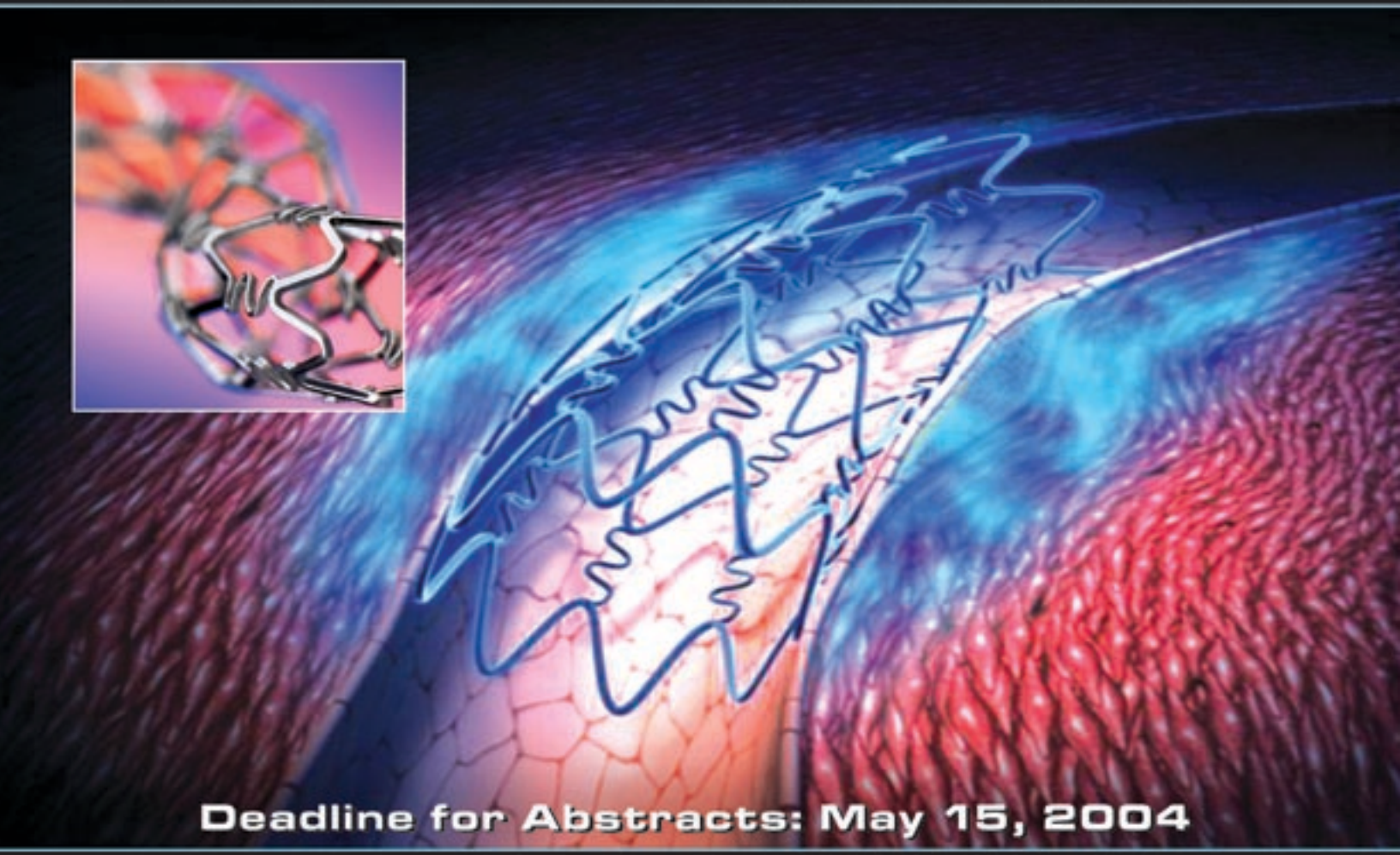
Society for Biomaterials

Biomaterials in Regenerative Medicine: The Advent of Combination Products

A special symposium held in conjunction with the Biomedical Engineering Society 2004 Fall Meeting



Deadline for Abstracts: May 15, 2004

Abstract categories include:
- Frontiers in combination products
- Material-Cell interactions
- Material-drug/DNA interactions
- Host Response
- Novel materials
- Industry/FDA forum "Translation from Discovery to Development" (Chair: Robert Nerem)

Invited speakers include:
- Julia Babensee
- Chris Chen
- Jeffrey Hubbell
- Bob Langer
- Ann Marie Schmidt
- Duncan Stewart
- Sam Stupp

Log on to **www.biomaterials.org** for information about submitting your abstract;
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