From the pages of Design News

Breakthrough Developments in Medical Design

By Doug Smock -- 5/15/2006

Rapid-fire developments in polymer technology are creating breakthroughs in medical design that can build billion-dollar markets overnight as the explosive recent growth of the drug-eluting stent business has shown. The next big thing in medical design is implanted devices made of biodegradable (also called bioabsorbable or resorbable) plastic compounds.

The use of biodegradable polymers in orthopedics dates backs to the 1980s, but various metals, particularly titanium, have dominated due to their superior strength and because of problems related to biodegradables. For example, rapid bulk erosion of the polymer causes tissue reaction. Significant technological advances in polymer engineering are about to unleash a new wave of design developments for the melt-away matter.

Key design developments to watch:

- New coronary stents use biodegradable materials for coatings or for the entire structure. Biodegradables have the potential to revolutionize the $5 billion annual stent market almost overnight because they create opportunities for re-treatment and elimination of drug residues used to treat restinosis, or renarrowing of the artery.
- New site-specific drug-delivery devices treat cancer, wound or macular degeneration and then disappear.
- Fracture-fixation devices, such as screws, pins, plates or mesh from metals, such as titanium, stainless steel or cobalt chrome will rapidly convert to new biodegradable fixtures that are stronger and break down on predetermined schedules.

A new Frost & Sullivan research report predicts that use of biodegradable materials for implants will grow 7.5 percent a year compared to 2.4 percent for all materials used in implants. "Bioabsorbable polymers are being clinically researched by many implant manufacturers to use in cardiovascular stents, meshes and spinal fusion, as well as hip and knee transplants," comments Balaji B. Capaloor, senior research analyst at Frost & Sullivan.

Biodegradables are rapidly gaining favor in orthopedics with doctors and patients because they require no follow-up surgery to remove them. They also allow transfer of loads to healing bone and soft tissues; are compatible with magnetic-resonance imaging; and avoid complications, such as corrosion, sometimes associated with metal implants. Another advantage of biodegradables is that injection molders are now mass producing the very expensive and thermally unstable polymers. These molders include Phillips Plastics of Hudson, WI and Mar-Lee Industries of Fitchburg, MA.

Only a few monomers have gained acceptance for use in approved medical-orthopedic devices. These include polylactic acid (PLA), polygolic acid (PGA), polycaprolactone (PCL), polydoxanone (PDO) and poly-trimethylene carbonate (TMC). Creation of copolymers from these monomers greatly extends engineering opportunities. For example, TMC makes compounds tougher and more malleable. Even within the PLA family, several combinations are possible.

A key question for engineers to consider is the extent of crystallinity in the polymer structure. Polymers, such as PGA, with semicrystalline structures are better suited for load-bearing applications because they have better mechanical strength. Increasing the polymers' crystallinity can boost their mechanical properties by increasing their level of crystallinity.

One of the leading orthopedic-technology developers is Finnish company Inion, which is only 6 years old. Its products include biodegradable polymer plates that find use in hand, ankle, and dental repair. The material retains load-bearing strength for about 12 weeks and then weakens, allowing the repaired bone to gradually adapt to bearing loads. "Typically, the material will break down over the next 18 to 24 months," comments Auvo Kakkinen, CEO of Inion and a former orthopedic surgeon. "The process is harmless, and the resulting energy is absorbed into the body's cells."

British company Smith & Nephew last year launched a system using bioabsorbable screws to attach graft tissue in anterior cruciate ligament surgery. The tapered fixation screw is injection-molded from poly-L-lactic acid (PLLA).

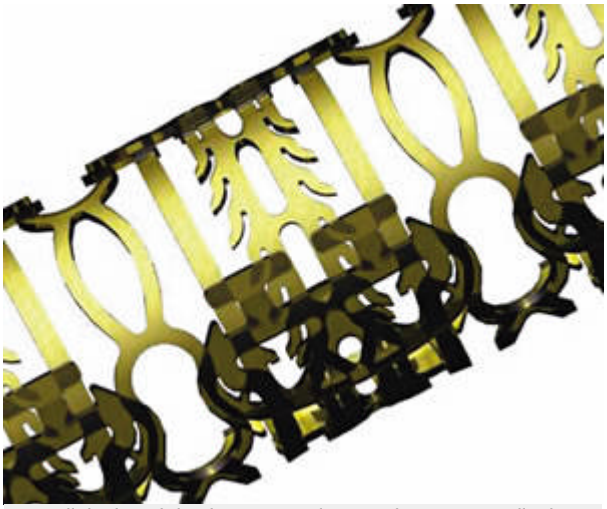
Disappearing Devices

The next phase of technological development focuses on the use of bioabsorbable polymers in devices that are implanted in the human body using newly-engineered polymers that have highly tailored degradation schedules.

The New Jersey Center for Biomaterials, headed by Rutgers University professor Joachim Kohn, has engineered new polymer structures for use by device makers Reva Medical in San Diego, CA and SurModics of Eden Prairie, MN. Reva asked Kohn to develop a polymer it could use in its slide-and-lock coronary stent, which uses a mechanical system to expand within a coronary artery. A series of stent elements slides open and then locks into place. The design allows for substantial reductions in stent-strut thickness in a variety of materials, including bioresorbable polymers. In previous stent designs, a surgeon expands a balloon inside the stent when an X-ray indicates that the stent is in place. The balloon bends and deforms the metal structure, which is often covered with a durable polymer that distributes drugs to the diseased area.

"The bioresorbable device is currently in the development stage," comments Cheryl Liberatore, director of business development for Reva. "The preclinical work is substantially complete, and the company is

poised for a first-in-man clinical trial in the near term."



Preclinical work is almost complete on the Reva Medical slide-and-lock coronary stent made with bioasborbable polymers.

Kohn developed an enhanced version of polyDTE carbonate for use in the Reva stent. His experiments included addition of iodine to allow X-ray visibility, polyethylene glycol to make the material less adhesive to components and avoid clotting, and acidic co-monomer to fine-tune biodegradation schedules. His team at Rutgers used computer models, a new screening assay and other tools to determine optimal quantities of each new ingredient.

Boston Scientific, one of the two leading stent manufacturers, has an option to buy Reva. Some clinicians believe that using bioabsorbable polymers will allow stents to treat more lesions per patient than metallic stents or to treat different vascular diseases for which metal stents are less desirable. CEO James R. Tobin of Boston Scientific commented at a plastics conference last year, however, that use of stents to treat other vascular diseases is still a long way off.

Another important player is MediVas, also of San Diego, which uses amino acid-based-polyester amides (PEA), to make bioabsorbable stents. MediVas has agreements with several technology players in the coronary-stent market, including Boston Scientific, and is also studying bioabsorbable devices that doctors can attach to cancer tumor cells or backs of eyes, where they would dispense medications and then disappear.

Also on the horizon are bioasborbable polymer scaffolds that physicians can seed with human stem cells and place in locations to repair arteries or other damaged human tissue. Concordia Fibers of Coventry, RI, produces Standard Biofelt using PGA in 20-cm by 30-cm felts. The thicknesses can be 1 to 5 mm, and the bulk density can be 25 to 100 mg/cc. Concordia Fibers' work in tissue engineering is based on the work of Dr. Robert Langer, M.D., at the Massachusetts Institute of Technology. (See "Medical Miracles," Aug. 15, 2005, at http://rbi.ims.ca/4923-511.)

"All applications of Biofelt are currently in preclinical and animal-trial stages, but we do expect that some of these will reach human clinical trials in the next couple of years," comments Art Burghouwt, executive vice president of Concordia Fibers. "The cell seeding, proliferation and differentiation is more the issue than the behavior of the polymers and scaffolds."

TYPICAL PROPERTIES OF SELECTED BIORESORBABLE POLYMERS Polymer	**Crystallinity**	**Tensile strength (MPa)**	**Tensile modulus (GPa)**	**Approximate time for complete resorption (months)**
PDO/PDS	Semi-crystalline	30	1.5	Six
PGA	Semi-crystalline	60 to 80	5-7	Six to 12
PGA-co-TMC	Semi-crystalline	60	2.4	12 to 15
85:15 PDLLA/GA	Amorphous	40 to 50	2	Six to 12
PDLLA	Amorphous	40 to 50	2	12 to 15
PLLA	Semicrystalline	60 to 70	3	More than 36
PCL	Semicrystalline	20 to 25	0.4	More than 36

Source: David Farrar, Smith & Nephew Research Centre

Web Resources

Material's developers:

The New Jersey Center for Biomaterials: http://rbi.ims.ca/4923-501	**Purac America**: http://rbi.ims.ca/4923-502	**Absorbable Polymer Technology**: http://rbi.ims.ca/4923-503

Device Developers:

Medivas: http://rbi.ims.ca/4923-504	**Reva Medical**: http://rbi.ims.ca/4923-505	**SurModics**: http://rbi.ims.ca/4923-506
Inion: http://rbi.ims.ca/4923-507	**Smith & Nephew**: http://rbi.ims.ca/4923-508	

Molders:

Phillips Plastics: http://rbi.ims.ca/4923-509	**Mar-Lee Industries**: http://rbi.ims.ca/4923-510	