RESOMER® polylactic acids are completely resorbed into the body

HEALING BONES WITH POLYMERS

Broken bones, torn tendons, and damaged intervertebral discs are painful and impair quality of life. Evonik's Medical Devices Project House develops materials that support healing and can spare patients further surgery. The first products are now being launched on the market

TEXT
KARIN ASSMANN

Perfect lightweight structure and high resilience: Bones combine maximum strength with minimal weight

Soccer players live dangerously. According to the German insurance association GDV, every fourth injury in this game is a fracture. To get the injured players back on their feet fast, surgeons often use screws, plates, wires, and pins to set the bone fragments and stabilize them until healing is complete. The fracture site gradually ossifies, the bone tissue regenerates, and the implants become superfluous. "Metal implants are usually removed after 12 to 24 months; for the patient this means more surgery, followed by extra time for recovery," says Dr. Andreas Karau, who is responsible for Biomaterials in Evonik's Health Care Business Line.

But metal is not the ideal material for treating fractures, because metal implants are much less elastic than bone. They therefore bear the mechanical forces exerted at the fracture site particularly well—too well, in fact, as Karau explains: "Bones need constant mechanical loading to regenerate and to maintain their density and strength. The absence of physiological stress can slow down the healing process." In the case of implants that remain in the body long-term, this may even lead to the shielded bone degenerating in the course of time. "This is known in medicine as the stress shielding effect. To prevent this, metal implants are often removed after a few months when the fracture has healed," says Karau.

A better approach is to make implants from a material that would allow mechanical stress to be exerted on the affected bone instead of intercepting it. This is where polymer-based devices have the edge: They are considerably more elastic than metals, and hence prevent the stress shielding effect. Evonik's experts have even taken the idea a step further: Implants made from RESOMER® biodegradable polymer offer the additional advantage of being resorbed by the body as the bone heals. Ideally, a bioresorbable polymer would be chosen in such a way that the strength of the implant is reduced as healing progresses and the load-bearing capacity of the fracture site increases. This eliminates the need for a subsequent intervention to remove the implant—which reduces the burden on the patient, the risk of infection, and, not least, the cost of treatment.

Evonik initiated systematic development of improved materials for orthopedic surgery in the Medical Devices Project House in Birmingham (USA) in 2014. This site was selected because the USA is the largest regional market for medical devices, with a share exceeding 40 percent; the size of the global medical devices market is currently €300 billion and is growing annually by about six percent. "We develop new solutions that help avoid additional surgery or accelerate the healing process," says Balaji Prabhu, head of the project house. →

Invertebral disc prostheses made of VESTAKEEP® restore the natural height of a disk segment

"We were able to customize implants by using printable biopolymers"

ANDREAS KARAU

For example, torn tendons are held in place with screws and pins made of RESOMER®

POLYMERS GAINING GROUND

Polymers, however, make up only about ten percent of the total implant market. "For many applications, such as artificial hip and knee joints or the stabilization of load-bearing bones, the available plastics that are approved for medical devices are simply not strong enough," says Prabhu. By contrast, polymeric materials are gaining ground in the treatment of fractures of the hands, feet, jaw, or skull, and for reconstruction of tendons in the shoulder, knee, or spine: A good 50 percent of implants in this area are made of polymers.

Evonik has been active in this market for many years and offers a wide range of polymer materials, including the RESOMER® brand of biodegradable polymers based on polylactic acids. Medical device manufacturers use these to produce screws, pins, and small plates that are degraded in the body after a specified period. Evonik also offers the polyetheretherketone VESTAKEEP®, which is used to make implants for the spine, mouth, jaw, and skull; such applications require both biocompatibility and good mechanical properties.

But the potential of these polymer materials in medical technology is far from exhausted. "If biopolymers could be processed by 3D printing, it would be possible to customize implants for each individual patient and operation," says Karau.

Around 25 researchers are working in the project house to realize this vision. "Most of them were freshly recruited, because it takes very specific expertise in a variety of different fields to develop new solutions and bring them to market readiness," says Karau. Some researchers, for example, have gained experience working for high-profile manufacturers of medical devices or in academia, while others have worked on the development of aerospace engineering materials. "So we're optimally positioned," adds Prabhu.

FIRST PRODUCT READY FOR MARKET LAUNCH

The Health Care Business Line is in the process of launching a product developed by the project house; this is a composite of RESOMER® polylactic acid and a synthetic hydroxyapatite filler. Hydroxyapatite, which makes up 70 percent of human bone, is the most common biomineral in the human body. "By combining RESOMER® and hydroxyapatite we can offer a composite whose mechanical properties are very similar to natural bone. Implants made from this material support bone regeneration and prevent the stress shielding effect," says Karau.

The properties of the two materials complement each other perfectly. RESOMER® provides biodegradability: It is completely degraded in the body to carbon dioxide and water, causes no inflammatory reaction, and is non-toxic. And it has yet another important advantage: "We can control the rate of degradation of the composite very precisely by varying the composition, chain length, and degree of crystallinity of the polylactic acids," says Prabhu. The biodegradable polymer can break down within a few weeks or over several months, depending on how long the bone and surrounding tissue require for regeneration.

Hydroxyapatite, an extremely hard material, performs two functions in the composite: It improves the mechanical strength of the polymers, and it promotes the healing process, known as osseointegration, in which bone cells are laid down on the surface of the implant. The biomineral is incorporated into the regenerating bone while the RESOMER® is slowly degraded. "At the same time, the hydroxyapatite serves as a buffer. During the degradation of RESOMER®, the pH of the surrounding tissue may fall slightly. Hydroxyapatite stabilizes the pH, thus improving osseointegration," says Prabhu.

However, a suitable pre-compounded composite for this purpose has not so far been available on the market. "Manufacturers of medical devices either had to compound the material (mix the individual raw materials to produce the composite) themselves, or commission a service provider to do so. And this processing step is not trivial," says Karau. The processing conditions, above all, are critical: Non-ideal conditions result in inhomogeneous dispersion of the hydroxyapatite in the polymer or cause a degradation reaction of the polymer.

Balaji Prabhu,
Head of the Medical Devices Project House

But the Project House has cracked the problem: "We can now manage this step on the commercial scale," says Karau. The Business Line can now offer composite materials of different compositions that manufacturers of medical devices can process directly by injection molding to produce the required part, without the need for an intermediate step. "Feedback from selected partners who have already received samples of the material has been overwhelmingly positive. The new product has sparked considerable interest," says Karau.

A CAGE FOR THE SPINAL COLUMN

A second focus of the Project House is VESTAKEEP®. "In chemical terms this is a biocompatible polyetheretherketone," says Evonik expert Marc Knebel, who is responsible for Medical Devices & Systems in the High Performance Polymers Business Line. "It is used in orthopedic implants that will remain in the mouth, jaw, skull, and, in particular, the spine over the long term."

A typical VESTAKEEP® product is an intervertebral disc implant. These look like small cages with a central cavity that is important for correct functioning; that's why they are also known as spine cages. For a slipped disc, doctors may advise removing the disc and replacing it with an implant of this type to restore the natural distance between the vertebrae," says Knebel. "Over time the bone material then grows into the cage, bridging neighboring vertebrae."

As Knebel explains, VESTAKEEP® is particularly suitable here due to the properties of the material: "The elasticity of VESTAKEEP® is comparable to that of bone, so that implants of this material prevent stress shielding of adjacent vertebrae."

However, a challenge with spine cages is that they may migrate, or subside, in the post-implantation phase. "Until ossification is sufficiently well advanced, the ridged surface of the implant ensures adequate stability through its clamping action," says Knebel. The VESTAKEEP® experts have even devised a trick to accelerate the healing process: A composite of VESTAKEEP® and the biomineral hydroxyapatite is expected to facilitate the growth of bone cells on the implant surface, allowing the vertebral bodies to fuse faster.

Here again, the temperature that is required in the production process presents a major obstacle, since it must be above 400 °C. The solution is a modified hydroxyapatite that is easily processed →

Initial successes with 3D printing: The project house has successfully produced molded parts made of RESOMER® powder through selective laser sintering

On the test bench: An injection molding prototype made of the newly developed composite material consisting of RESOMER® and hydroxylapatite

The Medical Devices Project House in Birmingham (Alabama, USA)

NEW COMPETENCE CENTER

Like all of Evonik's project houses, the Medical Devices Project House was a temporary organization. When it ended as scheduled on March 31, 2018, the Health Care Business Line (as the major user) took over its operation as a competence center that is also available to other business lines. The competence center will provide application technology support for the sales and marketing of the new products. It will also initiate projects and partnerships with customers and will continue working on existing projects.

3 QUESTIONS FOR PROF. DR. DOMINIK MEYER

Implants made of various polymers are also used at the Balgrist University Hospital in Zurich. The deputy chief physician of the orthopedics department talks about his experiences with plastic implants

What motivated you to use implants made of plastic?
Most of these materials have already been used since the 1980s. Their quality has improved quite a bit since then, and as a result they are a very good alternative in many areas today. In the case of screws, it's often important to ensure that they can be resorbed by the body. They disappear within three to six months and make it unnecessary to operate again on the patient. This is where bioresorbable plastics demonstrate their strengths.

What other advantages do the plastic alternatives offer?
Implants made of plastic are very useful if the patient requires radiation therapy, for example, because the radiation is scattered less widely. The use of plastic is also advisable for MRTs.

What has to happen so that plastics can be used even more often in the future?
In some cases, the strength could be increased. Plastic is a good material for the skull or the hand. But bioresorbable plastics in particular are not yet suited for high levels of strain such as those sustained by the thigh bone, for example.

at high temperatures and ensures very good bone growth. The process is currently being ramped up to commercial scale, and the launch of the new composite is slated for 2019. Its name, VESTAKEEP® Osteoconductive, indicates the ability of the composite to act as a scaffold and facilitate natural bone growth.

PRINTED IMPLANTS

Evonik's researchers in Birmingham are also pursuing the idea of developing printable RESOMER® polymers for medical technology. Should a patient with, for instance, skull or facial trauma require an implant, computed tomography can be employed to determine its exact form. Software then sends the data to a printer that fabricates the implant. A patient-specific implant is thus available within a matter of hours and the patient can undergo surgery.

However, this remains a vision. "Currently, the surgeon selects the most appropriate implant from a number of standard sizes: Individually fabricated polymer implants for individual patients are not available," says Prabhu. This is a serious drawback, but no implantable polymer materials have been available so far that give consistently high print quality and also meet the stringent regulatory and property requirements for medical technology. For example, polylactic acids now available on the market for industrial 3D printing contain additives that make the material printable in the first place, but these very additives prohibit its use in medical devices.

"We're working on making our biodegradable RESOMER® polymers usable for 3D printing in medical devices," says Dr. Thomas Riermeier, head of the Pharma Polymers & Services Product Line at Health Care. The aim is to bring to market materials with the appropriate documentation for the most common printing processes: powders for selective laser sintering (SLS) and filaments for fused deposition modeling (FDM).

With FDM, a filament of the polymer is fed to an extruder in the 3D printer, heated to melting point, and extruded through a nozzle. The component is built up layer by layer. "It's vital that the filament has a stable geometry suitable for the purpose and does not change chemically when melted. And it must deliver reproducible results, even on printers from different manufacturers," says Riermeier about the requirements of the material.

With SLS, by contrast, a laser moves over a powder bed, sintering only certain defined areas of the uppermost particle layer on the surface of a powder bed. These areas solidify upon cooling. After each layer is completed, the powder bed is lowered, a new layer of material is applied, and the process is repeated until the complete part has been produced, layer by layer. "For optimal results the polymer powder should have a suitable particle diameter and good flowability. This latter requirement is especially challenging for us: While free-flowing additives are commonly used in industrial applications, this is of course impossible in medical devices because they are not approved for this purpose," says Riermeier.

The project house researchers have already achieved some success with both printing methods. They have developed processes that produce RESOMER® powder and RESOMER® filaments of the right type. The first test parts have been printed to investigate how the material behaves during printing and to assess the properties of the printed component. The next step will be to provide manufacturers of medical devices with research samples, enabling them to carry out their own printing tests.

But there are regulatory hurdles to be overcome before the first printed implants can be deployed in healthcare environments. Who will print the device—the hospital, the printer manufacturer, or a service provider? How will consistent quality be assured? Who approves a freshly manufactured implant? "Our aim is to be ready with the appropriate products as soon as these issues have been resolved," says Riermeier. On the basis of the results achieved so far, the chances are good that this goal will be achieved.