Titanium in Difficulties

PEEK. In addition to surgical instruments and endoscopes, implants have become an important field of application for PEEK. The major reasons for the success of this polymer include its mechanical properties, its transparency to x-rays and its biocompatibility.

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According to a study conducted by Frost & Sullivan, back pain is one of the most common complaints in the USA – in 2005 alone, Americans visited doctors just under 20 million times because of spinal column and spinal disk problems. Sometimes, only surgical intervention can help to alleviate the pain: Every year, more than 800,000 operations are performed on the spinal column in the USA. Depending on the age and symptoms, common methods of treatment include disk removal (diskectomy) or removal of parts of spinal vertebrae (laminectomy), replacement of vertebrae by implants and stabilization (non-fusion) or stiffening (fusion) of the corresponding segment of the spinal column with implants.

When it comes to manufacturing implants or medical instruments, more and more manufacturers of medical products for spinal surgery as well as for traumatology and orthopedics turn to polyetheretherketone (PEEK) **(Fig. 1)**. The material is biocompatible, inert with respect to body fluids and can be easily formed to yield individual implants. Compared to titanium, the classic implant material, it offers the additional benefits of transparency to x-rays and an elasticity similar to that of bone. Because of its outstanding properties, PEEK has, in the meantime, become one of the most important thermoplastic material substitutes for titanium implants.

Since implants are supposed to last a lifetime, the materials used for them must be both biostable and capable of withstanding mechanical loads. For a long time, this was the exclusive domain of titanium or cobalt-chromium. In the meantime, however, more and more polyetheretherketone (PEEK) implants are being used, inasmuch as they can be machined more readily from semi-finished blanks or be produced via injection molding, which offers even greater design freedom. Compared to titanium or other metal alloys, there are also numerous other benefits.

Elastic and Transparent to X-Rays

For instance, metallic implants encounter limitations when it comes to imaging methods that physicians use during operations, when tracking the healing process and when checking the results. Because of their density, metals block x-rays and produce artifacts in a C-arm x-ray unit and also during computer tomography (CT) as well as during magnetic resonance imaging (MRI). These prevent observation of the bone tissue behind the implant, making reliable image evaluation difficult.

Because of its transparency to x-rays, PEEK (for instance, Vestakeep, supplier: Evonik), on the other hand, is invisible during CT and MRI scans and permits bone growth and the healing process to be assessed readily **(Fig. 2)**. In certain cases, however, it is desirable to see the implant, e. g. to check the fit of the implant, and this is also possible with modification of the resin.

An additional drawback of metals is the high modulus of elasticity, which is considerably greater than that of bone material. As a consequence, the implant absorbs most of the mechanical load instead of the bone. This so-called stress shielding effect can have wide-ranging consequences: Since bones need to be exposed to mechanical stress in order to regenerate during the healing process, on the one hand, and retain their long-term strength, on the other, healing may be slowed and the stress-shielded bone actually degenerate in the course of years.

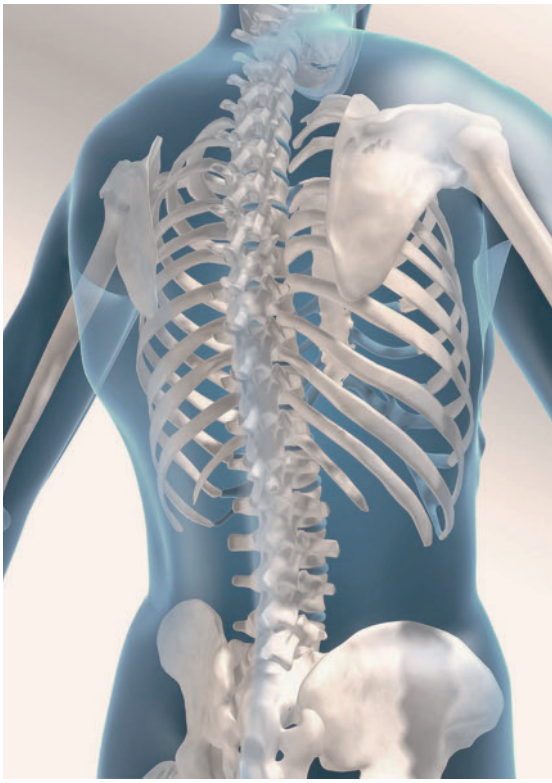

Fig. 1. The spinal column region represents a major field of application for PEEK implants today (photo: Sebastian Kaulitzki, www.fotolia.com)

In contrast to metals, PEEK has a lower modulus of elasticity, or greater elasticity, on the order of that found in bone material **(Fig. 3)**. This prevents the stress shielding effect, so that the bone is not relieved completely of mechanical stress when in contact with the implant and can thus retain its strength over many years.

A Resin for Harsh Environmental Conditions

Both its x-ray transparency and its ability to prevent the stress shielding effect have contributed to PEEK having become the most significant thermoplastic alternative to metallic implant materials in recent years. This relatively new high-performance plastic has been on the market →

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	Vestakeep M	Vestakeep I
USP Class VI	x	x
Acute systemic toxicity	x	x
Subcutaneous irritation	x	x
Implantation test 7 days	x	x
Hemocompatibility		x
Implantation subcutaneous 28 days		x
Genotoxicity		x
Subchronic systemic toxicity		x

Table 1. Biocompatibility tests stipulated by ISO 10993

since only the beginning of the 1980s and is used primarily when components must withstand harsh environmental conditions – for instance, high temperatures, corrosion as the result of exposure to salts, solvents, acids and other etching substances or extreme mechanical loads.

The reason for this is the aromatic, semi-crystalline nature of the PEEK polymer. Because of its chemical structure and morphology, it has exceptional resistance to wear, abrasion, hydrolysis, corrosion and chemicals. Furthermore, PEEK is characterized by high dimensional stability because of its low moisture uptake, high rigidity in conjunction with low weight, high heat deflection temperature, a continuous use temperature of 260 °C and its ability to be processed in many ways. Compared to other resins, PEEK offers the best combination of inert behavior and heat deflection temperature. Important nonmedical fields of application include semiconductor production, oil exploration, motor vehicles and aviation, where it is increasingly displacing aluminum, titanium or steel in aircraft.

Sterilizability

For medical applications of PEEK, important characteristics in addition to the mechanical properties and x-ray transparency include the exceptional sterilizability and biocompatibility.

Many other polymers encounter limitations when a combination of washing – drying – chemical cleaning – steam sterilization is used for hygienic cleaning. This is not the case with PEEK: Even after long-term exposure to hot steam, and ethylene oxide and gamma rays, this high-performance plastic retains its original properties unchanged and, as a consequence, can be sterilized without difficulty by means of all common methods – an important prerequisite, for instance, for use in multi-use surgical instruments. Since the polymer can also be colored easily, color coding of instruments is also possible.

The Finished Medical Product is the Critical Factor for Biocompatibility

Biocompatibility is the deciding factor when it comes to determining the basic suitability of a material for use as an implant – the material must be neither cytotoxic, mutagenic nor carcinogenic, have no allergenic properties and must also be stable in the biological environment. Verification of biocompatibility, however, must always be conducted on the finished medical product, since the products biocompatibility can change as a result of processing and combining with other materials.

The biocompatibility requirement of the finished medical product depends on both the type of contact (skin, blood, fatty tissue etc.) and the duration of contact. The biological assessment of medical products thus depends on the intended use. DIN EN ISO 10993 incorporates numerous international standards regarding biocompatibility testing and governs selection of the tests that are relevant for a particular application.

Nevertheless, certain material tests are meaningful, since they provide important information about suitability in the final end product. In addition to DIN EN ISO 10993, the US Pharmacopoeia (USP) "General Chapter <88>" describes testing of plastics for medical products and permits assignment, depending on the application, to Classes I to VI, with the plastics in Class VI having to satisfy the most stringent requirements. Here, too, the basic principle is, of course, that the biocompatibility of the final end product must be assured.

Extensive Biocompatibility Tests Passed

Evonik Industries has had the biocompatibility of its PEEK polymer from the Vestakeep product family – which is based primarily on the high chemical resistance – confirmed in extensive investigations by an independent testing institute. Depending on the type and duration of the body contact, two different PEEK variants are offered. The Vestakeep M variant is suitable for brief contact involving surgical instruments, for instance. Vestakeep I, in contrast, is suited for extended contact such as that required in the case of implants **(Table 1)**. The formulations of these polymers are targeted to provide high biocompatibility and an "in vitro" batch test for cytotoxicity to DIN EN 10993-5 offers additional security.

On the basis of the investigations, Vestakeep I molding compounds satisfy numerous requirements for medical applications **(Table 2)**.

It can be seen that the Vestakeep I polymers are inert with respect to body fluids and have no adverse effects in the standardized biocompatibility tests: They are

United States Pharmacopoeia Testing: <88> "Biological Reactivity Testing In Vivo" Class VI:
Acute Systemic Toxicity Test: 4 various extraction media (70 °C/24 h) Irritation Test – Intracutaneous Injection Test: 4 various extraction media (70 °C/24 h) Implantation Test: In Vivo Implantation Test: intramuscular, 7 days
Additional tests conducted with reference to ISO 10993. These include investigation of toxicity, sensitization, irritation, subchronic toxicity, genotoxicity and implantation:
Cytotoxicity as stipulated in ISO 10993-5 Hemocompatibility as stipulated in ISO 10993-4 Intracutaneous reactivity as stipulated in ISO 10993-10 Sensitization as stipulated in ISO 10993-10 Acute systemic toxicity as stipulated in ISO 10993-11
Subchronic toxicity as stipulated by 10993-11
Genotoxicity (Ames Test) conducted as stipulated in EN ISO 10993-3 and OECD Genotoxicity (Chromosome Aberration Test) conducted as stipulated in EN ISO 10993-3 Genotoxicity (Mouse Lymphoma Test) as stipulated in ISO 10993-3 OECD 476
Implantation In Vivo Implantation intramuscular 12 weeks as stipulated in ISO 10993-6

Table 2. According to investigations, Vestakeep I grades satisfy numerous requirements for medical applications

Fig. 2. Transparency to x-rays is a benefit of PEEK implants, since in contrast to titanium implants will grow inside the implant can be confirmed

not toxic, cause no reddening of the skin or edema and are not biologically reactive. In intramuscular implantation tests, neither loss of color, encapsulation, infections, bleeding nor necroses could be observed. Investigations of hemocompatibility and subchronic toxicity showed nothing unusual either. Specifications, production and production-accompanying documentation were modified to satisfy the demanding requirements of medical technology **(Table 3)**. It is further possible to distinguish Vestakeep I products from technical PEEK products.

Consistent Quality an Important Prerequisite for Medical Devices

Medical products that are intended for long-term contact with body tissue must satisfy especially stringent quality requirements for registration in Europe or the USA. On the one hand, manufacturers must prove that the materials are suitable for the particular application and, on the other, document how they will assure consistent quality.

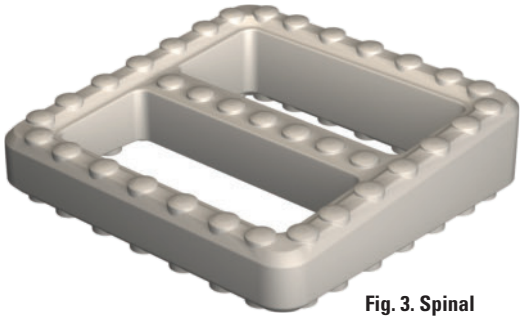

Fig. 3. Spinal implant: the greater elasticity of Vestakeep compared to that of titanium reduces stress peaks at the interface between bones and the spinal implant

For instance, when processed by means of extrusion or injection molding, the different cooling rates have an effect on the material properties of PEEK. Moreover, the duration and temperature of any subsequent thermal processing have a direct effect on the crystallinity of PEEK polymers and thus on their mechanical properties. This means that the material properties can be controlled, but also that errors during the production process can affect the quality. As a resin supplier, Evonik guarantees consistent quality of the materials used, the production processes and the PEEK polymers via certified and validated work procedures and a reliable quality assurance system.

	Vestakeep G	Vestakeep M	Vestakeep I
Duration of tissue contact		> 30 days	up to 30 days
ISO 9001:2008	x	x	x
Material traceability	x	x	x
Cytotoxicity batch test		x	x
Special production method			x
FDA Device Master File			x
"No change" agreement			x
Batch test for extractable substances			x
Cleanroom packaging			x

Table 3. Additional quality attributes of Vestakeep grades for medical applications compared to technical products

This information, some of which is confidential, has been provided to the Food and Drug Administration (FDA) in the USA in the form of a Device Master File. This simplifies registration of a new implant by customers: If a medical product manufacturer applies for registration in the USA, the FDA can research all relevant information regarding the materials used in the respective documentation.

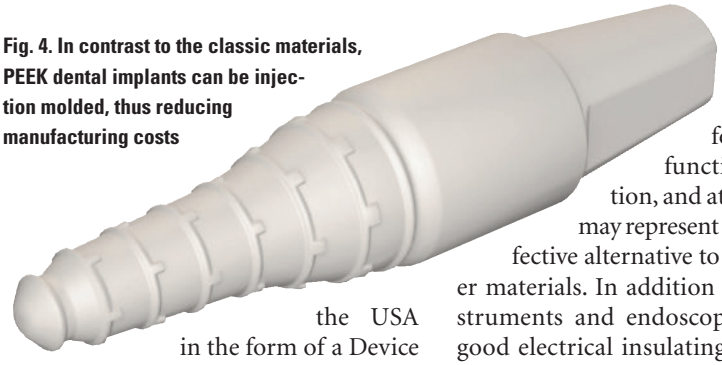

Fig. 4. In contrast to the classic materials, PEEK dental implants can be injection molded, thus reducing manufacturing costs

Furthermore, Evonik offers application-related advice regarding production of the implants, which because of the small numbers involved are usually machined from semi-finished blanks und are produced via injection molding only in the case of larger quantities **(Fig. 4)**. This is based on extensive know-how regarding all processing techniques, a team specialized in medical technology and outside medical consultants who ensure that we are on the same page as the customer. What is behind this is not only the thought of providing comprehensive service, but also our own self-interest: Since life expectancy is rising continually, the risk of spinal disorders is increasing as well – and with it the probability of having to need an implant oneself.

Conclusions

PEEK is normally used in medical products, because of its benefits: It saves weight, provides greater design freedom and the opportunity for increased function integration, and at the same time may represent a more cost-effective alternative to metals or other materials. In addition to surgical instruments and endoscopes, where the good electrical insulating properties of PEEK are beneficial, implants are a major field of application. Typical applications include spinal implants, orthopedic implants, dental implants as well as surgical implements for trauma surgery, where broken bones must be fixed in place or bone fragments replaced. ■

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