Polymer Stents

Implants. Absorbable stents for treating blocked blood vessels offer advantages over commercially available stents. In a project, first a biodegradable material was developed, which combines the advantages of different materials. Then molds for manufacturing a stent by injection molding were developed and constructed.

Fig. 1. Left: stent profile as an open half-shell (for demolding), b) right: stent in a wound condition (implant expanded) (figures: IKV)

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One of the most frequent causes of death in Germany is coronary heart diseases, such as angina pectoris, myocardial infarction and arteriosclerotic heart diseases, which are responsible for 152,366 deaths per year [1]. That corresponds to 17.7 % of all registered deaths in 2010. The causes of these deaths are arteriosclerotic circulatory problems of the organs due to changes in the vascular wall [2].

In 1977, the improvement of catherization led to the first minimal-invasive operation, in which the stenotized vessel is enlarged by a balloon catheter (PCI) [3]. However, this involves damage to the vascular wall, which, in conjunction with the elastic recovery forces of the vascular wall, can cause re-narrowing of the treated vessel cross-section (re-stenosis) [2]. The essential advantages of a PCI, such as low cost, and particularly the minor seriousness of the intervention, are only relevant if the enlarged vascular lumen is maintained. To support the vascular wall, stents are used. They are cylindrical implants resembling a scaffold.

When arteriosclerosis is treated by means of stent therapy, re-stenosis can also occur as a result of neointimal hyperplasia. To reduce the re-stenosis rate after stent implantation, tests have been performed on the material used and on design modifications. To further reduce the thickness of the stent struts, for example, the latest generation of stents consist of a tantalum core with a surrounding 316L stainless steel cover, and therefore have a strut thickness of only 29 µm [4]. A change of the configuration of the stent struts could also achieve a considerable reduction of the re-stenosis rate [5]. Furthermore, stents can be

Translated from Kunststoffe 2/2012, pp. 62–65. **Article as PDF-File** at www.kunststoffe-international.com; Document Number: PE110956

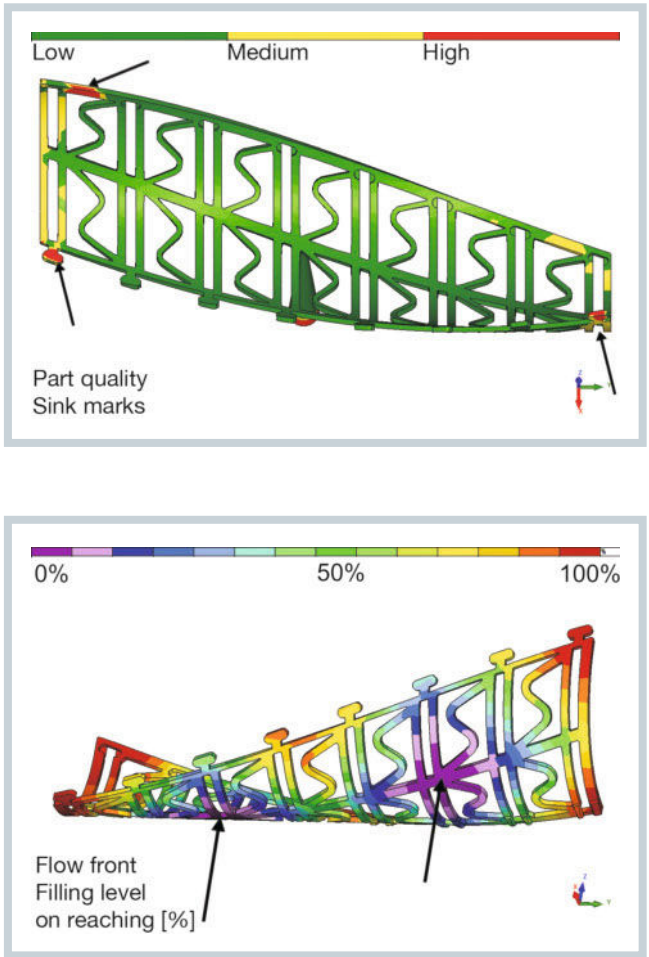

Fig. 2. Top: sink marks (arrows) with conventional sprue, bottom: mold filling with dual gate (arrows) and uniform part filling

provided with passive coatings, which may be no more than a barrier layer, or with active coatings that release drugs [6]. Even though the introduction of drug-coated stents did not solve the problem of re-stenosis, its frequency could be reduced to a fraction of its previous level. The permanent implantation of a foreign body (risk of inflammatory reactions) is thus the principal problem and ultimately is not desirable [4], which is why stents made of biodegradable materials are currently developed. Another advantage of absorbable stents is the possibility of treating re-stenosis with another stent at the same place, since, unlike with metal stents, there are no structures remaining that would obstruct the treatment.

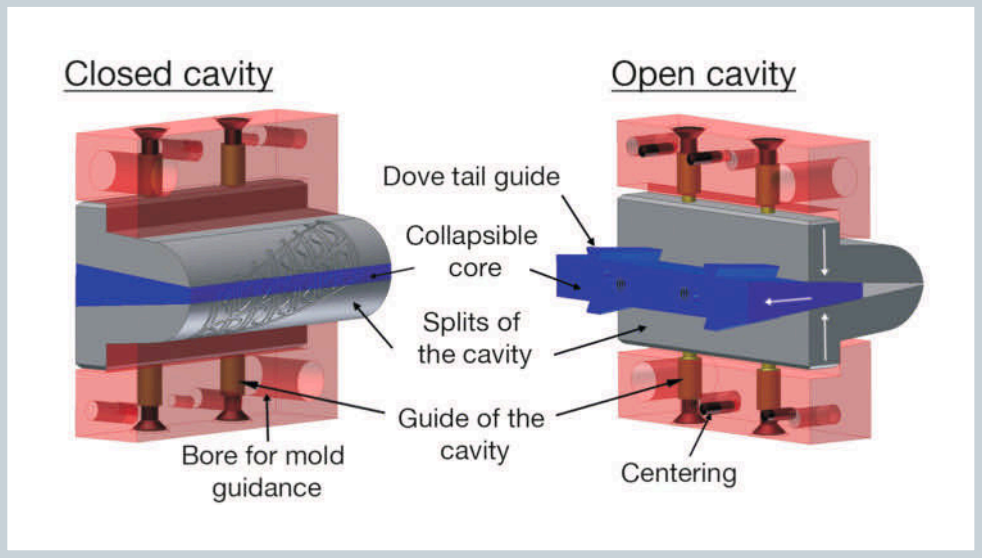

Fig. 3. Cavity of the stent mold

"Cell Adhesion at Vascular Interfaces"

The project "Cell Adhesion at Vascular Interfaces" involves researchers and developers from various scientific and engineering disciplines. The principal goals of the project are

- from a medical point of view, researching the healing of the vascular wall after stent implantation;
- from biological and chemical point of view, conceptualization of the adhesion of endothelial cells (cells of the vascular wall) to technical surfaces; and
- from an engineering point of view, coating a nitinol stent with endothelial cells, developing a biodegradable material and investigating possible manufacturing processes.

In the engineering and biochemical disciplines, a non-biodegradable nitinol stent is first coated with a biodegradable polymer and biofunctional proteins, which allow adhesion of endothelium cells to the stent. The aim is to achieve improved tissue integration and lower inflammatory reactions of the implant.

Then the non-absorbable nitinol stent with the polymer coating is replaced with an absorbable polymer stent. A material is being developed for this purpose that compensates the existing disadvantages of the absorbable polymers. With a new material, possible manufacturing processes for an absorbable stent must be subsequently investigated.

Material Development

The development of absorbable materials is advanced in medical technology. For example, these materials are established as suture materials or orthopedic implants. Aliphatic polyesters, such as polylactides (PLA) or polyglycolides (PGA), have predominantly become established due to their good biodegradability. The most important disadvantage of polyesters for the use in stents is, in particular, their poor mechanical properties, which can be compensated by combining them with polyamides. In the course of the project this combination of materials, known as polyesteramides (PEA), will be enhanced.

Polyesteramide, with various amide fractions, is synthesized from ε-caprolactam in polycaprolactone (PCL), and an initiator system as starting materials. At the Institute of Technical and Macromolecular Chemistry (ITMC) at the RWTH Aachen University, Germany, it is possible to study the mechanical properties on tensile test bars, because the bars can be injection molded directly following reactive extrusion process. As the fractions of amide increase, it is possible to significantly increase the tensile strength with a Young's modulus that is comparable to that of PCL. In addition, the different PEAs have elongations at break in the range of polyamide (approx. 150 %).

Manufacturing Process for an Absorbable Stent

Commercially available metal stents are frequently made from cylinders by laser machining. In principle, laser machining is also suitable for processing biodegradable polymers. However, this is a two-stage process in which a cylindrical semi-finished product is manufactured and then processed by laser machining.

A single-stage method for producing stents is injection molding. It has already become established for commercially available biodegradable products, such as absorbable screws for fixing in bones [7].

Injection Mold for Manufacturing a Stent

The cylindrical construction of a stent poses a particular challenge for demolding the part during injection molding. During solidification from the melt, plastics undergo shrinkage, which in the case of a cylindrical part, means shrinkage onto the mold structure. This makes damage-free demolding difficult or impossible for a delicate strut structure. For the mold design, therefore, a stent with an open profile has been developed, as shown in **Figure 1, left**. Because of the closure and slide mechanism, the stent can be wound for implantation **(Fig. 1, right)**. In this concept, individual stent struts are not axially deformed as normal in order to reduce the stent size for implantation, but the material is uniformly curved across the circumference. In preliminary tests, this geometry was produced from a flat semi-finished product of PCL by laser machining. After the stent has been rolled up at ambient temperature and ex- →

panded again, it remains plastically deformed, i. e. the part retains a curvature of about 180°. To prevent excessive loading and failure of the stent, it is already produced as a half-shell by injection molding.

The mold design was accompanied by a filling simulation, since mold filling represents a challenge in view of the high aspect ratio and the small flow channels of the stent geometry. The simulation shows that complete mold filling is only possible under the following conditions:

- Hot-runner sprue with dual gate,
- variotherm mold temperature control.

Figure 2, top, shows the part quality with a conventional pin gate. At the end of the flow path, the part has sink marks, since no effective holding pressure can be applied within the sealing time. The bottom figure shows the hot-runner system with dual gate. Variotherm mold temperature control is also taken into account in the simulation, i. e. a wall temperature analysis is performed, and used as basis for the part filling simulation. Despite the asymmetrical melt distribution due to the stent struts, uniform filling of the part can be seen.

For demolding the half-shell with undercuts, the cavity is designed as a split mold with collapsible core. Thanks to the simple opening movement of the cavity, the core can first be retracted causing the splits of the cavity to execute a perpendicular relative movement and the part is deformed without ejector pins. As the movement continues, the mold is then opened completely via a mandrel and the part can be removed. **Figure 3** shows the cavity; the white arrows represent the described movements.

By replacing the shaping inserts, it is possible to investigate various stent designs with the new mold inserts.

Summary and Outlook

For medical reasons, absorbable stents for treating blocked blood vessels offer advantages over commercially available stents. Within this project, first a biodegradable material was developed, which combines the advantages of different materials, such as mechanical strength and good biodegradability. Subsequently, molds for injection molding a stent were developed and constructed. The injection molding simulation shows that it is possible to manufacture a delicate stent structure. The manufactured stents should then be mechanically and toxicologically tested to validate their loading strength and biocompatibility through animal tests. In the continuation of the project, the absorbable stents are surface treated to achieve an improvement of the stent's biofunctionality. ■

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Other examples of the strict requirements on mold technology, not only in medical technology, will be presented by the IKV in over 40 lectures and 4 workshops at the 26th International Plastics Technology Colloquium, which will be held in Aachen, Germany, on March 7 and 8, 2012.

→ **www.ikv-kolloquium.de**

ACKNOWLEDGEMENT

The work described above is supported financially by the RWTH Aachen University, within the Exploratory Research Space in the Boost Fund Project "Cell Adhesion at Vascular Interfaces".

REFERENCES

1 Statistisches Bundesamt: Fachserie 12 Reihe 4: Gesundheitswesen. Todesursachen in Deutschland. Gestorbene in Deutschland an ausgewählten Todesursachen 2010. Wiesbaden, Sept. 23, 2011, number of the article: 2120400107005
2 Wintermantel, E.; Ha, S.-W.: Medizintechnik. Life Science Engineering. 4. Aufl., Springer-Verlag, Berlin Heidelberg 2008
3 Grüntzig A.R.; Senning, A.; Siegenthaler, W.E.: Nonoperative Dilatation of Coronary-Atery Stenosis – Percutaneous Transluminal Coronary Angioplasty. The New England Journal of Medicine 301 (1979) 2, pp. 61–69
4 Wieneke, H.; Böse, D.; Haude, M.; Eggebrecht, H.; Konorza, T.; Naber, C.; Erbel, R.: Koronare Stents. Von der Idee zum High-Tech-Implantat. Medizinische Klinik 100 (2005) 8, pp. 505–511
5 Rogers, C.; Edelman, E.R.: Endovascular stent design dictates experimental restenosis and thrombosis. Circulation 9 (1995) 1, pp. 2,995–3,001
6 Wieneke, H.; Sawitowski, T.; Wnendt, S.; Fischer, A.; Dirsch, O.; Karoussos, I.A.; Erbel, R.: Stent coating: a new approach in interventional cardiology. Herz 27 (2002) 6, pp. 518–526
7 Von Oepen, R.: Entwicklung spezieller Maschinen- und Verarbeitungstechniken zur Herstellung resorbierbarer Implantate. RWTH Aachen, dissertation, 1994

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