BIORESORBABLE SELF-EXPANDED VASCULAR STENTS - THE PREELIMINARY RESULTS

PIOTR DOBRZYNSKI[1]*, MICHAŁ SOBOTA[1], ANNA SMOLA[1], JANUSZ KASPERCZYK[1], GRZEGORZ KOKOT[2], WACŁAW KUŚ[2]

[1] CENTRE OF POLYMER AND CARBON MATERIALS, POLISH ACADEMY OF SCIENCES, POLAND
[2] FACULTY OF MECHANICAL ENGINEERING, THE SILESIAN TECHNICAL UNIVERSITY, POLAND
*E-MAIL: P.DOBRZYNSKI@CMPW-PAN.EDU.PL

[ENGINEERING OF BIOMATERIALS 138 (2016) 41]

Introduction

Because of frequently encountered late complications related to implantation even the latest generation of vascular stents, optimal treatment of coronary heart and peripheral artery disease, including acute coronary syndromes entails the need to search for new solutions. Fully biodegradable scaffolds represent the most ambitious emerging stent technology. The rationale is to provide a stable vascular stents in the short term, thus minimising restenosis due to vascular recoil, constrictive remodelling and loose intimal dissection flaps [1,2]. Thermoplastic poly-L-lactide (PLLA) is the most frequently used in the manufacturing of this type of scaffolds, which are formed similarly to the typical metal stents, via laser cutting to the final stent shapes previously fabricated by extrusion of mini-tubes. Currently being clinically used balloon-expanded stents such as ABSORB or Igaki – Tamai stent are received this way. However most interesting looks the possibility to form this type of tools with the help of new stunning technology - microinjection moulding, which should greatly cheapening of their production and overcomes stents shape design restrictions related to the used so far manufacturing method with laser punching. Injection moulding allows to remove troublesome problems in giving the stent's final permanent shape too. The application of bioresorbable materials presenting shape memory temperature close to body temperature additionally should simplify construction and increases reliability of stent delivery systems.

The main goal of our research is to obtain such a system for implantation of bioresorbable vascular stents, which will be obtained by the micro-injection moulding, additionally self-expanded because their shape memory behaviour induced by increase of temperature generated on the guide catheter. In this paper the results of optimization studies of the composition of the polymer, which will be used for forming the stents as well as results of designing of their target shape are presented.

Materials and Methods

L-Lactide, glycolide (Glaco Ltd. China) and trimethylene carbonate -TMC (Foryou Medical Devices Co. Ltd. China) were purified by recrystallization from ethyl acetate solution and dried in a vacuum oven at room temperature. Initiators and catalysts: zirconium(IV) acetylacetonate, zinc(II) acetylacetonate monohydrate, 1,4-butanediol (Aldrich Corp.) were used as obtained. The "primitive" stents was obtained with using devices set; Thermo Scientific HAAKE MiniLab & HAAKE MiniJet.

Results and Discussion

On the basis of previous studies [3,4], the terpolymer of L-lactide, glycolide and trimethylene carbonate, obtained via Ring Opening Polymerization (ROP) of L-lactide and glycolide, conducted with presence of the aliphatic oligocarbonate as a macroinitiator was the selected material designed to forming the stents. The macroinitiator is also obtained by ROP of the cyclic TMC catalysed with zinc compound in the presence of 1,4-butanediol. The resulting oligomer having an average weight of about 6,000 g/mol does not contain more than 1-2% of monomer, and the chains are terminated with hydroxyl groups at both ends. Without further purification, this oligomer was used in the second stage of the synthesis, played role of macroinitiator. Prepared on this way final triblock terpolymer shows a specific construction of the chain, which defines the central block carbonate connected by both sides with the L-lactide/glycolide copolymer chains presented segmented microstructure. This special terpolymer chain structure resulted good mechanical properties and shape memory behaviour induced by temperature slightly higher than body. The technology of synthesis of the terpolymer in a bench scale was elaborated, what allowed to produce a suitable amount of the polymer granulate to further processing. With using laboratory injection moulding machine were obtained the first "primitive" model of the stent in order to develop the procedure of crimping on the catheter and for monitoring the phenomenon of self-expansion of the stent caused by the temperature rise. Then, using the obtained data the optimizing of the geometry of the target stent was carried out, taking into account the stress state in the proposed element, the processing conditions and the planed method of implantation too. The design of the stent shape was completed on the basis of the analysis of strength properties, thermal analysis and coupled with the use of numerical modelling with finite element method [5]. The resulting final optimal shape of the stent was the basis to manufacture of precise injection mould with dimensions tolerance of less than 0.02 mm. The works on its manufacturing are currently being finalized. Soon we will begin the attempts of receiving the target stents, with using already specially prepared microinjection moulding machine - MicroPower 15 (Wittmann-Battenfeld GmbH). This device makes it possible to obtain mouldings of small dimensions and mass below one gram with the accuracy of a few microns.

Conclusions

At the present stage of research the primitive model of stents was formed with using the injection moulding technology. Synthesized by us biodegradable L-lactide/glycolide/trimethylene carbonate terpolymer turns to be fully capable to this type of processing and the final shape was at the same time the programmed permanent shape. Developed the ways of crimping stent on the catheter and set the rise temperature to about 41°C permitting its self-opening within a few seconds. With the use of numerical modelling, optimal shape of the stent was designed, which was used next for the implementation of the appropriate injection mould.

Acknowledgments

A financial support has been provided by the National Center for Research and Development, project no. PBS3/A9/38/2015 – BSM Stent "Obtaining of self-expanding, polymeric and biodegradable, drug-eluting vascular stents".

References

[1] Mintz GS, Popma JJ, Pichard AD, Kent KM, Satler LF, Wong C, et al. Circulation 1996;94:35–43.
[2] Serruys PW, Kutryk MJB, Ong ATL. N Engl J Med 2006;354:483–95.
[3] Smola A., Dobrzynski P., Cristea M., Kasperczyk J., Sobota M., et al., Polym. Chem. 2014;5;2442-2452.
[4] Rychter P, Pamula E, Orchel A, Posadowska U, et al., 2015. J Biomed Mater Res Part A 2015, 103A, 3503-3515.