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Development of a limbal fixation mechanism for a minimally invasive implantable glaucoma microstent

Abstract: Glaucoma represents a chronic eye disease that becomes increasingly prevalent worldwide. Therapies are commonly based on the reduction of intraocular pressure (IOP). Implant devices for micro-invasive glaucoma surgery (MIGS) represent a promising therapy option in refractory cases but suffer from limitations in long term efficacy or from dislocation associated complications. Our approach of an innovative drug-eluting glaucoma microstent for MIGS was presented previously. Within the current work we developed concepts and prototypes of a mechanism for the fixation of our glaucoma microstent in the region of the corneal limbus. A tripod and a haptics design of the fixation mechanism were developed and manufactured. Semifinished products were tested with regard to dimensional stability and mechanical properties according to the standard ANSI Z80.27-2014. Considering the mechanical properties of ocular target tissues, a gelatin based in vitro model for the measurement of microstent retention force was developed. Retention force testing of microstent prototypes in vitro resulted in a proof of concept for the fixation mechanism. Future studies will focus on the use of smaller fixation fibers, for example commercially available suture material, and on an overall miniaturization of the fixation mechanism enabling the use of our applicator device with a 22G x 1½” cannula.

Keywords: Glaucoma, microstent, fixation, ANSI, minimally invasive glaucoma surgery, micro-invasive glaucoma surgery, MIGS.

https://doi.org/10.1515/cdbme-2020-3056

1 Introduction

Glaucoma as a chronic eye disease causes structural damage to the optic nerve resulting in permanent loss of visual acuity and finally in blindness. With increasing and aging of the population glaucoma becomes more and more prevalent, worldwide [1].

Any glaucoma therapy is based on intraocular pressure (IOP) reduction. Therefore, micro-invasive glaucoma surgery (MIGS) using ab interno implantable glaucoma drainage devices (GDD) represents a promising approach. We previously presented our innovative concept of a drug-eluting glaucoma microstent for MIGS (Fig. 1) [2,3].

Figure 1: Glaucoma microstent for MIGS: valved inflow area (blue) including a fixation mechanism in the region of the corneal limbus and an anti-fibrotic drug-eluting coating in the outflow area (orange) (A); schematic representation of microstent release from the cannula of the applicator device (B).
Stable intraocular fixation represents a crucial aspect of ab interno implantable devices. The XEN Gel Stent (Allergan plc, Dublin, Ireland), a tubular MIGS device for drainage of aqueous humour into the subconjunctival space, is made of glutaraldehyde cross-linked porcine gelatin. Fixation of the XEN Gel Stent results from swelling of the tube in the hydrous intraocular environment. Nevertheless, complications like stent dislocation into the anterior chamber associated with the necessity for re-interventions were reported [4].

The current work focuses on the development of a limbal fixation mechanism suitable for our minimally invasive implantable glaucoma microstent. Therefore, microstent prototypes including fixation mechanisms were manufactured and tested. Testing of geometric and mechanical properties was conducted according to ANSI Z80.27-2014 “American National Standard for Ophthalmics – Implantable Glaucoma Devices”.

2 Materials and methods

2.1 Concept for a limbal fixation mechanism for glaucoma microstents

The concept of a limbal fixation mechanism is based on flexible fibers attached to the outer surface of the glaucoma microstent (Fig. 2.).

![Figure 2: Concepts for limbal fixation mechanisms for glaucoma microstents in the region of the corneal limbus: tripod design (A) and haptics design (B) in crimped (loaded into cannula of applicator device) and expanded state (after release from cannula of applicator device), respectively.](image)

The concept of microstent implantation into subconjunctival or suprachoroidal space using different applicator devices was described previously [2,3]. The MIGS-procedure is based on a 22G x 1½” cannula (inner diameter $ID_c = 0.47$ mm, outer diameter $OD_c = 0.70$ mm, length $l_c = 40$ mm) [2]. The microstent itself ($ID_m = 0.20$ mm, $OD_m = 0.36$ mm, $l_c = 10$ mm) fits loosely into this cannula [3]. Considering the inner cannula diameter, overall microstent diameter in the crimped state must not exceed 0.47 mm. On the other hand in the expanded state the outside diameter of the fixation mechanism should be at least 0.70 mm.

2.2 Manufacturing of microstent prototypes with limbal fixation mechanism

Tubular specimens as microstent base body were manufactured from polycarbonate based silicone elastomer in a dip-coating process as described previously [2].

As a basis for the fixation mechanism, flexible fibers with an aspired diameter of $D_f = 50$ µm were manufactured from poly-L-lactide (PLLA, Resomer L210, Evonik Healthcare GmbH, Essen, Germany) by means of a twin-screw extruder (HAAKE MiniLab II, Thermo Fisher Scientific, Karlsruhe, Germany). Extrusion processing was conducted at 220 °C using a 1.9 mm nozzle, a screw rotation speed of 1 min$^{-1}$ and a manual haul-off. Fiber diameter was measured by means of a biaxial laser scanner (ODAC 32 XY, Zumbach Electronic AG, Orpund, Switzerland).

Attachment of fiber segments to the outer surface of the microstent base bodies was conducted by means of 4% polycarbonate based silicone elastomer in chloroform (Sigma Aldrich Corp., St. Louis, MO, USA) as adhesive.

2.3 Testing of semifinished products and microstent prototypes

2.3.1 Dimensional stability and morphological characterization

According to ANSI Z80.27-2014 dimensional stability of microstent base bodies and PLLA-fibers was analyzed after immersion in 0.9% NaCl for 14 days at (35 ± 2) °C.

Morphological characterization of microstent prototypes was carried out by means of scanning electron microscopy (SEM, Quattro S, Thermo Fisher Scientific, FEI Deutschland GmbH, Dreieich, Germany) in low vacuum mode without the use of a conductive layer.

2.3.2 Mechanical testing

Mechanical properties of microstent components were analyzed before and after immersion in 0.9% NaCl for 14 days at (35 ± 2) °C. Tensile testing was carried out using a
universal testing machine Zwick/Roell Z0.5 (Zwick GmbH & Co. KG, Ulm, Germany) equipped with a 20 N load cell at 37 °C. A clamping length of 18.5 mm was used. Elastic modulus \( E \) was calculated as secant between the strain values \( \varepsilon = 0.05\% \) and \( \varepsilon = 0.25\% \) at a cross head speed of 1 mm·min\(^{-1}\). Further testing was conducted at 40 mm·min\(^{-1}\). Tensile strength \( \sigma_m \) and failure strain \( \varepsilon_b \) were determined.

For evaluation of microstent retention force \( F_r \), an \textit{in vitro} model based on porcine gelatin (RAPS Aspic Powder, 150 Bloom, RAPS GmbH & Co. KG, Kulmbach, Germany) was developed (Fig. 3).

The elastic modulus of ocular target tissues like the choroid or the sclera ranges between 4 kPa to 387 kPa or 24 kPa to 4,470 kPa depending on tension range and tissue orientation, respectively [5]. For comparison purposes, elastic modulus of porcine gelatin was determined for concentrations of 65, 70, 75 and 80 mg·ml\(^{-1}\) water by means of compression testing at 37 °C and a cross head speed of 10 mm·min\(^{-1}\). Rectangular gelatin block specimens with a profile of 10 mm x 10 mm and a height of 6 mm were used.

Prior to retention force testing, microstent prototypes were implanted into porcine gelatin by means of an insertion tube (\( ID_t = 1.2 \text{ mm}, \ OD_t = 1.3 \text{ mm} \)). A mandrel retained the microstent in position while the insertion tube was withdrawn. Retention force testing was conducted at 37 °C and a cross head speed of 5 mm·min\(^{-1}\).

### 3 Results

#### 3.1 Microstent prototypes with limbal fixation mechanism

Microstent base bodies with reproducible dimensions, \( ID_m = (0.20 \pm 0.00) \text{ mm} \) and \( OD_m = (0.36 \pm 0.02) \text{ mm} \) \((n = 17)\) and reproducible surface quality were manufactured. PLLA-fibers with diameters ranging from 50 µm ≤ \( D_f \) ≤ 150 µm were provided (Fig. 4).

#### 3.2 Morphological and mechanical characterization

Immersion of microstent base bodies and PLLA-fibers in 0.9% NaCl for 14 days at (35 ± 2) °C shows no influence on dimensional stability. Outer diameter before and after immersion was (370.3 ± 30.0) µm and (372.8 ± 26.3) µm for base bodies and (70.0 ± 0.0) µm and (73.1 ± 0.1) µm for PLLA-fibers \((n = 3)\).
The results of the mechanical characterization of microstent components before and after immersion in 0.9% NaCl for 14 days at \((35 \pm 2) ^\circ C\) were summarized in Tab. 1.

**Table 1:** Mechanical properties elastic modulus \(E\), tensile strength \(\sigma_m\) and failure strain \(\varepsilon_b\) of microstent components base body \((n = 6)\) and PLLA-fiber \((n = 10)\) before (dry) and after immersion in 0.9% NaCl for 14 d; mean value ± standard deviation, respectively.

<table>
<thead>
<tr>
<th></th>
<th>(E) [N·mm(^{-2})]</th>
<th>(\sigma_m) [N·mm(^{-2})]</th>
<th>(\varepsilon_b) [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>base body</td>
<td>dry</td>
<td>9.1 ± 2.5</td>
<td>18.7 ± 4.2</td>
</tr>
<tr>
<td></td>
<td>14 d NaCl</td>
<td>7.1 ± 1.5</td>
<td>18.0 ± 2.5</td>
</tr>
<tr>
<td>PLLA-fiber</td>
<td>dry</td>
<td>1,735.7 ± 50.3</td>
<td>11.4 ± 6.2</td>
</tr>
<tr>
<td></td>
<td>14 d NaCl</td>
<td>1,632.7 ± 61.6</td>
<td>20.2 ± 8.7</td>
</tr>
</tbody>
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Compression testing of porcine gelatin with concentrations of 65, 70, 75 and 80 mg·ml\(^{-1}\) yielded an elastic modulus of 1.2, 2.0, 3.2 and 4.2 kPa, respectively. Therefore a gelatin concentration of 80 mg·ml\(^{-1}\) was used for the retention force in vitro model.

Retention force of microstent prototypes with a fixation mechanism in a tripod design as well as prototypes without fixation mechanism was analyzed. Exemplary force distance curves are shown in Fig 6.

**Figure 6:** In vitro measurement of microstent retention force: exemplary force distance curves and photographs of testing glaucoma microstent prototypes with a fixation mechanism (tripod design) and without a fixation mechanism

A retention force of \((22.5 \pm 10.7)\) mN and \((14.8 \pm 4.3)\) mN was measured for microstent prototypes with and without a fixation mechanism \((n = 3)\), respectively.

**4 Discussion**

The presented methods are suitable for manufacturing and testing of minimally invasive implantable glaucoma microstents including a limbal fixation mechanism. Immersion of microstents according to ANSI Z80.27 shows negligible influence on dimensional stability and mechanical properties. The presented fixation prototypes were used for a proof of concept but could not jet be used in combination with our applicator device [2,3]. Future studies will focus on adaption of the mechanical properties of the retention force in vitro model [5]. Moreover, further development is necessary with regard to adequate dimensions and reproducible quality of the fixation mechanism. In this context the use of approved and commercially available 1-0 suture material (diameter ranging from 0.020 mm to 0.029 mm) in combination with fs-laser technologies represent promising approaches.

**Author Statement**

Research funding: Financial support by the Federal Ministry of Education and Research within RESPONSE "Partnership for Innovation in Implant Technology" is gratefully acknowledged. Conflict of interest: Authors state no conflict of interest. Acknowledgement: Support of S. Bode, L. Knorre, J. Paulsen and C. Unverricht is gratefully acknowledged.

**References**


