Stefan Siewert*, Wolfram Schmidt, Sebastian Kaule, Stefanie Kohse, Michael Stiehm, Franziska Kopp, Thomas Stahnke, Rudolf Guthoff, Niels Grabow and Klaus-Peter Schmitz

Development of a microstent system for minimally invasive glaucoma surgery

Abstract: Glaucoma is the leading cause of irreversible blindness worldwide. An increased intraocular pressure (IOP) is known as major risk factor. Currently, drainage devices that are implanted by means of minimally invasive glaucoma surgery (MIGS) represent a promising approach for IOP lowering. Commercially available devices for MIGS suffer from unregulated drainage involving ocular hypotony. Furthermore, long term drainage capability of current devices is limited by fibrotic encapsulation processes. Therefore, our group focusses on the development of a valved drug-eluting microstent for MIGS. Within the current work, we developed two alternative injector devices for minimally invasive microstent implantation. Both injector devices were based on a cannula in which the microstent is loaded and a mandrel inside the cannula. Injector device *A* is designed to push the microstent out of the cannula and injector device *B* is designed to withdraw the cannula above the microstent. Manufacturing of injector devices was conducted using rapid prototyping. Simplified polymeric microstents were manufactured from polycarbonate based silicone elastomer. Simulated use was performed in a silicone eye model. The presented injector devices were suitable for minimally invasive *ab interno* microstent implantation into suprachoroidal space. Ongoing miniaturization of the microstent system will allow the use of a 22 G cannula in future *ex vivo* experiments.

Keywords: glaucoma drainage device, microstent, minimally invasive glaucoma surgery

https://doi.org/10.1515/cdbme-2017-0164

***Corresponding author: Stefan Siewert:** Institute for Implant-Technology and Biomaterials e.V., Friedrich-Barnewitz-Str. 4, 18119 Rostock-Warnemünde, Germany, e-mail: stefan.siewert@uni-rostock.de
Wolfram Schmidt, Stefanie Kohse, Niels Grabow, Klaus-Peter Schmitz: Institute for Biomedical Engineering, Rostock University Medical Center, Friedrich-Barnewitz-Str. 4, 18119 Rostock-Warnemünde, Germany
Sebastian Kaule, Michael Stiehm, Klaus-Peter Schmitz: Institute for ImplantTechnology and Biomaterials e.V., Friedrich-Barnewitz-Str. 4, 18119 Rostock-Warnemünde, Germany
Franziska Kopp, Thomas Stahnke, Rudolf Guthoff: Department of Ophthalmology, Rostock University Medical Center, Doberaner Str. 140, 18057 Rostock, Germany

1 Introduction

Glaucoma is the leading cause of irreversible blindness worldwide [1]. Characteristic structural damage of the optic nerve and functional visual impairment usually results from increased intraocular pressure (IOP), caused by disturbed aqueous humour dynamics. Recently, a novel generation of glaucoma drainage devices emerged as a promising approach for minimally invasive glaucoma surgery (MIGS) [2]. Commercially available devices for MIGS suffer from unregulated drainage and the resulting risk of ocular hypotony. Furthermore, long term drainage capability of current devices is limited by fibrotic encapsulation processes [3].

Our group focusses on the development of a valved drug-eluting microstent for MIGS (see **Figure 1**). Drainage of aqueous humour from the anterior chamber of the eye into the suprachoroidal space is regulated by means of a micromechanical valve [4]. A drug-eluting coating in the outflow area of the microstent inhibits fibrosis [5].

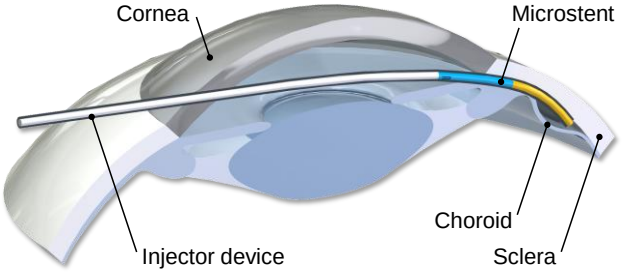

Figure 1: Concept of a microstent system for minimally invasive glaucoma surgery: valved inflow area of the microstent (blue) without and outflow area (orange) with drug-eluting coating.

Within the current work, we developed an injector device for minimally invasive microstent implantation.

2 Materials and methods

2.1 Manufacturing of microstents

Simplified polymeric microstents were manufactured in a semiautomatic dip-coating process (KSV NIMA Dip Coater, Biolin Scientific Holding AB, Stockholm, Sweden). Polymer solution of 4% (w/v) polycarbonate based silicone elastomer (Chronosil 80A, AdvanSource Biomaterials Corp., Wilmington, MA, USA) in Chloroform (Sigma Aldrich Corp., St. Louis, MO, USA) was used.

After measurement of tubing diameter by means of a biaxial laser scanner (ODAC 32 XY, Zumbach Electronic AG, Orpund, Switzerland), dipping mandrels were removed and specimens were dried four days at 40°C in vacuo. Morphological analysis was conducted using environmental scanning electron microscopy (ESEM; Philips XL 30, Philips, Amsterdam, the Netherlands) at a vacuum pressure of 1.2 mbar and an accelerating voltage of 10 kV.

2.2 Development of injector devices

Design of two alternative injector devices was developed using Creo Parametric 3.0 (PTC Inc., Needham, MA, USA). Both injector devices were based on a cannula in which the microstent is loaded and a mandrel inside the cannula. Injector device *A* is designed to push the microstent out of the cannula and injector device *B* is designed to withdraw the cannula above the microstent (see **Figure 2**). Manufacturing of injector devices was conducted using a 3D printer and polylactide filament (Ultimaker 2, Ultimaker B.V., Geldermalsen, Netherlands).

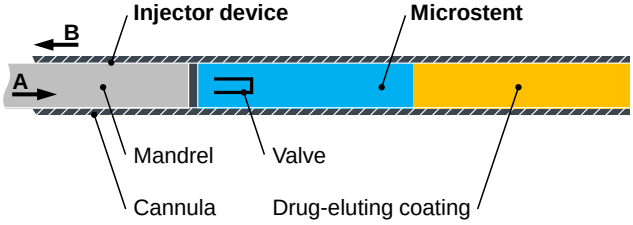

Figure 2: Schematic representation of the microstent loaded into the injector device for minimally invasive glaucoma surgery; Two alternative functional principles: a mandrel pushes the microstent out of the cannula (*A*) or the cannula is withdrawn above the microstent (*B*).

For analysis of applicability of injector devices, a simplified two-piece silicone eye model was developed and manufactured based on 3D printed casting molds (see **Figure 3**).

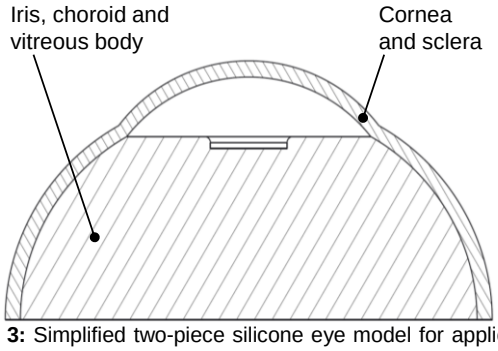

Figure 3: Simplified two-piece silicone eye model for applicability testing of injector devices.

Two-component silicone (Elastosil RT 601 A/B, Wacker Chemie AG, Munich, Germany) with a Shore hardness of 33 A was used for manufacturing of the eye model.

3 Results

3.1 Manufacturing of microstents

Manufactured polymeric microstents with an inner diameter of *ID* = 0.3 mm and a length of *l* = 10 mm showed a smooth surface (see **Figure 4**).

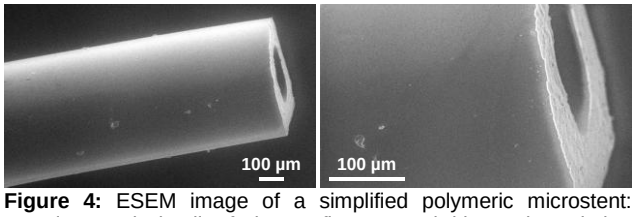

Figure 4: ESEM image of a simplified polymeric microstent: overview and detail of the outflow area (without drug-eluting coating).

An outer diameter of *OD* = 0.59 ± 0.04 mm (*n* = 10) allowed the use of injector devices with a 20 G (*ID* = 0.65 mm, *OD* = 0.90 mm) cannula.

3.2 Development of injector devices

Prototypes of the injector devices *A* and *B* are shown in **Figure 5**. Microstent implantation into the silicone eye model is illustrated in **Figure 6**. After paracentesis, the injector device *A* was inserted into the anterior chamber and advanced to the opposing chamber angle, where the microstent was deployed into suprachoroidal space. Injector device *B* was advanced beyond the chamber angle and the cannula was withdrawn above the fixed microstent.

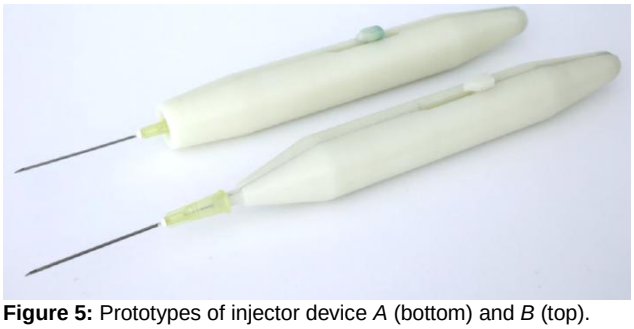

Figure 5: Prototypes of injector device *A* (bottom) and *B* (top).

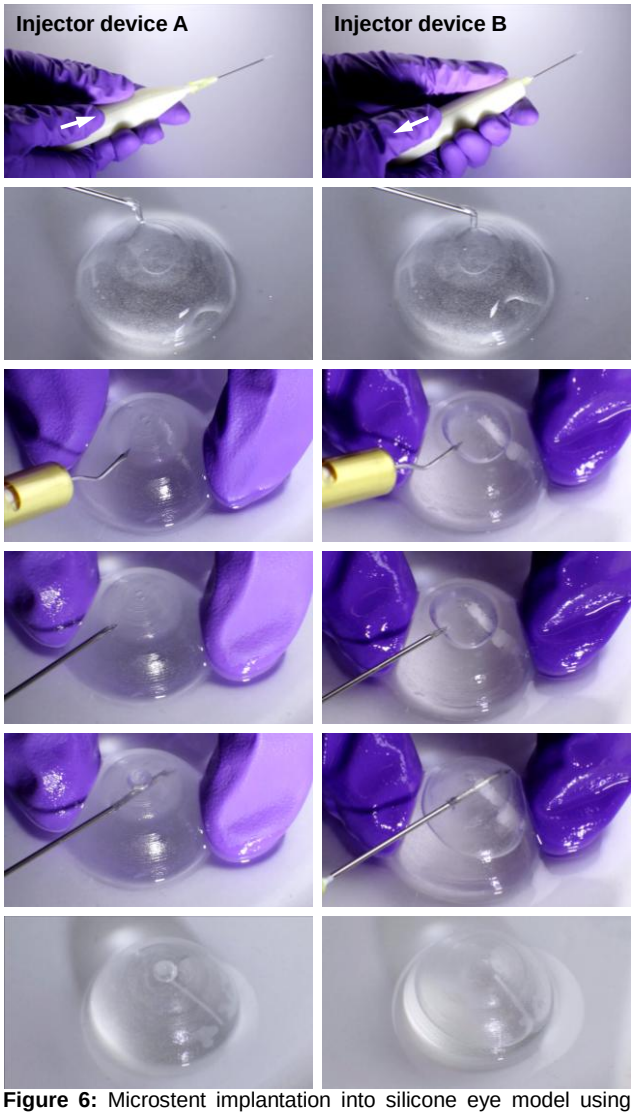

Figure 6: Microstent implantation into silicone eye model using the injector devices *A* and *B*; Top down: handling of the injector device, wetting of the silicone eye model, paracentesis, insertion of injector device into the anterior chamber, microstent implantation into suprachoroidal space and microstent localization after completion of the procedure.

4 Discussion

The commercially available CyPass System (Alcon, Fort Worth, TX, USA) uses an injector device with a 23 G (*OD* = 0.60 mm) access for suprachoroidal implantation. As a continuous tube, the CyPass Micro-Stent is fixed on an internal guidewire during implantation. Our microstent concept is based on a micro-mechanical valve for regulation of IOP within physiological boundaries. Since the distal tubing lumen is closed, an internal guidewire is not feasible. Therefore we used a cannula as external guidance.

The presented injector devices were suitable for minimally invasive *ab interno* microstent implantation into the suprachoroidal space. Allowing an exact guidance of the microstent, injector device B represents the preferred approach. Ongoing miniaturization of our microstent will enable the use of a 22 G (*ID* = 0.47 mm, *OD* = 0.70 mm) cannula in future *ex vivo* implanttations.

Author's Statement

Research funding: Financial support by the Federal Ministry of Education and Research (BMBF) within RESPONSE "Partnership for Innovation in Implant Technology" is gratefully acknowledged. Conflict of interest: Authors state no conflict of interest. Informed consent: Informed consent is not applicable. Ethical approval: The conducted research is not related to either human or animals use

References

[1] Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol 2006;90(3)262-7.

[2] Saheb H, Ahmed IIK. Micro-invasive glaucoma surgery: current perspectives and future directions. Curr Opin Ophthalmol 2012;23(2)96-104.

[3] Hoeh H, Ahmed IIK, Grisanti S, Grisanti S, Grabner G, Nguyen QH, Rau M, Yoo S, Ianchulev T. Early postoperative safety and surgical outcomes after implantation of a suprachoroidal micro-stent for the treatment of open-angle glaucoma concomitant with cataract surgery. J Cataract Refract Surg 2013;39(3)431-437.

[4] Siewert S, Schultze C, Schmidt W, Hinze U, Chichkov B, Wree A, Sternberg K, Allemann R, Guthoff R, Schmitz KP. Development of a micro-mechanical valve in a novel glaucoma implant. Biomed Microdevices 2012;14(5)907-920.

[5] Hovakimyan M, Siewert S, Schmidt W, Sternberg K, Reske T, Stachs O, Guthoff R, Wree A, Witt M, Schmitz KP, Allemann R. Development of an Experimental Drug Eluting Suprachoroidal Microstent as Glaucoma Drainage Device. Transl Vis Sci Technol 2015;4(3):14.