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Magnetically actuated glaucoma drainage device with adjustable flow properties after implantation

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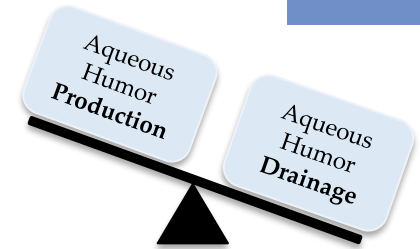
Abstract

Glaucoma is a leading cause of preventable blindness worldwide. A rise in the intraocular pressure (IOP) is a major risk factor for this disease, and results from an elevated resistance to aqueous humor outflow from the anterior chamber of the eye. Glaucoma drainage devices provide an alternative pathway through which aqueous humor can effectively exit the eye, thereby lowering the IOP. However, post-operative IOP is unpredictable and current implants are deficient in maintaining IOP at optimal levels. To address this deficiency, we are developing an innovative, non-invasive magnetically actuated glaucoma implant with a hydrodynamic resistance that can be adjusted following surgery. This adjustment is achieved by integrating a magnetically actuated microvalve into the implant, which can open or close fluidic channels using an external magnetic stimulus. This microvalve was fabricated from poly(styrene-*block*-isobutylene-*block*-styrene), or 'SIBS', containing homogeneously dispersed magnetic microparticles. "Micro-pencil" valves of this material were fabricated using a combination of femtosecond laser machining with hot embossing. The glaucoma implant is comprised of a drainage tube and a housing element fabricated from two thermally-bonded SIBS layers with the microvalve positioned in between. Microfluidic experiments involving actuating the magnetic micro-pencil with a moving external magnet confirmed the valving function. A pressure difference of around 6 mmHg was achieved which is sufficient to overcome hypotony (i.e. too low IOP) – one of the most common post-operative complications following glaucoma surgery.

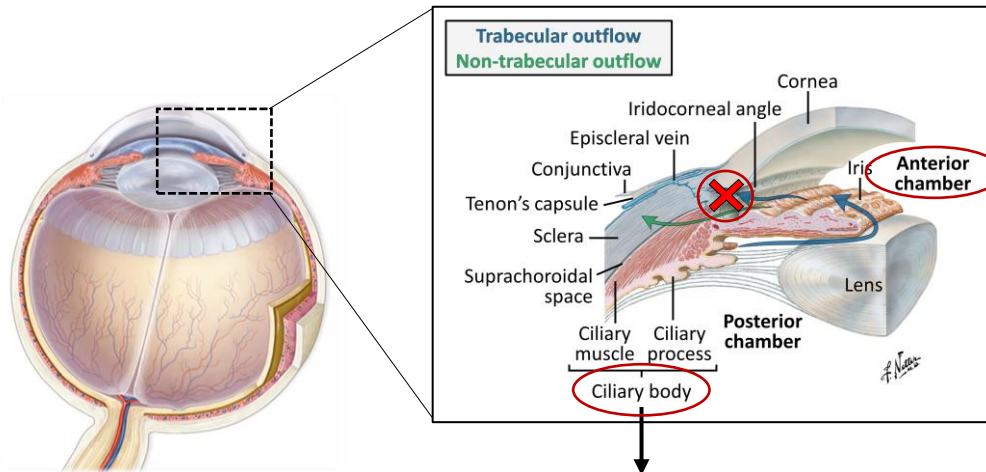
Keywords: Glaucoma; Intraocular pressure (IOP); Adjustable glaucoma implant; Magnetic microvalve; Microfabrication.

Introduction – What is glaucoma?

- Eye disease characterized by optic nerve damage and visual field loss
- Leading cause of irreversible blindness worldwide, with over **70 million people affected!**
- Most important known risk factor: **elevated intraocular pressure (IOP)**



Aqueous humor dynamics:



Continuous production
of aqueous humor
(2,5 μ L/min)



High IOP damages the
optic nerve



(mmHg) 6 10 20



Normal IOP

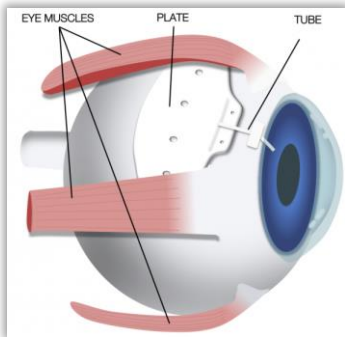
Glaucoma

Introduction – Current treatment options

- ✓ Pharmacological medication
 - ✓ Laser treatment
 - ✓ Surgery – ↑ Aqueous humor drainage
- } ↓ Aqueous humor production OR ↑ Aqueous humor drainage

Glaucoma drainage devices
 Bypass the eye's natural outflow pathways to provide an alternative/artificial route for aqueous humor to effectively exit the eye, thereby reducing IOP

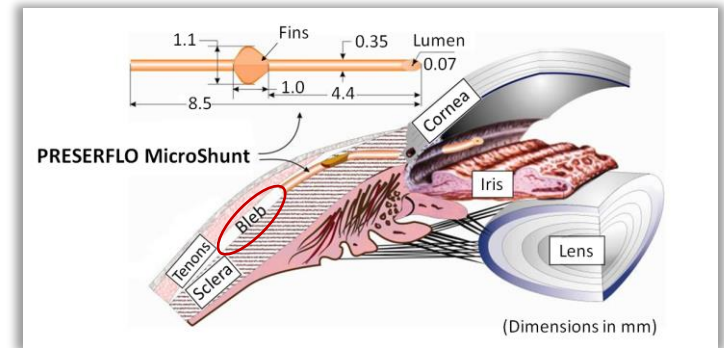
Baerveldt® implant



The Ahmed® Glaucoma Valve



PRESERFLO™ MicroShunt

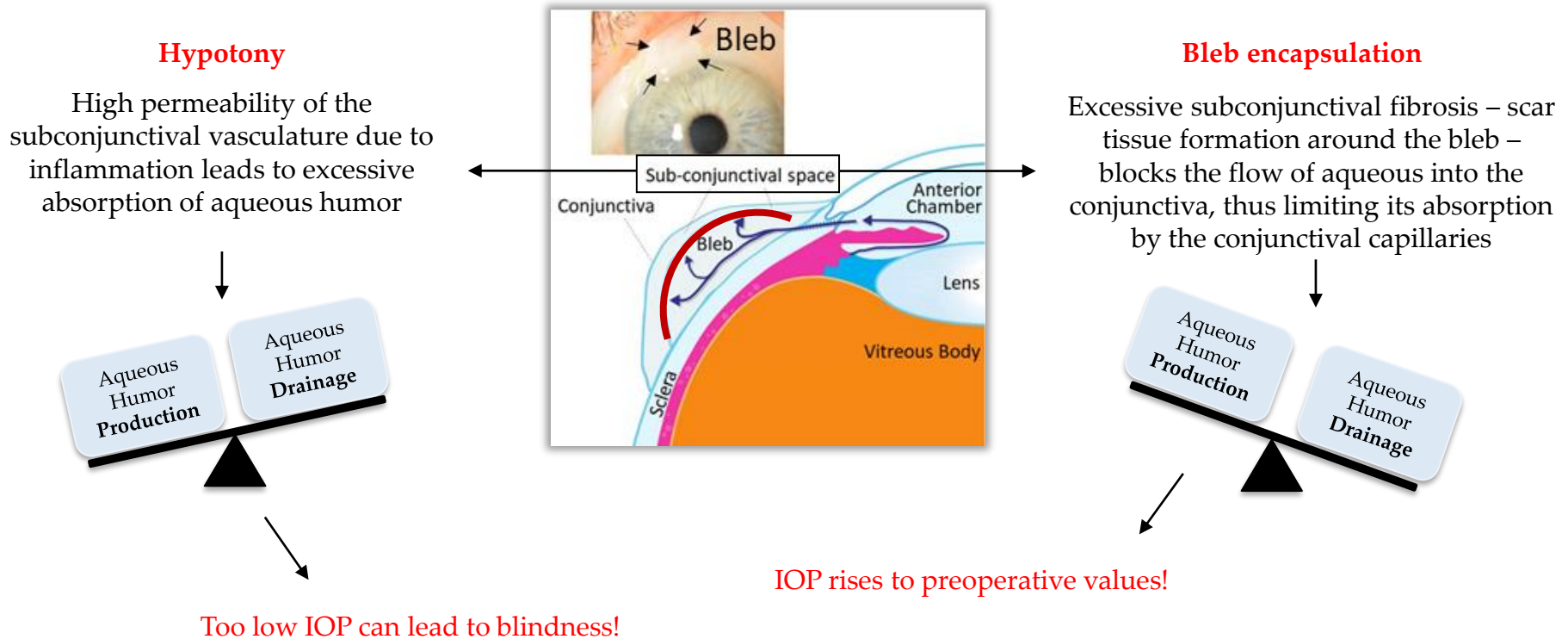


- ✓ Most glaucoma implants drain aqueous humor into the so-called “bleb”
- ✓ Aqueous humor in the bleb is then absorbed by the subconjunctival microvasculature

Introduction – Glaucoma drainage devices

Most common postoperative complications

- ✓ **Hypotony** – 5 mmHg or less (usually occurs in the early postoperative period)
- ✓ **Bleb encapsulation** (occurs weeks/months after surgery)



Introduction – Aim of the project

- ✓ Current glaucoma implants provide always the same fluidic resistance; thus, fluid flow cannot be adapted according to each patient's needs (**not all patients suffer from hypotony or bleb encapsulation!**)

Solution

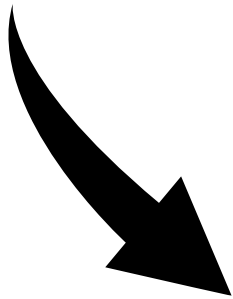
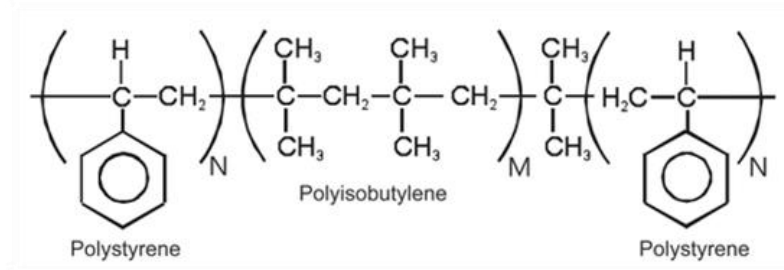
- ✓ Design and fabricate a novel **SMART GLAUCOMA DRAINAGE DEVICE** with **flow control** properties

Flow of aqueous humor through the implant will be adjusted if necessary, after surgery and non-invasively, through the actuation of a **stimuli-responsive valve** integrated in the implant!

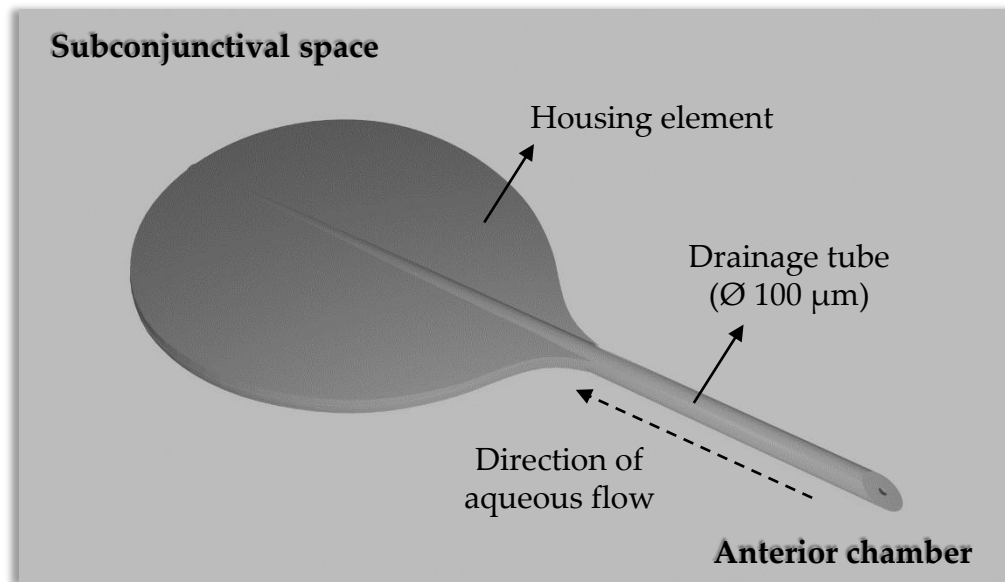
- ✓ Fabricate the stimuli-responsive microvalve and develop smart solutions to integrate it into the implant
- ✓ Evaluate the flow control properties of the smart implant by carrying out microfluidic experiments
- ✓ **Final goal:** produce potential implant prototypes that can be used for animal testing

Magnetically adjustable glaucoma implant

- ✓ Smart implant is comprised of a drainage tube and a housing element, both made from a highly biocompatible, bioinert material called **poly(styrene-*block*-isobutylene-*block*-styrene), or SIBS**:

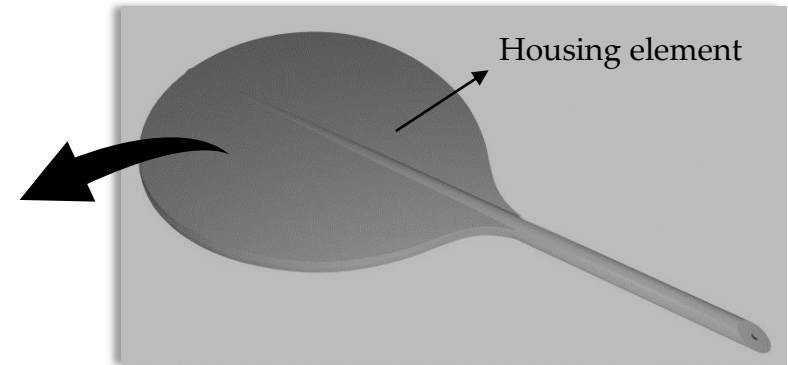
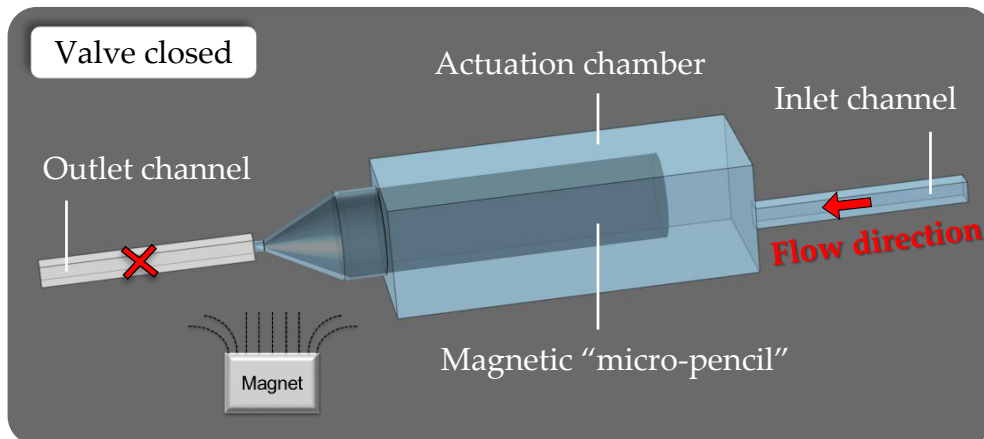
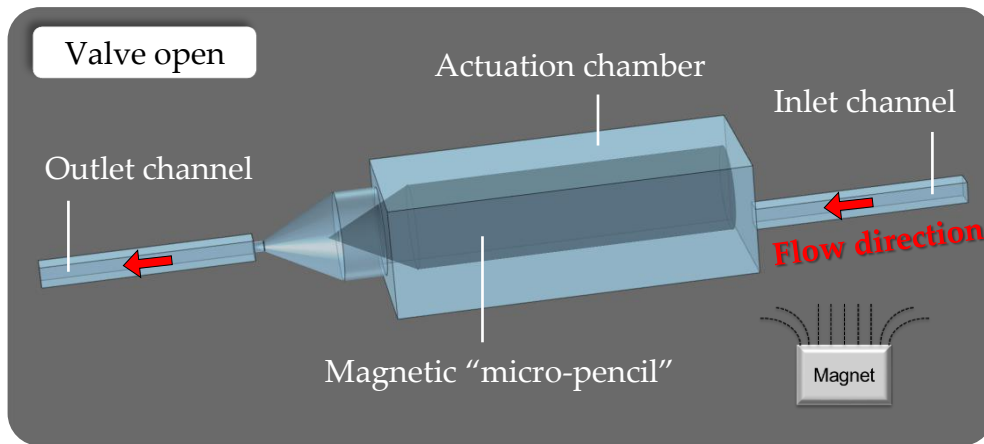


Smart implant:



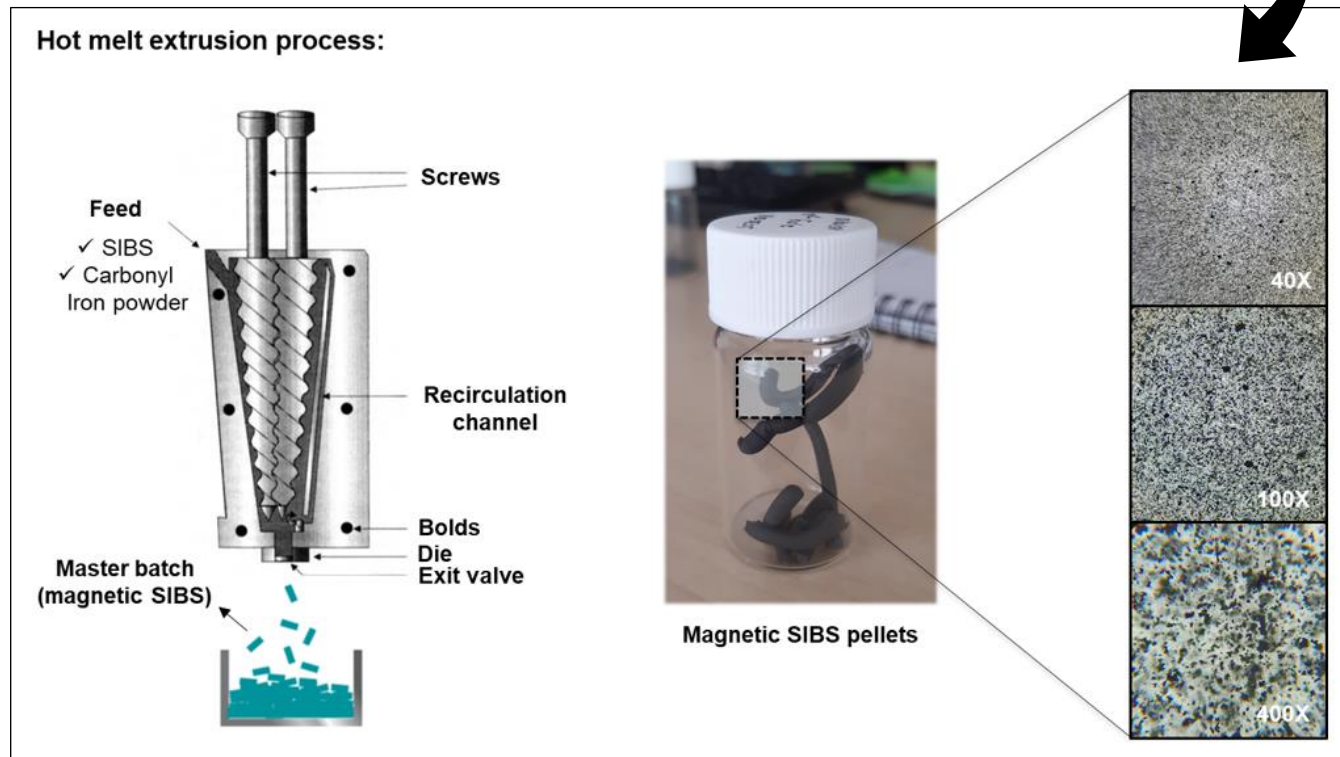
Magnetically adjustable glaucoma implant

- ✓ The housing element of the smart implant contains an actuation chamber where the microvalve, with the shape of a “micro-pencil”, is positioned
- ✓ An external magnet is used to move this microvalve to the open or closed positions: (i) when open, the device is in a “high flow” mode; (ii) when closed, the device is in a “low flow” mode:



Fabrication of the magnetic microvalve

- ✓ The magnetic microvalve is made from SIBS mixed with carbonyl iron powder (CIP): SIBS:CIP = 1:1 (w/w)
- ✓ Hot melt extrusion with mixing was used to fabricate the batch material (magnetic SIBS)



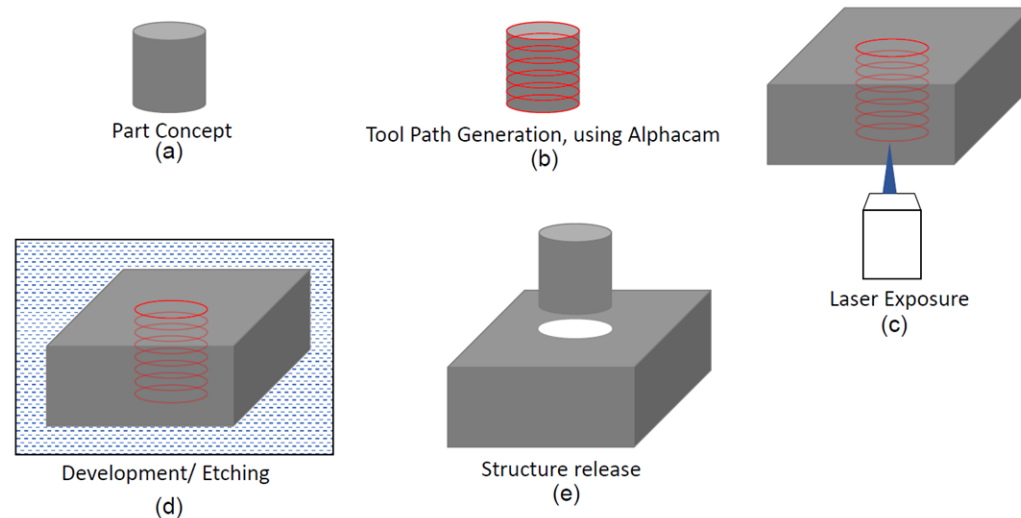
Fabrication of the magnetic microvalve

- ✓ The micro-pencil valve mold was fabricated using the FEMTOprint



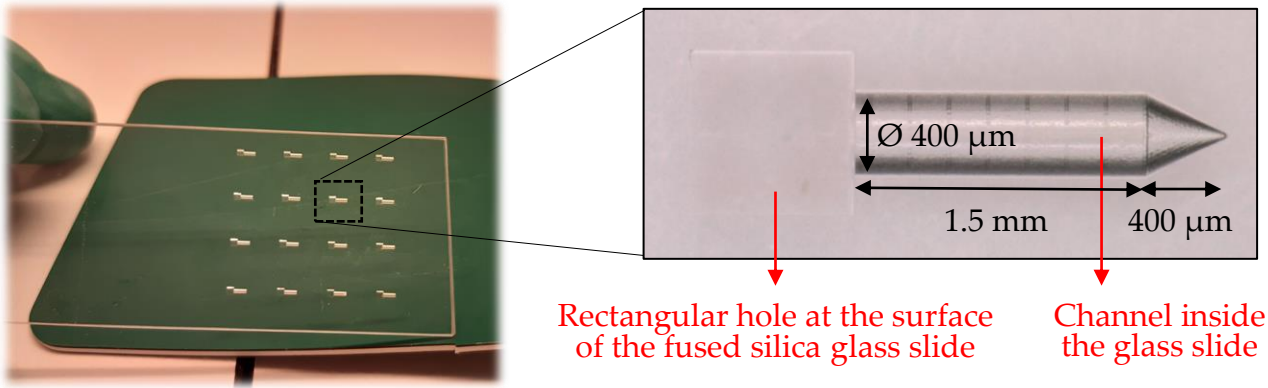
Femtosecond laser machining process:

- ✓ Modifying a material by exposing to femtosecond laser in a desired pattern followed by its etching to complete the machining process.



Fabrication of the magnetic microvalve

- ✓ FEMTOprint micro-pencil mold



Machining and etching times:

- ✓ Machining \approx 6h
- ✓ KOH etching \approx 48h

Magnetic Micro-Pencil:

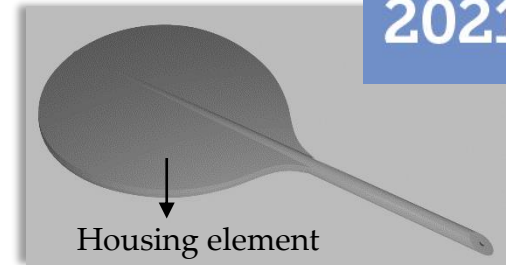


Hot embossing:

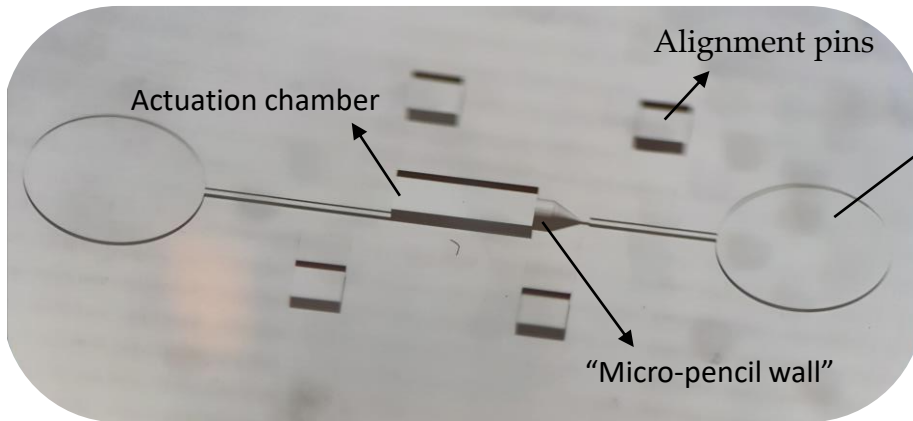
- ✓ FEMTOprint micro-pencil mold and Magnetic SIBS pellets are “sandwiched” between two brass plates
- ✓ 150 °C, 15 min, 5 tons

Fabrication of the housing element

- ✓ Housing element fabricated from two thermally-bonded SIBS layers with channels
- ✓ Molds for top and bottom layers were fabricated using the FEMTOprint



FEMTOprint mold for top layer:

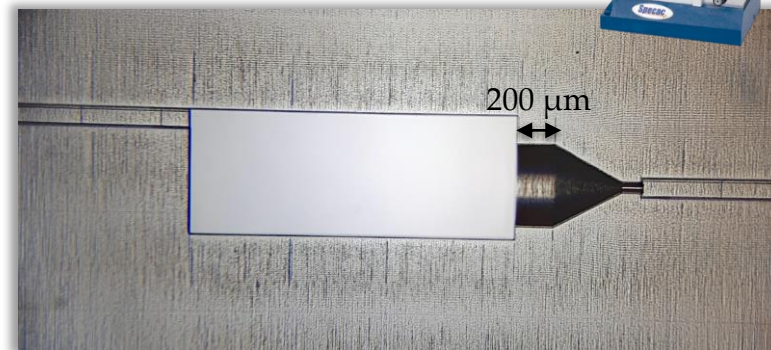


Inlet and outlet ports used for *in vitro* microfluidic experiments

Machining and etching times:

- ✓ Machining \approx 12h
- ✓ KOH etching \approx 7h

Replica-molded SIBS top layer:

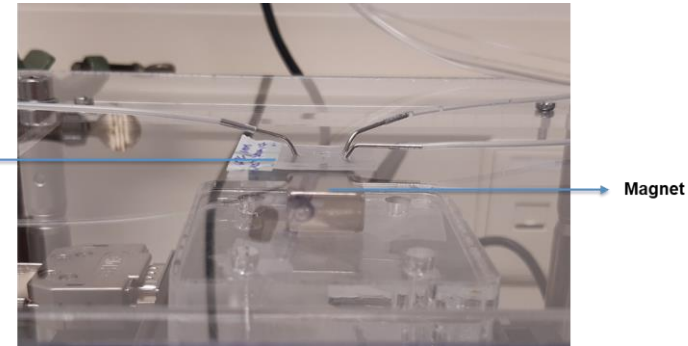
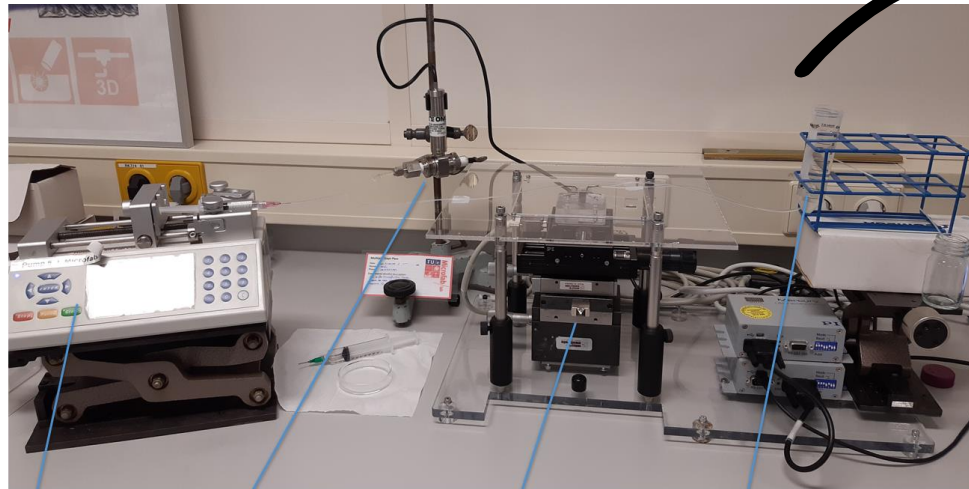


Hot embossing:

- ✓ 150 °C, 15 min, 5 tons

Setup for microfluidic experiments

- ✓ Aim: evaluate how the pressure upstream the implant (IOP) changes when the microvalve is moved to the closed or open positions.



Syringe pump:
pumping DI water
at 2.5 $\mu\text{L}/\text{min}$

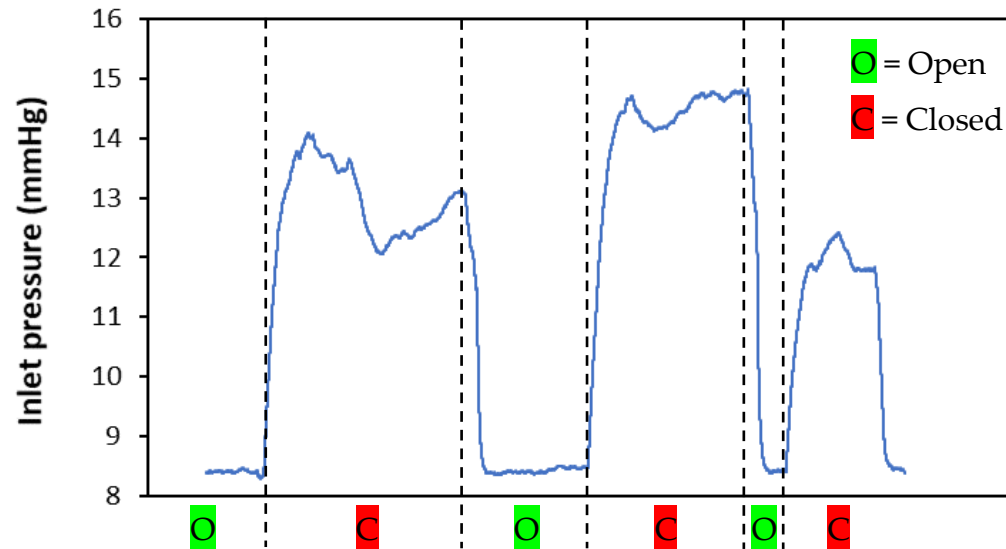
Pressure transducer:
measuring the pressure
upstream the device (inlet)

X,Y and Z stages:
move the magnet in one direction
at a pre-defined velocity

Outlet of the device connected to a column of
water of 6.8 cm, which corresponds to 5
mmHg (mimicking the pressure in the bleb)

It is expected that the pressure
upstream the device increases when
the microvalve is moved to the closed
position!

Microfluidic experiment result



- Closed position: **IOP increase up to 6 mmHg**
- Pressure difference achieved is sufficient to overcome hypotony (i.e. too low IOP)
- Pressure difference varies slightly between open/closed cycles

Conclusions

- ✓ The magnetic SIBS batch material was successfully fabricated using the hot melt extrusion process
- ✓ The femtosecond laser machining process is an effective technique to fabricate the molds for both the device and the microvalve
- ✓ Microfluidic tests have shown that, when in the closed state, the magnetically actuated microvalve can provide a sufficient hydrodynamic resistance that leads to an increase in the pressure upstream the implant (IOP)
- ✓ Pressure difference achieved is sufficient to overcome hypotony

Future work

- ✓ Leaching tests, as well as biocompatibility tests, need to be performed on the magnetic SIBS material
- ✓ Bonding experiments will be carried out to evaluate the influence of pressure, temperature and time on the bonding strength of the housing element
- ✓ A technique to connect the drainage tube with the housing element will need to be developed

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Santen

INNFOCUS

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Thank you for your attention!

