

# DEVELOPMENT OF A TEST FACILITY FOR MICROFLUIDIC CHARACTERIZATION OF GLAUCOMA DRAINAGE DEVICES

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**Abstract:** Microfluidic characterization plays an outstanding role in the development of glaucoma drainage devices. Here, we describe the optimization of an existing test facility with regard to measurement of small volumetric flow rates in the range of 1  $\mu\text{l}/\text{min}$  to 40  $\mu\text{l}/\text{min}$  in a minimized testing time. The existing test facility is extended by a flow sensor and validated by microfluidic characterization of glass capillaries. Finally, two micro-mechanical valve prototypes are successfully analysed with regard to opening and closing pressure.

**Keywords:** Microfluidics, Micro-mechanical valve, Glaucoma drainage device, Microstent

## Introduction

Glaucoma along with diabetic retinopathy and macula degeneration are common causes of blindness. Due to demographic development prevalence of glaucoma will increase in the future with an estimated number of 900.000 cases in Germany by 2030 [1].

Long term clinical results prove safety and efficacy of glaucoma drainage devices (GDD) in treatment of refractory glaucoma. Today the implantation of GDD is increasingly suggested for patients with uncontrollable intraocular pressure (IOP) despite of medical therapy or laser treatment [2, 3].

For lowering of IOP, the major task of GDD is the drainage of aqueous humour from the anterior chamber into another eye compartment. Therefore microfluidic characterization plays an outstanding role in the development of GDD. Previously we presented a test facility for microfluidic characterization of GDD that was based on measurement of mass flow as a function of the pressure difference [4]. The measurement of small volumetric flow rates in the range of 1  $\mu\text{l}/\text{min}$  to 40  $\mu\text{l}/\text{min}$  was time consuming. Depending on the desired resolution of pressure difference steps, the characterization of a single implant took up to one day.

Therefore we describe an improvement of our test facility with regard to the measurement of small volumetric flow rates in a short time period.

## Methods

The functionality of our test facility (Fig. 1) was previously described in detail [4]. The GDD is fixed in the flow chamber (c) and exposed to a pressure difference between two hydrostatic heads (a, b). For control of hydrostatic heads there are two pressure sensors (DMP 331, SUKU Druck-

und Temperaturmesstechnik GmbH, Germany) ( $p_1$ ,  $p_2$ ) and two magnetic valves (6011, Christian Bürkert GmbH & Co. KG, Germany) ( $v_1$ ,  $v_2$ ) in combination with a fluid reservoir (d) and a collecting tray on a scale (Sartorius CP225 D, Sartorius AG, Germany) (e). The test facility is encased by a climatic chamber (SI60D, Bibby Scientific Limited, UK). The original setup allows a measurement of mass flow as a function of the pressure difference and is suitable for volumetric flow rates above 40  $\mu\text{l}/\text{min}$  in an acceptable time period.

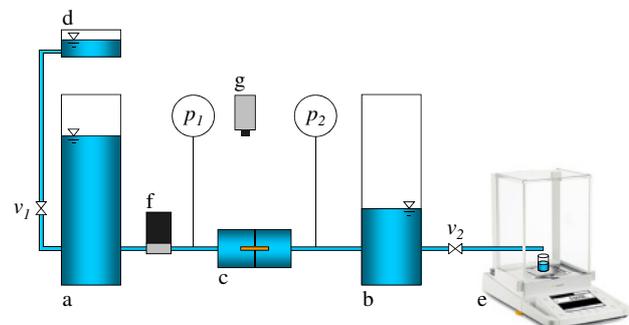


Figure 1: Test facility for microfluidic characterization of GDD (scheme): hydrostatic heads (a, b), flow chamber with GDD (orange) (c), fluid reservoir (d), collecting tray on scale (e), flow sensor (f), pressure sensor ( $p_1$ ,  $p_2$ ), magnetic valve ( $v_1$ ,  $v_2$ ) and camera system (g)

With regard to the measurement of small volumetric flow rates in the range of 1  $\mu\text{l}/\text{min}$  to 40  $\mu\text{l}/\text{min}$ , the existing test facility was extended by a flow sensor (SLG1430-480, Sensirion AG, Switzerland) (f) which is connected in series to the flow chamber. Additionally, for the observation of motion of micro-mechanical valves, a camera system (VRmFC-22/C-PRO camera, VRmagic GmbH, Germany; VZM 600i zoom lens, Edmund Optics, USA) (g) was integrated in the test facility. Measurement software was designed using LabVIEW 11.0.1 (National Instruments, USA). Validation of the improved test facility is done by microfluidic characterization of glass capillaries (minicaps CE 0,5  $\mu\text{l}$ , Hirschmann Laborgeräte GmbH & Co. KG, Germany). Finally, the improved test facility is used for microfluidic characterization of two different micro-mechanical valves designed for the application on a novel microstent for glaucoma therapy. Micro-mechanical valves (width 200  $\mu\text{m}$ , length 500  $\mu\text{m}$  and cutting width 30  $\mu\text{m}$ ) were manufactured by femtosecond (fs)-laser micromachining of silicone tubing ( $d_i = 300 \mu\text{m}$ ,  $d_o = 640 \mu\text{m}$ ,  $l = 10 \text{ mm}$ , Silastic Rx-50, Dow Corning Corporation, USA) [4]. To analyse the influence of the valve flap thickness, wall thickness of silicone tubing in the range of the valve is reduced to 65  $\mu\text{m}$  at the first and to

135  $\mu\text{m}$  at the second prototype. Microfluidic characterization is carried out at 22°C using ultrapure water with a dynamic viscosity of 0.955 mPas [4].

## Results

The volumetric flow rate through glass capillaries, measured with the improved test facility, corresponds very well to theoretical values, calculated by Hagen-Poiseuille equation (Fig. 2). Theoretical values do not consider in- and outflow effects which gives an explanation for the minimal deviation between theory and measurement at large pressure differences.

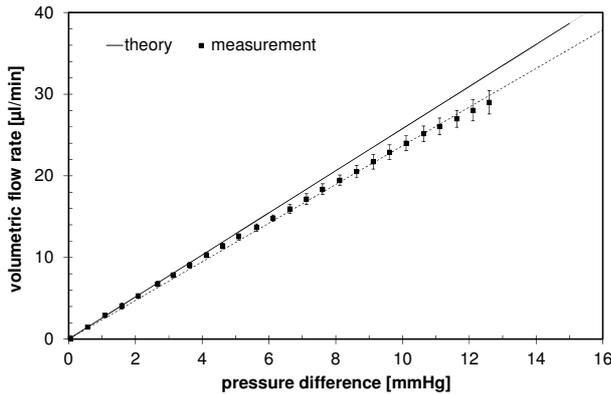


Figure 2: Theoretical and measured volumetric flow rate through glass capillaries ( $d_i = 170 \mu\text{m}$ ,  $l = 31.90 \text{ mm}$ ,  $n = 5$ )

The two fs-laser machined valves are shown in Fig. 3. Microfluidic characterization exhibits different valve characteristics, depending on valve flap thickness (Fig. 4). Measurement curves offer a pronounced hysteresis, in particular for the valve flap thickness 65  $\mu\text{m}$ .

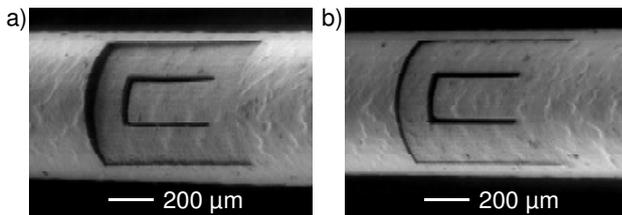


Figure 3: Scanning electron microscopy of two fs-laser-machined micro-mechanical valves: valve flap thickness 65  $\mu\text{m}$  (a) and 135  $\mu\text{m}$  (b)

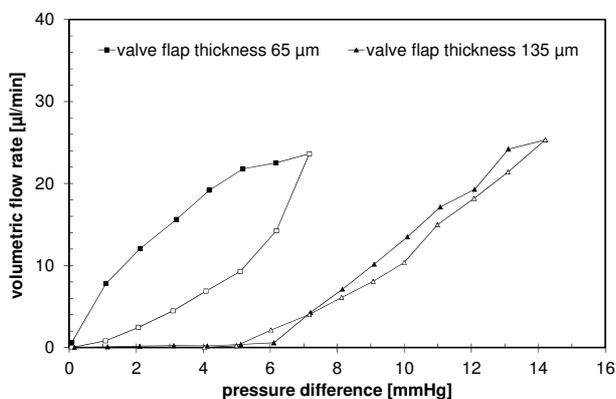


Figure 4: Measured volumetric flow rate through the two different micro-mechanical valves with increasing (filled marks) and decreasing (blank marks) pressure difference

Opening and closing pressure are defined as pressure difference where a volumetric flow rate of at least 1  $\mu\text{l}/\text{min}$  is measured. Valve opening and closing pressures are extracted from the measurement and summarized in Tab. 1.

Table 1: Measured opening and closing pressure of the two different micro-mechanical valves

valve flap thickness [ $\mu\text{m}$ ]	opening pressure [mmHg]	closing pressure [mmHg]
65	< 1	1
135	7	5

The camera system is fully integrated in the measurement-software and allows an on line imaging of the GDD and the valve, respectively. Individual images can be captured any-time manually or automatically at every pressure step.

## Discussion

The optimized test facility is suitable for microfluidic characterization of GDD. Measurement time, especially for small volumetric flow rates, was successfully minimized. The characterization of a valve, e.g. with the valve flap thickness 135  $\mu\text{m}$ , took less than half an hour which is almost 60 times faster compared with the previous facility. The resolution with regard to pressure difference steps can be enhanced up to 0.1 mmHg due to the minimized measurement time. This allows a precise determination of opening and closing pressures as shown for the two valve prototypes.

In future investigations the optimized test facility will be used for the precise design of micro-mechanical valves for the application on a novel microstent for glaucoma therapy.

## Acknowledgement

This project was partially funded by the Federal Ministry of Education and Research (BMBF) within the research project REMEDIS “Höhere Lebensqualität durch neuartige Mikroimplantate” and by the research funding FORUN 2012 of the Universitätsmedizin Rosstock.

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