Polymeric Micro Check Valve for Glaucoma Treatment
Considering Rate of Aqueous Humor Formation

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Abstract: This paper describes a novel glaucoma drainage device (GDD) to regulate intraocular pressure (IOP) considering the rate of aqueous humor formation. The device functionally consists of a polymeric cannula (silicone tube) and a micro check valve (PDMS: polydimethylsiloxane). The check valve has three layers: a top layer (cover), which has rounded edges to reduce fibrosis, an intermediate layer (thin movable valve membrane), and a bottom layer (base plate). A feedforward channel is employed in the top layer to prevent reverse flow by compensating the pressure of the outlet channel. The thickness of thin the PDMS membrane was determined considering the cracking pressure and the rate of aqueous humor formation. The cracking pressure in-vitro test was conducted at 15 mmHg, which lies within the normal intraocular pressure range (10 ~ 20 mmHg). The experimental mean value and standard deviation of the flow rate at the cracking pressure was 2.18 ± 0.69 µL/min, which is confirmed to cover the rate of aqueous humor formation in the normal human eye (1.5 ~ 3.4 µL/min). Flow in a reverse direction was not observed.

1 INTRODUCTION

Glaucoma is an eye disorder associated with abnormally increased intraocular pressure (IOP) due to occlusion of Schlemm's canal. It permanently induces resultant visual field loss and progressive blindness by damaging the optic nerve system. Three types of glaucoma treatment methods are mainly used to lower the IOP, including medication, laser surgery, and glaucoma surgery depending on the severity. One of the methods of refractory glaucoma treatment is a drainage device to surgically lower the IOP (Shuchi and Louis, 2010). Many researchers have worked to develop such a drainage device for glaucoma patients. Typically, Molteno, Krupin, Baerveldt, and Ahmed valves are commercially available devices, which usually consist of two components, namely, a cannula and a base plate. The plate is fixed onto the cornea with sutures, and the cannula shunts aqueous humour from the anterior chamber into the reservoir (Brian A Francis et al.,

1998).

Recently, many efforts to develop a drainage device using microfabrication technologies, called microelectromechanical systems (MEMS), have taken advantage of size reduction and batch processes. In particular, micro check valves are effective drainage valves for glaucoma patients, because they easily control the cracking pressure for regulation of the intraocular pressure and effectively prevent unexpected reverse flow and/or dust from outside the eyeball. However, unsuitable device shapes, such as sharp edges of the plate and cannula, and non-biocompatible materials can cause failures, such as inflammatory reactions. Also, the complicated fabrication of the valve membrane (for instance, using gray-scale photomask or through-hole process) might induce a severe variance in cracking pressure and/or flow rate (Jeffrey Chun-Hui Lin et al., 2010), (Seunghwan Moon et al., 2012). This paper presents a novel glaucoma drainage device (GDD) with a micro check valve, whose flow

rate is determined considering the rate of aqueous humor formation. The device was realized by a simple fabrication process using all-polymeric biocompatible materials. The fabricated device was experimentally evaluated in terms of flow rate, cracking pressure, and reverse flow.

2 DESIGN

Figure 1 shows the configuration of the proposed GDD with a leakage barrier and a valve membrane. The GDD functionally comprises a silicone cannula and a PDMS micro check valve. The PDMS valve consists of s three layers. The top layer contains a feedforward channel including a valve membrane to prevent reverse flow from outside the eyeball. The top and intermediate layers have several anti-delay holes to reduce the pressure delay between the feedforward channel and the fluidic channel. The bottom layer comprises a fluidic channel and a leakage barrier to maintain the appropriate cracking pressure.

The base plate has a fitting cavity into which the tip of the cannula is inserted. Suturing holes are commonly formed onto all three layers to mount the device on the eyeball for implantation.
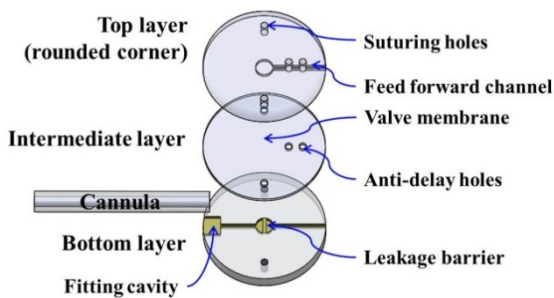

Figure 1: Schematic of the glaucoma drainage device (GDD) fabricated by the MEMS process.

3 OPERATION PRINCIPLE

Figure 2 shows the operation principle of the GDD with a micro check valve that is normally closed. When the intraocular pressure (P_i) is higher than the external pressure (P_e) plus the cracking pressure (P_c), the valve membrane is deflected upward; therefore, the aqueous humor generated from the anterior chamber can flow out of the eyeball. When P_e is greater than or equal to the intraocular pressure (P_i), the membrane returns to its initial shape because the feedforward channel is employed, preventing reverse flow by compensating for the applied pressure of the outlet channel.
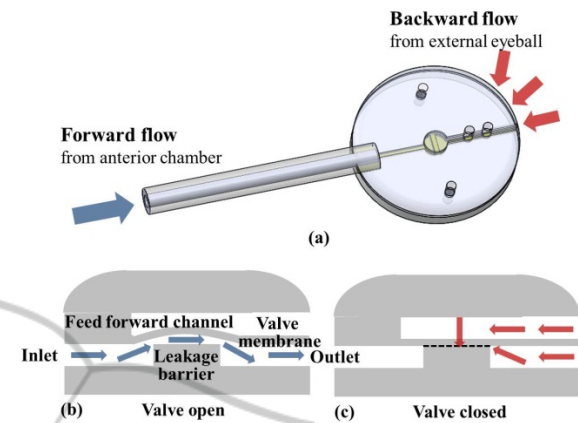

Figure 2: Operation principle of the micro check valve for regulating intraocular pressure: (a) bird's eye view, (b) the check valve in open state, and (c) the check valve in closed state. Dashed line represents the interface that makes physical contact with no stiction.

4 FABRICATION

Figure 3 shows the fabrication sequence of the proposed GDD. First, a mold for the top layer was fabricated using a negative photoresist (PR; SU-8). The 100 μm-high SU-8 was patterned on a silicon substrate. Second, another mold for rounding the corners of the top layer was fabricated using an isotropic process of deep reactive-ion etching (DRIE). Third, the molds were aligned after pouring uncured PDMS (Sylgard® 184, Dow Corning) on the round mold. Fourth, the PDMS replica was separated from the molds after curing at 60°C for 2 hours in a convection oven.

The intermediate layer, which is used to actuate the valve, was fabricated by spin coating of uncured PDMS on the glass, and it was cured under the same conditions.

For the bottom layer, a PDMS replica was peeled off of the patterned SU-8 mold. Next, parylene of 1 μm thickness was deposited onto the PDMS replica of the bottom layer using LPCVD (PDS2010, Specialty Coating Systems). Then, the PR was selectively patterned on the parylene layer. After selective etching of the parylene layer using reactive ion etching (RIE), the PR was removed. Finally, the PDMS bottom layer was dipped into acetone and buffered hydrofluoric acid (BHF) to remove the residual PR and silica-like layers, respectively (Yinhua Lei et al., 2011).

The top and intermediate layers were bonded

after treatment with O_2 plasma, and they were punched for fabrication of the anti-delay hole using a micro punch (Harris Uni-core). Then, the bottom layer was assembled with the top and intermediate layer after O_2 plasma treatment, and it was punched to shape the main body and suturing holes. The cannula (TYGON® S-54-HL Microbore tubing) was inserted into the fluidic channel and fixed with biocompatible bond (Henkel Loctite Corp.).

Microscopic images of the fabricated PDMS replica of the top and bottom layers are shown in figure 4.

Figure 5 shows a photo image of the fabricated GDD whose diameter and thickness are 7.7 mm and 1 mm, respectively. The length of the cannula can be individually adjusted considering the status of the patient in surgery.

Top layer   **Bottom layer**

Figure 4: Microscopic images of the fabricated PDMS replica of the top and bottom layers.
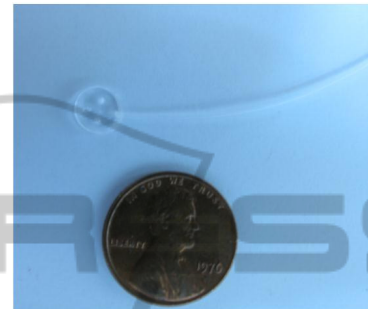
Figure 5: Image of the fabricated glaucoma drainage device

5 IN VITRO TEST

The flow characteristics of the micro check valve are shown in figure 6. A balanced salt solution (BSS), which has properties similar to those of the aqueous humor, was used to measure the flow rate using an electronic balance (AdventurerTM AR2140). Prior to the application of hydrostatic pressure to the inlet (cannula), the device was dipped into BSS to maintain experimental conditions similar to those of an in vivo experiment.

The membrane thickness of the device was 58 μm, and the diameter of valve membrane was 500 μm. Every data point of the fabricated GDD was obtained three times at 3 min intervals for the applied pressure.

Figure 7 shows the experimental flow rates of the proposed GDD with respect to the applied pressure. The results show that the flow rate is proportional to the applied pressure when the applied pressure is larger than the cracking pressure. The cracking pressure was 15 mmHg, which lies within the intraocular pressure range of normal patients (10 ~ 20 mmHg). The mean value and standard deviation of the flow rate were 2.18 ± 0.69 μL/min at cracking pressure, which is large enough to cover the rate of aqueous humor formation in a normal human eye (1.5 ~ 3.4 μL/min). Meanwhile, reverse flow was not
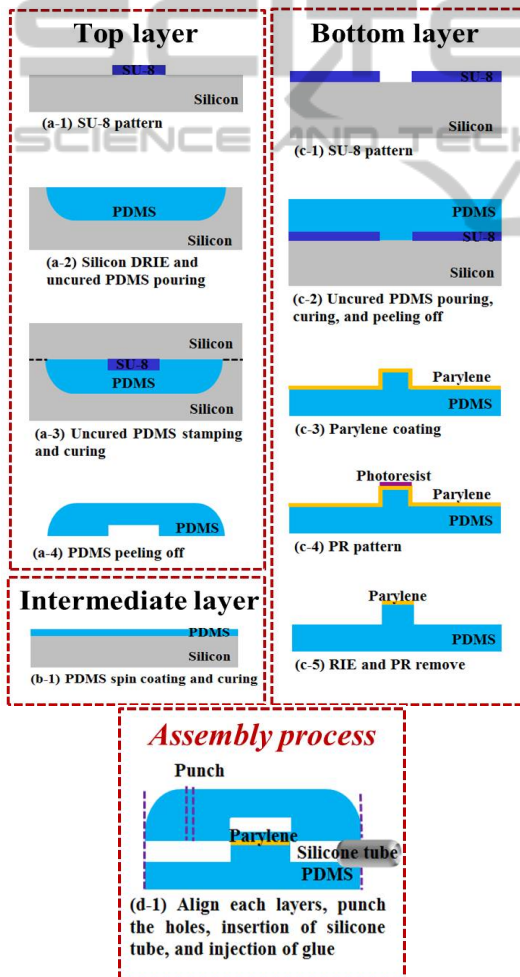

Figure 3: Fabrication sequences of glaucoma drainage devices (GDD); (a) the top layer (cover), (b) the intermediate layer (valve membrane), (c) the bottom layer (base plate), and (d) the assembly process of the three layers and cannula.
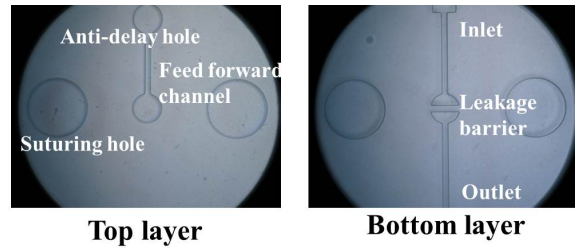
observed when hydrostatic pressure (up to 30 mmHg) was applied to the outlet and the feedforward channel. The in-vitro test results demonstrate that the proposed GDD has high potential for the treatment of glaucoma in view of cracking pressure, flow rate, and the prevention of the unwanted reverse flow.
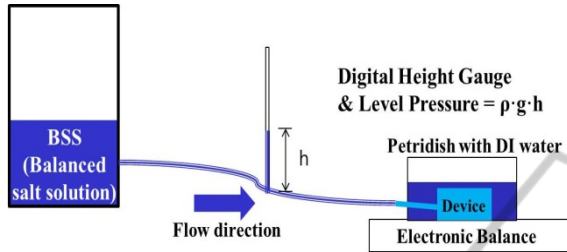

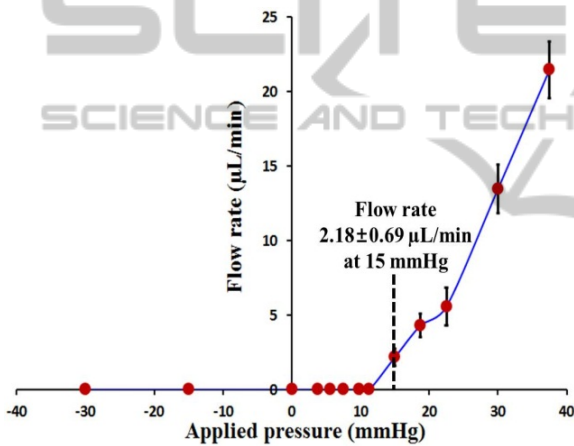Figure 6: Illustration of experimental setup to measure the flow rate of the fabricated GDD.

Figure 7: Flow rate of the proposed GDD (glaucoma drainage device) with respect to applied pressure. (thickness of valve membrane: 58 um, diameter of valve membrane: 500 um; cracking pressure: 15 mmHg).

6 FURTHER WORKS

The fabricated glaucoma drainage device will be mounted on a rabbit's eye for further study. Reliability testing (cracking pressure, flow rate, and reverse flow) will be carried out, and inflammatory reaction will be investigated through the in-vivo animal test.

REFERENCES

Brian A. Francis, Andres Cortes, Janet Chen, and Jorge A. Alvarado, 1998. *Opthalmology*, 105(9); 1708-1714

Jeffrey Chun-Hui Lin, Feiqiao Yu, and Yu-Chong Tai, 2010. *IEEE 23rd International Conference on Micro Electro Mechanical Systems (MEMS)*, 1107 - 1110

Seunghwan Moon, Seongmin Im, Jaeyong An, Chang Ju Park, Hwang Gyun Kim, Sang Woo Park, Hyoung Ihl Kim, and Jong-Hyun Lee, 2012. *Biomed Microdevices*, 14; 325–335

P. Shuchi, R. P. Louis, 2010. *Seminars in Ophthalmology*, 25(5-6); 265–270

Yinhua Lei, Yaoping Liu, Wei Wang, Wengang Wu, and Zhihong Li, 2011. *Lab Chip*, 11; 1385