IMPLANTABLE MICROVALVE-PACKAGED GLAUCOMA DRAINAGE TUBE

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ABSTRACT

This paper presents the first tube-type microvalved glaucoma drainage device (GDD) incorporating two parylene-based micro check valves in a needle-implantable form factor for minimally invasive implantation. Dual micro check valves are exploited in back-to-back configuration to realize a specified pressure-bandpass flow regulation profile for effective intraocular pressure regulation. Post-fabrication packaging of the microvalves in a glass capillary tube carrier facilitates hypodermic needle implantation of the device to the anterior chamber of the eye. This capillary tube then effectively provides a regulatory eye fluid drainage control with minimal surgical complications. Bench top flow tests successfully characterize the pressure/flow rate behavior of the tube device consistent with our design in the 0-200 mmHg and 0-80 μ L/min regulation ranges. In addition, preliminary *ex vivo* implantation test of tapered hollow tube mockup verifies the concept of subconjunctival tube placement with proposed device dimensions, which is promising for future study of tube implantation.

INTRODUCTION

Glaucoma is associated with abnormally high intraocular pressure (IOP) due to a patient's inability to drain excessive eye fluid from the anterior chamber of the eye through trabecular meshwork [1]. If not reduced with adequate treatment, the high IOP would continuously suppress and damage a patient's optical nerves as the disease progresses, leading to loss of vision or even total blindness in the end. Current clinical treatment involves medication typically in the form of eye drops with dosages depending on the severeness of the disease. However, it accompanies with certain concerns such as difficulty of continuous treatment, inefficient dosage style, and potential side effects or patient refractoriness to the drug composition. In order to have an alternative addressing those issues, glaucoma drainage device (GDD) has been a desirable with the concept of physically draining the excessive intraocular fluid through the artificial drainage path so as to reduce the associated IOP. Such a device should be capable of regulating the IOP to be below 20 mmHg while not causing hypotony (i.e., IOP < 5 mmHg) with time. It is further necessary to have the valve closed if high IOP (e.g., >50 mmHg) happens due to normal external interferences like eye rubbing or bumping. Therefore, it is ideal to have dual back-to-back valves consisting of an opened normally-closed (NC) valve above 20 mmHg and a closed normally-open (NO) valve above 50 mmHg in order to realize the desirable pressure-bandpass flow regulation.

Micromachined valves have long been widely made and used in microfluidic devices for flow controls in micro-total-analysis systems (μ TAS) [2][3]. In 2007, Chen et al. reported on-chip surface-micromachined parylene-based dual check valves with a potential application of using them as a passive IOP regulator [4]. To accomplish a stand-alone implantable device, however, the microvalves must be extensively released and packaged into a capillary tube to become a real valve-in-tube system for real device implantation. As a result, a novel post-microfabrication tube packaging technology using an auxiliary glass capillary tube as a coupler in this work is developed to help us assemble the valve

system. These valves have smaller planar size than the inner diameter (I.D.) of the coupling tube so that the valve surface would not be contaminated during packaging and such makes it easier to load the valves into appropriate capillary tubes. A subconjunctival needle implantation would be executed to mimic the normal aqueous humor drainage pathway (Figure 1). As such, the shape and length of the capillary tubes are also carefully designed so that the implantation can be performed using a specific needle-in-needle introducer setup. The front end of the tube is tapered for convenient device placement after injected from the needle with not penetrating the conjunctiva. The length is chosen based on that the back end of the tube can still be observed through cornea during surgery.

Figure 1: Subconjunctival implantation idea of the GDD implanted through the anterior chamber of the eye.

DESIGN

In microflow control component design of the glaucoma drainage tube, one NC valve is chosen to achieve the necessary low-pressure-off response and one NO valve is chosen to behave as a high-pressure stopper (Figure 2). Dual NC and NO parylene micro check valves artificially regulate the intraocular fluid drainage without any external power consumption, further control the IOP drainage profile of glaucoma patients. The back-to-back configuration prevents the GDD from water leakage if the fluid flows in the opposite direction. In NO valve design, the twisted-arm tether length is carefully designed considering the stiction effect to guarantee free-standing valve membrane after release [5]. On the contrary, the NC valve utilizes a stiction process that normally happens during drying process [6]. This self-stiction effect facilitates spontaneous anchoring of the NC valve with predetermined cracking pressure by pre-stressing the center sealing part of the valve through straight tethers connecting to the anchoring part (Figure 3). It greatly simplifies the multi-layer parylene micromachining process into single-layer parylene deposition. Both NC and NO valves are made separately by surface micromachining parylene C, which is biocompatible (USP Class VI grade) and compatible with CMOS/MEMS processes. The mechanical properties of the microvalves were simulated using COMSOL Multiphysics™ to design their pressure/flow rate characteristics. The cracking pressure and the fluidic conductance of the device can be controlled by the geometry and numbers of the tethers, the thickness of parylene, and the height difference between stiction anchoring part and the center sealing part.

In order to fulfill a real implantable GDD, valves are designed with circular releasing trenches on the back side of the wafer (Figure 3) to be introduced in an extra coupling capillary during packaging. All valves are encircled by 65 μm wide, 150 μm deep grooves defined by DRIE on the top side for convenient assembly afterwards. The I.D. of the coupling tubes is 320 μm , which is slightly larger than the 300 μm valve diameter. The outer diameter (O.D.) of the coupling tube is 400 μm , smaller than the I.D. of the outside protecting tube. The protecting tube can perfectly accommodate the valves given its 530 μm I.D., and it fits into 19-gauge needle given its 670 μm O.D. so that hyperdermic needle implantation is feasible. The front tip of the protecting tube is tapered to be 30° for convenient device placement at subconjunctiva site. The length of the protecting tubes could be trimmed to 2-10 mm depending on the size of individual eye for good observation during surgery.

Figure 2: Schematics of valve-in-tube system: (left) Combination of one NC valve and one NO valve with a coupling tube; (right) Final finished valve-in-tube system.

Figure 3: Cross-section of NC valve design.

FABRICATION AND PACKAGING

The fabrication process started from growing thermal oxide on silicon wafer surface (Figure 4). Through-wafer holes and releasing trenches of the valves were etched using backside DRIE until 50 μm silicon membranes were left. A three-step lithography was performed to create three different heights of sacrificial photoresist for the NC valve. A 150 μm deep groove was created surrounding the valves using additional DRIE after parylene C coating and patterning for convenient coupling tube packaging alignment afterwards. Through holes were then opened by completely etching away the silicon membrane so as to strip the sacrificial photoresist with acetone. After photoresist stripping and air drying of the devices, stiction happened on NC valves and the anchoring parts bonded onto wafer surfaces, providing the necessary pre-stressed force. Figure 6 shows the completed devices after air drying.

The microfabricated valves were packaged into a glass

capillary tube to fulfill the valve-in-tube system. The coupling tube was attached to the valve with a tiny epoxy drop gently applied onto the alignment groove (Figure 5). The valve-with-coupler package was then inserted into the protecting tube and the entire tube-in-tube system was further secured by epoxy sealing (Figure 7). The finished valved tube could be trimmed to 2-10 mm long, suitable for 19-gauge needle implantation (Figure 8).

Figure 4: Fabrication process flow: (a) NC valve; (b) NO valve.

Figure 5: Valve-in-tube system packaging procedure: (a) NC valve; (b) NO valve. Two valves share opposite packaging direction.

Figure 6: Micrographs of fabrication results: (a) NC valve with fixed-end tether boundary; (b) NC valve with flexible-end tether boundary; (c) NO valve with free-standing twisted-arms.

Figure 7: Valve packaging results: (a) NC valve and (b) NO valve in the tube; (c) Top view of NC valve inside a coupling tube.

Figure 8: Final valved tube results: (a) 2 mm long NC valved tube; (b) 2 mm long NO valved tube; (c) 6 mm long valved tube with 30 degree tapered tip; (d) Tapered valved tube in 19-gauge needle. 1 div. in pictures = 1 mm.

TEST AND DISCUSSION

Bench top test

Two different testing setups were built up for valve-on-chip and valve-in-tube test (Figure 9), respectively. Water was chosen as the working fluid to simulate the intraocular environment. Controlled pressure-driven water flow was injected and monitored by pressure gauge with tuning resolution up to 0.01 psi (~0.5 mmHg). For on-chip valve test, working fluid flowed into a customized jig with specially designed channels conducting water to fluidic ports of the tested valves. For valved tubes, an adapter was introduced to connect from columns of the testing setup to

valved tubes with different diameter. A protective tubing sleeve was also used to protect the valved tubes and provided tightly mounting. The flow rate was calculated from measuring the flowing speed of water front in the columns of the testing setup.

Pressure/flow testing results are shown in Figure 10. For NC valves, it could be shown that there is a good agreement with data from valves on chips and valves in tubes. The characterization results of NC valve show that cracking pressure was measured approximately 0.2 psi (~10 mmHg), which is consistent with our valve simulation results. No water flow was observed under pressure loading below cracking pressure point, giving the support that the sealing part was well pressed by the four straight tether arms with the predetermined snapping force. This result also indicates that the epoxy well secured the valved tube opening with no water leakage. NO valves were characterized directly in valved tubes. No significant cracking pressure was obtained during tests. The high-off behavior with greatly decreased flow rate from approximately 1.0-1.5 psi (~50-75 mmHg) was demonstrated. A small amount of water leakage was observed because of the misalignment of fluidic ports of the valves occurred from the nature of double-sided pattern alignment on the wafer throughout the fabrication processes.

Figure 9: Schematic of testing setup: (a) Customized testing jig was used to test valve on chip; (b) An adapter was used to test valve-in-tube system.

Figure 10: Testing results: (a) NC valve with fixed-end boundary; (b) NC valve with flexible-end boundary; (c) NO valve tested in tube.

Figure 11: (a) Needle in needle introducer setup; (b) A hollow tube subconjunctivally implanted into an enucleated porcine eye; (c) Testing dye shunted into the hollow tube.

Ex vivo implantation test

An implantation test using an enucleated porcine eye model and a tapered hollow tube mockup was performed to verify the implantation concept. A customized needle-in-needle introducer using 19-gauge and 25-gauge needles was developed to facilitate the minimally invasive needle incision and device injection (Figure 11) that the tube device would not dislodge during introducer retraction. Testing dye was injected into the hollow tube and it drained out to the diffusive subconjunctival location as expected. Dual-valve tube packaging is currently underway for further study and analysis.

CONCLUSION

A new post-microfabrication tube packaging technology has been developed to facilitate a valve-in-tube device for intraocular pressure regulation. Testing results have verified that valved tubes can be secured with epoxy with no observable water leakage. The finished tubes are designed with a form factor for needle-based minimally invasive implantation. Both normally-close and normally-open valves have been characterized respectively with experimental verification that their pressure/flow rate behaviors meet the IOP regulation requirements. *Ex vivo* implantation using tapered hollow tube prototype was performed with successful testing dye drainage demonstration. Optimized tube lengths can be determined from preliminary surgery results and incorporated in future GDD design. The coupling tube can serve as an adaptor to realize a back-to-back dual valve system as a practical pressure-bandpass IOP regulator (Figure 12).

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Figure 12: Schematic of a back-to-back dual-valved IOP regulator.

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