Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

Novel Micromachined Valved Glaucoma Drainage Devices

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Abstract: **In this work two novel valve devices are proposed for treatment of glaucoma. By opening or closing, the proposed valves can be used to reduce high pressures in the eye (hypertony), or prevent low pressures in the eye (hypotony) respectively. These devices work based on the buckling of fluid channel connected to the anterior chamber of the eye. The first proposed valve is fully mechanical while the second proposed device is magnetically driven.**

Keywords: Glaucoma Drainage Devices (GDD), Aqueous Humor, Intra Ocular Pressure (IOP), Mechanical Valve, Magnetic Valve, MEMS, Microfabrication.

1. INTRODUCTION

Glaucoma is a common disease of the eye, and is the second leading cause of blindness in the world, according to the World Health Organization. Devices that are surgically inserted into the eye to cure glaucoma by increasing the outflow of the aqueous humor are referred to by a variety of names. Perhaps the most common name is glaucoma drainage device (GDD). Other names include glaucoma filtration implant (GFI) and combinations including the words implant, shunt or drain. Glaucoma in most cases is caused by raised pressure within the eye.

There are presently three main therapies for glaucoma: treatment with drugs, glaucoma filtration surgery (GFS), and implantation of a GDD. The choice of therapy is dependent on the patient and is influenced by a number of factors. These factors include: the risks associated with the treatment, the likelihood of its success and the clinical presentation of the patient [1].

GDDs developed so far have reliability issues including: unreliable opening under high pressure conditions, unreliable closing under low pressure conditions and unreliable opening pressures. Therefore there is still lots of research work required to improve the design of GDDs [2]. The motive behind our proposed GDD mechanisms is to improve the design of GDDs and increase treatment success rates, such that GDDs are more often selected as a treatment method [2].

This paper addresses the main problems of previous GDD designs, and proposes two novel devices as solutions. The proposed new devices take advantage of the state-of-the-art micro-electro-mechanical sensor (MEMS) technology and advancements in microfabrication technology. Section two contains an introduction to glaucoma and GDDs, section three of the paper explains the proposed valve mechanisms. Section four describes the performed experiments, which is followed by discussion and conclusion sections.

2. GLAUCOMA DRAINAGE DEVICES

In this section the glaucoma disease is briefly introduced and the glaucoma drainage devices are explained as the main context of this research.

2.1. Eye and Glaucoma

The small volume in front of the eye's lens is of most interest in this research. This volume is divided into two parts by the iris, which controls the aperture of the lens. The volume between the iris and the cornea is the anterior chamber (250 μl) and the volume between the iris and lens is the posterior chamber (60 μl). Both chambers are filled with a clear liquid known as aqueous humour [2].

With reference to Figure.1, the aqueous humor passes through the pupil into the anterior chamber, and thereafter drains out of the eye into the canal of Schlem. Normal intraocular pressure is typically about 15±4 mm Hg, but may rise to 21 mm Hg. Pressures within the eye above this range are considered as abnormal pressures. This high pressure is one of the main reasons and also symptom of glaucoma.

The balance between the rate of formation and the rate of drainage of aqueous, adjusts the pressure in the eye. The rate of formation of aqueous is relatively constant at 2-2.5 μl/min while the outflow varies. Many forms of glaucoma are caused by a reduction in the outflow of aqueous, leading to an increase in IOP, thus, increasing the outflow is desirable to reduce the IOP in the eye [1].

2.2. Glaucoma Drainage Devices

Devices that are surgically inserted into the eye in order to increase the outflow of the aqueous are called glaucoma drainage devices (GDDs). GDDs create an alternate aqueous pathway by channeling aqueous from the anterior chamber through a long tube to an equatorial plate inserted under the conjunctiva.

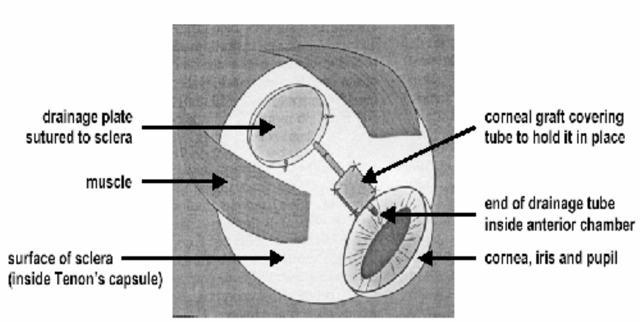

Figure.1. Schematics representation of a GDD [2]

GDDs are being used more frequently in the treatment of glaucoma. All known GDDs use a tube to feed aqueous from the anterior chamber. The tubes used so far are mainly made of silicone. Differences between the devices lie in the nature of the arrangements for drainage and pressure control [2].

Figure.1 shows the general arrangement of a typical drainage device and its position in the eye. After the device is implanted, the body reacts to it as foreign object and begins to encapsulate it with fibrous tissue, forming a bleb. This bleb is extremely important in the operation of the device, because it is the principal source of resistance to the flow of aqueous through the device. Aqueous humor flows freely out of the anterior chamber, through the tube and onto the drainage plate, from where it would spread across the surface of the sclera with minimal resistance. The bleb must grow to a suitable size to regulate the pressure. This is a major feature which determines the success or failure in an individual case.

The first GDD was proposed by Molteno [2] [4] and its design inspired other researchers to develop similar devices. Products from multiple manufacturers, including the Molteno implant, Ahmed glaucoma implant [5], and Baerveldt [6], are examples of aqueous drainage/shunt devices, implanted to reduce IOP in the anterior chamber of the eye. The basic design of these devices is similar. A silicone tube shunts aqueous humor from the anterior chamber to a fibrous capsule surrounding a plate positioned at the equatorial region of the globe. Many studies have demonstrated that these devices are comparable and are effective in treating patients with glaucoma [2].

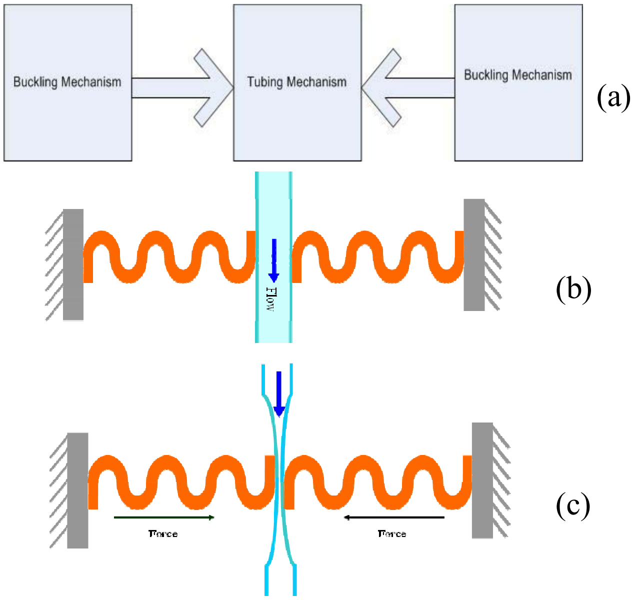

Figure.2. a) The general buckling mechanism. b) The proposed un-powered valve for adjusting eye pressure. c) The valve closes the pathway when there is a pressure drop in the eye to avoid hypotony

Each product has a different group of supporters in the surgical community. The Baerveldt is probably the most popular among glaucoma specialists. This is because of its bigger surface that reduces the chance of post inflammation. The Ahmed is the easiest to implant, so is more popular among surgeons who have less experience dealing with the common problems following glaucoma surgery. The Molteno has the longest track record, and no shunt has ever been found to give better results. Molteno implant requires surgery in both superior quadrants, which takes longer time. That is probably why Ahmed and Baerveldt implants, have gained such popularity.

As stated previously there is still no ideal GDD and there are several problems that should be solved about them. The most important problems that affect the design of GDDs are immediate hypotony and overgrowth of the bleb, tube fit and blockage and valves not closing [2][3]. Loss of pressure (Hypotony) immediately after the operation is a major problem that has to be overcome as well.

Prior to bleb formation, there must be some other resistance in the flow path. So far, the known techniques include implanting the tube several weeks after the drainage plate, temporarily obstructing the tube either by clamping it shut or filling it with material. These problem-solving techniques have themselves a number of complications including: variable delay in curing raised IOP and need for second operation [7]. A GDD that can prevent hypotony would be a very valuable device. This research work has its focus on solving this problem by methods that are explained in the next section.

3. DEVICE MECHANISMS

In this section according to the background presented in the previous section first the mechanical valve and then the magnetic valve are introduced.

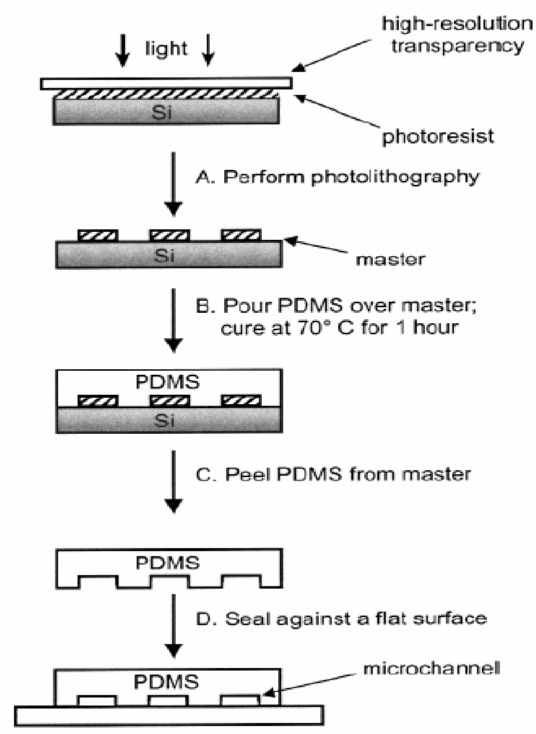

Figure.3. The fabrication process followed in this project to fabricate the PDMS channels which is based on soft lithography idea [15]

3.1. Mechanical device

The general idea for this device is to buckle a tube containing aqueous when the pressure is dropped in the eye. Thus, there are two subsystems that interact to provide the proposed mechanical valve. The tubing system that provides the pathway for the aqueous humor and the pressure system that buckles the tube according to its input pressure, i.e. IOP. The two springs on both sides of the flow pathway control its diameter. The elasticity of these springs can be adjusted by the pressure of the air inside them. The proposed valve mechanism is shown in Figure.2.

By changing the elasticity of springs one can get different forces applied to the tube. Therefore by adjusting the pressure inside the springs we will have the flow pathway closed for pressures lower than 5mmHg. This will inhibit the eye from hypotony. On the other hand, the following self-control happens: while the pressure in the eye increases the valve starts opening steadily. The opening of the valve lets aqueous to flow out and this finally results in the pressure drop in the eye. The obtained valve is not an on-off valve but rather a continuous operation valve.

The proposed fabrication process for the device combines two new fabrication technology, Buried Channel Technology (BCT) [9] and parylene micromolding [10] [11].

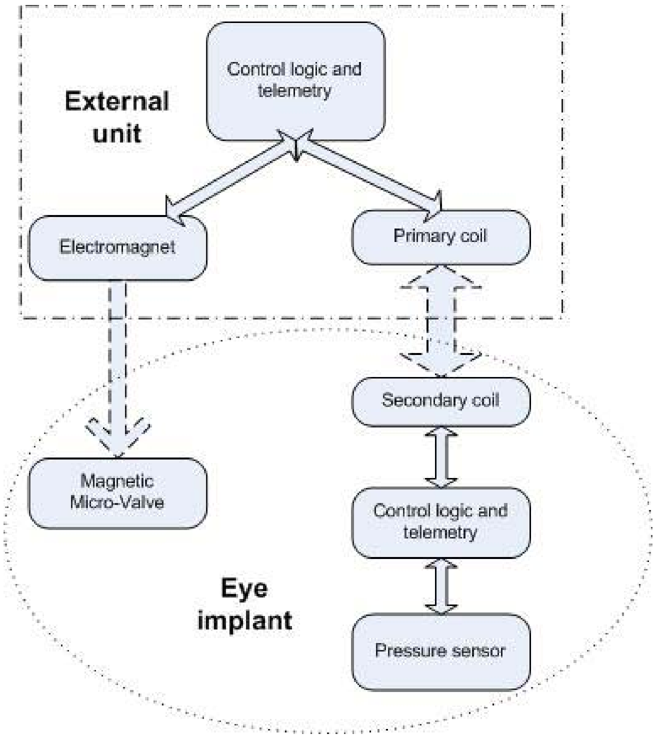

Figure.4 The block diagram of the proposed system for the magnetic actuated GDD. The IOP is sensed and sent out to the external unit in which the decision is made to open or close the magnetic micro-valve according to the measured IOP.

BCT is a method for the fabrication of micro channels under the bulk silicon. This method can be used for applications, such as channels, cavities, and connector holes in the bulk of silicon wafers. In this research BCT is proposed as a method to provide the required silicone mold for the parylene micromolding which deposits parylene in a very thin thickness on the top of the mold.

3.2. Magnetic device

The proposed magnetic valve mechanism is based on a method of fabricating elastomeric components in microfluidic systems based on deformation of elastic materials impregnated with magnetic components. Reference [17] provides the background information on magnetically modified elastomeric materials. Controllable miniature electromagnets are used to activate switching valves to control the eye pressure.

Whitesides and Xia [15] proposed an alternative, non-photolithographic set of microfabrication methods named soft lithography. This process can be seen in Figure.3 Multilayer soft lithography is a technique that combines soft lithography with the capability to bond multiple patterned layers of elastomers [16]. Multilayer structures are constructed by bonding layers of elastomer, which are separately cast from a micromachined mold.

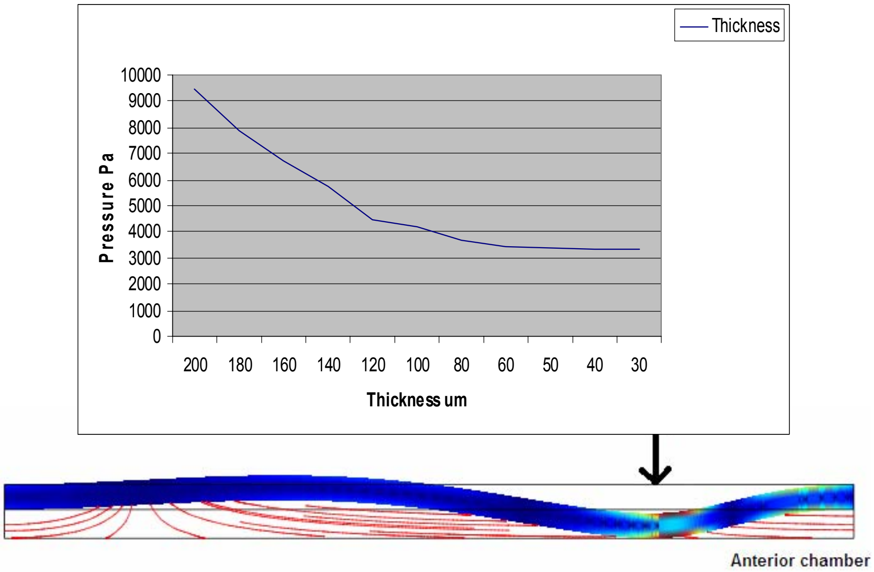

Figure.5. The simulation results for different thickness of the tubing system for input pressure of 5mmHg.

The proposed device in this paper is an extension of methods for rapid prototyping of fluidic microchannels based on replica molding of elastomers, such as PDMS. Silicone polymers such as PDMS have: high compliance, and micropumps [16]. By combining elastomers with magnetic materials and using electromagnets in the substrate, active valves can be fabricated. This approach is simpler and allows miniaturization, by removing the need for macroscopic supplies of external pneumatic switches [15].

For ferromagnetic force, the magnetic pressure F/A (force per unit area) between an electromagnet and a ferromagnetic material is approximately $F/A=B^2/2\mu_0$, where B is the flux density, and μ_0 is the permeability of free space. The flux density B can be estimated with magnetic circuit approximations or calculated using finite element analysis software [17].

The proposed magnetic valve is considered to be used in a system that can be seen in the block diagram of Fig.5. The pressure sensor can be embedded in the same system or an already designed pressure sensor can be used for sensing IOP [19] [20] [21]. In this system the eye pressure is sensed and whenever it falls lower than the 5mmHg the electromagnet instructs the proposed magnetic valve to close, avoiding the hypotony in the eye.

The flux density B can be estimated with magnetic circuit approximations or calculated using finite element analysis software. Saturation generally makes it difficult to obtain fields greater than 1 T this sets a practical upper limit to approximately 400 kPa of actuation pressure. In practice, we would expect to see less pressure, since the actuator needs to work against the elastomer modulus, and the magnetic high elongation, and good sealing properties, making them useful valving materials. Elastomer-based, valving strategies have been reported, who described pneumatic methods for deforming elastomeric microchannels to form microvalves circuits are not optimized [17]. In this research work the main focus is on the fabrication of the magnetic microvalve. The development of the general system of Figure.4 is considered as the next stages of the research in future.

4. EXPERIMENTS

In this section the results of the simulation for the mechanical valve and the fabrication of the channel for the magnetic valve are presented.

4.1. Finite Element Simulation

Using finite element method the tubing subsystem was simulated and the amount of the required force for buckling the tube was calculated. This force can be seen in Figure.2.c. The simulation was done in the lower limit of required IOP which is 5mmHg. As explained in section three we want the tubing to be closed at this particular pressure. For these simulations the force was applied to 1 mm of the tube length and the total length of the tube was 2 cm. Parylene was used as the structural material of the tube with the modulus of elasticity of 2.4 giga-pascal. COMSOL multiphysics software was used for simulation [8] and simulation results can be seen in Figure.5.

As can be seen from the bottom of the Figure.5, the simulation has been done for upper half of the tube to be brought down half way, thus, the same amount of force on the bottom side of the tube will buckle the whole valve.

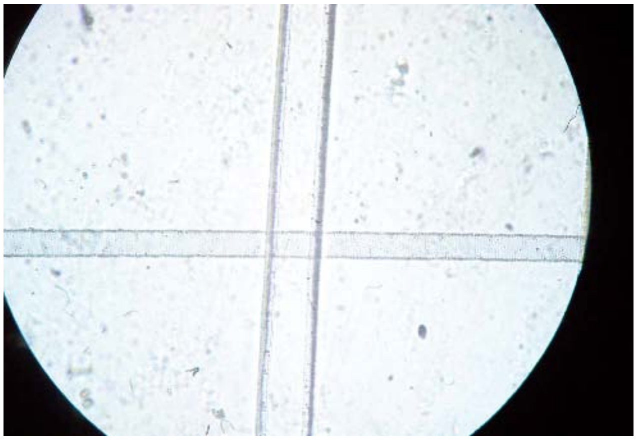

Figure.6. The PDMS channels the horizontal channel is 75 micron and the vertical channel is 200 micron in width. The channels are 10 microns high.

As expected by decreasing the thickness of the tube the required buckling force has also decreased. From 50 microns there is not a significant decrease in the amount of required force because of the decrease in the thickness.

The results of these simulations will be used in the next step of simulation which is the simulation of the buckling system. The buckling system, either magnetic or mechanical, should be able to provide the calculated force of the current simulation as can be seen in Figure.2.C and Figure.5. Proposed valve system stops the hypotony in the eye while eye pressure drops to 5 mmHg. This pressure is an important criterion that can determine the design of the buckling system.

As explained in the previous section parylene is considered as the structural material for the fabrication of the mechanical valve. This is because of the compatibility, mechanical characteristics and the particular fabrication technology for Parylene that enables us to deposit it in very thin thicknesses. For aqueous liquid, water was used in the simulation process.

4.2. Microchannel fabrication

For the fabrication of the magnetic valve PDMS was used as explained previously because of its mechanical properties, its ability to be shaped in soft lithography process and the ease to be impregnate by magnetic materials. For the magnetic valve and in this step of the project the micro channels were fabricated according to the Figure.3 process. GE RTV 615 was used as the PDMS pre-polymers and SU8-10 [18] was used as the master mold. Different channel widths of 75, 100, 150 and 200 µm were fabricated as network of parallel channels. The channel height was designed to be 10 µm by spinning the SU8 photoresist in 3000 rpm for 30 seconds. The mixture of the prepolymers A and B of RTV 615 was poured on this SU8 master mold and was cured in 70°C for one hour. Another network of PDMS was sealed on the top of this network which had a different mixture ratio of prepolymers. This different ratios of primary prepolymers made the adhesion of the two layers possible as can be seen in Figure. 6.

This has been so far very similar to [15] which resemble a pneumatic valve; the next step is to impregnate the prepolymers with Iron powder to be able to close the valve magnetically [17]. This way by sensing the IOP in the eye, while it drops under 5mmHg the valve is closed magnetically to avoid hypotony.

5. DISCUSSION

Both proposed valves in this research are based on the buckling of fluid channel connected to the anterior chamber of the eye as can be seen in Figure.1. Simulations were done to approximate the amount of force required to buckle the mechanical valve. The fluid channels were fabricated for the magnetic device using soft lithography technique. These channels are the main body of the proposed magnetic valve. The same simulation strategy can be used for the magnetic valve to estimate the amount of magnetic field required to buckle the PDMS channels.

For the mechanical valve, after the simulation and approximation of all required thicknesses and pressures the next step would be the fabrication of the device. For device fabrication a combination of two new technologies of Buried channel technology [9] and parylene micromolding [10] were proposed to be used.

For the magnetic valve the microchannels are fabricated and the next step is the impregnation of the PDMS with iron. This will give magnetic properties to the polymer. The channels were implemented as a network of parallel channels, so in case one of them is being buckled by aqueous humor’s particles, others will still continue functioning.

The proposed mechanical valve is a continuous operating valve while the magnetic valve is an on-off valve. The other advantage of the mechanical valve is that, it is fully mechanical, not needing to be electrically powered. As the proposed magnetic valve is supposed to be used together with a microelectronic system, its operation requires electrical power as can be seen in Figure.4. This power will be supplied to it wirelessly which makes the proposed design complicated compared to the mechanical valve.

The magnetic valve offers some advantages compared to the mechanical valve. The first advantage is the ability to continuously monitor the IOP that can give the possibility of monitoring the eye condition to the eye specialist. The second advantage of the magnetic valve is more accurate control on the pressure while the mechanical valve can not offer these because of its mechanical limitations.

6. CONCLUSION

In this paper new devices were proposed as a valve for glaucoma treatment. For both mechanisms after the completion of device fabrication there is a need for an in-vitro setup to test the functionality of the device before trying in the eye. A proper test setup can be found in [14] that consist of a syringe pump connected to a glass standpipe via a 3-way stopcock.

The next step in this research is the completion of the magnetic valve based on the already fabricated channels. The development of the full system of Figure.4 is intended in further work. The buckling mechanism used in this research is not limited to the mechanical and magnetic mechanisms explained in this paper, and other methods such as electrowetting are also among feasible options [22].

ACKNOWLEDGEMENTS

I would like to thank Dr. Bonnie Gray and Fartash Vasefi for their important helps in SFU microfabrication laboratory.

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