A New Adjustable Glaucoma Drainage Device

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Purpose. This work is focused on the testing of a new experimental noninvasively adjustable glaucoma drainage device (AGDD) that allows for the control of its outflow resistance to modulate intraocular pressure (IOP) in a customized fashion.

Methods. Six AGDDs were directly connected to a pressure transducer and a perfusion system continuously delivering saline solution at rate of 2 μL/min. The steady-state pressure was measured and reported as a function of the angular position of the AGDD disk. Ex vivo experiments were conducted on six freshly enucleated rabbit eyes. The IOP was measured, and the flow rate was increased with a syringe pump to simulate elevated IOP associated with glaucoma. After insertion of the implant in the anterior chamber, the position of the disk was sequentially adjusted.

Results. The relation between the pressure drop and the angular position of the AGDD disk is nonlinear. The functional range lies between 80° and 130°, which allows for four or five different reproducible adjustment positions. Above 130° the implant is considered to be closed (no outflow), and below 80° it is considered to be open (minimum resistance to flow).

Conclusions. The resistance to outflow of the experimental AGDD can be adjusted to keep IOP in the desired physiological range. This feature could be useful for addressing the risk of hypotony in the early postoperative stages and could provide a means to achieve optimal IOP under a wide range of postoperative conditions.

Keywords: glaucoma, drainage device, shunt tube, filtering surgery, adjustable glaucoma

Glaucoma is one of the leading causes of blindness in the world,[1,2] and lowering the intraocular pressure (IOP) to prevent optic nerve damage is one of the solutions to control glaucoma progression. Medication is the primary therapy used for patients suffering from glaucoma. However, for some patients, pharmacological solutions may be inefficient and surgical procedure is required.[3]

Several glaucoma filtering techniques exist, and most of them have demonstrated efficacy in lowering IOP.[4–6] They all aim at decreasing the resistance to aqueous humor outflow by creating an flow pathway additional to the conventional ones. For several decades, trabeculectomy[7] was one of the most frequently used surgical techniques. However, recent studies have shown a positive trend in the use of drainage devices in glaucoma surgery while the rate of trabeculectomy is decreasing.[6] The increasing popularity of filtering devices can be attributed to the fact that IOP is reduced in a way that is associated with fewer side effects compared to established techniques.[8]

The Ex-PRESS mini shunt is a stainless steel implant inserted under a scleral flap, and the operation is similar to the trabeculectomy.[9,10] Even if the rate of early hypotony decreased using this kind of device compared to classic trabeculectomy, the rate of complications remained comparable.[11–13] This implant aims at improving the way trabeculectomy works. However, as for all filtering procedures, the lack of proper IOP control can lead to postsurgical complications. Hypotony remains one of the main complications in the early steps postsurgery, and proper control of the IOP through the adjustment of the aqueous humor egress would probably help minimize the occurrence of such postoperative complications.

With regard to that prospect, the ideal filtering device would consist of an adjustable resistor valve that, upon proper adjustment, would take into account the postoperative hypotony and allow for customized adjustments of the IOP.

In this study we present the very first report of a novel adjustable glaucoma drainage device. Preliminary results from in vitro perfusion tests and ex vivo studies on enucleated eyes demonstrate that the model device is able to effectively and reproducibly control the resistance to aqueous humor (AH) egress.

Materials and Methods

Adjustable Glaucoma Drainage Device

Figure 1 shows the adjustable glaucoma drainage device (AGDD) (Fig. 1a) and its external control unit (CU) (Fig. 1b), which is used to read the functional position of the implant and to adjust its fluidic resistance. The concept of the AGDD was invented by Stergiopulos[14] and later developed and patented by Bigler and Stergiopulos.[15] The AGDD is designed to drain AH with a resistance to outflow that can be externally regulated. The implant is inserted surgically under a scleral flap in a manner similar to the Ex-PRESS shunt.[4] It is composed of a deformable silicone (MED-4830; NuSil, Carpinteria, CA) tube (outer diameter 0.3 mm, internal diameter 0.2 mm), which drains AH from the anterior chamber into a bleb formed in the scleral space. For a given rate of drainage, the IOP depends on

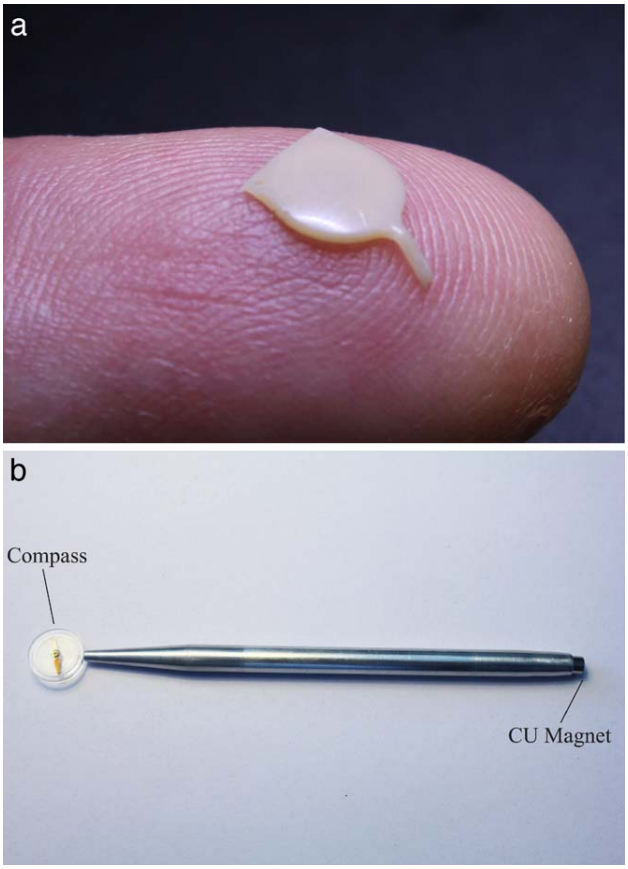

FIGURE 1. Picture of the adjustable glaucoma drainage device (**a**) and its control unit (**b**).

the fluidic resistance of the tube. The implant contains a mechanism (Fig. 2) that allows for a variable compression of the tube, altering its cross-sectional area accordingly and thus changing the fluidic resistance. The various levels of compression in the tube are achieved by rotating a magnetic disk around a shaft, which is eccentric to its axis of symmetry. The angular position of the magnetic disk defines the length of the tube that is compressed as well as the degree of radial compression.

The external measurement/adjustment device, also termed control unit (CU), is depicted in Figure 1b. The CU has been designed to help the physician perform two essential functions: measure the functional (angular) position of the implant, and perform a noninvasive adjustment of this functional position in order to optimize the drainage characteristics (fluidic resistance) of the implant. The measurement of the angular position of the magnetic disk is performed with the use of a flat compass, which is situated in one of the two ends of the CU. The magnetic needle is colored to indicate the "north pole," and the transparent cover slip or the outer rim of the compass housing contains gradations for easier reading of the angular position of the needle. The other extremity of the CU contains a permanent magnet for performing the adjustment. To adjust the angular position of the implant, the operator first reads the actual angular position of the implant's magnetic disk by placing the compass above the implant (Fig. 3). Once the angular position is read, the operator flips the CU 180° to bring the CU magnet into the vicinity of the implant in order to magnetically couple the external magnet to the internal magnetic disk. The operator then drags the magnet in

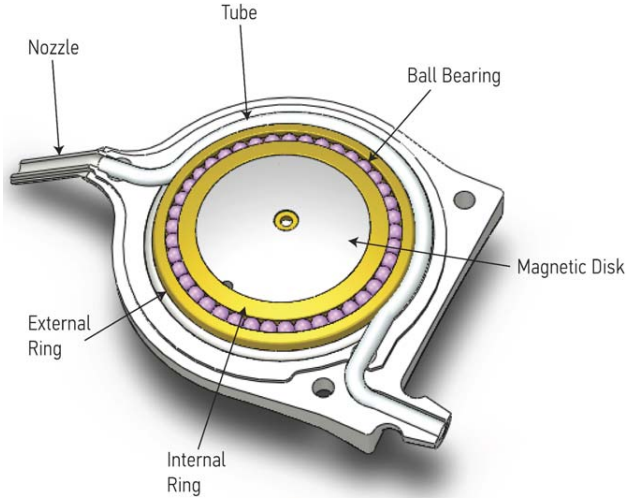

FIGURE 2. Synthetic image depicting details of the mechanism of the AGDD. Under the steering effect of external magnetic fields, the magnetic disk of the implant turns around an eccentric axis pushing or radially retracting the external ring of the ball bearing mechanism. The radial motion of the external ring leads to a change of the cross-sectional area of the elastic tube, thereby modifying its fluidic resistance.

a clockwise or counterclockwise direction along a circular arc around the implant, thus forcing the internal magnetic disk to rotate accordingly. The operator verifies the new angular position of the implant using the compass again.

The mechanism (Fig. 2) and the tube of the AGDD are encapsulated within two shells made of synthetic polymer (PEEK Optima; Invibio, Lancashire, UK). These shells are hermetically shielded to protect the mechanism from tissue contact and fluid entry, which could jeopardize its functionality over time. The AH enters the tube through the nozzle and exits at the backside of the implant, totally shielded from implant's interior. To optimize the positioning of the device under a scleral flap, the shells and the mechanism have been designed to match the radius of curvature of the human eye.

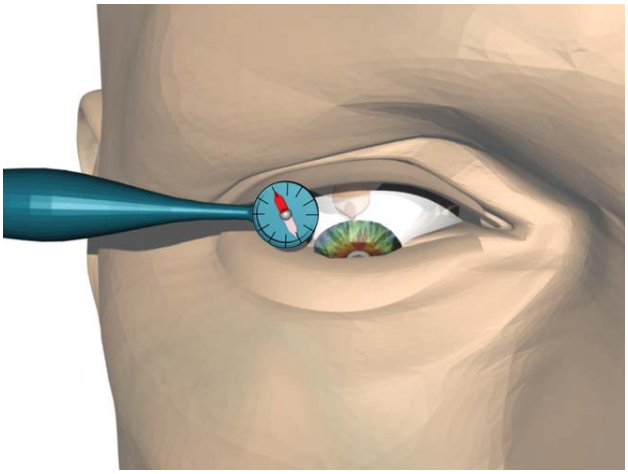

FIGURE 3. Synthetic image showing the positioning of the implant within the scleral flap and the compass of the CU, which is used to read out the angular orientation of the implant's magnetic disk. The operator may adjust the angular position of the implant using the CU magnet.

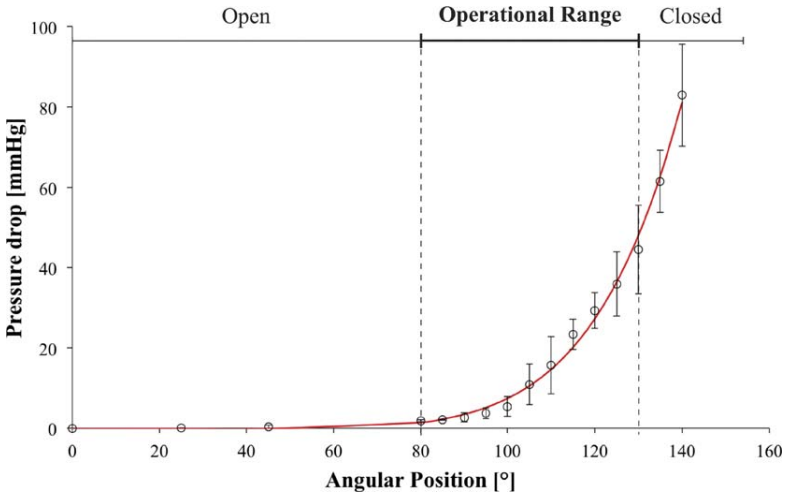

FIGURE 4. In vitro measurements of the pressure drop versus the angular position of the magnetic disk. The operational range is between 80° and 130°. Values are given as average ± standard deviations ($n = 6$). The operational range of the device is defined as the angular range between its fully closed and fully open position. The fitted curve corresponds to a power law: $f(x) = a^*x^b + c$, where $a = 4.81^*10^{-14}$, $b = 7.056$, and $c = -0.15$. $R^2 = 0.99$.

In Vitro Experimentation

The AGDD was connected to a syringe pump (SP210iw; World Precision Instruments, Sarasota, FL) pushing saline solution through the implant's tube at a rate of 2 μL/min. The saline solution would flow out of the distal end of the tube into the atmosphere. Pressure upstream of the implant was measured with an electronic manometer (BLPR2; World Precision Instruments). The manometer was connected to a data acquisition card (DAQPad-6015; National Instruments, Austin, TX) to give real-time pressure readings via a custom interface (LabView 9.0; National Instruments).

The angular position of the implant was changed using the CU. The magnet's angular position was adjusted from 0° to 180° (in 5° steps), and the steady-state pressure was recorded at each position. Three sets of data of pressure versus angular position were obtained for each implant. Experiments were conducted on six different implants.

Ex Vivo Experimentation

Six freshly enucleated eyes (postmortem time less than 4 hours) from white New Zealand rabbits were obtained from a local farm. The eye was held on a brace, and the anterior chamber was cannulated with a 24-gauge catheter (Optiva W; Smiths Medical, Rossendale, UK) filled with saline solution that was delivered by a syringe pump at a rate of 20 μL/min during the experimentation. The catheter was inserted between the anterior plane of the iris and the posterior surface of the cornea. The system was connected to an electronic manometer, and real-time pressure reading and recording were performed as for the in vitro experiment after implantation of the device. The angular positions of the magnetic disk were adjusted from 0° to 180° at intervals of 5°.

Surgical Procedure

The eye was maintained on the mounting unit, and a 24-gauge cannula (Optiva W; Smiths Medical) was inserted into the anterior chamber. The cannula was connected to a water column containing saline solution so that physiological ocular rigidity was maintained throughout the surgery. The height of the column was set to pressurize the eye at 25 mm Hg. A square scleral flap, 7 × 7 mm, was cut using a crescent sapphire blade down to 1 mm from the limbus. A 24-gauge needle was then used to poke the scleral wall and to enter the anterior chamber, creating a hole for entering the device's nozzle into the anterior chamber. Because the nozzle was inserted in the space between the cornea and the anterior surface of the iris, care was taken not to touch either of these structures. The implant was secured using two single point nylon 10-0 sutures, and the scleral flap was repositioned and sutured using two single point nylon 10-0. Finally, the 24-gauge cannula was connected to the syringe pump delivering 20 μL/min, which was deemed necessary to maintain IOP above 21 mm Hg.

Outflow Facility Measurement

Details of outflow facility measurement have been reported previously.[16,17] Briefly, the anterior chamber was perfused first with a defined flow rate (2 μL/min). After a stable IOP level was reached, the flow rate was changed to a higher value until another stable IOP level was reached. The outflow facility (OF) was then calculated using the Goldman equation

$$OF = \Delta Q / \Delta IOP \quad (1)$$

where $Q1$ and $Q2$ are successive inflow rates (μL/min), $\Delta Q = Q2 - Q1$, and $\Delta IOP = P2 - P1$, with $P1$ and $P2$ representing IOP at $Q1$ and $Q2$, respectively (mm Hg).

Statistics

The results were expressed as the mean and standard deviation (mean ± SD). The paired Student's t-test was used to assess the differences in pressure drop among the several angular positions. $P < 0.05$ was considered statistically significant.

RESULTS

In Vitro Experimentation

The relationship between the pressure drop and the adjustment is nonlinear (Fig. 4). From position 0° to 80° the resistance of the tube is equal or close to 0 ($P = 0.2$), meaning

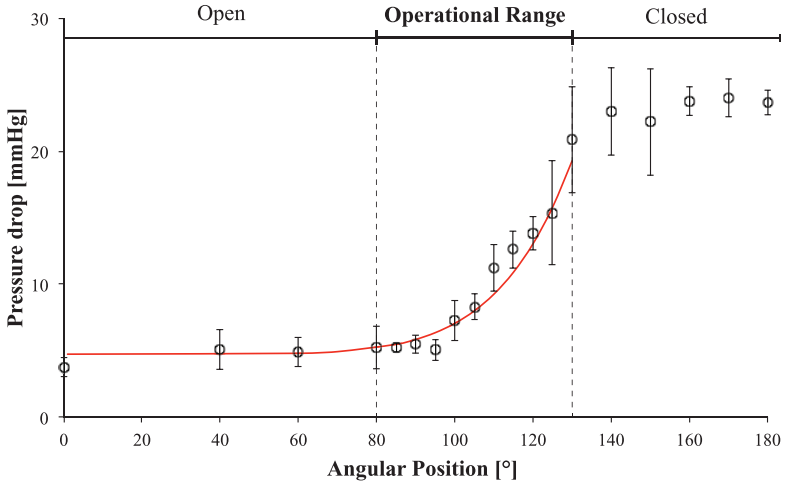

FIGURE 5. Ex vivo measurements of the pressure drop as function of the angular position of the magnetic disk. The implant was surgically placed into its intended anatomical position under a scleral flap in enucleated rabbit eyes. Values are given as average ± standard deviations ($n = 6$). The operational range of the device is defined as the angular range between its fully closed and fully open position. The fitted curve corresponds to a power law: $f(x) = a^*x^b + c$, where $a = 2.26^*10^{-14}$, $b = 7.004$, and $c = 4.739$. $R^2 = 0.98$.

that the AGDD configuration is fully open. From position 120° or higher the pressure drop is high (>30 mm Hg) and adjustments become less accurate.

Significantly different pressure drops may be achieved every 10° ($\Delta\theta$) from 90° to 130° ($P < 0.05$). With steps under 10°, differences in pressure are no more statistically significant. This means that the angular resolution of the device is approximately 10°.

The resistance of the AGDD to aqueous outflow when totally open (position 0°) is equal to 0.05 mm Hg/min/μL.

Ex Vivo Experimentation

The outflow facility before surgery was 0.33 ± 0.09 μL/mm Hg/min and after implantation was 1.27 ± 0.19 ($P < 0.05$). To maintain high pressure in the eye, the flow rate was increased to 20 μL/min, resulting in an IOP of 23 ± 2.5 mm Hg when the implant was in a fully closed position.

The angular position of the AGDD was adjusted in steps of 5°, and the IOP at the new steady state was recorded (Fig. 5). The IOP range from the fully closed to fully open position ranged from 23 ± 2.5 to 3.7 ± 0.7 mm Hg ($P < 0.05$).

Intraocular pressure versus angular position curves from in vitro and ex vivo measurements (Figs. 4, 5) were fit with an empirical power law ($y = a^*x^b + c$). The corresponding values were $b = 7.056 \pm 0.706$ for in vitro and $b = 7.004 \pm 1.297$ for the ex vivo experimentation, demonstrating, as expected, an identical exponent in the power law for the in vitro and ex vivo experiments.

DISCUSSION

In this study, we have tested a new experimental AGDD that allows for noninvasive and nontraumatic adjustment of the fluidic resistance of the shunt, thereby offering a customized control of IOP. The present in vitro and ex vivo experiments are the first steps to validate the fluidic characteristics and performance of this new implant. Results show that the drainage device described in this study can be adjusted by varying the angular position of the disk using an external magnet, thus modifying the cross-sectional area of the draining tube and changing its fluidic resistance. The resistance may vary from infinite (fully closed position) to a minimal value (fully open position), allowing the user to select over a wide range of IOPs.

The working range for the angular position of the implant is situated between 80° and 130°. Angular positions outside of this range correspond to fully open ($\theta \leq 80°$) or fully closed configurations ($\theta \geq 130°$). Within this working range and given the fact that the angular resolution is on the order of 10°, there are effectively four or five distinctly different positions that the user can select with good confidence in order to alter the resistance. This means that there is not only a binary system (open/closed) configuration, but also the possibility to selectively set the resistance of the implant and thus adjust IOP in accordance with different patient needs.

The pressure drop across the implant for a given flow rate is nonlinearly related to the angular position of the implant's disk. The angular position of the magnetic disk of the implant defines the degree of compression of the elastic tube, which defines the internal cross-sectional area of the tube and thus its fluidic resistance. According to Poiseuille's law, the hydraulic resistance (R_H) to flow is inversely proportional to the radius (r) of the tube to the power 4 ($R_H \propto (1/r^4)$). Thus when the hydraulic inner radius of the tube becomes smaller (due to compression by the magnetic disk), the resistance increases by the power of 4; for example, a reduction by half of the diameter leads to a 16 times increase of the resistance. For the particular implant design, the degree of compression is nonuniform along the tube and is nonlinearly dependent on the angular position θ. An empirical fit of the pressure drop versus angular position of the magnetic disk shows that pressure drop is proportional to the angle of adjustment to the seventh power. The resistance has therefore a very strong nonlinear dependence on the angular position of the disk. The nonlinearity of the system might be a limitation, as it reduces the number of adjustment points, making the system very sensitive to the angular position. An ideal system would exhibit a linear adjustment of the resistance as a function of the angle of the disk. In that case, the angular working range would be greater and the angular precision on the adjustment would be less stringent.

During the ex vivo experiments, eyes were artificially maintained at a pressure above 21 mm Hg to mimic glaucoma conditions. High flow rates were used to stabilize IOP at such a high level. This is mainly due to higher outflow facility of cadaveric eyes and to leakages occurring all around the insertion point of the implant's nozzle. The tests on the enucleated eyes demonstrated the efficacy and reproducibility of the AGDD to decrease IOP at various levels, depending on its angular position. Minimal pressures reached after total opening of the AGDD were slightly higher than zero due to high flow rates used in these experiments.

Based on these laboratory investigations, we plan to test the AGDD on an experimental animal model to confirm these initial results and to further evaluate the biocompatibility, controllability, and efficacy of such a device implanted in a living eye. The ultimate goal will be to conduct a clinical trial on patients suffering from medically uncontrolled glaucoma requiring a filtering procedure. In that event, the fine-tuning of the AGDD would be performed postoperatively according to the IOP measurements. For instance, if the IOP was too high (e.g., above 20 mm Hg), the clinician would set the position of the magnetic disk of the AGDD in a new orientation to decrease its fluidic resistance and thus lower IOP. Conversely, if the IOP was too low (e.g., below 5 mm Hg), the clinician could modify the orientation of the disk to increase the resistance to aqueous egress, resulting in an increase of the IOP. In the early postoperative period, and when hypotony is present, the operator could set the AGDD in a fully closed position that would help increase the IOP, thus contributing to minimizing the problem of persistent postoperative hypotony and potentially decreasing the complications related to hypotony. The scenario envisioned above is speculative and needs to be verified through in vivo experiments in animals and in appropriately designed clinical studies.

In conclusion, this study demonstrates that the resistance to AH egress can be selectively changed with an AGDD. This device provides various outflow resistances that can be adjusted to bring IOP to clinically acceptable values. The adjustment can be performed simply and noninvasively using an external CU. The in vitro results presented here need to be confirmed in vivo on animals and humans. Specifically, critical aspects that cannot be studied in vitro, such as biocompatibility, complications related to filtration, overall safety, and efficacy of the AGDD, will be investigated on an animal model before proceeding to a pilot human trial. The simplicity of the device, the relative ease with which resistance is adjusted over a wide range, and the standard way of implanting allow us to hypothesize that this first-ever AGDD may prove to be a valuable tool in the surgical treatment of glaucoma.

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