Performance of a Temperature-controlled Shape-memory Pupil Expander for Cataract Surgery

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Abstract

Purpose: Current pupil expanders are inadequate to reduce stresses and strains induced on the iris tissue. We manufactured an optimized shape-memory expander, performed *ex vivo* and *in vivo* validation of this device, and compared its performance with that from existing devices.

Setting: National University of Singapore and SingHealth Academy.

Design: Prospective randomized blinded assessment of iris anterior surface images.

Methods: We manufactured the shape-memory expanders by over-molding and inserted them into *ex vivo* porcine and *in vivo* monkey eyes for validation. To compare devices, 45 fresh *ex vivo* porcine eyes were purchased to test the Malyugin ring (10), Oasis iris expander (13), iris hooks (11) and our shape-memory expander (11). After insertion and removal of the devices, the eyes were fixed and the iris images were analyzed.

Results: Our expander was successful in pupil expansion for both *in vivo* and *ex vivo* experiments. Subsequent *ex vivo* devices' comparison revealed IPE loss in 36.4% of eyes for the iris hooks, 30.8% for the Oasis expander and 20.0% for the Malyugin ring. Sphincter tears were observed in 27.3% of eyes for the iris hooks and 10.0% for the Malyugin ring. No observable tissue irregularities were discovered from using our shape-memory expander.

Conclusion: We were able to optimize our pupil expansion device to minimize stresses exerted onto the iris tissue. These *in vivo* and *ex vivo* experimental validations demonstrate efficacy in engineering design, and further highlight the translational potential of smart materials in implant development to improve patient healthcare.

Introduction

Cataract surgery is the most performed surgery worldwide with this disease affecting over 20 million people[1]. This number is estimated to increase to over 30 million by 2020[2, 3] driven by an increase in the global elderly population. The surgery is done by replacing the cloudy natural lens with an artificial intraocular lens[4]. To do so requires a sufficiently large pupil for unobstructed surgical maneuvers. Therefore, pharmacological drugs such as phenylephrine, tropicamide and cyclopentolate are used to relax the sphincter muscle and constrict the dilator muscle prior to surgery[5, 6]. Despite this, small pupils may persist due to reduced muscle accommodation from aging[7] or as a result of ingestion of drugs (e.g. tamsulosin[8]), long term miotic drug usage (e.g. pilocarpine[9]) and pseudoexfoliation[10].

To remedy persisting small pupils, surgeons may deploy techniques such as mechanical stretching[10] and sphincter cuts[11, 12] to stretch the iris. Pupil expander devices may also be deployed to provide external mechanical support. These devices include iris hooks[13-15] (MicroSurgical Technology, Redmond, WA, USA), Malyugin ring[12] (Malyugin Ring 2.0, MicroSurgical Technology, WA, USA), Bhattacharjee ring[16] (B-HEX pupil expander, Med Invent Devices, Kolkata, India), Oasis iris expander (6.25 mm and 7.00 mm, Oasis Medical Inc, San Dimas, CA, USA), Perfect Pupil[17, 18] (Milvella Limited, North Sydney NSW, Australia), APX dilator[19] (Assia Pupil Expander, APX Ophthalmology Ltd., Haifa, Israel) and i-Ring[19-21] (Beaver-Visitec International, Inc. (BVI), Waltham, MA, USA). They function by engaging the iris margin and providing support to keep the pupil enlarged during cataract surgery.

An issue with many pupil expanders lies in the method of iris margin engagement, where focal points of iris contact induce high stress concentrations and

potentially increase the risk of iris damage[22]. Iris hooks and the APX dilator engage the iris at 4 distinct locations to form a quadrilateral pupil, forming a non-physiological opening with high localized stresses. The Oasis iris expander, Bhattacharjee and Malyugin rings also form non-physiological openings with 6 or 8 contact points that reduces these point forces. The ideal expansion requires full circumferential iris margin engagement, which is only currently adopted by the i-Ring[21, 23]. However, the i-Ring, like the Oasis iris expander, Bhattacharjee and Malyugin rings, requires additional surgical maneuvers for positioning[12, 16]. By stretching the spring-like devices across the anterior chamber at the multiple engagement points, large tissue stresses beyond the physiological range are generated that could potentially distort and tear the iris tissue[20, 24]. In addition, the need for current mechanical devices to be dragged cross the pupil for iris engagement in cases of a small pupil may induce trauma[25] and iridodialysis[26, 27]. We previously conducted a theoretical finite element modeling study showing reduced stresses on the iris tissue predicted by a uniform circular expansion design[28]. In the current study, we applied this design experimentally and developed a novel pupil expander to improve on the cumulative shortcomings of existing devices.

We propose the use of shape-memory technology[29] to enhance the cataract procedure. A shape-memory material is able to configure and “memorize” a specific shape at a specific transition temperature. At a lower temperature, this material is flexible and can be compacted. A heat stimulus provides the energy for the shape-memory polymer to deform back to its configured shape upon reaching the transition temperature in a controlled manner. Implementing this material in a pupil expander allows for insertion into smaller incisions while retaining its ability to mechanically induce a large pupil. Moreover, expansion of the pupil occurs gradually, slowly stretching the pupil to avoid sudden tissue enlargement.

In this paper, we aim to: (1) describe the design and construction of an optimized shape-memory material to expand the pupil, (2) validate its performance in *ex vivo porcine* and *in vivo* monkey experiments and (3) compare our pupil expander with commercially available devices using *ex vivo* porcine eyes.

Methods

Molding and Manufacturing the Shape-memory Pupil Expander

We purchased shape-memory material from SMP Technologies Inc. (MP Resin and Hardener, Tokyo, Japan). To determine the maximum transition temperature allowed, we measured the *in vivo* anterior chamber temperature in a non-human primate (NHP) under surgical conditions using a small custom-made temperature sensor. The measured temperature reading was 34.0°C after filling the anterior chamber with viscoelastic.

Our custom shape-memory material was manufactured with a glass transition temperature (T_g) of 30.0°C. Below T_g, the polymer can be folded and physically manipulated into compact shapes. Heating the polymer above T_g will supply the required energy for the polymer to return to its programmed shape. The target shape was set by polymerizing the shape-memory material in a custom mold with the desired shape and dimensions of our pupil expander.

3-dimensional (3D) printing was used to manufacture molds using the MakerBot 2.0 (Stratasys, New York, USA) with acrylonitrile butadiene styrene (ABS) as the printing material. The mold was 3D printed with a resolution of 50 µm for the center insert and 100 µm for the top and bottom molds. Dimensions of the mold and pupil expander were optimized to minimize the thickness of the device (300 µm) (**Figure**

1A, B and D), while ensuring full engagement at the iris margin and sufficient force for mechanical pupil dilation.

The shape-memory polymer was prepared by potting. The resin and hardener were first placed under vacuum (< 200 mTorr) for an hour to evaporate the water within the polymers. The resins were then mixed and stirred for approximately 1 minute and placed under vacuum again for 1 minute to remove the effervescence. The final mixture was poured into the mold and left to set overnight. After removal from the mold, the device was trimmed using a pair of Vannas scissors (Ref:1-111, Duckworth & Kent Ltd., Baldock, England) to remove the excess material prior to testing (**Figure 1C**).

Ex vivo Validation of Our Shape-memory Pupil Expander in Enucleated Porcine Eyes

Eleven enucleated porcine eyes were purchased from Primary Industries Ltd. (Singapore Food Industries Pte Ltd., Singapore). Fresh porcine eyes were purchased and transported back to the laboratories whereupon experiments were conducted immediately and completed within 6 hours post-mortem.

To ensure that the tissues maintained their properties similar to those *in vivo*, we kept the enucleated eyes in a modified Krebs-Henseleit buffer solution similar to the protocol performed by Whitcomb et. al.[30] The buffer solution was composed of a Krebs-Henseleit buffer (Product Number K3753, Merck KGaA, Darmstadt, Germany) composed of the following: 10.0 mM D-glucose, 1.2 mM $MgSO_4$, 1.2 mM KH_2PO_4, 4.7 mM KCL, 118 mM NaCl, and added with 25 mM $NaHCO_3$ and 1.25 mM $CaCl_2$. The solution was oxygenated with 95% O_2 and 5% CO_2 to maintain a pH of 7.5. This kept the sphincter and dilator muscle tissues active to provide pupil constriction. Thus, we

were able to induce pharmacological constriction for small pupil expander insertion to provide validation of our device's function.

Fresh eyes were placed in a warm and moist medium above a rubber heating pad (12 V / 10 W Silicone Rubber Flexible Heating Pad, O.E.M Heaters, MN, USA). A temperature sensor was used to maintain a steady temperature of 34.0°C (±1°C) (TE333 Temperature Controller, XCSource, Hong Kong) as was measured *in vivo*. A power transducer (72-10505 DC Bench Power Supply, TENMA Corporation, Tokyo, Japan) was used to power the heating pad (10 W) and temperature sensor (9 V, 0.1 A). At the Singapore National Eye Centre (SNEC), an ophthalmic microscope (OPMI 1 FR Pro, Zeiss, Jena, Germany) was used to enhance surgical vision and a DSLR camera (Canon EOS 800D, Tokyo, Japan) was used to record the experiments. Pilocarpine was administered to obtain a small pupil (2 drops of 2 % Isopto® Carpine, Alcon Laboratories, Inc., Texas, United States). Our shape-memory pupil expander prototypes were manufactured to provide optimal specifications for the porcine eyes: compact width of under 2.0 mm, expanded circular diameter of 7.0 mm, 300 µm overall thickness.

Insertion of the shape-memory pupil expander was performed in a similar manner to existing techniques, and consisting of several important steps[9] (**Figure 2**). First, a triangle blade (Ref: 72-2661, Surgical Specialties México, Corredor Tijuana-Rosarito 2000, Mexico) was used to make a 2.65 mm incision at a 30° to 40° angle near the cornea periphery. Viscoelastic solution is usually injected to maintain the shape of the anterior chamber, but not used in our study to prevent dilation from its use.

Second, an injector was used to deliver the compacted circular shape-memory pupil expander into the anterior chamber (**Figure 2A**). Since we did not have a custom-made injector, we used the Malyugin ring injector (Ref: MAL-1002-1, MicroSurgical Technology, Redmond, Washington, United States), although similar injectors from devices such as the Oasis iris expander would also perform the same function. Retraction of the circular device flattened it to a hyperellipse shape to fit the injector lumen. The 34.0°C ambient physiological temperature within the anterior chamber provided energy for the flattened device to deform back to a circular shape (**Figure 2B**).

Third, a Sinskey hook (Ref: 0105109, John Weiss & Son Ltd., Milton Keynes, United Kingdom) was utilized to maneuver and adjust the device into position (**Figure 2C**). To engage the iris margin, the Sinskey hook was used to pull and deform the pupil expander, then pushing the polymer to enlarge the pupil after iris engagement. This action was performed about 3 to 5 times, between 20 to 30 seconds depending on the individual condition of each pupil. Since the device deforms only from the user's manipulation, the iris tissue would not be overstretched from engagement (**Figure 2D**). The result was a 7 mm circular expanded pupil that was protected at the iris margin from any external manipulations (**Figure 2E**).

Last, to remove the pupil expander, the Sinskey hook was used to disengage the pupil expander from the iris margin at the incision site. This was done by hooking the device at the edge and flipping it upwards. The Malyugin ring injector was then inserted to hook the disengaged corner and retract the device. This process was performed swiftly and required no additional surgical maneuvers, leaving an atraumatic pupil (**Figure 2F – H**).

In vivo Validation of Our Shape-memory Pupil Expander in Non-Human Primates

Following optimization and successful validation in *ex vivo* porcine eyes (**Figure 3**), we proceeded to test our pupil expander in specific pathogen-free (SPF) NHPs (Macaca Fascicularis) of approximately 6 – 7 years of age. Since the NHP's eye is significantly smaller, we scaled our device to have the following specifications: compacted diameter of 1.5 mm, expanded diameter of 5.0 mm, 300 µm overall thickness.

Experiments were conducted at the SingHealth Experimental Medicine Centre (SEMC) at the Singapore Eye Research Institute (SERI). Intra-operative optical coherence tomography (OCT) imaging (Zeiss RESCAN 700 Integrated Intraoperative OCT, Carl Zeiss Meditec, Jena, Germany) was also utilized in conjunction with the surgical microscope to validate the position of the device.

The monkeys were anaesthetized with ketamine. The periocular area was cleaned with povidone-iodine 10%. A wire lid speculum was placed to separate the eyelids, and topical povidone-iodine 5% was instilled onto the ocular surface for a few minutes prior to the surgery. An operating microscope was positioned over the eye undergoing surgery. The same surgeon operated on all the monkeys, using a standardized aseptic surgical technique: two self-sealing wounds were made with a blade into the anterior chamber temporally and for a right-handed surgeon 90 degrees away. The temporal wound allowed insertion of the devices whilst the other was for manipulation. Viscoelastic (Healon, AMO, Illinois, USA) was injected into the anterior chamber and the expander device was utilized to open the pupil to 5 mm. The procedure for insertion and deployment in the primate's eye was identical to that of the *ex vivo* porcine eye. The compact device was inserted using a pair of straight

conjunctival forceps (Ref: 2-500-4N, Duckworth & Kent Ltd., Baldock, England) following application of the viscoelastic solution. The choice of forceps was to insert the device into a smaller incision. A Sinskey hook was utilized, when necessary, to position and adjust the device. After the device was fully deployed, iris cross-sectional images were taken using the intra-operative OCT.

All experiments were performed in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research, and were approved by the Institutional Animal Care and Use Committee (IACUC) of the SEMC located in the Singapore General Hospital (SGH). The SEMC has accreditation by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

Performance Comparison of our Shape-Memory Expander with Commercially-Available Devices

To evaluate the efficacies of our shape-memory pupil expander, we selected three commercially available pupil expanders for comparison. We selected the iris hooks because they are used by surgeons internationally. We also selected the Oasis iris expander and the Malyugin ring expander, this latter being recognized as one of the best devices currently available. In addition to the 11 porcine eyes used for validation with our pupil expander, another 34 eyes were purchased for this comparison. Eyes were placed in the aforementioned Krebs-Henseleit buffer and pilocarpine was used to obtain a small pupil prior to pupil expansion. All experiments were conducted within 6 hours post-mortem.

Malyugin ring. The technique used for deploying the Malyugin ring (Ref: MAL-1002-1, MicroSurgical Technology, Redmond, Washington, United States) was similar to that described in recent literature. The device was retracted into the injector and

delivered into the anterior chamber. Using the Malyugin ring manipulator (Ref: MAL-1003, MicroSurgical Technology, Redmond, Washington, United States), opposite ends of the loops were engaged by flexing and dragging these loops to engage the iris margin to obtain a final pupil diameter of 7 mm (**Figure 3A**). The reverse procedure was performed for removal of the device from the iris margin, and the injector was used to remove the Malyugin ring from the anterior chamber.

Oasis iris expander. The technique used for deployment of the Oasis iris expander (Ref: 9700, OASIS® Medical, Inc., Glendora, CA, United States) was similar to the Malyugin ring and described in the provided manual. The injector hooks onto the straight connectors for retraction within the injector lumen. The Sinskey hook was used to engage the opposite ends of the 4 engagement points with the iris margin to obtain a final pupil diameter of 7 mm (**Figure 3B**). The reverse procedure was performed for removal of the device from the iris margin, and the injector was used to remove the Oasis iris expander from the anterior chamber.

Iris hooks. The technique used for deploying the iris hooks (MST Iris Hook, Ref: MIH-0001-1, MicroSurgical Technology, Redmond, Washington, United States) was similar to that described in current literature. Four stab incisions were made to the cornea and the hooks were inserted to engage the iris margin. Tightening was performed individually until the maximal diameter of the pupil reached 7 mm (**Figure 3C**). The reverse was performed to remove the iris hooks.

A total of 45 eyes were used for this comparison: 10 eyes for the Malyugin ring, 13 for the Oasis iris expander, 11 for the iris hooks and 11 for the shape-memory pupil expander. After experimentation, the eyes were immersion fixed in 10% neutral buffered formalin solution for 24 hours. The irides were then isolated under a fume

hood and stored again in the 10% neutral buffered formalin solution. All the eyes tested were included in the results, without any exclusions.

Images of the fixed irides were taken under a microscope with a DSLR camera (Canon EOS 800D, Tokyo, Japan) and lens (Canon EF-S 10-18mm f/4.5-5.6 IS STM, Tokyo, Japan). A primary image of the iris was taken, followed by zoomed in sections of each quadrant of the tissue for a more accurate analysis (**Figure 4**). In order to remove bias during results analysis, the iris samples were blind graded by randomization and evaluated separately by an independent clinician. Analysis was done by manually marking the areas of tissue affected during the procedure, and image analysis was performed to measure the marked images. Analysis was classified into two complications: iris pigment epithelium (IPE) loss (defined as a section of missing dark pigment of the IPE at the iris margin) and sphincter tear (defined as a discontinuity of the circular shape of the sphincter tissue at the iris margin). Using ImageJ[31] (v1.50i, National Institutes of Health, USA), the circumferential lengths of tissue damage at the iris margin were measured (**Figure 4D**). The pupil diameters before device insertion were also measured using the smaller radii, since the porcine pupil is elliptical rather than circular.

Results

Manufacturing of our Shape-memory Device Prototype

The prototypes were made using potting, requiring custom-designed molds to encase the polymer. 3D printed molds were successfully manufactured with the 50 µm resolution of the 3D printer. The resultant molds were able to provide the 300 µm overall thickness desired but lacked smoothness in the U-shaped curvature. The

cross-sectional thickness of the device was measured to be approximately 80 µm, with an opening measuring approximately 140 µm for engagement of the iris margin.

Ex vivo and in vivo Validation of Shape-memory Device Prototypes

The *ex vivo* porcine iris experiment was performed in accordance with standard cataract surgery protocol[9, 32]. When inserted into the anterior chamber using a pair of forceps, the device was able to deform upon reaching the transition temperature within the anterior chamber. This deformation was slow and controlled because of the inherent shape-memory polyurethane properties. This prevented any sudden external forces which may cause trauma to surrounding tissues. Only a Sinksey hook was needed to manipulate the pupil expander. The device was disengaged from the iris margin with the Sinskey hook and was easily retracted into the injector for all 11 samples tested, leaving the minimally traumatized pupil (**Figure 2**).

The *in vivo* experiments were also successfully conducted by an experienced senior consultant. The device was optimized following the initial experiments with the NHPs. The device was successfully delivered into the anterior chamber and guided to the iris margin with a Sinskey hook. After deployment, we were able to verify that the pupil expander engaged the iris margin using the intra-operative OCT (**Figure 5**). A 6-month follow-up examination showed no complications such as inflammation or ocular hypertension on the primate, indicating biocompatibility using the polyurethane material.

Performance Comparison of the Selected Pupil Expanders

Comparison of the 4 pupil expander devices showed mostly IPE loss and minor sphincter tears (**Table 1**). Sphincter tears are always accompanied with IPE loss at the same location. Iris hooks fared the worst: out of the 11 tested samples, 3 exhibited

small sphincter tears and 4 exhibited IPE loss. Of the 10 samples tested with the Malyugin ring, 1 exhibited a small sphincter tear and 2 exhibited IPE loss. Iris samples tested with the Oasis iris expander did not exhibit sphincter tears, but 4 out of 13 samples exhibited IPE loss. The shape-memory pupil expander performed the best, with no observable sphincter tears or IPE loss. The mean pupil diameters before device insertion were 5.50 ± 0.876 mm for the Malyugin ring, 5.35 ± 0.576 mm for the Oasis iris expander, 5.27 ± 0.768 mm for the iris hooks and 5.10 ± 0.743 mm for the shape-memory expander.

Discussion

Previously, using numerical biomechanical methods[28], we identified the unmet need of a well optimized pupil expander for cataract surgery, capable of uniformly engaging the iris margin and smoothly increasing the pupil diameter to avoid potentially deleterious stresses and strains on the iris tissue. The present study provides the first proof of concept for such a device, that utilizes a shape-memory polymer-based smart material. We demonstrated here its successful application via *ex vivo* and *in vivo* experimental testing in porcine enucleated eyes and NHPs. Our novel pupil expander could potentially accommodate even smaller pupil sizes than other commercially available devices could.

Reduced Manipulation to the Iris Tissue Benefits Both Clinicians and Patients

With the use of devices such as iris hooks and APX dilator, multiple parts are required to be deployed individually. For the iris hooks, 4 or sometimes 5 hooks are inserted, creating high point stresses that greatly increases the risks of tissue tearing[14, 22, 33]. Similarly, the APX dilator's scissor-like claws contact the iris at 4 distinct locations.

Although the pupil is enlarged directly, both devices create additional corneal incisions, creating further tissue damage.

In the case of the Malyugin ring, i-Ring and Oasis iris expander, the opposite issues were observed. Though only requiring the standard primary and secondary corneal incision for cataract surgery, and only deployed into the anterior chamber, there are additional device manipulations. Both devices need to engage the iris margin, stretching the iris tissue excessively in order to engage the opposite ends. Especially when engaging the final corner, the pupil has already been enlarged significantly. Pushing the device to the opposite corner creates significant stresses that are clinically sub-optimal.

We designed our shape-memory pupil expander to address these two main issues. By adopting a more flexible design, the device is able to deform instead of overstretching the iris tissue. With the U-shaped cross section, the pupil expander can engage the entire iris margin, exerting uniform stresses on the iris tissue while protecting it from external forces such as accidental tears from surgical tool manipulations[34]. The circular shape provides minimum distributed stresses on the tissues, with full expansion not exceeding the designed maximum diameter, avoiding unnecessary stresses[28].

Slow and Constant Pupil Expansions Allow for Optimized Expansion Duration

While the type of pupil expansion is important, the speed at which the tissue is stretched also plays a role in determining whether damage is induced[22, 33]. Like most tissues in the human body, the iris tissue behaves in a viscoelastic manner[35, 36]. Fast expansions can create large stresses, which may result in tears. Existing devices mostly utilize the flexible, spring-like properties of a plastic like polypropylene. The use

of shape-memory material close to the T_g allows for a slower deformation speed that can avoid sudden pupil stretching.

By optimizing the T_g of the polymer, it is possible to control and adjust how fast the device uncoils. Our clinician feedback revealed that the ideal duration to deploy the device is between 20 and 30 seconds after device insertion into the anterior chamber. We designed our shape-memory material to slowly deform over 10 to 20 seconds after insertion, thereafter simple manipulation is conducted to position the device.

A Circular Expanded Pupil is Also Suitable for Femtosecond Laser Surgery

Femtosecond laser-assisted cataract surgery has been gaining popularity in recent years[37]. The use of pupil expanders could enhance the safety of the procedure by maintaining a dilated pupil for extended durations[38, 39]. Before the laser is used, there is a waiting period of about 15 minutes after the pharmacological drug is administered. The drug could wear off in a shorter duration for some patients, resulting in a smaller pupil. Further 1% atropine drops can be administered to limit pupil constriction, but this is not a fail-safe solution[38]. With the use of our custom circular pupil expander, an optimal 7 mm pupil could be maintained throughout the procedure to ensure patient safety and surgical success. This is not optimal with non-circular devices like the Malyugin and Bhattacharjee rings, and completely impossible for devices with external protrusions like the iris hooks and APX dilator, because they would interfere with the suction cup placed on the cornea[40, 41].

Additionally, it is believed that the anterior capsulotomy is the main trigger for an increase of prostaglandins in the aqueous with femtosecond laser-assisted cataract surgery. The resulting miosis has been somewhat but not completely mitigated by the

use of nonsteroidal anti-inflammatory drugs. The longer the wait between the laser portion and the phase emulsification portion of the surgery, the worse the miosis is[42]. The use of an optimized mechanical device may be helpful in alleviating this problem.

Existing Devices have Specific Drawbacks and Removal is Cumbersome

Usually in a hospital, the variety of pupil expanders available is limited to focus on perfecting the technique in one or two devices. Comparison between multiple devices is therefore uncommon and impractical. The versatility of the current device circumvents some disadvantages of existing alternatives. The method of incision and the size of the small pupil are two areas of concern with currently limited viable solutions[10]. For this study, porcine irides were utilized to obtain a larger pool sample and since the pupil expander experiments were all performed by the same person, it is possible to provide an unbiased comparison of the various devices.

Iris hooks take the longest to deploy and remove[13], and the small contact points with the greatest potential to damage soft tissues. While it allows for flexibility in positioning and varying pupil size, it is less practical in providing a sufficiently large pupil unless the tissue is retracted significantly[43]. Multiple stab incisions are not ideal either, since healing after corneal incisions can be slow and incomplete[44-46]. More recent devices, including ours, have been more efficient in this regard by eliminating additional incisions.

The Oasis iris expander works very similar to the many variations of ring devices in the market. However, the rigidity in material could be a concern. The connectors between the 4 loops can be weak and break easily, as happened during the first attempt to retract the expander into the retractor. Subsequently, care was taken to assist the device retraction using a pair of forceps by flattening the sides.

Additionally, once in the anterior chamber, the device would not retain its square shape, but remained slightly deformed in a rectangular shape from the bent curved connectors. The material construction is a hard polypropylene that may require excessive force to flex in order to engage the loops. The hard plastic against the soft iris tissue could be the reason for iris chafing and IPE loss in several samples. This was our motivation to utilize a soft polymer that can be more easily deformed and reduce the chance of damaging the iris tissue.

While the Malyugin ring may be very popular due to the ease of deployment, removal is significantly more challenging. The Oasis iris expander has specific shielded holes where the Sinskey hook is positioned, the Malyugin ring relies on a custom manipulator tool to hook onto the expander. The manipulator tool would contact the iris tissue during removal, and it is easy for the iris margin to get caught between the devices. At these 4 loops, the iris tissue may accidentally be dragged and torn. Additionally, the Malyugin ring is designed to be a continuous loop glued at the ends. During removal, one of the loops will always get stuck during retraction into the injector. Since it is a one-use device, forceful retraction is possible, but that would bend the device upwards or downwards, potentially contacting the corneal endothelium and inducing further trauma. Our shape-memory pupil expander encompasses a continuous U-shape cross section, eliminating the risk of getting caught by the iris. It is also easily removed, taking less time and effort in comparison to existing methods.

Limitations

The intended design consisted of a U-shaped cross section that can engage the iris margin. However, due to the low resolution of our 3D printer, the curved edges were right angled instead. This resulted in a rectangular cavity for the cross section.

In addition, the surface finish for the completed device was imperfect, with rough edges and surfaces. However, as a first proof-of-principle, this lab-made device was successful for both *ex vivo* and *in vivo* testing.

Additionally, the polymer used for testing would ideally be manufactured differently from the prototypes tested. We used potting to mold the device individually, whereas injection molding pellets would be better utilized for large scale production. With injection molding, the resolution and surface finish for the prototypes would be within acceptable tolerances (± 5 µm).

Comparison of the various pupil expanders would benefit from a larger sample size. This should allow for a greater pool of data for analysis and an accurate representation of the complication percentages. However, that would require a huge number of devices which is not practical with porcine data.

Finally, since testing of the device was in *ex vivo* porcine or healthy *in vivo* cynomolgus eyes, we have yet to follow up the procedure with phacoemulsification. Therefore, we will need to conduct further studies to ensure that there are no potential complications that may arise from the use of our shape-memory pupil expander.

Conclusion

We have developed an optimized pupil expansion device designed to minimize and limit the amount of stresses exerted onto the iris tissue. The *in vivo* and *ex vivo* experimental validations presented herein provide proof of concept of the device's efficacy, and further highlight the translational potential of smart materials in the development of other ophthalmological implants to improve patient healthcare.

What was known

- Current pupil expander devices are made of hard plastic materials and ring expanders utilize the tension-spring effect of the plastic during iris engagement, over-stretching the iris in the process.
- Removal of pupil expanders can sometimes be more difficult than their deployment.

What this paper adds

- A novel pupil expander that is made of a shape-memory polyurethane that could deform to prevent over-stretching of the iris tissue during device deployment.
- *Ex vivo* and *in vivo* animal experimental validation of the novel shape-memory pupil expander, as well *ex vivo* comparison with commercially available pupil expander devices to quantitatively and qualitatively compare each device.

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Figure 1: A. The computer-aided designs (CAD) cross-section drawing of the mold design. **B.** The device is designed to be 300 µm, with the thickness of the device approximately 80 µm. **C.** Processing of the shape-memory pupil expander after allowing it to set overnight. The polymer is separated from the mold and initially contains excess material. It is manually cut and trimmed down using a pair of Vannas scissors until a satisfactory shape is obtained. **D.** The final thickness of the device is measured to be approximately 300 µm.

Figure 2: *Ex vivo* porcine eye validation of the shape-memory pupil expander. **A.** Insertion of the pupil expander into the anterior chamber using a Malyugin ring injector. **B.** The ambient temperature slowly opens the device to a more circular shape. **C.** A Sinskey hook is used to position the device to engage the iris margin. **D.** The device deforms instead of overstretching the iris for engagement. **E.** Complete iris margin engagement to provide a 7 mm pupil. **F – H.** Removal of the pupil expander. The Sinskey hook is used to flip up and disengage one section of the device, and the Malyugin ring injector is used to grab and swiftly retract the device, revealing an atraumatic pupil.

Figure 3: Images from the *ex vivo* porcine study for each of the devices tested. Fully engaged pupils from the **A.** Malyugin ring, **B.** Oasis expander, **C.** Iris hooks and **D.** Our shape-memory pupil expander. All devices are expanded to a maximal diameter distance of 7 mm.

Figure 4: Images of the isolated porcine irides taken from the microscope for processing. **A.** First a 2× zoom image is taken, followed by **B – F.** multiple 4.5× zoom images for clear image analysis. **D.** Loss of IPE is noted and measured at the locations marked by the red boxes, performed by blind grading. *Note that the iris has been isolated from the eye and is therefore not regularly shaped.

Figure 5: A. Intra-operative optical coherence tomography (OCT) image from monkey undergoing insertion of pupil expander device. **B.** The cross-sectional image of interest is the sub-image across the blue arrow. The device successfully engaged the iris margin. The outline of the pupil expander is represented by the white dotted lines.