Electronic Supplemental Information

Device Description

Table S1 Dimensions of the prototype ocular drug delivery device.

	Specification	Value
Reservoir	Reservoir Dimensions (W x L)	7 mm x 7 mm
	Reservoir Wall Thickness	1 mm
	Reservoir Internal Volume	57.15 µL
	Support Pillars in Reservoir (W x L x H)	0.5 mm x 0.5 mm x 0.1 mm
Cannula	Cannula Dimensions (W x L)	1 mm x 10 mm
	Support Pillars in Tube (W x L x H)	0.4 mm x 0.4 mm x 0.1 mm
Valve	Valve Orifice	305 µm
	Valve Seat (W x L x H)	0.4 mm x 0.4 mm x 0.1 mm
	Refill Needle	30 gauge non-coring

The size and shape of the prototype drug delivery device was based on the available space in the human ocular orbit. The size, shape and placement of the device are not anticipated to cause trauma or irritation to ocular tissues; the device size and shape are intentionally modeled after commercially available glaucoma drainage devices, which have already been tested for patient comfort and approved for implantation. The drug delivery device was implanted in male Dutch belted pigmented rabbits for initial acute *in vivo* studies to demonstrate device functionality; a smaller second generation device whose size is more appropriate for a rabbit eye will be used for chronic biocompatibility studies.

The drug delivery device has mechanical actuation that is patient controlled. Dose volume is a function of pressure and duration of said pressure on the device. Additional device components such as multiple valve configurations and reservoirs can be developed to prevent the risk of accidental overdose by the patient through non-compliance or unintended use. However, the second generation drug delivery device will incorporate an automatic system which is electrically controlled and will address accidental dosing.

Device Fabrication

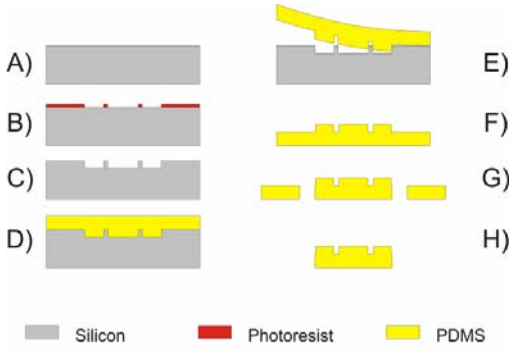

Figure S1 Fabrication process to create a silicon master and mold PDMS replicas. A) Silicon substrate; B) spin and pattern PR etch mask; C) etch substrate to form mold for device layer; D) pour PDMS onto mold and cure; E) remove patterned PDMS sheet from mold; F) place PDMS on flat cutting surface; G) separate PDMS replicas from molded sheet; and H) clean and prepared replica for device assembly.

Silicon masters, which where etched using DRIE, were selected over other material (i.e. SU-8 molds), for ease of fabrication and robustness of the resulting mold. Furthermore, accelerated curing of the PDMS required placing the mold into an oven at elevated temperatures (70 ºC). SU-8 is susceptible to thermal stresses and may crack or delaminate from a substrate surface when exposed to rapid changes in temperature.

A mixing ratio for PDMS (10:1 base to curing agent) was chosen because this ratio is well characterized in other research papers. Additionally, this ratio resulted in a solid device capable of withstanding surgical manipulation while maintaining enough flexibility for the cannula to achieve the high bending radius necessary for implantation.

In Vivo Experiment: Phenylephrine Delivery

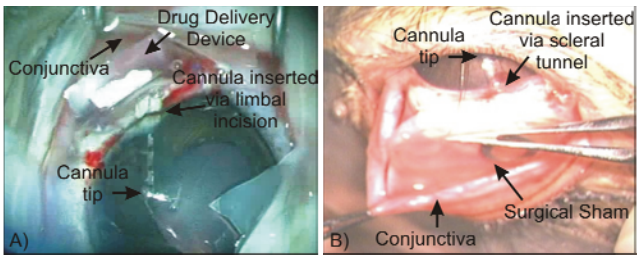

Figure S2 Images of A) drug delivery device and B) surgical sham placed *in vivo*. The cannula of the drug delivery device is inserted into the anterior chamber of the eye through a limbal incision while the cannula of the surgical sham is inserted via scleral tunnel.

Originally, the cannula was inserted into the anterior chamber through a limbal incision, a small cut made between the cornea and sclera. However, dispensed liquid would leak through the incision around the cannula. Sutures were used to close the incision around the tube, but caused the cornea to wrinkle. Therefore, subsequent *ex vivo* and *in vivo* testing were conducted using a scleral tunnel. This is an established surgical technique and has reduced leakage dramatically. A scleral tunnel is a standard technique used for

implanting glaucoma drainage devices and is formed by using a fine blade to create a thin pathway in the thick scleral tissue that terminates in the interior of the eye.

Surgical shams of the device were fabricated to provide rapid prototyping of the device to incorporate improvements to the device design. The sham also provided a model on which to refine surgical techniques and optimize component placement on the device.

While it is possible to deliver smaller volumes, a single 22.5 μL bolus was selected due to volume metering limitations of syringes used for intraocular injection and surgeon-controlled delivery. Additionally, 22.5 μL of 10% phenylephrine delivers an equivalent amount of drug during standard intraocular injections of 150 μL of 1.5% phenylephrine.[1] For intraocular injection, the 22.5 μL volume of phenylephrine (10% weight ratio) mix was delivered into the eye using a syringe (PTFE Luer Lock 25 μL Syringe, Hamilton Company, Reno, NV). For device-based delivery, 22.5 μL was delivered from the device by filling the 57 μL device reservoir and emptying half of the contents into the eye using forceps to apply pressure to the reservoir. The surgical sham reservoir (141 μL volume) was filled. Again, half of the reservoir volume was dispensed into the eye by depressing the reservoir with a cotton swab. The surgical sham does not contain a check valve, therefore a larger volume of phenylephrine was dispensed into the eye because some of the dispensed liquid backflows into the device when the pressure on the reservoir is removed.

1. B. Lundberg and A. Behndig, *Journal of Cataract and Refractive Surgery*, 2003, **29**, 2366-2371.