



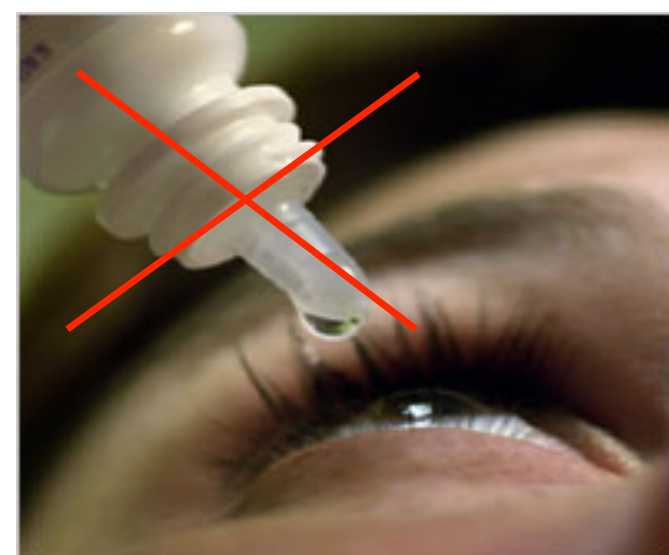
### Purpose

Atropine drops have been studied in the treatment of myopia progression<sup>1</sup>. The most effective concentrations cause excessive, fixed pupillary dilation, photophobia, near vision blur and possible toxic light levels to the retina, presenting obstacles to this treatment. We explored whether sustained, micro quantities of atropine could be released from a topical matrix device, as evidenced by continuous but modest pupil dilation, with preserved pupil functioning and minimal light sensitivity and visual blur.

### Methods

Preliminary experiments with our Topical Ophthalmic Drug Delivery Device (TODDD) confirmed expected dosing efficacy equivalent to standard clinical eye drops. For the desired myopia progression application, these results indicated trial of a hundred-fold decrease in drug concentration in the TODDD device from that which caused the typical clinical drop result of a fixed dilated pupil lasting over a week.

For this study the subject, CL, inserted one device in the left eye and wore it continuously for over 60 days. The other eye functioned as the untreated control. Pupil measurements were taken at least daily using a Jaeger Nearpoint Vision Card's pupil gauge. Lighting conditions were varied to confirm the treated pupil's constriction and dilation function.



### Advantages of TODDD™ Platform

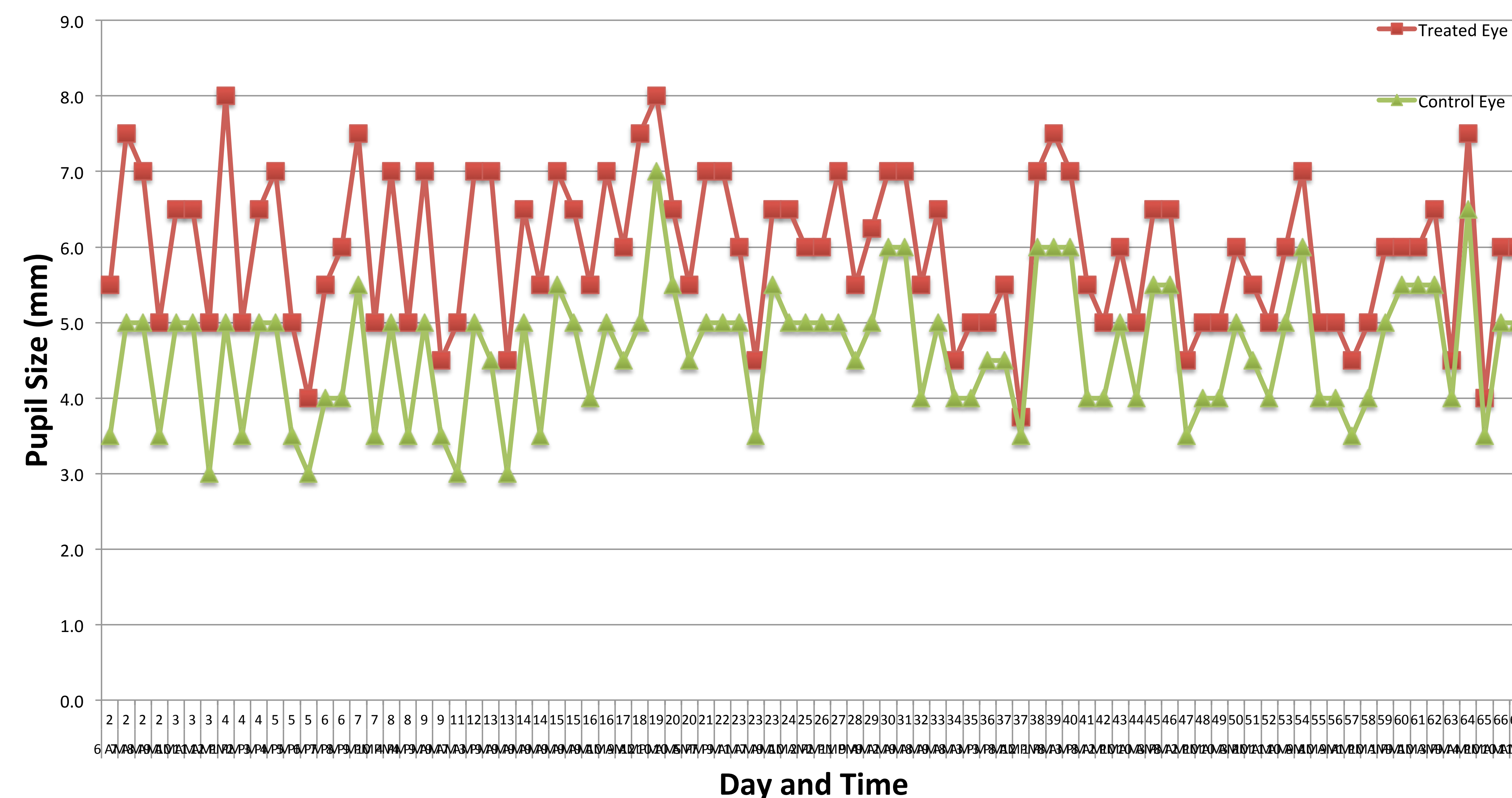
- ✦ Eliminates prevalent eye drop insertion and dosing issues
- ✦ Incorporates the drugs and combinations of drugs currently prescribed as eye drops
- ✦ Fewer compliance issues. Continuous, 90+ day 24/7 release of drug, eliminating patient dosing regimen
- ✦ Preservative free
- ✦ Tolerated well and presence easily confirmed
- ✦ Simple replacement in less than a minute
- ✦ Fewer, perhaps elimination of, systemic side-effects from excess drug in eye drops
- ✦ Can incorporate less suitable for aqueous formulations

### Results

For the entire sixty days that the device was worn, the treated eye had a clinically detectable larger pupil compared to the eye with no treatment, for all measurements (avg 1.50 mm through 60 days, p<<.001, paired t-test). The 0.05% dose did not fix and dilate the pupil at any time during treatment. After moderate blur and mild glare the first evening of treatment only, there were no visual symptoms of light sensitivity or blur throughout the study. The device yielded good comfort and did not eject from the eye or interfere with customary glasses and soft contact lens wear.

### Single Low-dose Atropine TODDD™ Treatment in One Eye

Pupil sizes - TODDD with myopia control agent in one eye (top line)



### Discussion

Most sustained ocular drug delivery attempt to duplicate the known effects of standard dose eye drops, with perhaps improved compliance and decreased local and systemic side effects. In the case of atropine for myopia progression however, the goal is not to duplicate the fixed pupil dilation and cycloplegia (paralysis of near focus) of standard dose eye drops, but rather to avoid those more anterior eye effects, while still delivering much smaller amounts of drug continuously to maintain myopia treatment effects, most likely at the retina. While preliminary studies confirmed that TODDD can deliver doses of drugs for weeks or months that sustain the standard clinical effects of daily drop use, for the application of myopia progression treatment a very low sustained dose atropine device was studied.

Results were consistent with published studies of myopia progression treatment effects of various doses of atropine drops, that indicated lower dose drops, while providing far more tolerable levels of side effects, and potential for less rebound progression upon cessation of treatment, also had lower clinical effects achieved during treatment. As the drops are still a pulse dose received once per day (in the evening to avoid symptoms from the temporary pupil dilation of even the low dose drops), there is a complete 24-hour shut-off between drop instillations of the applied drug delivery concentration gradient at the front of the eye, so that less drug is driven toward the back of the eye following each dose. A sustained release device provides a constant source of drug 24/7 at the ocular surface to continuously drive the drug deep into the eye.

### Conclusions

The study established intraocular continuous very low dose atropine delivery, as demonstrated by an increased pupil size vs. the control eye at every measurement over 60 days. Dosing remained low enough to continuously prevent symptoms of blur and light sensitivity. That the pupil remained reactive to changes in ambient light, rather than fixed and dilated as with standard atropine eye drop dosing, we believe contributes to the comfort of such treatment. Any cycloplegic effect, while not detected in this patient, needs to be further investigated in the young myopic population. If confirmed by prospective clinical trials, these findings would offer novel treatments for myopia progression.

### Reference

1. Chia, A., Lu, Q.S., and Tan, D. Five-year clinical trial on atropine for the treatment of myopia 2: myopia control with atropine 0.01% eyedrops. Ophthalmology. 2016; 123: 319-399

### TODDD™ - Topical Ophthalmic Drug Delivery Device

Designed for uninterrupted (24/7) drug delivery for 7 – 90+ days

**Device design** – Utilizes modified contact lens design features and new elements to fit the eye under the eyelid, specifically away from the cornea, to provide sustained comfort, retention, stability and large drug load capacity.

- Central curvature
- Peripheral curves
- Edge apex contours
- Edge lift
- Corneal relief curve
- Elevated lobes
- Fits under the eyelid
- No intrusion onto the cornea or into the visual field
- No inter-blink surface drying or deposits
- No issues of hypoxia or corneal inflammation

### TODDD™ Positioning and Stability



Subject with TODDD™ in place

Photo credit: R. Gutner, O.D.



### TODDD™ Large Drug Load Capacity