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14. ABSTRACT

Thousands of soldiers experience eye injuries in combat per year. When such injuries occur, corticosteroid eye drops are prescribed in order to prevent ocular inflammation. However, eye drops have low bioavailability, with only 1-7% of the drug reaching the eye, and are often administered incorrectly. In addition, the frequent administration of drops (as often as once per hour) can be cumbersome and result in poor adherence. We propose that wearing a corticosteroid-eluting contact lens worn continuously for one week would be a more convenient alternative while providing greater bioavailability. In *in vivo* studies, rabbits wearing the TCL had aqueous humor (AH) concentrations of API greater than or equal to AH concentrations from rabbits given corticosteroid eye drops. Ocular distribution of drug with TCL wear was comparable to or greater than hourly drops through seven days of TCL wear. Optical clarity studies demonstrate light transmission greater than 95%. We demonstrated efficacy of the TCL in rabbit models of anterior uveitis and corneal neovascularization.

15. SUBJECT TERMS

None listed

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1. **INTRODUCTION:** The purpose of this project is to create a contact lens which dispenses steroids to the eye in a sustained matter. Such lenses could be used to prevent conditions such as posttraumatic inflammation. In addition, a steroid eluting contact lens could potentially treat a variety of conditions such as anterior uveitis. Using a contact lens to treat ophthalmic conditions could improve efficacy and patient adherence; therefore prevent complications, particularly with frequent dosing regimens.
2. **KEYWORDS:** contact lens, controlled release, uveitis, corticosteroid, controlled drug delivery, corneal neovascularization
3. **ACCOMPLISHMENTS:**

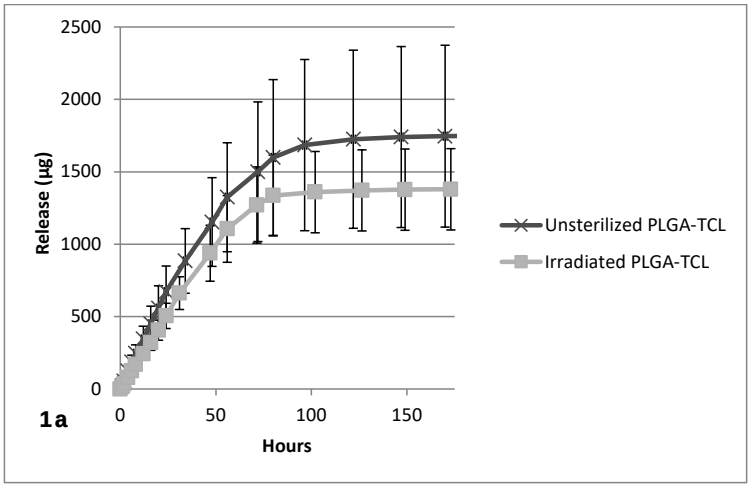
- **What were the major goals of the project?**
  - Aim 1: Develop a therapeutic contact lens (TCL) that could sustain drug release for seven days at therapeutic levels in an *in vitro* study.
  - Aim 2: Demonstrate drug flux comparable to therapeutic levels in the aqueous humor of TCL wearing rabbits for seven days.
  - Aim 3A: Demonstrate TCL efficacy in the treatment of anterior uveitis.
  - Aim 3B: Demonstrate TCL efficacy in the prevention of corneal neovascularization.
- **What was accomplished under these goals?**

Aim 1:

- Development of the TCL
  - We created contact lenses containing a drug polymer film consisting of dexamethasone and PLGA. Dexamethasone (Spectrum Chemical, New Brunswick, NJ) and PLGA (85-15 DLG 7E, Evonik DeGussa, Birmingham, AL) were dissolved in hexafluoroisopropanol (Sigma, St. Louis, MO) at a 1:1 ratio (60 mg/mL for each component). Drug-polymer films were created by solvent casting and encapsulated in methafilcon, a HEMA-based hydrogel. A 6mm aperture was created using a biopsy punch and the film within the punch was removed.
  - Benchtop release was performed by releasing lenses in 5mL phosphate buffered saline (PBS) at 37^{0}C, on a rotating shaker at 64 rpm. At predetermined timepoints of intervals between 1 hour and 24 hours, the lenses were removed and placed in a fresh solution of PBS
  - We also investigated several alternative polymers that are not-biodegradable, which would have the advantage of longer storage in a hydrated state. We attempted to make TCLs using a variety of polymers. ~~Some, such as Nylon-6 and ethylene vinyl alcohol, distorted the shape of the lens. Others such as P~~poly vinyl butyral (Sigma) and Eudragit® S100 (Evonik) produced usable lenses with 5-7 days sustained release.~~, though the drug loading was limited~~

~~due to solubility.~~ We used the PLGA-TCL for further studies due to the higher loading and cumulative release.

- Quantification of the TCL by HPLC
  - A Dynamax ICS5000+ HPLC system was used to quantify benchtop HPLC release. The mobile phases were acetonitrile and 0.1% trifluoroacetic acid in deionized water, with a flow rate of 1.0 mL/min. Samples were analyzed by UV detection at 250 nm.
  - Dexamethasone mean total release in the PLGA-TCL was 1750 micrograms (Figure 1A). The drug was released in a large burst over the first two days (Figure 1B) and continued to release at a lower concentration from days 3-7 in the study.



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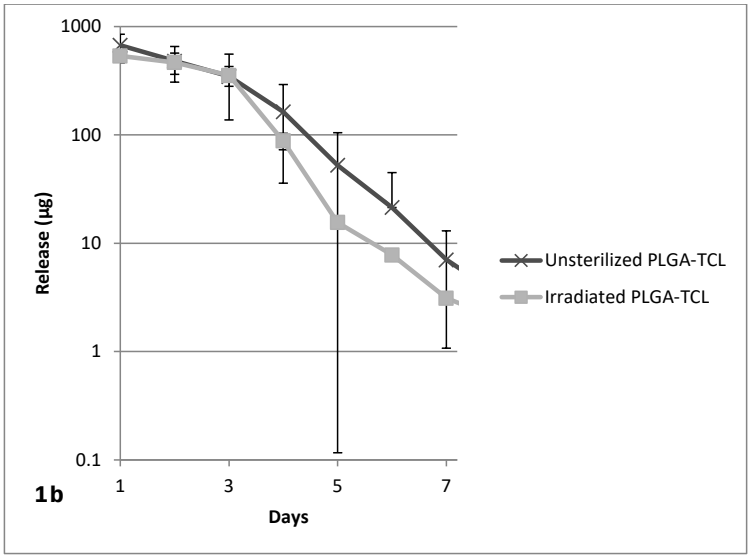


Figure 1. Cumulative (a) and daily (b) *in vitro* release from the PLGA-TCL.

- Cumulative release from the non-hydrolyzable polymers was decreased compared to the PLGA-TCL (Figure 2). ~~Work is ongoing to increase drug loading within the non-hydrolyzable TCLs.~~

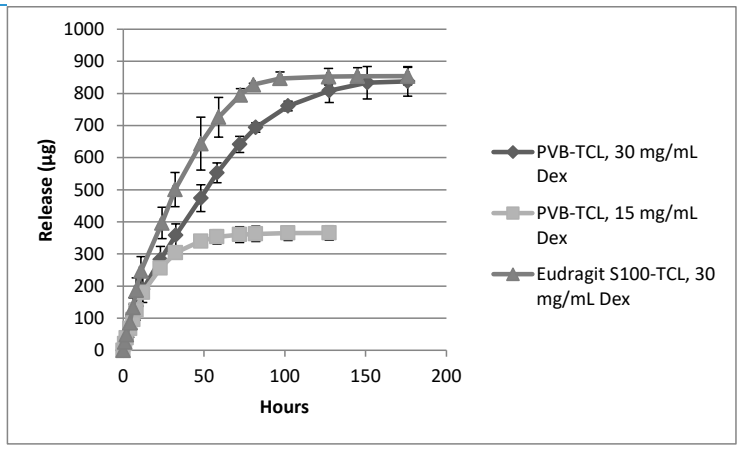


Figure 2. Cumulative i*n vitro* release of TCLs using non hydrolyzsable polymers. Polymer concentration for all lenses was 30 mg/mL.

- Characterization of the TCL

    - Sterilization methods were examined for the PLGA-TCL (hereafter the TCL). The ability to sterilize medical devices without adversely altering their function is a key component for clinical use. Autoclaving is an advantageous form of sterilization to use due to its low cost and ease of use. However, the high temperatures used in autoclaving and cause the drug and/or polymer to deteriorate. Gamma radiation sterilization can be performed while controlling the temperature of the medical device. However, significant costs can be incurred in equipment and the extensive regulatory requirements in working with radioactive substances. Due to known PLGA instability at high temperatures, PLGA-TCLs were only sterilized using gamma radiation. Medical devices using PLGA are typically sterilized in this manner, though gamma radiation often results in chain scission of polymers from the induction of free radicals (Lee JS et. al. 2003 Macromolecular Research 11(5) 352-6)
    - Vials with TCLs were packed in dry ice in an insulated container for temperature control and sterilized in a Gamma Cell 220E Cobalt 60 Irradiation Unit (Atomic Energy of Canada LTD, Ottawa, Canada) with a total dose administration of 25 kGy. Release from the lenses post sterilization was unchanged compared to unsterilized TCLs (Fig. 1).

    - TCLs were tested for optical clarity using a Lambda 1050 UV/Vis/NIR spectrophotometer with integrating sphere per ISO 18369-4 standards (reference ISO here). Hydrated PLGA-TCLs were placed in a 5 x 20 mm quartz cuvette (LambdaX, Nivelles, Belgium) and position within the spectrophotometer such that the light beam passed through the center of the lens. The beam was attenuated by a 6mm aperture in accordance with ISO procedure. Average light transmission was calculated over the visible light spectrum (390-700 nm). Lenses used in this study were TCLs, clear plano contact lenses (Kontur Contact Lens, Hercules, CA) and Air Optix® cosmetic plano contact lenses (Alcon Laboratories, Fort Worth, TX). Average light transmission from the PLGA-TCLs was 98.09 ±0.71%. This value is close to 99.9± 0.78% from the clear contact lens, and much higher than the cosmetic contact lenses (Fig. 3).

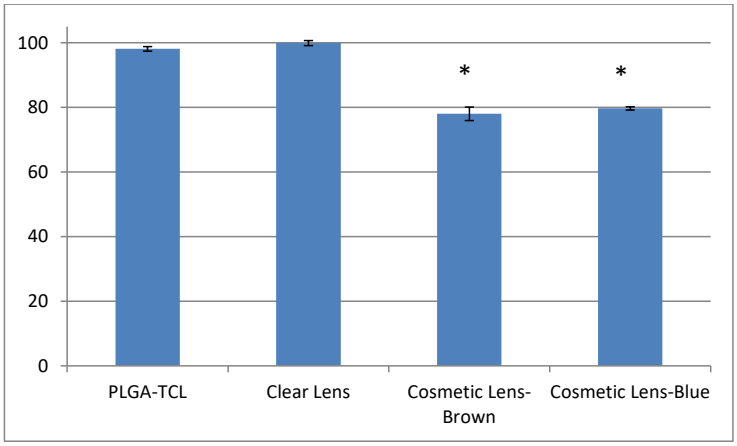


Figure 3. Light transmission results for PLGA-TCLs. n=4 per group. *p<0.001 compared to PLGA-TCL by Student t-test.

- Morphology of the TCLs was performed by anterior segment optical coherence tomography (AS-OCT). This technique is frequently used in clinical practice to examine the cornea. AS-OCT provides cross-sectional images of the PLGA-TCL at different positions in the lens. The OCT demonstrated a film encapsulated within the contact lens hydrogel. The thickness of the film is 130-150 μm (Fig. 4).

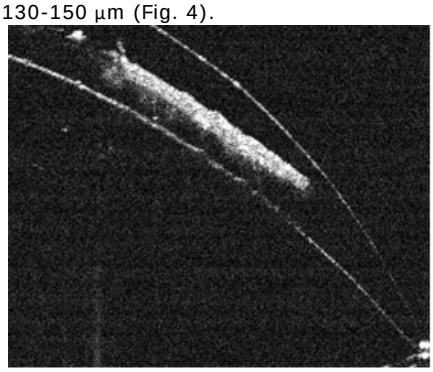


Figure 4. Representative OCT image of TCL.

- Cytotoxicity of the TCL
  - The minimum elution media (MEM) assay as described by ISO 10993-5 was used to assess cytotoxicity of the TCL-DDS (International Organization for Standardisation, 10993-5 (2009)). L929 murine fibroblasts were in 96 well plates at a density of $1x10^5$ cells/mL. TCL-DDS were immersed in DMEM at a SA/V ratio of 6 cm^2/mL for 24 hours at 37°C. 100 μL of this media (extract) was applied neat to the cells. To test the effects solely attributed to the API, dexamethasone alone was tested in additional wells. In order to increase the solubility of dexamethasone in water, the drug was added to DMSO at

concentrations (1.5%) that have not bee reported to be cytotoxic. Cells were incubated with extract or components for 24 hours. MTT Assay (Abcam, Cambridge MA) was used to measure cell viability and compared to untreated cells. Cell viability for was compared to untreated cells.

- Dexamethasone has been shown to be cytotoxic at levels that are well tolerated in humans and animals. For instance, dexamethasone has been reported to be cytotoxic to L929 cells in concentrations as low as 0.5 µM (Zhang, Y.Yue, M. Chang. *Biomedicine & Pharmacotherapy* 96 (2017) 443–449). Therefore, it was anticipated that TCL-DDS, which release 90µg/mL in the media under ISO 10993-5 testing conditions, would show less cell viability than untreated cells.
- TCL cell viability compared to untreated cells was 75±22% (Fig. 5). Because TCL released 90 µg/mL in the media, we measured cytotoxicity of dexamethasone alone at this concentration (90 µg/mL), twice as high (180 µg/mL) and much lower (18 µg/mL) drug concentrations. We found that dexamethasone alone showed cell survival rates of 38±18%, 60±10%, and 68.7±10.4% for 180, 90, and 18 µg/mL, respectively, compared to untreated cells. Cell survival for dexamethasone180 µg/mL was significantly less than 90 µg/mL (p=0.02) and 18 µg/mL (p=0.004). There was no difference between 90 and 18 µg/mL (p=0.17).

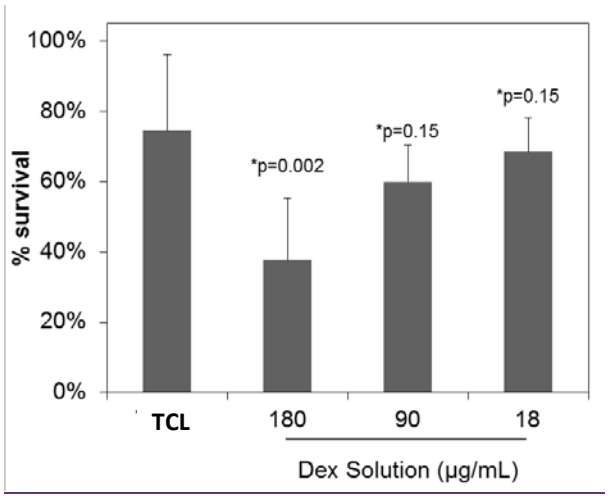


Figure 5. Cytotoxicity of TCL compared to dexamethasone solution alone. n≥6. p-values determined by unpaired Student t-test.

Aim 2:

- Aqueous humor concentrations from TCL wear by rabbits:
    - New Zealand White (NZW) rabbits (n=4) wore the TCLs. At 3, 6, 12, 24 hours, and 2-7 days, aqueous humor (AH) was withdrawn. Drug content in the AH was measured by LC/MS-MS. Drug concentrations were compared to rabbits given 0.1% dexamethasone drops either hourly or four times daily.
    - Drug concentrations from the TCL met or exceeded concentrations from hourly drops through 7 days of TCL wear (Fig. 6). The TCL drug concentrations were significantly greater than from drops through 96 hours and at 144 hours. The amount of drug present in the TCL was as much as two orders of magnitude greater than from the drops.

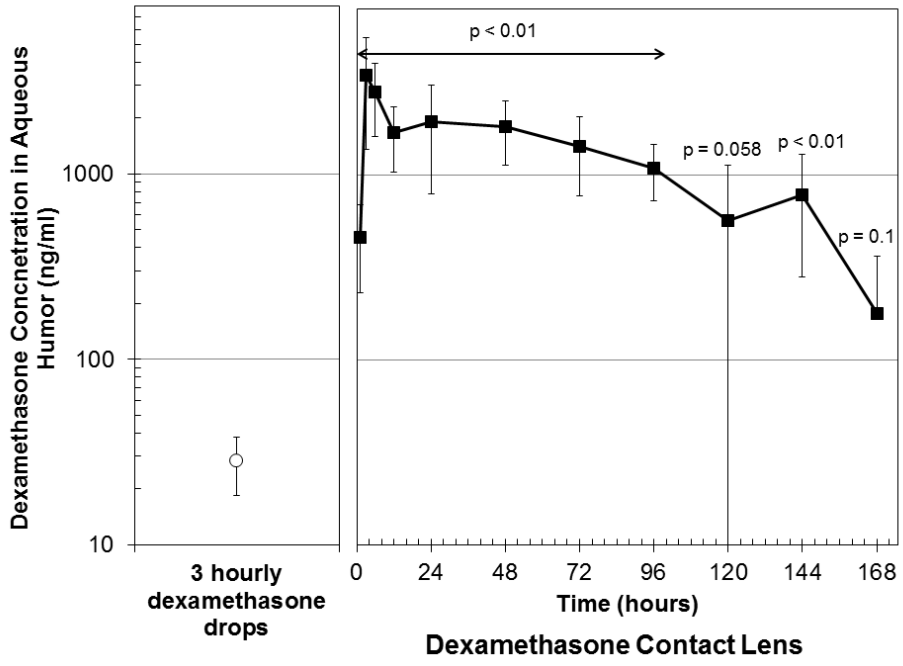


Figure 6. Aqueous humor levels of dexamethasone as obtained from Dex-lens (right) as compared to 3-hourly dexamethasone drops (left). n=4. p –values as compared to hourly drops by student t-test.

- Drug distribution throughout the ocular tissues with TCL wear
    - New Zealand White rabbits (n=4) (Charles River Laboratories, Wilmington, MA) wore the TCLs. At 6 hours and 1, 2, 5 and 7 days, the rabbits were sacrificed and the eye was enucleated. The eye was dissected and the following tissues were collected: retina, vitreous humor, choroid, sclera, cornea, and iris (with ciliary body). The tissues were homogenized and the drug extracted using methanol. Drug content was measured by LC/MS-

MS. Drug concentrations were compared to rabbits given 0.1% dexamethasone drops either hourly for eight hours.

- Drug concentrations were higher for the TCLs than the drops at 6 hours and 1 day in all categories (Fig. 7). The only exception was sclera at 6 hours, for which only one sample was successfully processed. Drug levels for the TCL were also higher for the drops in the sclera at 2 days, and higher in the cornea, iris, and retina at 2 days and 5 days. At all other time points, the TCL drug levels were comparable to drops with the exception of the choroid at day 7, in which the drops were higher. An interesting finding was that while topical medications do not normally have high concentrations at the back of the eye, the TCL retina concentrations were 100 times greater than drops at 2 days. Potentially, the TCL could be used to treat diseases in the back of the eye.

- All rabbit eyes were evaluated for biocompatibility by ophthalmologist examination, IOP checks, and pachymetry. There was no evidence of toxicity, irritation, or other adverse effects from the TCLs.

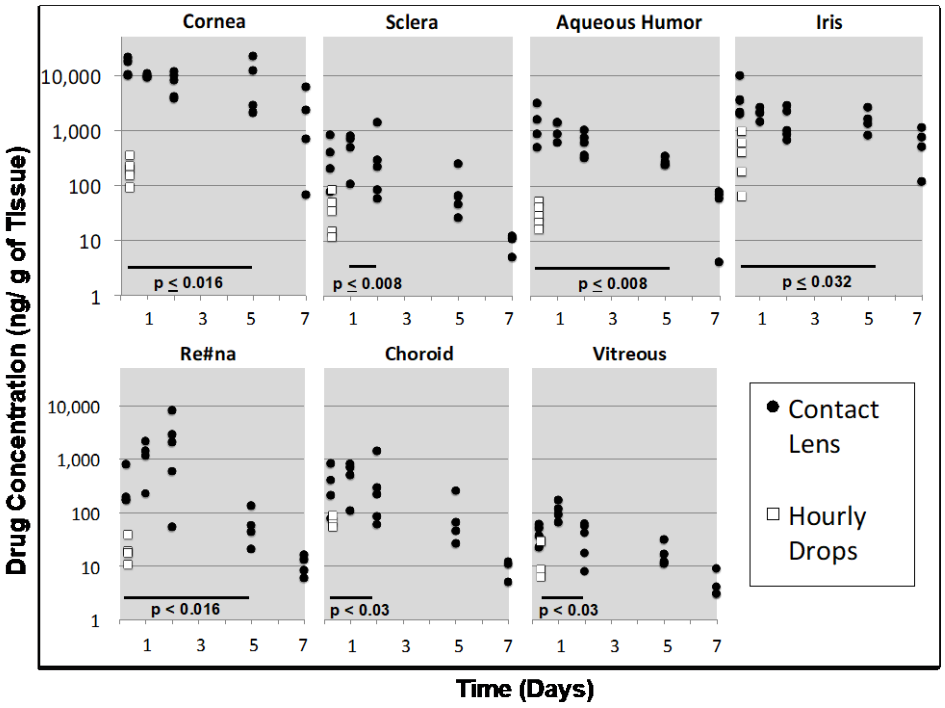


Figure 7. Dex concentrations from in ocular tissues for up to 7 days of TCL wear, compared to Dex drops for 8 hours. n≥4. Statistical comparisons by Mann-Whitney U.

Aim 3a

- Treatment of anterior uveitis using the TCL in a rabbit model
    - Rabbits were injected with lipopolysaccharides in the anterior chamber to induce anterior uveitis. Rabbits were divided into one of three groups (n=5): TCL, hourly dexamethasone drops, or hourly saline drops (negative control). Treatment began immediately after induction. Aqueous humor samples were taken on days 1, 3 and 5 of the study to measure aqueous humor (AH) protein, a marker of inflammation.
    - Protein in the aqueous humor was quantified by Bradford Assay (Bio-Rad, Hercules, CA).
    - Aqueous humor protein levels peaked on Day 1 after LPS injection in the animals treated with saline drops (Fig. 8). The aqueous humor protein levels in the saline group remained significantly higher than baseline throughout the study with p-values of 0.0006, 0.0003, and 0.0094 on day 1, day 3, and day 5 (Student t-test). Rabbits treated with dexamethasone drops also had significantly greater aqueous humor protein concentrations on day 1 ($p = 0.04$) compared to baseline, but the not on day 3 ($p=0.77$) or day 5 ($p=0.18$). Previous studies that used LPS intracameral injections to induce inflammation found similar trends with inflammatory markers peaking during the first 24 hours and decreasing thereafter *(15, 16, 18)*. Animals treated with D-lenses did not have an increase in aqueous humor protein concentration following the LPS injection (Student t-test compared to baseline: day 1, $p=0.88$; day 3, $p= 0.55$; and day 5, $p= 0.67$). When compared to animals treated with saline drops, rabbits treated by D-lenses had significantly less protein concentrations on day 1 ($p=0.028$) and day 3 ($p = 0.016$), but not on day 5 ($p=0.25$). Rabbits treated with dexamethasone drops also had significantly less inflammation than those treated with saline drops on day 1 ($p=0.034$) and 3 ($p=0.015$), but not on day 5 ($p=0.25$). We also examined white blood cell count concentrations in the AH but found no significant differences among the groups.

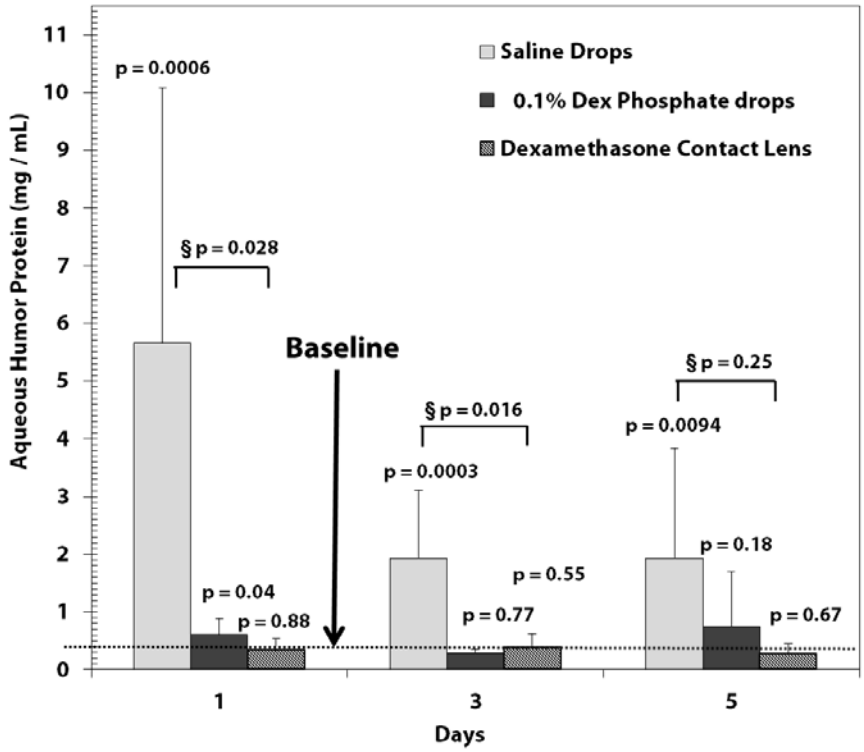


Figure 8. In vivo efficacy for treatment of induced anterior uveitis. Aqueous humor protein concentration after lipopolysaccharide endotoxin injection into the aqueous humor followed by treatment with: hourly sterile saline solution 0.9% for 5 days, hourly dexamethasone 0.1% ophthalmic solution for 5 days, or dexamethasone-eluting contact lenses worn for 5 days (n = 5). Data are means ± SD. § p-values = comparison between saline drops and dexamethasone-eluting contact lenses using Student t-test and all other p-values represent comparison from the baseline of the same animal by Student t-test.

Aim 3b:

Prevention of corneal neovascularization using the TCL in a rabbit model

- Pilot study. Rabbits had photographs taken of the right eye. Then 7-0 silk sutures placed in the corneal stroma of the right eye. Four different patterns of suture were placed, one in each of four rabbits (Figure 9). On days 2, 5 and 7 of the study, the rabbits underwent a slit lamp exam and additional photographs were taken (Figure 10). On day 7, the rabbits were euthanized and both corneas were removed for additional analysis. Corneal neovascularization was assessed by measuring vascularized surface area on day 7 from the photographs using ImageJ.

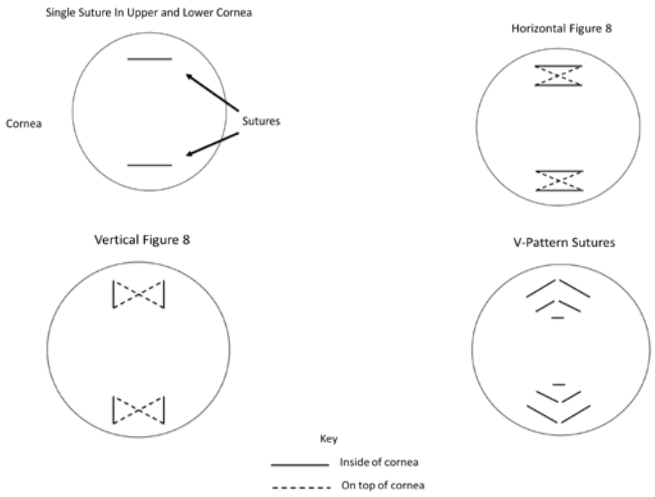


Figure 9. Suture patterns used in corneal neovascularization pilot study.

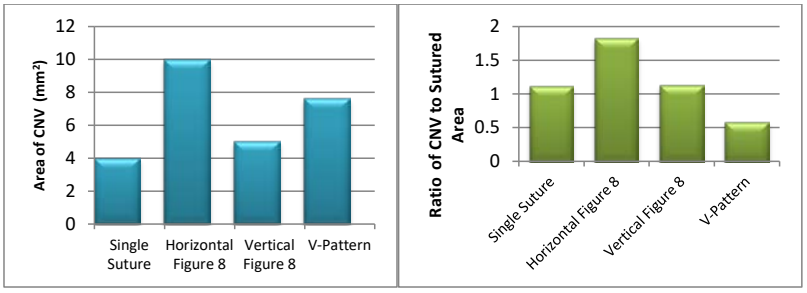


Figure 10. Results of image analysis from CNV pilot study (n=1). The horizontal Figure 8 suture had the largest area of CNV (a) and the highest ratio of CNV to sutured area.

- Based on the CNV area, the horizontal figure 8 suture was chosen for the full study.
- Corneal Neovascularization Efficacy Study. New Zealand White rabbits had 7-0 silk sutures placed in the corneal stroma of the right eye. Sutures were placed in a figure 8 pattern in the superior and inferior cornea (Figure 11). Upon initial suture placement, rabbits underwent a slit lamp exam with photographs, ocular coherence tomography, and had digital photographs taken with a SLR camera. On day 5, the slit lamp exam was repeated to assess corneal neovascularization. On day 7, the rabbits once again underwent slit lamp photographs, OCT, and camera photographs. Then the rabbits were euthanized and both corneas were

removed for additional analysis. Corneal neovascularization was assessed by measuring:

- Vascularized surface area from the photographs using ImageJ.
- VEGF-A and VEGF-R2 in the cornea using qRT-PCR.
- CD-45+ cells using flow cytometry.

- The groups studied (n=6) were:
  - TCL group
  - Dexamethasone sodium phosphate drops (0.1%), given hourly for 8 hours per day for seven days.
  - Vehicle contact lens group, in which the lens is fabricated with a polymer film but contains no dexamethasone.
  - No treatment

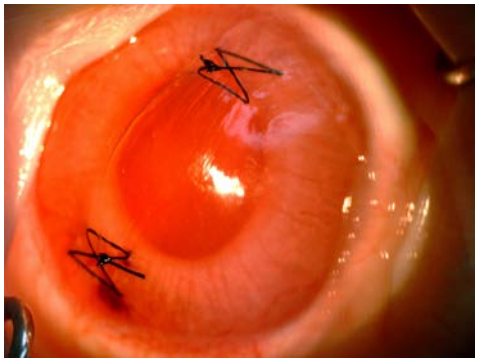


Figure 11. Rabbit eye with figure 8 sutures in the superior and inferior cornea.

- Two masked observers independently evaluated the slit lamp images for the following:
  - Area of corneal neovascularization. The area was traced using ImageJ. OCT images were used to translate the area from pixels to mm^2
  - Fluorescein staining, using the NEI fluorescein staining scale

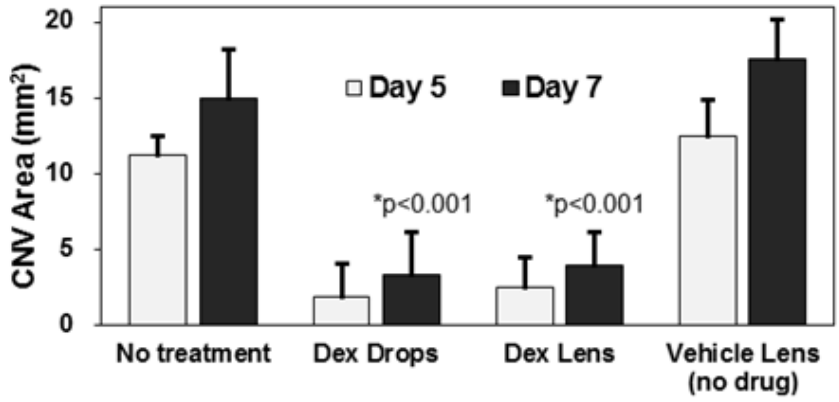


Figure 12. CNV area of rabbits undergoing treatment with the TCL, a vehicle contact lens, dexamethasone ophthalmic solution, or no treatment (n=6 per group).

- The CNV area was significantly lower on Day 5 and Day 7 in the TCL group compared to the no treatment group (Figure 12). There were no differences between the Dex drops group and the TCL group. There was also no difference in CNV area between the no treatment group and the vehicle contact lens group on either date, indicating the contact lens itself does not reduce CNV.

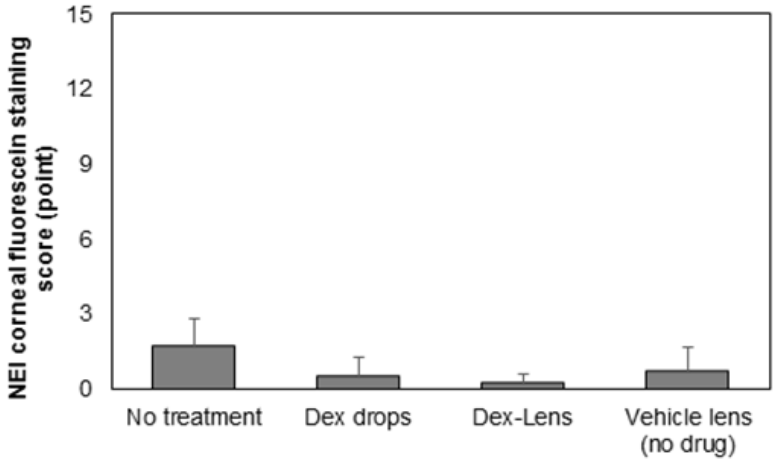


Figure 13. NEI corneal fluorescein staining scores for rabbits in CNV study. Scale is from 0 to 15.

The corneal staining, a measure of corneal health and epithelial defects, showed no differences among all four groups (Figure 13). Scores on the NEI corneal fluorescein staining scale ranged from 0-5, out of a possible 15. The contact lens was not responsible for significant corneal epithelial defects.

- The inferior cornea was excised from each eye for analysis by flow cytometry. An 11mm corneal trephine was used to ensure the same amount of cornea was present in each sample. The TCL group had a significantly lower CD45+ percentage than the no treatment group. There was no significant difference between the no treatment group and the vehicle contact lens group (Figure 14). This demonstrates the TCL suppressed inflammation in the sutured eye to the same extent as dexamethasone solution, and there was no effect from the contact lens itself.

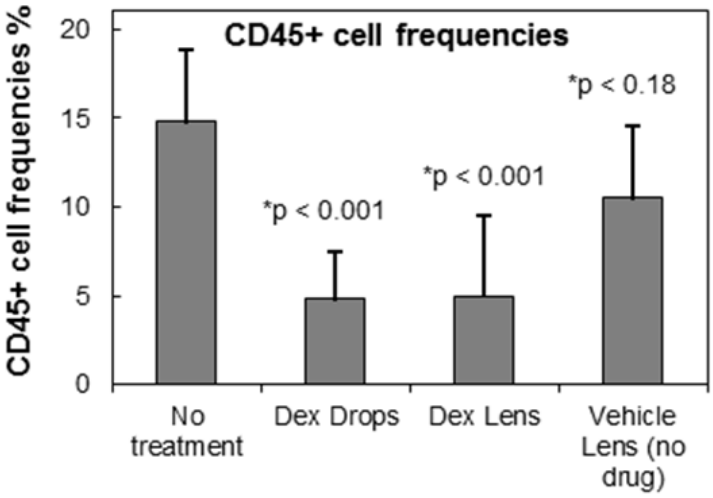
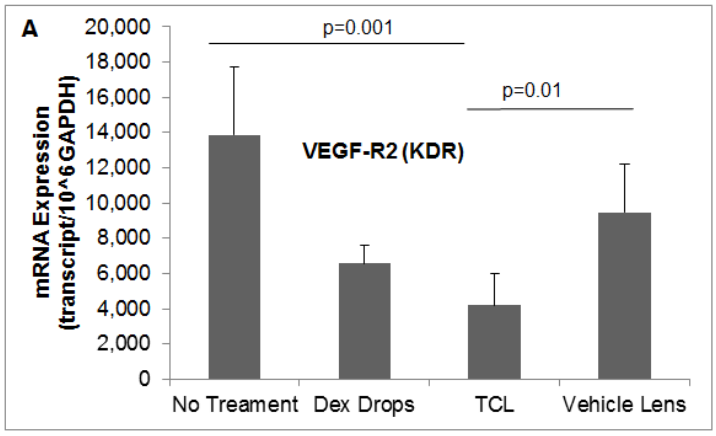


Figure 14. CD45+ cell frequencies (n=6). Statistical analysis performed by unpaired Student t-test with Bonferroni correction. *p<0.005 compared to no treatment

- qRT-PCR was performed on the superior cornea to evaluate mRNA expression of VEGF-A and VEGF-R2 (Figure 15). VEGF-R2 (KDR) is a receptor that was downregulated in the TCL group compared to the no treatment and vehicle lens group. For VEGF-A, the Dex drops group had signifcantly lower mRNA expression than both the TCL and the vehicle lens. The TCL had greater downregulation compared to the vehicle lens. No significant differences were seen in comparison to the no treatment group. The Dex drops group may have had greater downregulation

due to the manner of dexamethasone delivery (pulsatile vs continuous). The amount of dexamethasone in the later days of the study was more likely greater in the drops compared to the TCL, although the bioavailability of the dexamethasone delivered from drops may not be greater. However, since VEGF R2 is significantly downregulated in the TCL, ligand binding for VEGF-A is limited.



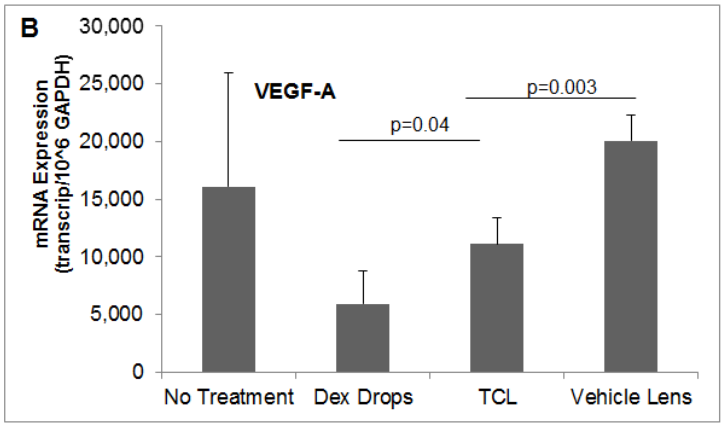


Figure 15. mRNA expression of a) VEGF-R2 and b) VEGF-A from sutured corneas (n=4 to 6) *

- **What opportunities for training and professional development has the project provided?**

  Ms. Amy Ross has learned the indications for ophthalmic usage of corticosteroids (e.g, prevention of ocular wound inflammation) and the typical treatment regimens for clinical use. She has examined measurement techniques of dexamethasone and developed a high pressure liquid chromatography method for quantification.

  Ms. Ross also learned how to perform a Bradford protein quantification assay in preparation for efficacy studies in the use of anterior uveitis. She familiarized herself with techniques for homogenizing ocular tissues and the extraction of dexamethasone from said tissues.

  Dr. Lokendra Bengani was trained on the use of animals in biomedical research. He learned appropriate techniques for handling rabbits and administering drugs to rabbits. He also learned how to use ImageJ for image analysis.

- **How were the results disseminated to communities of interest?**

  Presented in part at local and national meetings.

- **What do you plan to do during the next reporting period to accomplish the goals?**

Nothing to report

4. **IMPACT:**

- **What was the impact on the development of the principal discipline(s) of the project?**

Nothing to report

- **What was the impact on other disciplines?**

  Nothing to report.

- **What was the impact on technology transfer?**

Nothing to report.

- **What was the impact on society beyond science and technology?**

Nothing to report.

5. **CHANGES / PROBLEMS:**

- **Changes in approach and reasons for change**

Nothing to report.

- **Actual or anticipated problems or delays and actions or plans to resolve them**

Nothing to report.

- **Changes that had a significant impact on expenditures**

Nothing to report.

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and / or select agents**

Nothing to report.

- **Significant changes in use or care of human subjects**

Nothing to report (not applicable).

- **Significant changes in use or care of vertebrate animals.**

Approval for *in vivo* studies described in Aims 2 and 3 was submitted to SERI IACUC on July 13, 2015 and approved October 23rd, 2015. No changes to SOW regarding vertebrate animals.

- **Significant changes in use of biohazards and / or select agents**

Nothing to report.

6. **PRODUCTS:** *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**

Preliminary data presented at Glaucoma New Horizons 360, February 2016.

Poster Presentation: "Pharmacokinetics and Efficacy of a Steroid-Eluting contact lens" Military Vision Research Symposium, March 2017

Poster Presentation: "Inhibition of Corneal Neovascularization by Dexamethasone-Eluting Contact Lenses in a Rabbit Model" Military Vision Research Symposium, March 2017

Poster Presentation: "Poster: "Pharmacokinetics and Efficacy of a Steroid-Eluting contact lens" Military Vision Research Symposium, March 2017

Poster Presentation: "Inhibition of Corneal Neovascularization by Dexamethasone-Eluting Contact Lenses in a Rabbit Model" The Association for Research and Vision in Ophthalmology (ARVO) Annual Meeting, May 2017

Oral Presentation: "Inhibition of Corneal Neovascularization by Dexamethasone-Eluting Contact Lenses in a Rabbit Model" Controlled Release Society Annual Meeting, July 2017

Poster Presentation: "Inhibition of Corneal Neovascularization by Dexamethasone-Eluting Contact Lenses in a Rabbit Model" International Society for Contact Lens Research, August 2017

Oral Presentation: "A Corticosteroid Eluting Contact Lens for Ocular Inflammation" Military Health Services Research Symposium, August 2018 (planned)

- **Journal publications**

Two manuscripts are in preparation:

- "Retinal drug delivery with sustained-release steroid-eluting contact lenses"

- "Safety and in vivo efficacy of a dexamethasone-eluting contact lens for inhibition of corneal neovascularization and inflammation"

Books or other non-periodical, one-time publications.

Nothing to report.

- **Other publications, conference papers, and presentations.**

Nothing to report.

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

Nothing to report.

7. **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

- **What individuals have worked on the project?**

Joseph B. Ciolino, M.D.-Dr. Ciolino provided oversight over all aspects of this project, including data analysis and interpretation.

Lokendrakumar C. Bengani, Ph.D.-Dr. Bengani performed animal studies and contributed to data analysis and interpretation.

Amy Ross-Ms. Ross developed the TCL formulation and conducted *in vitro* release studies and characterization.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report.

- **What other organizations were involved as partners?**

  Although they were not paid from this award, Lt. Col. J. Richard Townley of Lackland AFB used the TCLs to conduct a study of preventing corneal haze post photorefractive keratotomy in rabbits. Their study found the TCL reduced central haze at a level comparable to dexamethasone drops given four times daily. Lt. Col. Townley also provided guidance on this project.

Sustained corticosteroid release from a novel contact lens drug delivery system for the treatment of ocular inflammation and corneal neovascularization.

MR130201

PI: Joseph B. Ciolino **Org:** Schepens Eye Research Institute **Award Amount:** $1,000,000

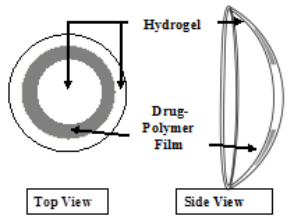
Study Aims

- Aim 1: Development and *in vitro* testing of a steroid-eluting contact lens.
- Aim 2: *In vivo* evaluation of biocompatibility and drug flux.
- Aim 3: *In vivo* evaluation of efficacy in animal models of ocular inflammation and corneal neovascularization.

Approach

We will develop a steroid-eluting therapeutic contact lens (TCL) that will consists of a thin drug-polymer film encapsulated within the periphery of a typical hydrogel contact lens. We will study drug release profile *in vitro* (Aim 1) and then the drug flux into the eye *in vivo* and compare it to that of steroid drops (Aim 2). Finally, we will test its efficacy in treating ocular inflammation and corneal neovascularization (Aim 3).

Steroid-eluting therapeutic contact lens



We will use our innovative approach to develop a steroid-eluting contact lens for the treatment of ocular inflammation and cornea neovascularization.

Timeline and Cost

Activities CY	14	15	16	
Aim 1: Development and *in vitro* testing				
Aim 2: *In vivo* evaluation of biocompatibility and drug flux.				
Aim 3: *In vivo* evaluation of efficacy				
Estimated Budget ($)	**$372**	**$314**	**$314**	**$000**

Updated: (05/14/18)

Goals/Milestones

CY14 Goal – To demonstrate in vitro drug release at therapeutic levels for 7 days.

x Drug quantification using high-performance liquid chromatography

CY15 Goals – XTCL in vivo drug flux into the aqueous humor that is equal to or exceeds steroid eye drops

x Place TCL on eyes for one week and compare drug flux into the eye to the current standard of care (steroid eye drops)

CY16 Goal – In vivo demonstration of efficacy

X Demonstrate the effectiveness of TCL to treat intraocular inflammation and corneal neovascularization, compared to eye drops

Budget Expenditure to Date

Projected Expenditure: $1,000,000

Actual Expenditure: $ 999,628.00