



Treatments for Neurotrauma

Steroid-releasing Therapeutic Bandage Contact Lens

Ocular trauma commonly results from blast injuries. Ocular wound healing begins with an inflammatory stage that is associated with pathological sequelae. Researchers at the Schepens Eye Research Institute (Boston, Massachusetts) developed a corticosteroid-releasing therapeutic bandage contact lens (TCL) that can be used to prevent trauma-related ocular inflammation and scarring. The TCL has the potential to also change the treatment of other ocular inflammatory conditions, such as post-operative inflammation.

The concept of contact lens drug delivery dates back to the 1960's (US patent # 2,976,576); however, sustained and controlled delivery has historically been a significant challenge (*Wichterle and Lim 1956*). Unmodified commercial contact lenses can absorb medications, but all of the drug is released over several hours. In contrast to other drug-eluting contact lens designs that used a particulate approach to control drug release, the researchers took a macroscopic approach that consists of a thin drug-polymer film encapsulated within the periphery of a typical hydrogel contact lens which maintains a clear central aperture that allows unimpeded light and oxygen transmission (Figure 1). Using this novel system, they developed a steroid-eluting contact lenses capable of releasing therapeutic amounts of dexamethasone in a controlled manner for up to a week.

The researchers demonstrated that TCLs provide sustained drug flux in animals and proof-of-concept effectiveness in two animal models of inflammation. Ocular drug flux studies found that TCLs delivered dexamethasone to the front and back of the eye at levels that were 100s to 1,000 times greater than those of hourly commercial dexamethasone drops (*Kobashi et al. 2017b*).

To study efficacy, the researchers compared TCLs to hourly administration of commercial dexamethasone eye drops in animals. Anterior uveitis was induced by injection of lipopolysaccharide (LPS) endotoxin into the aqueous humor. Protein levels in the aqueous humor served as an objective and quantitative measure of inflammation. Three days after LPS injection, we found statistically significantly less aqueous humor protein concentrations for animals treated with TCLs (0.29-0.22 milligrams per milliliter, $p = 0.016$) and with hourly dexamethasone drops (0.29-0.07 milligrams per milliliter, $p = 0.015$) compared to untreated animals (1.92-1.19 milligrams per milliliter) as shown in Figure 2 (*Bengani and Ciolino 2017*).

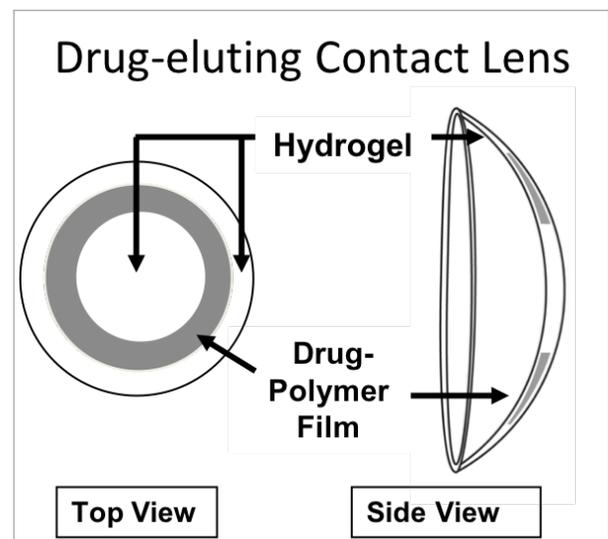


FIGURE 1: Drug-eluting contact lens schematic. (Figure used with permission from the authors)





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In another study, the researchers studied the efficacy of TCLs, hourly dexamethasone drops, and a vehicle contact lens (no drug) for the prevention of corneal neovascularization (CNV), which was induced by placing 7-0 silk sutures along corneas of animals. The extent of neovascularization was compared between treatment groups by two cornea fellowship-trained masked observers who measured the area of CNV (millimeter²) from slit lamp photographs taken on day 7 as shown in Figure 3 (U.S. patent # 2,976,576) (Ciolino *et al.* 2017, Kobashi *et al.* 2017a, 2017b). TCLs were far more effective in reducing CNV compared to no treatment or vehicle contact lenses, and similar to hourly dexamethasone drops. The measured CNV area was validated by biomarkers in the cornea, such as levels of Vascular Endothelial Growth Factor and the number inflammatory cells.

In summary, steroid-eluting contact lenses can limit scarring of the eye following ocular trauma. They can be used to treat ocular trauma in Service members in the battlefield, clinic, or after surgery.

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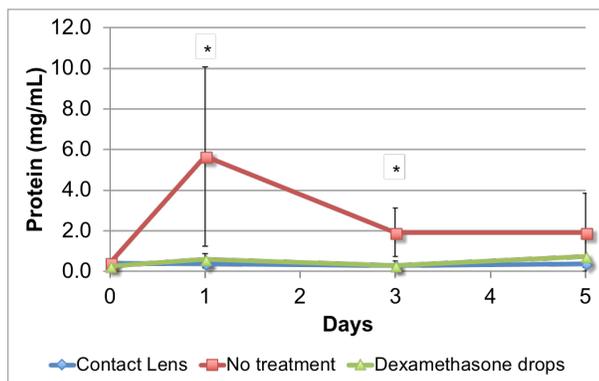


FIGURE 2: Aqueous humor protein concentration before (day 0) and after LPS endotoxin injection into the aqueous humor followed by treatment with: hourly sterile saline solution 0.9 percent, hourly dexamethasone 0.1 percent ophthalmic solution, or dexamethasone-eluting contact lenses worn for five days (n = 5 per group). Data are means ± standard deviation. Rabbits treated by dexamethasone drops and dexamethasone-eluting contact lenses had significantly less aqueous humor protein than those treated with saline drops at day one and three. *p<0.05 by Student t-test (Figure used with permission from the authors)

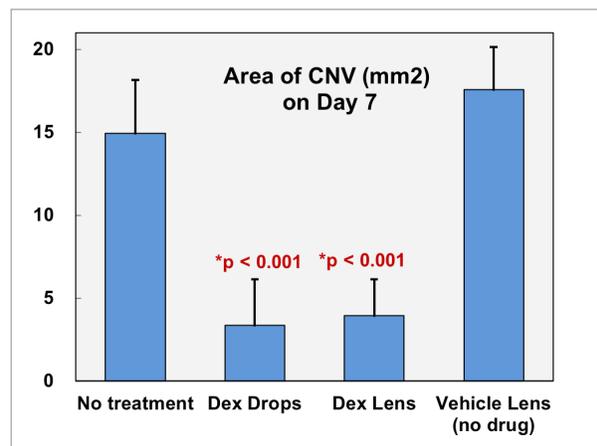


FIGURE 3: Corneal neovascularization area in suture-induced CNV measured from slit lamp images by two masked cornea experts. * compared to no treatment. (Figure used with permission from the authors)





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