



**Illinois Eye**  
ILLINOIS EYE AND EAR INFIRMARY



# Effect of Intraocular Enoxaparin on Postoperative Fibrosis in a Juvenile Rabbit Model of Lensectomy

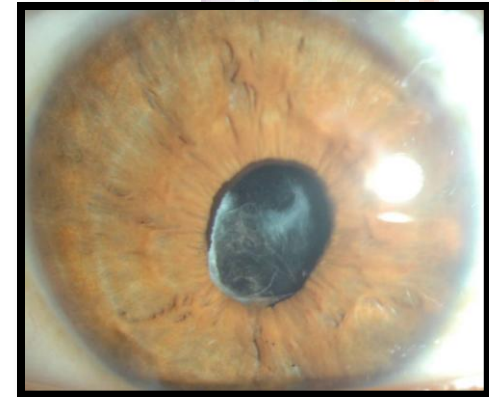
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# Introduction

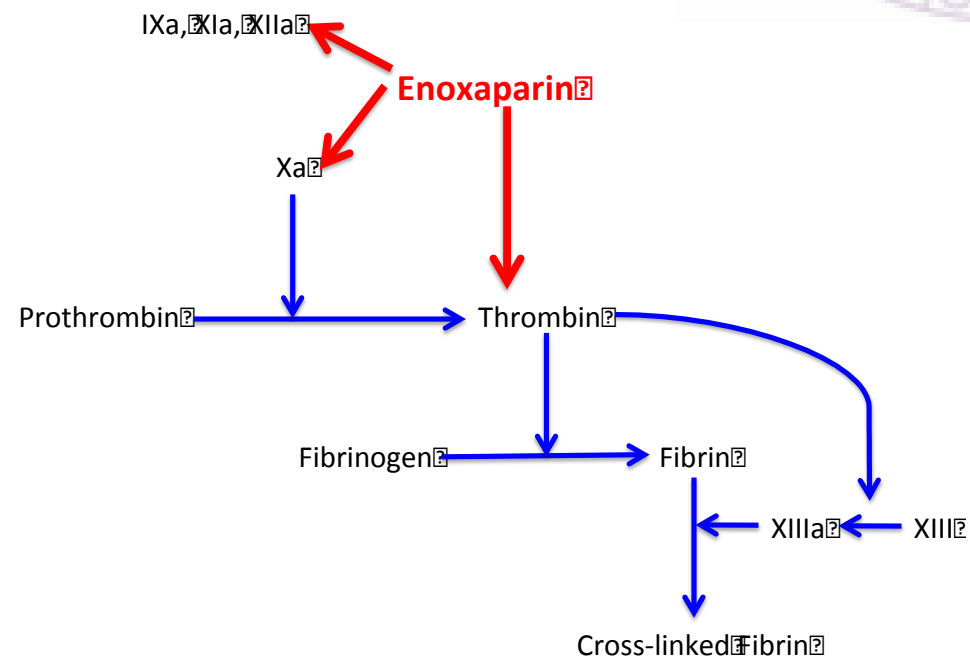
- Intraocular surgery in children has a higher incidence of postoperative fibrosis and inflammation compared to adults.
- One of the most common intraocular surgeries is for congenital cataract, with an estimated US prevalence 13.6/10,000 infants.<sup>2</sup>
- Steroids are the mainstay of postoperative care, but complications still occur including obscuration of the visual axis from membrane formation, synechiae, high intraocular pressure, and the need for reoperation.<sup>3</sup>
- Prevention of postoperative fibrosis and inflammation in pediatric patients will improve the clarity of the visual axis, reduce reoperation rates, and improves visual outcomes.
- Rabbits are an ideal animal model of pediatric cataract surgery postoperative inflammation and fibrosis because the anterior chamber is anatomically similar to the human eye with a robust response to lens extraction.<sup>4</sup>



Fibrin membrane in a child after lensectomy with IOL implantation<sup>1</sup>

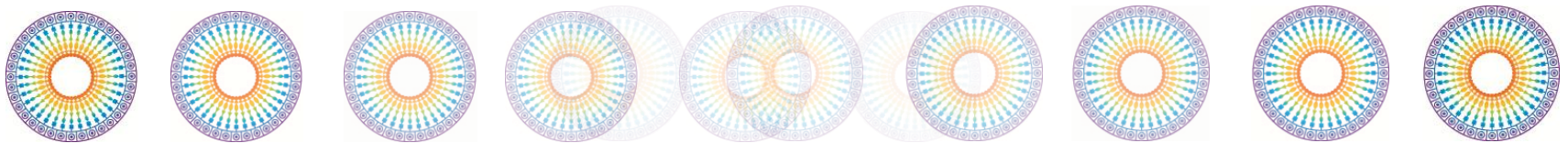
# Introduction

- Fibrin is formed from the conversion of fibrinogen to fibrin by thrombin.
- Heparin has been noted to decrease fibrin formation as well as have some anti-inflammatory properties.<sup>5</sup>
- Enoxaparin is a low molecular weight heparin with a longer half-life than heparin.
- Enoxaparin inactivates thrombin through binding to anti-thrombin III. It also inhibits protease Xa with stronger inhibition than heparin, preventing the conversion of prothrombin to thrombin.



# Purpose

- To investigate the efficacy and safety of a low molecular weight heparin, enoxaparin, for the prevention of postoperative fibrosis and inflammation after lensectomy in a juvenile rabbit animal model.



# Methods

All experiments were approved and in compliance with Animal Care Committee at the University of Illinois at Chicago.

- Subjects: 15 Juvenile (6 week old) New Zealand White rabbits

## Surgery

- Rabbits were anesthetized with intramuscular (IM) ketamine and xylazine
- Unilateral lens extraction surgery was performed as follows:
  - *A clear-corneal incision was made with a 20G MVR blade*
  - *A continuous curvilinear capsulorhexis was made and the lens was removed in its entirety using a Simcoe irrigation-aspiration*
  - *Wounds were closed with buried 10-0 nylon suture*
- Using a 30G needle on a syringe, 0.1cc Balanced Salt Solution (BSS) or enoxaparin was injected into the anterior chamber of the operated eye at the completion of surgery
- Topical erythromycin antibiotic was given for 3 days postoperatively
- Analgesia with subcutaneous buprenorphine was given for the first postoperative day and as needed for the next 3 days



# Methods

## **Study groups**

- Control (BSS, 0.1ml intracameral injection) – 8 subjects
- Treatment (Enoxaparin 0.1ml of 100 mg/ml intracameral injection) – 7 subjects

## **Measures**

Performed under sedation with IM ketamine and dexmedetomidine

- Anterior chamber examinations were performed on Days 2 to 7 and weekly thereafter
- Optical coherence tomography (OCT) signal strength (Spectralis OCT, Heidelberg Engineering) was measured daily from 2 to 7 days postoperatively and then weekly for a month
- Electroretinography (ERG) studies (UTAS E3000 Visual Diagnostic System, LKC Technologies) were performed between postoperative week 2 and 3

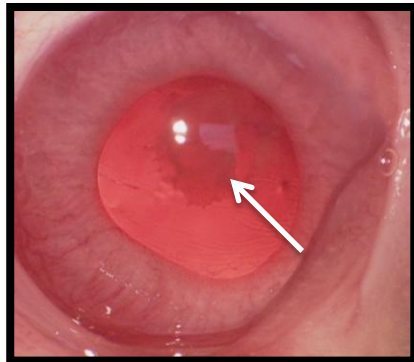


# Results – Anterior Chamber Exam

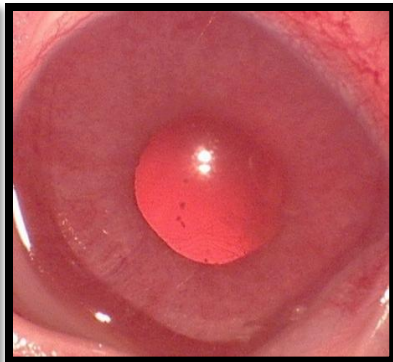
## Juvenile rabbit lensectomy

- Induced anterior chamber fibrin clot formation (white arrow) in 75% of the 8 control rabbits between postoperative days 2 through 4
  - Fibrin clots were resolved by 7 days postop without intervention
- None of the 7 rabbits treated with enoxaparin developed a fibrin clot or membrane
  - One subject in the treatment group had anterior chamber blood in first two days after the operation which resolved within 2 days without intervention

*2 Days Postop*

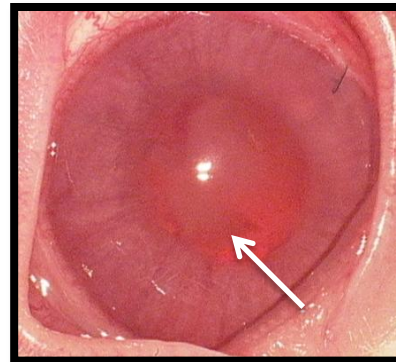


Control

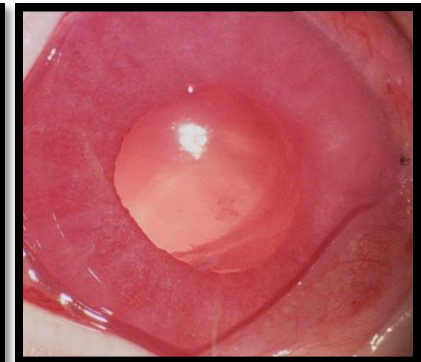


10mg Enoxaparin

*3 Days Postop*



Control



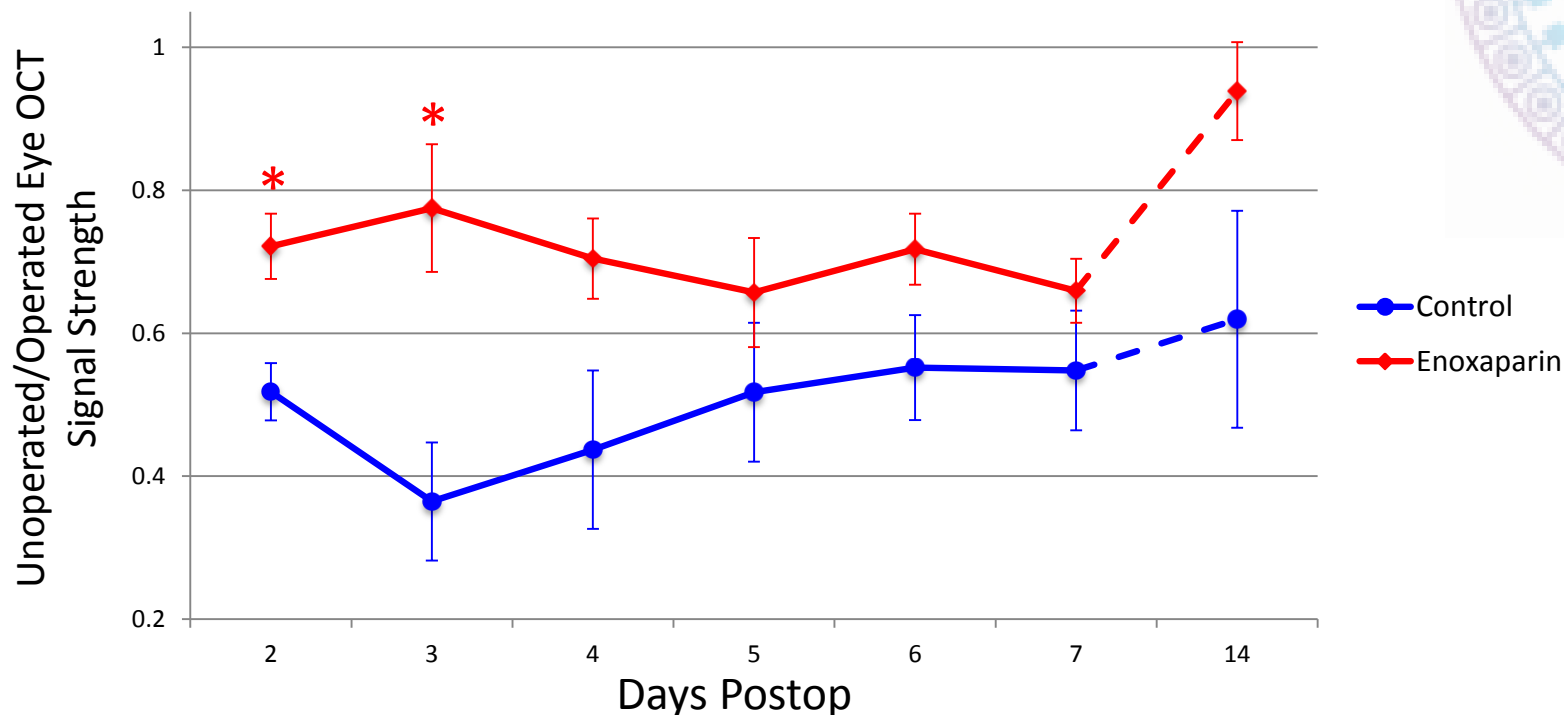
10mg Enoxaparin

Anterior chamber of 6 week-old rabbits after clear lens extraction.

A fibrin clot can be seen in the anterior chamber of control rabbits but not enoxaparin (arrow).

# Results- OCT Signal Strength

Comparison of the ratio of the unoperated/operated eye OCT signal strength of control or enoxaparin-treated rabbits

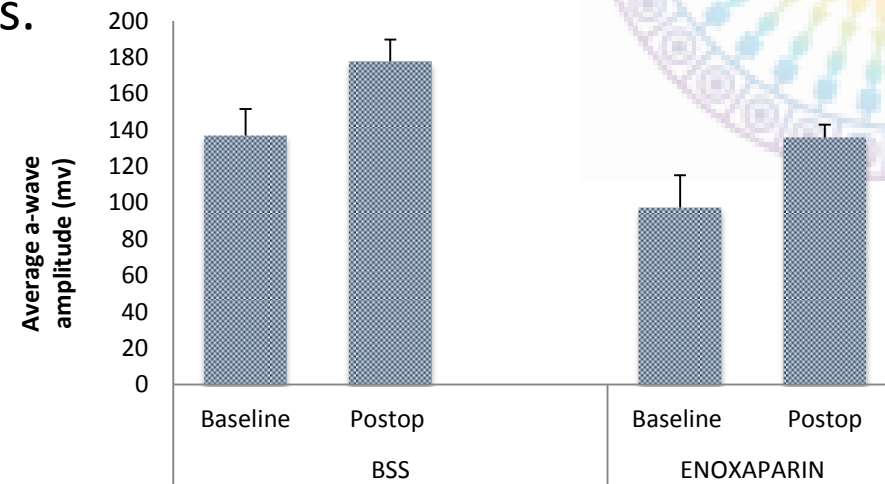
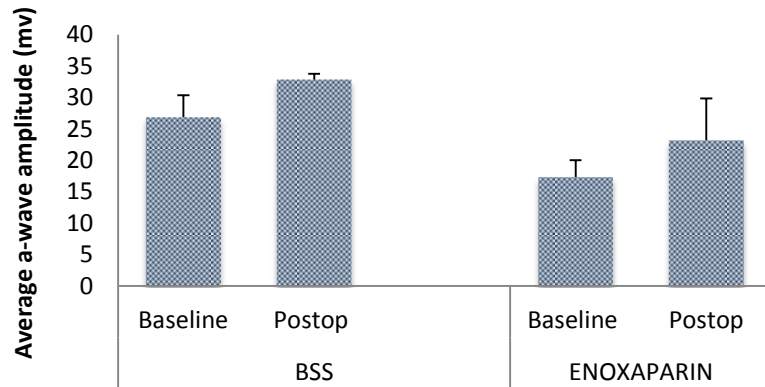


- The group of eyes treated with enoxaparin had increase in signal strength ratio compared to controls (ANOVA,  $p < 0.001$ )
- These differences of individual days were significant on postop 2 and 3 (\*,  $p < 0.05$ , error bars are SEM)

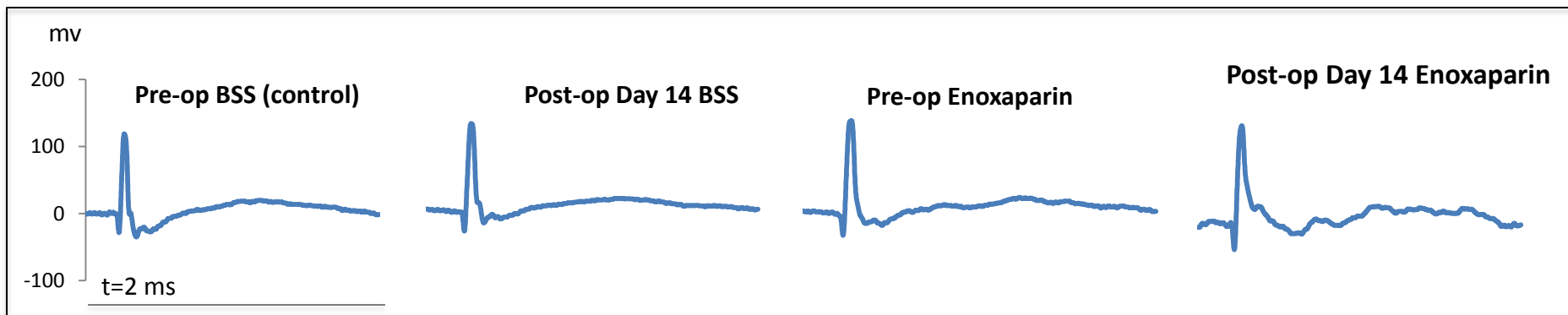


# Results – ERG

- Electroretinogram (ERG) studies in both control and Enoxaparin treated eyes showed an increase in a-wave and b-wave amplitude three weeks postop. This observation could be due to an ongoing retinal development in juvenile rabbits.

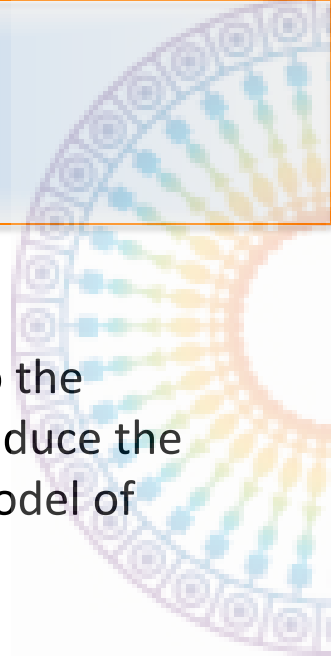


*Dark adapted ERG using dark flash stimulus before and two weeks after surgery*



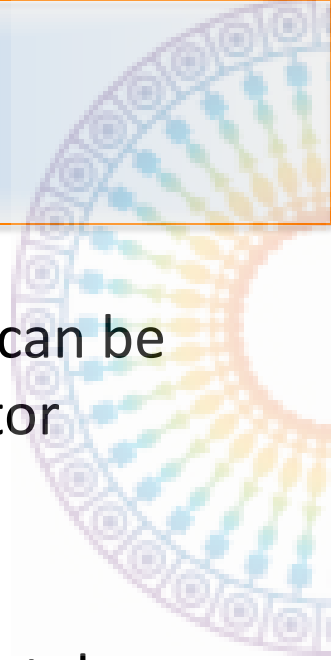
# Discussion

- Intraocular enoxaparin, a low molecular weight heparin, injected into the anterior chamber at the completion of lens extraction surgery may reduce the formation of fibrin and improve clarity of the visual axis in a rabbit model of lensectomy.
- The only randomized clinical trial of children using enoxaparin in the irrigating solution did not find a significant benefit except for reduced inflammation in the first week postoperatively.<sup>6</sup>
  - *The dose of enoxaparin used in this trial (40 mg medication diluted into 500cc of balanced salt solution) was significantly less than 10mg into the anterior chamber at the conclusion of surgery.*
- The use of intraocular medications such as enoxaparin could potentially augment or may help reduce dependency on corticosteroids in the immediate postoperative period.



# Conclusions

- A juvenile rabbit animal model of clear lens extraction can be used to quantify the clarity of the visual axis and monitor retinal toxicity with candidate medications.
- Enoxaparin injected into the anterior chamber immediately after lens extraction may reduce the formation of fibrin and improve clarity of the visual axis in a rabbit model of lensectomy.
- Intraocular enoxaparin does not appear to have toxic effects on the retina by ERG.



# References

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