

Evaluation in Canines of a Novel Device for Suprachoroidal Drug Delivery

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INTRODUCTION

- The suprachoroidal space (SCS) has long been known as a potential space for drug delivery. Several studies using microneedles in rabbits, pigs, and humans have demonstrated this access to be minimally invasive and costefficient for drug delivery to the retina and choroid ^{1,2}.
- The Everads Injector, a novel delivery technology that employs blunt dissection of the scleral and choroidal tissues to open a channel to access the SCS, was recently reported to be both tolerable and effective in delivering AAVs in NHP studies^{3,4}, as well as safe, feasible, and tolerable for clinical use ⁵.
- The purpose of this study was to evaluate the injection method and distribution of two distinct dyes into the canine SCS using the Everads Injector (Everads Therapy).

METHODS

- A total of 4 (1 male and 3 females) Beagle dogs, ranging in age from 1 to 2 years, were used in this study.
- Ophthalmic examinations, including slit lamp biomicroscopy and indirect ophthalmoscopy, were performed prior to and immediately after dosing.
- All animals were anesthetized and received a suprachoroidal injection of 200 µL of BSS with ICG in the right eye and BSS with FITC-Dextran (MW: 500,000) in the left eye.
- During dosing, thermal images were captured using a handheld thermal imaging camera (TC004 Topdon[®]).
- Intraocular pressure (IOP) was measured using a rebound tonometer (TonoVet Plus®) before, immediately after, and 30 minutes after dosing.
- Confocal Scanning Laser Ophthalmoscopy (cSLO) and autofluorescence (AF) images were captured immediately after dosing using the Spectralis ® HRA/OCT imaging platform (Heidelberg Engineering).
- Eyes dosed with ICG were collected for dissection immediately after the procedure, and eyes dosed with FITC-Dextran were fixed in 8% formalin, embedded in OCT media, and serially cryosectionned along a frontal plane⁶.

Group	Eye	Test Material	Dose Level	Dose Concentration	Dose Volume	# of Males	# of Females
1	OD	BSS with ICG	25 mg	2.5 mg/ml	200 µL	1	3
	OS	BSS with FITC- Dextran (MW:500,000)	10 mg	50 mg/ml	200 µL		

Table 1. Study Design



Figure 1. Everads Injecto



Figure 2. Representative thermal images showing correct delivery to the SCS with change in local temperature of the scleral surface as a result of the test material entering the SCS (blue area at T = 6 sec). Scleral surface temperature normalizes as test material's temperature equilibrates while dispersing in the SCS at T = 16 sec.

RESULTS

- Thermal images obtained during dosing indicated successful delivery into the SCS (Figure 2).
- Ophthalmic examination: no dye was observed in the vitreous humor immediately post-dosing, as well as no retinal detachment or hemorrhages associated with SCS dosing.
- IOP values increased up to 4-fold immediately post-dosing compared to baseline; however, they returned to baseline values within 30 minutes (Table 2).
- cSLO and AF images showed a wide distribution of the dye across the fundus (Figure 3) that was confirmed to be in the SCS through dissection for ICG-injected eyes (Figure 4) and by IHC on the FITC-Dextran injected eyes (Figure 5).



Figure 3. Representative cSLO image showing no dye was observed in the vitreous and AF image showing wide distribution of FITC-Dextran in the SCS.



Table 2. IOP Results

Animal ID	Evo	IOP (mmHg)						
Animarid	суе	Baseline	IMPD	30 min PD				
	OD (ICG)	21	41	20				
1	OS (FITC-Dextran)	20	67	20				
2	OD (ICG)	22	73	10				
۷	OS (FITC-Dextran)	20	22	9				
	OD (ICG)	21	92	20				
3	OS (FITC-Dextran)	20	66	22				
A	OD (ICG)	20	99	24				
4	OS (FITC-Dextran)	18	57	25				
OD = right eve: OS = left eve: IMPD = Immediately Post Dose [.] PD = Post Dose								

Figure 4. Representative image showing ICG or FITC-Dextran staining in the suprachoroidal space.



Figure 5. Images from eyes injected with FITC-Dextran showing 360-degree fluorescence in the SCS and sclera from the ora serrata to the posterior pole confirming 100 % coverage of the SCS.

CONCLUSION

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 - SI, ND, SVS and WAB None
 - YB: consultant to Everads and holds stock options
 - KMT and HD: employees at Everads and hold stock options

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• Injection into the SCS with the Everads Injector offers a simple and minimally invasive method to deliver drugs throughout the entire SCS of adult canine eyes that can be translatable to human eyes.

https://abstracts.euretina.org/2024/lb24-157-3858/r/rec5jxj51GsymuUJY

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