Treatment Efficacy and Biocompatibility of a Biodegradable Aflibercept Microsphere-hydrogel Drug Delivery System

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Financial Disclosure

- US Patents pending “Microsphere-hydrogel drug delivery system”
- NIH research grants

Summary

- We demonstrated that one injection of our 6-month aflibercept-drug delivery system (DDS) had a similar treatment efficacy compared to the multiple bolus injections of aflibercept

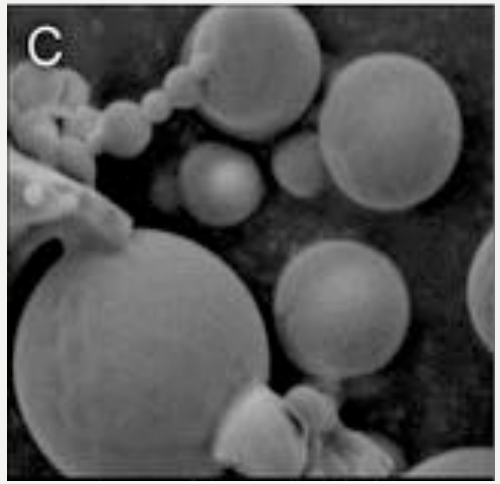
- There were no long-term functional and morphological abnormalities due to DDS injection

Anti-VEGF Therapy

- Intravitreal anti-VEGF therapy has become the first-line treatment and standard of care for wet AMD and other retinal vascular diseases

- All anti-VEGF agent therapies share a common limitation:
  - In order to be effective, a monthly (bimonthly) injection is required for durations of two years and often longer

Our Drug Delivery System (DDS)



Aflibercept-loaded microspheres

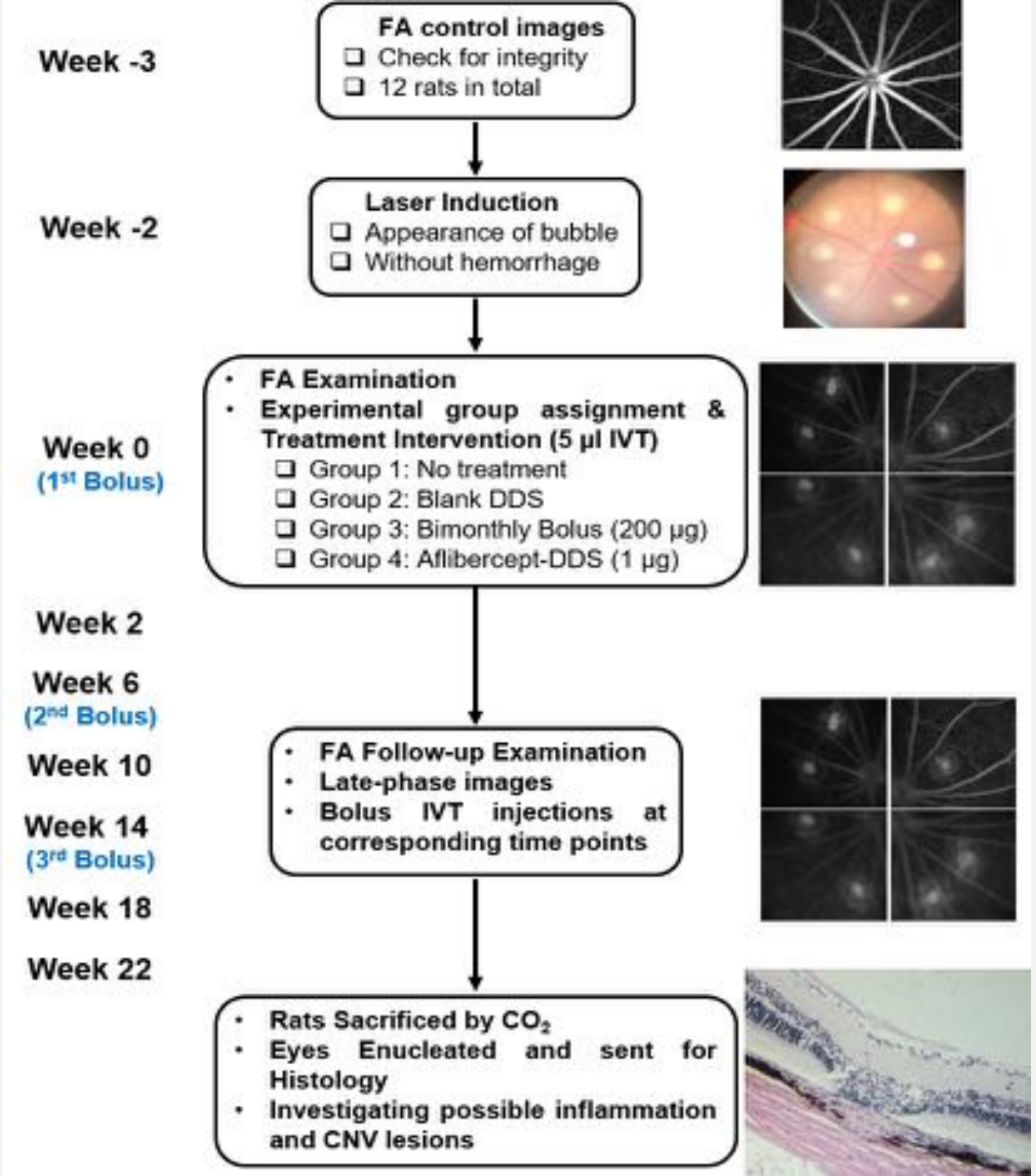
Thermo-responsive Hydrogel

- Biodegradable PLGA microspheres
  - Encapsulate Aflibercept
  - Technique to stabilize/protect the protein during manufacture process
- Biodegradable thermo-responsive hydrogel
  - Confines the microspheres to a specific delivery site
  - Eliminates inflammation caused by microsphere degradation
  - Acts as another barrier for sustained delivery
- Injectable via small gauge needles (26-30 gauge needle)
  - Intravitreal injection

Osswald and Kang-Mieler (2016)

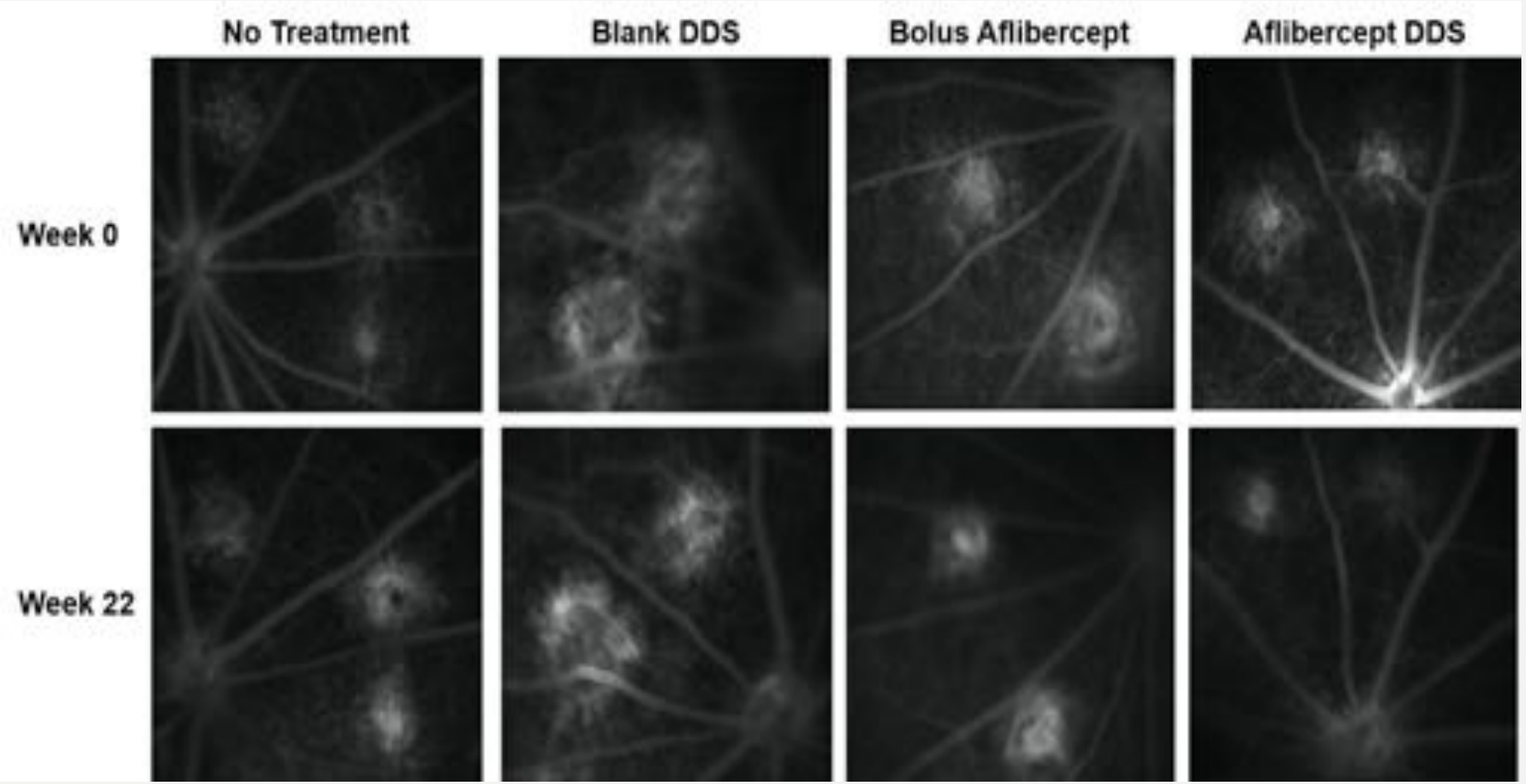
Goal of This Study

- To evaluate the treatment efficacy and biocompatibility of our biodegradable DDS
  - Treatment efficacy of aflibercept-DDS in a laser-induced CNV rodent model
  - Biocompatibility of blank-DDS (no anti-VEGF) in a normal rodent model

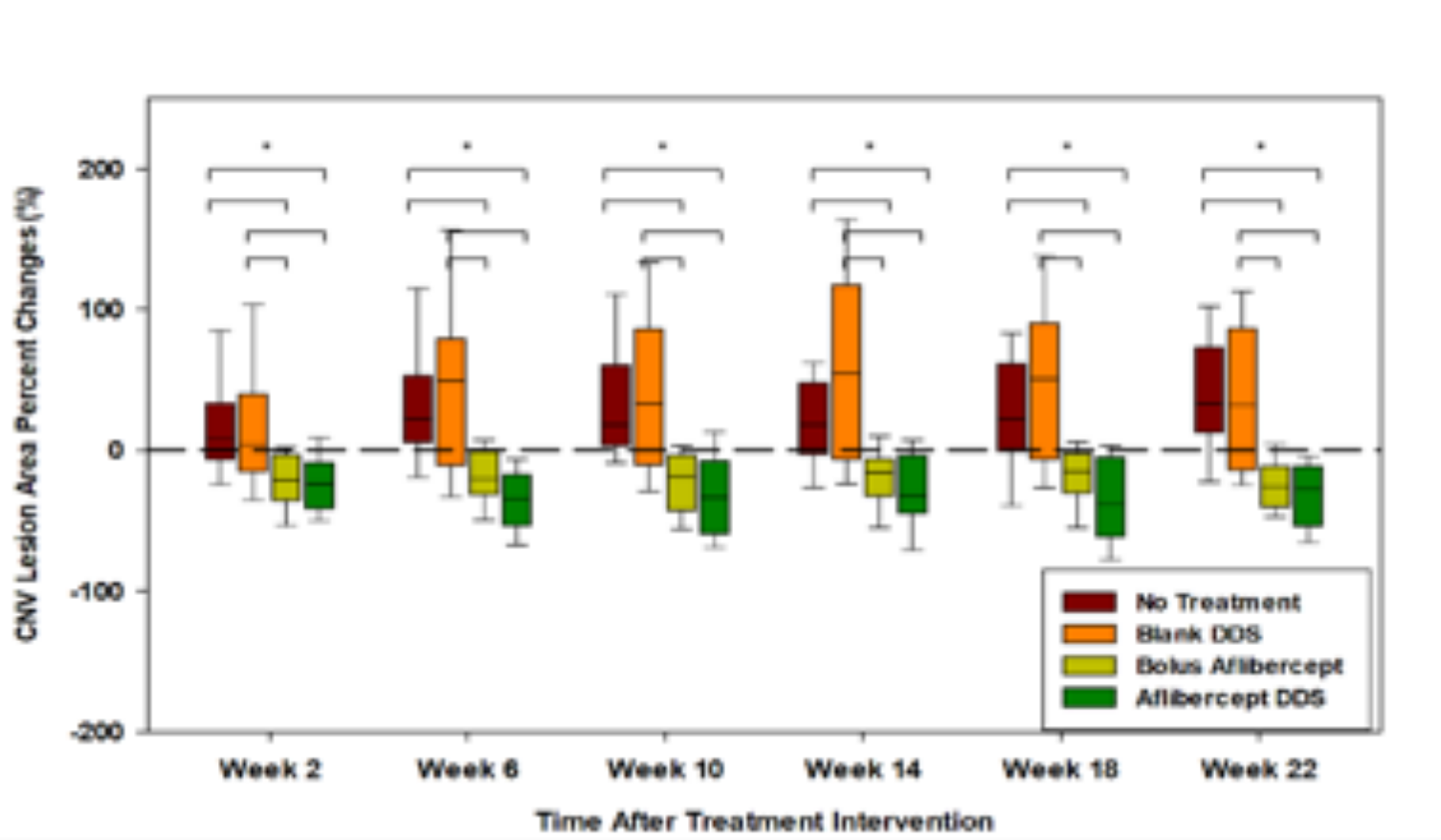


Schematic experimental design for aflibercept-DDS CNV study

Representative FA Images of CNV



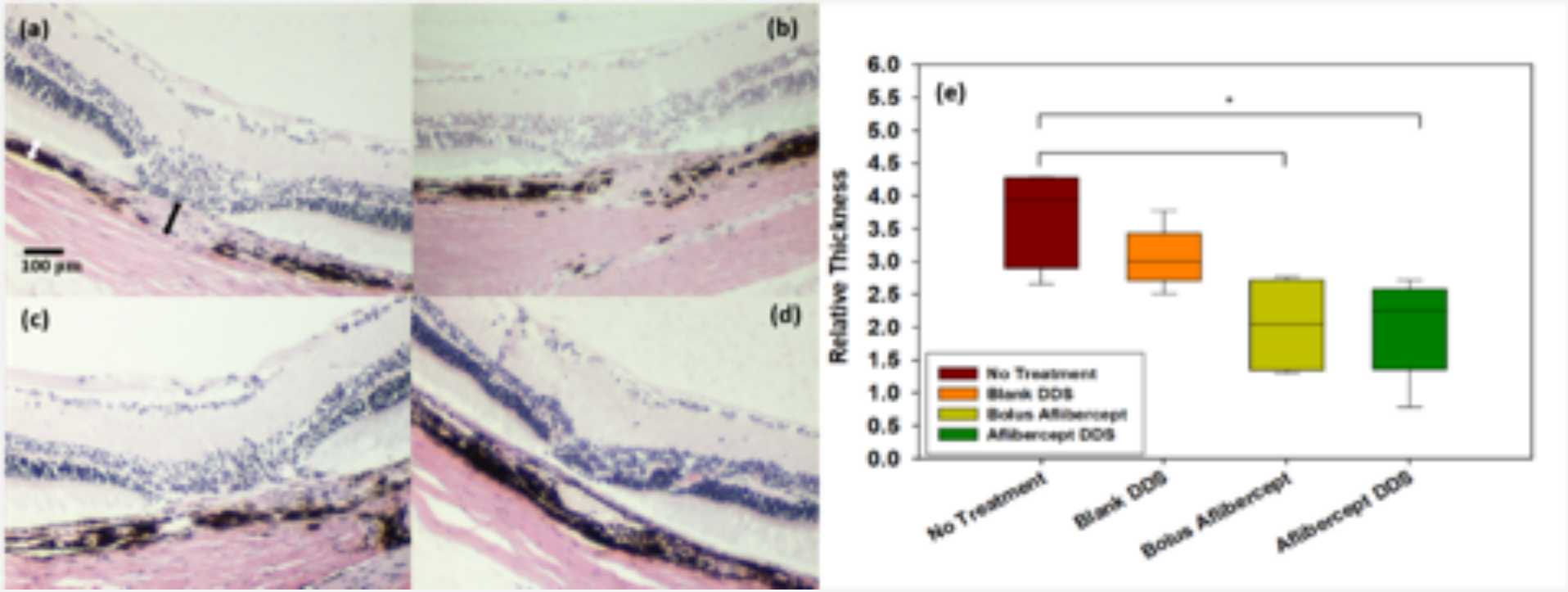
Effect of Aflibercept on CNV Lesion



- CNV lesion areas measured based on FA images and use of Multi-Otsu Threshold image analysis method

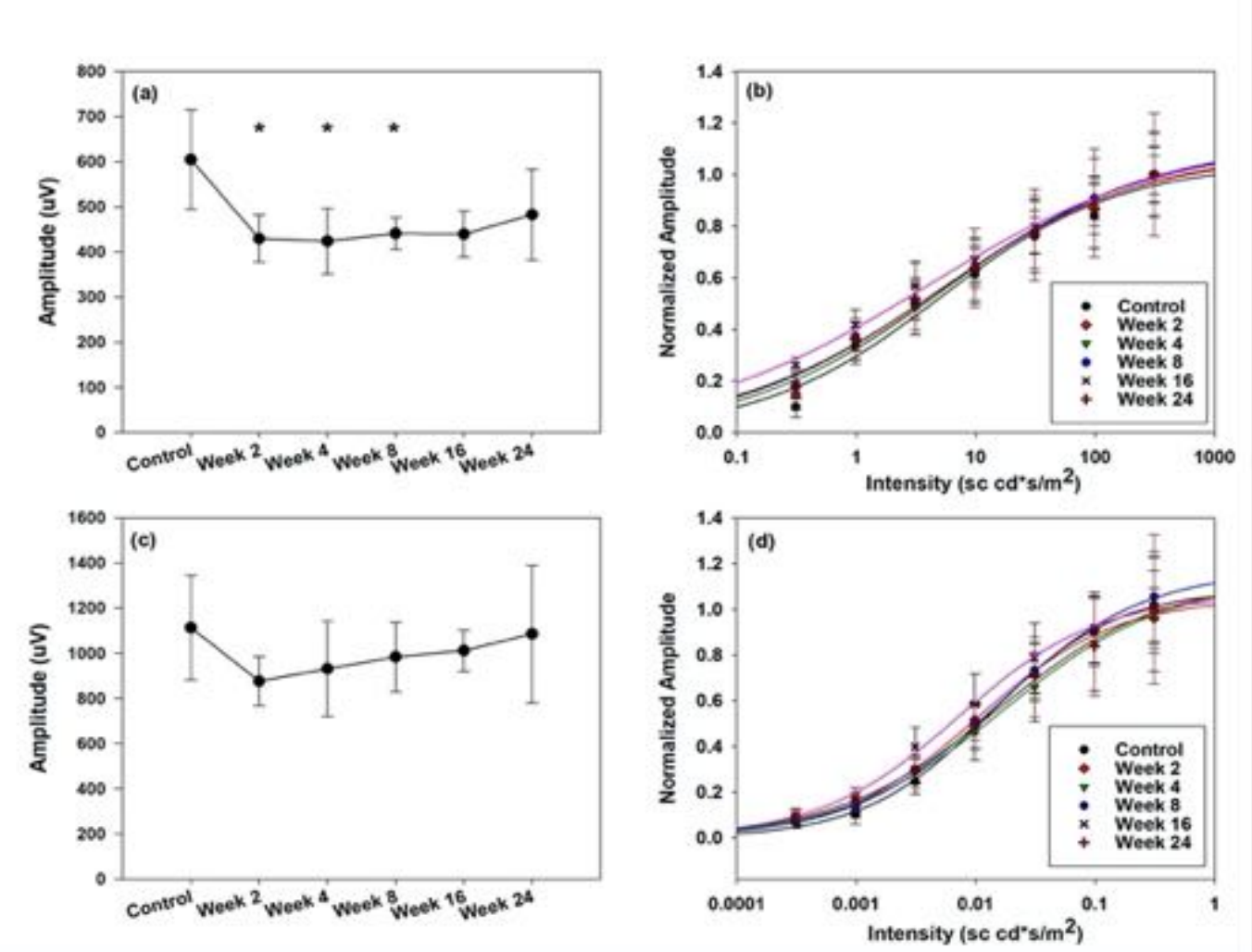
- DDS group showed a similar reduction in CNV compared to bolus treatment group
- DDS group received an overall lower dose (1 μg total vs. 600 μg total in bolus group)

Histological Analysis of CNV Lesions



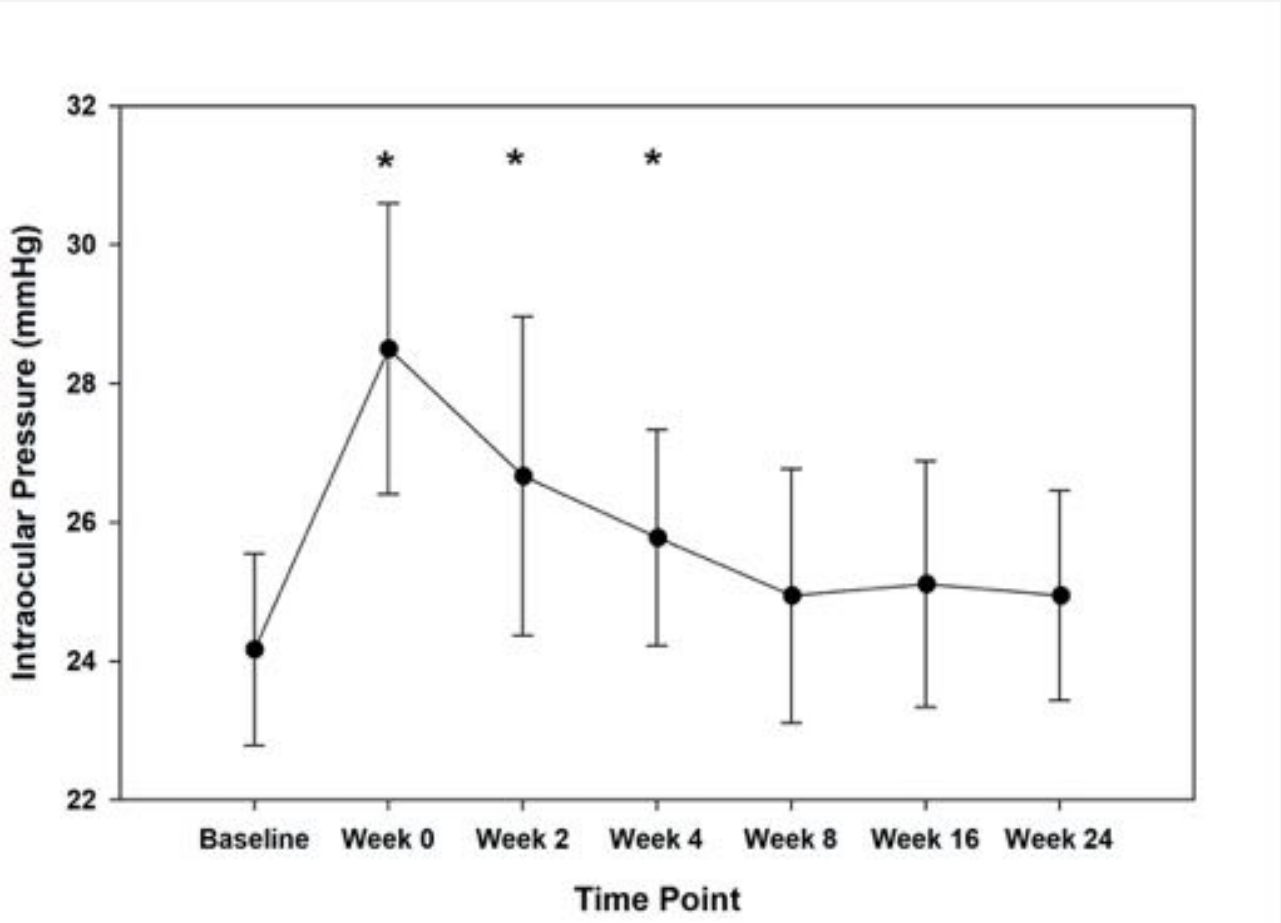
- Aflibercept-DDS group showed a similar reduction in CNV compared to the bolus aflibercept IVT treatment group

Scotopic ERG Responses Pre- and Post- Blank-DDS Injection



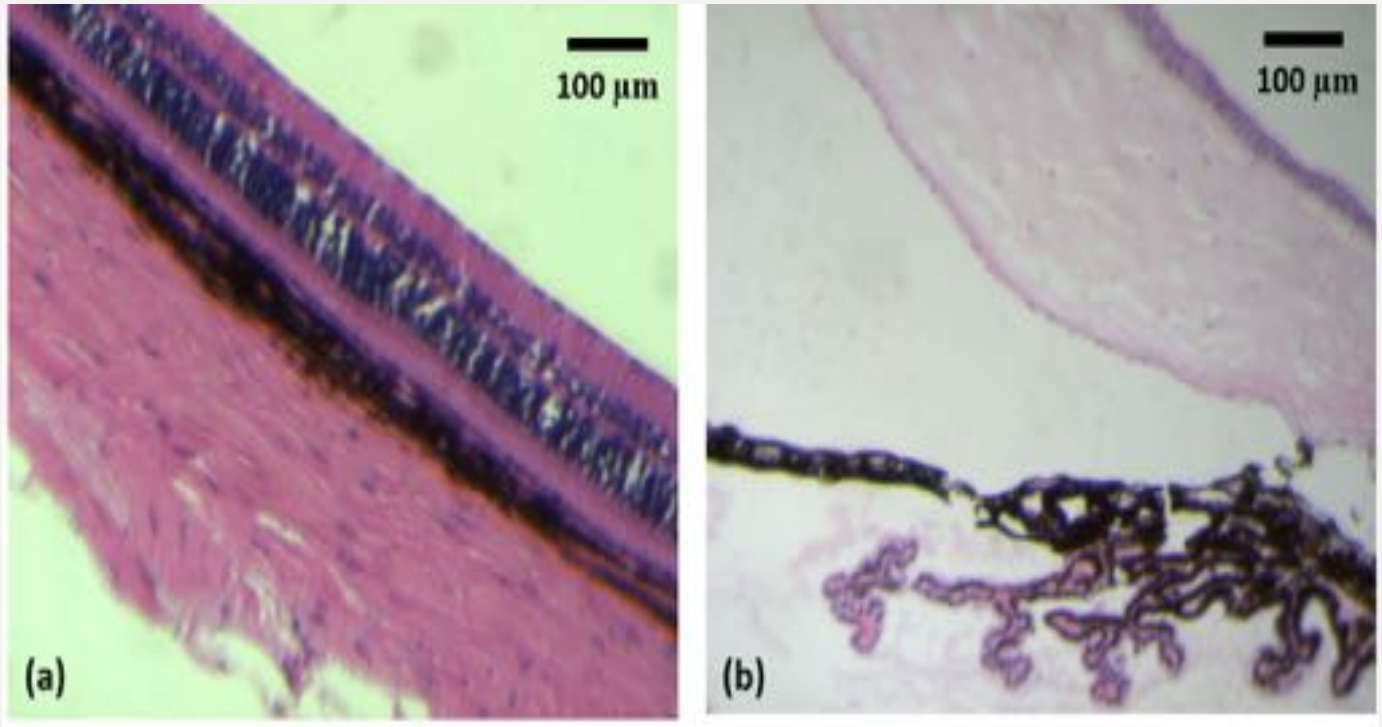
- Small transient changes in the maximal a-wave amplitude and the b-wave sensitivity
- No long-term physiological effects

IOP Measurement Pre- and Post-IVT Injection of Blank-DDS



- Transient increase in IOP immediately after DDS IVT injection
- IOP returned to baseline

Endpoint Histopathology of Blank-DDS IVT Injection



- No signs of chronic inflammatory responses or foreign body reactions in both the posterior and anterior segments.

Summary

- Aflibercept-DDS group received an overall lower dose (1 μg total vs. 600 μg total in bolus group), but had a similar CNV reduction compared to the aflibercept-bolus IVT injection treatment group
- Transient changes in ERG and IOP were observed with no long-term effects
- No chronic inflammation or other abnormalities were observed

Summary

- In this study, we demonstrated that our aflibercept-DDS was effective, safe and well-tolerated
- Our aflibercept-DDS is advantageous over current IVT bolus regimen in terms of less injections and lower overall dose needed

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