

Oral scutellarin treatment preserves retinal structure and visual function in a retinal neurodegeneration model

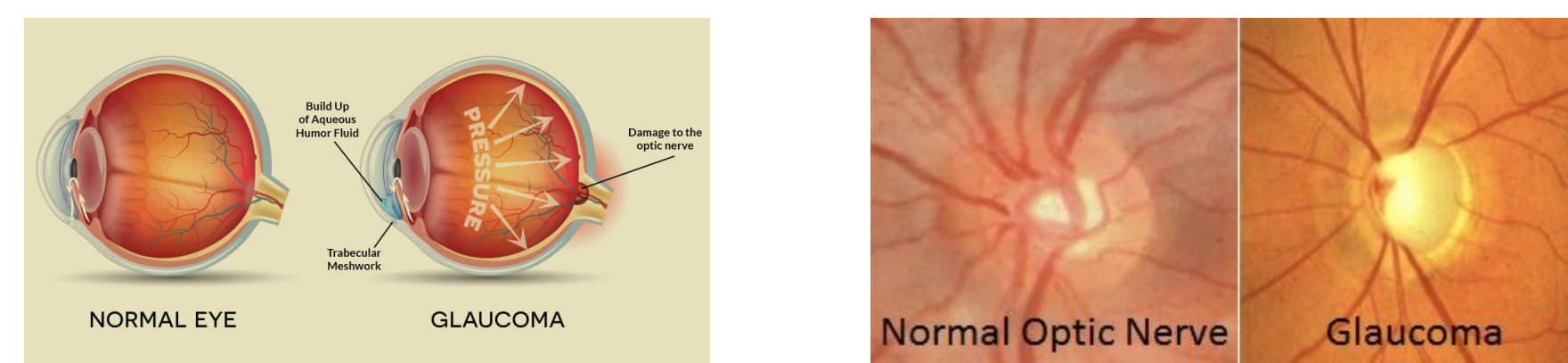
Eva Yarsky, Jingyuan Zhu, Anoop Sainulabdeen, Krystal Akers, Vishnu Adi, Jeffrey R. Sims and Kevin C. Chan

Department of Ophthalmology, NYU Grossman School of Medicine, NYU Langone Health, New York University, New York, NY

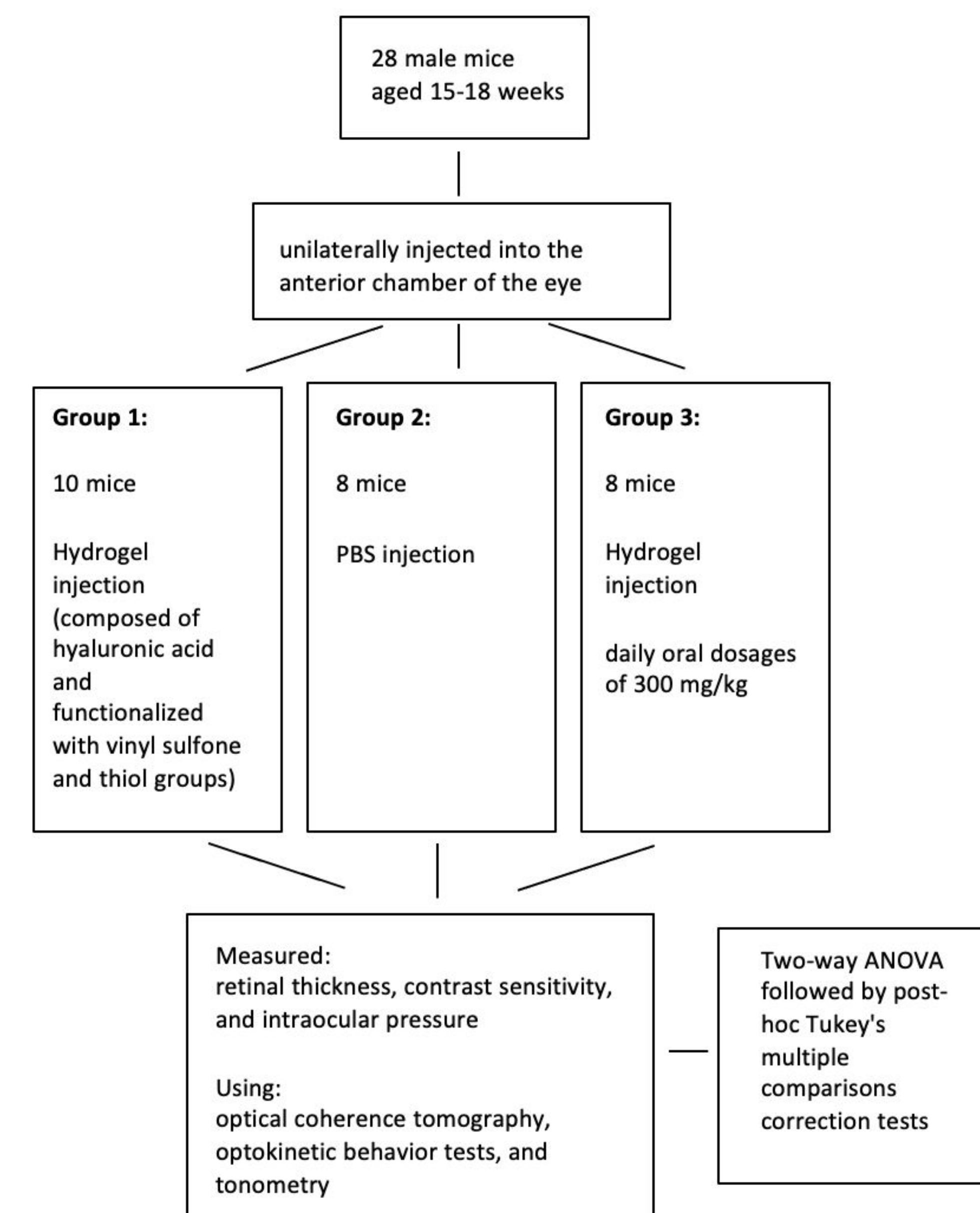
Introduction

Glaucoma is a neurodegenerative disease that is characterized by elevated IOP (intraocular pressure) and results in RGC (retinal ganglion cell) death, leading to irreversible blindness. It is difficult to study glaucoma in a pre-clinical setting because there are currently no *in-vivo* glaucoma models which maintain optical clarity and allow for retinal imaging. Present models rapidly degrade and are not conducive to longitudinal studies. Scutellarin is a plant extract from the herb *Erigeron breviscapus*. A Flavone glucuronide (5,6,4'-trihydroxyflavone-7-O-glucuronide), It has been shown to have protective effects on inflammation.

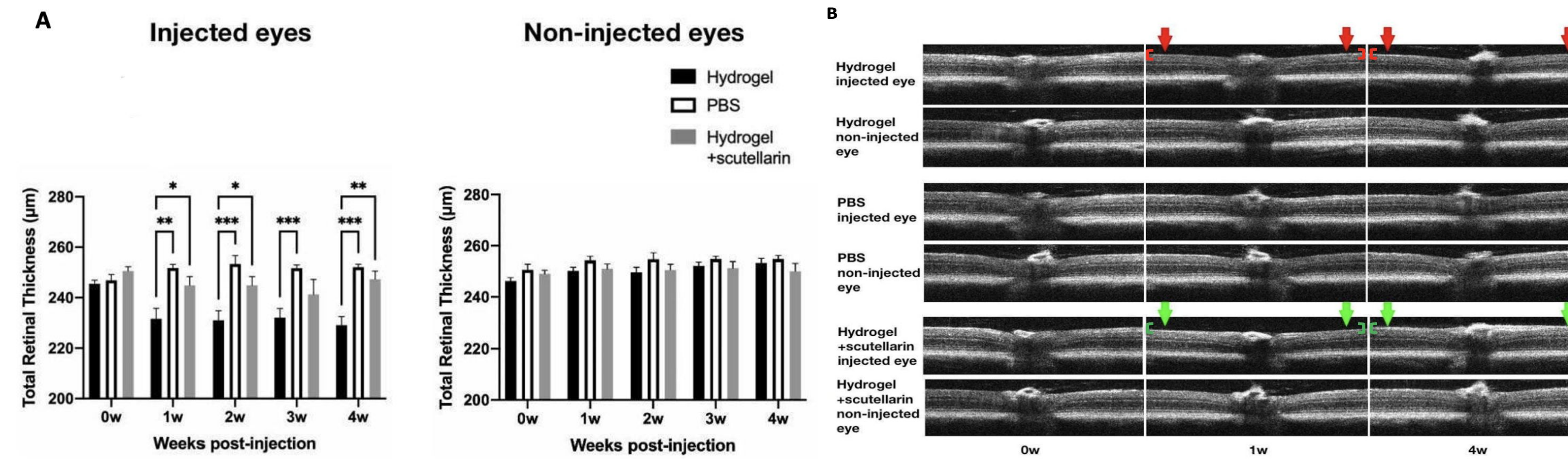
Purpose: Analyze whether the administration of oral scutellarin alleviates the effects of glaucoma while testing the efficacy of a new hydrogel model that relies on a gelatinous polymer combination being injected into the anterior chamber of the eye and stimulating glaucoma.



Experimental protocol

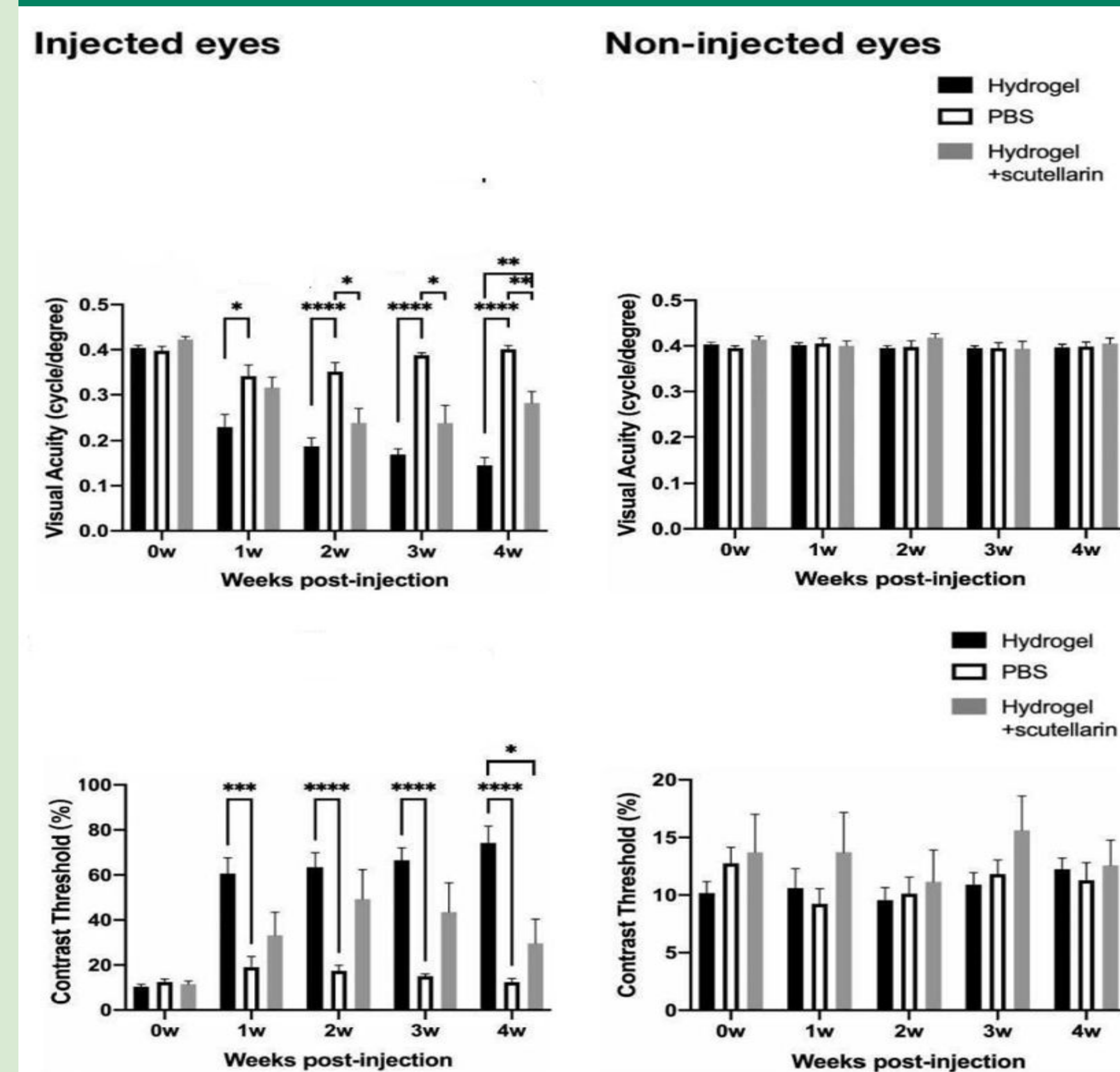


Scutellarin improves retinal thinning



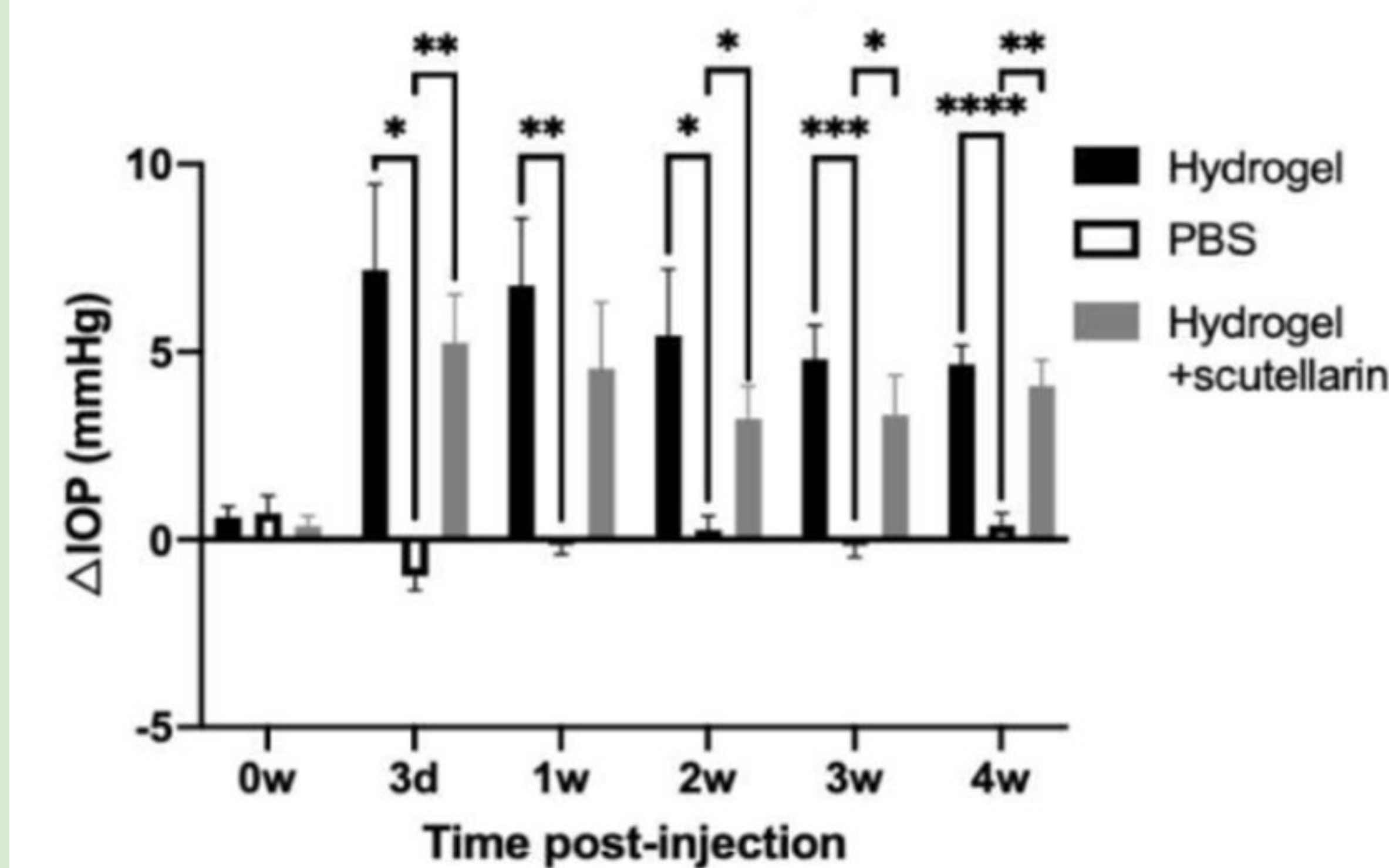
Analysis of effects of scutellarin on total retinal thickness. (A) Quantitative comparison of total retinal thickness across Group 1, Group 2 and, Group 3. (B) Cross sectional retinal images from both injected and non-injected eyes of a representative mouse in each of the 3 groups at 0 weeks, 1 week, and 4 weeks, generated using optical coherence tomography. Red arrows and brackets indicate significant retinal thinning in the injected eye of the hydrogel-only group. Green arrows and brackets indicate less extreme retinal thinning in the injected eye of the hydrogel+scutellarin group.

Mild effect on vision



Quantitative analyses for visual acuity and contrast threshold in the injected (left column) and non-injected eyes (right column) for Group 1, Group 2, and Group 3.

No effect on IOP



Inter eye comparison of IOP after unilateral intracameral injections. Intraocular pressure was measured over the course of five weeks for Group 1, Group 2, and Group 3.

Conclusions and discussion

TRT:

- Greater retinal thinning in injected eyes of the hydrogel-only group than in the injected eyes of hydrogel+scutellarin group ($P < 0.01$).

Optokinetic response:

- No significant difference in optokinetic responses between the three groups ($P > 0.05$).
- VA (visual acuity) and CT (contrast threshold) was reduced to a greater extent in the hydrogel-only than in the hydrogel+scutellarin groups.

IOP:

- Inter IOP difference was significantly higher in the hydrogel only group and the hydrogel+scutellarin group when compared to the PBS group ($P < 0.01$).
- No significant difference between Δ IOP of hydrogel-only and hydrogel+scutellarin groups ($P > 0.05$).

Discussion:

- Hydrogel model was effective at mirroring the effects of glaucoma by increasing the IOP while maintaining a clear optical media over a long term period.
- Scutellarin had a significant effect on improving retinal thinning and visual behavior deficits.
- The administration of scutellarin had no significant effect on retinal thickness, IOP, or optokinetic measurements.
- The study was limited by the bioavailability and physiological fluctuations from anaesthesia during IOP measurements.

Future directions

- Hydrogel Model can be applied to future, longitudinal glaucoma neurodegeneration studies.
- Scutellarin should be studied as a neurotherapeutic agent for diseases that do not involve elevated IOP.
- Bioavailability of oral scutellarin can be increased by binding it to B12 derivatives-modified nanoparticles.
- Anesthesia based data fluctuations can be avoided in future studies by introducing behavioral training and awake IOP measurements.

Acknowledgements

Department of Ophthalmology, NYU Grossman School of Medicine, NYU Langone Health, New York University, New York, NY
 • Including Jingyuan Zhu and Kevin C. Chan.