

Intraoperative Pressure Levels for Creating Blebs During Subretinal Delivery of Ocular Gene Therapy

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Summary

- These data characterize the intraoperative pressure levels for creating retinal blebs during sub-retinal delivery of gene therapy.
- There was slight variation in the intraoperative pressure levels required to initiate a retinal bleb across conditions.
- There appeared to be greater variation in maximum intraoperative pressure levels for bleb propagation with higher pressures required for younger patients.
- These results will allow us to further refine our surgical technique for subretinal delivery of ocular gene therapy.

Mendelian diseases of the outer retina

Clinical challenges:

- Often progressive and lead to blindness
- >100 genes known to be affected
- Effective therapy must **correct** or **replace** photoreceptors

Be able to treat *every* affected person

Optimization of retinal gene therapy

Increasing Efficacy

- Photoreceptor transduction: Vector, Route, Dose
- Timing in various disease state

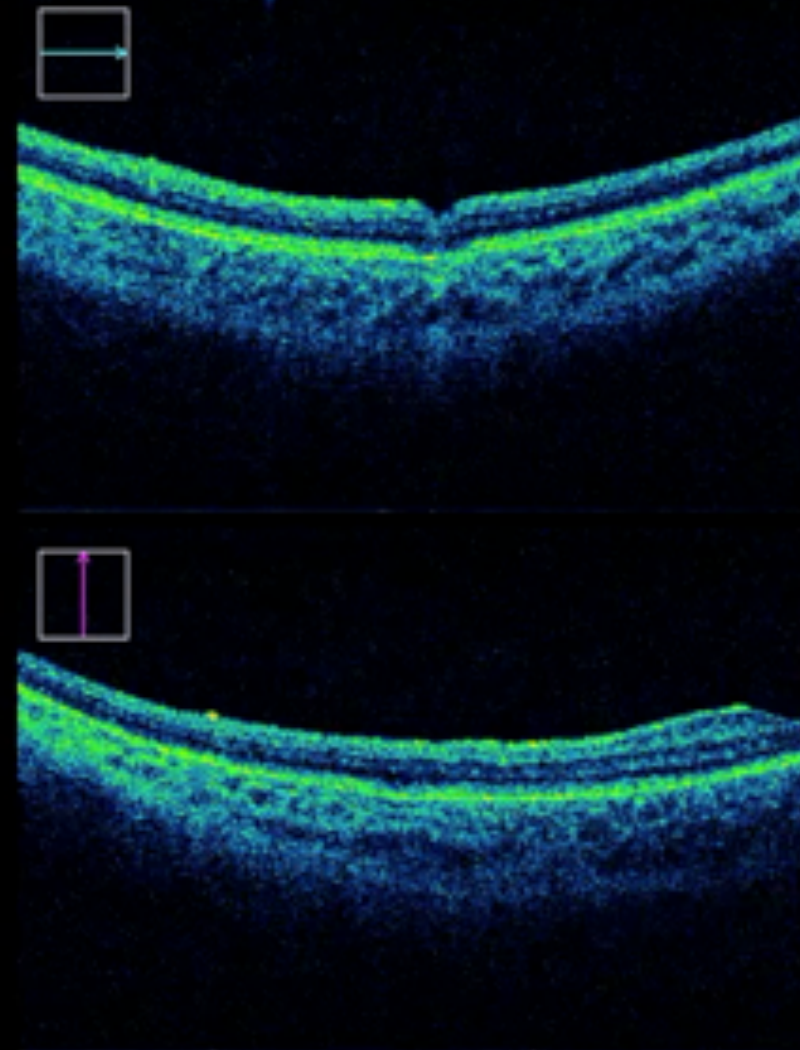
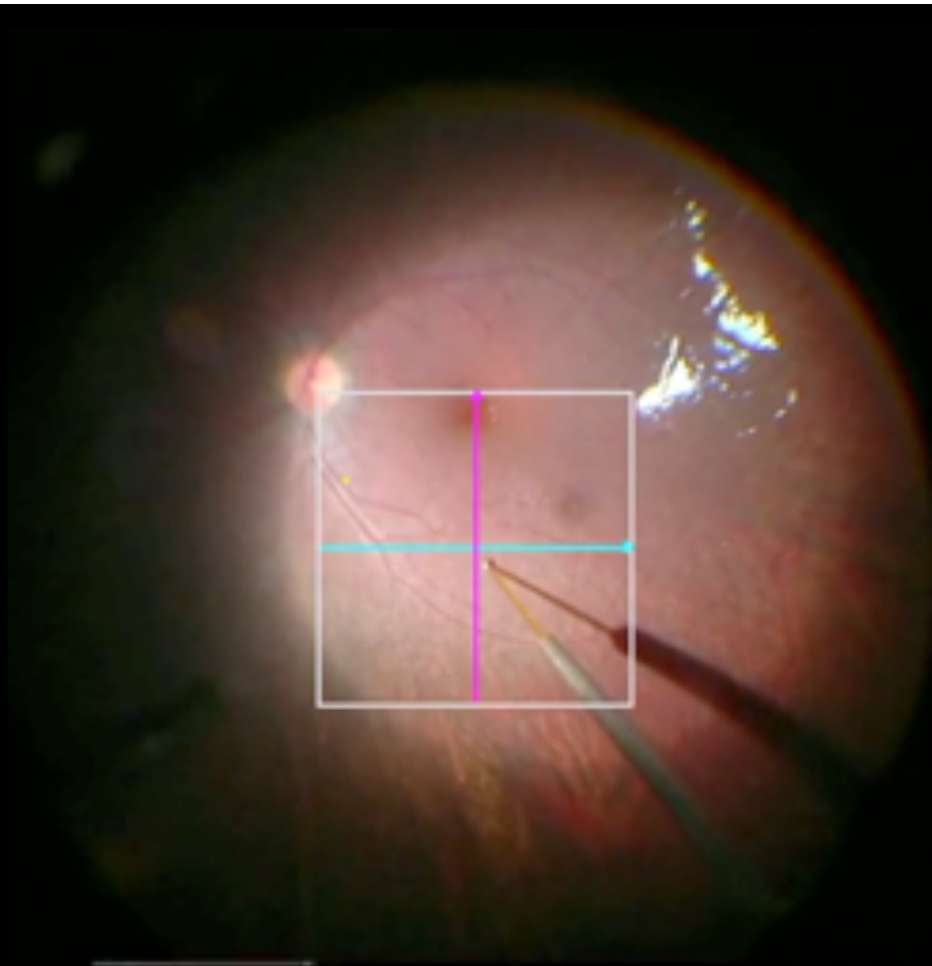
Decreasing Failure Rate & Complications

- Rejection/Inflammation/Tumorigenicity
- Good manufacturing practice
- **Improve safety of subretinal injections and surgical protocols**

Subretinal injection technique



CASEY EYE
Institute



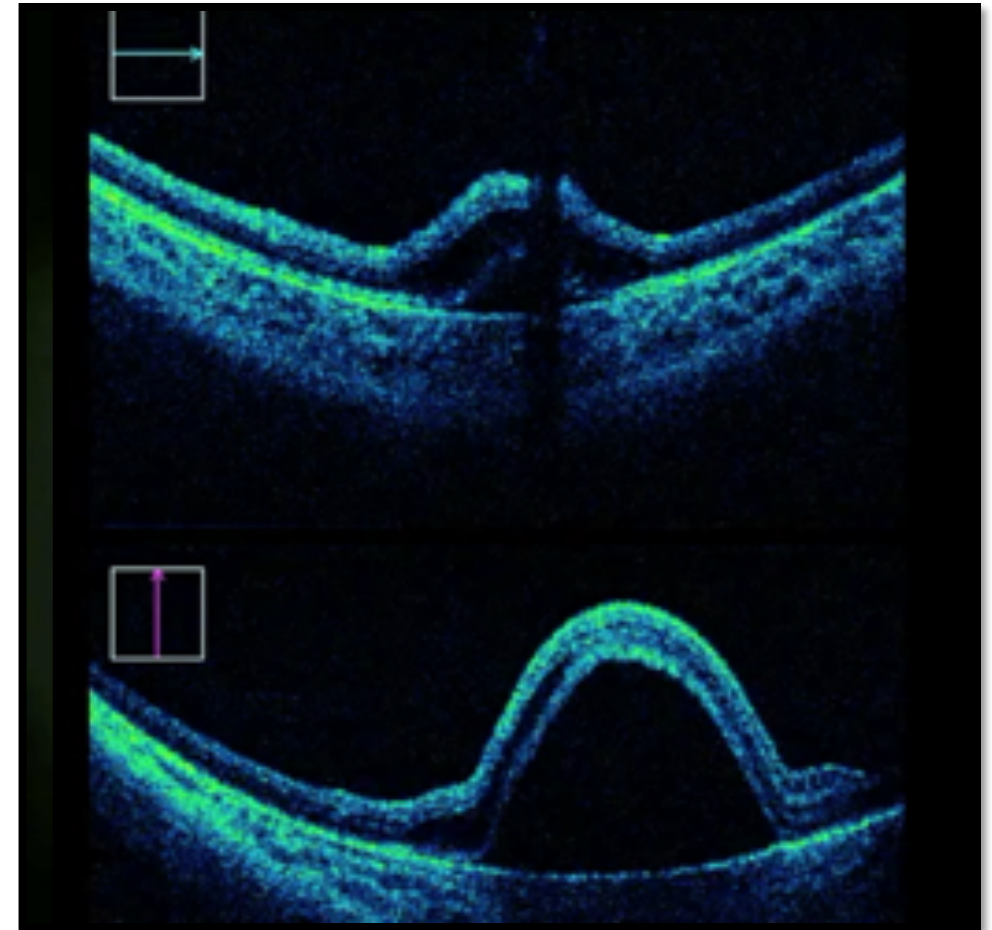
Project specific aims

- To characterize the intraoperative pressure levels for creating retinal blebs during subretinal delivery of ocular gene therapy.

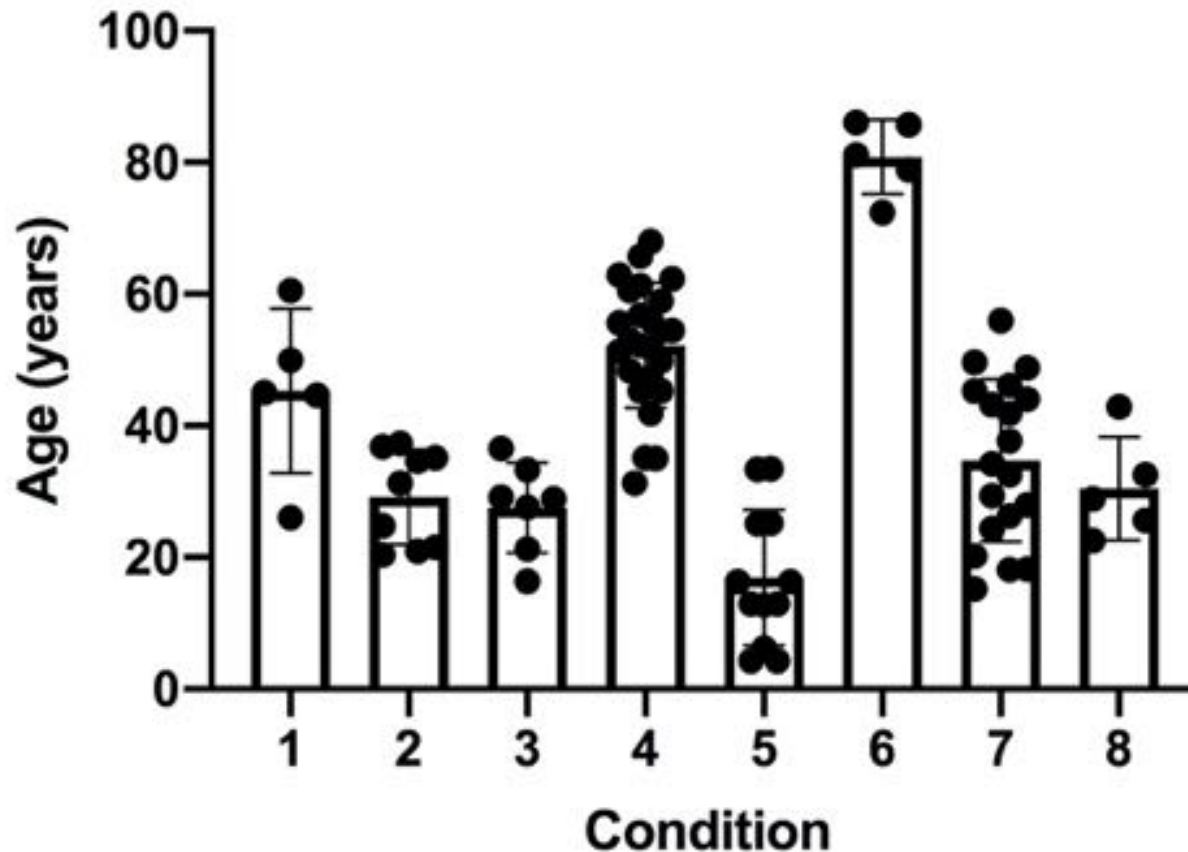
- To evaluate age and condition as related to surgical difficulty

BSS pre-bleb:

- Max pressure
 - Pre intra-op and post-op
- Bleb propagation:**
- Coherence tomography data
 - Min & max pressures
 - Conditions

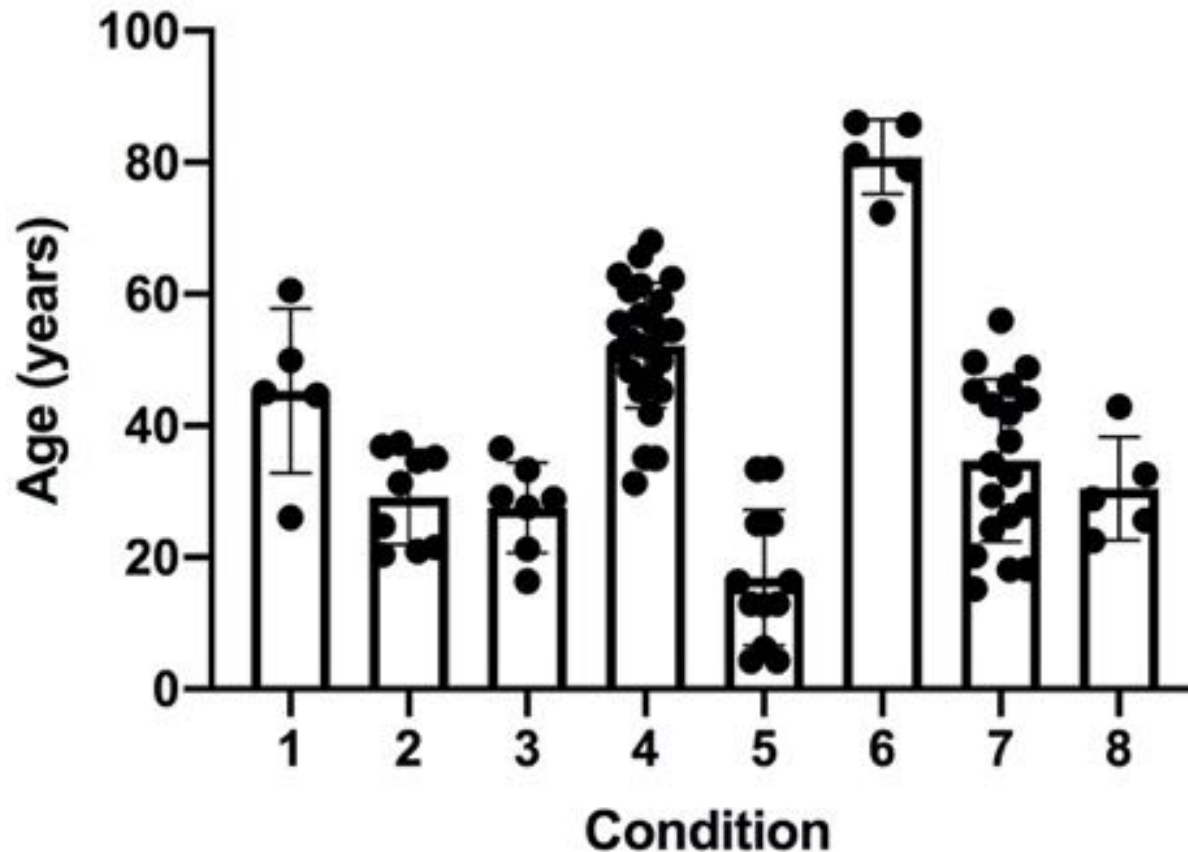


Subretinal gene therapy at CEI



- **112** ocular gene therapy patients
- **56** treated using pneumatic-assisted subretinal delivery
- Various conditions
- Median age: 36.5yrs (4—86)

Subretinal gene therapy at CEI

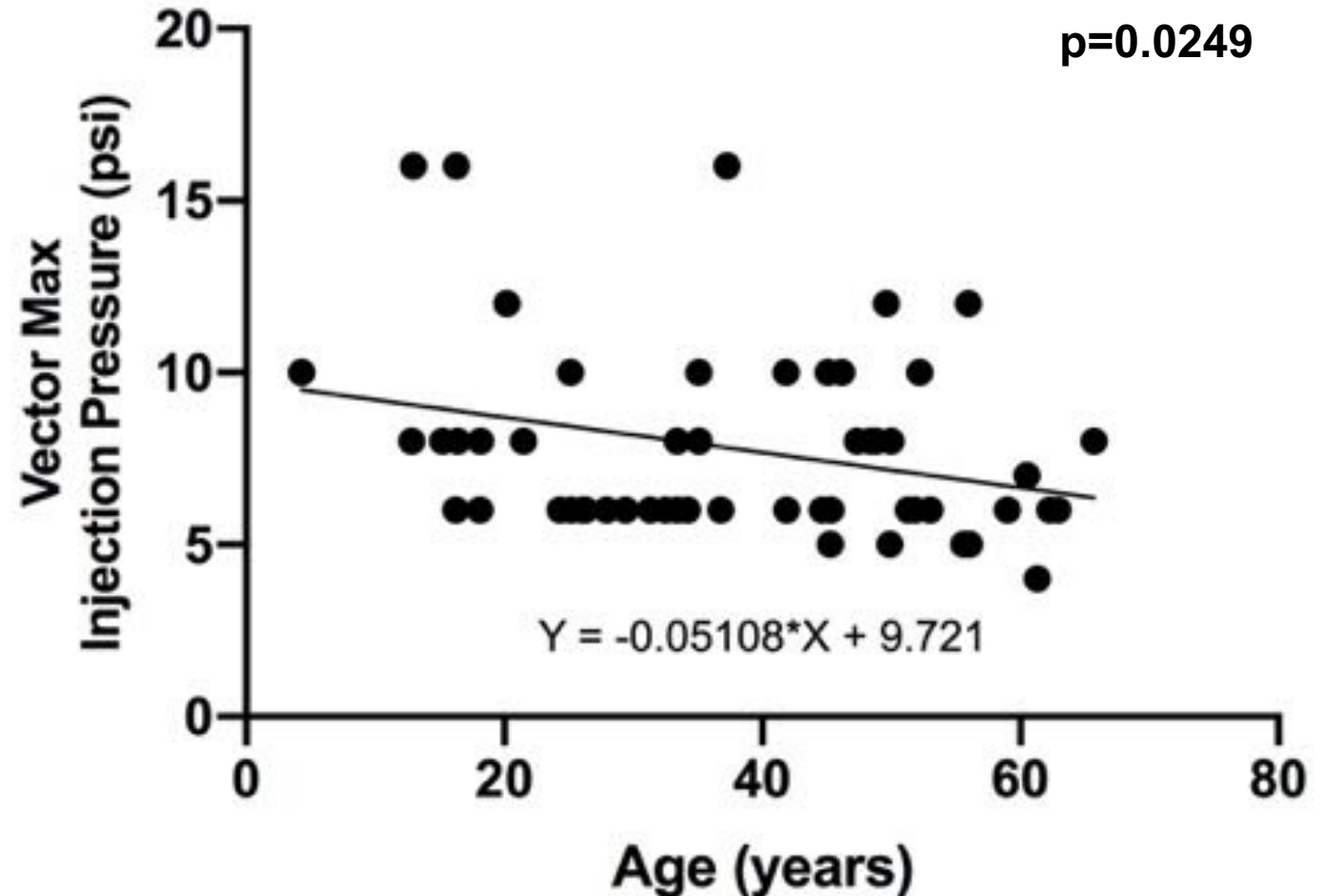


- **BSS pre-bleb formation:**
 - Average volume: 39.8 μ L
 - Range: 10—100 μ L
 - Average Max Pressure: 9.5 PSI (8.8—10.1 PSI)
 - Range: 4—20 PSI

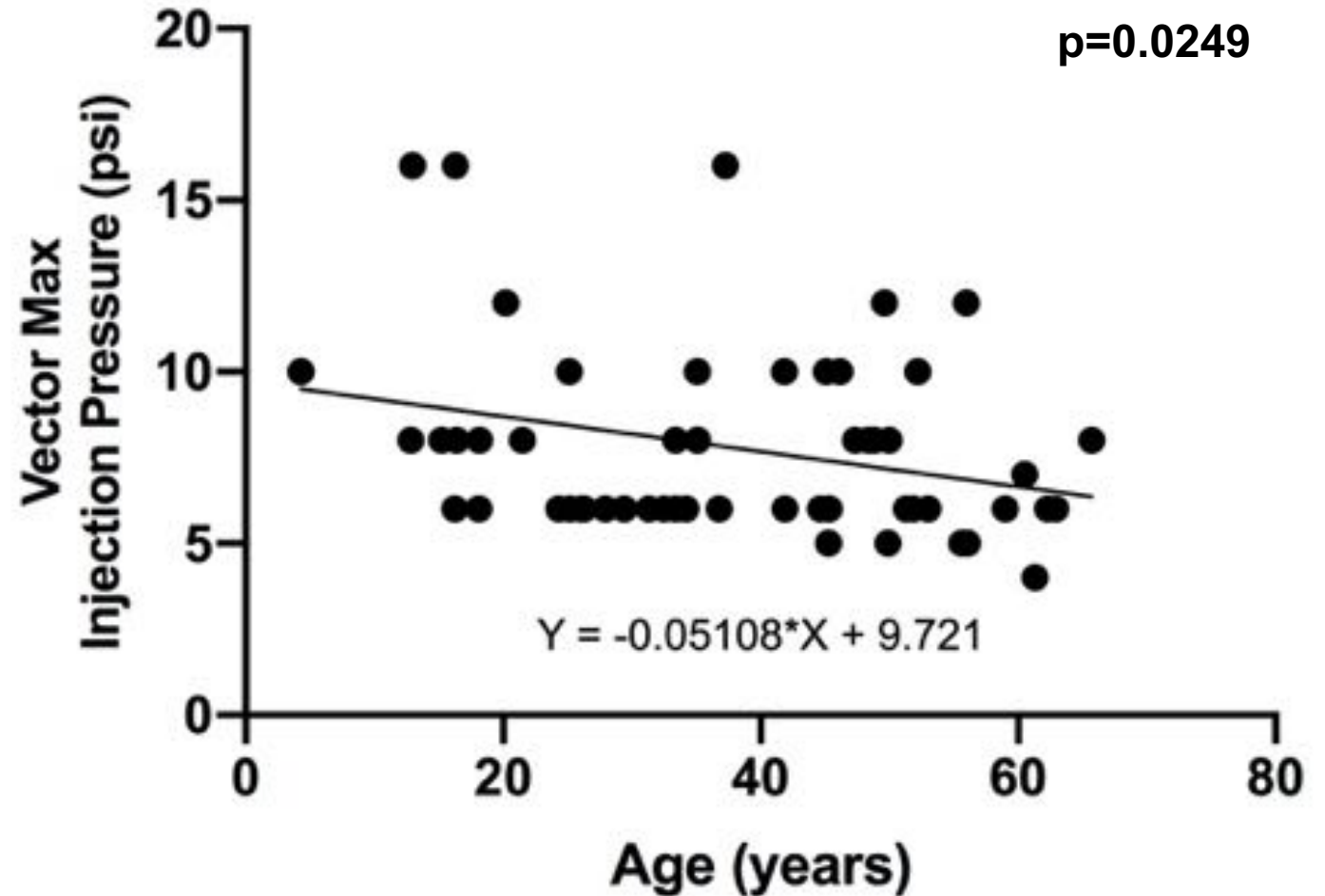
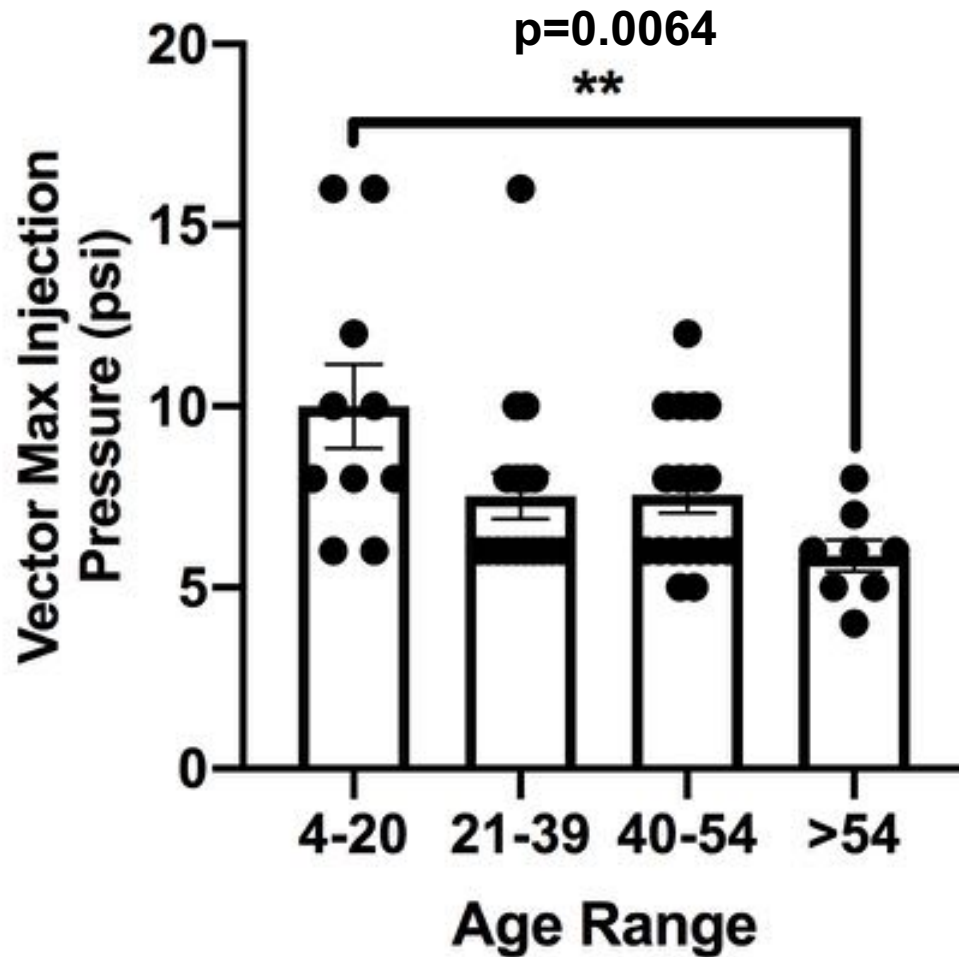
Retinal bleb propagation for vector delivery

■ Bleb propagation:

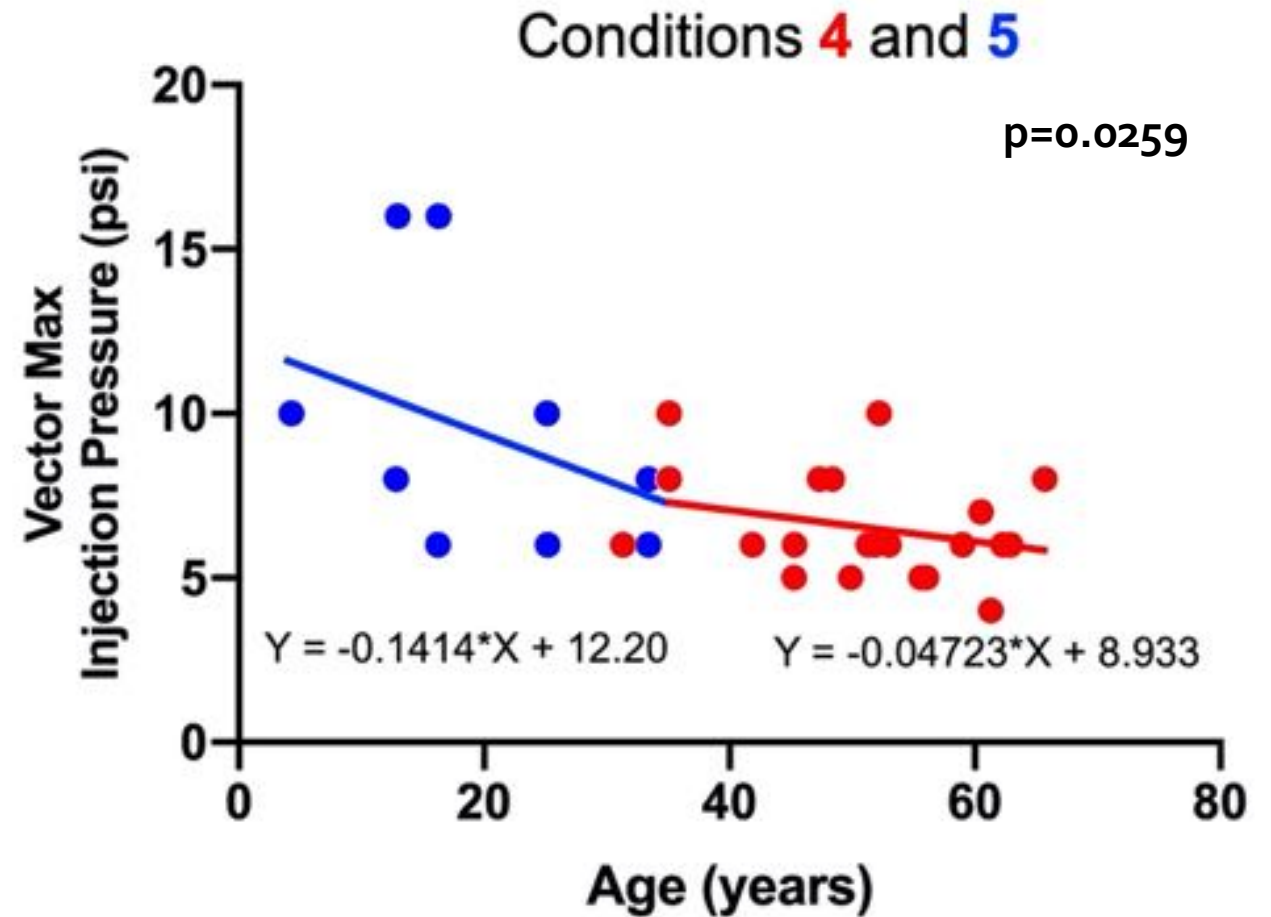
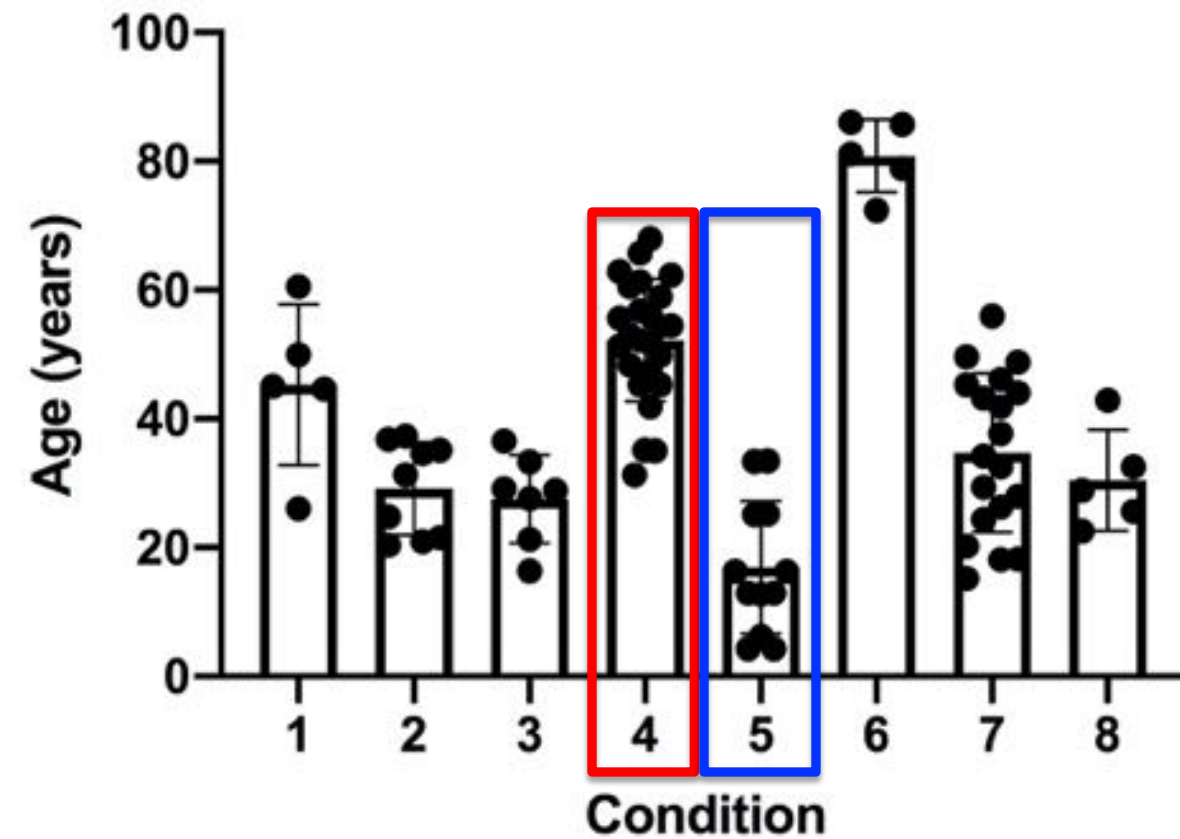
- Average volume: 211.5 μ L
 - Range: 20—450 μ L
- Average min pressure: 4.4 PSI (3.7—5.3 PSI)
 - Range: 2—10 PSI
- Average max pressure: 7.7 PSI (6.6—9.6 PSI)
 - Range: 4—16 PSI



Age affects maximum vector injection pressure



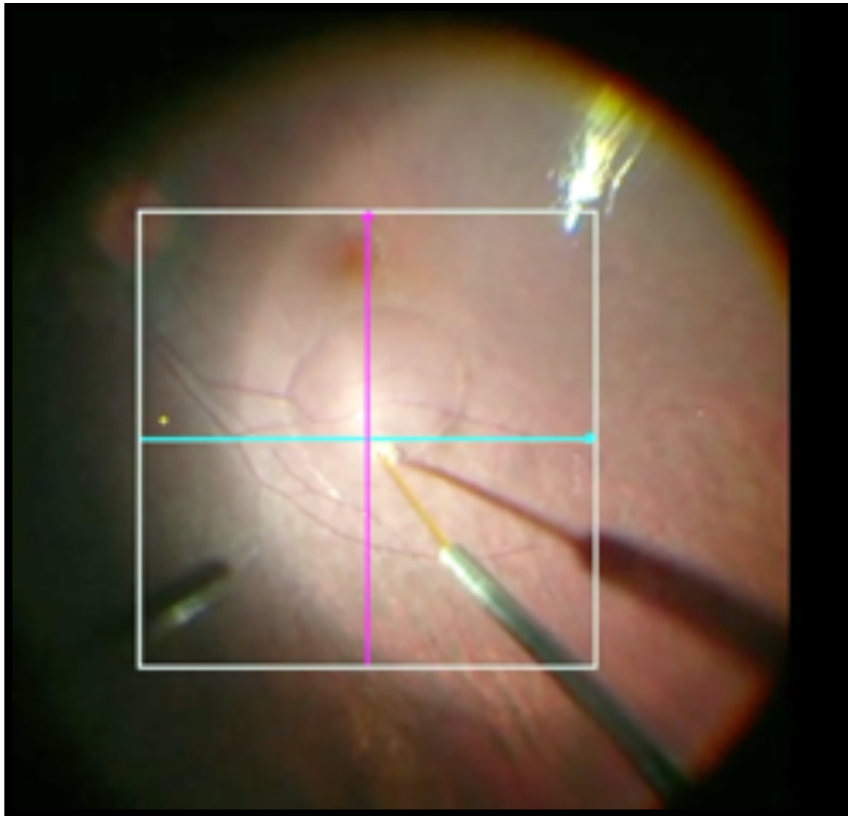
Age affects maximum vector injection pressure



Optimizing subretinal injections

■ Future studies:

- Long-term evaluation of post-operative OCT and outcomes stratified by age, condition, and intra-operative injection pressures
- Continued review of intra-operative OCT and video to evaluate angle of retinotomy, vector egress, etc.
- Comparison of outcomes, including vision, complication rates (macular hole), microperimetry, etc.



Conclusions

- The eye is an excellent target for gene therapy.
- These data characterize the intraoperative pressure levels for creating retinal blebs during sub-retinal delivery of gene therapy.
- There was slight variation in the intraoperative pressure levels required to initiate a retinal bleb across conditions.
- There appeared to be greater variation in maximum intraoperative pressure levels for bleb propagation with higher pressures required for younger patients.
- These results will allow us to further refine our surgical technique for subretinal delivery of ocular gene therapy.

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