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

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

To evaluate age and condition as factors related to surgical difficulty and outcomes.

To compare intra-op and post-op optical coherence tomography data across conditions.

**BSS pre-bleb:**
- Max pressure

**Bleb propagation:**
- Min & max pressures
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: 39.8µL
    - Range: 10—100µL
  - Average Max Pressure: 9.5 PSI (8.8—10.1 PSI)
    - Range: 4—20 PSI
**Bleb propagation:**

- **Average volume:** 211.5µL
  - **Range:** 20—450µL
- **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

\[ Y = -0.05108 \times X + 9.721 \]
Age affects maximum vector injection pressure

p = 0.0064

p = 0.0249

Right panel: Regression analysis

Y = -0.05108X + 9.721

p = 0.0249
Age affects maximum vector injection pressure

Conditions 4 and 5

\[ Y = -0.1414X + 12.20 \]

\[ Y = -0.04723X + 8.933 \]
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.
References

Dr. Andreas Lauer
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