Duke Eye Center

Microscope-integrated optical coherence tomography guided volumetric measurements of subretinal blebs created by a novel suprachoroidal approach

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- **Joseph A. Izatt:**
  - Leica Microsystems: patents, royalties
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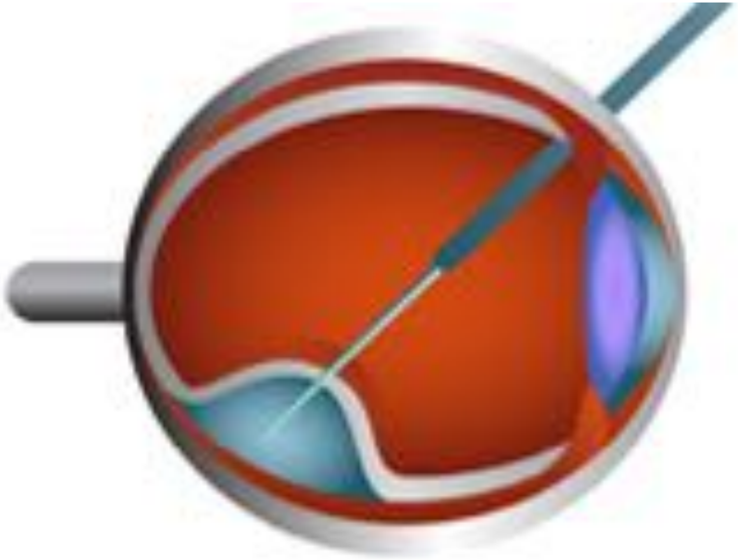
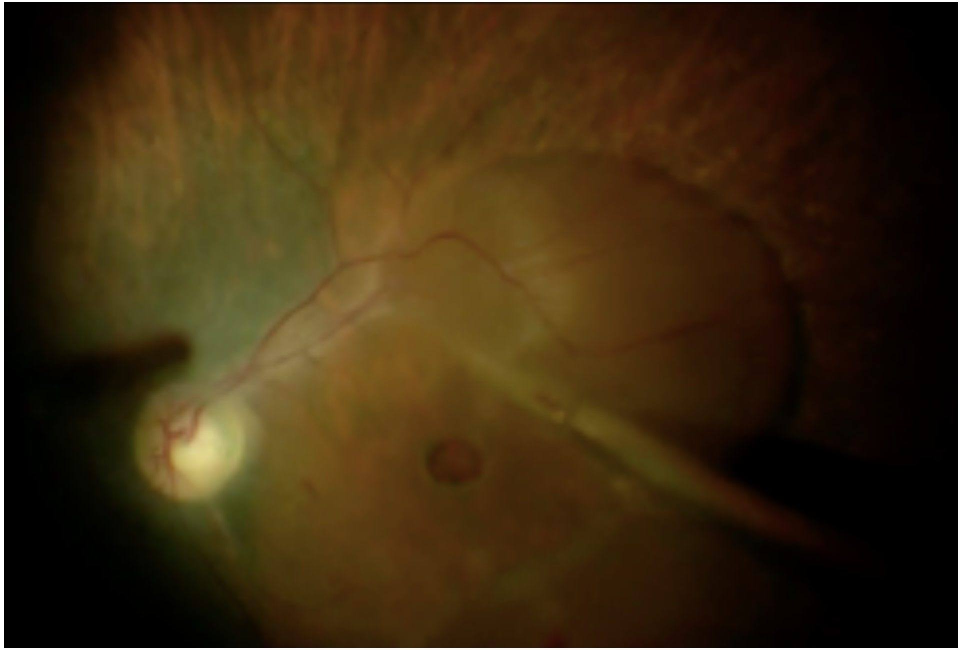
Summary

- The volume of subretinal blebs created by a novel suprachoroidal cannula was calculated by a microscope-integrated OCT (MIOCT) image-based method with accuracy and precision
- The mean volume delivered into the subretinal space as measured by the MIOCT imaging method was 82.48% of the expected injection volume

Subretinal Drug Delivery





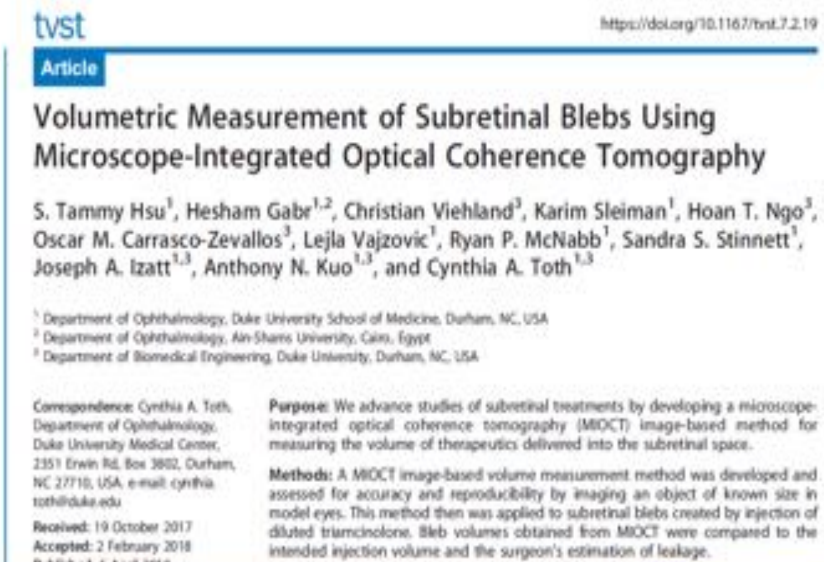
Source: https://physicians.dukehealth.org/articles/mioct-facilitates-accurate-measurement-subretinal-injection-volumes

Limitations of Current Surgical and Visualization Techniques

- Technical challenges of vitrectomy in pediatric population
- Poor visualization of subretinal space
- Reflux of viral vector into the vitreous cavity
- Uncertainty of volume delivered

Volume Loss During Subretinal Injections

- Sub-retinal injection of 50 μL attempted in 11 porcine eyes
- In 7/11 eyes, reflux of fluid into vitreous cavity observed
- In remaining four eyes, volume loss calculated to be between 12-72%



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Article

Volumetric Measurement of Subretinal Blebs Using Microscope-Integrated Optical Coherence Tomography

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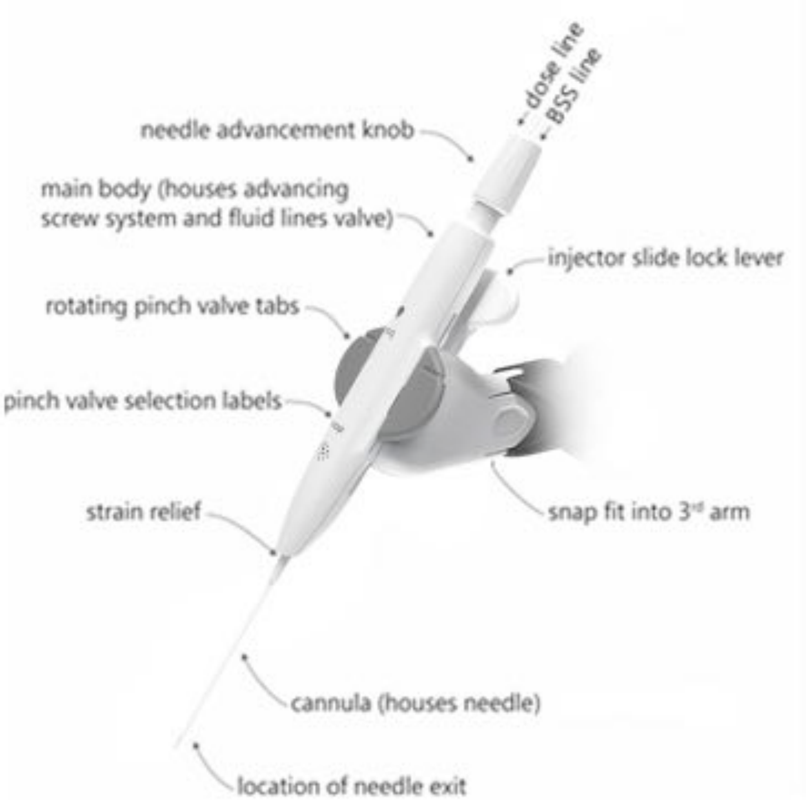
Purpose: We advance studies of subretinal treatments by developing a microscope-integrated optical coherence tomography (MIOCT) image-based method for measuring the volume of therapeutics delivered into the subretinal space.

Methods: A MIOCT image-based volume measurement method was developed and assessed for accuracy and reproducibility by imaging an object of known size in model eyes. This method then was applied to subretinal blebs created by injection of diluted triamcinolone. Bleb volumes obtained from MIOCT were compared to the intended injection volume and the surgeon's estimation of leakage.

Subretinal Delivery via Suprachoroidal Approach



Safety and Efficacy of Subretinally Administered Palucorcel for Geographic Atrophy of Age-Related Macular Degeneration

Phase 2b Study

Jeffrey S. Heier, MD,[1] Allen C. Ho, MD,[2] Michael A. Samuel, MD,[3] Tom Chang, MD,[3] Christopher D. Riemann, MD,[4] John W. Kitchens, MD,[5] Jason S. Slakter, MD,[6] Yannek I. Leiderman, MD, PhD,[7] Rand Spencer, MD,[8] George A. Williams, MD,[9] Sheila B. Hickson-Curran, MCOptom,[10] Michael Keane, MS,[10] James S. Baldassarre, MD,[10] for the Prelude Study Group

Purpose: To evaluate safety and successful use of a novel subretinal delivery system and suprachoroidal surgical approach and safety and activity of human umbilical tissue–derived cells (palucorcel) via a novel delivery system in patients with geographic atrophy (GA).

Design: Multicenter, open-label phase 2b study.

Participants: Participants were 55 to 90 years with GA secondary to age-related macular degeneration (AMD) and best-corrected visual acuity (BCVA) of 20/80 to 20/800. Exclusion criteria included neovascular AMD in the intervention eye, glaucoma with intraocular pressure of 25 mmHg or more, or other significant ophthalmologic conditions.

Methods: Participants received a subretinal injection of palucorcel, 3.0×10^5 cells in 50 µl, using the custom-designed delivery system and surgical procedure.

Main Outcome Measures: Safety assessments included treatment-emergent adverse events (AEs), immunologic assessments, and ophthalmologic evaluations. Efficacy was evaluated as change in mean number of BCVA letters from baseline, proportion of participants gaining 15 BCVA letters or more, and growth rate of GA lesions at 12 months.

Results: Surgery and palucorcel administration were performed in 21 participants at 8 sites by 8 different surgeons. At baseline, median total area of GA was 13.4 mm^2 and median BCVA was 43 letters in the intervention eye. Eye-related AEs occurred in 76% of participants (16/21), including conjunctival hemorrhage ($n = 5$), retinal hemorrhage ($n = 4$), and vitreous floaters ($n = 4$). Most AEs were mild and resolved within 1 month. No serious AEs, no retinal detachment or perforation, and no significant changes in intraocular pressure occurred. At month 12, mean change in BCVA from baseline was −5.9 letters correct (standard deviation, 13.0 letters correct) in the intervention eye and −3.7 letters correct (standard deviation, 9.0 letters correct) in the fellow eye. No participants showed improvement of 15 letters or more in the intervention eye, and 3 participants lost more than 15 letters by month 1. No apparent effect of treatment was observed.

Conclusions: Palucorcel was delivered successfully to the targeted subretinal site using a novel delivery system and suprachoroidal approach for most participants; however, improvement in GA area, retardation of growth, or visual acuity were not demonstrated. *Ophthalmology Retina 2020;4:384-393*

Objectives

Utilize microscope-integrated OCT to:

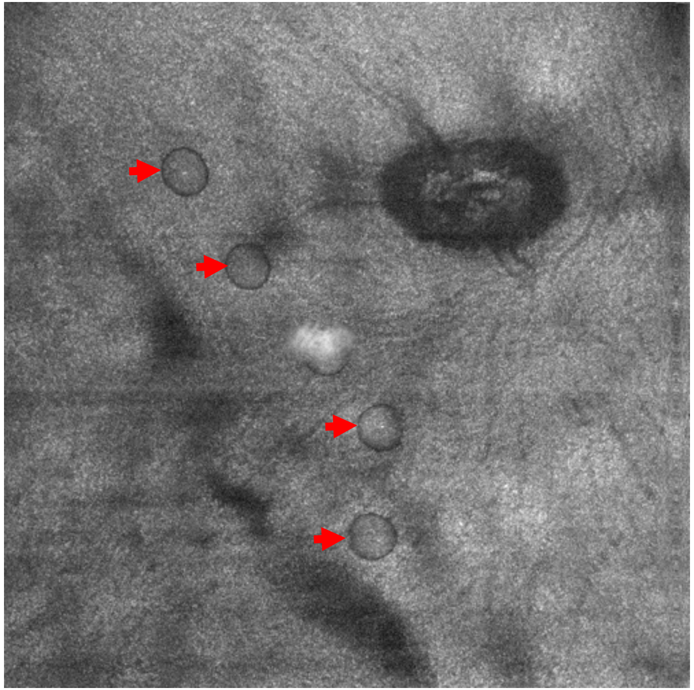
- Improve surgical visualization of the subretinal space, including wider field viewing system
- Obtain intraoperative imaging of subretinal blebs created by suprachoroidal approach
- Utilize image processing and segmentation to calculate volume of subretinal blebs
- Develop automated segmentation for more rapid calculation of subretinal bleb volume

Hypothesis

- Microscope-integrated optical coherence tomography can measure the volume of subretinal blebs created by a suprachoroidal approach
- Measurements are feasible using a wider field viewing system than high magnification contact lens
- Aimed to achieve less than 20% loss of volume delivery relative to intended volume using suprachoroidal approach

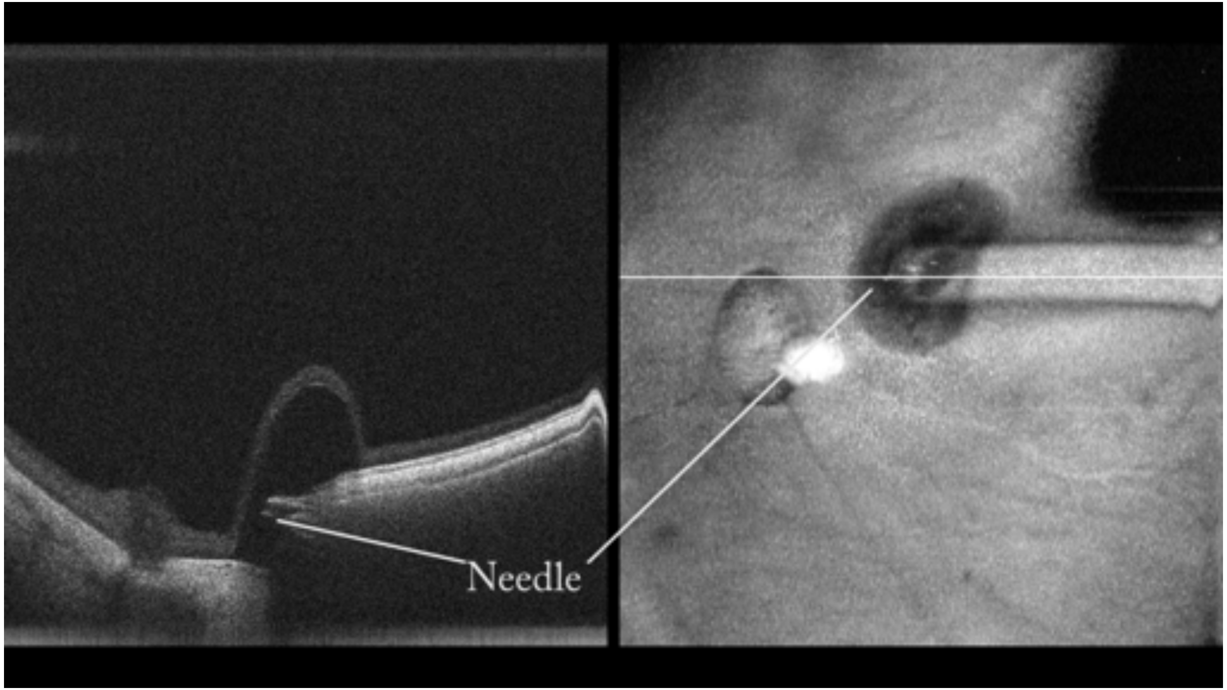
Methods- Model calibration

- Objects of known size (ceramic alumina spheres, 1 mm diameter) surgically inserted onto epiretinal space of ex-vivo porcine eyes
- Spheres imaged and segmented
- Number of voxels in image summed and used to create voxel to mm^3 calibration factor

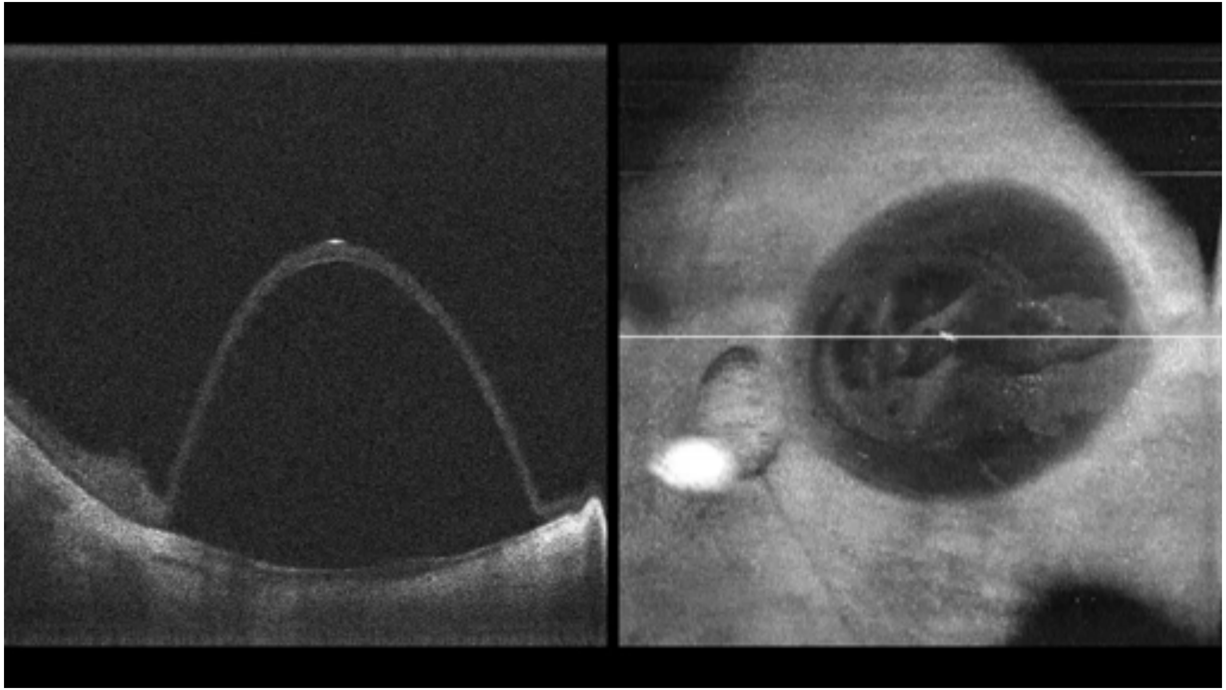


Methods: Subretinal Bleb Creation

Entry Bleb



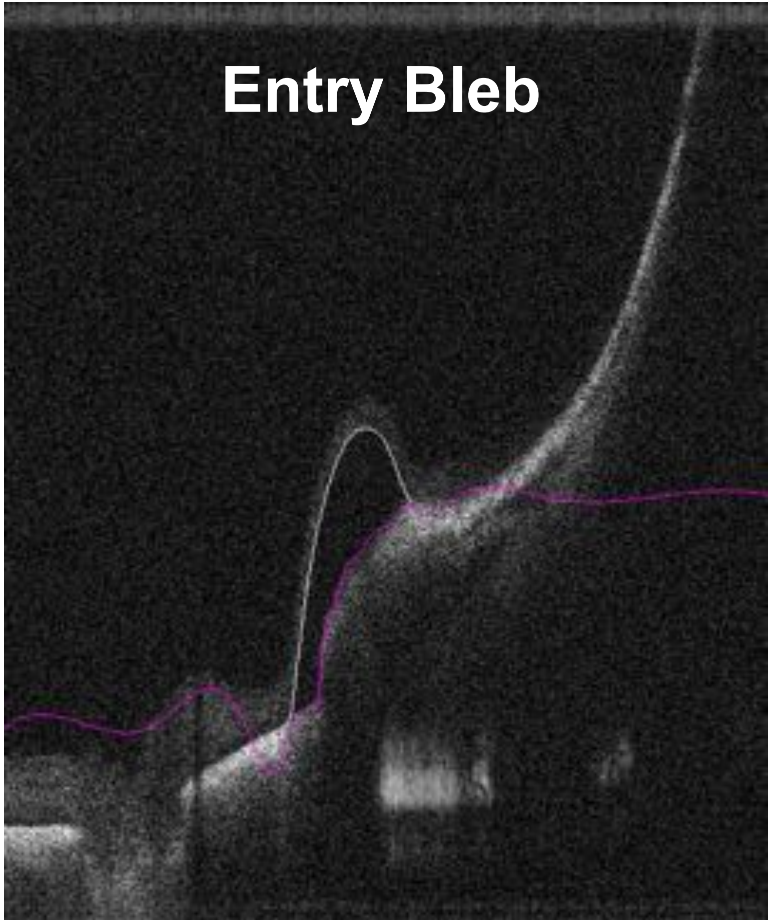
Full Bleb

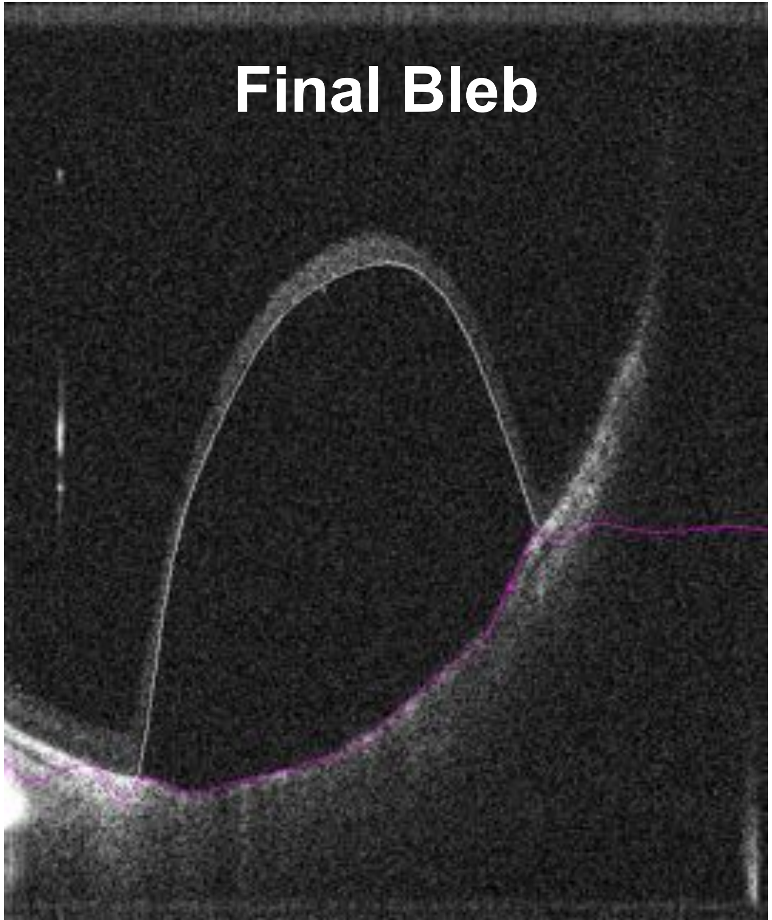


Methods

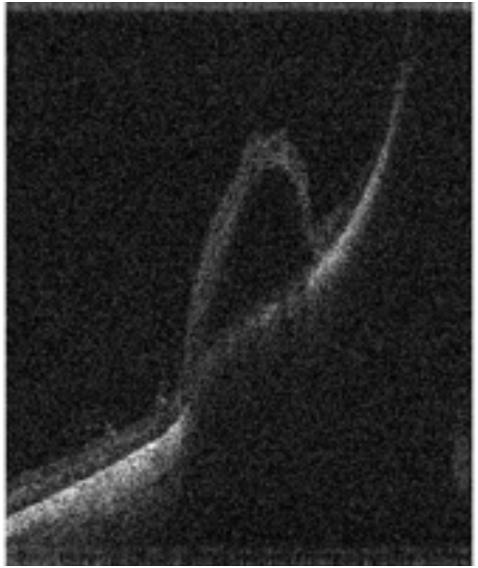
- Blebs created and imaged successfully in 26 eyes
- Manual segmentation completed on entry and full blebs for the 10 eyes with the best image quality
- Bleb volumes generated from voxel to mm^3 using prior calibration
- Segmented blebs used as input training for deep-learning algorithm for automated segmentation

Manual Segmentation

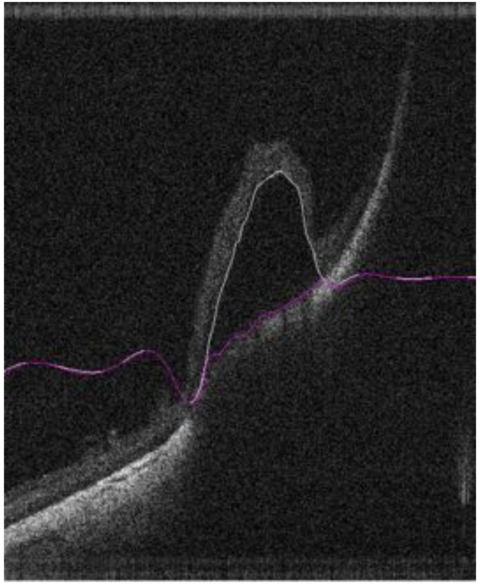




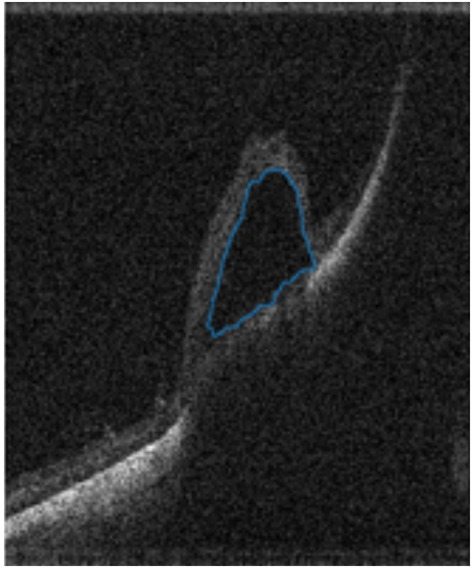
Unsegmented



Manual Segmentation



Autosegmentation



Results- Volume injected by devices

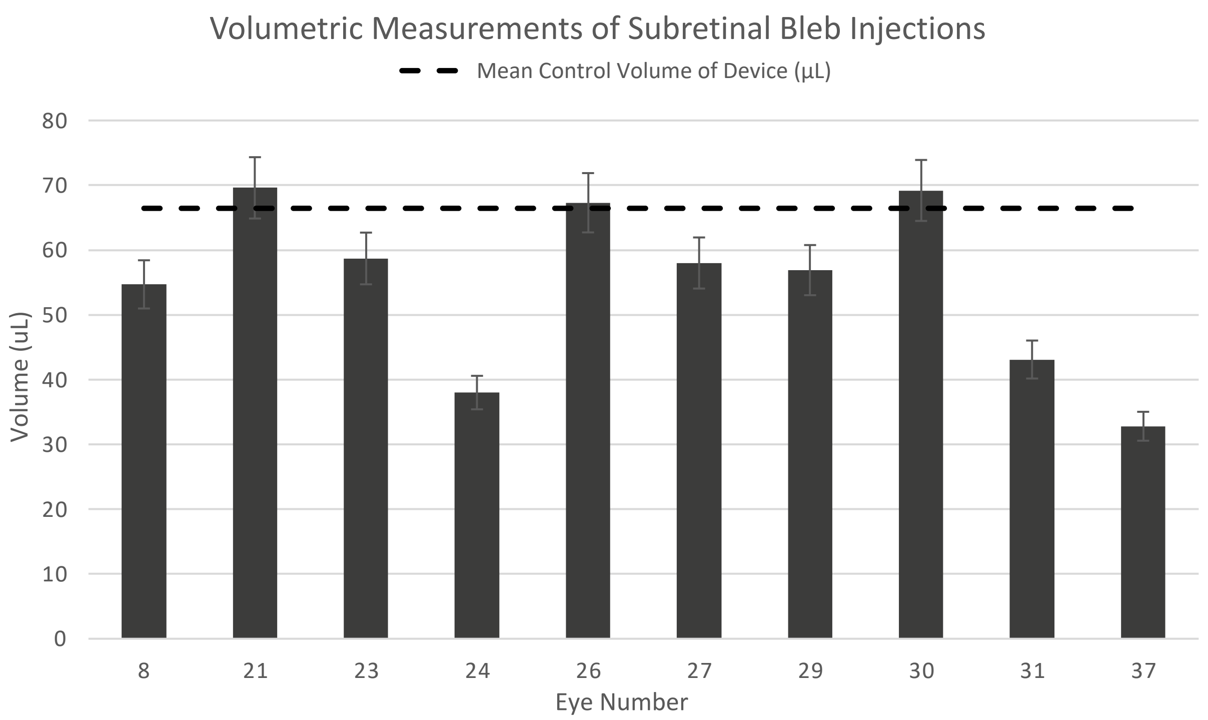
Device 1		Device 2	
Measurement #	Volume (µL)	Measurement #	Volume (µL)
1	67.6	1	66.5
2	66.4	2	67.5
3	66.6	3	67.1
4	64.9	4	67.3
5	68.3	5	66.0
6	66.2	6	68.7
7	65.9	7	66.8
8	67.5	8	65.9
9	68.7	9	66.7
10	56.8	10	67.3
Mean Injected Volume for Devices 1 and 2: **66.44 µL**			
Standard Deviation: **2.4 µL**			

Results: Bleb Volume Measurements

Eye	Eye Length (mm)	Entry Volume (mm^3)	Final Volume (mm^3)	Injected Volume (mm^3)
8	28.0	7.00	61.7	54.7
21	27.8	7.21	76.8	69.6
23	27.4	2.33	61.1	58.7
24	27.6	7.79	45.8	38.0
26	27.7	4.84	72.2	67.3
27	28.3	4.34	62.3	58.0
29	28.0	3.47	60.4	56.9
30	28.3	5.32	74.5	69.2
31	28.4	5.31	48.4	43.1
37	27.0	3.77	36.6	32.8
mean±standard deviation	**27.9±0.420**	**5.14±1.68**	**60.0±12.4**	**54.8±12.3**

Injected Bleb Volume Measurements

$$Net\ volume = Final\ volume\ - Entry\ volume$$



Volume Loss During Subretinal Injections

- Mean bleb volume: 82% of mean intended delivery volume
- In seven out of ten blebs, the bleb achieved 80% or greater of the mean intended volume
- Min, Median, Max volume: 32.8 µL, 57.45 µL, 69.6 µL (50%, 14%, 1% error)

Conclusions

- MIOCT can be used to measure the volume of subretinal blebs with precision and accuracy under high-magnification or wide-field viewing systems
- Use of MIOCT provides a method for visualization and quantification of subretinal drug delivery
- Suprachoroidal approach delivered a mean of 80% of intended injection volume to subretinal space

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- Sina Farsiu, PhD
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- Christian Viehland, PhD