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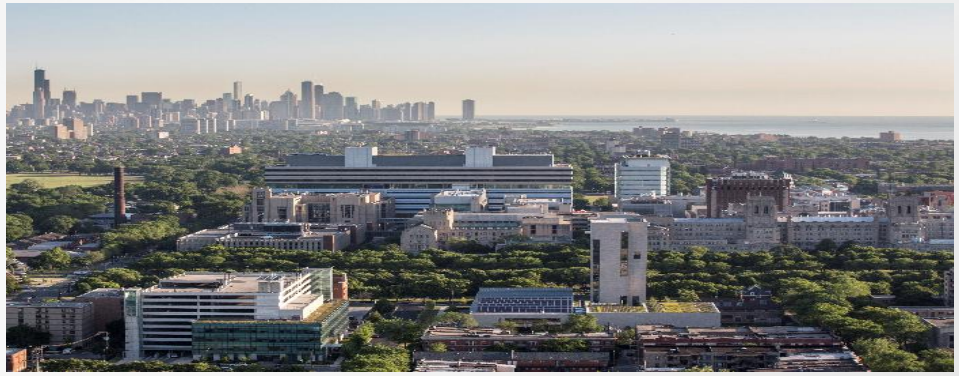

Multimodal Imaging Analysis for Suprachoroidal Injection Across Species: A Retina Surgeon's Perspective

Seenu M. Haripradad, MD
Shui-Chin Lee Professor of Ophthalmology
Interim Chair
Chief, Vitreoretinal Service
University of Chicago Department of Ophthalmology

Thomas Ciulla, MD, MBA
Clearside Biomedical, Inc.

Cherry Wan, PhD
Clearside Biomedical, Inc.

THE MACULA SOCIETY established in 1977
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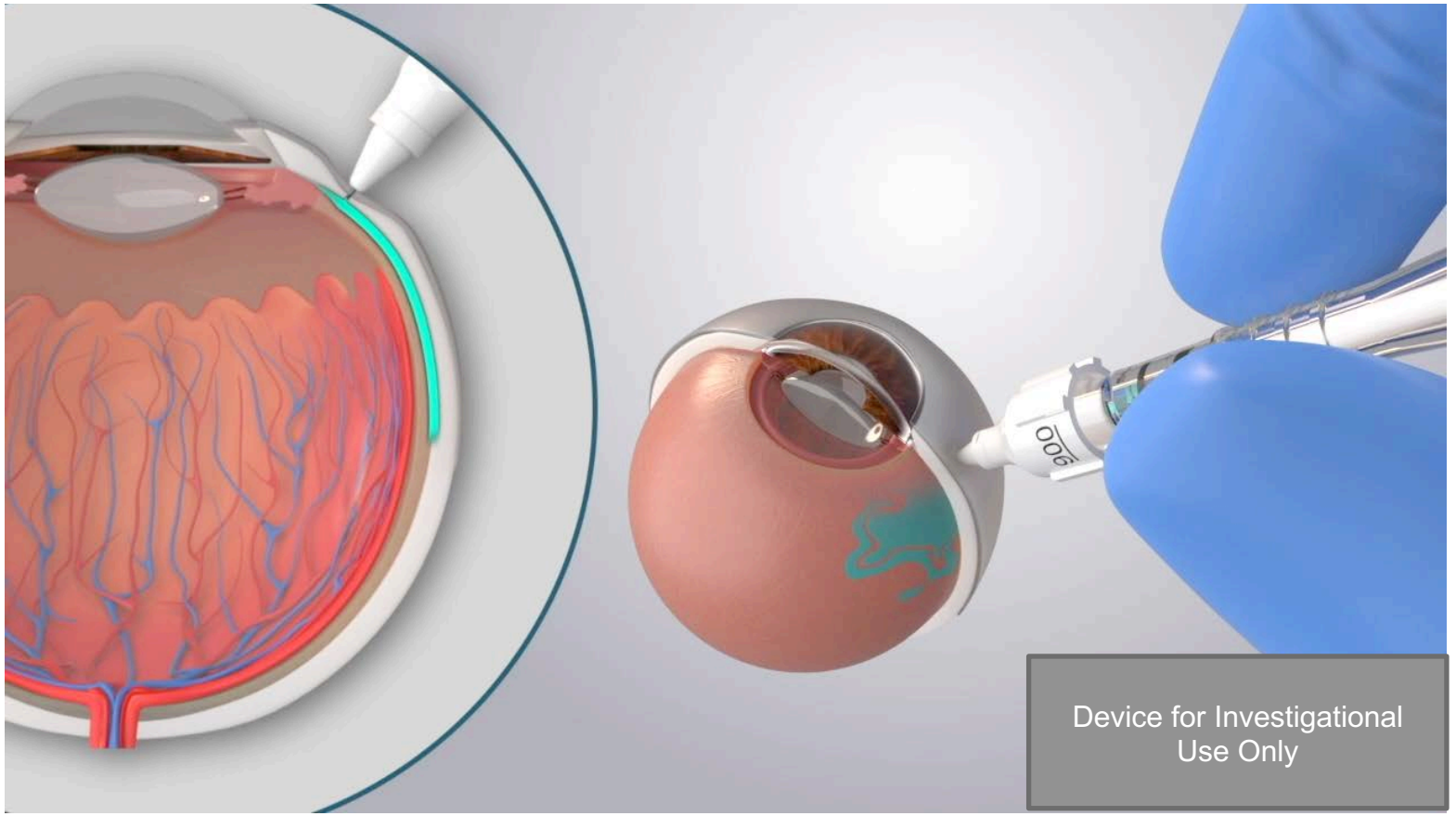
FEBRUARY 6-7, 2021

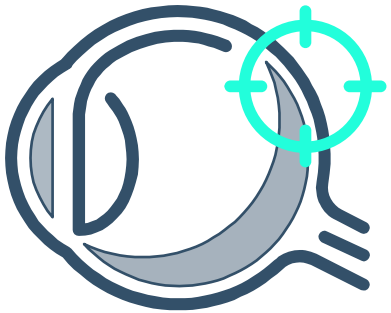
Financial Disclosures

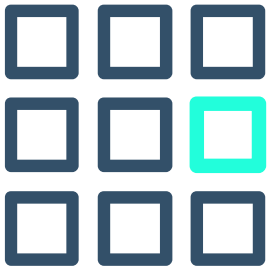
- SH: Clearside Biomedical, Allergan, EyePoint Pharmaceuticals, Alimera Sciences, Novartis, Spark, Biogen, Graybug, Regeneron, Bausch & Lomb- Consultant or Speaker's Bureau
- TC: Clearside Biomedical- Employee & Stockholder
- CW: Clearside Biomedical- Employee & Stockholder

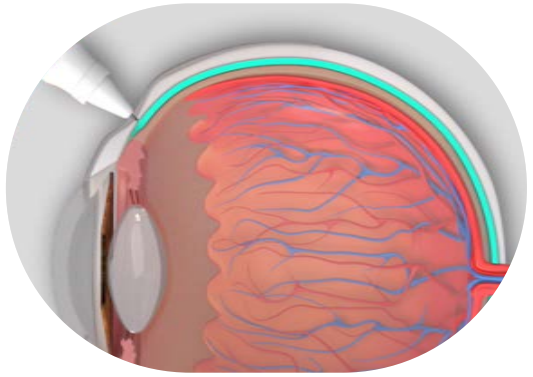
In-office suprachoroidal injections with a Microinjector are well tolerated in clinical trial patients to date



Core Advantages of Treating Via the Suprachoroidal Space







TARGETED

The back of the eye is the location of many irreversible and debilitating visual impairments[1]

for efficacy

COMPARTMENTALIZED

Drug is compartmentalized in the suprachoroidal space, which helps keep it away from non-diseased tissues[2]

for safety

BIOAVAILABLE

Fluid spreads circumferentially and posteriorly when injected within the suprachoroidal space, bathing the choroid and adjacent areas with drug[3]

for durability

Sources: PK = pharmacokinetic | 1. Rai UDJ, Young SA, Thrimawithana TR, et al. The suprachoroidal pathway: a new drug delivery route to the back of the eye. Drug Discov Today. 2015;20(4):491-495. 2. Chiang B, Jung JH, Prausnitz MR. The suprachoroidal space as a route of administration to the posterior segment of the eye. Adv Drug Deliv Rev. 2018;126:58-66. 3. Moisseiev E, Loewenstein A, Yiu G. The suprachoroidal space: from potential space to a space with potential. Clin Ophthalmol. 2016;10:173-178.

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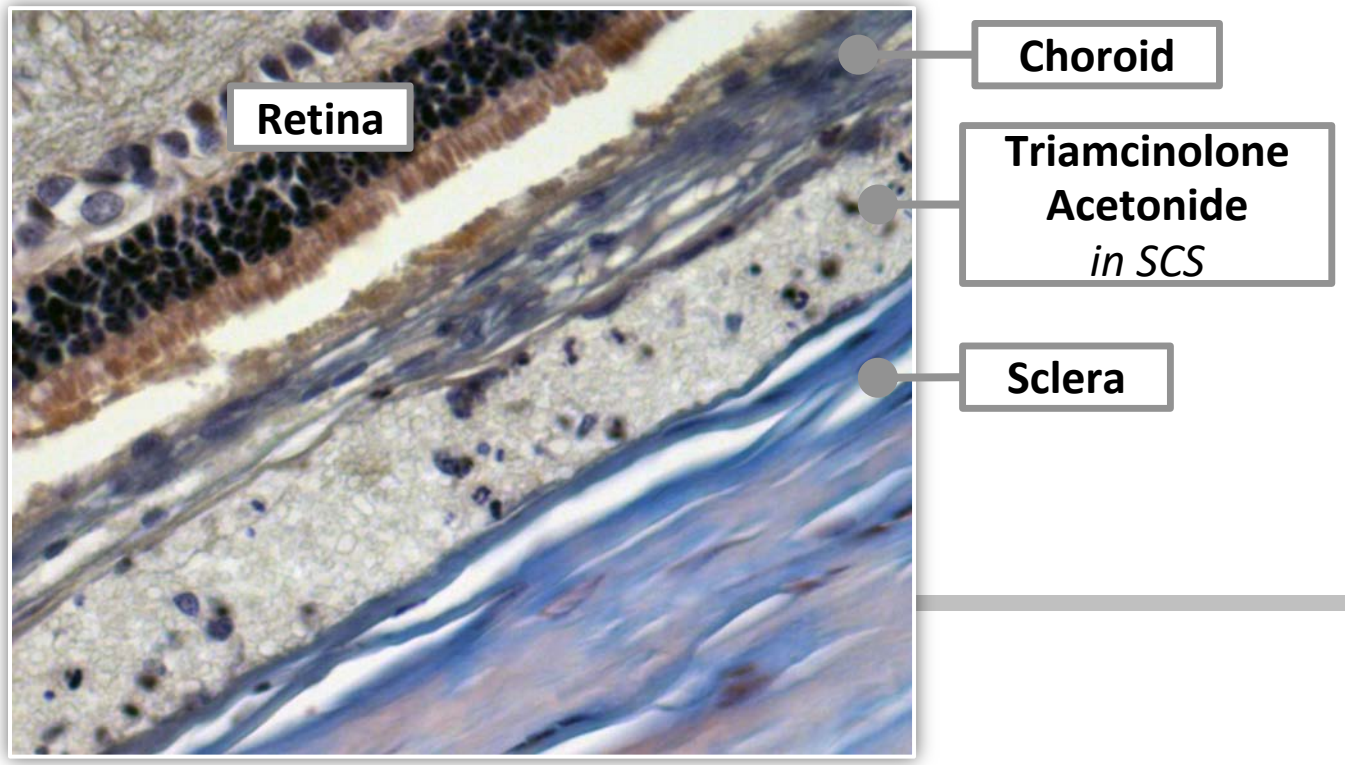
Article

Clinical Characterization of Suprachoroidal Injection Procedure Utilizing a Microinjector across Three Retinal Disorders

Chen-rei Wan[1], Barry Kapik[1], Charles C. Wykoff[2], Christopher R. Henry[2], Mark R. Barakat[3], Milan Shah[4], Rafael V. Andino[1], and Thomas A. Ciulla[1]

Methods: Datasets from six clinical trials across three diseases…



Conclusions: Both the user survey and the correlation analysis demonstrated that SC injection is well accepted by physician-investigators, and the two needle lengths accommodate a wide range of anatomic and demographic variables.

Translational relevance: These results…suggest that SC injection could be readily adopted in clinical practice for targeted compartmentalized delivery of ocular therapeutics.

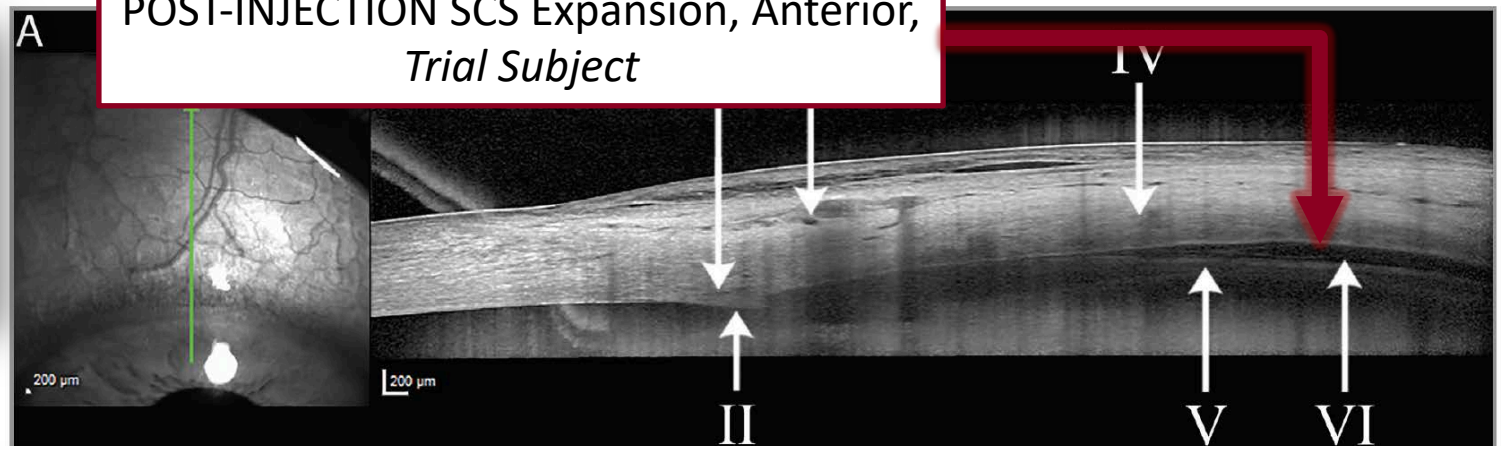
OCT images show expansion of the SCS post injection, followed by a reduction to pre-injection levels one month following injection

CLINICAL SCIENCE

Suprachoroidal Space Alterations Following Delivery of Triamcinolone Acetonide: Post-Hoc Analysis of the Phase 1/2 HULK Study of Patients With Diabetic Macular Edema

Shaun I. R. Lampen, BS; Rahul N. Khurana, MD; Glenn Noronha, PhD; David M. Brown, MD; Charles C. Wykoff, MD PhD

POST-INJECTION SCS Expansion, Anterior, *Trial Subject*



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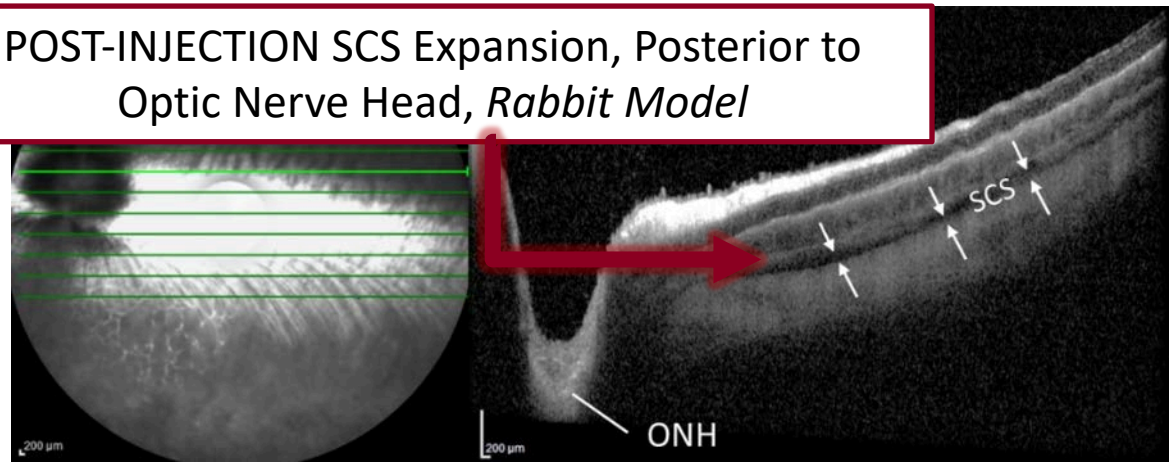
Article

Suprachoroidally Delivered DNA Nanoparticles Transfect Retina and Retinal Pigment Epithelium/Choroid in Rabbits

Viral S. Kansara[1], Mark Cooper[2], Ozge Sesenoglu-Laird[2], Leroy Muya[1], Robert Moen[2], and Thomas A. Ciulla[1]

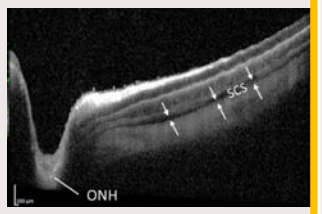
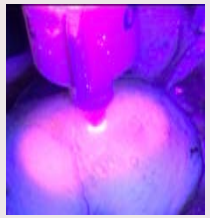
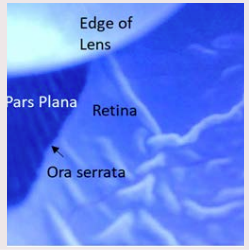
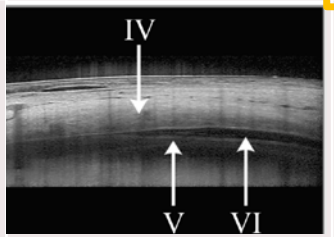
POST-INJECTION SCS Expansion, Posterior to Optic Nerve Head, *Rabbit Model*



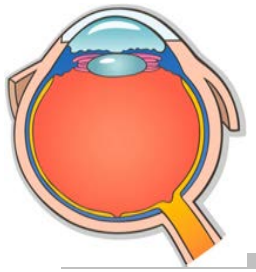
Lampen SIR, Khurana RN, Noronha G, Brown DM, Wykoff CC. Suprachoroidal Space Alterations Following Delivery of Triamcinolone Acetonide: Post-Hoc Analysis of the Phase 1/2 HULK Study of Patients With Diabetic Macular Edema. Ophthalmic Surg Lasers Imaging Retina. 2018;49(9):692-697. doi:10.3928/23258160-20180831-07, Add additional citation

Kansara VS, Cooper M, Sesenoglu-Laird O, Muya L, Moen R, Ciulla TA. Suprachoroidally Delivered DNA Nanoparticles Transfect Retina and Retinal Pigment Epithelium/Choroid in Rabbits. *Transl Vis Sci Technol*. 2020;9(13):21. Published 2020 Dec 15. doi:10.1167/tvst.9.13.21

Novel imaging methodologies of suprachoroidal and IVT injections characterize injectate spread in ex vivo models

	In Vivo		*Ex Vivo*		
	External Photography Surgeon Perspective	**OCT**	**Fluorescing Dye Injection under UV**	**Post Injection Cryofreeze + Sectioning**	**Real Time Vitreous View (Endoscopy)**
Suprachoroidal Porcine / Rabbit Models					
Intravitreal Porcine Model					
Patient Clinical Trials					

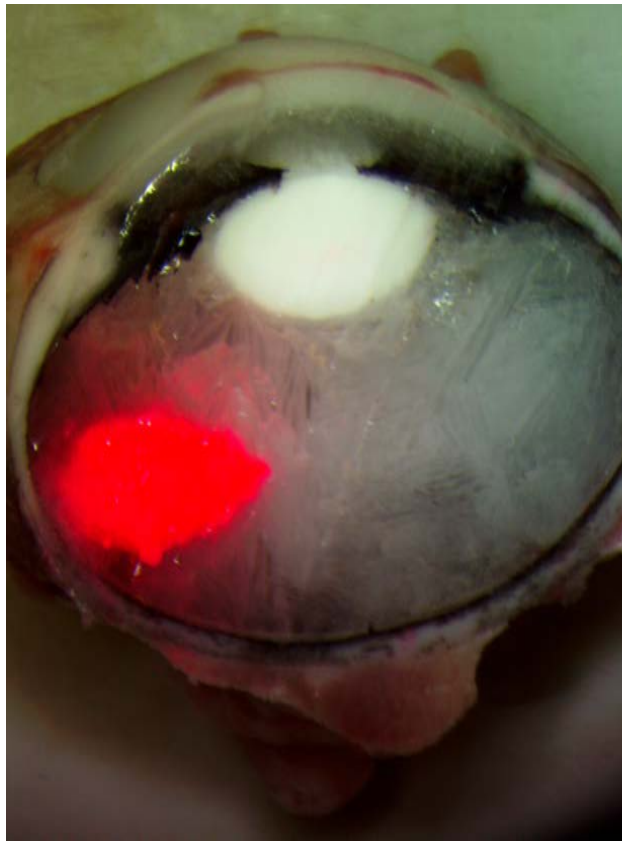
Fluorescing Dye under UV:
IVT injection shows no visible injectate;
Suprachoroidal injection shows circumferential, posterior spread



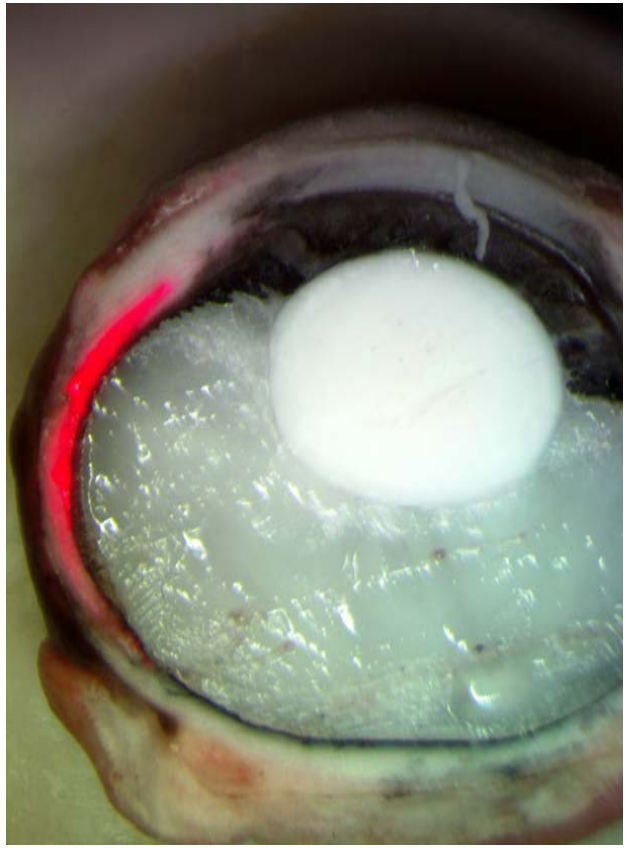
For Reference: Images oriented per cross-section diagram above

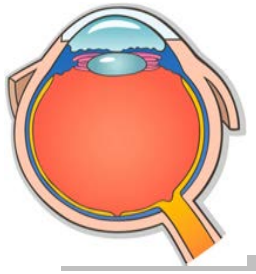
Post-Injection Cryofreeze and Sectioning:
IVT injection shows injectate bolus in vitreous;
Suprachoroidal injection shows circumferential, posterior spread

IVT Injection



Suprachoroidal Injection



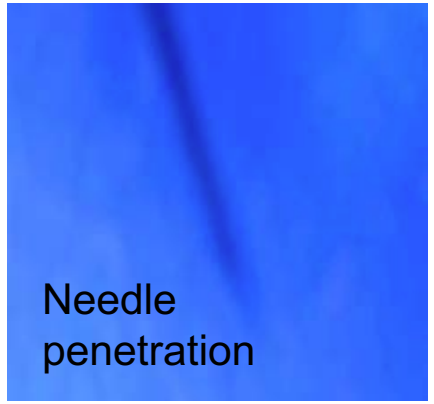


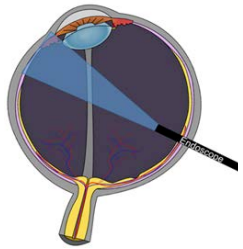
For Reference: Images oriented per cross-section diagram above

Vitreous View (Endoscopy):

IVT injection shows needle tip followed by injectate bolus;
Suprachoroidal injection shows localized tissue depression, then expansion

IVT Injection





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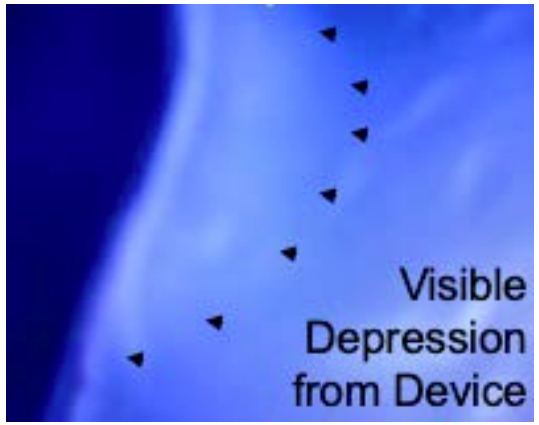
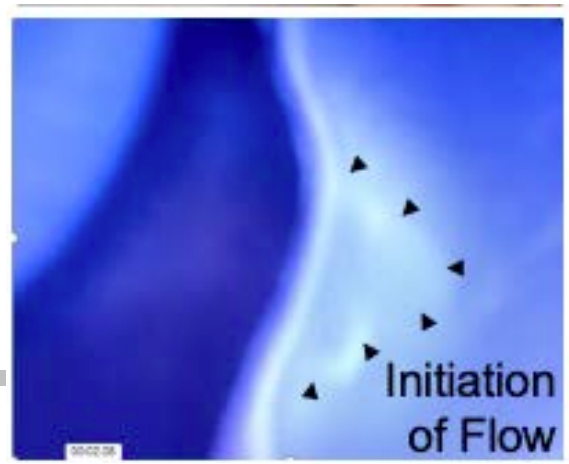
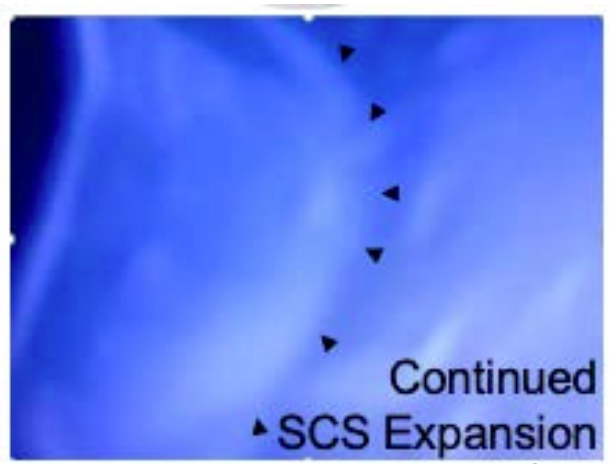
Suprachoroidal Injection







Conclusion

- Imaging of suprachoroidal injections demonstrates
  - acute opening of the SCS
  - circumferential, posterior spread of injectate
  - compartmentalization of injectate to posterior tissues

- These multimodal imaging methodologies support the potential of suprachoroidal injections to target affected tissue layers in chorioretinal disorders.

THANK YOU