Prevent Blindness®
Bringing Americans to Eye Care

2018 Focus on Eye Health National Summit:
Research to Impact

Promising Practices Emerging from NEI Partnerships

--- moderator ---

James Jorkasky

Alliance for Eye and Vision Research

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Promising Practices Emerging from NEI Partnerships

Michael Steinmetz, PhD
National Eye Institute

Stephen Rose, PhD
Foundation Fighting Blindness

Cynthia A. Toth, MD
Duke Eye Center; Member, ARVO "Telling the Story of OCT" Steering Committee

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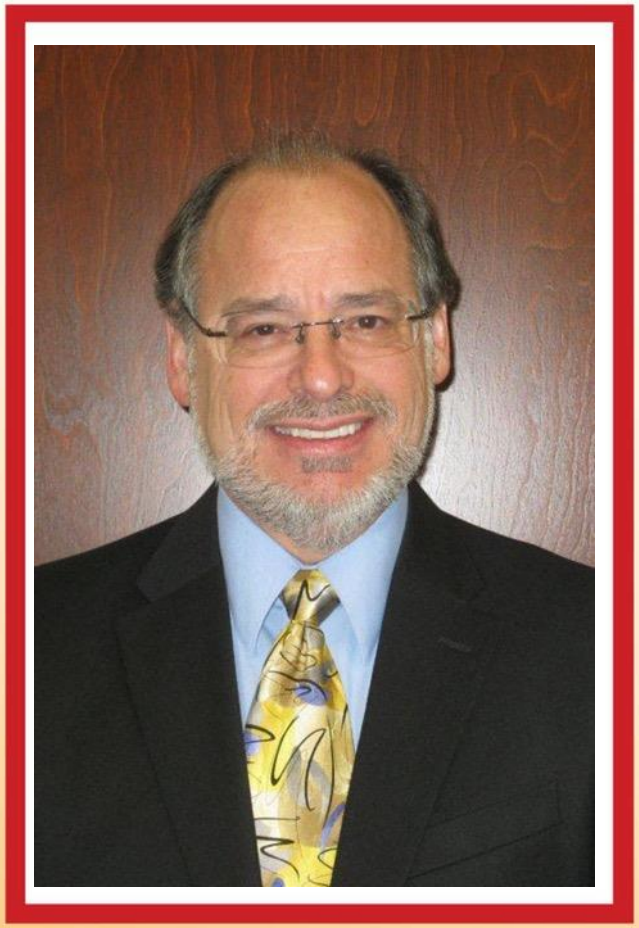

Advancing Eye Health Through Partnerships with Other Federal Agencies

Michael Steinmetz, PhD

Acting Deputy Director and

Director, Division of Extramural Science Programs

National Eye Institute

Advancing Eye Health Through Partnerships with Other Federal Agencies

- BRAIN Initiative
- Collaborative Research in Computational Neuroscience (CRCNS)
- NEI – Department of Defense Vision Research Program Collaboration

Brain Research through Advancing Innovative Neurotechnologies (BRAIN)

- Revolution in our understanding of the brain
- Develop and apply innovative technologies
- Dynamic picture of cells and circuits
- Understanding of activity at the speed of thought
- Treat, cure and prevent brain disorders

BRAIN Federal Partners

- 10 Institutes and Centers at NIH
- National Science Foundation (NSF)
- Defense Advanced Research Projects Agency (DARPA)
- U.S. Food and Drug Administration (FDA)
- The Intelligence Advanced Research Projects Activity (IARPA)

BRAIN Non-Federal Partners

- 5 private foundations
- 2 private research institutes
- 7 private and public universities and systems
- 11 companies

BRAIN Alliance Coordination

- Open lines of communications
- Public-private partnerships
- Shared funding opportunities and accomplishments
- Annual investigators meeting – open to public

Collaborative Research in Computational Neuroscience (CRCNS)

- Exploit computational methods to understand complex neurobiological systems
- Provide theoretical and technical foundations for understanding principles and dynamics
- Guiding experimental design and data analysis
- Building predictive models for testing new theories and hypotheses
- Encourage true collaborations between mathematicians and bench scientists

CRCNS Partners

- 6 Directorates and Offices at the National Science Foundation (NSF)
- 9 Institutes and Centers at the National Institutes of Health (NIH)
- German Federal Ministry of Education and Research (BMBF)
- French National Research Agency (ANR)
- United States-Israel Binational Science Foundation (BSF)
- Japan's National Institute of Information and Communications Technology (NICT)

CRCNS Mechanics

- NSF solicits applications requiring empirical and theoretical partners
- NSF provides scientific and technical review
- NIH peer-review staff participate to assure NIH requirements met
- NIH program staff select highly meritorious applications that are relevant to the Institute's mission
- Selected applications are approved for NIH funding by the Institute's Advisory Council
- Foreign components of international collaborations are funded by the relevant foreign funding agency

NEI-DOD Vision Research Program Collaboration

- DOD goal is to foster innovative military-relevant research to prevent, mitigate and treat military-relevant eye injuries and disease in war fighters and veterans
- Includes basic science, translational and clinical studies related to the treatment and restoration of visual function
- Clear overlap with the NEI mission in these areas
- NEI participates on the DOD program panel to provide advice and guard against duplicative efforts
- Outstanding science is proposed each year that goes unfunded due to lack of financial resources

NEI-DOD Vision Research Program Collaboration

- New collaboration modeled off the CRCNS program is currently under development
- DOD will solicit and review applications
- NIH review staff will participate in review to assure NIH policies are followed
- NEI will select highly meritorious applications that are particularly relevant to the NEI mission
- Selected applications will be approved for NIH funding by the National Advisory Eye Council
- NEI expects to bring new investigators to our portfolio and advance eye health in areas that are relevant to the missions of the DOD and the NEI

Summary

The NEI actively seeks collaborations with other Institutes and Centers at the NIH, with other federal agencies, private research institutes, foundations, academic institutions and private companies in order to share information and leverage outside investigators, research activities and funding in order to advance eye health

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Stephen Rose, Ph.D.

Chief Scientific Officer
Foundation Fighting Blindness

NEI builds the intellectual infrastructure

- NEI support of basic discovery research is the foundation upon which essentially all ocular therapeutic development is based.
- NEI funding of more external translational awards and in conjunction with the NIH National Center for Advancing Translational Science is moving these discoveries into preclinical studies

Outside Funders leverage NEI discoveries

- Foundation Fighting Blindness (FFB) and other non-government funders support preclinical development of potential treatments coming from the NEI support.
- FFB supports start-up companies spun out of academic institutions to develop these preventions, treatments, and cures.

Outside Funders leverage NEI discoveries

- Prime example is LUXTURNA™ from Spark Therapeutics for LCA2 caused by a mutation in the RPE65 gene.
- The RPE65 gene was identified by Michael Redmond in the NEI intramural program.
- FFB supported linking the RPE65 gene to LCA2 and the preclinical studies necessary to allow a clinical trial.

Outside Funders leverage NEI discoveries

- This FFB support led to early gene therapy clinical trials that showed success in restoring vision; NEI also supported a separate early gene therapy clinical trial for LCA2
- Results of these trials led to the formation of Spark Therapeutics that took the LCA2/PRE65 gene therapy across the finish line to gain FDA approval.

Outside Funders leverage NEI discoveries

- LUXTURNA™ is now the only FDA approved gene therapy for a genetic disease in the United States.
- The clinical trials treated over a hundred individuals with severe vision loss and restored partial vision to essentially all.
- Four individuals have been treated now that LUXTURNA™ is commercially available.

Outside Funders leverage NEI discoveries

- LUXTURNA™ would not have happened if NEI didn't support discovery research and non-governmental support from groups like FFB wasn't available for clinical development.
- This public-private partnership is paramount to bringing preventions, treatments and cures to those vision impaired individuals who could benefit.

Outside Funders leverage NEI discoveries

- Other endeavors include the Glaucoma Research Foundation, BrightFocus Foundation and JDRF, for example, co-funding research and clinical development based on NEI support over the years in discovery and translational research support.

Public-Private partnerships lead to success

- This type of public-private partnership extends into all ocular diseases, including but not limited to other inherited rare retinal degenerations, Glaucoma, Uveitis, diabetic retinopathy, and other vision robbing conditions.
- NEI research support leads to findings that allow many high quality shots on goal for clinical treatments supported by outside funders, like FFB, Glaucoma Research Foundation, BrightFocus and others.

Public-Private partnerships lead to success

- NEI has a robust Small Business Innovation Research (SBIR) program with many start-ups and biotech companies that are building on NEI discovery research.
- This includes development of small molecule drugs, biologics, ocular imaging technology and devices.

Public-Private partnerships lead to success

- The SBIR support has led to many approved products that also had non-NEI funding, such as the Argus II retinal prosthesis, Optical Coherence Tomography (OCT), Visual Aide Services Using Camera-Enabled Mobile Phones and others.

Public-Private partnerships lead to success

- The NEI support is necessary for development of sight saving interventions and technologies and non-government support like the Foundation Fighting Blindness' is important to help see these advances make it to the those in need and make sure they retain or even recover vision.

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FOUNDATION FIGHTING BLINDNESS

Prevent Blindness
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Promising Practices Emerging from NEI Partnerships

Cynthia A. Toth, MD

Joseph AC Wadsworth
Professor of Ophthalmology &
Professor of Biomedical Engineering
Duke University

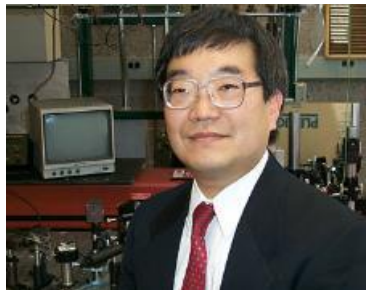
Promising Practices Emerging from NEI Partnerships

Development of Intraoperative and Pediatric Optical Coherence Tomography (OCT)

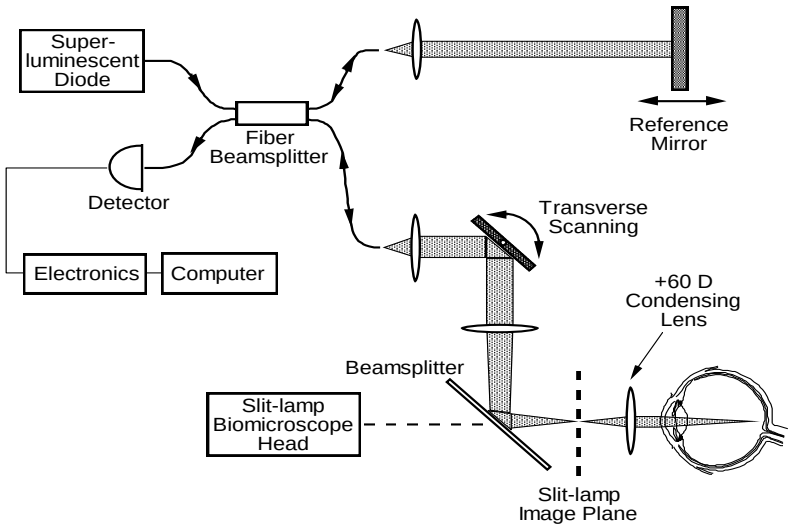
Biomedical engineering partnerships have revolutionized eye care

Optical Coherence Tomography (OCT)

- Novel light-based micron-scale imaging
- Reveals cellular microstructure



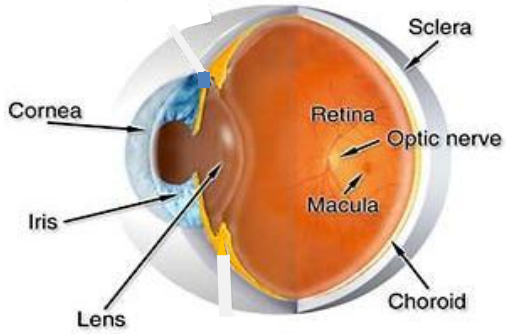
Prof. James Fujimoto- MIT



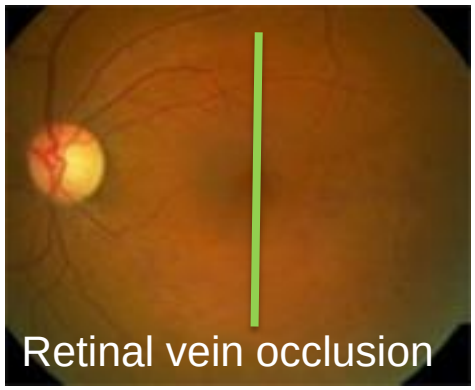
Swanson EA, Izatt JA, Hee MR, Huang D, Lin CP, Schuman JS, Puliafito CA, Fujimoto JG. Optics Letters 1993, 1864-6.

Optical Coherence Tomography (OCT)

- A new method to examine the retina
- Changes the way we diagnose and monitor eye disease

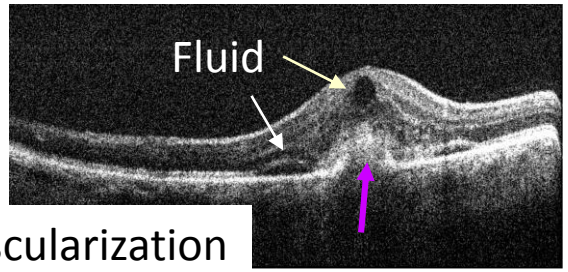


Traditional view



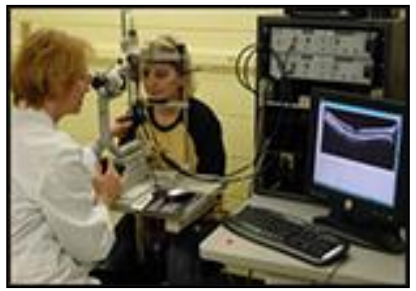
OCT view

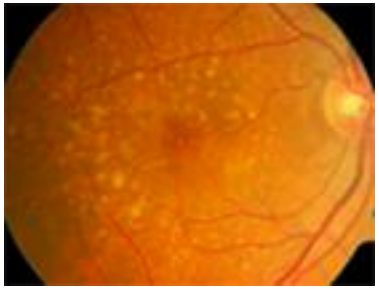
OCT in Age-Related Macular Degeneration

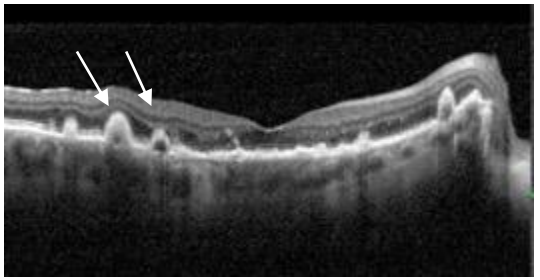


Neovascularization

Comparison of Age-related Macular Degeneration Treatment Trials (CATT)







Age-related Eye Disease Studies 2 (AREDS2) Ancillary SDOCT Study

Expand advanced imaging

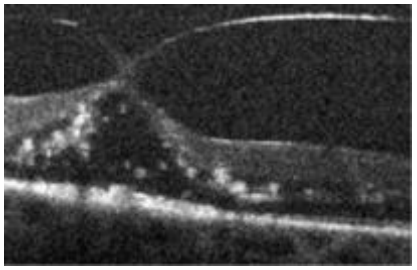
- In Surgery

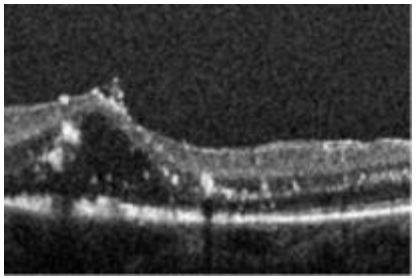
- For Children

OCT imaging in Surgery

- Portable system
- Pause to image

Joseph Izatt

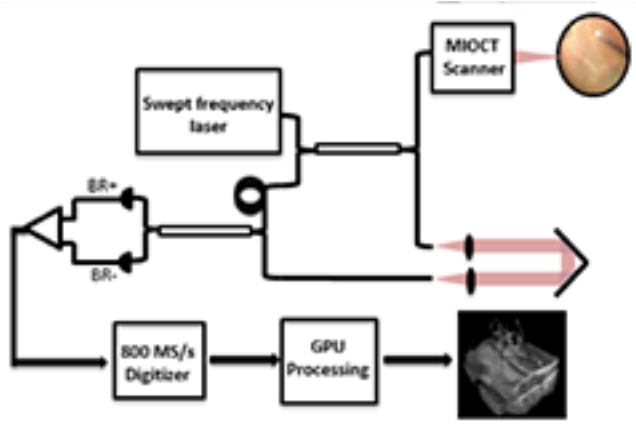




-**Dayani PN, Maldonado R, Farsiu S, Toth CA** Retina, 2009
-**Scott AW, Farsiu S, Enyedi LB, Wallace DK, Toth CA.** AJO, 2009
-**Ehlers JP, Kernstine K, Farsiu S, Sarin N, Maldonado R, Toth CA.** Arch Ophthalmol. 2011

NEI-funded Biomedical Research Partnership Grants

Joseph Izatt & Cynthia Toth



- **Microscope-Integrated Scanner**

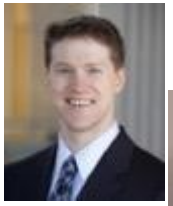
Yuankai Kenny Tao

- **Swept Source 1060 nm OCT**

Oscar Carrasco-Zevallos

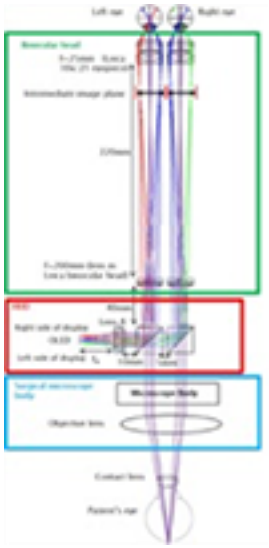
Christian Viehland

- **Graphic Processor Unit-based High Speed Volumetric Image Computation and Rendering**



Brenton Keller

Moseph Jackson-Atogi

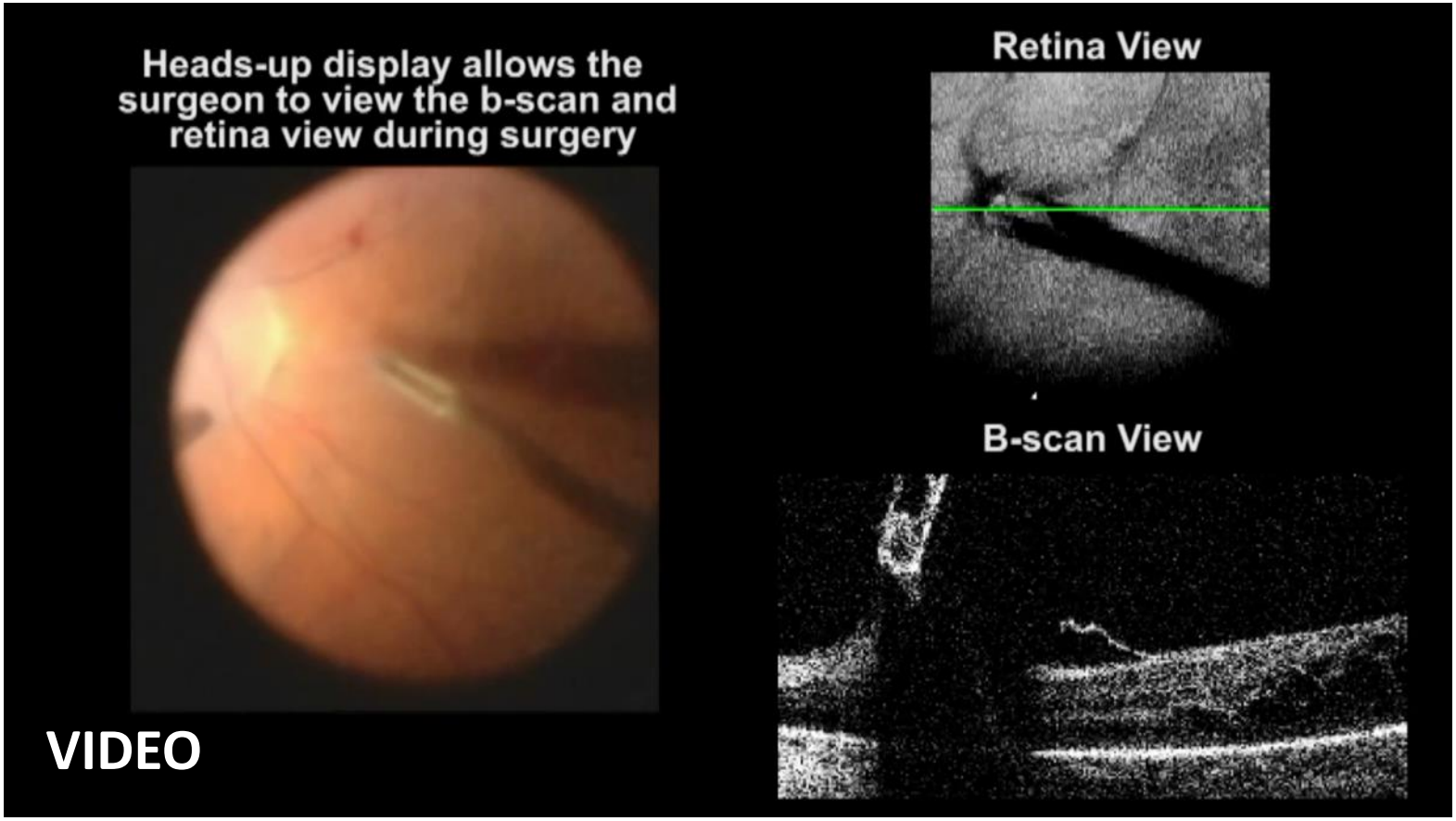


- **Stereo Heads up Display**

Liangbo Linus Shen

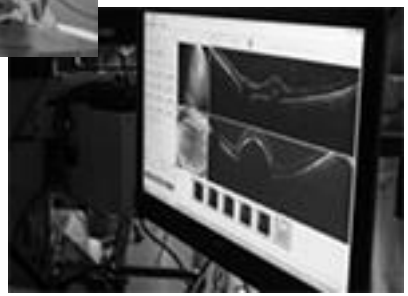
Tao YK et al Optics Letters 2010
Carrasco-Zevallos et al Nature Scientific Reports 2016
Viehland C et al, Biomed. Opt. Expr. 2016.
Shen L et al Biomed Opt Express. 2016

Translational Research

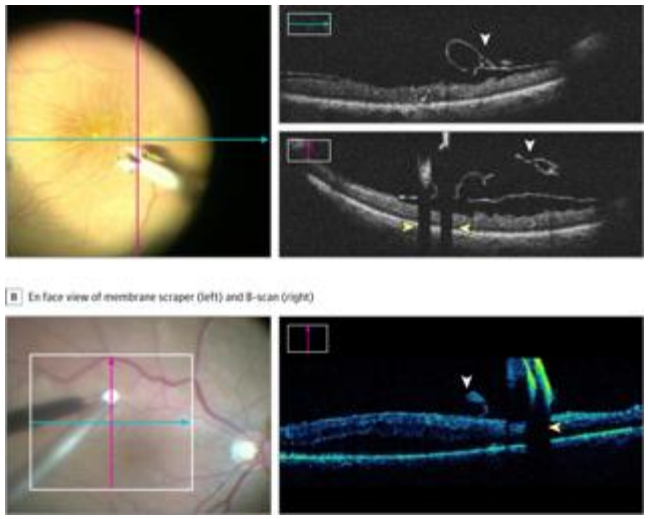


Commercialization

Bioptigen/Leica EnFocus 2300



Zeiss Rescan



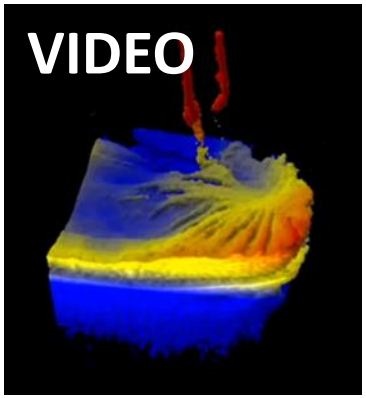
Runkle A et al. Ophthalmic Surg Lasers Imaging Retina. 2017

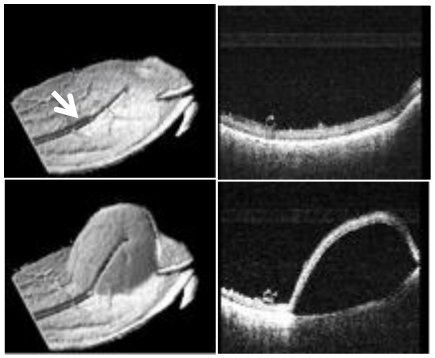
Ehlers JP et al. JAMA Ophthalmol. 2015

NEI-funded Biomedical Research Partnership Grants

- Surgeon training
- Improved visualization
- Precise delivery of subretinal materials for gene and stem cell therapies

Bleicher, I et al
ARVO 2018





Hsu, ST et al
TVST 2018

Why use OCT in the Nursery

- Retinopathy of prematurity (ROP) examination is complex
- To view & photograph the retina, white light is used; many camera systems contact the eye
- OCT provides important information using infrared illumination and without contacting the eye

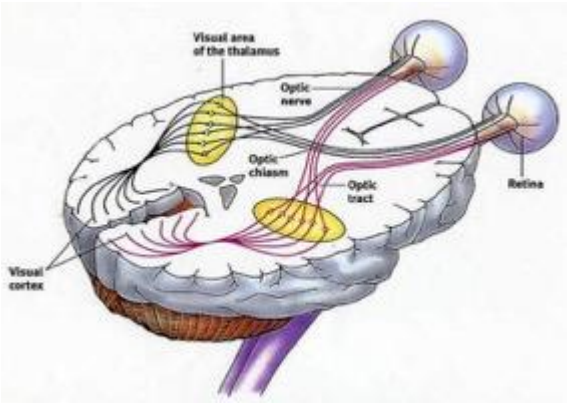
www.aapos.org retinopathy of prematurity; Prakalapakorn et al. JAAPOS 2014

Rothman AL et al
Retina 2015
Video 2

Why use OCT in the Nursery

- The retina is the entry to the visual pathway

- The visual pathway makes up over 25% of the brain

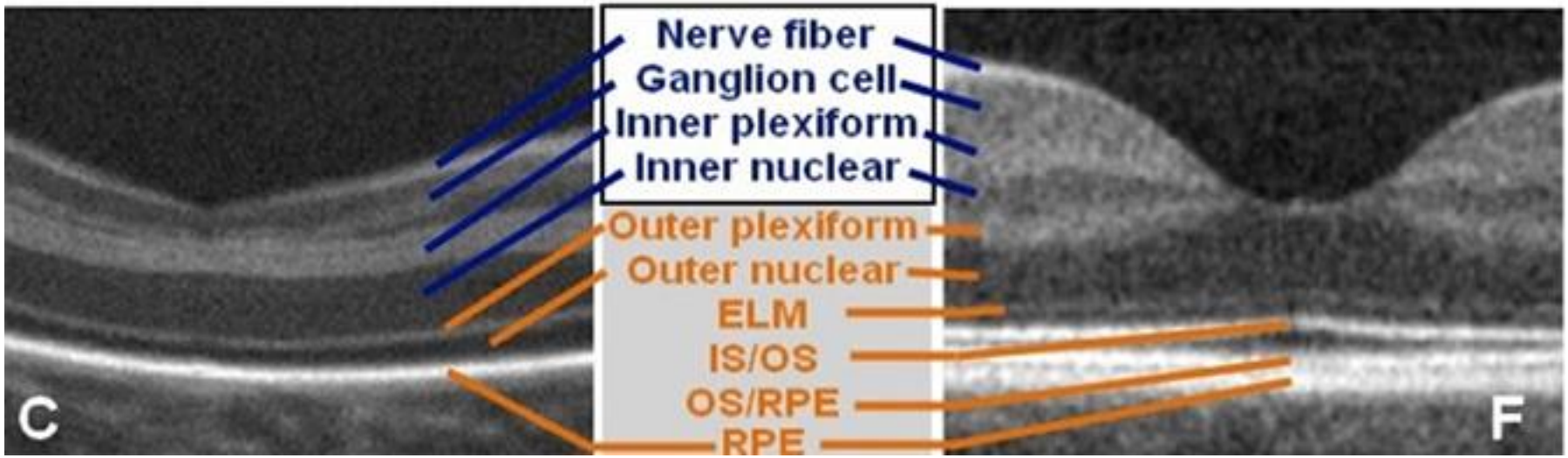


- The brain is the last major organ to develop

The premature infant retina is actively developing while in the nursery

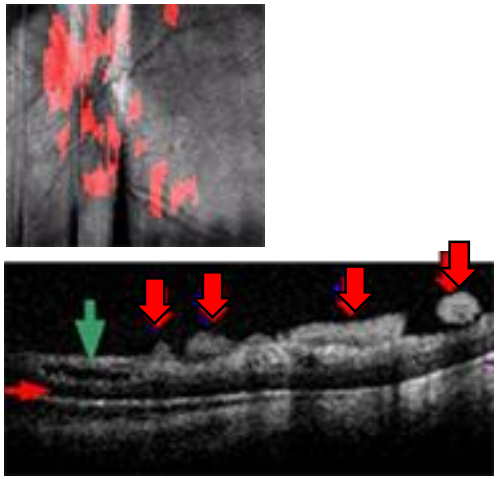
OCT of Premature Infant Retina

OCT of Adult Retina

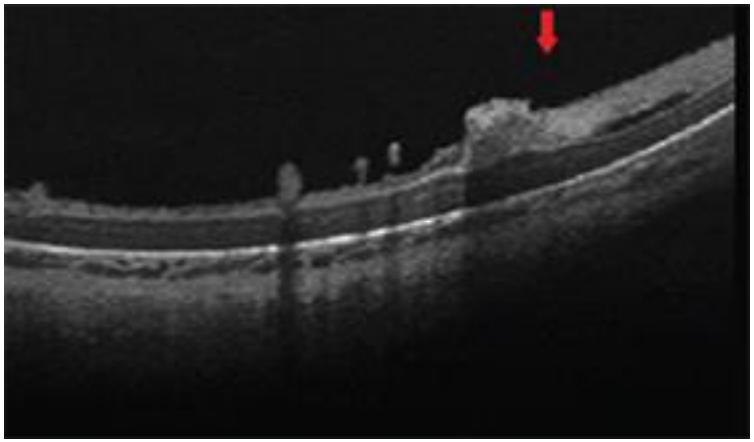


Maldonado RS et al. *Ophthalmology.* 2011

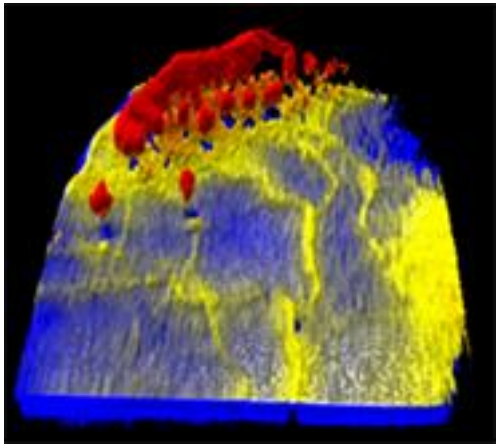
Bedside OCT imaging reveals patterns of development of abnormal blood vessels and neural tissue in retinopathy of prematurity (ROP)



Chavala SH et al
Ophthalmol 2009



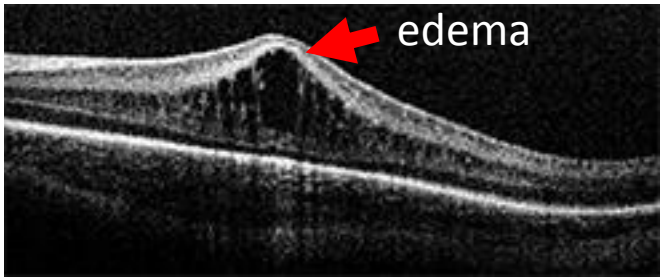
Chen X et al
Ophthalmol Retina, 2018



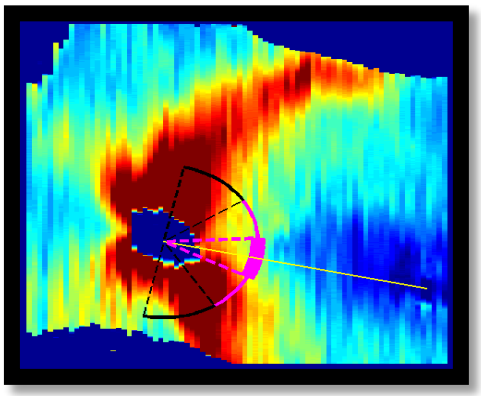
Mangalesh, S et al ARVO presentation 2017

Infants (like adults) **have retinal findings revealed only by OCT**

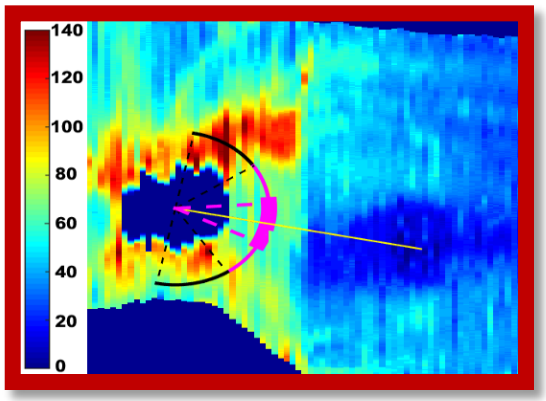
- Edema



- Nerve fiber layer thinning



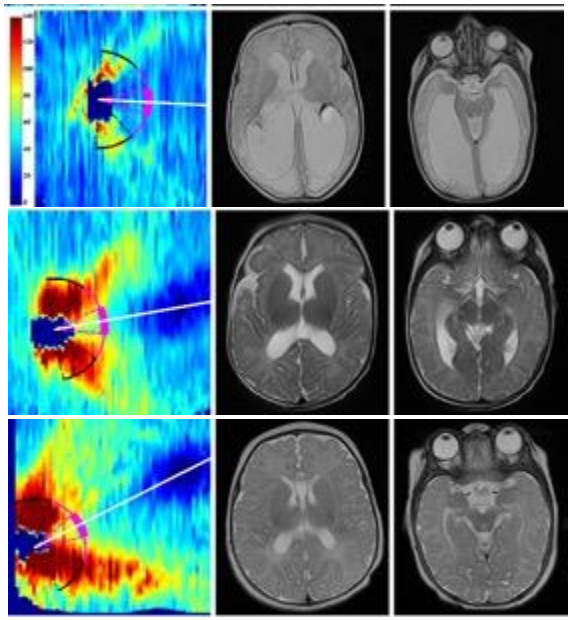
Normal



Severe thinning

Bedside retinal OCT findings in premature infants relate to the brain

- Edema has been associated with poor neurodevelopment
- Thin retinal layers have been associated with brain injury and poor neurodevelopment

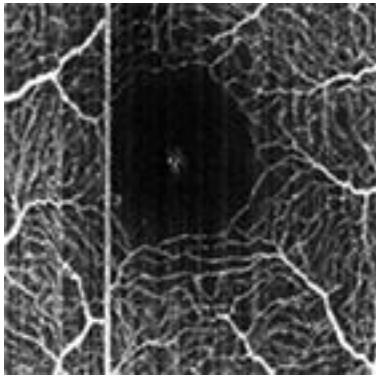


Rothman AL et al. *Ophthalmology*. 2014

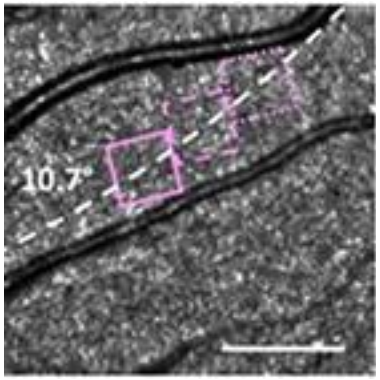
Rothman AL et al. *AJO*. 2015

Recent imaging technology advances

- Non-contact handheld OCT imaging of retinal vascular flow
- Higher speed and adaptive optics imaging
- Image processing, analytics and clear age-referenced outputs



Christian Viehland
SPIE
2018

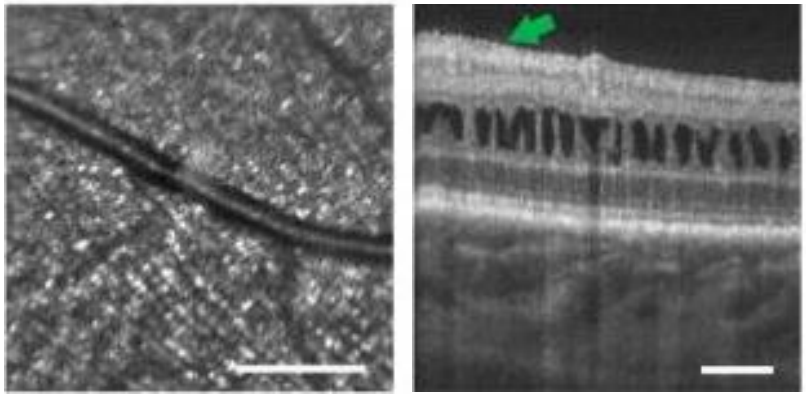


LaRocca F et al
Cone mosaic in
14 month old toddler
Nat Photonics 2016

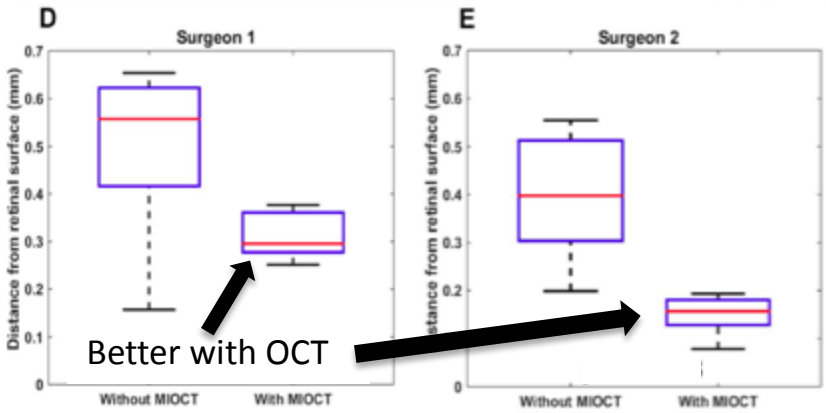
Meeting clinical needs

- Early assessment of eye-brain development and disease
- Surgical guidance to improve surgical accuracy and outcomes

Retinoschisis

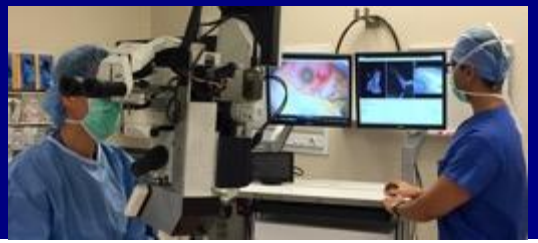


LaRocca F et al Nat Photonics 2016



Carrasco-Zevallos et al. Scientific Reports 2016

Research Collaborators



NIH Biomedical Research Partnership Grant R01-EY023039, “Intraoperative OCT Guidance of Intraocular Surgery" (Izatt/Toth MPI), NCRR UL1 RR024128; R21 EY019411, EY02132, R01-EY025009, P30-EY005722, K23-EY028227

The Hartwell Foundation, Research to Prevent Blindness, Retina Research Foundation

Toth Laboratory
- Ramiro Maldonado
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- Rachelle O’Connell
- Du Tran Viet
- Michelle McCall
- Katrina Winter
- Neeru Sarin
- Eric Yuan
- Monica Sevilla
- Vincent Tai
- DH Nam
- Adam Rothman
- Philip Desouza
- S Tammy Hsu
- Isaac Bleicher
- Hesham Gabr
- Amy Tong
- Shwetha Mangalesh
- Jonghyun Lee

Retina
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- Glenn Jaffe
- Daniel Ting
- Mila Oh
- Dilraj Grewal
- Paul Hahn
- Tamer Mahmoud
- Scott Walter
- Bozho Todorich
- Michael Seider
- Justis Ehlers
- Adrienne Scott
- Annie Lee
- Tomas Moreno
- Sai Chavala
- Pouya Dayani
- Prithvi Mruthyunjaya
- Xi Chen

Biomedical Engineering
- **Joseph Izatt**
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- Brenton Keller
- Christian Viehland
- Linus Shen
- Gar Waterman
- Justin Migicz
- Francesco Larocca
- Derek Nankivil
- Theo DuBose
- Moseph Jackson-Atogi

Cornea
- **Anthony Kuo**
- Neel Pasricha
- Christine Shieh
- Ryan McNabb
- Pam Bhullar

Pediatric Neuroradiology
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Sina Farsiu Laboratory
- Stephanie Chiu
- David Cunefare

Cole Eye Institute
- Sunil Srivastava
- Justis Ehlers
- Kenny Tao

Neonatology/Peds Neurology
- Michael Cotton
- Katie Gustafson
- Carolyn Pizoli
- Joanne Finkle

Pediatric Ophthalmology
- Sharon Freedman
- David Wallace
- Laura Enyedi
- Mays El-Dairi

Biostatistics
- Maureen Maguire (Penn)

Telling the story of OCT

- Sharing the public benefit from investments in vision research
  - Videos
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