Macular OCT characteristics in a cohort of preterm infants

Cynthia A Toth


Department of Ophthalmology, Duke University
*Department of Biomedical Engineering, Duke University
**Center for Preventive Ophthalmology and Biostatistics, University of Pennsylvania
Financial Disclosures

• Alcon & Hemosonics – royalties (Toth)
• Unlicensed and pending patents (Toth)
• Research support:
  National Eye Institute: R01EY250009, P30 EY005722 (Toth)
  National Institute of Health: EY02827 (Chen)

Other Authors: No Financial Conflict

1. I will discuss investigational pediatric SSOCT systems
2. All use of investigational devices in human subjects was with prior consent and under IRB approved protocols.
• OCT is an alternative method of analyzing neurovascular retina in ROP
• First report of the full BabySTEPS 36 week data in infants screened for ROP
  – Macular edema severity is associated with ROP Stage but not pre-Plus/Plus disease
  – Choroidal thickness is associated with pre-Plus/Plus disease but not ROP Stage
• Different retinal and choroidal thickness response to ROP may reflect their different location relative to the blood-eye barrier

Summary
BabySTEPS (STudy of Eye imaging in Preterm infantS) Summary:

To improve preterm infant health care via novel bedside ocular neurovascular imaging

AND

Characterize from imaging, the early indicators of ROP, poor vision and neurological development

FOR FUTURE USE

to determine disease and development and monitor response to treatment.
65% of infants in Early Treatment of ROP Study had subnormal visual acuity at school age

- 50-70% of VPT infants worldwide develop significant neuro-developmental impairment

- ROP may represent only one striking vascular aspect in a continuum of delayed, diseased and abnormal neurovascular development of the brain and retina

To improve preterm infant health care via novel bedside ocular neurovascular imaging

AND

Characterize from imaging, the early indicators of ROP, poor vision and poor brain/neurological development

FOR FUTURE USE
to monitor response to treatment.
Methods

Site: Duke Intensive Care Nursery and Duke Regional Nursery

Study Design: Prospective, longitudinal, observational study in preterm infants

Inclusion Criteria: ≤1500 g birthweight or ≤30 weeks gestational age; eligible for ROP screening
Data collection and work flow

Infant health & Ocular Exam Findings

Collection & entered into RedCap software

OCT imaging

DARSI Lab (Duke Advanced Research in SS & SDOCT Imaging)

Research MRI

MRI reading center at WashU

Visual acuity

Teller acuity @ 9 months

Neurodevelopmental outcomes

Bayley scales @ 2 years

Data analysis by Center for Preventive Ophthalmology and Biostatistics at UPenn
Total infants enrolled in BabySTEPS

Infants with any OCT imaging

Infants with OCT imaging at 36±1 weeks PMA

- 118 infants enrolled
- 11 infants transferred before OCT imaging
- 5 infants died before OCT imaging
- 10 infants discharged or transferred or died
- 4 infants treated for ROP OU
- 2 infants imaged after 37 weeks

- 102 infants with OCT imaging
- 85 infants/170 eyes
- One eye treated for ROP prior to 36 weeks

- Treatment-free visit per child closest to 36 weeks PMA: 169 eyes
## Demographics of the study cohort

<table>
<thead>
<tr>
<th>Demographic information</th>
<th>Preterm N=85</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational Age (wks), mean (SD)</td>
<td>28 (2)</td>
</tr>
<tr>
<td>Birth Weight (gm), mean (SD)</td>
<td>976 (269)</td>
</tr>
<tr>
<td>Age at imaging for cross-sectional analysis (wks, PMA), mean(SD)</td>
<td>36 (0.6)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>43 (51)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>African-American</td>
<td>38 (45)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>5 (6)</td>
</tr>
<tr>
<td>Asian</td>
<td>3 (3)</td>
</tr>
<tr>
<td>More than one</td>
<td>39 (46)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>7 (8)</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>78 (92)</td>
</tr>
</tbody>
</table>
### ROP exam findings in 169 untreated eyes at 36 weeks PMA

<table>
<thead>
<tr>
<th></th>
<th>OD  N=84* (%)</th>
<th>OS  N=85 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ROP stage at the time of imaging</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 0</td>
<td>47 (56)</td>
<td>48 (57)</td>
</tr>
<tr>
<td>Stage 1</td>
<td>14 (17)</td>
<td>15 (18)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>22 (26)</td>
<td>20 (23)</td>
</tr>
<tr>
<td>Stage 3</td>
<td>1 (1)</td>
<td>2 (2)</td>
</tr>
<tr>
<td><strong>Plus disease at the time of imaging</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>80 (95)</td>
<td>80 (94)</td>
</tr>
<tr>
<td>Pre-Plus</td>
<td>1 (1)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Plus</td>
<td>3 (4)</td>
<td>1 (1)</td>
</tr>
<tr>
<td><strong>ROP Zone at the time of imaging</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zone I</td>
<td>8 (10)</td>
<td>9 (11)</td>
</tr>
<tr>
<td>Zone II</td>
<td>57 (68)</td>
<td>58 (68)</td>
</tr>
<tr>
<td>Zone III</td>
<td>16 (19)</td>
<td>15 (18)</td>
</tr>
<tr>
<td>Fully Vascularized</td>
<td>3 (4)</td>
<td>3 (3)</td>
</tr>
<tr>
<td><strong>Subsequent ROP Therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bevacizumab &amp; laser</td>
<td>4 (5)</td>
<td>5 (6)</td>
</tr>
<tr>
<td>Laser</td>
<td>3 (3)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>No Therapy</td>
<td>77 (92)</td>
<td>77 (91)</td>
</tr>
</tbody>
</table>

*One eye of one infant excluded for analysis due to early treatment for ROP*
Evolution of Infant OCT Imaging

Duke investigational SSOCT hand-held devices (compact, lighter & high-speed)

- OCT hand-piece does not contact the eye
- Near infrared light is comfortable to view
- Pupil dilation is not mandatory

Scott AW et al. AJO 2009
Chong GT et al Arch Ophthalmol 2009
Chavala SH et al Ophthalmol 2009
Maldonado RS, et al. IOVS 2010
Tran-Viet et al. Retina 2017
Viehland et al BOE 2019
OCT is an alternative method for imaging and analyzing neurovascular retina in infants with ROP.

We extracted thickness data from the eyes at 36 weeks PMA.

Seely et al., TVST 2020 in press

Mangalesh et al., Graefes Arch Clin Exp Ophthalmol 2019
Foveal OCT was successfully captured in both eyes for all 85 infant OCT imaging sessions.

Quality of OCT volumes of the fovea:

\[ n = 129 \text{ eyes} \]

- Excellent = 19%
- Acceptable = 67%
- Poor (but useful for some grading) = 14%
- Unusable = 0%
Qualitative & Quantitative OCT image analysis

Qualitative OCT features:
- Vitreous pathologies: Opacities, clumps, foci
- Macular edema: Presence and severity
- Severity of edema: Mild, Moderate, Severe
- Photoreceptor development: ELM & EZ presence
- Retinoschisis & retinal detachment

Layer Thicknesses at fovea and across foveal center (DOCTRAP Program)
- Retinal thickness
- RNFL+ GCL+IPL
- Inner nuclear layer
- Outer retina
- Choroid
Macular Edema in infants at 36±1 week PMA

Severity of Macular Edema

- None: 40% (Video a)
- Mild: 22% (Video b)
- Moderate: 23% (Video c)
- Severe: 16% (Video d)

Retinal thickness at fovea

- None
- Mild
- Moderate
- Severe

Inner nuclear layer thickness at fovea

- None
- Mild
- Moderate
- Severe

Choroidal thickness was not associated with macular edema severity or retinal thickness

p<0.001
Association between retinal layer thickness at foveal center and ROP stage

<table>
<thead>
<tr>
<th>ROP Stage</th>
<th>Retinal thickness at fovea (µm)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stage 2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage of ROP</th>
<th>Inner nuclear layer (µm)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td></td>
<td>0.006</td>
</tr>
<tr>
<td>Stage 2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Retinal thickness, RNFL+GCL+IPL, INL and outer retinal thicknesses were associated with ROP stage but not with plus disease.
Association between choroidal thinning & Plus disease

Choroidal thickness vs ROP Stage

- No Plus
  - Choroid at fovea: 275µm
  - Choroid across 1mm: 284µm

- Plus disease
  - Choroid at fovea: 130µm
  - Choroid across 1mm: 126µm

p=0.002

Choroidal thickness vs Plus disease

- No Plus
  - Choroid at fovea: 275µm
  - Choroid across 1mm: 284µm

- Plus disease
  - Choroid at fovea: 130µm
  - Choroid across 1mm: 126µm

p=0.062
Summary

- OCT is an alternative method of analyzing neurovascular retina in ROP
- First report of the full BabySTEPS 36 week data in infants screened for ROP
  - Macular edema severity is associated with ROP Stage but not pre-Plus/Plus disease
  - Choroidal thickness is associated with pre-Plus/Plus disease but not ROP Stage
- Different retinal and choroidal thickness response to ROP may reflect their different location relative to the blood-eye barrier
Analysis of Retinal Microanatomy in Retinopathy of Prematurity to Improve Care: Study of eye-brain development in preterm infants (Baby STEPS) Group

Study Chair: Cynthia A. Toth, MD;
Co-investigators: Xi Chen, MD, PhD; Charles M. Cotten, MD; Maysantoine El-Dairi, MD; Sina Farsiu, PhD; Sharon F. Freedman, MD; Kathryn E. Gustafson, PhD; Joseph Izatt, PhD; Carolyn Pizoli, MD; Sasapin Grace Prakalapakorn, MD; Lejla Vajzovic, MD; Christian Viehland, PhD; David Wallace, MD;
Post-doctoral Fellow: Shwetha Mangalesh, MBBS;
Senior Research Program Lead: Michelle McCall, BA, MCAPM;
Research Program Leads: Joanne Finkle, RN, JD; Neeru Sarin, MBBS;
OCT Imagers: Du Tran-Viet, BS; Ryan Imperio, BS; William Raynor, BS;
Data Analysts: Stephanie Chiu, PhD; Heena Divecha, MS; Vincent Tai, MS; Katrina P. Winter, BS;
Medical Student: Kai Seely, BS

Principal Investigator: Maureen G. Maguire, PhD;
Co-Investigator: Gui-Shuang Ying, PhD;
Statistician: Brendan McGeehan, MS

Funding: NIH R01 EY250009, P30 EY005722