A spectral-domain OCT study of formerly premature children.

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Preceptor: Dr. Recchia
Background: Optical coherence tomography (OCT)

- OCT analogous to ultrasound imaging
- Non-invasive
- Uses light waves
- Many applications in ophthalmology
**Background: OCT**

<table>
<thead>
<tr>
<th>Zeiss Stratus OCT</th>
<th>Zeiss Cirrus HD-OCT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time Domain</strong></td>
<td><strong>Spectral Domain</strong></td>
</tr>
<tr>
<td>(Meditec, Dublin, CA)</td>
<td>(Meditec, Dublin, CA)</td>
</tr>
<tr>
<td>Acquires 6 linear B-scans</td>
<td>Acquires 200 linear B-scans</td>
</tr>
<tr>
<td>Fewer data points sampled</td>
<td>More data points sampled</td>
</tr>
<tr>
<td>Slower scanning time</td>
<td>Faster scanning time</td>
</tr>
<tr>
<td>Resolution: up to 10 microns</td>
<td>Better resolution: up to 5 microns</td>
</tr>
<tr>
<td>More concern for eccentric fixation and technical skills</td>
<td>Less concern for eccentric fixation and technical skills</td>
</tr>
</tbody>
</table>
Background: SD vs TD OCT

Spectral Domain

Time Domain

Courtesy of Zeiss Whitepaper
Background: Prematurity

Visual Acuity at 10 Years in Cryotherapy for Retinopathy of Prematurity (CRYO-ROP) Study Eyes

Effect of Retinal Residua of Retinopathy of Prematurity

Cryotherapy for Retinopathy of Prematurity Cooperative Group®
Background: Prematurity

- Escedy et al (2007) noted increase central retinal thickness in formerly premature children

- Stratus OCT

- Mainly due to presence to ROP
Recchia et al (2007) showed OCT abnormalities in ROP patients - first to suggest that changes may be vestiges of prematurity.
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Limitations

- Technologically
- Methodologically
Hypothesis:

OCT abnormalities are more common in formerly premature children than in full term children.
OCT and prematurity

Study questions:
1. Is there a difference in macular thickness between premature and full-term children?
2. Is there a difference in foveal contour between these groups?
3. Are the OCT findings correlated to the presence of ROP or another variable?
Methods

- IRB approval for prospective study
- Records of formerly premature infants born prior to 1/1/2001 (treated in the Vanderbilt NICU)
- Control group matched for age and refractive error
Methods

- Group I: premature with ROP
  (<32 weeks gestational age)

- Group II: premature without ROP
  (<32 weeks gestational age)

- Group III: full term
  (>36 weeks gestational age)
Methods

- Gestational age, birth weight, ROP status obtained from records
- Cycloplegic refraction
- Best corrected visual acuity
Methods

- Quantitative primary outcome measures (OCT)
  - central subfield thickness
  - inner (ring) macular thickness
  - outer (ring) macular thickness
  - total macular volume
Methods

- Qualitative primary outcome measures (OCT)
  - presence of foveal depression
  - preservation of retinal layers
Methods

- OCT data were reviewed by a trained physician (FMR) masked to the birth history of the patient.

- Quality of all scans was assessed and any scans with a signal strength less than 8/10 were discarded.

- For each eye, a 6 x 6 mm macular cube and 5-line macular raster line scan were interpreted individually.
Results: Eyes

- 76
  - 38 patients completed study

- 9
  - One eye nystagmus, one eye phthisical, two eyes uncooperative, five monocular status

- 6
  - Six eyes from three patients – could not determine ROP/non-ROP status

- 2
  - From one pt with a poor OCT scan

59
  - Eyes of 32 patients
### Results:

**TABLE 1**

<table>
<thead>
<tr>
<th></th>
<th>ROP</th>
<th>Premature</th>
<th>Full-term</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients</strong></td>
<td>12</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td><strong>Number of Eyes</strong></td>
<td>24</td>
<td>16</td>
<td>19</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>10.2 +/- 2.0</td>
<td>9.9 +/- 2.3</td>
<td>11.2 +/- 2.7</td>
</tr>
<tr>
<td><strong>Gestational age (weeks)</strong></td>
<td>27.3 +/- 1.1**</td>
<td>28.9 +/- 2.0**</td>
<td>&gt;38.0</td>
</tr>
<tr>
<td><em>p=0.0014</em></td>
<td><em>p=0.0014</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Birthweight (grams)</strong></td>
<td>1081 +/- 301</td>
<td>1169 +/- 429</td>
<td></td>
</tr>
<tr>
<td><strong>Average refractive error (sph)</strong></td>
<td>+0.24 +/- 0.99</td>
<td>-0.79 +/- 2.26</td>
<td>-0.55 +/- 1.69</td>
</tr>
</tbody>
</table>
Results: Central subfield thickness

- ROP: 301.8 (p < 0.0001)
- Premature: 278.9 (p = 0.0728)
- Full-term: 265.1
Results: Inner ring retinal thickness

- ROP: 322.1 μm (p = 0.2612)
- Premature: 315.4 μm (p = 0.0571)
- Full-term: 326.1 μm (p = 0.4330)
Results: Outer ring retinal thickness

ROP: 286.4um  p=1.0000
Premature: 286.4um  p=0.8373
Full-term: 284.8um  p=0.7515
Results: Total macular volume

- ROP: 10.19 mm³, p=0.6546
- Premature: 10.12 mm³, p=0.7987
- Full-term: 10.06 mm³, p=0.8251
<table>
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<tr>
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<th>ROP</th>
<th>Premature</th>
<th>Full-term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent Foveal Depression</td>
<td>4/24 = 16.7%</td>
<td>0/16 = 0%</td>
<td>0/19 = 0%</td>
</tr>
<tr>
<td>Blunted Foveal Depression</td>
<td>10/24 = 41.7%</td>
<td>8/16 = 50%</td>
<td>0/19 = 0%</td>
</tr>
<tr>
<td>Normal Foveal Depression</td>
<td>10/24 = 41.7%</td>
<td>8/16 = 50%</td>
<td>19/19 = 100%</td>
</tr>
<tr>
<td>Preservation of Retinal Layers</td>
<td>15/24 = 62.5%</td>
<td>8/16 = 50%</td>
<td>0/19 = 0%</td>
</tr>
</tbody>
</table>
Results: Central subfield thickness: inner ring thickness

- **ROP**: 0.939
- **Premature**: 0.886
- **Full-term**: 0.813

Significance levels:
- **ROP**: $p < 0.0001$
- **Premature**: $p = 0.0006$
- **Full-term**: $p = 0.0127$
Results: Gestational age effect?

Macular Thickness vs. Gestational Age

Pearson’s: -0.61
Discussion:

- Significant effect of gestational age
- Non-significant effect of ROP
- In contrast to prior studies which suggest that ROP is the major determinant of OCT abnormalities
Discussion: Foveal development

- Foveal depression occurs by a reduction of inner (ganglion cell and inner nuclear) layers of the retina
- Evident by 24-25 weeks of gestation
- Continues until four months postnatally

Diagram from Provis et al.
Discussion: Foveal development

- Mintz-Hittner et al described smaller foveal avascular zone (FAZ) in formerly premature children.

- Provis et al showed that the formation of the FAZ (vascular border) precedes foveal depression.

- These two processes may be interrelated.
Discussion: Foveal development

- Prematurity may change retinal oxygenation

- Disruption of FAZ and foveal formation
  - Blunted/absent foveal depression
  - Thickened central macula
  - Preservation of retinal layers

- Interestingly, most of our patients had excellent visual acuity
Limitations

- Selection bias (less severe ROP, less severe neurological disease)
- Non-matched gestational age
- Most ROP staging obtained indirectly through NICU discharge summaries
- Inter-rater variability of ROP
Conclusions

- OCT findings such as increased central macular thickness and foveal depression blunting may represent hallmarks of prematurity.

- These findings can be associated with normal visual acuity.
Clinical relevance

- Greater use of OCT in evaluation of patients with decreased visual acuity
- OCT abnormalities may not represent ocular disease
- Research studies in which numerical cutoffs are made for inclusion or evaluation of therapeutic response
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References

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- Provis JM, Sandercoe T, Hendrickson A. Astrocytes and blood vessels define the foveal rim during primate retinal development. IOVS 2000; 41(10), 2827-2836.