Baseline OCT Predictors Associated with Three-Year Change in Dark Adaptation in Age-related Macular Degeneration

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Summary

- Status of age-related macular degeneration (AMD) and baseline AMD stage associated with significant changes in rod intercept time (RIT) at 3 years
- Baseline OCT predictors of change in RIT at 3 years include:
  - Hyperreflective foci
  - Atrophy
- Developing new subretinal drusenoid deposits (SDD) at 3 years associated with significant impairments in RIT
Background

• Dark Adaptation (DA) has been recognized as functional measure for AMD
• Limited evidence that certain OCT features are associated with DA
• Limited knowledge about DA progression over time
• To assess the relationship between baseline OCT features and three-year changes in DA, in a cohort of patients with AMD and a control group
Methods

• Prospective longitudinal study recruited patients with AMD and control subjects age >50 years

• Complete ophthalmic examination and multimodal imaging

• AMD classification using color fundus photographs and AREDS grading by two graders and one senior grader
Methods

• Spectral Domain OCT (Heidelberg)
  • High Resolution Volume 20x20
  • 97 scans, 15 frames

• We evaluated OCT for the following:
  • Classic drusen
  • Reticular drusen
  • Ellipsoid disruption
  • Atrophy
  • Subretinal fluid
  • Intraretinal fluid
  • Hyperreflective foci
  • Outer retinal tubulations
  • CNV / fibrosis
  • PED
Methods

- Dark Adaptation: AdaptDX (MacuLogix Inc.)
  - Extended protocol (20 minutes)
  - 15 min rest between the two eyes
  - Excluded eyes with fixation error >30%
- Rod Intercept time (RIT) measurements done at
  - Baseline exam
  - 3-year exam
- Multilevel mixed level models for the inclusion of 2 eyes of the same patient
## Results

### Characterization of DA

<table>
<thead>
<tr>
<th>Baseline AMD stage</th>
<th>Baseline</th>
<th></th>
<th></th>
<th>3 years</th>
<th></th>
<th></th>
<th></th>
<th>RIT change in minutes Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>RIT mean ± SD</td>
<td>RIT abnormal n (%)</td>
<td>RIT &gt; 20 min n (%)</td>
<td>RIT mean ± SD</td>
<td>RIT abnormal n (%)</td>
<td>RIT &gt; 20 min n (%)</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Control</td>
<td>13</td>
<td>5.4 ± 3.1</td>
<td>3 (23)</td>
<td>0 (0)</td>
<td>6.1 ± 2.7</td>
<td>5 (38)</td>
<td>0 (0)</td>
<td>0.7 ± 2.4</td>
</tr>
<tr>
<td>Early AMD</td>
<td>3</td>
<td>5.7 ± 4.1</td>
<td>1 (33)</td>
<td>0 (0)</td>
<td>7.5 ± 3.5</td>
<td>1 (33)</td>
<td>0 (0)</td>
<td>1.8 ± 2.0</td>
</tr>
<tr>
<td>Intermediate AMD</td>
<td>26</td>
<td>14.2 ± 2.5</td>
<td>22 (85)</td>
<td>11 (42)</td>
<td>16.6 ± 5.3</td>
<td>24 (92)</td>
<td>16 (62)</td>
<td>2.4 ± 4.2</td>
</tr>
</tbody>
</table>
## RIT at 3 Years

<table>
<thead>
<tr>
<th></th>
<th>Beta coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AMD stage baseline</strong></td>
<td>4.83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Phakic baseline</td>
<td>4.61</td>
<td>0.123</td>
</tr>
<tr>
<td>Gender</td>
<td>-1.21</td>
<td>0.618</td>
</tr>
<tr>
<td>RIT baseline</td>
<td>0.81</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Ellipsoid zone disruption</strong></td>
<td>4.63</td>
<td>0.007</td>
</tr>
<tr>
<td><strong>SDD</strong></td>
<td>5.90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SDD &gt;2 ETDRS fields</td>
<td>5.38</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Classic drusen</strong></td>
<td>7.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hyper reflective Foci</td>
<td>4.11</td>
<td>0.067</td>
</tr>
<tr>
<td>Atrophy</td>
<td>2.69</td>
<td>0.393</td>
</tr>
</tbody>
</table>

*Accounting for age*
Baseline Predictors of RIT Change

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Beta coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMD stage baseline</td>
<td>1.69</td>
<td>0.026</td>
</tr>
<tr>
<td>Phakic baseline</td>
<td>0.11</td>
<td>0.977</td>
</tr>
<tr>
<td>Gender</td>
<td>-0.76</td>
<td>0.605</td>
</tr>
<tr>
<td>DA baseline</td>
<td>-0.096</td>
<td>0.567</td>
</tr>
<tr>
<td>Ellipsoid zone disruption</td>
<td>0.49</td>
<td>0.757</td>
</tr>
<tr>
<td>SDD</td>
<td>1.26</td>
<td>0.405</td>
</tr>
<tr>
<td>SDD &gt; 2 ETDRS fields</td>
<td>2.88</td>
<td>0.480</td>
</tr>
<tr>
<td>Classic drusen</td>
<td>2.16</td>
<td>0.153</td>
</tr>
<tr>
<td><strong>Hyper reflective Foci</strong></td>
<td><strong>3.96</strong></td>
<td><strong>0.018</strong></td>
</tr>
<tr>
<td>Atrophy</td>
<td>-0.39</td>
<td>0.927</td>
</tr>
</tbody>
</table>

Only patients that at baseline reached RIT within 20 minutes (n= 31 eyes)
## Subgroup Analysis—Eyes RIT > 20 Baseline

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Beta coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ellipsoid zone disruption</td>
<td>-0.029</td>
<td>0.787</td>
</tr>
<tr>
<td>SDD</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>SDD &gt; 2 ETDRS fields</td>
<td>-0.035</td>
<td>0.676</td>
</tr>
<tr>
<td>Classic drusen</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Hyper reflective Foci</strong></td>
<td><strong>0.124</strong></td>
<td><strong>0.024</strong></td>
</tr>
<tr>
<td>Atrophy</td>
<td><strong>0.178</strong></td>
<td><strong>0.004</strong></td>
</tr>
</tbody>
</table>

Accounting for age

**Baseline OCT predictors accounting for age**

- Ellipsoid zone disruption: $-0.029$, $P = 0.787$
- SDD: NA, $P = NA$
- SDD > 2 ETDRS fields: $-0.035$, $P = 0.676$
- Classic drusen: NA, $P = NA$
- Hyper reflective Foci: $0.124$, $P = 0.024$
- Atrophy: $0.178$, $P = 0.004$
Discussion
Subretinal Drusenoid Deposits

• Of those with SDD at baseline (n= 23), 48% (n=11) had DA more than 20 (i.e. unable to reach RIT during 20 minutes of testing). At 3 years, this number increased to 65% (n= 15). No significant worsening of RIT.

• Of the 19 eyes without SDD at baseline, only 3 developed SDD at 3 years. Significant association between developing SDD and RIT change (p=0.042).
Summary

• Baseline AMD stage and AMD vs controls associated with significant changes in RIT at 3 years
• Baseline OCT predictors of change in RIT at 3 years include:
  • Hyperreflective foci
  • Atrophy
• Developing new SDD at 3 years associated with significant impairments in RIT
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