Quantifying the Rate of Ellipsoid Zone Loss in Stargardt Disease

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FINANCIAL DISCLOSURES:

No financial disclosures
MY ROLE IN THIS RESEARCH:

Please answer which of the following portions of the research you participated in:

☑️ Conception and design of the work/project
☑️ Acquisition of data
☑️ Analysis and interpretation of data
☑️ Creation and/or critical review of the presentation
INTRODUCTION:

- Stargardt disease: slowly progressive inherited retinal disorder
- Characterized by accumulation of lipofuscin in the RPE and variable degrees of macular atrophy$^{1,2}$
INTRODUCTION:

• Traditional studies of progression of Stargardt disease track RPE atrophy (on fundus autofluorescence (FAF))$^{3-8}$
INTRODUCTION:

- Photoreceptor abnormalities (compared to RPE atrophy)\textsuperscript{9-14} are:
  - More widespread
  - Occur earlier in the disease pathophysiology
INTRODUCTION:

- Photoreceptor integrity (as seen as the ellipsoid zone (EZ) on OCT$^{15-17}$
- Correlates retinal function: visual acuity, sensitivity on microperimetry, multifocal ERG response
PURPOSE:

To examine the extent that tracking the EZ on OCT can monitor disease progression in Stargardt Disease and how it compares to tracking RPE on FAF
METHODS:

Subjects:
- Retrospective review
- Retina Division at the Wilmer Eye Institute
- Stargardt patients with ABCA4 mutation
- Follow up > 12 months
METHODS:

**Imaging:**

**OCT:**
- SD-OCT macula volume scans (Spectralis)
- Central 20° x 20° with 49 B-scans
- NIR-R fundus image

**FAF:**
- Conventional FAF (Spectralis)
- Central 30° x 30°
Area of EZ loss
NIR-R

Area of RPE loss
FAF

Comparison
Composite
METHODS:

Statistical Analysis:

• Yearly rate of EZ loss: change in area of EZ loss over period of follow up

• Yearly rate of RPE loss: change in area of RPE loss over period of follow up
METHODS:

Reliability:

- One randomly chosen scan per patient re-analyzed by primary grader (intra-grader reliability)
- Same subset re-analyzed by a second grader (inter-grader reliability)
- Intraclass correlation (ICC) based on a two-way mixed effect model
RESULTS:

• 16 patients
• 15/16 contributed both eyes to the study
• Mean age 33 years (range 10-60 years)
• Follow up
  • Mean 2 years (range 1-5 years)
### RESULTS: Reliability

<table>
<thead>
<tr>
<th></th>
<th>ICC (EZ on OCT)</th>
<th>ICC (RPE on FAF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-Grader</td>
<td>0.99</td>
<td>0.99</td>
</tr>
<tr>
<td>Inter-Grader</td>
<td>0.99</td>
<td>0.96</td>
</tr>
</tbody>
</table>
Bland-Altman Plot
Area of EZ loss is larger than area of RPE loss

$p<0.01$
Rate of EZ loss is similar to RPE loss
Representative Patient #1
Figure A: Initial, Fovea, Year 2

Fovea:

Area: 6.67mm²

Figure B: Year 2, Fovea

Area: 8.25mm²

Figure C: Initial, Superior Macula

Initial

Figure D: Year 2, Superior Macula

Year 2
Initial

NIR-R

6.67mm²

FAF

2.54mm²

Composite

Year 2

NIR-R 0.79mm²/year

8.25mm²

FAF 1.29mm²/year

5.13mm²

Composite
Representative Patient #3

Rate of loss (mm²/year)

EZ

RPE

0.31 ± 0.31

0.33 ± 0.38
CONCLUSIONS:

- Tracking EZ loss on OCT is reliable (inter and intra-grader)
- Area of EZ loss is larger than RPE loss
- Rate of EZ loss is similar to rate of RPE loss
- Advantages of tracking EZ loss
  - Correlates better with retinal function compared to RPE atrophy
  - Occurs earlier in the disease pathophysiology of STGD so can better monitor early stage disease
REFERENCES:

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