Introduction

The ellipsoid region of the photoreceptor inner segments is easily identified in the latest generation of spectral domain OCT as the first (or 3) hypo-reflective bands located on the outer aspect of the neurosensoric retina; this band has been termed ellipsoid zone (EZ). Seventy-five percent of the volume of the ellipse region is accounted for by mitochondria, providing the energy essential for phototransduction processes. It is therefore not surprising that the integrity of the EZ seen on OCT is related to retinal sensitivity. The Radial Shape Discrimination (RSD) test is a global hyperacuity visual function test requiring images of the target to fall on a structurally and functionally intact area of the retinal photoreceptor mosaic.

We investigated the relationship between EZ hyper-reflectivity over the foveal area and performance on a handheld version of the RSD test in participants with age-related macular degeneration (AMD). We hypothesised that participants with more disruption to the EZ band would show worse RSD performance.

Methods

Participants

Clinical sample of participants attending AMD service were included:
- BCVA better than 0.4 logMAR
- Any stage of early/intermediate AMD but no neovascular (nAMD) or central geographic atrophy
- nAMD, being monitored/treated.

Procedures

RSD and BCVA were tested in clinic with appropriate up to date optical correction, always before OCT. Both eyes were always examined.

Ellipsoid Zone Disruption (EZD)

Foveal EZD was defined as a continuous section of a B-scan (falling within the central ring of the ETDRS grid) where the EZ (Fig. 3) was either absent or hyporeflective (yet not completely missing), and which might be accompanied by drusen (Fig. 4). The lengths of all B-scans where the EZ was intact and disrupted were summed and transformed into a percentage of the total. The level of EZD disruption was categorised into 3 groups: “intact EZ”, “less than 20%”, and “more than 20%” disruption.

Results

Participants (n=49, 45 females) were 77±8 years old (mean±SD, range 57 to 91 years). OCT data from all b 78% (65 53% had some EZ disruption at the fovea.

Fig 5: Radial shape discrimination (RSD) and best corrected visual acuity (BCVA) for study eyes of participants with intact ellipsoid zone (EZD=0%), less than 20% and more than 20% of EZD disruption. A statistically significant difference was seen in mean RSD (p<0.05) but not in mean BCVA (p>0.05). Error bars indicate 95% CI. Boxes above show groups age, mean EZD and mean BCVA.

Discussion

While drawn assessment in colour fundus photographs is the current gold standard to assess change in severity of early AMD, foveal drusen alone do not correlate well with visual function. The advent of high resolution OCT has given rise to new potential markers of relevance to AMD, one of which is the integrity of the EZ. It has been reported that EZ integrity is related to retinal sensitivity measured by microneurometry®, suggesting that a loss of EZ hyperreflectivity indicates loss of functional photoreceptors (although not necessarily their death).

Theoretically, normal thresholds for EZD (in the hyperacuity range) are only achievable with a relatively intact photoreceptor mosaic over the area of retina on which the image of the RF pattern falls. Our results are consistent with loss of functional photoreceptors in early AMD causing a decrease in the ability to globally process radial frequency patterns, leading to worse RSD thresholds.

Conclusions

- A statistically significant decrease in EZ dysfunction is linked to disruption of EZD in eyes with early AMD at risk of developing nAMD.
- The EZD test, as used here, is easy to operate and handle and, unlike BCVA, can be used in unsupervised self monitoring of vision.
- Given the emergence of effective treatments for nAMD and the need for early detection, we are currently investigating the ability of the EZD test to detect early nAMD (EDMAD project).

References


Links

Please feel free to scan

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Table 1: Overall OCT quality.

Rating Definition

Good Correct scan positioning, no evidence of significant artifacts or noise 00% (79%)
Fair Pester than “Good”, but enough evidence to proceed with the grading 13% (7)
Ungradable Quality too poor to proceed with grading 7% (5)

Ellipsoid Zone Disruption (EZD)
The level of EZD in study eyes influenced RSD scores (p=0.01) but did not affect BCVA (p=0.89, Fig 5).

While the proportion of total RSD variance explained by EZD was small (Partial η2=0.02) there was a clear statistically significant linear trend in the data (Polynomial contrasts, p=0.003). The effect of EZD was much more noticeable when the fellow, nAMD eyes were included in the analysis, confirming more of the AMD spectrum (Fig 6). A stronger correlation was seen for RSD (Pearson’s r=0.61) than for BCVA (Pearson’s r=0.45). The slopes of the regression lines for RSD and BCVA (R2=0.045,0.005 and 0.00290.004 respectively) were statistically significantly different (p=0.0005). Results remained unchanged when 0% and 100% EZD were excluded from the analysis and study eyes and fellow eyes were randomised in order to avoid both eyes of the same participant included in the analysis.

Drusen and foveal thickness

64% of participants with EZD also had large drusen at the fovea (defined as ≥70μm in maximum height, including the RPE). No statistically significant difference in RSD was observed between those with EZD only and those with EZD and drusen (mean difference in RSD: 0.05 logMAR, F(1,42)=1.01, p=0.32). Mean BCVA CST was 283±23 (95%CI 277 to 287 μm). No statistically significant correlation was seen between CST and RSD (Pearson’s r=0.012, p=0.25) after the effect of age was accounted for.

Fig 5: 5 Radial shape discrimination (RSD) and best corrected visual acuity (BCVA) for study eyes of participants with intact ellipsoid zone (EZD=0%), less than 20% and more than 20% of EZD disruption. A statistically significant difference was seen in mean RSD (p<0.05) but not in mean BCVA (p>0.05). Error bars indicate 95% CI. Boxes above show groups age, mean EZD and mean BCVA.

Fig 6: Relationship between the amount of EZ disruption and central visual function (RSD, left and BCVA, right) for study eyes and fellow nAMD eyes, covering a wider sample of the spectrum of AMD. A stronger association (r=0.61 to 0.41) and steeper linear regression slope (β=0.85±0.0005 and 0.0029±0.0004) were seen for RSD compared to BCVA.

Fig 7: Examples of EZD (arrow) occurring on its own (top) and with large drusen (bottom).