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Autofluorescence Measurements in Choroideremia

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Background & Purpose

Choroideremia (CHM) is a progressive X-linked retinal degeneration affecting the choroid, retinal pigment endothelium (RPE) and outer retina. Fundus autofluorescence (AF) has a distinctive pattern of AF loss in CHM but this has not previously been quantified. We set out to i) determine the repeatability of measuring the residual AF area loss for use in monitoring CMH; ii) correlate AF area loss with patient age, thus producing a standardised predicted rate of progression against which clinicians may compare their own patients; and iii) provide insights the underlying anatomical changes occurring in eyes with CHM.

Methods

Progression With Age

Choroideremia.

Fifty consecutive CHM patients (100 eyes) attending outpatient clinics at the Oxford Eye Hospital underwent AF analysis with Heidelberg Spectralis. Area of residual AF was traced using the tool available in Heidelberg Eye Explorer. Bland-Altman analysis was used to calculate the coefficient of repeatability. The rate of progression with age was calculated and maps of the remaining area of AF created using GIS software; FME (Safe Software Inc, Canada) and QGIS version 2.6 (open source GIS software).

In choroideremia centripetal loss of AF typically progresses steadily over a patient's lifetime.

By analysing a cohort comprising a range of ages, it is possible to predict the average rate

and extent of AF area loss (Figure 2). The y-intercept allows for the fact that the optic disc

does not display natural AF so an image which includes the optic disc cannot display 100%

AF. The gradient of the line is the rate of residual retinal loss, known as the Oxford Index for



Bland Altman Analysis

A Bland Altman analysis 16 was performed to establish the test-retest variability of our method for measuring the area of retained AF as a percentage of the total area photographed on a 55⁰ image (Figure 1). The image comprises a total of 10 eyes from 10 patients divided into two groups: Ia) absolute residual area < 10mm2, and Ib) absolute residual area of AF \geq 10mm². The CR was 0.3% for patients with an area of < 10mm² and 0.7% for patients with an area of ≥ 10 mm².



Figure 2: Oxford Index calculation for remaining retinal area in eyes with choroideremia. Age is plotted on a linear scale and area on a log scale due to the logarithmic nature of the relationship. The equation defines the Oxford Index and shows the relationship between remaining retina and age. Taking into account the log axes, the Oxford Index for the remaining retina can be defined as $\log y = -0.04 * age + 2.53.$



Maps of Remaining Retinal Area



A composite image of the right eyes is presented on the left and a composite image of the left eyes is create a map of areas of residual retina in choroideremia. Across a cohort of 100 eyes (50 right and 50 left), less than five eyes on each side had retained AF around the optic disc, whereas up to 40 eyes for each side had preservation of AF around the fovea. There was a preservation at increasing distance from the fovea. The pattern of demonstrate relative conservation in the vertical meridian. Similarly

Conclusions

- \succ We have shown AF is a repeatable and useful outcome measure for monitoring CHM progression.
- > The Oxford Index for Choroideremia provides clinicians with a simple tool for quickly assessing the extent of an individual patient's progression as compared to the age-matched mean.
- > We have provided a map of where the retina is most robust and this can help in understanding disease pathogenesis as well as directing future treatment.









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