Visual Field Estimation Using Artificial Intelligence-Imaging Analysis In Patients With Retinitis Pigmentosa

**Introduction**

Inherited retinal disorders (IRDs) are a varied group of conditions with a wide range of effects on the visual experience.1 It is reported that over 5 million people worldwide are affected with an IRD, or approximately 1 every 2000 individuals.2,3 They are the leading cause of blindness and visual disability in the working-age population of Australia and UK.4,5 The most common type of IRD is retinitis pigmentosa (RP), a rod-cone dystrophy with a prevalence of roughly 1 in 3000 individuals.6

Patients affected by RP typically present with night blindness and peripheral field loss. The disease is often monitored by multimodal testing such as retinal imaging, visual field (VF) testing, visual acuity, and contrast sensitivity.1,7 By doing multiple tests, the aim is to capture both retinal structure and function and follow this over time, as the disease slowly progresses. Although this approach is ideal to comprehensively capture patients’ visual experience, often not all tests are available due to cost, time, and staff readiness, especially in the public health environment.

VF testing is a key parameter in visual assessment, necessary to define levels of visual impairment by public health organisms such as the World’s Health Organization.8 However, in practice, it can be time consuming, needing multiple attempts to reach a reliable result, more so in children and patients with severe visual impairment. Recent advances have been made to predict VF based on structural parameters such as optical coherence tomography (OCT) in patients with glaucoma.9,10 An initial study in 18 eyes with RP found a good correlation between kinetic perimetry and OCT ellipsoid zone (EZ),11 and a more recent approach used ultra-widefield fundus autofluorescence (FAF) images to estimate visual acuity, field, and central retinal sensitivity in eyes with RP.12

X-linked RP (XLRP) accounts for up to 15% of all RP cases,13 usually having a rather severe presentation in males, being symptomatic in childhood and rapidly progressing to severe visual impairment by the fourth decade of life.14 Variants in retinitis pigmentosa GTPase regulator (*RPGR*) are the predominant cause of X-linked retinitis pigmentosa (XLRP), accounting for 70-80% of cases.15 *RPGR*-associated RP follows a classical rod-cone dystrophy pattern, and structure-function correlations have been attempted in the past, where autofluorescence findings were found highly correlated with electrophysiology testing.16,17

In this paper, we used artificial intelligence (AI) to assist on predicting patients’ VF based on easy and fast to acquire blue FAF and OCT imaging, potentially aiding towards more efficient patient care.

**Methods**

Fifty-nine male patients with genetically confirmed *RPGR*-associated RP participated in a natural history study that took place in Moorfields Eye Hospital (London, UK). Informed consent was obtained from all patients, ethical approval was provided by the local ethics committee and the study honoured the tenets of the Declaration of Helsinki.

The patients had consistent OCT (Heidelberg Spectralis, Heidelberg Engineering, Inc., Heidelberg, Germany) and Octopus VF (Hagg-Streit AG, Bern, Switzerland) on every visit (every 6 to 12 months for 5 years) with both eyes separately. Macular OCT volume scans using XXXXXXXX scans density and XXXXXXXXX protocol were acquired by specialized technicians, capturing the central 20 degrees of the macula, with the fovea being in the centre of the scan. An automated segmentation algorithm XXXXXXXXXXXXX was used to detect the foveal scan and measure transfoveal EZ width and EZ area. Heidelberg macular blue FAF images were also automatically analysed and the area of the hyperautofluorescent ring was detailed.

Raw VF data was extracted directly using EyeSuite software associated with Octopus and assessments with reliability factors above 25 were excluded from the analysis. Parameters such as mean sensitivity (MS), mean deviation (MD), diffuse defect (DD), and local defect (LD) were considered for analysis.18 Raw data was also imported to the Hill of Vision (HOV) software (XXXXXXXXXXX, Oregon, USA), obtaining total HOV values (VTOT), as well as central 20 (V20) and 30 degrees (V30) results.

Although most patients in this cohort have peripheral VF loss, given that the VF can capture up to 160° and the OCT acquired in this study only images 20/30°, a further analysis to obtain MS of the central 20 degrees of the VF was undertaken using R software XXXXXXXXXXXXXX…

MS estimation to visual field degrees was established using Hagg-Streit AG Perimetry Simulation (XXXXXXX), where a 20° field corresponded to ~19 dB MS and ~10 dB MD, a 10° field to ~9 dB MS and ~20 dB MD, a 5° field to ~3 dB MS and ~27 dB MD, and a 1° field to ~0.6 dB and 29 dB MD.

Single eye macular OCT and VF assessments that took place within a one-month range were linked together and the data was used for statistical analysis, using GraphPad Prism 8.0.2 (GraphPad Software, San Diego, CA, USA). Linear regressions and Pearson correlation were used, and the threshold of significance was set at p < 0.05. Variables that did not pass the Kolmogorov-Smirnov or Shapiro-Wilk normality tests (p >0.1) were normalized for statistical purposes.

**Results**

A total of 381 pairs of OCT and VF data of right (OD) and left (OS) eyes were analysed in this study, with up to 14 pairs per patient (OD and OS, during 7 visits). XX VF were excluded due to having a high RF, and 84 OCTs were not found automatically in the database, possibly due to patients not having the assessment within a month range of the VF testing.

There was a significant association between MS and EZ width (p <0.0001, Y-intercept 0.28, slope 0.13, Figure XX), with also a significant correlation between both parameters (<0.0001, R2 0.32). This means that in patients with RP, an EZ width of 1000 µm corresponds with a MS of ~6 dB, and a monocular field between 5 and 10°, while those with a 2000 µm EZ width will have a field between 10 and 20° with that eye (Figure XX).

EZ width was also significantly associated with MD (p <0.0001, Y-intercept 4.1, slope -0.12; Pearson p <0.0001, R2 0.27), and with DD (p <0.0001, Y-intercept 3.38, slope -0.12; Pearson p <0.0001, R2 0.29), but now with LD (p 0.16). Regarding HOV parameters, foveal EZ width was also significantly associated with VTOT (p <0.0001, Y-intercept 0.6, slope 0.03; Pearson p <0.0001, R2 0.21), V30 (p <0.0001, Y-intercept 0.6, slope 0.1; Pearson p <0.0001, R2 0.23), and V20 (p <0.0001, Y-intercept 0.23, slope 0.3; Pearson p <0.0001, R2 0.35, Figure XX).

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