Octopus 900 automated kinetic perimetry versus standard automated static perimetry in glaucoma practice

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Abstract

Purpose: The presence of central visual field loss does not infer the extent of peripheral visual field loss. In advanced stage glaucoma, we evaluated whether automated kinetic perimetry provided additional visual field information to that of central static perimetry.

Materials and Methods: We undertook a prospective cross sectional study of advanced stage glaucoma defined as stages 3-4. Visual field assessment for right and left eyes was undertaken within one clinic visit using the Octopus 900 G programme and kinetic strategy.

Results: We recruited 126 patients (170 eyes). Mean patient age at assessment was 55.86 years (SD 15.15). Mean kinetic reaction time was 1503.96ms (SD 801.68). Kinetic I4e was plotted in 71% of eyes with an unadjusted area of 2513.68 degrees^2 (SD 2397.91) and mean isopter radius of 23.16 degrees (SD 13.07). Kinetic I2e was plotted in 53.5% of eyes with an unadjusted area of 627.07 degrees^2 (SD 1291.94) and mean isopter radius of 7.47 degrees (SD 10.59). Increased reaction time was associated with a poorer visual field (p=0.001). Mean sensitivity, mean deviation and standard loss variance values on static perimetry were higher in patients who had a defined kinetic field boundary than in patients with no kinetic response to I4e stimulus (p=0.0001). However this corresponded to only small to medium correlation between static fields and existent kinetic fields: the presence of poor static fields did not always infer a poor kinetic visual field as poor static fields could also have good kinetic visual fields.

Conclusions: Although we confirmed a lack of agreement and only a small to medium correlation between the extents of central versus peripheral visual field loss, automated kinetic perimetry did provide additional peripheral (outside the static 30-degree central field) visual field information which was clinically useful in the presence of non-informative severely defected central visual fields.

Keywords

Standard automated perimetry; Automated kinetic perimetry; Glaucoma; Advanced stage; Octopus 900

Introduction

Kinetic perimetry is an essential perimetry assessment in many areas of ophthalmology practice including the assessment of young children, patients with poor vision or severely restricted visual fields and for patients with posterior hemisphere brain injuries [1-5].

For patients with glaucoma, the usual choice of visual field assessment is a threshold strategy to assess the central 24 to 30 degrees of the visual field of right and left eyes individually. In clinical practice a number of issues arise with these central assessment programmes. For patients with late-stage disease, the central programme can show severe visual field loss but does not provide information about the peripheral visual field which is of use when indicating the 'functional' field of vision – that used by the individual in daily activities. Peripheral visual field impacts on quality of life. Whilst central vision is rated as having greatest importance for glaucoma patients, peripheral vision is of importance for mobility and tasks outside the home [6-8]. Where peripheral vision is affected, this leads to worse quality of life scores for items such as role limitation and peripheral vision [9,10].

Options for peripheral visual field assessment are static suprathreshold screening programmes or threshold programmes. However, these can have considerable test durations and/or may provide limited detail of the visual field loss [11]. A further alternative is to consider kinetic visual field assessment. Use of entirely automated kinetic perimetry is not commonly reported despite the wide acceptance of automated static perimetry. This is not surprising. Kinetic visual field assessment is often not used because of perceived longer test durations and need for experienced examiners. However, kinetic perimetry can be undertaken with shorter test durations in comparison to peripheral static suprathreshold and threshold assessments [11,12]. Traditionally kinetic perimetry was operated in manual mode, typically using a Goldmann perimeter. In the last decade, considerable advances have been made in the development of computerised kinetic perimetry. A move to computerised perimetry has enabled standardisation of certain features and removes examiner bias that exists in manual mode (for example, stimulus speed, randomisation of vector presentation) with additional advantages of auto-calibration, digital storage of test results, calculation of reaction times and availability of age-reference isopters.

The Octopus 900 perimeter provides 90 degree full field projection perimetry and facilitates both kinetic and static visual field assessment. The vectors chosen for kinetic perimetry can be preselected and run as an automatic test or performed 'live' (manual mode) choosing vectors for assessment dependent on patient responses during the test. Combining automated customised tests with live vectors results in semi-automated kinetic perimetry.

In this study we aimed to investigate the use of automated kinetic perimetry using the Octopus 900 in providing additional information about the full visual field in cases of advanced stage 3-4 glaucoma with considerable central visual field loss, to determine the proportion that retained useful peripheral visual field and to explore the duration of testing by automated kinetic perimetry. We hypothesised that this data could be used to provide a recommendation for transfer from the static to the kinetic assessment in cases where central visual field assessment no longer provides sufficient data on which to base clinical decisions.

Methods

Design

We undertook a prospective, exploratory, observational cross-section study. Institution ethical approval (Glaucoma Clinic New Delhi, India) was obtained and subjects provided informed consent.

Recruitment

The study recruited patients with visual field loss due to advanced glaucoma and who met our inclusion criteria. Consecutive subjects requiring visual fields were recruited from ophthalmology outpatient clinics between 2016-2017. Severe glaucoma was diagnosed according to the International Classification of Diseases (ICD) diagnostic code 9 (365.73) and 10 (7^{th} digit "3"). Diagnostic code 365.73 represents the glaucoma stage code for severe, advanced and end-stage glaucoma

consisting of “glaucomatous visual field abnormalities in both hemifields and/or loss within 5 degrees of fixation in at least one hemifield” [13,14]. ICD version 9 codes were updated in 2015 to version 10 codes which consist of seven digits [15]. The first three indicate the code category and the last four provide added detail. Where the last digit is “3”, this indicates severe glaucoma regardless of the type or cause of glaucoma. For example, H4010X3 represents unspecified open angle severe stage glaucoma.

Inclusion criteria

We included adult patients attending for visual field assessment with a diagnosis of severe or advanced glaucoma (stages 3-4), sufficient motor ability to sit at the perimeter unaided, ability to press the response button, sufficient cognitive ability to understand and follow instructions for performing the test, and willingness to undergo standard visual field assessments on the same day.

Exclusion criteria

We excluded patients with a diagnosis of stage 1-2 glaucoma, visual acuity worse than 1.0 logMAR, those unable to sit at the perimeter, those with unreliable visual fields, unable to follow instructions for performing the test or too ill to complete the full assessment.

Visual field assessment

The study protocol consisted of visual field assessment with both static G1 perimetry and kinetic perimetry on the same day. There was no defined order to visual field testing. The Octopus 900 perimeter G programme has a physiology-based grid of 59 test locations within the central 30 degrees [16]. Locations are clustered more closely together centrally (2.8 degree spacing) with five central foveal locations and 17 test locations in the macular region. Locations are spaced further apart peripherally with emphasis on locations in nasal step regions and with more test locations nasally than temporally. There is no weighted analysis of test locations. Test locations are distributed in a pattern to follow retinal nerve fibre bundles to facilitate the detection of glaucomatous visual field loss. Static visual field results were deemed unreliable if combined false negative and false positive responses exceeded 25%.

For the purposes of using automated kinetic perimetry, a standardised test was programmed using the Octopus 900 Eyesuite platform (Figure 1). Two stimuli of the same size (I: 0.25mm^2/0.009 degrees^2 area; 0.11 degree diameter) were used but of different intensities (4e: 1000 apostilb and 2e: 100 apostilb). Size I represents the smallest of the five target sizes used, and frequently selected, in kinetic perimetry [17,18]. Size I4e is the smallest and brightest target used to assess the peripheral visual field whilst size I2e is 10 decibels dimmer than size I4e and used to assess the central visual field. These targets correspond better to the area tested by the G1 static programme whilst also allowing for the smallest target appropriate to test the peripheral visual field boundary [17,18]. The peripheral visual field boundary and blind spot were assessed using the size I4e target. The central visual field boundary was assessed using the size I2e target. A minimum of twelve vectors were assessed for the peripheral visual field and eight for the central visual field, moving centripetally. In addition, 56 static points (14 per quadrant) are assessed within the central 30 degrees of the visual field using the I4e target. Where a visual field defect was found, this was further evaluated using additional vectors with direction of target movement perpendicular to the boundary of the field defect. Following assessment, the response points along each vector, including any additional vectors required to plot visual field deficits, were joined to form the isopter for I4e and I2e targets respectively. Refractive correction was used as required for the central visual field (static and kinetic perimetry) and for the peripheral visual field (kinetic perimetry).

Reaction time vectors were added for I4e and I2e stimuli; two vectors per stimuli and placed within the central 10 degrees of the visual field. These allow calculation of the latency, measured in milliseconds, between detection of the stimulus and response (pressing the perimeter response button).In kinetic perimetry, reaction time vectors are placed within the intact visual field area for the related isopter, i.e. after plotting a size I4e perimeter isopter, reaction times are plotted within this isopter in a seeing area using a size I4e reaction vector. The patient should be able to see the stimulus as soon as it is presented. Therefore, the time between stimulus presentation and the time the patient presses the response button, represents the reaction time for the patient. In turn, this allows adjustment of the visual field isopters to take into account the latency effect on the size of visual field [19]. With rapid response following presentation of the reaction time stimuli, the adjustment of visual field isopters is

minimal. However, where reaction times are delayed, isopter boundaries can be adjusted considerably. Delayed reaction times can be caused by variability from visual field loss but can represent cognitive delay, fatigue, age and visual field eccentricity [19,20]. Reaction time induces a systematic shift of the isopter or of the boundary of visual field loss in the direction of the target movement [19]. Thus, adjustment for reaction time can reduce variability for the isopter measurement [19].

Movement of the target on the Octopus perimeter was set at 5°/sec for central and peripheral isopters and 3°/sec for the blindspot. Area of visual field was calculated automatically on Octopus perimetry for each target (isopter) and the result provided as degrees^2. For each isopter, the peripheral extent (radius) of each vector was calculated and then the mean isopter radius calculated. Where more than one island of visual field was present, each was measured separately and measurements combined to give one value for the overall visual field.
Kinetic visual field results were deemed unreliable if patient fixation was considered poor by the examiner (by observation on the Octopus eye monitor) or if the blindspot could not be mapped (unless visual field loss prevented blindspot mapping). In such cases, the kinetic visual field testing would be terminated with no recording for the kinetic visual field.

Statistical analysis

Analyses were done using the statistical package SPSS version 25 (IBM SPSS Statistics, USA).

Glaucoma typically affects both eyes, thus two eyes from same patients may not be independent when considering analysis of visual field assessments [21]. Assessments are usually reported for the worst affected eye only. In this study we sought to evaluate visual field data available from kinetic versus static perimetry. We had all the data from both eyes for many subjects although some subjects only had data for one eye as the other eye was blind, hence we aimed to utilise all the data from all eyes as our primary analysis. For the purposes of sensitivity analysis, we also present results from worst eyes (see supplementary material). Worst eye was defined as the eye with greater mean deviation value on G1 static perimetry.

To evaluate normality of distribution of measurements from right and left eyes, a Kolmogorov-Smirnov test was used. If normality was concluded, then we conducted a general linear mixed effect model analysis for difference between eyes in mean sensitivity. The mean sensitivity was the dependent variable and the eye (right versus left) was treated as fixed factor and nested within patient. The patient was treated as a random factor.

Correlation analysis (Spearman ranked correlation) was used to compare measurements for visual field area versus mean isopter radius and reaction compensation, and non-parametric analysis (Mann Whitney test) for static perimetry global indices versus kinetic area and mean isopter radius.

Scatterplots include linear regression lines and Loess curves. The linear regression line assesses strength of linear association between two continuous variables with r^2 =0.0 indicating lack of linear association (i.e. lack of correlation). Correlation (r) is first assessed by its p-value (p) and then, if significant, the correlation is judged as none, small, medium or large if r is 0-0.1, 0.1-0.3, 0.3-0.5 or more than 0.5; i.e. when r^2 is 0-0.01, 0.01-0.09, 0.09-0.25 or more than 0.25 [22,23]. A non-directional p-value, i.e. two-sided alternative hypothesis, is used. The value of r^2 tells us how much variability is shared between variables. The Loess (locally estimated scatterplot smoothing) curve is a local nonlinear regression curve in which the fitting of each point is weighted towards the data nearest to that point. It makes no assumption about the association between variables and is used to visually observe the possible nature of the association between two continuous variables. It can be used as a modelling tool and provides a nonparametric regression that focuses on the fitted curve [24]. The fitted points and related standard errors do respect a particular estimate but are estimated to the whole curve [25]. The default span was set to alpha (α) values ranging from 0.60-0.80 as a trade-off to ensure sufficient data for an accurate fit in order to reduce variance, and to avoid an over-smoothed regression in order to reduce bias. Along the Loess curve, the cross section between the x and y axis relating to the main point of inflection along the curve, was used to indicate cut-off values between data represented along the x and y axes. We report the inflection point as a range of values, as observed for the range of (α) 0.60-0.80.

In this paper all global indices are reported as positive numerical values, including mean sensitivity, mean deviation and standard loss variance.

Results

Primary analysis: All patients / eyes

Results are presented for 126 subjects (170 eyes) with reliable visual field performance; 29 eyes at stage 3 and 141 at stage 4. The worst affected eye was right in 64 (50.8%) and left in 62 (49.2%). Mean age at time of testing was 55.86 years (SD 15.15; 58 [range 13-83]).

The G1 programme was completed for all 170 eyes. Kinetic perimetry with size I4e was attempted for all 170 eyes but with a detected visual field in 121 eyes. Kinetic perimetry with size I2e was attempted for all 170 eyes with a detected visual field in 89 eyes. Figure 2 displays one example of static and kinetic results for one patient.

Distribution of data across left and right eyes

Visual field assessment variables were confirmed to be normally distributed (Kolmogorov-Smirnov test). The area of visual field with size I4e and I2e, showed no significant difference between left and right eyes (p=0.978 and p=0.565 respectively). The mean isopter radius for the visual field with size I4e and I2e, showed no significant difference between the left and right eyes (p=0.863 and p=0.797 respectively, in a general linear mixed model).

Kinetic test duration and Reaction times

The mean duration of kinetic visual field assessment was 10.39 minutes (SD 1.67). Mean duration of static visual field assessment was 3.32 minutes (SD 1.07).

Reaction time calculations gave a mean of 1503.96ms (SD 801.68; min-max range 163-4289.

Kinetic area of visual field

Table 1 outlines values for kinetic and static visual field measurements.

Without reaction time adjustment

The area of visual field with size I4e was plotted for 121 eyes (71.2%) with a mean area of 2513.68 degrees^2 (SD 2397.91). Area of visual field with size I2e was plotted for 78 eyes (45.9%) with a mean area of 627.07 degrees^2 (SD 1291.94).

With reaction time adjustment

The mean area of visual field (for 121 eyes) with size I4e was 3519.40 degrees^2 (SD 2758.09). Area of visual field with size I2e was plotted for 89 eyes (52.35%) with a mean area of 971.54 degrees^2 (SD 1500.96). Eleven eyes did not have a visible field of vision for I2e without reaction time adjustment but which became visible and measurable once reaction time adjustment was made.

Difference in means with / without RT were significant for I4e and I2e isopters; p=0.001 (t-test).

Kinetic mean isopter radius

Without reaction time adjustment

The average mean isopter radius for size I4e was 23.16 degrees (SD 13.07) and for size I2e was 7.47 degrees (SD 10.59).

With reaction time adjustment

The average mean isopter radius for size I4e was 29.16 degrees (SD 13.43) and for size I2e was 11.93 degrees (SD 11.73).

Kinetic visual field comparisons

A significant association was found for reaction time in comparison to the difference in area from with/without reaction time adjustments for I4e and I2e (p=0.0001, p=0.001 respectively, Spearman rank correlation).

Some variability of the difference in area from with/without adjustment for I4e was explained by a linear relationship with reaction time (r 0.499, r^2 0.249, p<0.0001) athough a lot of variability remained unexplained. No variability of I2e was explained by reaction time (r 0.084, r^2 0.007, p=0.350). The variability in mean isopter radius from with/without reaction time adjustment for I4e can be explained to some extent

by a linear relationship with reaction time (r 0.644, r^2 0.415, p<0.0001), and the same for I2e (r 0.244, r^2 0.06, p=0.006).

There were a number of outliers who had longer reaction times with no subsequent increase in visual field area. This suggests that longer reaction times do not necessarily imply an increase in poor visual fields.

Area of visual field was compared to mean isopter radius (without reaction time adjustment) with significant correlations for both I4e and I2e (p=0.0001, Spearman's rank correlation). An almost linear relationship and high correlation was found between increasing area of visual field with increasing mean isopter radius measurements for both I4e and I2e (p=0.0001, r^2 0.837, 0.889 respectively without reaction time compensation; p=0.0001, r^2 0.851, 0.852 respectively with reaction time compensation).

Kinetic versus static visual field comparisons

Global indices from static G threshold perimetry were compared for patients who had a defined kinetic field boundary versus those who had no kinetic visual field boundary to size I4e (Table 2). Global indices of mean sensitivity, mean deviation and standard loss variance were significantly greater when a kinetic visual field could be plotted than when the kinetic visual field could not be plotted (p=0.0001 Independent t test). For example, mean sensitivity values were 8.66 decibels versus 2.52 decibels for plotted versus non-plotted I4e kinetic fields and 9.50 decibels versus 3.99 decibels for plotted versus non-plotted I2e kinetic fields. This gives strong evidence that there is an association between static values and availability of the kinetic assessment. Eyes that have kinetic values also have higher static values.

There was medium correlation for static mean sensitivity versus kinetic area of visual field for either size I4e or I2e (r 0.466, r^2 0.217, p<0.0001 and r 0.311, r^2 0.097, p=0.0004 respectively: Figure 3) and for static mean sensitivity versus kinetic mean isopter radius (r 0.597, r^2 0.357, p<0.0001 and r 0.406, r^2 0.165, p<0.0001 respectively: Figure 3). Low mean sensitivity (i.e. worst visual field) could have a low or high area of visual field, and vice versa for high mean sensitivity. Using the Loess curve to consider differences between mean sensitivity and area/mean isopter radius for kinetic visual fields, the point of inflection is approximately 8 decibels (range 7-9

decibels) for mean sensitivity versus kinetic I4e and approximately 13 (range 12-14 decibels) decibels for kinetic I2e.

There was medium correlation for static mean deviation versus kinetic area of visual field for either size I4e or I2e (r -0.416, r^2 0.173, p<0.0001 and r -0.277, r^2 0.077, p=0.0017respectively: Figure 4) and for static mean deviation versus kinetic mean isopter radius (r -0.539, r^2 0.290, p<0.0001 and r -0.363, r^2 0.132, p<0.0001 respectively: Figure 4). Using the Loess curve to consider differences between mean deviation and area/mean isopter radius for kinetic visual fields, the point of inflection is approximately 18 decibels (range 17-19 decibels) for mean sensitivity versus kinetic I4e and approximately 13 decibels (range 12-14 decibels) for kinetic I2e.

Sensitivity analysis: Worst eyes only

Taking only the worst eye for each patient, measurements were analysed for 126 subjects (126 eyes) with 18 eyes at stage 3 and 108 at stage 4. The worst eye was right in 64 (50.8%) and left in 62 (49.2%). Results for test duration, reaction times, kinetic area of visual field, kinetic mean isopter radius, and kinetic versus static visual field comparisons are shown in supplementary tables 1-2 and supplementary figures 1-6.

Discussion

We have evaluated central static automated perimetry versus automated kinetic perimetry to determine what added information may be obtained from kinetic perimetry of the central and peripheral visual field in advanced stage glaucoma.

In kinetic perimetry, area of visual field and mean isopter radius are two measurements that may be used to indicate the extent of visual field. Both measurements correlated highly with each other but with highest agreement when reaction time compensation was enabled. Reaction time is the time interval between the onset of a stimulus and the subject's response and is typically measured in milliseconds. In a normal population using suprathreshold perimetry, Artes and colleagues reported reaction times of 180-2000ms [26] Mean reaction times in our cohort was high at about 1504ms. Reaction times have been reported using semi-

automated kinetic perimetry (size III4e) in patients with advanced visual field loss [19]. Their mean reaction time recorded was 735ms overall (95% confidence intervals: 356-1515) but for glaucoma patients specifically, the mean reaction time was 794ms (95%CI: 391-1416). Our mean reaction time was higher but may be partially explained by the significant stages 3-4 visual field loss in our cohort and the use of kinetic stimulus sizes of I4e and I2e compared to size III4e; i.e. it is harder to see our target sizes in advanced disease.

Large inter- and intra-subject variability has been reported in normal populations but also in those with visual field loss [19,26]. Reaction times are not only based on cortical function but are indicative also of visual pathway damage [19]. Reaction time can be influenced by a number of factors including increasing age, fatigue, patient cognition and alertness but also the extent of visual field loss and with increasing eccentricity within the field of vision [19,20,26-28]. People with advanced visual field loss frequently have lengthy reactions times but some do not [20]. Reaction times are also reported as prolonged in the affected eye versus the non-affected eye. Thus, reaction time is an important factor influencing the variability of visual field responses and has therefore been proposed as a useful reliability indicator in kinetic perimetry [19]. Therefore, measurement of reaction time may allow determination of visual field due to true damage or because of increased reaction time [20].

Stimulus size is an important consideration in perimetry. In static perimetry, the default stimulus size is III. In kinetic perimetry the typical peripheral isopter size is I4e and I2e for central isopter size. For this study we chose these stimulus sizes for our static (G programme) and kinetic automated assessments to evaluate test completion and extent of visual field loss. Further, to consider test reliability we incorporated retest vectors for 20% of all tested vectors. Instead of repeated presentations, other studies have opted to measure more meridians [27,29]. Nevalainen and colleagues [29] studied advanced visual field loss due to glaucoma (stages 3-4) using a customised Octopus 101 central static programme alongside semi-automated kinetic perimetry using sizes I4e and III4e and 24 vectors per isopter. Additionally they used a size I3e or I2e target for central kinetic assessment. They determined that kinetic perimetry was comparable to automated static perimetry in terms of test-retest reliability and in determining the edges and area of visual field

loss in advanced cases. Further, their patients reported preference for the kinetic visual field assessment.

Monter and colleagues [12] compared mean deviation (24-2 static programme) to mean isopter radius in moderate glaucoma using a size III kinetic stimulus. To evaluate repeatability and counteract outlier responses, they included repeated presentations at the same meridians. A further study used sizes III4e and V4e in kinetic perimetry in comparison to an Octopus 900 32 static programme in patients with advanced glaucoma [30]. In their kinetic perimetry size V4e target was seen by all subjects whilst size III4e was not seen by many patients. This contrasts with previous studies in which III4e was seen by the majority of patients. Kinetic perimetry did define a peripheral visual field and/or central island in 54% of their patients – visual field areas not detected by static perimetry. Thus kinetic perimetry provided additional information undetected by static perimeter that was useful to the overall clinical examination of the patient.

In contrast to these studies [12,29,30], we used considerably smaller kinetic targets and could plot size I4e in 71% of eyes and I2e in 52.35% of eyes. We evaluated mean sensitivity and mean deviation values from static perimetry to consider whether these values could provide an indication for choice of kinetic stimulus size. We found a significantly higher mean sensitivity value (8.66 decibels) and lower mean deviation value (18.32 decibels) for patients in whom kinetic visual fields could be plotted. In comparison, Nowomiejska and colleagues [30] reported an average mean deviation response of 25.8 decibels (range 20.3-33.9) when using sizes III4e and V4e; responses consistent with our mean deviation values for patients who could not plot kinetic visual fields with size I4e. Thus, the higher the mean sensitivity and lower the mean deviation, the greater the size of kinetic stimulus size that should be used to plot peripheral visual field isopters.

The lack of prediction for the peripheral visual field status when based on the results of central visual field assessment has been discussed [12]. The extent of central visual field loss does not always infer similarly impaired, worse or better extent of peripheral visual field loss. Our results were consistent in finding small to medium correlation between the extents of central versus peripheral visual field loss. However, obtaining kinetic visual field results to outline the peripheral visual field did,

for some patients, provide useful additional information about the extent of visual field loss in the peripheral visual field to aid in clinical decision making and patient discussions.

Test duration was significantly longer for kinetic perimetry in comparison to central static perimetry. However our patients had severely impaired static fields and test duration was shorter than usual for central threshold static testing as a result. Based on our results, size I2e added little value so should, we suggest, be omitted from kinetic visual field assessment for advanced visual field loss. Our test duration for kinetic perimetry was not substantially different from that of other similar studies [12,30]. Furthermore, some patients could not detect size I4e and, in these cases, sizes III and/or V can be considered and perhaps be indicated by the mean deviation value of the central static field.

In our analysis, we used the Loess curve to compare differences between the mean sensitivity and mean deviation values obtained from static perimetry to the area calculations using stimulus sizes I4e and I2e obtained from kinetic perimetry. The Loess curve does not provide confidence values. We found the point of inflection to be within an overall range of approximately 7-14 decibels for mean sensitivity and 12-19 decibels for mean deviation for both I4e and I2e stimulus sizes. We therefore provide a clinical recommendation that at a minimum mean sensitivity level of approximately 10 decibels and/or a minimum mean deviation level of approximately 15 decibels on a static central visual field assessment, a switch should be made to using kinetic perimetry using size I4e. At mean sensitivity less than 10 decibels and mean deviation greater than 15 decibels, kinetic stimulus sizes of III4e and V4e could be considered.

We addressed a methodological issue with this paper. Many studies reporting visual field analysis present data from one eye: often the worst eye. We evaluated the distribution of data for all eyes in this study as our primary analysis and we present this as supplementary data. We subsequently ran a sensitivity analysis of worst eyes only to determine where significance lies when only focussing on the worst eye and where the sample size is smaller. We found no differences in distribution for right versus left eyes or for worst versus better eyes. Such evaluation of distribution is essential if wishing to combine results from all eyes in reporting data. Clearly

analysis and reporting of data is important in the context of the type of study. Reporting intervention outcomes often necessitates a determination of independent effect. Hence reporting data from one eye per subject is often appropriate where the condition affects both eyes. However, in studies of assessment comparisons (such as this present study) the question being asked is about the ability of each assessment/test to detect the same defect and that question is as important for each eye individually (as two independent comparisons) as for the subjects individually (as a single comparison). We have reported our methods and results in establishing the distribution of data and our subsequent decision to combine results versus solely presenting worst eye data only. As seen from our supplementary results, values were highly comparable for all eyes versus worst eyes only.

Limitations

Our study is limited by a number of factors. We report visual field results but did not collect visual acuity or fundus imaging for this study. We selected I4e and I2e stimuli for kinetic perimetry because of the frequent use of these stimuli when performing kinetic perimetry. Not all patients were able to discern this target size/brightness and we reflect on the choice of stimuli above.

Conclusions

In advanced stage glaucoma where central static perimetry results show substantially impaired visual fields, these results fail to provide sufficient information to contribute to clinical decision making for the monitoring of the disease. Choice of kinetic stimulus size may potentially be guided by the central static mean deviation indices. We recommend considering kinetic visual field assessment for advanced glaucoma at stages 3-4 once static mean sensitivity reaches levels of approximately 10 decibels and mean deviation of approximately 15 decibels. Additional information about the extent of involvement of the peripheral visual field may prove useful to the clinical discussion. Peripheral kinetic perimetry may confirm substantial visual field loss across the entire visual field or indicate areas of better/preserved visual field outside the central 30 degrees.

References

1. Cummings MF, van Hof-van Duin J, Mayer DL, Hansen RM, Fulton AB. (1988) Visual fields of young children. Behav Brain Res. 29: 7-16
2. Lepore FE. (2001) The preserved temporal crescent: the clinical implications of an ‘endangered‘ finding. Neurol. 57: 1918-21
3. Blamires TL, Reeves BC. (1996) Vision defects in patients with peri-chiasmal lesions. Optom Vis Sci. 73: 572-8
4. Agrawal S, Mayer DL, Hansen RM, Fulton AB. (2009) Visual fields in young children treated with Vigabatrin. Optometry and Visual Science. 86: 767-773
5. Donaghue SP. (1999) Perimetry techniques in neuro-ophthalmology. Curr Op Ophth. 10: 420-428
6. Sawada H, Yoshino T, Fukuchi T, Abe H. Assessment of the vision-specific quality of life using clustered visual field in glaucoma patients. J Glauc. 2014; 23:81–87
7. Rulli E, Quaranta L, Riva I, Poli D, Hollander L, Galli F, Katsanos A, Oddone F, Torri V, Weinred RN. et al. Visual field loss and vision-related quality of life in the Italian Primary Open Angle Glaucoma Study. Int J Sci Rep. 2018; 8: 619
8. Aspinall PA, Johnson ZK, Azuara-Blanco A, Montarzino A, Brice R, Adrian V. Evaluation of quality of life and priorities of patients with glaucoma. Invest Ophth Vis Sci. 2008;49:1907–1915
9. Burr JM, Kilonzo M, Vale L, Ryan M. Developing a preference-based Glaucoma Utility Index using a discrete choice experiment. Optom Vis Sci. 2007;84:797–808
10. Quaranta L, Riva I, Gerardi C, Oddone F, Floriani I, Konstas AG. Quality of Life in Glaucoma: A Review of the Literature. Adv Ther. 2016;33(6): 959–981.
11. Rowe FJ, Cheyne CP. Garcia-Finana M, Noonan CP, Howard C, Smith J, Adeoye J. Detection of visual field loss in pituitary disease: peripheral kinetic versus central static. Neuro-Ophth. 2015; 39: 116-24
12. Monter VM, Crabb DP, Artes PH. Reclaiming the periphery: automated kinetic perimetry for measuring peripheral visual fields in patients with glaucoma. Invest Ophth Vis Sci. 2016; 58: 868-875

13. Fellman RL, Mattox G, Ross KM, Vicchrilli S. Know the new glaucoma staging codes. Eyenet. 2011 (October); 65-66
14. WuDunn D. Monitoring patients with advanced glaucoma. Glauc Today. 2015 (September/October), 42-43
15. https://icd.who.int/browse10/2010/en#/H40-H42 [last accessed 12th May 2020]
16. Racette L, Fischer M, Bebie H, Hollo G, Johnson CA, Matsumoto C. Visual field digest. A guide to perimetry and the Octopus perimeter. 2016, 6th edition. Haag Streit AG, Switzerland
17. Wong AMF, Sharpe JA. A Comparison of Tangent Screen, Goldmann, and Humphrey Perimetry in the Detection and Localization of Occipital Lesions. Ophthal 2000;107:527–544
18. Rowe FJ, Hepworth LR, Hanna KL, Mistry M, Noonan CP. Accuracy of kinetic perimetry assessment with the Humphrey 850; an exploratory comparative study. Eye. 2019 Dec;33(12):1952-1960
19. Nowomiejska K, Conthein R, Paetzold J, Zagorski Z, Kardon R, Schiefer R. Reaction time during semi-automated kinetic perimetry (SKP) in patients with advanced visual field loss. Acta Ophth. 2010; 88: 65-69
20. Vonthein R, Rauscher S, Paetzold J, Nowomiejska K, rapp E, Hermann A, Sadowski B, Chaumette C, Wild JM, Schiefer U. The normal age-corrected and reaction time–corrected isopter derived by semiautomated kinetic perimetry. Ophth 2007;114:1065–1072
21. Bunce C, Patel KV, Xing W, Freemantle N, Dore CJ, Ophthalmic Statistics Group. Ophthalmic statistics note 1: unit of analysis. Brit J Ophth. 2014; 98: 408-412
22. Illowsky B, Dean S. Introductory Statistics. OpenStax, Houston, Texas. 2013. https://openstax.org/books/introductory-statistics/pages/12-4-testing-the-significance-of-the-correlation-coefficient [accessed 29th May 2020]
23. Cohen J. Statistical power analysis for the behavioural sciences. Routledge. 1988; ISBN 978-1-134-74270-7
24. Cleveland WS, Grosse E, Shyu WM. Local regression models. Chapter 8. Statistical Models in S. Editors: Chambers JM and Hastie TJ, Wadsworth & Brooks/Cole1992.
25. https://www.statsdirect.com/help/nonparametric_methods/loess.htm

26. Artes PH, McLeod D, Henson DB. Response time as a discriminator between true and false positive responses in suprathreshold perimetry. Invest Ophth Vis Sci. 2002; 43: 129-132
27. Nowomiejska K, Vonthein R, Paetzold J, Zagorski Z, Kardon R, Schiefer U. Comparison between semiautomated kinetic perimetry and conventional Goldmann manual kinetic perimetry in advanced visual fied loss. Ophth. 2005; 112: 1343-1354
28. Nowomiejska K, Brzozowska A, Zarnowski T, Rejdak R, Weleber FG, Schiefer U. Variability in isopter position and fatigue during semi-automated kinetic perimetry. Ophthalmologica. 2012;227(3):166-72.
29. Nevalainen J, Paetzold J, Krapp E, Vonthein R, Johnson CA, Schiefer U. The use of semi-automated kinetic permetry (SKP) to monitor advanced glaucomatous visual field loss. Gr Arch Clin Exp Ophth. 2008; 246: 1331-1339
30. Nowomiejska K, Wrobel-Dudzinska D, Ksiazek K, Ksiazek P, Rejdak K, Maciejewski R, Juenemann AG, Rejdak R. Semi-automated kinetic perimetry provides additional information to static automated permetry in the assessment of the remaining visual field in end-stage glaucoma. Ophth Phys Opt. 2015; 35: 147-154

Table 1: Visual field parameters

			Kinetic		Static
			I4e, n=121	I2e, n=89	III, n=170
Area (degrees^2)	Without RT	Mean	2513.68	627.07	
		SD	2397.91	1291.94	
Area (degrees^2)	With RT	Mean	3519.40	971.54	
		SD	2758.09	1500.96	
Mean isopter radius (mm)	Without RT	Mean	23.16	7.47	
		SD	13.07	10.59	
Mean isopter radius (mm)	With RT	Mean	29.16	11.93	
		SD	13.43	11.73	
Mean sensitivity (decibels)		Mean			6.94
		SD			5.58
Mean deviation (decibels)		Mean			20.04
		SD			5.67
Standard loss variance (decibels)		Mean			5.89
		SD			2.29
Diffuse defect (decibels)		Mean			17.13
		SD			7.86
Test duration (minutes)		Mean	10.39		3.32
		SD	1.67		1.07

Table 2: G programme global indices

Static perimetry N=170	**Kinetic perimetry: I4e (Mean values)**		**Kinetic perimetry: I2e (Mean values)**		**Significance (Independent t test)**
Global indices	**Area plotted N=121**	**Area not plotted N=49**	**Area plotted N=89**	**Area not plotted N=81**	
Mean sensitivity	8.66	2.52	9.50	3.99	P=0.0001
Mean deviation	18.32	24.46	17.47	22.99	P=0.0001
Standard loss variance	6.63	3.98	6.84	4.79	P=0.0001

Figure 1 Basic standardised kinetic strategy

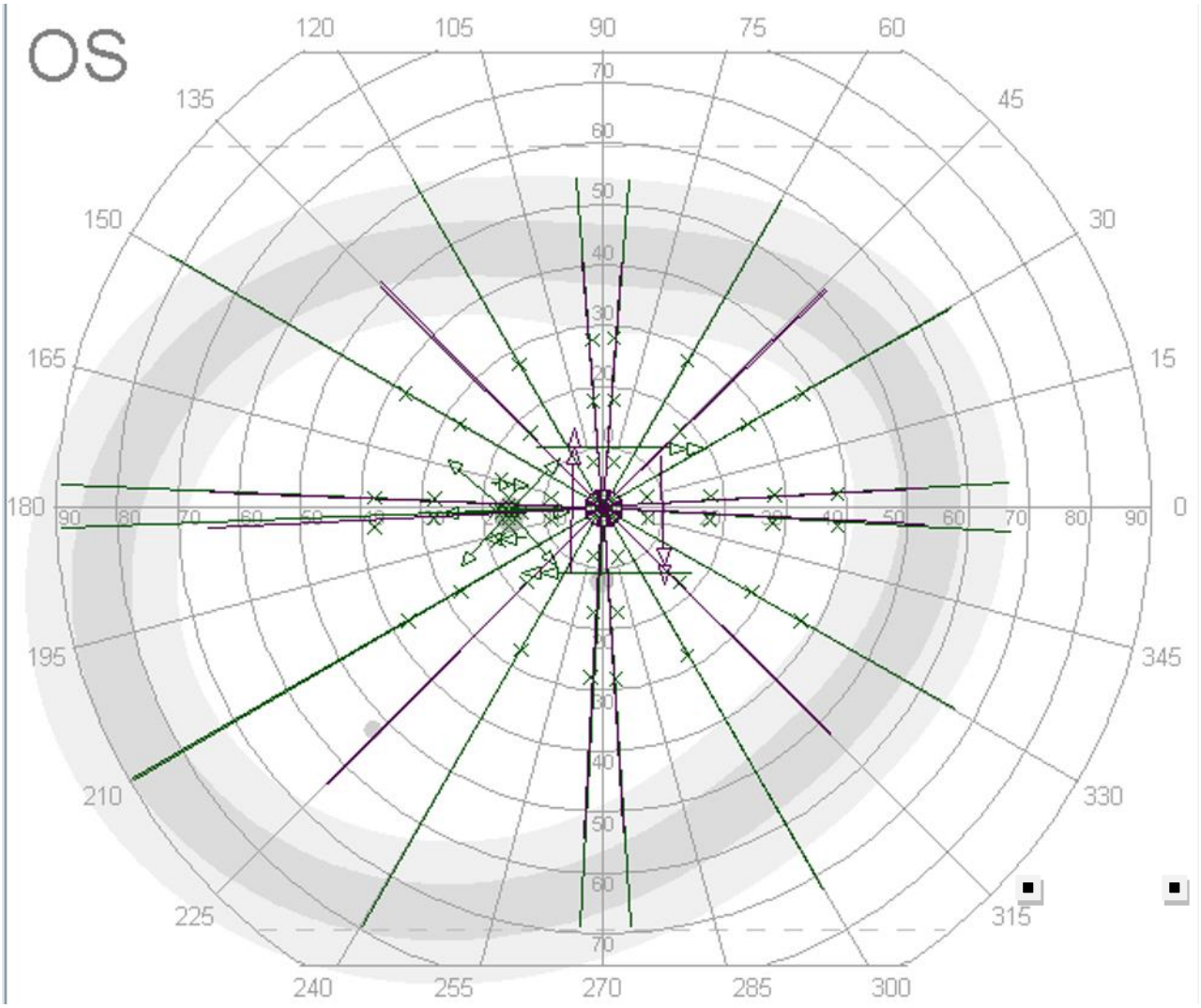
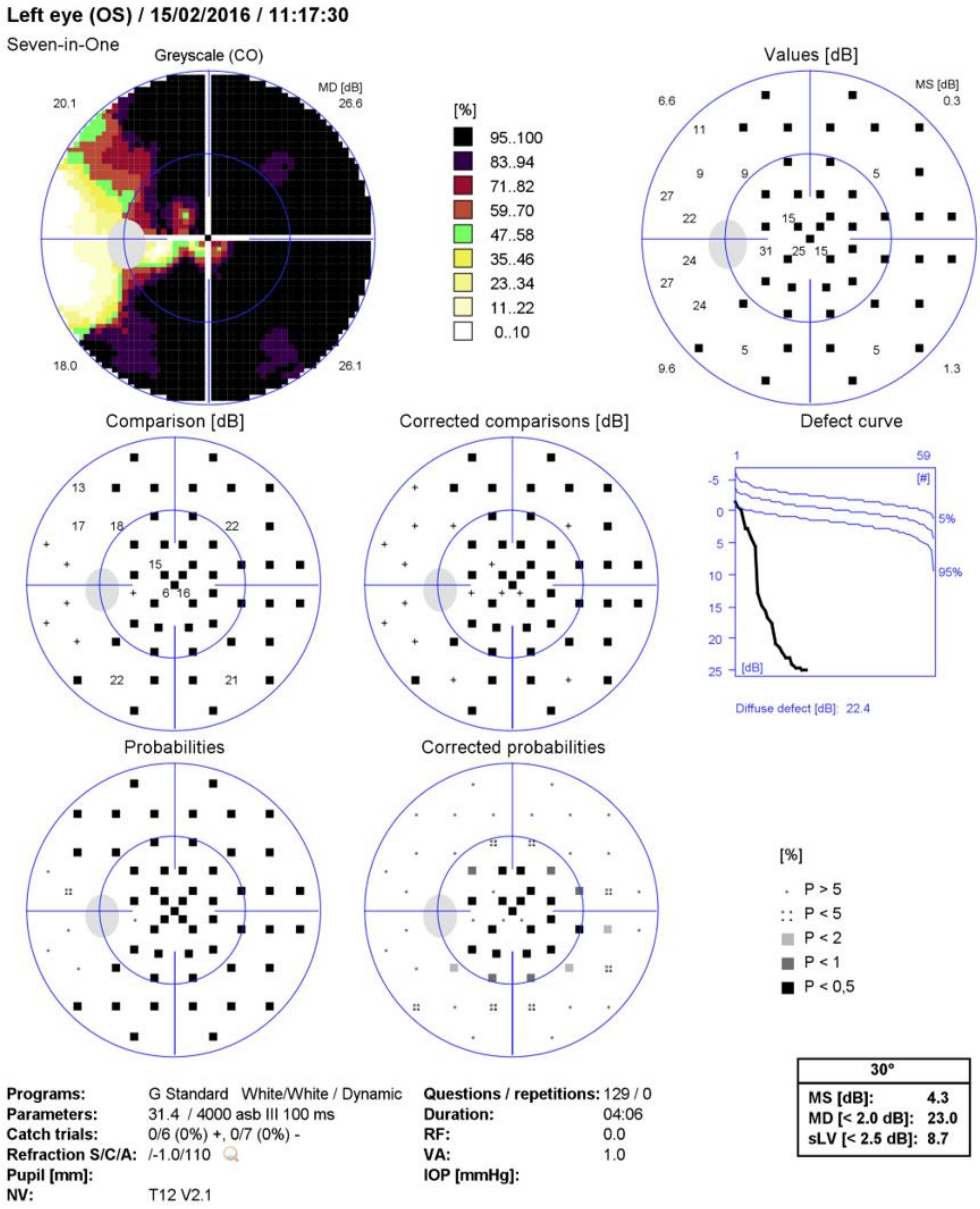
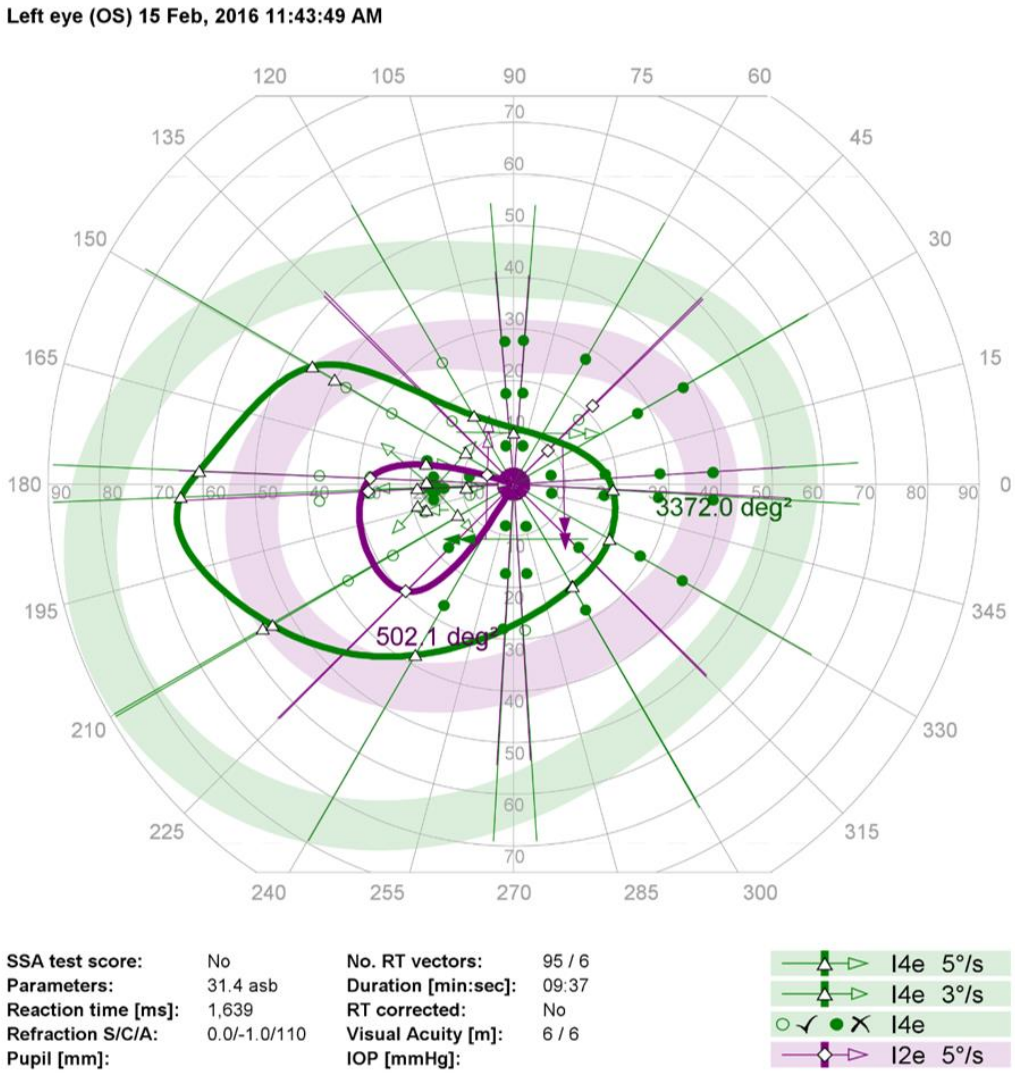


Figure 2: Illustrative results of static and kinetic perimetry

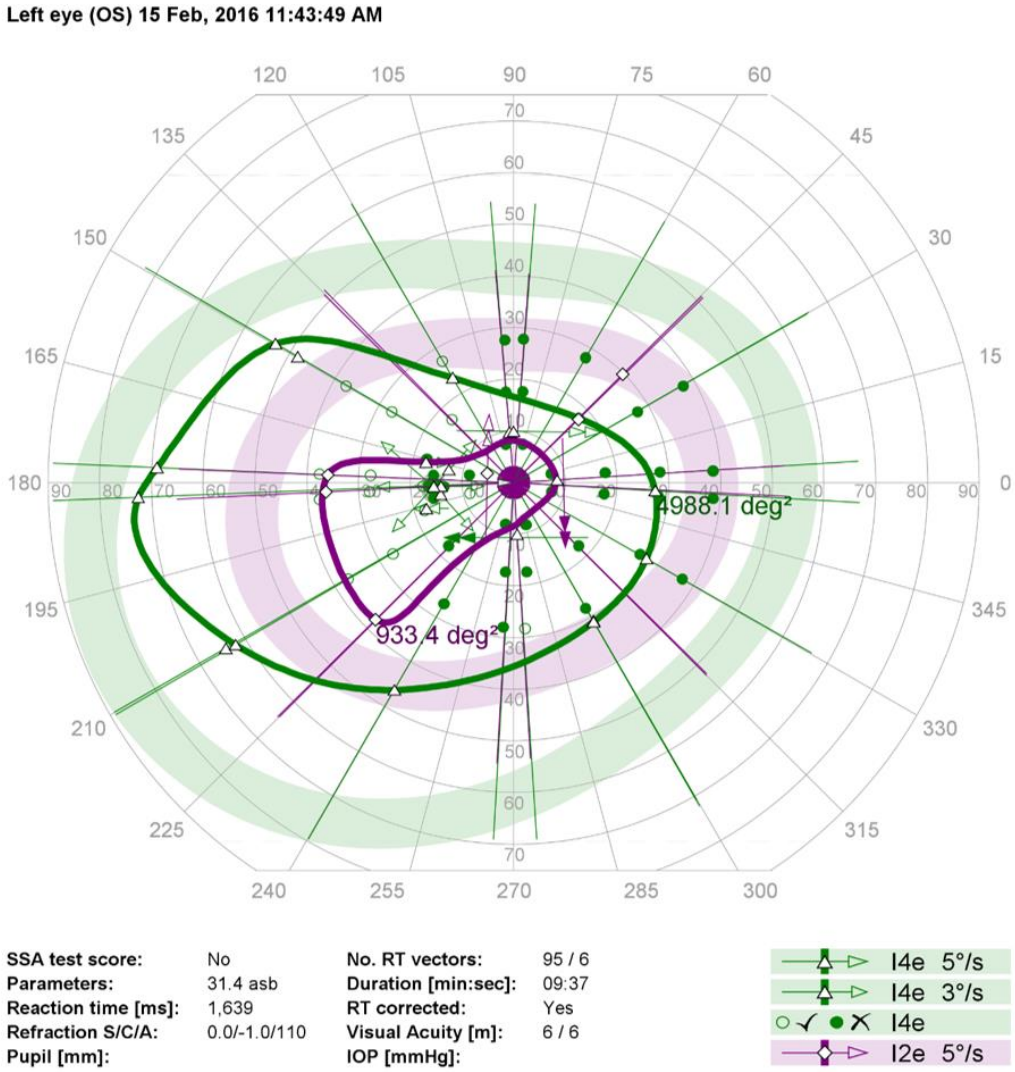
A – G1 static perimetry, left eye



B – Kinetic perimetry without reaction time adjustment, left eye



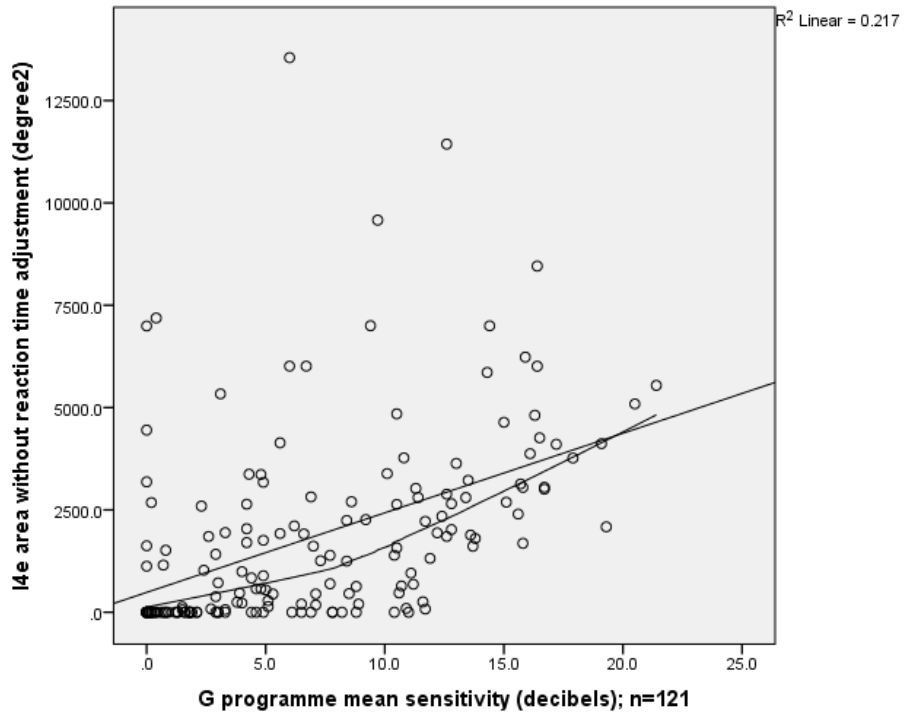
C – Kinetic perimetry with reaction time adjustment, left eye



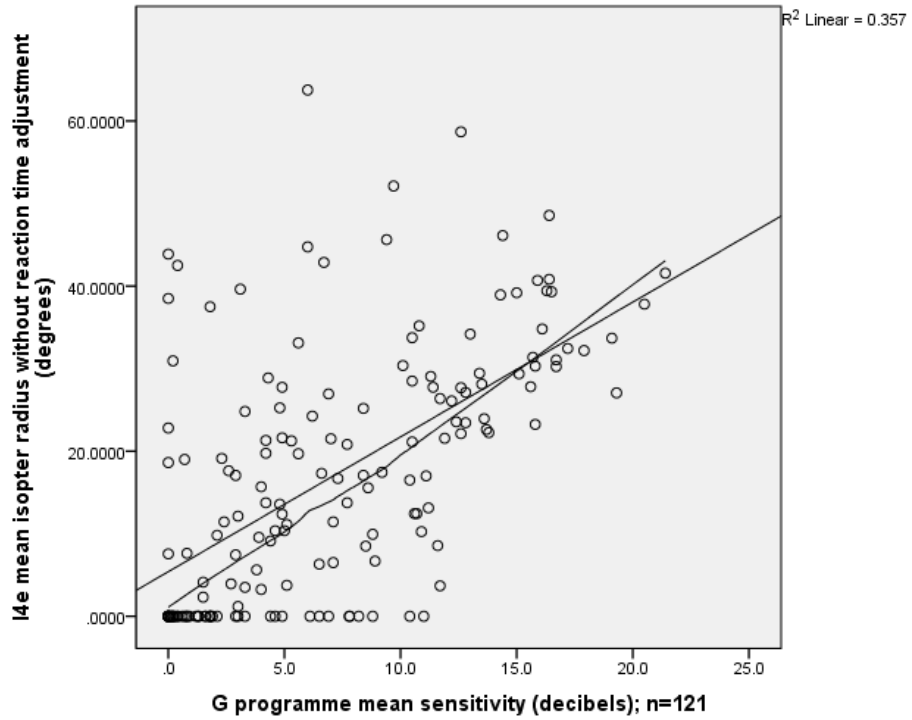
Static perimetry results shows a severely restricted visual field whilst kinetic perimetry display a good residual temporal visual field with increase in isopter area after reaction time adjustment.

Figure 3: Static perimetry mean sensitivity and kinetic perimetry

A – Mean sensitivity versus area; I4e

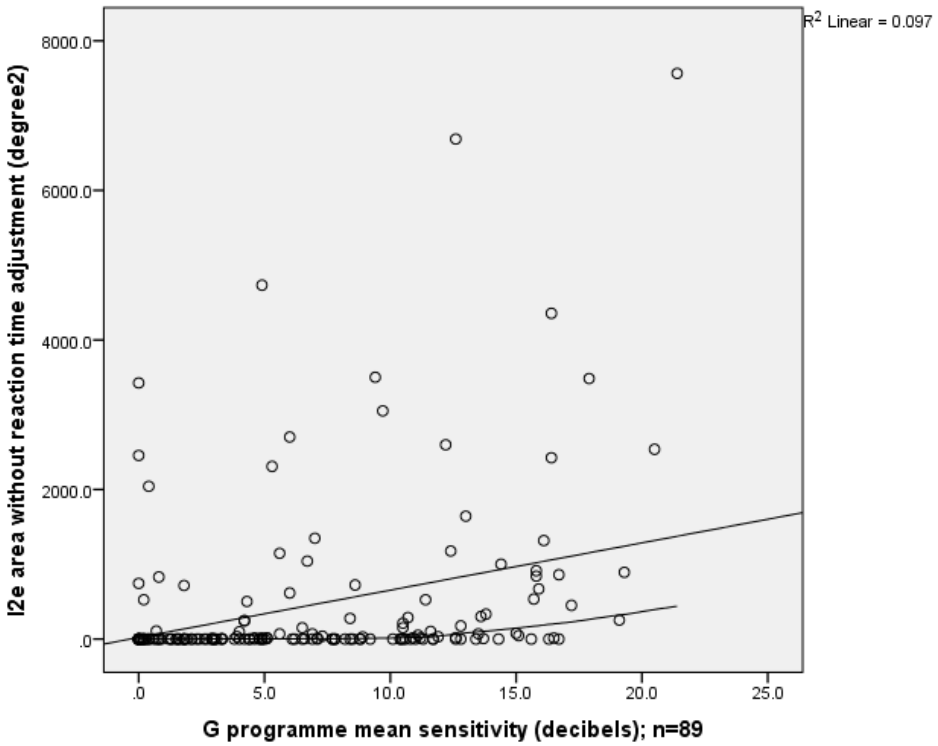


B – Mean sensitivity versus mean isopter area; I4e

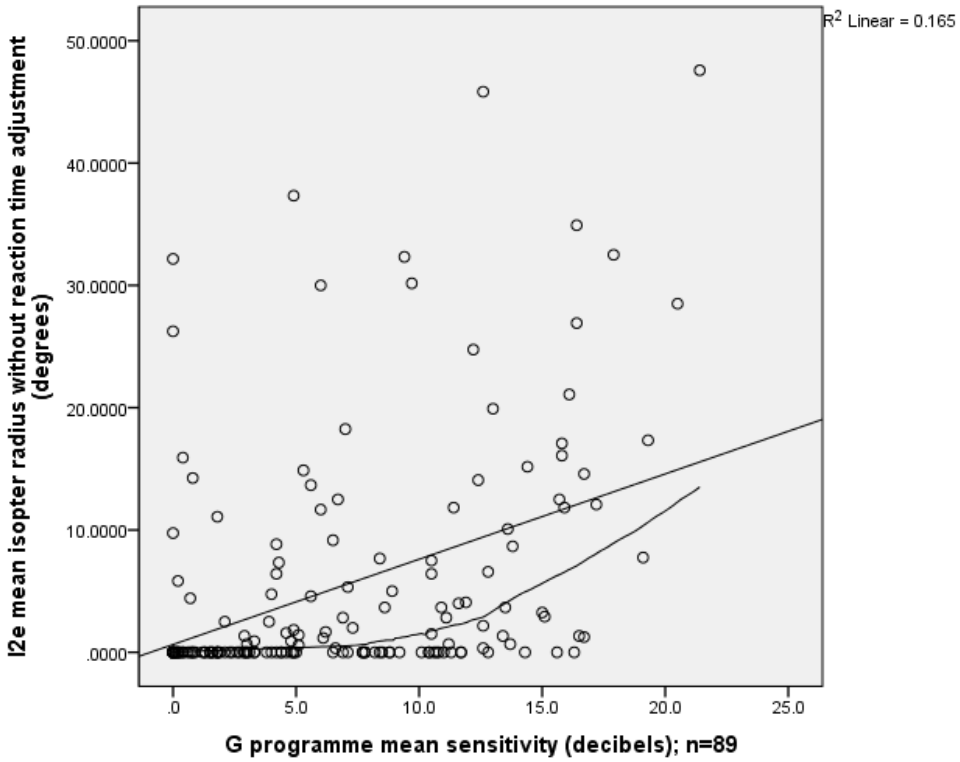


Linear regression line and Loess regression curve show medium and large correlations for size I4e - there was considerable variability for this difference (r 0.466, r^2 0.217, p<0.0001, and r 0.597, r^2 0.357, p<0.0001). The Loess point of inflection is approximately 8 decibels.

C – Mean sensitivity versus area; I2e



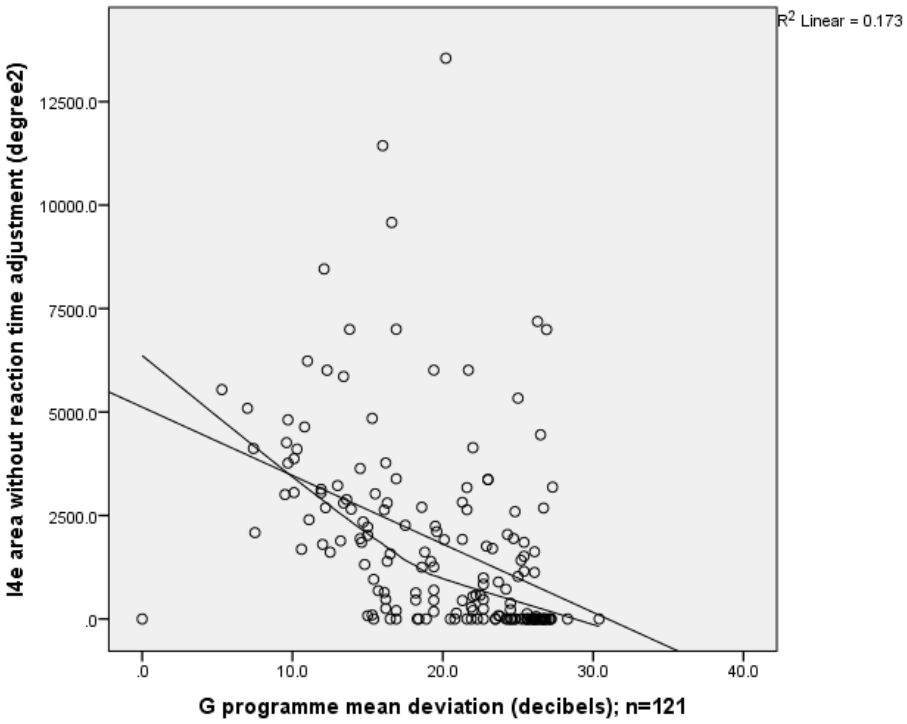
D – Mean sensitivity versus mean isopter area; I2e



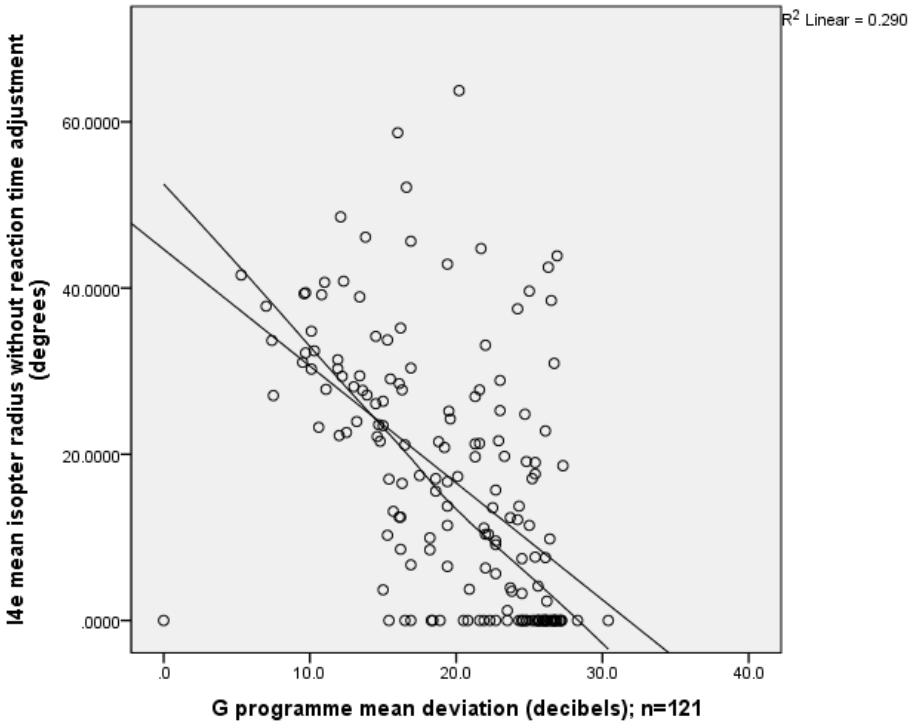
Linear regression line and Loess regression curve show medium correlations for size I2e- there was considerable variability for this difference (r 0.311, r^2 0.097, p=0.0004 and r 0.406, r^2 0.165, p<0.0001). The Loess point of inflection is approximately 13 decibels.

Figure 4: Static perimetry mean deviation and kinetic perimetry

A – Mean deviation versus area; I4e

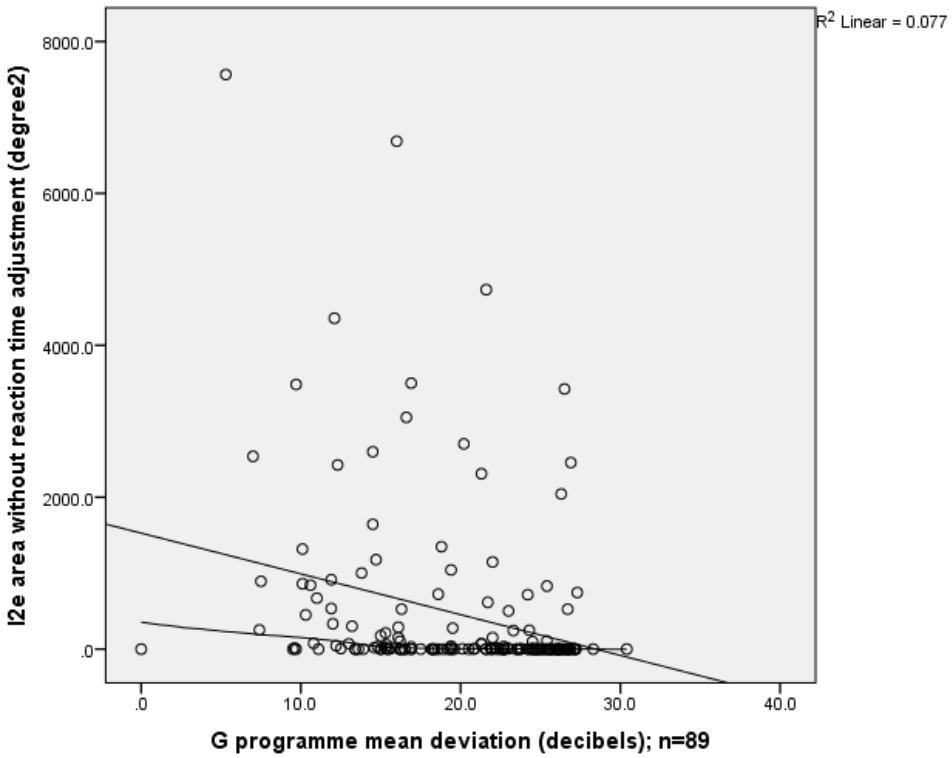


B – Mean deviation versus mean isopter radius; I4e

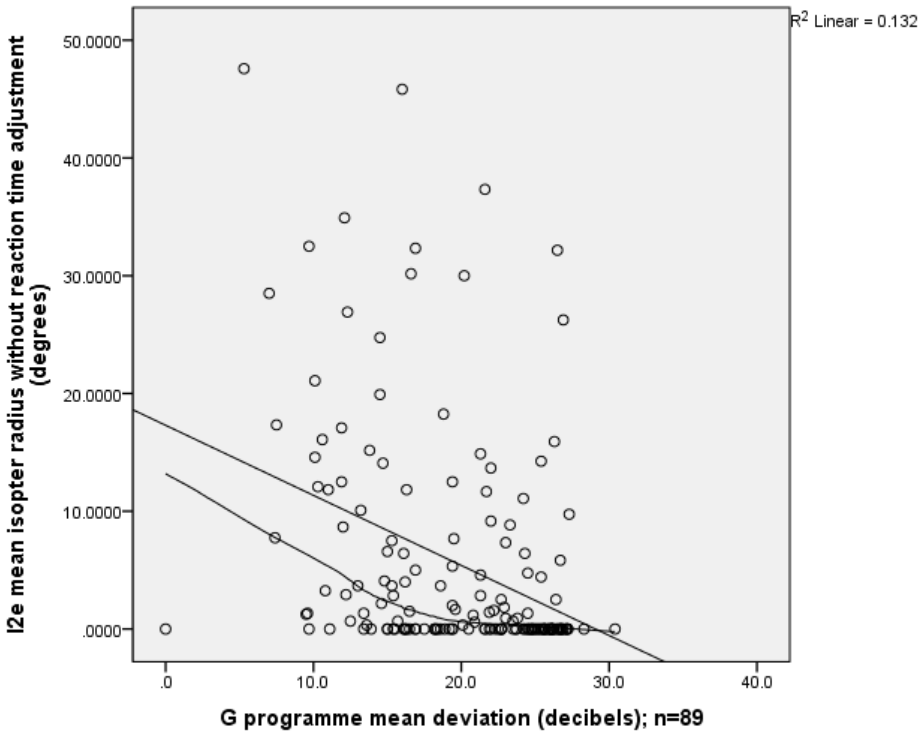


Linear regression line and Loess regression curve show medium and small correlations for size I4e- there was considerable variability for this difference (r -0.416, r^2 0.173, $p<0.0001$ and r -0.277, r^2 0.077, p=0.0017). The Loess point of inflection is approximately 18 decibels.

C – Mean deviation versus area; I2e



D – Mean deviation versus mean isopter radius; I2e



Linear regression line and Loess regression curve show large and medium correlations for size I2e- there was considerable variability for this difference (r -0.539, r^2 0.290, $p<0.0001$ and r -0.363, r^2 0.132, $p<0.0001$). The Loess point of inflection is approximately 13 decibels.

Supplementary table 1: Visual field parameters

			Kinetic		Static
			I4e, n=83	I2e, n=57	III, n=126
Area (degrees^2)	Without RT	Mean	2615.85	770.56	
		SD	2585.68	1488.66	
Area (degrees^2)	With RT	Mean	3592.65	1118.86	
		SD	2922.62	1727.26	
Mean isopter radius (mm)	Without RT	Mean	22.91	8.25	
		SD	14.13	11.97	
Mean isopter radius (mm)	With RT	Mean	28.84	12.33	
		SD	14.30	13.23	
Mean sensitivity (decibels)		Mean			6.21
		SD			5.58
Mean deviation (decibels)		Mean			20.60
		SD			5.91
Standard loss variance (decibels)		Mean			5.65
		SD			2.40
Diffuse defect (decibels)		Mean			18.05
		SD			7.98
Test duration (minutes)		Mean	10.43		3.28
		SD	2.04		1.10

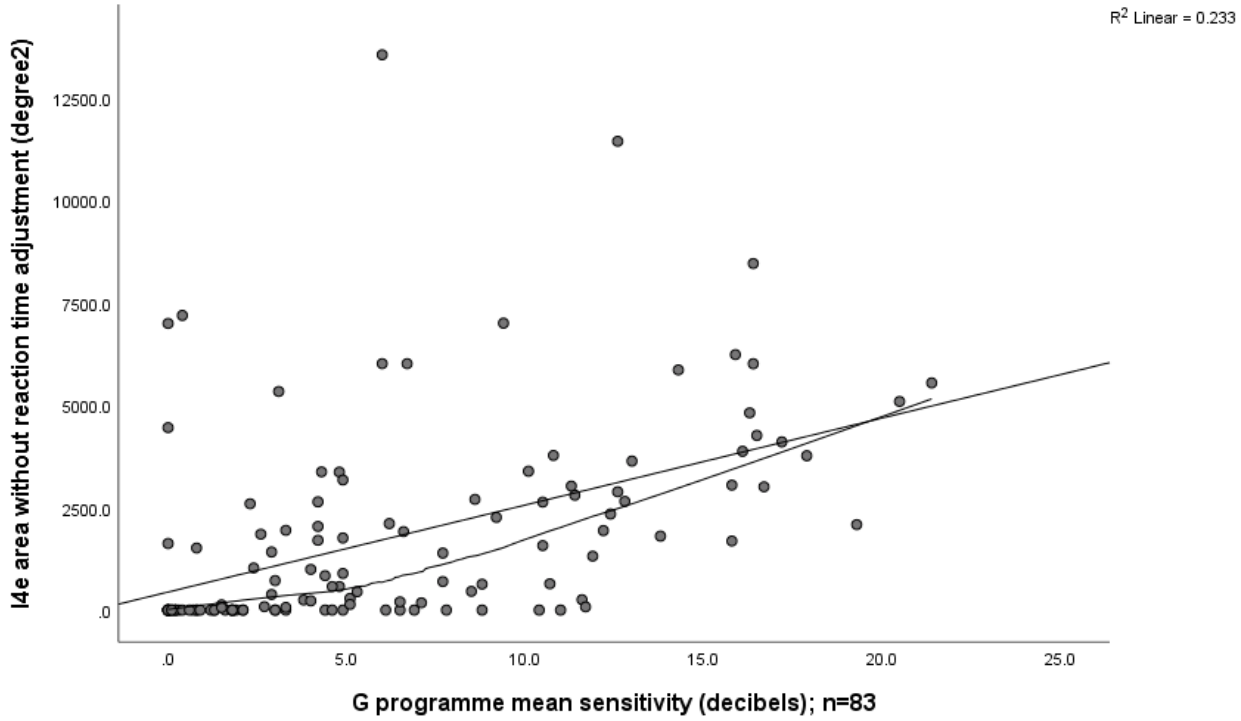
Supplementary table 2: G programme global indices

Static perimetry N=126	Kinetic perimetry: I4e (Mean values)	Kinetic perimetry: I2e (Mean values)	Significance (Independent t test)

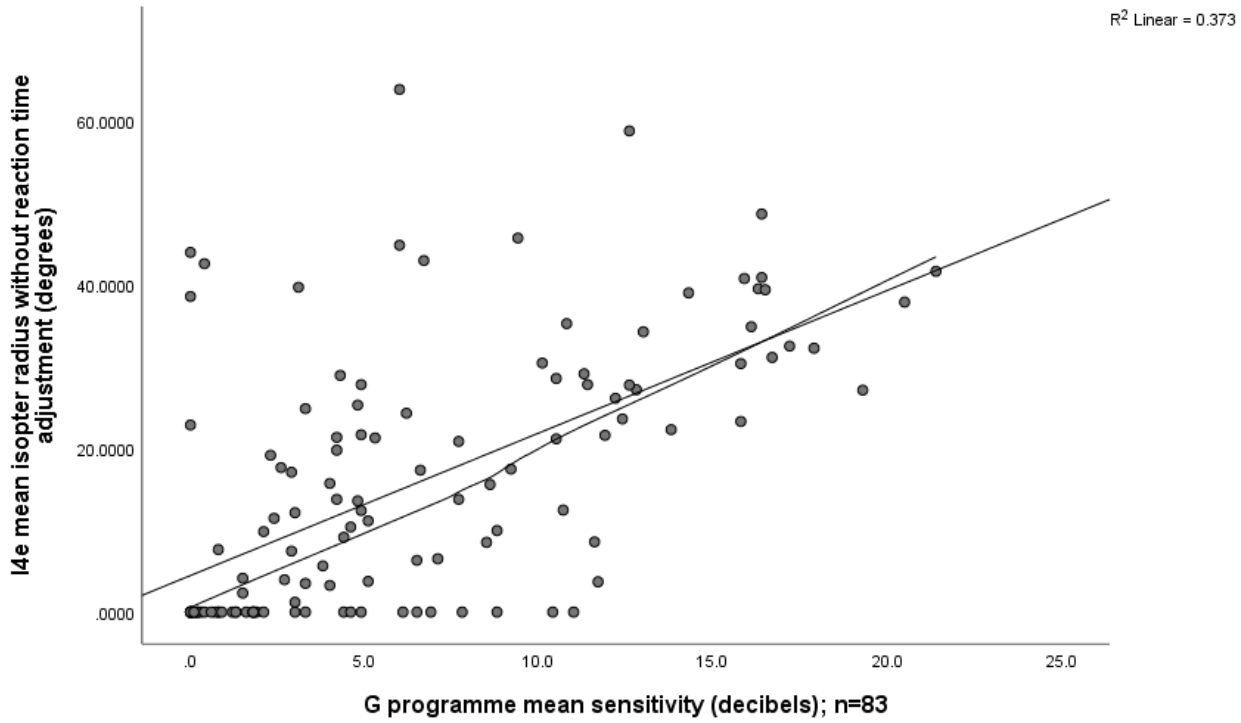
Global indices	Area plotted N=83	Area not plotted N=43	Area plotted N=57	Area not plotted N=69	
Mean sensitivity	8.25	2.37	9.30	3.76	P=0.0001
Mean deviation	18.82	24.57	17.76	23.24	P=0.0001
Standard loss variance	6.65	3.85	6.98	4.65	P=0.0001

Supplementary figure 1: Static perimetry mean sensitivity and kinetic perimetry – worst eyes

A – Mean sensitivity versus area; I4e

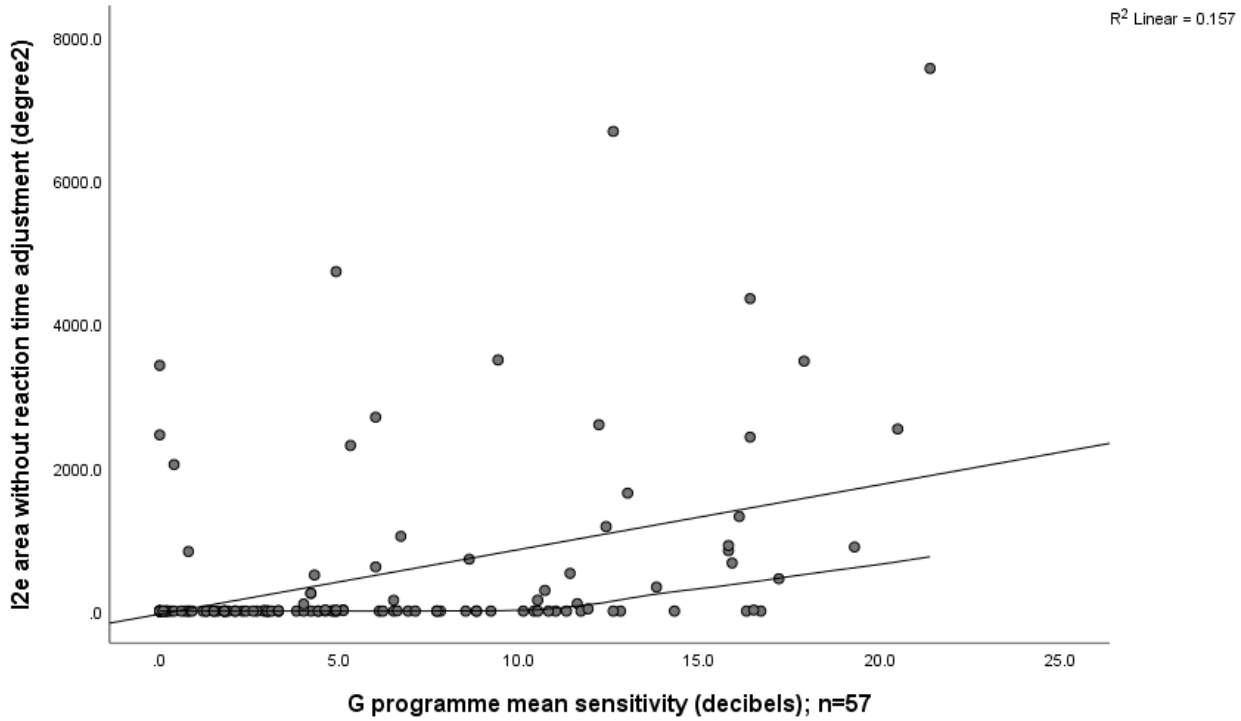


B – Mean sensitivity versus mean isopter area; I4e

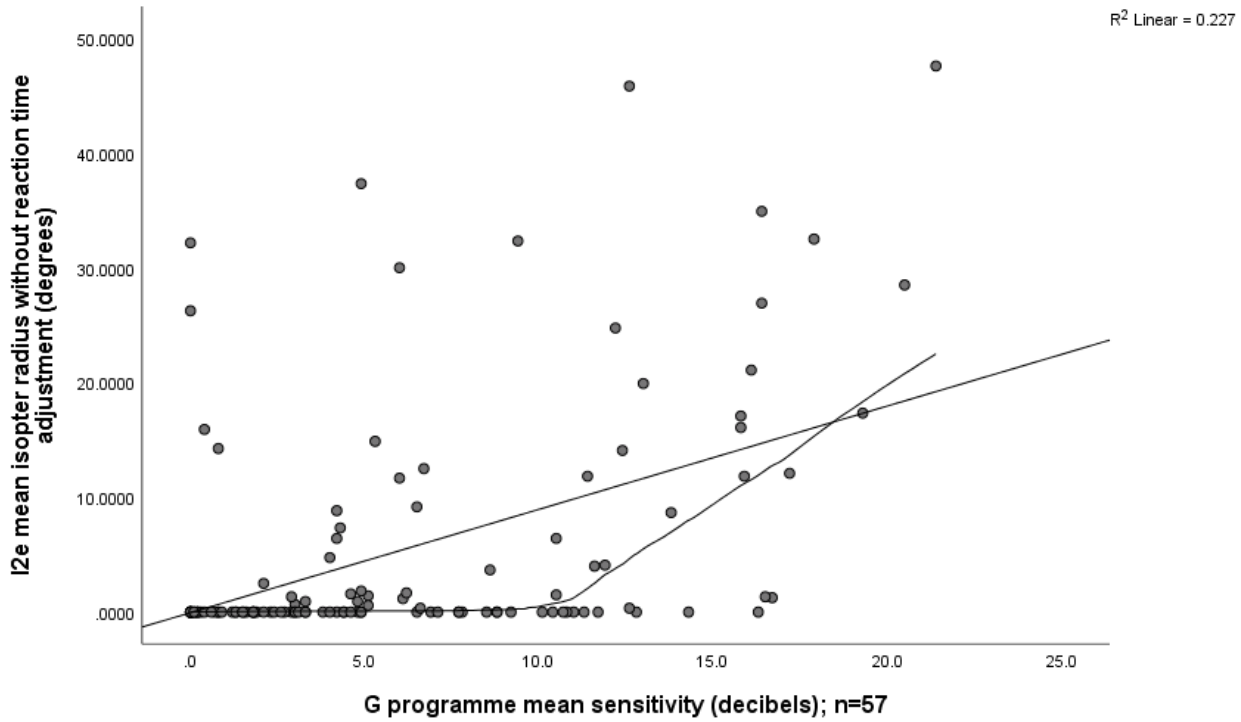


Linear regression line and Loess regression curve show correlations for size I4e - there was considerable variability for this difference (r^2 0.233, 0.373). Loess point of highest curvature is approximately 8 decibels.

C – Mean sensitivity versus area; I2e



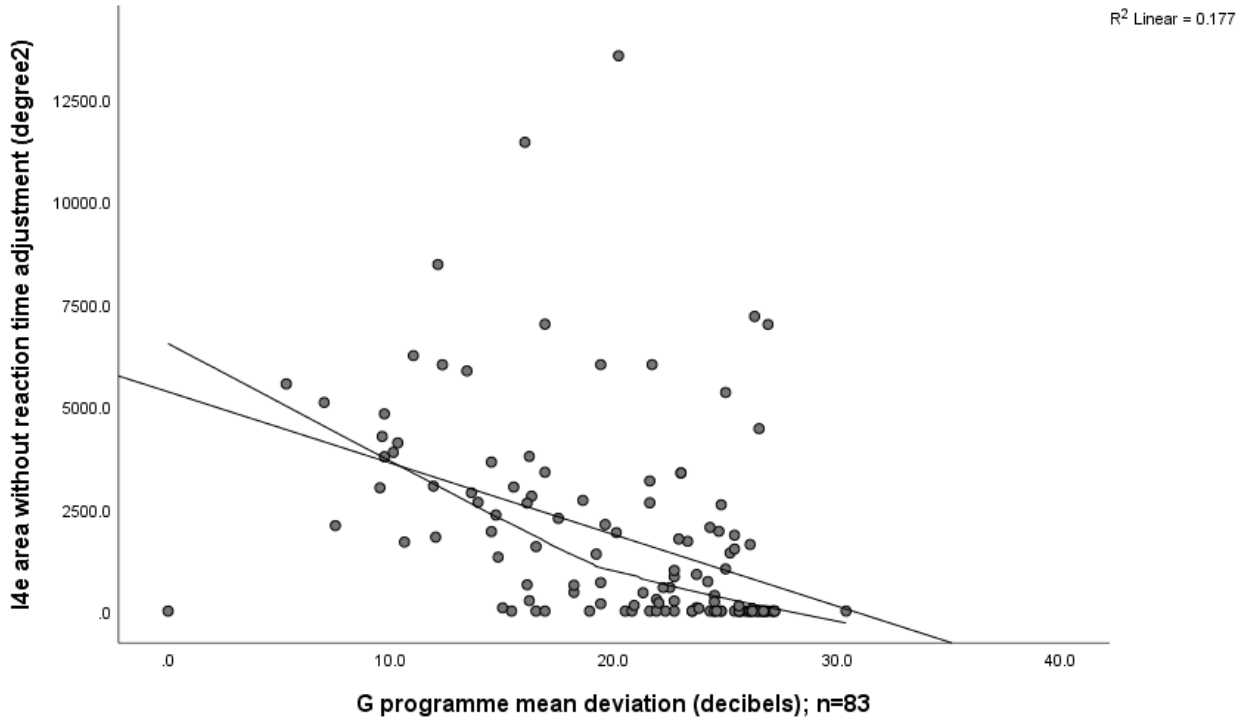
D – Mean sensitivity versus mean isopter area; I2e



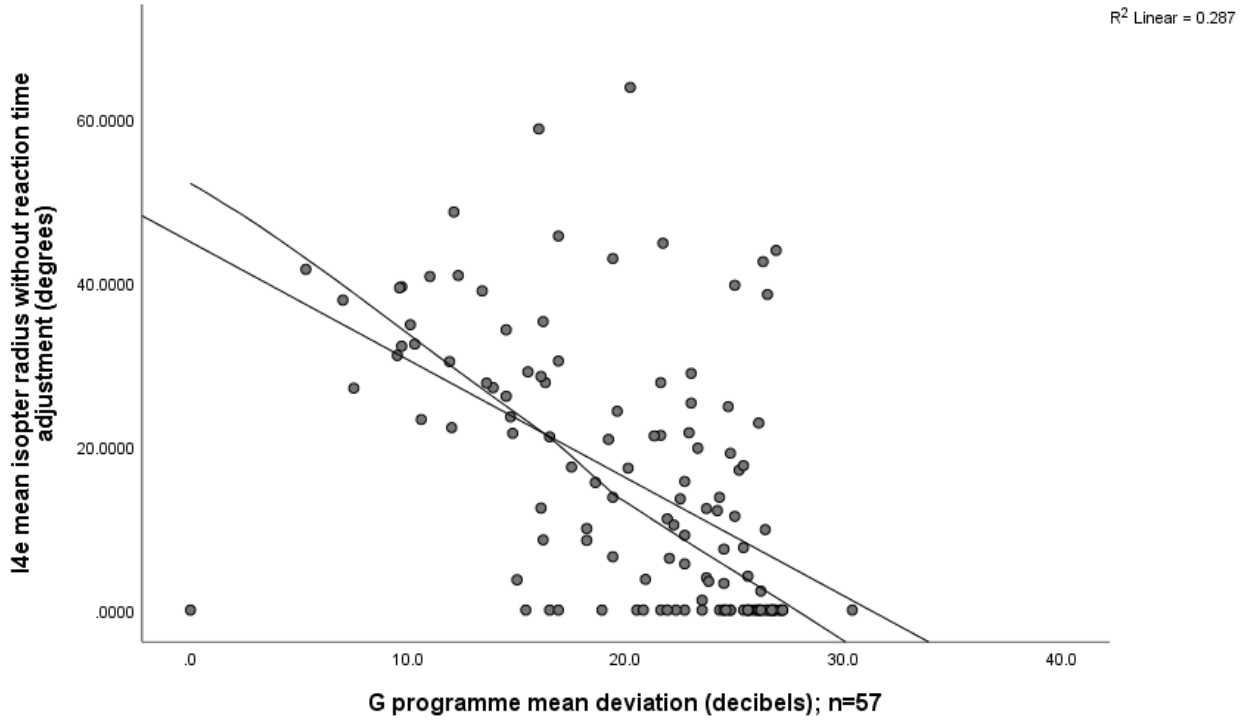
Linear regression line and Loess regression curve show correlations for size I2e - there was considerable variability for this difference (r^2 0.157, 0.227). Loess point of highest curvature is approximately 13 decibels.

Supplementary figure 2: Static perimetry mean deviation and kinetic perimetry – worst eyes

A – Mean deviation versus area; I4e

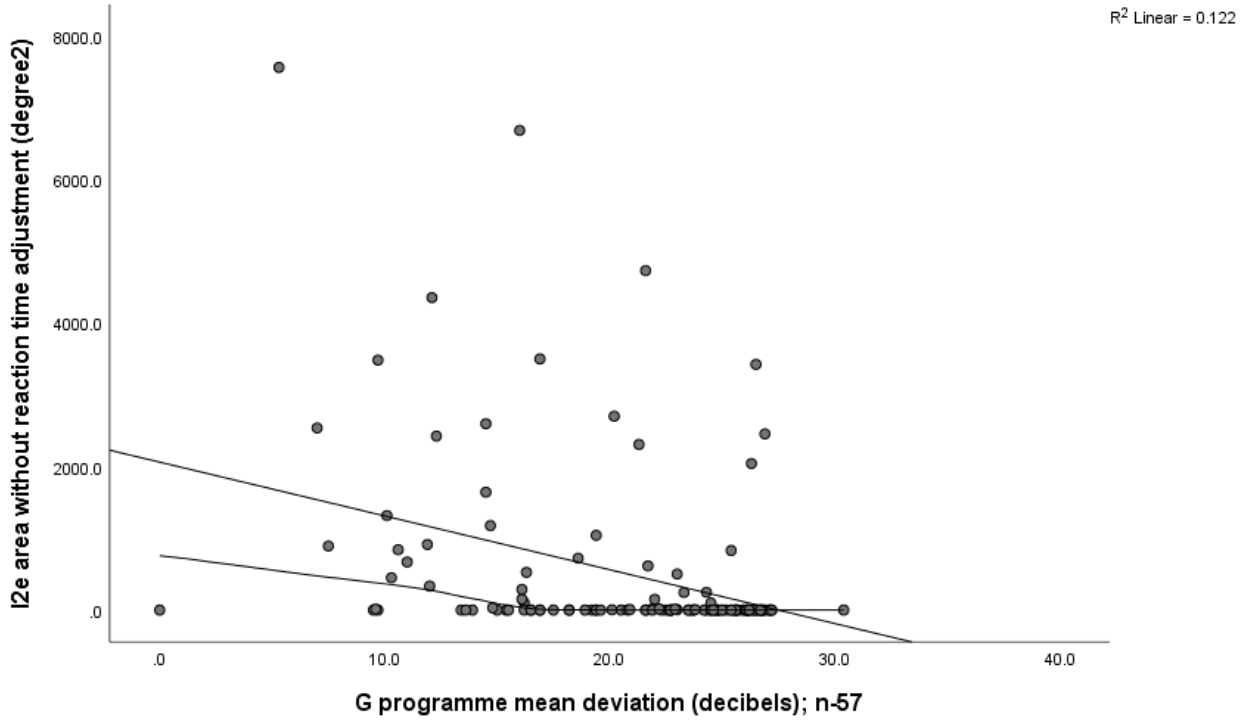


B – Mean deviation versus mean isopter radius; I4e

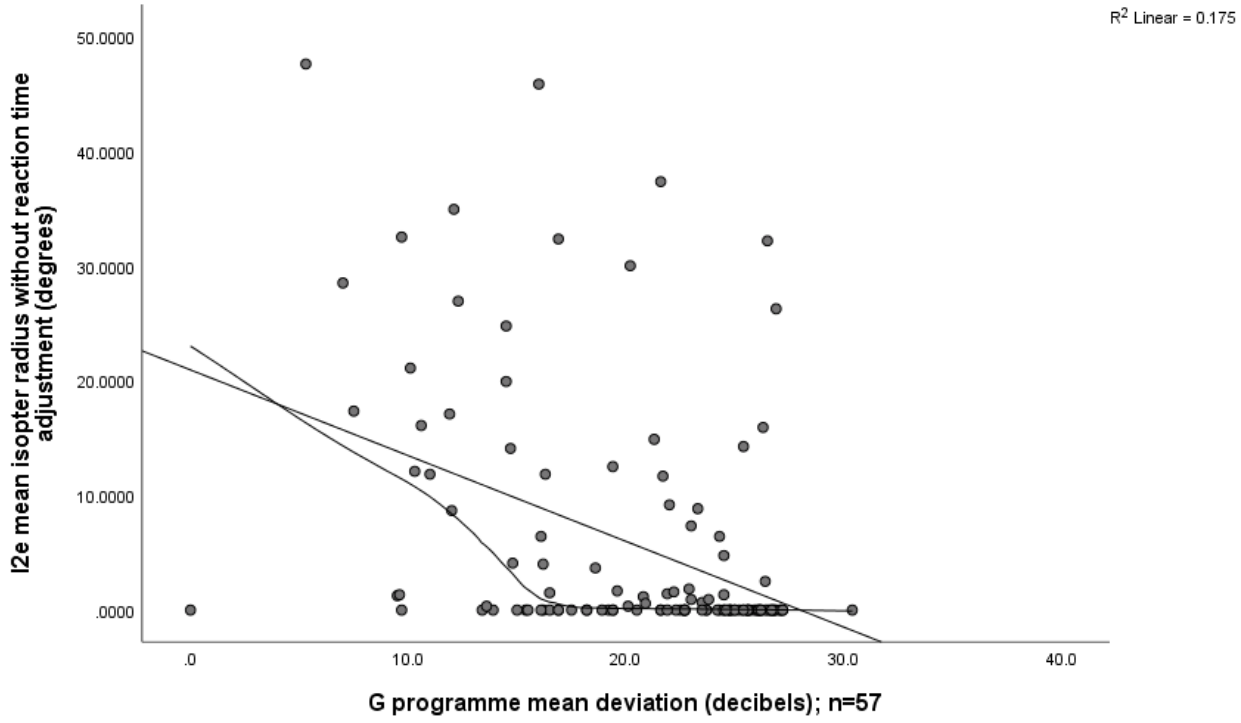


Linear regression line and Loess regression curve show correlations for size I4e - there was considerable variability for this difference (r^2 0.177, 0.287). Loess point of highest curvature is approximately 18 decibels.

C – Mean deviation versus area; I2e



D – Mean deviation versus mean isopter radius; I2e



Linear regression line and Loess regression curve show correlations for size I2e - there was considerable variability for this difference (r^2 0.122, 0.175). Loess point of highest curvature is approximately 14 decibels.