

## SCIENTIFIC CORRESPONDENCE

# Variability across the optic nerve head in scanning laser tomography

J C H Tan, D F Garway-Heath, R A Hitchings

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**Aim:** To characterise measurement variability in scanning laser tomography of the optic nerve head.

**Methods:** 21 normal and 21 glaucoma subjects underwent same and separate day test-retest Heidelberg retina tomograph imaging by the same and different operators.

**Results:** Rim area was most reproducible among parameters. Its variability tended to be highest temporally and increased ( $p < 0.05$ ) with testing involving different operators and visits. Nature of regional variability differed between glaucoma and normal eyes and between standard and 320  $\mu\text{m}$  reference planes.

**Conclusions:** Rim area is reproducible and potentially useful as a marker of progression. Pattern of variability and the influence of different reference planes, disease, operators, and visits should be considered when evaluating progression.

Scanning laser tomography of the optic nerve head (ONH) is reproducible,<sup>1–5</sup> but in what way it should be used to evaluate glaucoma progression remains to be determined. To judge progression, measurement variability needs to be distinguished from true change, for which a detailed understanding of reproducibility is needed. Variability in Heidelberg retina tomograph (HRT) image analysis may be influenced by blood vessels, cardiac pulsation,<sup>6</sup> and the ONH's variably sloped, excavated surface.<sup>1–3, 7</sup> Progression is not uniform over the ONH<sup>8–11</sup> and its detection is likely to be influenced by test conditions and variability in different ONH regions. We studied the reproducibility of different topographic parameters, from which one was selected to assess variability regionally. Whether testing involving different operators and visits affects variability was studied in normal and glaucoma eyes. Then the possibility that different reference planes vary in reproducibility was investigated.

## METHODS

### Study subjects

Twenty one normal (mean visual field MD = +0.11 dB) and 21 age matched glaucoma subjects (MD = -4.6 dB) attending a glaucoma research clinic at Moorfields Eye Hospital underwent repeat testing. All were experienced with tests in this study. Selection was not restricted by severity of visual field defects nor ONH appearance. Normal subjects had (1) intraocular pressure (IOP) <22 mm Hg, (2) repeatedly normal Humphrey 24-2 visual fields (Humphrey Instruments Inc, CA, USA) with advanced glaucoma intervention study (AGIS)<sup>12</sup> visual field scores = 0, (3) no concurrent ocular disease, (4) no family history of glaucoma, (5) refractive errors less than plus or minus 6D, and were (6) aged >40 years. Glaucoma patients

had (1) pretreatment IOP >21 mm Hg on at least two occasions, (2) reproducible Humphrey 24-2 field defects with AGIS scores >0, (3) open anterior chamber angles, and (4) no known ocular disease other than glaucoma. Glaucoma patients were treated medically, had IOP <22 mm Hg, and treatment did not change between tests.

### Imaging

Test-retest HRT imaging (software v2.01; Heidelberg Engineering, Germany) was by experienced operators in both eyes of all subjects. Eyes were imaged in random order. Three well centred 10° images were acquired at each session. Corneal curvature, scan depth and focus settings were kept constant. Pupils were not dilated.

Subjects attended two test visits separated by 6–8 months. Each visit had two imaging sessions, an hour apart. The same operator scanned in both sessions on the first visit, and one session of the second visit. A separate operator scanned in the second session of the second visit. Imaging sessions were ordered randomly. Variability was analysed along four lines: (1) intraoperator-intravisit, (2) intraoperator-intervisit, (3) interoperator-intravisit, and (4) interoperator-intervisit.

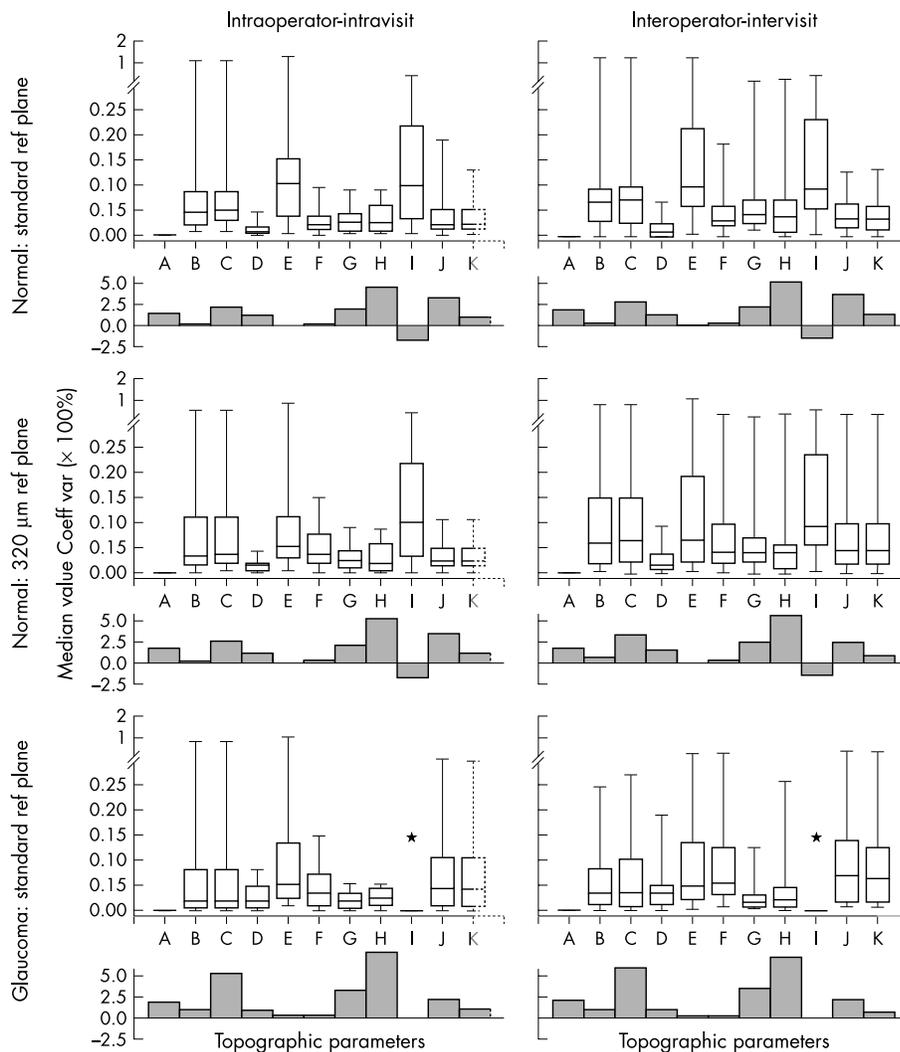
### Analysis

Mean topography images from one randomly selected eye of each subject were analysed. All images had pixel mean SD <50  $\mu\text{m}$ . Contour lines, all drawn by the same observer (JT), were exported to test-retest images. For global analysis, topographic parameters (see Fig 1) were analysed by two reference planes: (1) standard reference plane set 50  $\mu\text{m}$  posterior to contour line height between 350° and 356° (HRT software v1.11 to 2.01),<sup>13, 14</sup> and (2) 320  $\mu\text{m}$  reference plane offset by 320  $\mu\text{m}$  posterior to the mean height of the reference ring (HRT software v1.09 to 1.10).<sup>14</sup> For regional analysis, a single reliable parameter was assessed in 30° sectors round the ONH (0–360°).

Parameter variability was compared using the coefficient of variation (CV). Regional variability was analysed as described by Bland and Altman.<sup>15</sup> Significance testing was by the Wilcoxon signed rank test (Mann-Whitney test) to determine if sector variability (differences) changed with different operators and visits.

## RESULTS

In Figure 1, CV for both reference planes tended to increase with different test operators and visits. Apart from disc area, the rim area of the CV was lowest and reasonably proportioned to its point estimates. In normal eyes, median rim area CV for intraoperator-intravisit and interoperator-intervisit testing was 1.1% and 1.6% respectively for the 320  $\mu\text{m}$  reference plane; and 1.5% and 2.3% respectively for the standard reference plane. A comparable pattern was seen in



**Figure 1** Variability of topographic parameters measured by coefficient of variation (CV). Graphs: top row = normal eyes, standard reference plane (ref plane); middle row = normal eyes, 320 µm reference plane; bottom row = glaucoma eyes, standard reference plane. Left column = intraoperator-intravisit testing, right column = interoperator-intervisit testing. Only standard reference plane analysis for glaucoma eyes shown (pattern in 320 µm reference plane data similar). Box plots = median, first, and third quartiles, error bars = 95% percentiles. Bar graphs = corresponding point estimates. X-axis: A = disc area, B = cup area, C = cup-disc area ratio, D = rim area, E = cup volume, F = rim volume, G = mean cup depth, H = maximum cup depth, I = cup shape measure, (\* data were not analysed in glaucoma as cup shape values ranged from negative to positive, making it difficult to analyse CV meaningfully. Negative and positive values represent a skew towards low or high values in the height distributions of the cup respectively. Nevertheless, normal eyes gave a reasonable estimation of cup shape variability), J = retinal thickness, K = retinal cross sectional area.

glaucoma; 95% percentiles for rim area CV by either reference plane did not exceed 9% in normal and 12% in glaucoma.

In Figure 2, agreement intervals for regional rim area in normal eyes tended to peak temporally (0–90°, 270–360°) irrespective of the reference plane. Variability tended to increase with different operators and visits, especially temporally and with the standard reference plane. A similar increase was seen in glaucoma but its pattern varied between reference planes: standard reference plane variability was highest nasally but 320 µm reference plane variability was highest temporally. Schematic diagrams show that sector variability was significantly less ( $p < 0.05$ ) in intraoperator-intravisit testing compared with intraoperator-intervisit, interoperator-intravisit, or interoperator-intervisit testing for both reference planes, though their patterns differed.

## DISCUSSION

Our results indicate that different test operators and visits affect reproducibility independently, and that this varies by reference plane and ONH region. Previous studies of parameter variability have not addressed the influence of different operators, visits, or reference planes in mean images.<sup>4,5</sup> One study that measured global pixel variability reported that different visits did not significantly affect variability, though a trend was seen.<sup>16</sup> We studied discrete regions of rim area and our results agree with Jonescu-Cuyper *et al.*,<sup>17</sup> who found that

variability was generally less (median 30%) in same day repeat imaging than imaging separated by 1 day to 1 year.

Some points should be noted. Firstly, cup area CV was higher than for rim area because its point estimates were small relative to variability (SD/mean) rather than cup area being more variable per se. In fact, SD for cup area and rim area were similar ( $p > 0.05$ ). Secondly, cup shape had high variability, suggesting its limited usefulness in longitudinal evaluation (although it has been suggested for diagnosis<sup>7</sup>). It could be that tilting and image decentring between images changes cup shape to cause variability. Thirdly, the possibility that progression occurred between visits in glaucoma cannot be excluded. However, such change manifesting as bias was not seen in global rim area agreement analysis (separate analysis; not shown).

Possible reasons for the observed patterns of variability are, firstly, the ONH is often tilted temporally and inferiorly so that the reference plane is more superficial in the ONH temporally than nasally. Slight shifts may lift the reference plane above the temporal but not nasal rim surface to artefactually reduce rim area temporally. In glaucoma, the ONH could become depressed relative to the surrounding retina, causing the reference plane to lie more superficially in the nerve and measurements to be more variable. Secondly, reference plane shifts should affect the temporal rim-cup more than in steeper nasal regions. Thirdly, the standard reference plane is fixed to a small 6° section of the inferotemporal contour line, where it

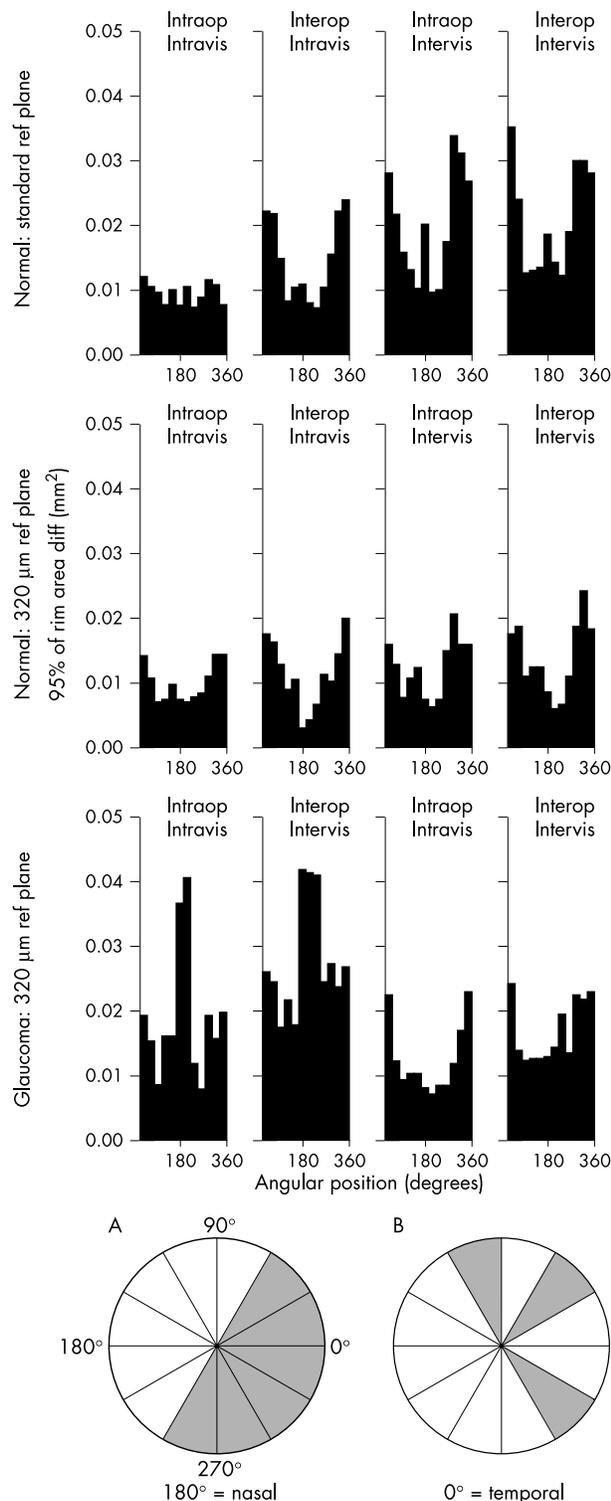


Figure 2 Bar graphs for regional variability in rim area. Top row = normal eyes, standard reference plane (ref plane); middle row = normal eyes, 320 µm reference plane; bottom row = glaucoma eyes, standard and 320 µm reference plane. Intraop intravis = intraoperator-intravisit agreement, interop intravis = interoperator-intravisit agreement, intraop intervis = intraoperator-intervisit agreement, interop intervis = interoperator-intervisit agreement. Each bar = 95% agreement interval for a 30° sector of rim area. Sectors located on ONH circumference (0–360°), with 0° = temporal, 90° = superior, 180° = nasal, 270° = inferior. Schematic diagrams show sectors in which variability increased significantly (normal eyes,  $p < 0.05$ ) with testing by different operators or in different visits. A = standard reference plane, B = 320 µm reference plane; both left eye aspects. Shaded regions = 30° sectors with significantly greater ( $p < 0.05$ ) intraoperator-intervisit, interoperator-intravisit, or interoperator-intervisit variability compared with intraoperator-intravisit variability. 0° = temporal, 90° = superior, 180° = nasal, 270° = inferior.

“pivots.” Image tilting or reference plane shifts may cause more variation nasally opposite the pivot.

Rim area is reproducible and potentially useful as a marker of progression. Its variability differs between regions of the ONH, is influenced by testing involving different visits and operators, and varies with reference planes. These features can be expected in standard reference plane analysis of HRT II images and should be considered when evaluating progression. It seems that a reference plane that is stable relative to the ONH is vital to optimising reproducibility and should be explored further.

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**Authors’ affiliations**

J C H Tan, D F Garway-Heath, R A Hitchings, Moorfields Eye Hospital and Institute of Ophthalmology, London, UK

Correspondence to: Professor R A Hitchings, Glaucoma Research Unit, Moorfields Eye Hospital, City Road, London EC1V 2PD, UK; roger.hitchings@virgin.net

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