EXTENDED REPORT

Detecting glaucoma with RADAAR: the Bridlington Eye Assessment Project

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Aims: To develop a diagnostic algorithm using rim/disc area asymmetry ratio (RADAAR) to discriminate between normal and glaucomatous eyes using the Heidelberg retina tomograph (HRT).

Methods: RADAAR was calculated by dividing rim/disc area ratio of the larger disc by that of the smaller disc. RADAAR normal tolerances in each disc sector were generated using 611 population based normal elderly individuals (mean age 72.5 years). Overall status for each individual was equal to the worst disc sector. Sensitivity was assessed in 45 patients with open angle glaucoma.

Results: RADAAR variance was significantly greater in glaucoma compared with normality in all disc sectors ($p < 0.001$). Normal RADAAR limits were not dependent on age or sex. Overall, at the 99th percentile limit, the diagnostic algorithm's specificity was 95.1% with a sensitivity of 55.6%. Males with glaucoma showed greater RADAAR variance than females. Corresponding sensitivity of the diagnostic algorithm was 63.0% and 44.4% in males and females respectively, although this difference was not statistically significant ($p = 0.43$).

Conclusion: The RADAAR diagnostic algorithm detected glaucoma with moderate sensitivity but was limited by significant numbers of glaucoma patients with symmetrical optic disc changes. RADAAR may have greater sensitivity in males than in females although this requires confirmation in further studies.

Asymmetry of neuroretinal rim configuration is a well recognised component in the diagnosis of glaucoma.¹ It is also a risk factor for progression of ocular hypertensive patients to glaucoma.² With the development of digital imaging technologies (such as the Heidelberg retina tomograph, HRT) comes the possibility of measuring asymmetry of optic nerve head parameters accurately enough to use asymmetry to discriminate between normal and glaucomatous eyes. In spite of this potential, we found only one study examining the usefulness of asymmetry measures in glaucoma diagnosis using HRT.³ The authors constructed the RADAAR measure (rim area to disc area asymmetry ratio) and found it was significantly correlated with intraocular pressure and degree of glaucomatous optic nerve damage in glaucoma patients. However, they were unable to test the ability of RADAAR to discriminate between normal and glaucomatous eyes in the absence of a suitable reference range developed on normal patients. We have recently published normative RADAAR values based on a population based sample of normal elderly subjects participating in the Bridlington Eye Assessment Project.⁴ By comparing the two eyes of each patient, asymmetry has the potential to reduce parameter variability by providing a measure which accounts for inter-individual variation because of patient factors such as age,⁵⁻⁷ sex,⁸ disc area,⁶ refraction,⁷ image acquisition,¹⁰ and contour placement on the optic disc.¹¹ Thus, inter-individual comparisons in cross sectional (diagnostic) studies may become more valid.

Our aim was to develop a diagnostic algorithm using RADAAR and to test its specificity in these normal patients, and its sensitivity when applied to patients with a new diagnosis of glaucomatous optic neuropathy.

PATIENTS AND METHODS

Normal subjects: the Bridlington Eye Assessment Project

Normal subjects were recruited from a population based sample examined as part of the Bridlington Eye Assessment

Project (BEAP). The methodology of BEAP has been previously described.⁸ Briefly, the project is a screening exercise for eye disease in patients over 65 years of age living in the town of Bridlington, England. Patients registered blind or partially sighted, bed bound or with dementia, and those moving into or out of the area during the study were excluded. Patients underwent a comprehensive eye examination, logMAR visual acuity testing (Bailey Lovie No 4 Chart, National Vision Research Institute of Australia) and automated suprathreshold visual field testing with the Henson Pro 5000 perimeter (Tinsley Instruments, Croydon, UK). A single stimulus, supra-threshold central 26 point test was employed. This was automatically extended to a 68 point test if a defect was detected. After instillation of tropicamide 1% into both eyes, systematic slit lamp biomicroscopy was performed with specific disc, macular, and periphery findings being noted. Finally, Heidelberg retina tomograph II images (HRT II, Software Version 1.4.1.0, Heidelberg Engineering GmbH, Dossenheim, Germany) were obtained.

BEAP had seen 2065 patients at the start of this study in October 2004. Normality was defined with the following criteria applied to both eyes: (1) intraocular pressure less than or equal to 21 mmHg; (2) normal visual field determined by suprathreshold automated examination; and (3) corrected logMAR acuity of at least 0.3 (Snellen equivalent 6/12). Exclusion criteria were (1) history of glaucoma; (2) use of ocular pressure lowering treatment; and (3) splinter haemorrhages observed clinically on the optic disc. No attempt was made to exclude patients on the basis of a neuroretinal rim configuration clinically suspicious for glaucoma. A total of 880 patients were defined as normal. All subjects were white. Informed consent was obtained from all participants and a local ethics committee approved all methodology. All methods adhered to the tenets of the

Abbreviations: BEAP, Bridlington Eye Assessment Project; CDR, cup/disc ratio; HRT, Heidelberg retina tomograph; MD, median difference; RADAAR, rim area/disc area asymmetry ratio

Table 1 Global and sectoral RADAAR measures in 611 normal individuals and 45 patients with glaucoma (mean (SD))

Parameter	Normals	Glaucoma	p Value*
G RADAAR	0.97 (0.11)	1.06 (0.43)	0.23
T RADAAR	0.98 (0.28)	1.12 (0.76)	0.91
TS RADAAR	0.98 (0.19)	1.10 (0.67)	0.47
TI RADAAR	0.98 (0.22)	1.56 (1.79)	0.52
N RADAAR	0.99 (0.10)	1.07 (0.50)	0.55
NS RADAAR	0.98 (0.13)	1.15 (0.75)	0.48
NI RADAAR	1.00 (0.13)	1.08 (0.43)	0.99

*Student's *t* test.

G, global, T, temporal; TS, temporal-superior; TI, temporal-inferior; N, nasal; NS, nasal-superior; NI, nasal-inferior.

Declaration of Helsinki guidelines for research in human subjects.

Glaucoma subjects

Glaucoma patients were recruited retrospectively over 2 years from the practice of a glaucoma consultant (SAV) at Queen's Medical Centre, Nottingham. Patients were included if they met all of the following criteria: (1) new diagnosis of open angle glaucoma made by the consultant or senior fellow; (2) visual field loss consistent with glaucoma; and (3) corrected logMAR acuity of at least 0.3. Minimal criteria for glaucomatous visual field defect were as follows: glaucoma hemifield test outside normal limits, pattern standard deviation with a *p* value of <5%, or a cluster of three points in the pattern deviation plot in a single hemifield (superior or inferior) with *p* value of <5%, one of which must have a *p* value of <1%. A visual field test was excluded if any of the reliability indices were greater than 20%. A total of 95 patients fitting the above criteria for glaucoma were recruited.

Confocal scanning laser ophthalmoscope assessment

Patients were imaged with HRT II, with the scanner's focus being adjusted according to the patient's refraction, and to obtain the best image. The optic disc contour line was drawn on all images by one investigator (MJH). HRT II then calculated disc area (mm²), reference height (mm), and further stereometric parameters including rim area (mm²) and rim/disc area ratio. Each of these parameters were expressed for the global disc, and for six individual disc sectors (temporal, temporal-superior, temporal-inferior,

nasal, nasal-superior, nasal-inferior). Subjects with an image mean pixel height standard deviation greater than 50 μ m in either eye were excluded from further analysis. We calculated rim area/disc area asymmetry ratio (RADAAR) in a similar way to Harasymowycz *et al*, by dividing the the rim/disc area ratio of the eye with the larger disc by that of the smaller disc.³ The choice of method in calculating asymmetry measures is important. Most of the previous studies calculating asymmetry parameters did so on a left/right basis,^{5 12 13} though the recent study by Harasymowycz *et al* used a bigger disc/smaller disc comparison.³ It has been previously demonstrated that cup area increases to a larger degree than rim area with increases in disc size.^{8 14} For consistently defined limits of normality, asymmetry measures should therefore be calculated by comparing eyes on the basis of disc size, rather than laterality. In contrast with Harasymowycz *et al*, for most analyses we did not then remove the left hand tail of the histogram by taking the inverse of values less than 1 (smaller rim/disc area ratio in the smaller disc). This preserved any relevant information contained asymmetrically in the right and left sides of the curve. Disc area ratio was calculated by dividing the area of the larger disc by that of the smaller disc.

RADAAR diagnostic algorithm

In all, 95% and 99% limits of normality for RADAAR were defined non-parametrically (by rank percentiles) globally and for each sector in the sample of normal patients. Although there was a relation between RADAAR and disc area asymmetry, this was only significant in two sectors, even then only accounting for approximately 1% of the variance. No attempt was therefore made to correct for this relation. For each disc sector, RADAAR between the 2.5th and 97.5th percentiles of normality was defined as "within normal limits," between the 0.5th and 2.5th or 97.5th and 99.5th was defined as "borderline," and outside of the 0.5th or 99.5th percentiles was defined as "outside normal limits." Overall status for each individual was equal to the worst status of any of the global or sectoral RADAAR measures. Statistical analyses were undertaken using SPSS 12.0.2 (Statistical Package for Social Sciences, SPSS, Inc, Chicago, IL, USA).

RESULTS

Study group characteristics

After exclusion of subjects with unacceptable image quality, the final study sample consisted of 622 normal individuals, and 45 patients with glaucoma. On average, the normal subjects were older than the glaucoma patients (mean age 72.5 (SD 4.8) and 62.1 (14.1) years respectively, *p*<0.001, Mann-Whitney U test). After subjective examination of RADAAR values, 11 normal subjects were further excluded as extreme outliers, leaving 611 normal individuals for further analysis. Average visual field mean deviation in the worse eye of each of the glaucoma patients was -6.9 dB.

Figure 1 Box plot comparing nasal-superior RADAAR measure in 611 normal individuals and 45 patients with glaucoma. Solid horizontal line indicates median value, box extent indicates interquartile range, circles represent outliers and asterisks represent extreme cases.

Table 2 Area under ROC curves and sensitivities (Sn) at fixed specificities (Sp) for discrimination between normal individuals (n = 611) and patients with glaucoma (n = 45).

Parameter	ROC curve area (SE)	Sn/Sp (Sp>95%)	Sn/Sp (Sp>80%)
G RADAAR	0.81 (0.04)	42/95	71/80
T RADAAR	0.65 (0.05)	22/95	42/80
TS RADAAR	0.73 (0.04)	42/95	49/80
TI RADAAR	0.79 (0.04)	36/95	58/80
N RADAAR	0.79 (0.04)	40/95	64/80
NS RADAAR	0.74 (0.05)	44/95	56/80
NI RADAAR	0.77 (0.04)	33/95	56/80

G, global; T, temporal; TS, temporal-superior; TI, temporal-inferior; N, nasal; NS, nasal-superior; NI, nasal-inferior.

RADAAR in normal individuals and glaucoma patients

Table 1 displays RADAAR values for the 611 normal individuals and 45 patients with glaucoma. There was no significant difference in central tendency (mean) of RADAAR between the normal and glaucoma groups. The variance of RADAAR values was consistently significantly greater in the glaucoma group compared with the normal group (Levene statistic for homogeneity of variance $p < 0.001$ for all sectors; shown graphically for the nasal superior sector in fig 1). There was no significant difference in central tendency (mean) or variance of any RADAAR measure between normal males and females. No significant correlation was found between any RADAAR measure in the normal group and age. Small but significant negative correlations were found between RADAAR in normals and disc area ratio only in the global and nasal sectors (Pearson's $r = -0.12$, $p = 0.004$ and -0.09 , $p = 0.03$ respectively). No significant correlation between age and any RADAAR measure was found in the glaucoma group. Males and females with glaucoma showed no difference in central tendency of any RADAAR, however, variance was greater in males than females for all RADAAR measures, reaching significance in the temporal-inferior and nasal-inferior sectors (Levene statistic for homogeneity of variance 14.3, $p < 0.001$ and 5.1, $p = 0.03$ respectively). Table 2 displays the area under ROC curves for the global and sectoral RADAAR measures when used to discriminate between the normal and glaucoma subjects (ROC curves for selected RADAAR measures plotted in fig 2). The global RADAAR measure had the greatest area under ROC curve, with the temporal measure having the smallest area.

Figure 2 Receiver operating characteristic (ROC) curves for global, temporal, and temporal-inferior RADAAR in discriminating 622 normal individuals and 45 patients with glaucoma.

RADAAR diagnostic algorithm

Table 3 displays summary classification based on this scheme for 611 normal individuals and 45 patients with glaucoma. The best discriminating sector was the global classification with a specificity of 95.1% and sensitivity of 42.2% at the 95% limit of normality. The overall classification returned a specificity of 78.5% and a sensitivity of 80.0% at the 95% limit of normality. χ^2 tests revealed highly significant associations between diagnostic classification and actual diagnosis in all sectors and for both sexes ($p < 0.001$). Figure 3 compares the results of the overall classification for each sex in the normal and glaucoma groups. In normal individuals the overall classification defined 77.2% of males and 79.6% of females as "within normal limits." In glaucoma patients the overall classification defined 63.0% of males and 44.4% of females as "outside normal limits." This trend to increased specificity and decreased sensitivity in females compared with males was not statistically significant (χ^2 0.69 with 2 degrees of freedom, $p = 0.71$ in normals, 1.71 with 2 degrees of freedom, $p = 0.43$ in glaucoma patients).

No statistically significant relation was found between disc area asymmetry (when ranked in two groups by the median value) and overall classification based on RADAAR (at the 99% limits of normality; χ^2 1.18, $p = 0.28$, and χ^2 with continuity correction 0.59, $p = 0.44$ in the normal and glaucoma groups, respectively). The effect of asymmetry in visual field index mean deviation on sensitivity was assessed by grouping difference in mean deviation in glaucoma patients into two ranks by the median value (median difference, MD 2.3 dB, minimum 0.0, maximum 19.0 dB). Of 22 glaucoma patients with difference in MD of 2.3 dB or less, nine were "outside normal limits." Of 21 patients with a difference in MD of greater than 2.3 dB, 15 were "outside normal limits" (χ^2_{trend} 3.96, $p = 0.05$).

DISCUSSION

Our study indicates that asymmetry in rim/disc area ratio can detect perimetrically defined glaucoma with a sensitivity of 80% and specificity of 78.5% at the 95% limit of normality. At the 99% limit specificity rose to 95.1% with a sensitivity of 55.6%. The relatively low sensitivity reflects the overlap in RADAAR between normal and glaucoma (illustrated in fig 1) indicating that symmetry is common in early to moderate glaucoma. It is possible that some of the normal subjects have preperimetric glaucoma. However, we have chosen to define glaucoma based on visual field because the problem of disagreement in classifying optic nerve heads clinically.^{15, 16} In our study, RADAAR in normal subjects showed no correlation with age or sex, and only a very small correlation with disc size asymmetry. We might therefore expect this diagnostic tool to perform similarly if tested in other white populations because of the consistency of the measure. Further studies are needed to confirm this. In addition, since all subjects comprising the normative data were white,

Table 3 Summary classification of disc sectors by RADAAR limits of normality

RADAAR result (%)	Global	Temporal	Temp/sup	Temp/inf	Nasal	Nasal/sup	Nasal/inf	Overall
Within normal limits	95.1 (57.8)	95.1 (75.6)	95.1 (60.0)	95.1 (60.0)	95.1 (57.8)	94.9 (64.4)	95.1 (64.4)	78.5 (20.0)
Borderline	3.9 (11.1)	3.9 (6.7)	3.9 (13.3)	3.9 (13.3)	3.9 (24.4)	4.3 (17.8)	3.9 (8.9)	16.6 (24.4)
Outside normal limits	1.0 (31.1)	1.0 (17.8)	1.0 (26.7)	1.0 (26.7)	1.0 (17.8)	0.8 (17.8)	1.0 (26.7)	4.9 (55.6)

Results (%) are shown for 611 normal elderly individuals and 45 patients with glaucoma (in parentheses). Results are shown for all disc sectors and for the overall analysis. RADAAR values within the central 95% of normative values were classed "within normal limits," between the 95% and 99% limits, "borderline" and outside the 99% limits, "outside normal limits."

Figure 3 Overall classification by sex according to RADAAR limits of normality. Results are shown for (A) 611 normal elderly individuals and (B) 45 patients with glaucoma.

further work is required to define the validity of RADAAR in other ethnic groups. As RADAAR variance was greater in glaucoma than normal for all disc sectors we included them all in the diagnostic model. However, ROC curves revealed that not all sectors were equally accurate in discriminating normal and glaucoma. Further research is required to determine the best combination of sectors to optimise specificity and sensitivity. In glaucoma patients, males exhibited significantly greater RADAAR variance than females in the temporal-inferior and nasal-inferior sectors, although the differences in sensitivity and specificity of the overall diagnostic method were not significant using a χ^2 test. We are not aware of any other studies having found a sex difference in optic nerve head asymmetry in glaucoma patients. Further studies are required to confirm this finding in other populations. Previous research has also demonstrated utility in structural asymmetry measures in glaucoma. RADAAR correlates with the severity of open angle glaucoma,³ and cup asymmetry is a risk factor for conversion from ocular hypertension to glaucoma.^{2, 17} Functional asymmetry in visual evoked potential perimetry can also detect early glaucoma.¹⁸ However, the Blue Mountains Eye Study found that vertical cup/disc ratio (CDR) asymmetry was not useful in identifying patients with glaucoma.¹³ The study measured optic disc parameters from stereo photographs, and derived asymmetry measures by subtracting the value of the right eye from that of the left eye. Possible reasons for the insensitivity of the method include the consideration of only vertical CDR asymmetry that may miss glaucoma manifesting in other disc sectors. Additionally, we have previously argued the need to calculate asymmetry based on a bigger disc/smaller disc comparison, rather than on a right/left basis.⁴ This ensures that the greater increase in cup size compared with rim size in bigger discs does not introduce additional "noise" into the asymmetry measure.

Image quality was a significant limiting factor in our study, with poor quality images resulting in the exclusion of 29% of normals and 53% of glaucoma patients. We have previously discussed reasons for poor image quality in the elderly⁸ such as cataract¹⁹ and advanced age.²⁰ The image quality in the glaucoma group was surprisingly poor given that all images were acquired by an experienced, trained operator. Any diagnostic algorithm will be of limited usefulness if significant numbers of patients produce unusable images. Another limitation of the study was the lack of data on refractive status. The Blue Mountains Eye Study found significant anisometropia (defined as greater than or equal to 1.0D spherical equivalent difference between eyes) in 14.7% of older individuals, with higher rates found in more elderly patients and those with cataract.²¹ Anisometropia may cause differential effects on image size, thus introducing inconsistency into the RADAAR measure. However, by dividing rim area by disc area, we anticipate that the ratio of rim/disc area asymmetry should remain relatively unaffected.

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REFERENCES

- 1 **Wolfs RC**, Borger PH, Ramrattan RS, *et al*. Changing views on open-angle glaucoma: definitions and prevalences—the Rotterdam Study. *Invest Ophthalmol Vis Sci* 2000;**41**:3309–21.
- 2 **Yablonski ME**, Zimmerman TJ, Kass MA, *et al*. Prognostic significance of optic disk cupping in ocular hypertensive patients. *Am J Ophthalmol* 1980;**89**:585–92.
- 3 **Harasymowycz P**, Davis B, Xu G, *et al*. The use of RADAAR (ratio of rim area to disc area asymmetry) in detecting glaucoma and its severity. *Can J Ophthalmol* 2004;**39**:240–4.
- 4 **Hawker MJ**, Vernon SA, Ainsworth G, *et al*. Asymmetry in optic disc morphometry as measured by Heidelberg retina tomography in a normal elderly population: the Bridlington Eye Assessment Project. *Invest Ophthalmol Vis Sci* 2005;**46**:4153–8.
- 5 **Hermann MM**, Theofylaktopoulos I, Bangard N, *et al*. Optic nerve head morphometry in healthy adults using confocal laser scanning tomography. *Br J Ophthalmol* 2004;**88**:761–5.
- 6 **Durukan AH**, Yucel I, Akar Y, *et al*. Assessment of optic nerve head topographic parameters with a confocal scanning laser ophthalmoscope. *Clin Experiment Ophthalmol* 2004;**32**:259–64.
- 7 **Nakamura H**, Maeda T, Suzuki Y, *et al*. Scanning laser tomography to evaluate optic discs of normal eyes. *Jpn J Ophthalmol* 1999;**43**:410–4.
- 8 **Vernon SA**, Hawker MJ, Ainsworth G, *et al*. Laser scanning tomography of the optic nerve head in a normal elderly population: The Bridlington Eye Assessment Project. *Invest Ophthalmol Vis Sci* 2005;**46**:2823–8.
- 9 **Wollstein G**, Garway-Heath DF, Hitchings RA. Identification of early glaucoma cases with the scanning laser ophthalmoscope. *Ophthalmology* 1998;**105**:1557–63.
- 10 **Miglier S**, Albe E, Guareschi M, *et al*. Intraobserver and interobserver reproducibility in the evaluation of optic disc stereometric parameters by Heidelberg Retina Tomograph. *Ophthalmology* 2002;**109**:1072–7.
- 11 **Garway-Heath DF**, Poinsoosawmy D, Wollstein G, *et al*. Inter- and intraobserver variation in the analysis of optic disc images: comparison of the Heidelberg retina tomograph and computer assisted planimetry. *Br J Ophthalmol* 1999;**83**:664–9.
- 12 **Saruhan A**, Orgul S, Kocak I, *et al*. Descriptive information of topographic parameters computed at the optic nerve head with the Heidelberg retina tomograph. *J Glaucoma* 1998;**7**:420–9.
- 13 **Ong LS**, Mitchell P, Healey PR, *et al*. Asymmetry in optic disc parameters: the Blue Mountains Eye Study. *Invest Ophthalmol Vis Sci* 1999;**40**:849–57.
- 14 **Budde WM**, Jonas JB, Martus P, *et al*. Influence of optic disc size on neuroretinal rim shape in healthy eyes. *J Glaucoma* 2000;**9**:357–62.
- 15 **Varma R**, Steinmann WC, Scott IU. Expert agreement in evaluating the optic disc for glaucoma. *Ophthalmology* 1992;**99**:215–21.
- 16 **Azuara-Blanco A**, Katz LJ, Spaeth GL, *et al*. Clinical agreement among glaucoma experts in the detection of glaucomatous changes of the optic disk using simultaneous stereoscopic photographs. *Am J Ophthalmol* 2003;**136**:949–50.
- 17 **Quigley HA**, Enger C, Katz J, *et al*. Risk factors for the development of glaucomatous visual field loss in ocular hypertension. *Arch Ophthalmol* 1994;**112**:644–9.
- 18 **Graham SL**, Klistorner AI, Grigg JR, *et al*. Objective VEP perimetry in glaucoma: asymmetry analysis to identify early deficits. *J Glaucoma* 2000;**9**:10–9.
- 19 **Zangwill L**, Irak I, Berry CC, *et al*. Effect of cataract and pupil size on image quality with confocal scanning laser ophthalmoscopy. *Arch Ophthalmol* 1997;**115**:983–90.
- 20 **Sihota R**, Gulati V, Agarwal HC, *et al*. Variables affecting test-retest variability of Heidelberg Retina Tomograph II stereometric parameters. *J Glaucoma* 2002;**11**:321–8.
- 21 **Guzowski M**, Fraser-Bell S, Rohtchina E, *et al*. Asymmetric refraction in an older population: the Blue Mountains Eye Study. *Am J Ophthalmol* 2003;**136**:551–3.