Published in final edited form as:

J Glaucoma. 2013 February ; 22(2): 65–72. doi:10.1097/IJG.0b013e31822e8e51.

African Descent and Glaucoma Evaluation Study (ADAGES): Asymmetry of Structural Measures in Normal Participants

Grant H. Moore, BA^{1,2}, Christopher Bowd, PhD², Felipe A. Medeiros, MD PhD², Pamela A. Sample, PhD², Jeffrey M. Liebmann, MD³, Christopher A. Girkin, MD⁴, Mauro T. Leite, MD², Robert N. Weinreb, MD², and Linda M. Zangwill, PhD²

¹NYU School of Medicine, New York, NY

²Ophthalmology, UCSD Hamilton Glaucoma Center, San Diego, CA

³Ophthalmology, New York Eye and Ear Infirmary, New York, NY

⁴Ophthalmology, Univ of Alabama at Birmingham, Birmingham, AL

Introduction

Primary open-angle glaucoma (POAG) is a bilateral disease¹⁻³ and inter-eye asymmetry in optic disc and retinal nerve fiber layer (RNFL) parameters occur commonly in early stages of the disease.⁴⁻⁷ Specifically, inter-eye cup-to-disc ratio asymmetry has been suggested to be a harbinger of glaucomatous damage⁸ and inter-eye asymmetry of the neuroretinal rim configuration has been reported to be an important element in the diagnosis of glaucoma as well as a risk factor for conversion to glaucoma in patients with ocular hypertension.⁹⁻¹¹ As retinal ganglion cell death is the primary pathological process in glaucoma, recent studies have also focused on asymmetry of RNFL thickness.¹²⁻¹⁴

The use of computerized imaging devices, such as the confocal scanning laser ophthalmoscope (CSLO) and the scanning laser polarimeter (SLP), has high utility to locate and objectively measure structural features including optic disc topography and RNFL thickness. Thus, the measurements provided by these devices are ideal for a variety of ocular parameters.

Given that changes in optic disc topography and RNFL thickness may both occur before loss of vision can be detected by standard automated perimetry in early glaucoma, the detection of abnormalities in these structures is important in the management of the disease. When this is considered alongside the fact that populations of African Descent (AD) have a higher susceptibility to POAG,¹⁵⁻¹⁹ attention must be given to determining whether differences in retinal structures exist between persons of African descent and persons of different races. Several studies have sought to establish normal ranges of asymmetry for optic disc

Corresponding Author: Linda Zangwill, PhD., 9415 Campus Pointe Drive, La Jolla, CA. 92093, Phone: 858-534-7686, Fax: 858-822-4951, Zangwill@glaucoma.ucsd.edu.

Author Disclosure Information: G.H. Moore: None. C. Bowd: F; Pfizer Inc. J.M. Liebmann: F; Carl Zeiss Meditec, Dyopsis Corp., Heidelberg Engineering, Optovue Inc., Topcon Medical Systems Inc.. C; Alcon Laboratories Inc., Allergan Inc., Dyopsis Corp., Optovue Inc., Pfizer Inc., Topcon Medical Systems Inc. C.A. Girkin: C; Alcon Laboratories Inc., Allergan Inc., Pfizer Inc. R; Heidelberg Engineering Inc., Optovue Inc., Merck Inc., Topcon Medical Systems Inc., Carl Zeiss Meditec Inc., Eyesight Foundation of Alabama. M.T. Leite: None. F.A. Medeiros: F; Alcon Laboratories Inc., Carl Zeiss Meditec Inc., Merck Inc., Pfizer Inc.. C; Alcon Laboratories Inc., Allergan Inc., Pfizer Inc. R; Alcon Laboratories Inc., Allergan Inc., Carl Zeiss Meditec Inc., Pfizer Inc., Reicherts Inc. R.N. Weinreb: F; Carl Zeiss Meditec Inc., Heidelberg Engineering GmbH, Optovue Inc., Pfizer Inc., Topcon Medical Systems Inc.. C; Alcon Laboratories Inc., Allergan Inc., Carl Zeiss Meditec Inc., Genetech Inc., Merck Inc., Optovue Inc., Pfizer Inc. L.M. Zangwill: F; Carl Zeiss Meditec Inc., Heidelberg Engineering GmbH, Optovue Inc., Topcon Medical Systems Inc.. R; Heidelberg Engineering GmbH.

topographies and RNFL thickness.^{4, 5, 12-14, 20, 21} However, little consideration was placed on race in these studies.

With this in mind, the current study was carried out to determine the degree of inter-eye asymmetry of optic disc topography and retinal nerve fiber layer (RNFL) thickness in healthy individuals of AD compared to those of European descent (ED) while also determining normal tolerance limits for asymmetry measured by the HRT-II CSLO (Heidelberg Retina Tomograph, HRT-II, Heidelberg Engineering, GmbH, Heidelberg Germany) and the GDx-VCC SLP (GDx-VCC; Carl Zeiss Meditec, Inc., Dublin, CA). These limits may, in turn, aid in the detection of early glaucomatous axonal loss.

Methods

Subjects

Study participants from the African Descent and Glaucoma Evaluation Study (ADAGES) and Diagnostic Innovations in Glaucoma Study (DIGS) who met the eligibility criteria outlined below were included in the analysis. Details of the ADAGES and DIGS methods have been described previously.²² In brief, the study was designed to prospectively evaluate structural and functional changes in glaucoma between individuals of AD and ED at 3 study centers, the Hamilton Glaucoma Center, Department of Ophthalmology, University of California, San Diego (UCSD), the Department of Ophthalmology, the New York Eye and Ear Infirmary (NYEE), and the Department of Ophthalmology, University of Alabama, Birmingham (UAB) as part of the ADAGES study.²² AD participants were all black Africans, and this group did not include any African individuals of Arabic or Caucasian descent. The same procedures and protocols were used at all 3 sites and are the same as those used in the DIGS at UCSD. Informed written consent was obtained from all participants and study methods were approved by the institutional review boards at all 3 sites. Methods adhere to the tenets of the Declaration of Helsinki and to the Health Insurance Portability and Accountability Act. Healthy control subjects were invited to join via advertisements family member recommendations and referrals by optometrists and community ophthalmologists.

All subjects underwent a complete ophthalmological examination, including a review of the medical history, determination of best corrected visual acuity, slit-lamp biomicroscopy, intraocular pressure (IOP) measurement with Goldmann applanation tonometry, gonioscopy, dilated fundus examination, simultaneous stereophotography of the optic disc and standard automated perimetry (SAP) in both eyes using the 24-2 program with the Swedish Interactive Thresholding Algorithm (SITA) of the Humphrey Visual Field Analyzer (Carl Zeiss Meditec Inc, Dublin, California, USA). Visual Field tests with more than 33% fixation losses, false negative errors, and false-positive errors were excluded. All eyes had open anterior chamber angles, a best corrected visual acuity of 20/40 or better, a spherical refraction within less than 5.0 diopters, and cylinder correction less than 3.0 diopters. 519 subjects met inclusion criteria and were included in this study.

Simultaneous stereoscopic color optic disc photographs (TRC-SS; Topcon Instrument Corp. of America, Paramus, NJ) were obtained on all participants. Photographs were reviewed with a stereoscopic viewer (Pentax Stereo Viewer II; Asahi Optical Co., Tokyo, Japan). Only photos with adequate quality were graded. All graders were masked to patient identification and other patient information. Discrepancies between two graders regarding whether an eye was healthy or glaucomatous were resolved by a third, experienced grader. By ADAGES definition, normal eyes were those with IOP<22mmHg, a normal stereophotography assessment, and no repeatable visual field damage (pattern standard

deviation [PSD] and glaucoma hemifield test within normal limits). Only participants with two “Normal” eyes were used in the current study.

Instrumentation

All patients underwent HRT-II imaging in each eye. The HRT-II is a confocal scanning laser ophthalmoscope, and its working principles have been described in other publications.²³ Software version 3.0 was used for this data analysis. The HRT-II’s software provides stereometric topographic measures of the optic disc relative to the reference plane or the curved surface. The standard reference plane was employed for measurements in this study. The HRT-II measurements of: global cup area, global cup volume below the reference plane, global rim area, and global rim volume were assessed in this study.

As described previously,^{22,24} experienced staff members from the Imaging Data Evaluation and Analysis (IDEA) Center at UCSD evaluated image quality and outlined the disc margin with the aid of available stereoscopic photographs of the optic disc. For HRT, good quality images were those with image standard deviation (SD) < 50 mm, even image illumination and good centering. Of the 1038 images acquired for this study, only 81 (7.8%) had an image SD < 20 mm, and only 3 (0.27%) had an image SD < 40.

Patients also underwent SLP imaging with the GDx-VCC. This device employs a near infrared laser beam with a wavelength of 785 nm to scan the ocular fundus. More detailed explanations of the working principles have been described elsewhere.^{25,26} The GDx-VCC measurement of average (TSNIT) RNFL thickness was analyzed in this study. Image quality was assessed by experienced IDEA Center graders masked to other test results. Only well-focused, evenly illuminated, and centered scans with residual anterior segment retardation < 12nm and standard deviation < 7μm, determined by GDx software, were included. Only images with typical scan scores (TSS) > 80 were included, since it has been shown that scans with TSS > 80 have minimal atypical scan patterns.^{27, 28} TSS is a continuous variable ranging from 0 to 100 and is the result of a support vector machine analysis of SLP data labeled for training based on the subjective appearance of each scan, with low TSSs indicating atypical scans and high TSSs indicating typical ones.²⁹ All patients were required to have had a reliable SAP Field, good quality HRT-II and GDx-VCC exams, and stereophotographs all within a six month period. When multiple exams occurred on the same date, the exam with the best quality score was used.

Asymmetry Analysis

Asymmetry between eyes was calculated for all HRT-II and GDx-VCC parameters. Several different methods of asymmetry calculation have been described in the literature.^{6, 7, 20, 21, 30, 31} In this study, absolute asymmetry was used. Absolute asymmetry was calculated by taking the absolute value of the right eye minus left eye parameter values. Although this formula does not directly account for inter-individual variation in optic disc and RNFL measures, the authors opted to account for this variation by adjusting for mean disc area and disc area asymmetry in multivariable analyses.

Statistical Analysis

The distribution of the absolute value of asymmetry between eyes was derived for HRT cup area, cup volume, rim area, rim volume, and GDx average RNFL thickness, and was used to identify values outside the normal range at the 95th percentile. Because asymmetry values were calculated as absolute values, the distributions calculated in this study were non-gaussian with the majority of asymmetry values near zero for optic disc topography and RNFL asymmetry measurements. Therefore, Mann-Whitney-Wilcoxon U tests were

performed for each of the asymmetry measurements to examine differences between AD and ED patients.

The relationships between HRT cup area, cup volume, rim area, rim volume, and GDx average RNFL thickness asymmetry and mean disc area, disc area asymmetry, axial length asymmetry, HRT-II standard deviation asymmetry, K-value asymmetry, mean K-value, and age were examined using univariate and multivariable models. Mean disc area and K-value were derived by taking the average of both eyes. Univariate models were performed first, and then the variables with p-values less than 0.05 were included as candidate explanatory variables in the multivariable models. In this study, P values < 0.05 were considered statistically significant. All statistical analysis was performed with JMP Version 8.01 (SAS Institute Inc, Cary, North Carolina, USA).

Results

Data for 519 participants (262 AD participants and 257 ED participants) were included in the analysis. Basic demographic, average disc area, and visual field MD (of the worse eye) by race are shown in Table 1. As expected, average disc area was larger in AD participants compared to ED participants ($p < 0.0001$). No statistically significant differences were found between AD and ED participants with regard to age, percentage of male participants, and MD of the worse eye. The average age of all participants in this study was 46 years (range 18-85).

The distributions of HRT Cup Area, Cup Volume, Rim Area, Rim Volume, and GDx VCC average RNFL thickness are presented in Figure 1. The medians and 95th percentiles for interocular asymmetry measurements for all participants and participants stratified by race (i.e., AD vs. ED) are shown in Table 2.

In general, AD participants had higher median values for asymmetry parameters. Specifically AD participants showed significantly higher median asymmetry in Cup Volume and Rim Volume (Mann-Whitney-Wilcoxon U test $p < 0.001$ and $p = 0.033$, respectively) compared to ED participants. HRT Cup Area, Rim Area, and GDx VCC Average RNFL thickness asymmetry median values did not vary significantly by race.

Univariate regression analyses were performed to determine how other parameters influenced asymmetry (Table 3). Square root transformations for the HRT optic disc topography and GDx VCC average RNFL asymmetry measurements were used for the univariate and multivariable analyses in order to stabilize the variance. In instances where the aforementioned asymmetries were plotted against another asymmetry measurement (i.e. axial length asymmetry), the square root transformation of the other measurement also was used (i.e. the square root of axial length asymmetry).

Mean disc area and disc area asymmetry were consistently associated with HRT topographic parameter asymmetry (Table 3 and Figure 2). Specifically, increased disc area asymmetry was most strongly associated with increasing rim area asymmetry ($R^2 = 24.5\%$, $p < 0.0001$) followed by cup area asymmetry ($R^2 = 11.1\%$, $p < 0.0001$), cup volume asymmetry ($R^2 = 4.72\%$, $p < 0.0001$), and rim volume asymmetry ($R^2 = 1.83\%$, $p = 0.0020$). Average RNFL thickness asymmetry however, was not associated with disc area asymmetry ($R^2 = 0.26\%$, $p = 0.2481$). Similarly, increased mean disc area was most strongly correlated with increased cup volume asymmetry ($R^2 = 23.1\%$, $p < 0.0001$), followed by cup area asymmetry ($R^2 = 16.2\%$, $p < 0.0001$), rim volume asymmetry ($R^2 = 2.12\%$, $p < 0.0009$), and rim area asymmetry ($R^2 = 1.30\%$, $p < 0.0092$), but not with increasing average RNFL thickness asymmetry ($R^2 = 0.111\%$, $p = 0.447$). In contrast, axial length asymmetry was not significantly associated with asymmetry of HRT topographic parameters or GDx RNFL

thickness. Other explanatory variables including age, corneal curvature, and HRT-II image quality (standard deviation) were not consistently associated with the magnitude of asymmetry (data not shown).

Based on the results of the univariate analyses, we evaluated the effects of race, mean disc area, and the square root transformation of disc area asymmetry on the square root transformations of cup area, cup volume, rim area, rim volume, and average RNFL asymmetry in multivariable analyses (Table 4). For cup area asymmetry, cup volume asymmetry, and rim volume asymmetry, the associations between both mean disc area and the square root transformation of disc area asymmetry were significant, but race was not. For rim area asymmetry, only the square root transformation of disc area asymmetry remained significant ($p < 0.001$). Neither race, mean disc area, nor the square root transformation of disc area asymmetry were significantly associated with changes in average GDx RNFL asymmetry.

Discussion

This study determined normal ranges of inter-eye asymmetry for several different HRT-II-measured optic disc topographies and GDx-VCC-measured RNFL thickness and showed that AD participants have significantly higher median cup volume asymmetry and rim volume asymmetry values compared to ED participants. However, in multivariable analyses that adjusted for mean disc area and disc area asymmetry, race was no longer significant.

Two studies have investigated the effect of race on RNFL thickness, although both studies included a relatively small number of AD participants (Budenz et al- 11 subjects [10.2%], and Mwanza et al- 51 subjects [18%]).^{12,14} The current study compared only healthy subjects of European and African descent, and it provided a significantly larger number of AD participants at 262 (50.5%). In our sample, AD participants showed larger median cup volume and rim volume asymmetry than ED. However, as indicated in the multivariable analyses, these differences by race were explained in part by the larger mean disc area and larger disc area asymmetries in the AD group. This is consistent with Hawker et al, who showed that disc area asymmetry was correlated with increased cup area, cup volume, and rim area asymmetries.⁵ Similarly, Zangwill et al and others have shown that differences in topographic optic disc measurements (not including asymmetry) between AD subjects and subjects in other racial groups can be explained, at least in part by a larger optic disc area in AD subjects.^{32,33} In the current study, both mean disc area and disc area asymmetry also showed significant positive correlations with cup area, cup volume, and rim volume asymmetries.

In contrast to previous reports,¹²⁻¹⁴ the current study placed more emphasis on total asymmetry and did not evaluate systematic differences by eye. Although these studies have consistently noted higher average RNFL thickness in the right eye, the mechanism behind this lateral predominance is poorly understood.¹²⁻¹⁴ Additionally, inconsistency exists regarding the laterality of RNFL thickness asymmetry on a per patient basis. With this in mind, we derived asymmetry by subtracting OS values from OD values, but eliminated laterality by taking the absolute value of the asymmetry value.

As increasing age results in thinner RNFL,³⁴⁻³⁷ we evaluated whether increased age affected asymmetry. Our results, with a larger age range of study participants [mean age of 46 years (range 18-85 years)], agreed with Hawker et al's study of elderly subjects [mean age of 72 years (range 65-89 years)].⁵ There was no correlation between age and asymmetry of optic disc topography measurements. Similarly to Mwanza et al, the current study did not find a relationship between increased age and increased average RNFL thickness asymmetry.¹²

This finding differs from those of two previous studies, one of which showed non-significant trending toward increased asymmetry while the other showed significantly increased RNFL thickness asymmetry with increasing age.^{14,38}

Previous studies reporting normal ranges for average RNFL thickness asymmetry have used earlier versions of scanning laser polarimetry^{20, 21} or OCT technology.^{12, 13} To the best of the authors' knowledge, a normal range of asymmetry for GDx-VCC-measured average RNFL thickness has yet to be reported. As the GDx-VCC is often used in clinical practice, this range is important. Unlike the optic disc topography asymmetry measurements, RNFL thickness asymmetry was not correlated with mean disc area or disc area asymmetry in this study. Hence, RNFL thickness asymmetry may be a more robust parameter to follow in patients with disc area asymmetry and larger mean disc area.

Unlike previous studies,^{12,14} the current study did not show a significant correlation between axial length asymmetry and average RNFL thickness asymmetry. The average axial length in the current study was 23.74mm (range= 20.7mm-26.5mm). It is likely that the limited range of axial length (truncated due to inclusion limits on refractive error) affected the strength of this correlation.

We also visually examined the HRT images of the participants that were outside the 95th percentile cut-offs for several variables in order to determine whether there are other clinical explanations for the relatively large asymmetry in these healthy eyes. Visual inspection of HRT images of 9 outliers suggested that cup area and cup volume were artificially low in some eyes, due in part to the presence of blood vessels within the cup included as part of the rim tissue by HRT software. In these cases in which the contra-lateral eye did not have large vessels within the cup, cup area and cup volume asymmetries were artificially high. An example of this type of asymmetry is shown in Figure 3. In the left eye reflectance image (lower right image), a large vessel is present in the inferonasal region. In the left eye topographic map (lower left image), this vessel registers as part of the rim (color-coded as green). A similar vessel is not present in the right eye and because of this, a larger than expected asymmetry results.

Other explanations for large asymmetries in HRT measures could be slight contour line misplacement in one eye increasing the inter-eye difference in disc area and other topographic parameters. Alternately, large asymmetries of some HRT measures could be due to inter-eye reference plane height asymmetry. A post hoc multivariable analysis with race, mean disc area, square root of disc area asymmetry, and square root of reference plane height asymmetry included in a single model, showed that both the square root transformations of rim area and rim volume were significantly associated with reference height asymmetry. However, with the exception of HRT rim volume in which the R^2 increased from 3% to 11%, the inclusion of reference plane height did not increase the amount of variability explained by the models (R^2 increased by less than 1.5%) (data not shown). Reference plane height asymmetry, then, should be considered when using asymmetry of rim volume to diagnose glaucoma.

In summary, the current study showed that after adjusting for mean disc area and disc area asymmetry in multivariable models, inter-eye asymmetry did not vary by race. Given that the main predictors of optic disc topography asymmetry are disc area and disc area asymmetry, physicians who rely on asymmetry as a sign of early glaucoma should take disc area and disc area asymmetry into consideration in their differential diagnosis. In addition, the results of this study suggest that there is little need for race-specific normative databases for asymmetry. Asymmetries with magnitudes outside the normal ranges of asymmetry

found in this study may suggest early glaucomatous optic neuropathy when used in conjunction with other risk factors for glaucoma.

Acknowledgments

Support: NEI Grants U10EY14267, EY019869, EY08208, EY11008, and EY13959; and Research to Prevent Blindness, Inc. (Medical Student Fellowship Grant).

References

1. Coleman AL. Glaucoma. *Lancet*. Nov 20; 1999 354(9192):1803–1810. [PubMed: 10577657]
2. de Voogd S, Ikram MK, Wolfs RC, Jansonius NM, Hofman A, de Jong PT. Incidence of open-angle glaucoma in a general elderly population: the Rotterdam Study. *Ophthalmology*. Sep; 2005 112(9):1487–1493. [PubMed: 16039716]
3. Weinreb RN, Khaw PT. Primary open-angle glaucoma. *Lancet*. May 22; 2004 363(9422):1711–1720. [PubMed: 15158634]
4. Harasymowycz P, Davis B, Xu G, Myers J, Bayer A, Spaeth GL. The use of RADAAR (ratio of rim area to disc area asymmetry) in detecting glaucoma and its severity. *Can J Ophthalmol*. Apr; 2004 39(3):240–244. [PubMed: 15180140]
5. Hawker MJ, Vernon SA, Ainsworth G, Hillman JG, MacNab HK, Dua HS. 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*. Nov; 2005 46(11):4153–4158. [PubMed: 16249493]
6. Hawker MJ, Vernon SA, Tattersall CL, Dua HS. Detecting glaucoma with RADAAR: the Bridlington Eye Assessment Project. *Br J Ophthalmol*. Jun; 2006 90(6):744–748. [PubMed: 16714266]
7. Ong LS, Mitchell P, Healey PR, Cumming RG. Asymmetry in optic disc parameters: the Blue Mountains Eye Study. *Invest Ophthalmol Vis Sci*. Apr; 1999 40(5):849–857. [PubMed: 10102281]
8. Fishman RS. Optic disc asymmetry. A sign of ocular hypertension. *Arch Ophthalmol*. Nov; 1970 84(5):590–594. [PubMed: 5478884]
9. Caprioli J, Miller JM, Sears M. Quantitative evaluation of the optic nerve head in patients with unilateral visual field loss from primary open-angle glaucoma. *Ophthalmology*. Nov; 1987 94(11):1484–1487. [PubMed: 3684222]
10. Yablonski ME, Zimmerman TJ, Kass MA, Becker B. Prognostic significance of optic disk cupping in ocular hypertensive patients. *Am J Ophthalmol*. Apr; 1980 89(4):585–592. [PubMed: 7369323]
11. Zeyen TG, Raymond M, Caprioli J. Disc and field damage in patients with unilateral visual field loss from primary open-angle glaucoma. *Doc Ophthalmol*. 1992; 82(4):279–286. [PubMed: 1306476]
12. Mwanza JC, Durbin MK, Budenz DL. Interocular Symmetry in Peripapillary Retinal Nerve Fiber Layer Thickness Measured With the Cirrus HD-OCT in Healthy Eyes. *Am J Ophthalmol*. Mar; 2011 151(3):514–521. e511. [PubMed: 21236402]
13. Park JJ, Oh DR, Hong SP, Lee KW. Asymmetry analysis of the retinal nerve fiber layer thickness in normal eyes using optical coherence tomography. *Korean J Ophthalmol*. Dec; 2005 19(4):281–287. [PubMed: 16491818]
14. Budenz DL. Symmetry between the right and left eyes of the normal retinal nerve fiber layer measured with optical coherence tomography (an AOS thesis). *Trans Am Ophthalmol Soc*. 2008; 106:252–275. [PubMed: 19277241]
15. Munoz B, West SK, Rubin GS, et al. Causes of blindness and visual impairment in a population of older Americans: The Salisbury Eye Evaluation Study. *Arch Ophthalmol*. 2000; 118(6):819–825. [PubMed: 10865321]
16. Sommer A. Glaucoma risk factors observed in the Baltimore Eye Survey. *Curr Opin Ophthalmol*. Apr; 1996 7(2):93–98. [PubMed: 10163329]
17. Sommer A. Epidemiology, ethnicity, race, and risk. *Arch Ophthalmol*. Aug. 2003 121(8):1194. [PubMed: 12912700]

18. Tielsch JM, Katz J, Quigley HA, Javitt JC, Sommer A. Diabetes, intraocular pressure, and primary open-angle glaucoma in the Baltimore Eye Survey. *Ophthalmology*. Jan; 1995 102(1):48–53. [PubMed: 7831041]
19. Tielsch JM, Sommer A, Katz J, Royall RM, Quigley HA, Javitt J. Racial variations in the prevalence of primary open-angle glaucoma. The Baltimore Eye Survey. *JAMA*. Jul 17; 1991 266(3):369–374. [PubMed: 2056646]
20. Kurimoto Y, Matsuno K, Kaneko Y, Umihira J, Yoshimura N. Asymmetries of the retinal nerve fibre layer thickness in normal eyes. *Br J Ophthalmol*. May; 2000 84(5):469–472. [PubMed: 10781509]
21. Essock EA, Sinai MJ, Fechtner RD. Interocular symmetry in nerve fiber layer thickness of normal eyes as determined by polarimetry. *J Glaucoma*. Apr; 1999 8(2):90–98. [PubMed: 10209724]
22. Sample PA, Girkin CA, Zangwill LM, et al. The African Descent and Glaucoma Evaluation Study (ADAGES): design and baseline data. *Arch Ophthalmol*. Sep; 2009 127(9):1136–1145. [PubMed: 19752422]
23. Girkin, CA. Principles of Confocal Scanning Laser Ophthalmoscopy for the Clinician 1ed. San Ramon: Jocoto Advertising; 2005.
24. Alencar LM, Zangwill LM, Weinreb RN, et al. A comparison of rates of change in neuroretinal rim area and retinal nerve fiber layer thickness in progressive glaucoma. *Invest Ophthalmol Vis Sci*. Jul; 51(7):3531–3539. [PubMed: 20207973]
25. Weinreb RN, Shakiba S, Zangwill L. Scanning laser polarimetry to measure the nerve fiber layer of normal and glaucomatous eyes. *Am J Ophthalmol*. May; 1995 119(5):627–636. [PubMed: 7733188]
26. Zhou Q, Weinreb RN. Individualized compensation of anterior segment birefringence during scanning laser polarimetry. *Invest Ophthalmol Vis Sci*. Jul; 2002 43(7):2221–2228. [PubMed: 12091420]
27. Medeiros FA, Alencar LM, Zangwill LM, Sample PA, Susanna R Jr, Weinreb RN. Impact of atypical retardation patterns on detection of glaucoma progression using the GDx with variable corneal compensation. *Am J Ophthalmol*. Jul; 2009 148(1):155–163 e151. [PubMed: 19375062]
28. Bagga H, Greenfield DS, Feuer WJ. Quantitative assessment of atypical birefringence images using scanning laser polarimetry with variable corneal compensation. *Am J Ophthalmol*. Mar; 2005 139(3):437–446. [PubMed: 15767051]
29. Medeiros FA, Bowd C, Zangwill LM, Patel C, Weinreb RN. Detection of glaucoma using scanning laser polarimetry with enhanced corneal compensation. *Invest Ophthalmol Vis Sci*. Jul; 2007 48(7):3146–3153. [PubMed: 17591884]
30. Hoffmann EM, Boden C, Zangwill LM, et al. Intereye spatial relationship of abnormal neuroretinal rim locations in glaucoma patients from the diagnostic innovations in glaucoma study. *Am J Ophthalmol*. May; 2007 143(5):781–787. [PubMed: 17379176]
31. Yang H, Downs JC, Burgoyne CF. Physiologic intereye differences in monkey optic nerve head architecture and their relation to changes in early experimental glaucoma. *Invest Ophthalmol Vis Sci*. Jan; 2009 50(1):224–234. [PubMed: 18775866]
32. Girkin CA, Sample PA, Liebmann JM, et al. African Descent and Glaucoma Evaluation Study (ADAGES): II. Ancestry differences in optic disc, retinal nerve fiber layer, and macular structure in healthy subjects. *Arch Ophthalmol*. May; 128(5):541–550. [PubMed: 20457974]
33. Zangwill LM, Weinreb RN, Berry CC, et al. Racial differences in optic disc topography: baseline results from the confocal scanning laser ophthalmoscopy ancillary study to the ocular hypertension treatment study. *Arch Ophthalmol*. Jan; 2004 122(1):22–28. [PubMed: 14718290]
34. Bowd C, Zangwill LM, Blumenthal EZ, et al. Imaging of the optic disc and retinal nerve fiber layer: the effects of age, optic disc area, refractive error, and gender. *J Opt Soc Am A Opt Image Sci Vis*. Jan; 2002 19(1):197–207. [PubMed: 11778725]
35. See JL, Nicolela MT, Chauhan BC. Rates of neuroretinal rim and peripapillary atrophy area change: a comparative study of glaucoma patients and normal controls. *Ophthalmology*. May; 2009 116(5):840–847. [PubMed: 19410941]

36. Budenz DL, Anderson DR, Varma R, et al. Determinants of normal retinal nerve fiber layer thickness measured by Stratus OCT. *Ophthalmology*. Jun; 2007 114(6):1046–1052. [PubMed: 17210181]
37. Alamouti B, Funk J. Retinal thickness decreases with age: an OCT study. *Br J Ophthalmol*. Jul; 2003 87(7):899–901. [PubMed: 12812895]
38. Funaki S, Shirakashi M, Funaki H, Yaoeda K, Abe H. Relationship between age and the thickness of the retinal nerve fiber layer in normal subjects. *Jpn J Ophthalmol*. May-Jun;1999 43(3):180–185. [PubMed: 10413251]

Figure 1.

Graph showing the frequency distribution of mean asymmetry (absolute value [right eye minus left eye]) in HRT cup area, cup volume, rim area, rim volume and GDx-VCC average RNFL thickness. N=519 pairs of eyes. All measurements were positive due to use of absolute value.

Figure 2.

Scatter plots showing univariate linear regression between the square root transformation of disc area asymmetry and the square root transformations cup area asymmetry, cup volume asymmetry, rim area asymmetry, rim volume asymmetry, and average RNFL thickness asymmetry. The graphs show that increased disc area asymmetry was correlated with increased asymmetry in all parameters except for average RNFL thickness asymmetry.

Figure 3.

This figure shows an HRT images from a participant with increased cup area and cup volume asymmetry due to a large blood vessel (indicated by arrows) occupying the inferonasal portion of the cup in the left eye that does not appear in the right eye. Note, the HRT-II topographic image is false color-coded. The red area represents the cup while the blue and green areas represent the neuroretinal rim²³.

Table 1**Demographic Information and Descriptive Statistics**

(mean and 95% CI unless otherwise indicated)

	African Descent	European Descent	P-value
N	262	257	
Age (years)	44.9 (43.3, 46.5)	47.1 (45.2, 49.0)	0.0794
Average Disc Area (mm ²)	2.04 (1.99, 2.10)	1.76 (1.71, 1.80)	<0.0001
% Male	88 (33.6%)	83 (32.3%)	0.7542
Visual field Mean Deviation (dB)(from worse eye)	-63 (-.78, -.48)	-0.54 (-.70, -.38)	0.4313

Table 2

Distributions of Optic Disc and Nerve Fiber Layer Measures by Race (N=519)

			African Descent	European Descent	ALL	p-value *
		n	262	257	519	
HRT Variables	Cup Area Asymmetry (mm ²)	MEDIAN (25%-75%)	0.11 (0.05, 0.19)	0.09 (0.04, 0.17)	0.1 (0.05, 0.18)	0.1537
		95% cut-off	0.42	0.32	0.39	
	Cup Volume Asymmetry (mm ³)	MEDIAN (25%-75%)	0.03 (0.01, 0.07)	0.02 (0.01, 0.05)	0.03 (0.01, 0.06)	0.0003
		95% cut-off	0.18	0.14	0.15	
	Rim Area Asymmetry (mm ²)	MEDIAN (25%-75%)	0.14 (0.07, 0.25)	0.14 (0.06, 0.22)	0.14 (0.06, 0.23)	0.2844
		95% cut-off	0.45	0.45	0.45	
GDx-VCC Variables	Rim Volume Asymmetry (mm ³)	MEDIAN (25%-75%)	0.075 (0.04, 0.12)	0.06 (0.03, 0.11)	0.07 (0.03, 0.12)	0.0326
		95% cut-off	0.22	0.22	0.22	
	TSNIT RNFL Thickness Asymmetry (μm)	MEDIAN (25%-75%)	2.15 (1.21, 3.79)	2.01 (0.89, 3.58)	2.06 (1.07, 3.71)	0.2636
		95% cut-off	6.23	6.40	6.25	

* Mann-Whitney Wilcoxon Test

HRT= Heidelberg Retina Tomograph

GDx-VCC = GDx Variable Corneal Compensation

TSNIT RNFL= Temporal, Superior, Nasal, Inferior, Temporal (Average) Retinal Nerve Fiber Layer

Table 3

Univariate Analyses showing association between Disc Area Asymmetry, Mean Disc Area, and Axial Length on Optic Nerve Head Asymmetry and Retinal Nerve Fiber Layer Asymmetry

	Square Root Disc Area Asymmetry (mm ²)			Mean Disc Area (mm ²)			Square Root Axial Length Asymmetry (mm)		
	Slope	R-Squared	P-value	Slope	R-Squared	P-value	Slope	R-Squared	P-value
Square Root Cup Area Asymmetry (mm²)	0.30	0.11	<.0001	0.15	0.16	<.0001	0.01	<.01	0.5239
Square Root Cup Volume Asymmetry (mm³)	0.14	0.05	<.0001	0.13	0.23	<.0001	0.01	<.01	0.7507
Square Root Rim Area Asymmetry (mm²)	0.48	0.25	<.0001	0.05	0.01	0.0092	-0.01	<.01	0.7892
Square Root Rim Volume Asymmetry (mm³)	0.09	0.02	0.002	0.04	0.02	0.0009	-0.01	<.01	0.3123
Square Root TSNIT RNFL Thickness Asymmetry (μm)	0.18	<.01	0.2481	<.01	<.01	0.9823	0.014	<.01	0.8291

TSNIT RNFL= Temporal, Superior, Nasal, Inferior, Temporal (Average) Retinal Nerve Fiber Layer

Table 4

Multivariable Analyses of Race, Mean Disc Area, and Disc Area asymmetry on Optic Nerve Head Asymmetry and Retinal Nerve Fiber Layer Asymmetry

Parameters (All are square root transformations)			Estimate	P-value
Global Cup Area Asymmetry (mm²)				
	Race		-0.01	0.4562
	Mean Disc Area		0.13	<.0001
	Square Root Disc Area Asymmetry		0.23	<.0001
Global Cup Volume Asymmetry (mm³)				
	Race		0.01	0.8064
	Mean Disc Area		0.12	<.0001
	Square Root Disc Area Asymmetry		0.09	0.0013
Global Rim Area Asymmetry (mm²)				
	Race		0.01	0.187
	Mean Disc Area		0.01	0.9391
	Square Root Disc Area Asymmetry		0.48	<.0001
Global Rim Volume Asymmetry (mm³)				
	Race		0.01	0.2966
	Mean Disc Area		0.03	0.0242
	Square Root Disc Area Asymmetry		0.08	0.0098
TSNIT RNFL Thickness Asymmetry (μm)				
	Race		0.04	0.2443
	Mean Disc Area		-0.05	0.518
	Square Root Disc Area Asymmetry		0.20	0.1968

TSNIT RNFL= Temporal, Superior, Nasal, Inferior, Temporal (Average) Retinal Nerve Fiber Layer