Detection of Glaucomatous Visual Field Changes Using the Moorfields Regression Analysis of the Heidelberg Retina Tomograph

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● PURPOSE. To evaluate the sensitivity and specificity of optic disk examinations performed using the Moorfields regression analysis (MRA) of the Heidelberg Retina Tomograph (HRT) in differentiating normal from glaucomatous eyes.

● DESIGN: Retrospective cross-sectional study.

● METHODS: Five hundred and nineteen patients were included in the study for a total of 193 normal eyes, 213 with suspected glaucoma (primary open-angle glaucoma [POAG]), and 113 with POAG. The intervention consisted of optic disk imaging by means of HRT I. A mean of three repeated images was analyzed using version 2.01 software. The optic disk was classified as "normal/outside normal limits" on the basis of the MRA. The visual field was examined using the DS 24 II program (Humphrey perimeter), with a glaucomatous visual field being defined on the basis of an abnormal Glaucoma Hemifield Test and a statistically significant corrected pattern standard deviation greater than 2 dB. The results obtained with MRA were compared with those obtained using the multivariate discriminant analysis (MDA) provided in the HRT I. The main outcome measures were sensitivity, specificity, and positive and negative predictive values of HRT examination.

● RESULTS: The sensitivity and specificity of the HRT-MRA examination were, respectively, 74% and 94% (83% and 75% with MDA) when the patients with suspected POAG were excluded from the analysis; the figures were 74% and 85%, and 41% and 94% (83% and 64%, and 60% and 75% with MDA) when the same patients were included as being normal or having POAG.

● CONCLUSIONS: In a broad clinical setting including normal subjects, patients with suspected POAG, and POAG patients, the HRT-MRA showed a high degree of diagnostic accuracy. The MRA was less sensitive but more specific than MDA. Greater diagnostic ability may be added by HRT-MRA examinations than by HRT-MDA to standard POAG diagnostic studies. (Am J Ophthalmol 2003;136:26–33. © 2003 by Elsevier Inc. All rights reserved.)

P RIMARY OPEN-ANGLE GLAUCOMA (POAG) IS STILL one of the major causes of blindness in the world. It involves the progressive loss of retinal ganglion cells and subsequent visual field damage. The loss of retinal ganglion cells is clinically detectable as a structural modification of the optic disk or as a loss of retinal nerve fiber layer reflectivity, particularly when using a blue or green light.[1,2] As the optic disk and retinal nerve fiber layer are usually evaluated by means of subjective techniques (ophthalmoscopy, retinography, and so forth), which are clearly based on the examiner's experience, it may be useful to introduce objective quantitative measurements that should improve the ability to discriminate normal from abnormal (glaucomatous) conditions.

Over the last few years, a number of new devices have been developed for this purpose, some of which provide a quantitative measure of a variety of optic disk parameters,[3,4] whereas others are designed to measure only the thickness of retinal nerve fiber layer,[5,6] or the whole retina.[7] The Heidelberg Retina Tomograph (HRT) is a scanning laser ophthalmoscope that allows a three-dimensional topographic analysis of the optic disk and retina. It provides rapid and reproducible measurements of optic disk topography on a pixel-by-pixel basis, as well as a reproducible analysis of various optic disk parameters.

The HRT has been widely investigated to assess the reproducibility of topographic measures[3,8–20] and their clinical validity in differentiating normal from glaucomatous optic disks, but the results are very different in terms of sensitivity and specificity[21–29] for a number of reasons. First, the facts that optic disk shapes and sizes vary widely

in the normal population and that there is a close correlation among disk, rim, and cup sizes[30,31] may negatively affect the use of one or more standard HRT measurements as a means of differentiating normal and glaucomatous optic disks.[22] Second, most of these studies involved small patient samples that included various proportions of normal (33%–67%) and glaucomatous cases. Third, the HRT stereometric parameters depend on the position of the reference plane along the "z" axis, which, as it is based on anatomical investigations,[32,33] is variable and unpredictable.[29] Finally, the different studies used different visual field criteria to define "glaucoma." It has been recently shown that visual field results poorly agree with the multidiscriminant analysis[21] and analysis of ranked segments distribution curves[34,35] used in the HRT I 2.01 software and that these two analyses had a low degree of clinical ability to detect glaucomatous visual fields defects in a large sample attending a standard clinical setting.[29]

The software implemented in the HRT II includes statistical analyses aimed at better discriminating normal from abnormal optic disks. It has been shown that the Moorfields regression analysis (MRA), which indicates normality, borderline, or abnormality on the basis of a comparison between the examined optic disk and a dedicated database of normal eyes, is highly capable of clinically discriminating normal and glaucomatous patients.[25] The advantage of the MRA is that it uses the global and sectorial rim area adjusted for disk size and age, which is believed to improve the specificity of the examination.

The aim of this study was to evaluate the clinical usefulness of HRT examinations by assessing the sensitivity and the specificity of HRT-MRA in detecting glaucomatous visual field changes. The study population included a large sample of healthy subjects, patients with ocular hypertension who are at higher risk of developing glaucoma, and patients with POAG, who are representative of the typical population in our clinical settings.

DESIGN

THIS WAS A RETROSPECTIVE STUDY PERFORMED IN ONE institutional center.

METHODS

THE STUDY POPULATION CONSISTED OF 519 PATIENTS AGED 25 to 81 years, attending the Glaucoma or Outpatient Services at S. Paolo Hospital in Milan. One eye was randomly chosen for each subject. The Institutional Review Board was informed about the protocol and ruled that no consent was needed because this was a retrospective chart review of data normally obtained in clinical practice. The inclusion criteria were 20/20 visual acuity, a clear lens, and a normal retina; the exclusion criteria were

myopia greater than −6 diopters, hyperopia greater than 4 diopters, optic disk abnormality (that is, drusen or a tilted disk), a history of neurophthalmologic diseases, a diagnosis of low-tension glaucoma and HRT images of poor quality.

All of the patients included in the study underwent a complete ophthalmologic evaluation: biomicroscopy of the anterior segment and intraocular pressure (IOP) measurements by means of Goldmann tonometry were made before pupillary dilation; the indirect ophthalmoscopic evaluation and HRT examination were carried out in mydriasis.

The normal subjects had an IOP of <22 mm Hg, and a normal visual field, as revealed by the Humphrey 750 DS 24 II program. Their Glaucoma Hemifield Test results were within normal limits, and they had a corrected pattern standard deviation of ≤2 dB.

The definition of patients with suspected POAG was based on the presence of IOP of ≥22 mm Hg without therapy and a normal visual field. For the purposes of the study, however, all of the patients with an IOP of ≥22 mm Hg, Glaucoma Hemifield Test results that were borderline or outside normal limits and a corrected pattern standard deviation ≤2 dB, or Glaucoma Hemifield Test results within normal limits and a corrected pattern standard deviation of > 2 dB were also included in this group.

Primary open-angle glaucoma was defined as the presence of an abnormal visual field consistent with glaucoma and a history of IOP of >21 mm Hg (without topical medical treatment). The glaucomatous visual field was defined on the basis of Glaucoma Hemifield Test results outside normal limits and a statistically significant corrected pattern standard deviation of >2 dB.[36] The visual field defects had to be present in two different visual fields within a time span of 6 months The last visual field has been used in determining the subject's category. The clinical appearance of the optic disk was used to exclude patients with particular patterns of the optic disk such as the presence of drusen or tilted disk but was not considered to classify subjects.

At the time of the study, IOP was ≤21 mm Hg (under topical medical treatment) either in patients with POAG or in patients with suspected POAG to rule out a possible bias in HRT evaluation induced by moderate differences in IOP among the three groups.[37]

The HRT (Heidelberg Instruments, Heidelberg, Germany) is a confocal scanning laser ophthalmoscope that uses a diode laser (wavelength 670 nm) to scan the retinal surface in three dimensions. A topographic image is usually taken as a series of 32 confocal images (that is, 32 optical sections) at 32 consecutive focal planes, each consisting of 256 × 256 pixels. The HRT examinations were performed using a 10-degree angle view.

Three topographic images were obtained for each eye, and a mean topographic image was analyzed using version 2.01 software. The optic margin was delimited by a contour line placed around the inner edge of Elschnig ring by two clinicians whose reproducibility has been previously eval-

uated,[20] and the operating software provided 12 predefined shape parameters. For this analysis, the reference plane was set at the standard value of 50 μm below the mean retinal surface at the temporal sector between 350 and 356 degrees.

The HRT classification of the optic disk was determined according to Wollstein and colleagues[25] and Mikelberg and colleagues.[21] The MRA classification is based on 112 normal Caucasian eyes and 77 early glaucomatous Caucasian eyes. The MRA takes into account the global and sectorial rim area corrected for global and sectorial disk area and uses three grades: "normal" if all of the measurements fall within the 95% confidence intervals (CI); "borderline" if at least one falls between the lower 95% and 99.9% CI; and "outside normal limits" if at least one rim area measurement is less than the lower 99.9% CI. To obtain data that could be better compared with those provided by Wollstein and colleagues,[25] the cases defined as being borderline were considered as being normal. The MRA is not implemented in the standard software of the HRT I and is today available as an add-on program, and it was provided to the authors by Heidelberg Engineering.

Multivariate discriminant analysis compares the eye under examination with a normative database on the basis of three of the predefined HRT parameters: rim volume, height variation contour, and cup shape measure, adjusted by age. The MDA classifies eyes as "glaucomatous" or "normal."

Three different analyses were performed. In analysis 1, the patients with suspected POAG were excluded. In analysis 2, the normal patients and those with suspected POAG were put in the same group. In analysis 3, the patients with known and suspected POAG were put in the same POAG group.

Statistical analysis was performed using SPSS (version 6.1) software (SPSS, Chicago, Illinois, USA). Sensitivity, specificity, diagnostic accuracy (the sum of true positive and negative observations divided by the total number of observations), positive predictive values (PPV), and negative predictive values (NPV) were calculated according to standard procedures. An independent two-tailed test was used to compare mean values between two groups. The one-way analysis of variance (ANOVA) test was used to compare means among groups. The χ^2 test was used to compare proportions.

RESULTS

OF THE 519 PATIENTS INCLUDED IN THE STUDY, 193 WERE normal, 213 had suspected POAG, and 113 had POAG. The group of patients with suspected POAG includes a substantial proportion of ocular hypertension patients with normal corrected pattern standard deviation and Glaucoma Hemifield Test results (177/213), ocular hypertension patients with borderline Glaucoma Hemifield Test and normal corrected pattern standard deviation (6/213),

and ocular hypertension patients with abnormal Glaucoma Hemifield Test or corrected pattern standard deviation (30/213). The mean age in the three groups was, respectively, 56.9 ± 11.1, 61.1 ± 12.2, and 68.0 ± 12.2 years; and the mean refraction was, respectively, 0.2 ± 1.8, 0.1 ± 2.1, and −0.2 ± 1.9. Difference in age among the three groups was statistically significant ($P < .01$). Difference in refraction among the three groups was not statistically significant ($P > .05$). The descriptive statistics of the visual field indices and HRT parameters are shown in Table 1. The ANOVA showed significant differences in all of these variables among the three groups.

Table 2 shows the HRT classification of the 519 patients.

The sensitivity, specificity, diagnostic accuracy, and PPV and NPV of the HRT examinations are shown in Table 3. The MRA was highly specific and sensitive when the patients with suspected POAG were excluded from the analysis. Its diagnostic ability remained high when the patients with suspected POAG were included in the normal group but was lower when they were included in the POAG group. The diagnostic accuracy of MRA was 87% in analysis 1, 82% in analysis 2, and 61% in analysis 3 (due to a considerable decrease in sensitivity). The MDA was highly sensitive but had a low degree of specificity. Its diagnostic accuracy was 78% in analysis 1, 68% in analysis 2, and 65% in analysis 3. The difference in diagnostic accuracy between MRA and MDA was statistically significant in analysis 1 ($P = .006$) and analysis 2 ($P < .0001$); the difference was not statistically significant in analysis 3 ($P = .123$). The sensitivity and specificity did not change when the eyes with a disk area out of the suggested MRA range (1.2–2.8 mm^2) were excluded from the analysis.

In analysis 1, MRA sensitivity linearly increased with progressively increasing mean deviation when the POAG patients were categorized according to mean deviation deciles values ($r^2 = 0.53$, $P = .016$). However, MRA sensitivity was fairly constant when POAG patients were categorized according to increasing mean deviation (up to approximately −12 dB) or corrected pattern standard deviation (up to approximately 9 dB); it definitely increased when mean deviation and corrected pattern standard deviation values were larger (Tables 4 and 5).

The MRA NPV was approximately at or above 90% in analyses 1 and 2, whereas PPV was approximately at or above 90% in analyses 1 and 3 (Table 3).

DISCUSSION

IN PATIENTS WITH POAG, OPTIC NERVE HEAD MODIFICA-tions and retinal nerve fiber loss may precede visual field glaucomatous alterations.[2,38–52] To plan a therapy designed to preserve visual function for as long as possible, it seems to be clinically appropriate to use instruments capable of

TABLE 1. Mean (SD) Values of Visual Field Indices and Heidelberg Retinal Tomography Measurements in Normal Subjects, Patients With Suspected POAG, and POAG Patients

	Normal	Suspected POAG	POAG	*P*
IOP	16.34 (1.26)	23.45 (1.93)	24.35 (1.82)	<.001
IOP at time of imaging	16.34 (1.26)	16.72 (1.36)	16.84 (1.39)	<.01
Mean deviation	−0.56 (1.48)	−1.14 (2.80)	−9.73 (7.13)	<.01
Corrected pattern standard deviation	0.82 (0.65)	1.55 (1.05)	7.34 (3.44)	<.001
Disc area	1.81 (0.38)	1.90 (0.42)	2.04 (0.47)	<.001
Cup area	0.45 (0.31)	0.67 (0.43)	1.18 (0.57)	<.01
Cup-disk area	0.24 (0.12)	0.33 (0.17)	0.56 (0.21)	<.01
Rim area	1.35 (0.24)	1.22 (0.29)	0.86 (0.35)	<.01
Cup volume	0.09 (0.11)	0.17 (0.17)	0.31 (0.22)	<.01
Rim volume	0.37 (0.13)	0.31 (0.13)	0.16 (0.10)	<.01
Mean cup depth	0.20 (0.08)	0.25 (0.11)	0.28 (0.11)	<.001
Maximum cup depth	0.56 (0.20)	0.61 (0.21)	0.61 (0.20)	.012
Cup shape measure	−0.19 (0.07)	−0.15 (0.08)	−0.08 (0.15)	<.01
Height variation contour	0.42 (0.11)	0.39 (0.10)	0.37 (0.13)	<.01
Mean RNFL thickness	0.26 (0.08)	0.23 (0.08)	0.15 (0.08)	<.01
RNFL cross-sectional area	1.23 (0.36)	1.12 (0.37)	0.73 (0.39)	<.01

IOP = intraocular pressure; POAG = primary open angle glaucoma; RNFL = retinal nerve fiber layer; SD = standard deviation.

TABLE 2. Heidelberg Retinal Tomography Classification by Groups

	Normal (n = 193)			Suspected POAG (n = 213)			POAG (n = 113)		
	+	±	−	+	±	−	+	±	−
Moorfields regression analysis	12	19	162	50	44	119	84	10	19
Multivariate discriminant analysis	48	—	145	100	—	113	94	—	19

+ = abnormal; ± = borderline; − = normal; POAG = primary open-angle glaucoma.
Borderline cases were considered as being normal.

TABLE 3. Sensitivity, Specificity, Diagnostic Accuracy, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of Heidelberg Retinal Tomography Examination in Detecting Glaucomatous Visual Field

	Sensitivity	Specificity	Accuracy	PPV	NPV
Moorfields regression analysis					
Analysis 1	74%	94%	87%	87%	89%
Analysis 2	74%	85%	82%	57%	92%
Analysis 3	41%	94%	61%	92%	48%
Multivariate discriminant analysis					
Analysis 1	83%	75%	78%	66%	88%
Analysis 2	83%	64%	68%	39%	93%
Analysis 3	60%	75%	65%	80%	52%

NPV = negative predicted values; POAG = primary open-angle glaucoma; PPV = positive predicted values.
Analysis 1, normal vs POAG patients; analysis 2, normal plus suspected POAG vs POAG patients; analysis 3, normal vs suspected POAG + POAG patients.

TABLE 4. Sensitivity of MRA and MDA, Excluding POAG Suspect Patients, in Detecting Glaucomatous Visual Field Ranked by Progressively Increasing Mean Deviation (Cut-off at 33rd and 66th Percentiles)

	Mean Deviation (dB)		
	<-5.82	-11.58	≥-11.58
MRA normal	13	13	3
MRA abnormal	25	25	34
Total	38	38	37
Sensitivity	66%	66%	92%
MDA normal	11	7	1
MDA abnormal	27	31	36
Total	38	38	37
Sensitivity	71%	82%	97%

MDA = multivariate discriminant analysis; MRA = Moorfields regression analysis; POAG = primary open-angle glaucoma.

TABLE 5. Sensitivity of MRA and MDA, Excluding POAG Suspect Patients, in Detecting Glaucomatous Visual Field Ranked by Progressively Increasing Corrected Pattern Standard Deviation (Cut-off at 33rd and 66th Percentiles)

	Corrected Pattern Standard Deviation (dB)		
	<5.32	8.98	≥8.98
MRA normal	14	11	4
MRA abnormal	23	26	35
Total	37	37	39
Sensitivity	62%	70%	90%
MDA normal	11	8	0
MDA abnormal	26	29	39
Total	37	37	39
Sensitivity	70%	78%	100%

MDA = Multivariate discriminant analysis; MRA = Moorfields regression analysis; POAG = primary open-angle glaucoma.

detecting glaucomatous alterations, particularly in the early stages of the disease.

A clinically relevant step in the process of assessing new diagnostic methods is to evaluate their diagnostic validity to establish whether they are useful in a clinical setting. We investigated the diagnostic accuracy of HRT in discriminating normal and glaucomatous eyes. The visual field-based definition of glaucoma is clinically relevant as it indicates definite functional loss, and it is the gold standard of the presence of glaucoma whenever new diagnostic tools are investigated.

A previous study found that MDA has a fair diagnostic ability,[29] and Wollstein and colleagues[25] have shown that the diagnostic ability of HRT-MRA to distinguish normal and early glaucomatous eyes is high (sensitivity, 84%, and sensitivity, 96%). Our study is the first attempt to make a

direct comparison between the two HRT analyses in the same population.

The results showed that MRA was highly sensitive and specific (diagnostic accuracy, 87%) when only normal and POAG patients were included in the analysis. The sensitivity was moderate and fairly constant, however, when mean deviation (an indicator of the global visual field defect) was within -12 dB, and it was extremely high only when mean deviation was larger. Our results could then confirm the results of Wollstein and colleagues[25] only partially. Conversely, MDA was highly sensitive but not very specific (diagnostic accuracy, 78%), as has been previously reported.[29]

The comparison of MRA and MDA showed that MRA was much more specific (Table 3). Both analyses showed different results when the patients with suspected POAG (typical of the clinical setting) were considered to be normal or as having POAG. The diagnostic accuracy of MRA was 82% in analysis 2 (MDA was 68%) and 61% in analysis 3 (MDA was 65%). This finding indicates that HRT diagnostic accuracy is 10 to 15 units greater using MRA when patients with suspected POAG are considered as being normal ($P < .001$), whereas it is not significantly lower using MRA when patients with suspected POAG are considered as having POAG ($P = .123$). Although the higher diagnostic accuracy of MRA over MDA observed in analyses 1 and 2 was not observed in analysis 3, our results seem to indicate that MRA can discriminate normal from POAG patients better than MDA even in a large sample including borderline patients (who represent a high proportion of the patients generally seen in the clinical setting). It is worth noting that, given the definitions of POAG and suspected POAG used in this study, the former group also includes patients with early glaucoma whereas the latter includes a substantial proportion of ocular hypertension patients with normal corrected pattern standard deviation and Glaucoma Hemifield Test results (177/213), ocular hypertension patients with borderline Glaucoma Hemifield Test and normal corrected pattern standard deviation (6/213), and ocular hypertension patients with abnormal Glaucoma Hemifield Test or corrected pattern standard deviation (30/213).

Interestingly, the diagnostic ability of MRA did not change when the analysis was restricted to the eyes whose disk area was within the range suggested by the manufacturer (1.2–2.8 mm^2), which can be interpreted as a further indication of the robustness of the MRA normative database, whose regression of rim on disk area also holds true for eyes whose disk size exceeds the lower or upper values of the model.

The MRA had a high PPV and NPV in analysis 1. Positive predictive value and NPV were clearly unbalanced when the patients with suspected POAG were considered as being normal or as having POAG. Although a correct interpretation of the predictive values must take into account the prevalence of the disease in the studied

population (which is high in this study, and does not necessarily reflect the prevalence of POAG in other clinical settings), it is worth noting that the probability of having/not having the disease when the test was positive/negative was high when the patients with suspected POAG were excluded from the analysis. As expected, however, PPV and NPV were negatively affected when the evaluation was made on the whole sample, which also consisted of a considerable number of patients with suspected POAG whose inclusion in the normal/POAG groups was definitely arbitrary.

These results may be interpreted in terms of improvements in the HRT software. Some of the previously reported limitations of HRT-MDA analysis are that it only provides a global disk analysis, does not take into account the size of the disk area, and includes an analysis of rim and cup measurements whose size may depend on the absolute position of the reference plane along the "z" axis.[29] The MRA is clearly better than MDA, as it globally and sectorially analyses rim area taking into account the close correlation between rim and disk area. However, as it only considers rim area, it is still affected by the problem of the absolute position of the reference plane along the "z" axis, and that may limit its clinical ability to distinguish normal and POAG eyes.[29]

Conversely, our findings may also be explained by a series of confounding factors. First of all, the gold standard used in our study may itself have some limitations. In fact, we referred to commonly used criteria to define the normal group, which, however, do not account for localized visual fields defects that might be undetected by the global indices. That in turn might affect the specificity of the studied method. Differently from the patient with suspected POAG or POAG, the normal subjects have been enrolled on the basis of a single normal visual field, which may have induced a potential selection bias. The criteria for defining normal and POAG eyes leave a large gap that may be filled by a considerable number of eyes with heterogeneous characteristics that are usually defined as borderline or suspected POAG in the clinical setting, particularly when IOP is ≥ 22 mm Hg. Moreover, including the patients with suspected POAG in the normal group (analysis 2) or POAG group (analysis 3) is totally arbitrary and may lead to biased results and conclusions. Second, it can be expected that some ocular hypertension eyes may have some glaucomatous alterations in the disk[44,45,47–49] or retinal nerve fiber layer.[39,41,43–45,52] Third, a number of ocular hypertensive eyes with normal visual field examination results may be false ocular hypertension cases because of an overestimation of IOP induced by a thicker cornea.[53–55] Moreover, the exclusion of normal tension glaucoma patients may have introduced a selection bias since controls and cases are not identified only on the basis of visual field but also of IOP, which means they have been enrolled with different inclusion/exclusion criteria.

Some limitations of our study may also have affected the results. First, our normal population was not representative of the general population, which may have induced a patient self-selection bias (those attending the ophthalmic department) or an investigator selection bias (the mean disk area was smaller in the normal patients than in those with known or suspected POAG). Second, the mean age of the three groups was different, which makes the comparison less accurate. However, unlike MDA, which takes into account only age, MRA better controls these limitations as it takes into account both disk area and age.

Our results also suggest that HRT-MRA may be capable of detecting optic disk abnormalities due to subclinical glaucoma in eyes with a normal visual field. If so, the gold standard may be inappropriate, as a number of studies have demonstrated that visual field alterations are preceded by structural damage that can be clinically detected by means of retinal nerve fiber layer evaluation, particularly in eyes with an increased IOP.[39,41,43–45,47,49,52] However, we did not specifically investigate this hypothesis, which can only be addressed by longitudinal studies.[56]

The HRT is a powerful optic disk imaging technique because it allows a three-dimensional reconstruction of the retinal surface and cupping and the acquisition of quantitative optic disk measurements, thus improving the follow-up of patients over time to monitor changes.[56–59] Over the last few years, attempts have been made to increase its diagnostic precision, and the results of this study show that the MRA provided in the HRT II as a means of distinguishing normal from glaucomatous eyes is diagnostically more accurate than the MDA analysis implemented in the HRT I. Moreover, these results are particularly relevant clinically, as they demonstrate the potential of an MRA examination to discriminate normal and POAG eyes in a sample that is completely different from that used to test the software.

The analysis of the slope of the "peripapillary nerve fiber layer surface" developed by Caprioli and colleagues,[26] which does not depend on a retinal reference plane, showed a sensitivity of 85% and a specificity of 80% in discriminating normal and glaucomatous eyes. The surface topography analysis developed by Swindale and colleagues,[28] which does not depend on the manual outlining of disk boundaries, had an overall classification accuracy of 89% in discriminating normal and glaucomatous eyes. The neural networks analysis developed by Bowd and colleagues,[60] which uses a series of global and regional HRT parameters, showed an extremely high degree of diagnostic accuracy in detecting glaucoma (the area under the receiver operating characteristic curve was approximately 0.96). Until the results of the former two studies (which suggest performing an optic disk analysis regardless of the reference plane) and of the latter one (which suggests the HRT analysis to be carried on by a trained neural network) are confirmed by larger cross-sectional or longitudinal investigations, HRT-MRA, despite the fair sensitivity

observed in the detection of early glaucomatous visual field defects, may add greater diagnostic ability than HRT-MDA to standard POAG diagnostics, given the higher specificity, which limits the number of false positive tests.

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