Imaging Technologies for the Diagnosis of Glaucoma

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Abstract
In this article we describe recent advances in imaging technologies that quantify the topography of the optic nerve head and retinal nerve fibre layer and their role in diagnosing glaucoma. These technologies include optical coherence tomography (OCT), scanning laser polarimetry (SLP, GDx) and confocal scanning laser ophthalmoscopy (CSLO, HRT). A review of recently published literature was carried out. The diagnostic performance of the different imaging devices is comparable and appears to be acceptable for the diagnosis of manifest glaucoma. The benefits of recent technological improvements need to be fully assessed. At the moment it is not clear which of the currently used imaging technologies is the most useful for diagnosis and management of glaucoma.

Keywords
Optical coherence tomography, scanning laser polarimetrey, confocal scanning laser ophthalmoscopy

Disclosure: The authors have no conflicts of interest to declare.
Received: 18 November 2009 **Accepted:** 21 December 2009 *DOI: 10.17925/EOR.2009.03.02.16*
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Glaucoma is a chronic neurodegenerative disease characterised by retinal ganglion cell death. The loss of retinal ganglion cells results in typical structural changes in the optic nerve head (ONH) and the retinal nerve fibre layer (RNFL) and in distinctive visual field (VF) defects. Glaucoma is a leading cause of blindness in Europe, with a prevalence of 1–2% of the adult population. Most patients with glaucoma are undiagnosed due to its asymptomatic course.[1]

Glaucoma diagnosis is based on the detection of the characteristic structural and/or functional changes and relies on the experience of the investigator. Most people diagnosed with glaucoma have corresponding structural and VF test abnormalities. However, in patients with early stages of the disease, the diagnosis may be challenging as they may show only VF or structural changes.

The detection of VF defects often occurs after there has been substantial structural damage.[2,3] Diagnosis of early glaucomatous optic nerve damage may be challenging even for experienced clinicians because of the wide variability of normal optic disc morphology. Sometimes the diagnosis of glaucoma in the absence of VF abnormalities is confirmed after monitoring patients and detecting structural changes in the optic nerve or RNFL.[4]

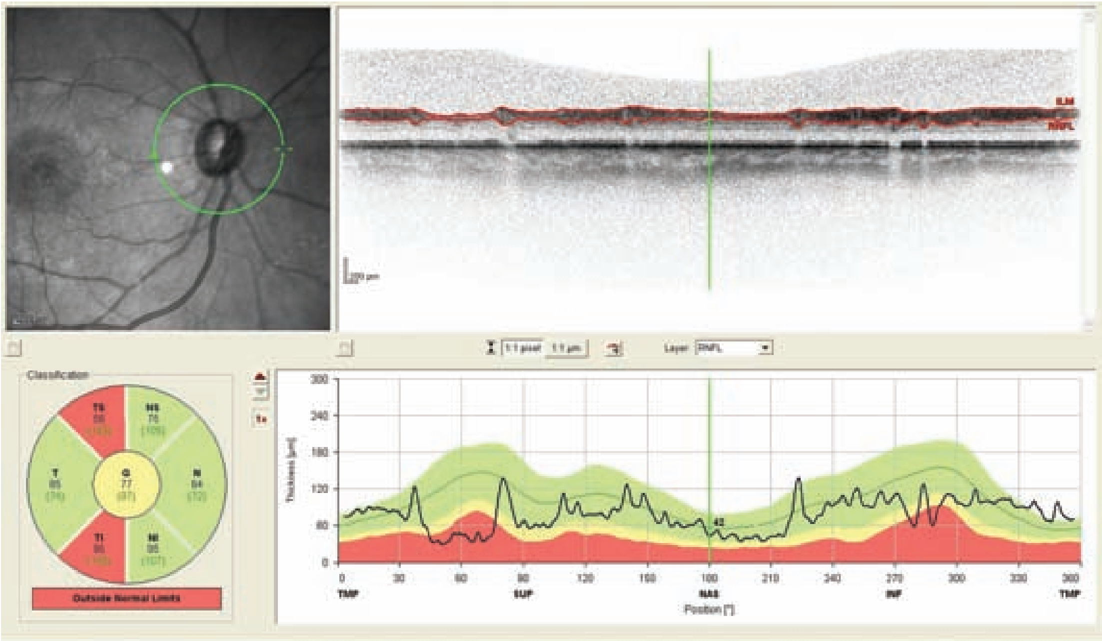
Until recently, the reference standard for recording ONH damage was stereophotography of the ONH and red-free pictures of the RNFL.[5,6] Recently introduced imaging devices are designed to facilitate the objective and quantitative assessment of the ONH and the RNFL: scanning laser polarimetry (SLP, i.e. GDx), confocal scanning laser ophthalmoscopy (CSLO, i.e. Heidelberg retinal tomography [HRT]) and optical coherence tomography (OCT) (see *Figure 1*). They can be used to detect early structural damage by focusing on glaucoma-relevant structures of the ONH and surrounding tissues and using a normative database to determine the probability of glaucoma. Imaging of the ONH and the RNFL for detecting glaucoma progression is another important aspect of glaucoma management. However, in this review we will focus only on the role of imaging technologies in the diagnosis of glaucoma. We will provide a brief description of the recent advances, and review the current literature on the diagnostic performance for glaucoma of these imaging devices.

Scanning Laser Polarimetry

SLP is designed to provide objective assessment of the RNFL thickness with potential use for diagnosis and follow-up. SLP is based on the principle that polarised light passing through the birefringence RNFL undergoes a detectable phase shift, which is linearly related to RNFL thickness.[7] The result is a 2D map of retardation around the optic disc. The software provides a discriminating classifier of glaucoma/normality named nerve fibre indicator (NFI), which is fully automated. To detect change over time, regression analysis can be performed.

The first GDx nerve fibre analyser contained a fixed compensating device to compensate for polarisation effects of cornea and lens. Because the parameters for corneal compensation are different for different eyes,[8] the current SLP systems (GDx Variable Cornea Compensator [VCC] and GDx Enhanced Corneal Compensator [ECC], Carl Zeiss Meditec, Inc., Dublin, CA) include a variable compensator that allows for individualised eye-specific compensation of anterior segment birefringence. The performance of SLP can be affected by

Figure 1: Print-out of a Spectral-domain Optical Coherence Tomograph



light scattering in the eye leading to a poor signal-to-noise ratio and atypical retardation patterns (ARPs).[9–11] The reason for ARPs is unknown, but as ARPs occur more in glaucomatous eyes than in normal eyes it has been hypothesised that it results from low signal-to-noise ratio when decreased reflectivity is present.[9] An analysis of the contribution of backscattered light from various depths to the total retardation map using spectral-domain OCT found that atypical retardation patterns in SLT are associated with deep penetration of the probing light beam into the strongly birefringent sclera.[12] To improve the accuracy, first the already-mentioned VCC,[13] then the software-based ECC[14] were introduced. It appears that GDx ECC performs better than VCC in the detection of glaucoma in early stages of disease.[11,15]

Confocal Scanning Laser Ophthalmoscopy

Confocal scanning laser ophthalmoscopy (CSLO) is an imaging tool that is designed to create a quantitative, 3D topographic picture of the ONH and the posterior segment surface. The currently used instrument, the HRT (Heidelberg Engineering GmbH, Dossenheim, Germany), uses a 670nm diode laser beam to scan the surface of the posterior segment. Based on the measurements of the ONH, the instrument generates a number of stereometric parameters, such as rim volume, rim area, cup shape or cup-to-disc ratio, that allow evaluation of the ONH for glaucomatous damage. The relevant ONH parameters are automatically generated by the instrument's software after identification of the optic disc border by the operator. It allows optic disc assessment to detect structural glaucomatous changes up to eight years earlier than visual field examination.[16]

The latest version of the CLSO, the HRT III, provides a large ethnic-selectable normative database and includes data analysis tools such as Moorfields regression analysis (MRA) and the Glaucoma Probability Score (GPS). Other technical improvements in the scaling and alignment of images have been made.

MRA is a linear regression that takes into account the relationship between optic disc size and rim area or cup-to-disc ratio. The MRA improves the diagnostic accuracy of the HRT by taking into consideration that neuroretinal rim area is affected by disc size and age.[17]

The GPS is an automated approach to the optic disc classifying procedure that eliminates operator-dependent factors, which are a source of variability. It is based on five glaucoma-specific parameters of the 3D shape of the optic disc and peri-papillary RNFL and provides disease probability values.[18]

The glaucomatous change can be assessed by topographic change analysis (TCA). TCA provides localised, objective and quantitative information about changes in the volume of the neuroretinal tissue. TCA describes significant repeatable changes in the neuroretinal rim volume by comparing the variability within a baseline examination with that between baseline examination and follow-up examination.[19]

Optical Coherence Tomography

OCT uses a scanning interferometer and a coherent infrared light (of 820–870nm) to obtain cross-sectional retinal images based on the reflectivity of the different retinal layers down to the retinal pigment epithelium.[20] OCT is a non-invasive, cross-sectional imaging technique that allows *in vivo* measurements of tissue thickness. The most commonly used time-domain OCT device (Stratus TD-OCT model 3000, Carl Zeiss Meditec, Inc. Dublin) has an axial resolution of approximately 10 microns and a transversal resolution of approximately 20 microns.

With the OCT the topography of the ONH can be assessed; however, the most important aspect of the OCT is the quantification of the RNFL thickness, which is measured using peri-papillary scanning around the optic disc. Because the RNFL is one of the layers with the greatest reflectance and because of its anterior location, it can be automatically segmented and measured by computer algorithms.

There are major recent developments of OCT, such as spectral-domain optical coherence tomography (SD-OCT), which permits

Table 1: Studies of Confocal Scanning Laser Ophthalmoscopy

Author	Imaging Device	Study Population	Reference Standard	QUADAS Item Y/N	Comments
Pablo, 2009[30]	HRT III	Early glaucoma vs normal	Stereoscopic photography	12/1	Ability of HRT to discriminate early glaucoma similar to assessment of stereophotographs
Saito, 2009[32]	HRT II	Early glaucoma vs normal	VF	10/3	Performance of GPS and MRA similar
Chauhan, 2009[54]	HRT III software	Longitudinal study of progressive glaucoma vs stable glaucoma	Monoscopic disc photographs	12/1	HRT performs at least as well as disc photographs to detect glaucoma progression (cave: monoscopic disc photographs)
Oddone, 2009[51]	HRT III	Different stages of glaucoma vs normal	VF	10/3	HRT parameters not good at early stages; sectorial analysis better than global analysis
Vizzeri, 2009[55]	HRT III	Longitudinal study of progressive glaucoma vs stable glaucoma	Stereoscopic photography	12/0 1 unclear	Agreement between progression identified by HRT and stereophotograph assessment was poor
Ferreras, 2007[33]	HRT III	Healthy vs glaucoma MRA vs GPS	Stereoscopic disc photography	11/2	GPS and MRA have similar diagnostic accuracy; both are influenced by optic disc size and severity of disease
Bowd, 2009[56]	HRT II	Patients enrolled in the Diagnostic innovations in Glaucoma Study	Progression in VF and/or stereoscopic disc photographs	9/1 3 unclear	TCA parameters can discriminate between progressing and stable eyes; low specificity in apparently non-progressing patients (?)
Ferreras, 2008[57]	HRT III	Healthy vs glaucoma	Stereoscopic photography and VF	12/1	Compared with HRT-provided parameters, the linear discrimination function (LDF) has higher diagnostic ability
Ohkubo, 2007[31]	HRT II	Healthy vs glaucoma; screening	Stereoscopic disc photography	8/4 1 unclear	HRT II outperforms non-mydriatic stereoscopic disc photograhy because of bad image quality in glaucomatous eyes
De Leon-Ortega, 2007[35]	HRT II vs HRT III	Healthy vs glaucoma; African vs European ancestry	Stereoscopic disc photography	9/3 1 unclear	MRA of HRT III showed highest diagnostic ability; GPS showed similar sensitivity but a considerably lower specificity than MRA
Moreno-Montanes, 2008[34]	HRT III	Healthy vs OHT and glaucoma	VF	7/2 4 unclear	Retrospective analysis of consecutive cases; GPS more sensitive but less specific than MRA; MRA and GPS agreement was low

GPS = glaucoma probability score; HRT = Heidelberg retina tomograph; MRA = Moorfields Regression Anaylsis; OHT = ocular hypertension; QUADAS = Quality Assessment of Diagnostic Accuracy Studies; TCA = topographic change analysis; VF = visual field.

much faster scanning and better axial resolution than TD-OCT. 3D OCT is also available and may be used to image the ONH. There are several SD-OCT devices commercially available, and it is likely that further developments will appear in the future.

It is unclear whether the new SD-OCT technology will improve the diagnostic performance with glaucoma. It seems that this may be the case as a more accurate measurement technique for assessment of the thickness of the retinal layers is provided. The capability of the new SD-OCT to detect localised RNFL defects, documented on stereophotographs, was investigated. All currently available SD-OCT instruments were able to confirm the structural glaucomatous damage.[21] It has been shown that RNFL thickness measurements obtained by SD-OCT correlated more strongly with localised visual field defects than scanning laser polarimetry.[22]

The relationship between RNFL thickness measured by time-domain (Stratus) and spectral-domain OCT (Cirrus HD; Carl Zeiss Meditec, Inc. Dublin) has been studied. A good correlation between the two instruments was found; however, when absolute values were compared, a significant difference in RNFL thickness was detected. Therefore, measurements are not interchangeable and cannot be compared directly. It was shown that RNFL measurements obtained by the Stratus OCT are generally higher than with the Cirrus OCT, except when the RNFL is very thin.[23–25]

Literature Review

We have reviewed the most recent studies on diagnostic accuracy of the above imaging technologies, and assessed the quality of the studies. For this purpose we conducted a comprehensive search of peer-reviewed literature in PubMed for the period January 2007 to June 2009. The search was limited to studies published in English-language journals. The following search terms were used: optical coherence tomography, scanning laser polarimetry, confocal scanning laser ophthalmoscopy and glaucoma. The search resulted in 326 citations. The abstracts of

Table 2: Studies of Scanning Laser Polarimetry

Author	Imaging Device	Study Population	Reference Standard	QUADAS Item Y/N	Comments
Toth, 2009[58]	GDx ECC	Healthy vs glaucoma	Visual field (progression)	12/1	Increased inter-visit standard deviation is an early sign of glaucoma progression
Sanchez-Cano, 2009[36]	GDx VCC	Healthy vs pre-perimetric glaucoma	Red-free digital RNFL photography	13/0	A new parameter calculated from the most significant sectors leads to better sensitivity in the diagnosis of pre-perimetric glaucoma
Medeiros, 2009[59]	GDx	Progressive vs stable glaucoma	Stereoscopic optic disc photography and/or visual fields	10/3	Eyes with progression in SAP or stereophotos had significantly higher rate of RNFL loss than stable eyes; even eyes that were not detected as progressing showed decline of RNFL thickness
Medeiros, 2007[15]	GDx ECC vs VCC	Healthy vs glaucoma	Stereoscopic optic disc photography and/or visual fields	9/3 1 unclear	GDx ECC performs better than VCC, especially at early stages of the disease
Baraibar, 2007[37]	GDx VCC	Healthy vs pre-perimetric glaucoma	Stereoscopic optic disc photography and red-free RNFL photography	13/0	Pre-perimetric glaucoma can be detected by GDx, and division into 12 RNFL sectors improves diagnostic reliablity
Sehi, 2007[11]	GDx VCC vs ECC	Healthy vs glaucoma	Perimetric glaucoma (VF and optic disc assessment)	6/4 2 unclear	SLP (ECC) reduces frequency and severity of atypical birefringence pattern (ABP) and improves correlation between RNFL measurements and visual function

ECC = enhanced corneal compensation; GDx = SLP = scanning laser polarimetry; RNFL = retinal nerve fibre layer; QUADAS = Quality Assessment of Diagnostic Accuracy Studies; SAP = standard automated perimetry; VCC = variable corneal compensation.

these articles were reviewed, and 35 studies comparing different imaging instruments or reporting diagnostic performance of each of the three instruments were found. Only prospective studies were included (see *Tables 1–3*).

The quality of the selected articles was assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool,[26,27] a quality assessment tool using 14 items (see *Table 4*). As the interpretation of the test results using imaging devices for glaucoma is fully automated, the QUADAS tool was modified slightly and item 12 was removed. Among the QUADAS items, some appear to be of critical importance, e.g. 'Was the spectrum of patients included in the study representative of the patients that will receive the test in clinical practice?' and 'Was an appropriate reference standard chosen?'[1,28]

Asking if a population is representative is important to understand how the imaging devices perform in 'real-life' conditions, when patients with some media opacity, other ocular co-morbidities or poor co-operation are examined. Refractive error, disc size, severity of glaucoma or operator-dependent factors can also influence the performance of the imaging instruments. Including a large proportion of patients with more severe disease is associated with increased sensitivity.[29]

Regarding the performance of HRT in diagnosing glaucoma, the data analysis tools MRA and GPS were assessed. The ability of HRT to discriminate between early glaucoma and normality was similar to the assessment of stereoscopic disc photographs by expert clinicians.[30] HRT could outperform stereophotography in one study, but the authors used non-mydriatic stereophotographs, which are not of optimum quality.[31] The diagnostic performance of MRA compared with GPS was judged to be similar in some studies,[32,33] while others reported a better performance of GPS[34] or MRA.[35]

Regarding SLP (GDx), two high-quality studies were detected (i.e. using an acceptable reference standard, including a spectrum of disease and patients that is similar to the patients in whom the instrument will be used in practice). In these two studies, SLP was able to detect pre-perimetric glaucoma[36,37] with reasonable accuracy. In other studies it was shown that ECC performed better than VCC.[11,15]

The performance of the different OCT instruments appears to be comparable.[38,39] The Stratus OCT has a rather poor performance in preperimetric glaucoma.[40,41] Differences in the RNFL configuration and thickness assessed by OCT were detected in eyes with OHT.[42,43]

Results of Studies Comparing Different Devices

The diagnostic performance of the different imaging devices is comparable and appears to be acceptable to diagnose glaucoma (see *Table 5*). However, there is very limited use in pre-perimetric glaucoma.[44,45] The performance of the GDx VCC in a glaucoma screening trial was reported. A combination of several GDx parameters appeared to be useful for detecting glaucoma in the population,[46] while the performance of HRT II was rated to be poor.

Frequency doubling technology (FDT) perimetry or stereoscopic disc examination by an experienced observer outperformed imaging devices in some studies.[47,48] However, when less experienced graders assess the optic disc, imaging devices provide higher diagnostic accuracy.[49]

Table 3: Studies of Optical Coherence Tomography

Author	Imaging Device	Study Population	Reference Standard	QUADAS Item Y/N	Comments
Leung, 2009[39]	Time vs spectral-domain OCT (Stratus vs Cirrus)	Glaucoma vs healthy	Visual fields	9/3 1 unclear	Diagnostic performance between the two OCT is comparable; poor agreement of measurements
Sehi, 2009[38]	Time vs Fourier-domain OCT	Glaucoma vs healthy	Visual fields	9/3 1 unclear	Comparable diagnostic performance
Zhong, 2009[41]	Stratus OCT	Pre-perimetric glaucoma vs healthy	Stereo colour photography	10/1 2 unclear	Sensitivity of Stratus OCT RNFL thickness parameters is low for detecting pre-perimetric glaucoma
Hougaard, 2007[60]	Stratus OCT	Glaucoma with mild VF defects vs healthy	Stereo and RNFL photography	10/2 1 unclear	OCT summary report parameters show only moderate diagnostic sensitivity, especially in patients with mild glaucoma; diagnostic potential of OCT not fully exploited
Anton, 2007[42]	Stratus OCT	Healthy vs patients with OHT and manifest glaucoma	Visual fields	9/3 1 unclear	RNFL and ONH parameters differentiate well between healthy and glaucomatous; significant differences between OHT and healthy eyes for some OHN parameters
Lee, 2009[61]	Stratus OCT	Glaucoma, progressing vs stable	Red-free RNFL photography	11/1 1 unclear	Stratus OCT detects progressive RNFL loss with high sensitivity and moderate specificity
Gyathso, 2008[43]	Stratus OCT	Healthy vs glaucoma and OHT	Red-free RNFL and colour stereoscopic photography	11/1 1 unclear	Only study that provides sample size calculation; Stratus OCT detects significant quantitative differences in RNFL thickness between all three groups
Nouri-Mahdavi, 2008[40]	Stratus OCT	Early disc or visual field changes vs normal	Stereoscopic photography and visual field	11/1 1 unclear	Interesting approach to define a reference standard; poor performance in patients with optic disc changes but normal fields (50%); better performance in more advanced disease
Hood, 2007[62]	Stratus OCT	Healthy vs glaucoma	Visual field (hemi-field test) and mVEP	7/4 2 unclear	OCT detects glaucoma confirmed with subjective and objective functional tests (cave: diagnostic performance assessed in advanced disease)

mVEP = multifocal visual evoked potential; OCT = optical coherence tomography; OHT = ocular hypertension; ONH = optic nerve head; QUADAS = Quality Assessment of Diagnostic Accuracy Studies; RNFL = retinal nerve fibre layer; VF = visual field.

Table 4: The QUADAS Assessment Tool

Item	Yes	No	Unclear
1. Was the spectrum of patients representative of the patients who will receive the test in practice?	( )	( )	( )
2. Were selection criteria clearly described?	( )	( )	( )
3. Is the reference standard likely to correctly classify the target condition?	( )	( )	( )
4. Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?	( )	( )	( )
5. Did the whole sample or a random selection of the sampe receive verification using a reference standard of diagnosis?	( )	( )	( )
6. Did patients receive the same reference standard regardless of the index test result?	( )	( )	( )
7. Was the reference standard independent of the index test (i.e. the index test did not form a part of the reference standard)?	( )	( )	( )
8. Was the execution of the index test described in sufficient detail to permit replication of the test?	( )	( )	( )
9. Was the execution of the reference standard described in sufficient detail to permit its replication?	( )	( )	( )
10. Were the index test results interpreted without knowledge of the results of the reference standard?	( )	( )	( )
11. Were the reference standard results interpreted without knowledge of the results of the index test?	( )	( )	( )
12. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?	( )	( )	( )
13. Were uninterpretable/intermediate test results reported?	( )	( )	( )
14. Were withdrawals from the study explained?	( )	( )	( )

QUADAS = Quality Assessment of Diagnostic Accuracy Studies.

Table 5: Studies Comparing Different Imaging Devices

Author	Imaging Device	Study Population	Reference Standard	QUADAS Item Y/N	Comments
Schrems, 2009[45]	Stratus OCT vs GDx VCC	Healthy, ocular hypertension, pre-perimetric glaucoma, perimetric glaucoma	Stereoscopic 15° colour photography	7/3 3 unclear	OCT and GDx comparable in the diagnosis of perimetric glaucoma; limited use in pre-perimetric glaucoma
Toth, 2009[46]	HRT II vs GDx VCC	Real-life glaucoma screening trial	Full glaucoma assessment (including VF and ONH evaluation)	12/1	Two reference standards during screening and final assessment; combination of several GDx criteria was useful for screening; poor performance of HRT
Windisch, 2009[48]	HRT, Stratus OCT, GDx VCC	Healthy vs glaucoma	Stereoscopic colour fundus photography	9/3 1 unclear	Red-free fundus photographs more appropriate to detect localised RNFL defects; 20–40% of localised RNFL defects were not detected by HRT, OCT or GDx
Vessani, 2009[49]	HRT III, GDx, Stratus OCT	Healthy vs glaucoma	Stereoscopic colour fundus photography	12/1	Diagnostic ability of imaging devices showed better performance than subjective assessment of the ONH by a general ophthalmologist but not by a glaucoma expert
Hong, 2007[47]	HRA I, GDx, Stratus OCT, FDT-Perimeter	Healthy vs glaucoma	Stereoscopic disc examination	10/3	FDT-Perimetry outperforms GDx, Stratus OCT RNFL photography using HRA
Sehi, 2007[11]	SLT (ECC) vs OCT	Healthy vs glaucoma	Dilated stereoscopic disc examination and VF	9/2 2 unclear	GDx ECC has stronger correlation than OCT
Pueyo, 2007[63]	SLT (VCC), Stratus OCT, HRT II	Healthy vs glaucoma	IOP, VF, stereoscopic optic disc photography	7/3 3 unclear	Best criteria discriminating healthy and glaucomatous eyes for each device were defined
Reus, 2007[44]	GDx VCC vs HRT I and stereophotography	Healthy vs glaucoma	Stereoscopic optic disc photography and visual fields	9/1 3 unclear	GDx VCC and HRT have a similar diagnostic accuracy
Naithani, 2007[64]	Stratus OCT vs HRT II	Healthy vs glaucoma (early or moderate VF defects)	Visual fields	7/3 3 unclear	OCT-based automated classifiers performed better than HRT classifiers; overall, performance is moderate: HRT 16.6% false-negatives (small discs) and 15% false-positives (larger discs)

ECC = enhanced corneal compensation; FDT = frequency doubling technology; GDx = SLP = scanning laser polarimetry; HRA = HRA = Heidelberg Retina Angiograph photography of RNFL; HRT = Heidelberg retina tomograph; IOP = intraocular pressure; OCT = optical coherence tomography; ONH = optic nerve head; QUADAS = Quality Assessment of Diagnostic Accuracy Studies; RNFL = retinal nerve fibre layer; SLT = scanning laser tomography; VCC = variable corneal compensation; VF = visual fields.

Among the most common limitations of the published literature, we would highlight that most studies compared eyes with already known and manifested glaucoma versus known healthy eyes. Four studies, two on OCT[40,41] and two on GDx,[36,37] investigated patients with pre-perimetric glaucoma. In only one study was the screening performance of an instrument (GDx) investigated.[46] For detecting pre-perimetric glaucoma, the performance of OCT was poor.[40,41] Both reports on GDx showed promise for detecting pre-perimetric glaucoma.[36,37] It has to be mentioned that several studies examined commercially unavailable detection algorithms that may have a higher diagnostic accuracy than the standard diagnostic tools.

Both GPS and MRA easily detected glaucoma in large discs but performed worse in smaller discs. In general it was shown that GPS is influenced to a greater extent by the disc size and is therefore outperformed by MRA.[50,51] It was suggested that GPS may be more useful to confirm a normal disc while MRA might be more helpful to confirm glaucoma suspects.[52] SLP (GDx VCC and ECC) has been shown to be influenced only minimally by optic disc size; however, repeatability of the measurements decreased with increasing severity of glaucoma.[53]

Conclusion

Recent advances in imaging devices for the assessment of optic disc morphology and RNFL thickness have the potential to greatly facilitate glaucoma diagnosis and monitoring of the disease. However, more high-quality studies on diagnostic accuracy are needed to define the role of imaging devices more precisely. At present is not clear which of the currently used imaging technologies is the most useful for diagnosis and management of glaucoma. ■

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1. Burr JM, Mowatt G, Hernandez R, et al., *Health Technol Assess*, 2007;11:iii–iv, ix–x, 1–190.
2. Sommer A, Katz J, QuigleyHA, *Arch Ophthalmol*, 1991;109:77–83.
3. Greaney MJ, Hoffmann DC, Garway-Heath DF, et al., *Invest Ophthalmol Vis Sci*, 2002;43:140–45.
4. Jonas JB, Müller-Berg JA, Schlötzer-Schreharth UM, Naumann GO, *Invest Ophthalmol Vis Sci*, 1990;31:736–44.
5. Sommer A, Pollak I, Maumanee AE, *Arch Ophthalmol*, 1979;97:1444–8.
6. Sommer A, Pollak I, Maumanee AE, *Arch Ophthalmol*, 1979;97:1449–54.
7. Weinreb RN, Dreher AW, Coleman A, et al., *Arch Ophthalmol*, 1990;108:557–60.
8. Greenfield DS, Knighton RW, Huang XR, *Am J Ophthalmol*, 2000;129:715–22.
9. Bagga H, Greenfield DS, Feuer WJ, *Am J Ophhtlamol*, 2005;139:437–46.
10. Sehi M, Ume S, Greenfield DS, *Invest Ophthalmol Vis Sci*, 2007;48:2099–2104.
11. Sehi M, Guaqueta DC, Feuer WJ, Greenfield DS, *Am J Ophthalmol*, 2007;143:272–9.
12. Götzinger E, Pircher M, Baumann B, et al., *Invest Ophthalmol Vis Sci*, 2008;49:5366–72.
13. Weinreb RN, Bowd C, Zangwill LM, *Arch Ophthalmol*, 2003;121:218–24.
14. Reus NJ, Zhou Q, Lemij HG, *Invest Ophthalmol Vis Sci*, 2006;47:3870–77.
15. Mederios FA, Bowd Ch, Zangwill LM, et al., *Invest Ophthalmol Vis Sci*, 2007;48:3146–53.
16. Zangwill LM, Weinreb RN, Beiser JA, et al., *Arch Opthalmol*, 2005;123:1188–97.
17. Miglior S, Guareschi M, Albe E, et al., *Am J Ophthalmol*, 2003;136:26–33.
18. Swindale NV, Stjepanovic G, Chin A, et al., *Invest Ophthalmol Vis Sci*, 2000;41:1730–42.
19. Chauhan BC, Blanchard JW, Hamilton DC, LeBlanc RP, *Invest Ophthalmol Vis Sci*, 2000;41;775–82.
20. Huang D, Swanson EA, Lin CP, et al., *Science*, 1991;254:1178–81.
21. Vizzeri G, Balasubramanian M, Bowd C, et al., *Opt Express*, 2009;17:4004–18.
22. Horn FK, Mardin CY, Laemmer R, et al., *Invest Ophthalmol Vis Sci*, 2009;50:1971–7.
23. Sung KR, Kim DY, Park SB, Kook MS, *Ophthalmology*, 2009;116:1264–70.
24. Knight OJ, Chang RT, Feuer WJ, Budenz DL, *Ophthalmology*, 2009;116:1271–7.
25. Vizzeri G, Weinreb RN, Gonzalez-Garcia AO, et al., *Br J Ophthalmol*, 2009;93:775–81.
26. Whiting PF, Rutjes AWS, Reitsma JB, et al., *BMC Med Res Methodol*, 2003;3:25.
27. Whiting PF, Westwood ME, Rutjes AWS, et al., *Med Res Methodol*, 2006;6:9.
28. Medeiros FA, Zangwill LM, Bowd C, et al. *Am J Ophthalmol*, 2005;139:1010–18.
29. Medeiros FA, Zangwill LM, Bowd CH, et al., *Invest Ophthalmol Vis Sci*, 2006;47:1008–15.
30. Pablo LE, Ferreras A, Fogagnolo P, et al., *Eye*, 2009;14 (Epub ahead of print).
31. Ohkubo S, Takeda H, Higashide T, et al., *J Glaucoma*, 2007;16:531–8.
32. Saito H, Tomidokoro A, Yanagisawa M, et al., *J Glaucoma*, 2009;18:227–32.
33. Ferreras A, Pajarin AB, Polo V, et al., *Ophthalmology*, 2007;114:1981–7.
34. Moreno-Monatnes J, Anton A, Garcia N, et al., *Am J Ophthalmol*, 2008;145:360–69.
35. De Leon-Ortega JE, Sakata LM, Monheit BE, et al., *Am J Ohthalmol*, 2007;144:525–32.
36. Sanchez-Cano A, Garaibar B, Pablo LE, Honrubia F, *Ophthalmologica*, 2009;223:256–62.
37. Baraibar B, Sanchez-Cano A, Pablo LE, Honrubia FM, *J Glaucoma*, 2007;16:659–64.
38. Sehi M, Grewal DS, Sheets CW, Greenfield DS, *Am J Ophthalmol*, 2009 (Epub ahead of print).
39. Leung CK, Cheung CY, Weinreb RN, et al., *Ophthalmology*, 2009;11:1257–63.
40. Nouri-Mahdavi K, Nikkhou K, Hoffmann DC, Law SK, Caprioli J, *J Glaucoma*, 2008;17:183–8.
41. Zhong Y, Shen X, Zhou X, Cheng Y, Min Y, *Clin Exp Ophahalmol*, 2009;37:262–9.
42. Anton A, Moreno-Montanes J, Blazquez F, et al., *J Glaucoma*, 2007;16:1–8.
43. Gyatsho J, Kaushik S, Gupta A, et al., *J Glaucoma*, 2008;17:122–7.
44. Reus NJ, De Graaf M, Lemij H, *Invest Ophthalmol Vis Sci*, 2007;48:1651–8.
45. Schrems WA, Mardin ChY, Horn FK, et al., *J Glaucoma*, 2009 (Epub ahead of print).
46. Toth M, Kothy P, Hollo G, *J Glaucoma*, 2008;17:639–46.
47. Hong S, Ahn H, Joo S, et al., *Ophthalmology*, 2007;114:210–15.
48. Windisch BK, Harasymowycz PJ, See JL, et al., *J Glaucoma*, 2009;93:225–300.
49. Vessani RM, Moritz R, Batsi L, et al., *J Glaucoma*, 2009;18:253–61.
50. Oddone F, Centofanti M, Rossetti l, et al., *Ophthalmology*, 2008;115:1358–65.
51. Oddone F, Centofanti M, Iester M, et al., *Ophthalmology*, 2009;116:1106–11.
52. Zangwill LM, Jain S, Racette L, et al., *Invest Ophthalmol Vis Sci*, 2007;48:2653–60.
53. Garas A, Toth M, Vargha P , Hollo G, *J Glaucoma*, 2009; in press.
54. Chauhan BC, Jain S, Racette L, et al., *Invest Ophthalmol Vis Sci*, 2007;48:2653–60.
55. Vizzeri G, Weinreb RN, Martinez de la Casa JM, et al., *Ophthalmol*, 2009;116:14–24.
56. Bowd CH, Balasubramanian M, Weinreb RN, et al., *Invest Ophthalmol Vis Sci*, 2009;50:691–701.
57. Ferreras A, Pablo LE, Larrosa JM, et al., *Ophthalmology*, 2008;115:775–81.
58. Toth M, Hollo G, *J Glaucoma*, 2008;17:571–7.
59. Medeiros FA, Alencar LM, Zangwill L, et al., *Invest Ophthalmol Vis Sci*, 2009;50:1675–81.
60. Hougaard JL, Heijl A, Bengtsson B, *J Glaucoma*, 2007;16:302–6.
61. Lee EJ, Kim TW, park KH, et al., *Invest Ophthalmol Vis Sci*, 2009;50:662–8.
62. Hood DC, Harizman N, Kanadani FN, et al., *Br J Ophthalmol*, 2007;91:905–7.
63. Pueyo V, Polo C, Larrosa JM, et al., *J Glaucoma*, 2007;16:173–7.
64. Naithani P, Sihota R, Sony P, et al., *Invest Ophthalmol Vis Sci*, 2007;48;3138–45.