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Emerging Technology: Optic Disc Imaging - Disease Monitoring

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Introduction
In addition to stereophotography, there are three quantitative imaging devices currently in widespread use for glaucoma management. These are confocal scanning laser tomography (Heidelberg retina tomograph [HRT]; Heidelberg Engineering, Heidelberg, Germany), scanning laser polarimetry with 'variable' corneal compensation (GDxVCC; Carl Zeiss Meditec Inc., Dublin, CA) and optical coherence tomography (StratusOCT; Carl Zeiss Meditec Inc., Dublin, CA). The performance of these devices for diagnosis [1] and identifying progression [2] has recently been reviewed. Some of the literature cited relates to older versions of these technologies, such as the GDx NFA (with 'fixed' corneal compensation) and OCT2 (which has reduced sampling in the axial direction compared with StratusOCT).

Current guidance
The AAO PPP [3] recommends the documentation of the Optic Nerve Head (ONH) and Retinal Nerve Fibre Layer (RNFL) appearance by imaging, photography, or drawing. The frequency of examination is advised as: 6 – 18 months for stable patients (depending on duration of control) and 2 to 12 months for patients with poorly-controlled IOP or signs of progression, and 6 – 24 months for glaucoma suspects (depending on risk level) and 3 – 12 months for high risk glaucoma suspects with poorly-controlled IOP.

The Royal College of Ophthalmologists' guidelines [4] recommend, at baseline, an ONH drawing "which may be usefully supplemented by disc photography +/or digital computerised scanning of the disc/nerve fibre layer". The frequency of monitoring depends on the level of IOP control achieved, the age of the patient and the severity of the disease. Progression may be confirmed by comparison of current status with baseline appearance.

The European Glaucoma Society guidelines [5] state that "imaging is likely to play a role in the future for longitudinal follow-up."

Recent evidence
In recent years, the evidence to support the application of imaging technologies for monitoring glaucoma has been building. However, there are barriers to the successful demonstration of the role of quantitative imaging in glaucoma progression detection. These include the lack of an external 'gold standard' for progression with which to compare the imaging devices [6,7,8] and the rapid progress in technology, which changes faster than typical glaucoma progresses.[6]

Recent evidence demonstrates that imaging and visual function tests for glaucomatous progression agree poorly [6,7,8] and challenges the prevailing view that imaging tools are more useful early in the course of the disease and visual function tests later in the course.[7,8]

Imaging techniques to monitor for progression

ONH photography

Photography has some advantages over quantitative imaging devices. For instance, features related to glaucoma progression, such as increasing peripapillary atrophy and disc haemorrhages, are evident in photographs, but are not readily apparent in other images.

The assessment of progression from photographs is subjective, although in trained hands sensitivity and agreement is fair. Repeat gradings from stereophotography have been evaluated for agreement and for the sensitivity and specificity of progression determination (with the Ocular Hypertension Treatment Study Endpoint committee as the reference standard). Agreement (kappa) ranged from 0.65 to 0.83, specificity from 98% to 100% and sensitivity from 64% to 81%.[9] Agreement between observers is better with stereoscopic than with monoscopic photography.[10]

The greatest barrier to the routine use of ONH photographs is the lack of appropriate viewing systems, although new technology is available that permits the viewing of stereoscopic photographs in 3-dimensions on the computer screen.[11]

Most studies report the performance of expert observers (and usually a consensus of experts) in identifying progression from ONH photographs. There are no reports of the ability of non-expert observers to identify progression.

Heidelberg Retina Tomograph (HRT)

An analysis technique, identifying change at the level of groups of pixels in the HRT images, has been developed.[12] This technique, Topographic Change Analysis (TCA), was tested in a longitudinal data set of 84 patients and 41 normal subjects, and followed for a median of 7.5 years. The criteria for change were adjusted to achieve similar progression rates with the HRT and visual field analyses.[7] When the specificity for HRT and visual field was approximately at 86 - 90% and 81 - 90%, respectively, 42% of the eyes with glaucoma were found to be progressing by each of HRT and visual field. However, the agreement for progression between the two was poor. This suggests approximately equal sensitivity of the HRT and visual field to detect progression in established glaucoma. Similar results have been reported for ocular hypertension.[8] 198 patients with ocular hypertension and 21 normal subjects were followed for a median of 6.0 and 5.3 years, respectively. When progression criteria for the HRT and visual field were matched to give about 90% specificity, the progression rates were similar, with 33% and 32% progressing by HRT and visual field criteria, respectively. Agreement, however, was poor, with only 12% of subjects progressing by HRT and visual field criteria. These findings suggest that both imaging and perimetry are required if progression is not to be missed in patients with ocular hypertension or early manifest glaucoma. However, studies have yet to identify the implication of identified structural progression for subsequent visual function.

GDx

Few data are available for this technology as a result of several changes in hardware and analysis software. However, polarimetry is likely to be able to detect progression because measurements discriminate well between normal and glaucomatous eyes,[13] predict glaucomatous visual loss in at-risk eyes,[14] and are highly reproducible.[15] In one study, limits of change were derived from a test retest study.[16] 17 eyes with a disc

hemorrhage were followed for an average of 30.7 months and 5 (29%) exhibited change in GDx NFA parameters greater than the limits for change. Progressive RNFL thickness change has also been documented following anterior ischaemic optic neuropathy[17] and traumatic optic neuropathy.[18]

Ocular Coherence Tomography (OCT)

Longitudinal data are scarce because technology development has resulted in hardware changes. However, OCT imaging is likely to be able to detect progression because OCT RNFL thickness measurements discriminate well between normal and glaucomatous eyes[19] and are highly reproducible.[20] There is one report of a longitudinal study in glaucomatous and glaucoma suspect subjects.[21] 64 eyes of 37 subjects were imaged over a median 4.7 years. OCT progression was defined as change from baseline greater than twice the device reproducibility error in 2 of 3 consecutive follow-up scans. VF progression was defined as a reduction in mean deviation of 2 dB from baseline in 2 of 3 consecutive visits. 22% of eyes progressed by OCT alone, 9% by VF alone and 3% by OCT and VF. The relative sensitivity of the OCT and visual fields to detect progression cannot be assessed directly in the absence of data regarding the specificity of the criteria applied.

The finding is similar to the reports of HRT progression, with relatively poor agreement between imaging and visual function measures of progression. There are various possible explanations to account for this. The most likely is that measurement 'noise' has masked some of the change, so that progression may be missed by either or both imaging and visual field testing. Alternatively, retinal ganglion cell dysfunction may result in visual function change, but without change in images. And change in images may represent alteration to non-neuronal structures, such as the lamina cribrosa. However, a tentative conclusion is that imaging and visual field testing should be performed in the follow-up of glaucoma patients and suspects.

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