

CLINICAL SCIENCE

Agreement between frequency doubling perimetry and static perimetry in eyes with high tension glaucoma and normal tension glaucoma

S Kogure, Y Toda, D Crabb, K Kashiwagi, F W Fitzke, S Tsukahara

Br J Ophthalmol 2003;**87**:604–608

Aims: To investigate the agreement in results between frequency doubling technology (FDT) and the conventional automated static perimeter in eyes with normal tension glaucoma (NTG) and high tension glaucoma (HTG).

Methods: 72 eyes of 36 patients, who had two or more experiences with the Humphrey field analyser (HFA) program C30-2, were examined with the screening C-20-1 program of FDT. The result of FDT at each of the 17 stimulus points was graded as one of four categories. 58 out of 76 test points of HFA were assigned to one of the 17 clusters corresponding to FDT test points. Each cluster was represented as the lowest (scotoma of HFA) or the highest (threshold of HFA) probability symbol of total deviation (TD) of the HFA test points included in the cluster. The agreement between scotoma/threshold of HFA and FDT results was evaluated for NTG and HTG.

Results: In a total of 65 eyes, the Spearman coefficients between the FDT and HFA (threshold/scotoma of HFA) were 0.599 and 0.515 ($p < 0.0001$), respectively. In the HFA mean deviation matched 20 HTG eyes and 20 NTG eyes, the number of points with abnormal FDT results were 102 and 62 in eyes with HTG and NTG, respectively. The eyes with HTG had more abnormal FDT results than NTG eyes ($p = 0.0014$, Mann-Whitney U test). The kappa coefficient between FDT and threshold of HFA in eyes with HTG and NTG was 0.288 and 0.520, respectively, and the agreement between FDT and scotoma of HFA was 0.480 and 0.439, respectively.

Conclusions: The best agreement of the results of FDT and HFA was observed in eyes with NTG using threshold of HFA. The eyes with HTG showed lower agreement with more abnormal points in FDT results, which suggests enough sensitivity of FDT in eyes with NTG, and higher sensitivity of FDT in eyes with HTG.

See end of article for authors' affiliations

Correspondence to:
Satoshi Kogure, MD,
Department of
Ophthalmology,
Yamanashi Medical
University, Tamaho,
Yamanashi 409-38, Japan;
skogure@
res.yamanashi-med.ac.jp

Accepted for publication
17 July 2002

The retinal ganglion cells of different sizes have distinct physiological functions. Small cells that project to the parvocellular layers of the lateral geniculate body belong to the "P-cell pathway" which conveys information on colour, high spatial frequency, and pattern discrimination, while large cells that project to the magnocellular layer belong to the "M-cell pathway" dealing with motion detection, low spatial frequency, and high temporal frequency.¹ Large optic nerve fibres (M-cell) are selectively lost in chronic experimental and human glaucoma.²⁻⁴ Therefore, tests operating on the M-cell pathway—that is, flicker perimetry and motion detection test, were thought to have advantages in the detection of early glaucoma.^{5,6}

Furthermore, there are two subtypes of M-cell. One is the Mx-cell, which has linear characteristic summation in receptive fields and another is the My-cell, that has a non-linear character. Testing of the My pathway appears to be a strong candidate for an effective screening procedure for glaucoma, because My-cells have a larger nerve fibre diameter and fewer redundancies than Mx-cells.⁷ The My-cell represents only 3%–5% of the total number of ganglion cells, indicating that the loss of even a single cell will lead to a distinct scotoma in the lattice of My-cell receptive fields.⁷

When a low spatial frequency sinusoidal grating undergoes high temporal frequency counterphase flicker, its perceived spatial frequency is twice its actual spatial frequency.⁸ This phenomenon, called frequency doubling illusion, is a result of the non-linearity of the My pathway in response to contrast.⁹

The frequency doubling technology (FDT) is a new perimeter that has a frequency doubling illusion stimulus with large sinusoidal grating.¹⁰⁻¹² Its efficacy for glaucoma

screening and early glaucoma detection has been reported.^{5,13-19}

It is surprising that FDT detects early or localised visual field defects in glaucomatous eyes, in spite of a large stimulus size (10×10 degrees). The question now arises: which is relevant to visual field defects in FDT, depth of scotoma or surviving highest sensitivity on conventional perimetry in that area (10×10 degrees)? It is expected that FDT will miss localised scotoma because of a response from an adjacent area. There is a further question which needs to be asked. Does the FDT work with the same effectiveness in eyes with normal tension glaucoma (NTG) and high tension glaucoma (HTG)? In this study, we investigated the agreement of results between FDT and conventional automated static perimeter in eyes with NTG and HTG.

PATIENTS AND METHODS

Patients

At the glaucoma clinic of the Yamanashi Medical University Hospital, consecutive patients with glaucoma and suspected glaucoma were enrolled in this study from February 1999 to May 1999.

The inclusion criteria are as follows.

- (1) Patients who had two or more experiences with the Humphrey field analyser (HFA) program C-30-2
- (2) The last result of HFA has a lower frequency of false positive error and false negative error of 33%.

The exclusion criteria are as follows.

- (1) Eyes with cataracts or other ocular disease except glaucoma

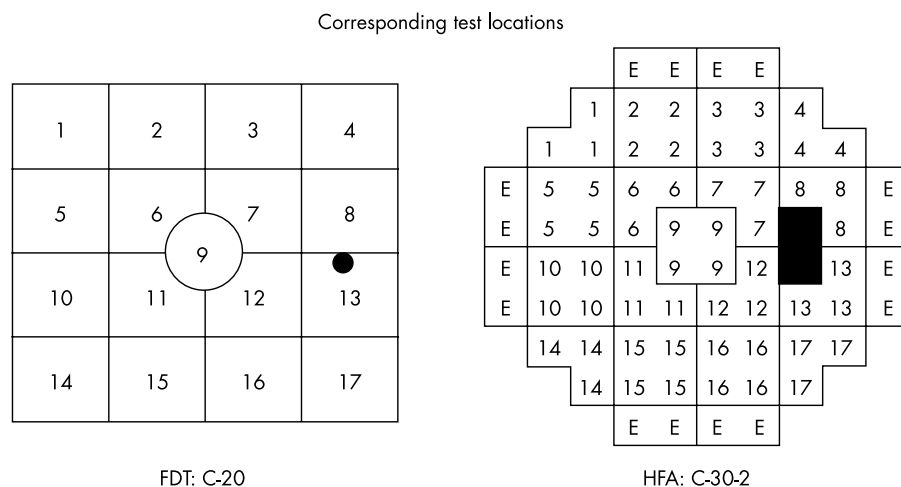


Figure 1 Test locations of Humphrey field analyser (HFA) program 30-2 and frequency doubling technology (FDT). The same location numbers (from 1 to 17) of FDT (left) and HFA (right) were compared.

- (2) Small pupil, 2.0 mm or less in a diameter
 (3) The result of FDT has false positive error of 33% or more.

Eyes with small pupils were excluded because the influence of a small pupil on FDT is significant.¹² The false positive results of FDT were not included because the false positive results of HFA were not included. The false negative result of FDT was not obtained with the current version of FDT.

Device

The frequency doubling perimetry (Frequency Doubling Technology; FDT, Welch Allyn Co, USA) screening program C-20-1 was performed for all subjects after a demonstration. Eyes with refraction of -7 dioptres or less were tested with their own glasses in accordance with the recommendations in the manufacturer's manual.

Methods of comparison

The program C-20-1 of FDT gives values with four grades at each of 17 test points for an eye. The criteria for these four grades (normal, mild loss, moderate loss, severe loss) are as follows.

- (1) *Normal*: sensitivity is equal to or better than the 1% probability level for normal in their age group
- (2) *Mild loss*: the 1% probability level stimulus was missed twice, but a higher contrast level target (0.5% probability level) was seen
- (3) *Moderate loss*: the 0.5% probability level target was not seen, but a maximum (100%) contrast target was seen
- (4) *Severe loss*: none of the target was seen.

Fifty eight of the 76 stimulus locations of the HFA central 30-2 program were divided into 17 clusters to correspond to the FDT. The stimulus points of FDT and the cluster of HFA are shown in Figure 1.

The total deviation (TD) of the HFA gives one of five grades of probability symbols (0.5%, 1%, 2%, 5%, and normal). We define the highest probability symbol of TD within a cluster and the lowest probability symbol of TD within the cluster as the "threshold of HFA" and "scotoma of HFA," respectively. The threshold of HFA means highest sensitivity surviving within the area of the cluster. The scotoma of HFA shows the extent of visual field damage. We show an example in Figure 2, in which the threshold and scotoma of HFA agree with the results of FDT. If the results of FDT agree with the threshold of HFA more than with the scotoma of HFA, it will be supposed that FDT will miss the steep scotoma.

If the pathogenic differences of glaucoma induce a difference in the agreement between the HFA and the FDT, the eyes with HTG and NTG were compared. To compare the

results from NTG and HTG patients with the same severity of glaucomatous field defects, the mean deviation of HFA had been matched for comparison.

The HTG consists of primary open angle glaucoma and ocular hypertension. The eye with ocular hypertension might have glaucoma damage which was not detected using HFA. To compare the early glaucoma damage, the normal tension glaucoma suspected eyes were included in NTG. The NTG suspected eye had a glaucomatous cupping of the optic disc with 0.8 or more cup to disc ratio, or nerve fibre layer defect with normal HFA.

The kappa was calculated for statistical analysis of agreement between categorical assessments. It has a range from 0 to 1, with 1 indicating perfect agreement. The values below 0.2 are considered to reflect "poor" agreement, while values above 0.6 indicate "substantial" agreement. The FDT results have four categories, while HFA results have five categories of probability level. To calculate the kappa, these categories were reduced to two categories. One was 1% probability level or less and the other was over 1% probability level.

RESULTS

Seventy two eyes of 36 patients out of 144 consecutive patients were randomly selected following inclusion and exclusion criteria. Seven of 72 eyes had a false positive error on FDT and were therefore excluded according exclusion criteria.

The mean age of the subjects was 63.7 (SD 11.8) years (range 31–79 years old). The visual acuity of the subjects ranged from 20/200 to 30/20. The mean deviation (MD) of HFA was -8.75 (8.93) dB (range -29.78 to 2.69 dB). The test time for the C-20-1 screening program was 80.3 (35.8) seconds (range 38–144 seconds).

In a total of 65 eyes, the Spearman coefficients between the FDT results and HFA results (threshold of HFA or scotoma of

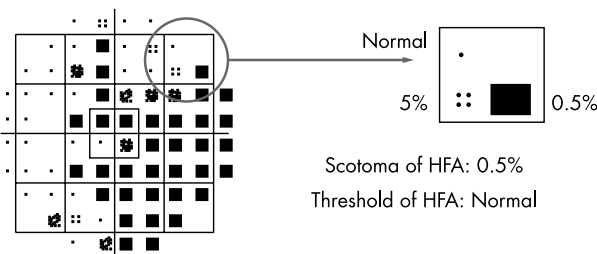


Figure 2 An example of evaluating a cluster of HFA. Threshold of HFA means the highest probability level of the total deviation in each cluster. Scotoma of HFA means the lowest probability level of the total deviation in each cluster. The threshold of HFA and scotoma of HFA of this figure are normal and 0.5%, respectively.

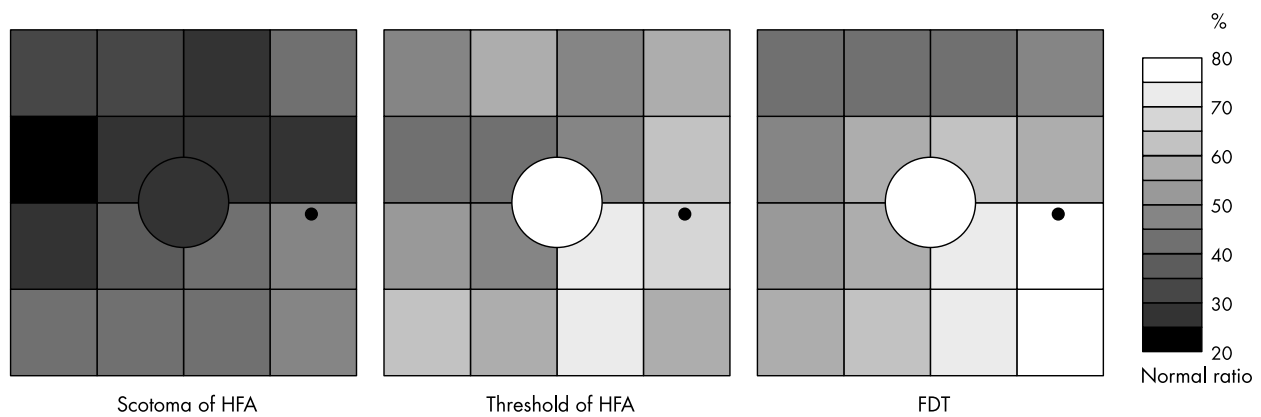


Figure 3 Normal ratio of each test location in HFA and FDT. In 65 eyes, the ratio of normal, 1% or higher probability level, was shown by a grey scale on each test location for FDT (right), threshold of HFA (centre), and scotoma of HFA (left).

Table 1 Agreement of results between frequency doubling technology (FDT) and Humphrey field analyser (HFA) with highest probability (threshold of HFA)

	HFA C30-2, highest probability (threshold of HFA)					
	High tension glaucoma (HTG)			Normal tension glaucoma (NTG)		
	Normal	Abnormal (p<1%)	Total	Normal	Abnormal (p<1%)	Total
FDT screening C-20-1						
Normal	225	13	238	268	10	278
Mild to severe loss	72	30	102	32	30	62
Total	297	43	340	300	40	340

Table 2 Agreement of results between frequency doubling technology (FDT) and Humphrey field analyser (HFA) with lowest probability (scotoma of HFA)

	HFA C30-2, lowest probability (scotoma of HFA)					
	High tension glaucoma (HTG)			Normal tension glaucoma (NTG)		
	Normal	Abnormal (p<1%)	Total	Normal	Abnormal (p<1%)	Total
FDT screening C-20-1						
Normal	201	37	238	227	51	278
Mild to severe loss	42	60	102	14	48	62
Total	243	97	340	241	99	340

HFA) were 0.599 ($p<0.0001$) and 0.515 ($p<0.0001$), respectively. The abnormal rates (probability level 1% or less) are shown in Figure 3 for FDT, threshold of HFA, and scotoma of HFA. The proportions of abnormal points were similar to one another. The distribution of abnormal points of FDT was, however, less in the central area (Fig 3).

The total of 65 eyes consisted of 21 NTG eyes and 44 HTG eyes. To compare the results from NTG and HTG patients with the same severity of glaucomatous field defects, the mean deviation of HFA had been matched between the HTG eyes and the NTG eyes. All 65 eyes were listed in order of MD of HFA. The pairing of NTG and HTG was selected with a difference within 1 dB of MD. Twenty out of 21 eyes with NTG were selected as pairs. The MD of the NTG group and of the HTG group was -4.63 (6.47) dB and -4.64 (6.69) dB, respectively. While the number of abnormal clusters with HFA results was almost even between NTG and HTG, the number of abnormal

points with FDT results was 102 and 62 in eyes with HTG and NTG, respectively (Tables 1 and 2).

Using the results of five graded probability levels of HFA or four graded probability levels of FDT, the eyes with HTG had significantly worse results on FDT ($p=0.0014$, Mann-Whitney U test) than those of NTG, while the difference of the results between the HTG eyes and NTG eyes was not significant on HFA ($p=0.6958$, Mann-Whitney U test).

The proportion of FDT results in the HFA cluster is shown in Figures 4 and 5. Between NTG eyes and HTG eyes, the numbers of abnormal HFA clusters were almost same. The number of abnormal FDT points, however, were more frequent in eyes with HTG, especially in a corresponding normal HFA cluster.

The agreement between the FDT results and the HFA results represented by threshold of HFA or scotoma of HFA was better in NTG patients than in HTG patients (Tables 1 and 2). The

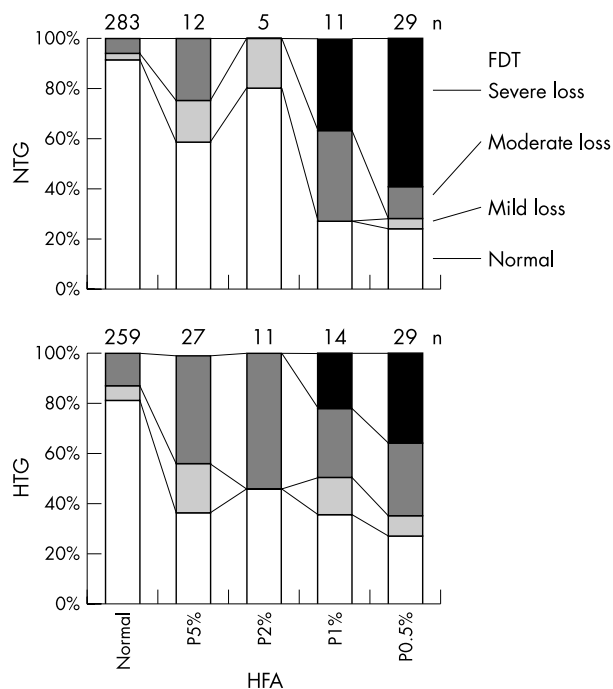


Figure 4 Ratio of FDT results for each probability level of HFA (threshold of HFA) in NTG eyes (top) and HTG eyes (bottom). While the proportion of abnormal clusters in HFA are similar between NTG eyes and HTG eyes, HTG eyes have twice as many abnormal FDT points in normal HFA clusters. (n = number of HFA clusters).

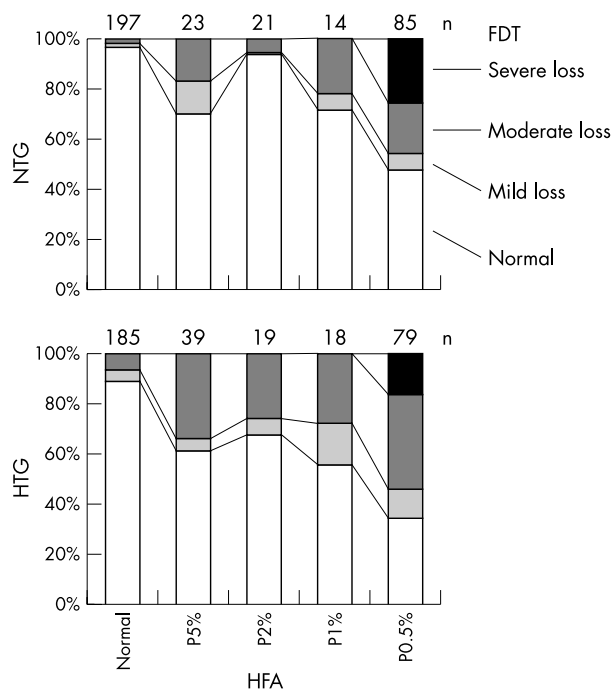


Figure 5 Ratio of FDT results for each probability level of HFA (scotoma of HFA) in NTG eyes (top) and HTG eyes (bottom). While the proportion of abnormal clusters in HFA are similar between NTG eyes and HTG eyes, HTG eyes have twice as many abnormal FDT points in normal HFA clusters. (n = number of HFA clusters).

kappa coefficient between FDT results and threshold of HFA in eyes with HTG and NTG was 0.288 and 0.520, respectively, and that between FDT results and scotoma of HFA was 0.480 and 0.439, respectively. The best agreement between FDT and HFA was between FDT and threshold of HFA (which means surviving light sensitivity) of NTG eyes.

DISCUSSION

In this study, we confirmed moderate agreement between the results of the new perimeter FDT and the results of conventional automated static perimetry, HFA. The results of FDT correlated well with the results of HFA.

In the comparison between MD matched HTG and NTG, the eyes with HTG showed more abnormal FDT points than those with NTG. Particularly, in the comparison with scotoma of HFA, 20% of normal HFA clusters in the HTG group showed abnormal FDT results. On the other hand, the normal HFA cluster of the NTG group had only 5% abnormal results on FDT. This suggests two possible reasons: (1) FDT was more sensitive than HFA in eyes with HTG, and (2) FDT could not detect the scotoma in eyes with NTG.

The kappa coefficient, which means the agreement between the HFA and the FDT, showed the best agreement with threshold of HFA in NTG eyes. This means that the threshold in FDT agreed with the highest threshold in the cluster of the HFA.

Hence, we can imagine that in the area of single cluster, which has both an intact area and scotoma, the intact area is aware of the sinusoidal grating of the FDT although there was a scotoma in the same cluster. Especially, FDT has very large square stimulus spots with adjoining spots. It is useful to detect the remaining sensitivity but not so useful for detecting scotoma. It was expected that FDT would not detect the localised scotoma before this study.

It has been reported that patients with NTG showed localised scotoma while those with POAG showed diffuse field defects.¹⁹⁻²⁵ If a localised scotoma could not be detected with FDT, it was expected that the HTG had better agreement in two perimeters than that of the NTG. However, the HTG had a lower agreement because of the disagreement in the normal HFA cluster. The FDT detected more abnormal points in the HTG group. This suggests that the FDT has enough sensitivity for NTG eyes, and is more sensitive to POAG or ocular hypertension and can detect early change.

The reason for the higher sensitivity in HTG with FDT is suggested by the next two assumptions; one was that HTG eyes had more severe disturbance of the My-cell pathway than NTG eyes; the other that FDT was more sensitive than HFA but could not detect the scotoma of NTG. As a result, NTG eyes had good agreement between FDT and HFA. We suggest that the reason for the lower sensitivity in NTG and for the lower number of abnormal results in the central visual field is that the square stimulus target is too large. Johnson reports higher sensitivity with smaller stimuli with his own frequency doubling perimeter.²⁶ Even though the FDT has enough sensitivity and specificity, we expect a higher sensitivity by FDT with smaller stimulus size.

After our first report about this study in September 1999 in Japan, many investigators have duplicated results that show POAG has more visual field defects in FDT than NTG.²⁷⁻²⁹ These reports support our results. Further study, however, is required to prove these mechanisms.

In conclusion, the FDT correlates with the conventional static autoperimeter, and has a higher sensitivity to HTG.

ACKNOWLEDGEMENTS

Presented at the 42nd Annual Meeting of ARVO, Fort Lauderdale, FL, USA 30 April 2000.

Proprietary interests: none.

Authors' affiliations

S Kogure, Y Toda, K Kashiwagi, S Tsukahara, Department of Ophthalmology, Yamanashi Medical University, Japan
D Crabb, Department of Mathematics, Nottingham Trent University, UK
F W Fitzke, Institute of Ophthalmology, University College London, UK

REFERENCES

- 1 **Sekuler R**, Blake R. *Perception* 3rd ed. Singapore: McGraw-Hill, 1994:102–79.
- 2 **Glovinsky Y**, Quigley HA, Dunkelberger GR. Retinal ganglion cell loss is size dependent in experimental glaucoma. *Invest Ophthalmol Vis Sci* 1991;**32**:484–91.
- 3 **Chaturvedi N**, Hedley-Whyte ET, Dreyer EB. Lateral geniculate nucleus in glaucoma. *Am J Ophthalmol* 1993;**116**:182–8.
- 4 **Dandona L**, Hendrichson A, Quigley HA. Selective effects of experimental glaucoma on axonal transport by retinal geniculate nucleus. *Invest Ophthalmol Vis Sci* 1991;**32**:1593–9.
- 5 **Johnson CA**. Early losses of visual function in glaucoma. *Optom Vis Sci* 1995;**72**:359–70.
- 6 **Anderson RS**, O'Brien C. Psychophysical evidence for a selective loss of M ganglion cells in glaucoma. *Vis Res* 1997;**37**:1079–83.
- 7 **Maddess T**, Henry GH. Performance of nonlinear visual units in ocular hypertension and glaucoma. *Clin. Vis Sci* 1992;**7**:371–83.
- 8 **Kelly DH**. Frequency doubling in visual responses. *J Opt Soc Am A* 1966;**56**:1628–33.
- 9 **Kelly DH**. Nonlinear visual responses to flickering sinusoidal gratings. *J Opt Soc Am A* 1981;**71**:1051–5.
- 10 **Johnson CA**, Samuels SJ. Screening for glaucomatous visual field loss with frequency-doubling perimetry. *Invest Ophthalmol Vis Sci* 1997;**38**:413–25.
- 11 **Sponsel WE**, Trigo Y, Hendricks J, et al. Frequency doubling perimetry (letter). *Am J Ophthalmol* 1998;**126**:155–6.
- 12 **Kogure S**, Membrey W, Fitzke F, et al. Effect of decreased retinal illumination on frequency doubling test. *Jpn J Ophthalmol* 2000;**44**:489–93.
- 13 **Kondo Y**, Yamamoto T, Sato Y, et al. A frequency-doubling perimetric study in normal-tension glaucoma with hemifield defect. *J Glaucoma* 1998;**7**:261–5.
- 14 **Quigley HA**. Identification of glaucoma-related visual field abnormality with the screening protocol of frequency doubling technology. *Am J Ophthalmol* 1998;**125**:819–29.
- 15 **Sponsel WE**, Arango S, Trigo Y, et al. Clinical classification of glaucomatous visual field loss by frequency doubling perimetry. *Am J Ophthalmol* 1998;**125**:830–6.
- 16 **Alward WL**. Frequency doubling technology perimetry for the detection of glaucomatous visual field loss [editorial]. *Am J Ophthalmol* 2000;**129**:376–8.
- 17 **Cello KE**, Nelson QJ, Johnson CA. Frequency doubling technology perimetry for detection of glaucomatous visual field loss. *Am J Ophthalmol* 2000;**129**:314–22.
- 18 **Patel SC**, Friedman DS, Varadkar P, et al. Algorithm for interpreting the results of frequency doubling perimetry. *Am J Ophthalmol* 2000;**129**:323–7.
- 19 **Caprioli J**, Spaeth GL. Comparison of visual field defects in the low-tension glaucomas with those in the high-tension glaucomas. *Am J Ophthalmol* 1984;**97**:730–7.
- 20 **Caprioli J**, Sears M, Spaeth GL. Comparison of visual field defects in normal-tension glaucoma and high-tension glaucoma [letter]. *Am J Ophthalmol* 1986;**102**:402–4.
- 21 **Chauhan BC**, Drance SM, Douglas GR, et al. Visual field damage in normal-tension and high-tension glaucoma. *Am J Ophthalmol* 1989;**108**:636–42.
- 22 **Hitchings RA**, Anderton SA. A comparative study of visual field defects seen in patients with low-tension glaucoma and chronic simple glaucoma. *Br J Ophthalmol* 1983;**67**:818–21.
- 23 **King D**, Drance SM, Douglas G, et al. Comparison of visual field defects in normal-tension glaucoma and high-tension glaucoma. *Am J Ophthalmol* 1986;**101**:204–7.
- 24 **Phelps CD**, Hayreh SS, Montague PR. Comparison of visual field defects in the low-tension glaucomas with those in the high-tension glaucomas [letter]. *Am J Ophthalmol* 1984;**98**:823–5.
- 25 **Zeiter JH**, Shin DH, Juzych MS, et al. Visual field defects in patients with normal-tension glaucoma and patients with high-tension glaucoma. *Am J Ophthalmol* 1992;**114**:758–63.
- 26 **Johnson CA**, Cioffi GA, Van BE. Frequency doubling technology perimetry using a 24–2 stimulus presentation pattern. *Optom Vis Sci* 1999;**76**:571–81.
- 27 **Kogure S**, Toda Y, Crabb D, et al. Comparison of results with frequency doubling perimetry and Humphrey C30-2 in eyes with high or normal tension glaucoma. *Invest Ophthalmol Vis Sci* 2000;**41**:suppl 87.
- 28 **Horikoshi N**, Osako M, Tamura Y, et al. Comparison of detectability of visual field abnormality by frequency doubling technology in primary open-angle glaucoma and normal-tension glaucoma. *Jpn J Ophthalmol* 2001;**45**:503–9.
- 29 **Matsuo H**, Tomita G, Suzuki Y, et al. Difference in FDT outcome in a normal hemifield between early-stage open angle glaucoma eyes with elevated and normal intraocular pressure. *Invest Ophthalmol Vis Sci* 2002;**43**:suppl 87. [ARVO abstract 2175]



Readers' favourite

Top 10

Click on the "Top 10" button on the homepage to see which are the best read articles each month

www.bjophthalmol.com



Agreement between frequency doubling perimetry and static perimetry in eyes with high tension glaucoma and normal tension glaucoma

S Kogure, Y Toda, D Crabb, et al.

Br J Ophthalmol 2003 87: 604-608

doi: 10.1136/bjo.87.5.604

Updated information and services can be found at:

<http://bjo.bmj.com/content/87/5/604.full.html>

References

These include:

This article cites 28 articles, 5 of which can be accessed free at:

<http://bjo.bmj.com/content/87/5/604.full.html#ref-list-1>

Article cited in:

<http://bjo.bmj.com/content/87/5/604.full.html#related-urls>

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections

Articles on similar topics can be found in the following collections

[Angle](#) (791 articles)
[Glaucoma](#) (779 articles)
[Intraocular pressure](#) (789 articles)
[Neurology](#) (1042 articles)
[Vision](#) (499 articles)
[Epidemiology](#) (766 articles)

Notes

To request permissions go to:

<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:

<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:

<http://group.bmj.com/subscribe/>