EVALUATION OF TWO SCREENING TESTS FOR FREQUENCY DOUBLING TECHNOLOGY PERIMETRY

CHRIS A. JOHNSON, GEORGE A. CIOFFI and E. MICHAEL VAN BUSKIRK

Devers Eye Institute, Discoveries in Sight Research Laboratory, Portland, OR, USA

Abstract

Purpose: To compare two screening procedures for frequency doubling technology (FDT) perimetry.

Methods: Both eyes of 52 normal subjects (aged 18-81 years), and one eye of 56 patients with glaucomatous visual field loss (25 early, 18 moderate, and 13 advanced visual field loss) were tested with the two FDT perimetry screening procedures. One procedure initially presents stimuli at the normal age-adjusted 1% probability level (C-20-1 test) and is designed to emphasize high specificity. The other test procedure initially presents stimuli at the normal age-adjusted 5% probability level (C-20-5 test) and is designed to enhance sensitivity. For both procedures, the authors determined sensitivity and specificity for one or more abnormal test points, two or more abnormal test points, and two or more clustered abnormal test points.

Results: Both test procedures demonstrated high sensitivity and specificity. As expected, sensitivity was highest for the C-20-5 test and specificity was highest for the C-20-1 test. Sensitivity decreased and specificity increased when results were evaluated according to the one abnormal point, two abnormal points and two clustered abnormal points, respectively. Both tests took slightly less than 45 seconds per eye for normal subjects, 60-80 seconds per eye for early glaucoma patients, 80-100 seconds per eye for moderate glaucoma patients, and 125 seconds per eye for advanced glaucoma.

Conclusions: Both of the screening tests for FDT perimetry exhibit high sensitivity and specificity, and demonstrate excellent efficiency. The findings suggest that the C-20-1 test (1% probability level) is probably most appropriate for large population-based screening purposes, whereas the C-20-5 test (5% probability level) is probably best suited for screening in a clinical ophthalmic setting.

Introduction

A low spatial frequency (less than two cycles per degree) sinusoidal grating undergoing high temporal frequency (greater than 15 Hz) counterphase flicker appears to have twice as many light and dark bars as are actually present, i.e., its spatial frequency appears to be doubled. This has been referred to as the frequency doubling effect and is presumably due to the preferential stimulation of nonlinear magnocellular (M cell) mechanisms that are most responsive to the spatiotemporal characteristics of the stimulus display\(^1\). The frequency doubling effect has been used as a method of screening...
for glaucomatous damage by Maddess and Henry\textsuperscript{1}, and has recently been adapted for visual field testing by Johnson and Samuels\textsuperscript{2}.

Recent investigations have reported that the commercially available version of frequency doubling technology (FDT) perimetry, produced jointly by Welch Allyn (Skaneateles Falls, NY) and Humphrey Instruments (San Leandro, CA), exhibits good clinical performance characteristics for evaluation of visual field loss in glaucoma\textsuperscript{2,3}. The full threshold test procedure for FDT perimetry has high sensitivity and specificity for detection of glaucomatous visual field loss\textsuperscript{2,3}, is capable of quantifying and classifying various stages of glaucomatous visual field damage\textsuperscript{4}, and is a sensitive procedure for detecting early damage in normal tension glaucoma\textsuperscript{5}. The original screening procedure, which presents stimuli at the age-adjusted 1% normal probability level, has also been reported to have high sensitivity and specificity for detection of glaucomatous visual field loss\textsuperscript{6}.

The purpose of the present investigation was to compare two different rapid screening strategies for FDT perimetry, the original screening test which presents stimuli throughout the central visual field at the normal age-adjusted 1% probability level (the C-20-1 test), and a new one which presents stimuli throughout the central visual field at the normal age-adjusted 5% probability level (the C-20-5 test).

\textbf{Methods}

We tested both eyes of 52 normal subjects aged between 18 and 81 years (average age, 46 years), and one eye of 56 glaucoma patients (aged 35 to 85 years, average age, 64 years). Although there was an average age difference between the normal subjects and the glaucoma patients of 18 years, this did not represent a confounding factor because all individuals were tested with stimulus values that had been adjusted for normal aging effects, according to the statistical model that has been developed for the commercial version of FDT perimetry. Thus, stimuli that are presented at the 5\% or 1\% probability levels are referenced to normal values that are applicable for the individual’s age at the time of testing.

The eyes of glaucoma patients were classified according to their mean deviation values for Humphrey Field Analyzer results. Twenty-five eyes had early glaucomatous visual field loss, defined as a reproducible defect characteristic of glaucoma with a mean deviation of -6 dB or better. Eighteen eyes had moderate glaucomatous visual field loss, defined as a reproducible defect characteristic of glaucoma and a mean deviation of between -6 dB and -12 dB. Thirteen eyes had advanced glaucomatous visual field loss, with a mean deviation of between -12 dB and -22 dB, in conjunction with a deficit that was characteristic of glaucoma.

Testing was performed with the Welch Allyn/Humphrey Instruments FDT perimeter. In addition to the two screening test procedures (described below), a full threshold FDT test (ref) was also conducted for reference purposes. All the test procedures used the central 20° (C-20) stimulus presentation pattern. This consisted of 17 target locations that included four stimuli per quadrant (10° squares) plus a central 5° diameter circular target. The stimulus display thus covers the central 20° radius of the visual field.

The original screening procedure developed for FDT perimetry, referred to as C-20-1, presents stimuli to the observer with a contrast level that 99\% of the normal population of
the same age is able to see (the age-adjusted 1% probability level). If the target is detected, it is assumed that contrast sensitivity is within normal limits, and no further testing is performed at that location. If it is missed, the same stimulus is presented at that location a second time. If it is missed again, the location is classified as having a ‘mild’ relative loss of sensitivity. It then presents a stimulus of higher contrast (the 0.5% age-adjusted normal probability level), and if this is missed, the location is classified as ‘moderate’ relative sensitivity loss. The test will then present a final stimulus at maximum (100%) contrast and if it is not detected, the sensitivity loss for that location is classified as ‘severe’ loss of sensitivity.

The second screening procedure (C-20-5) is quite similar, except that the contrast levels are slightly different. It begins by presenting stimuli at the contrast level corresponding to the normal age-adjusted 5% probability level (i.e., 95% of the normal population of that age can detect the stimulus). If the stimulus is detected, no further testing is performed at that location. If it is missed, then it repeats the presentation at the 5% probability level. If this is missed, it presents a stimulus at the 2% probability level, and if this is missed, the 1% probability level stimulus is presented. The results are presented in terms of \( p \geq 5\% \) (stimulus seen on initial presentation), \( p < 5\% \) (stimulus missed both times at the 5% level), \( p < 2\% \) (stimulus missed at the contrast corresponding to the 2% probability level), and \( p < 1\% \) (stimulus missed at the 1% probability level).

The C-20-1 screening test is designed to be a conservative strategy that optimizes specificity, whereas the C-20-5 screening test is designed to be a more liberal strategy that optimizes detection of early or subtle loss. We evaluated the results according to three simple algorithms. Screening test results were considered to be outside normal limits if: (1) a single location was abnormal (\( p < 1\% \) for C-20-1 and \( p < 5\% \) for C-20-5); (2) two locations were abnormal; or (3) two locations were abnormal and were adjacent to each other (two clustered points).

### Results

The upper graph in Figure 1 presents sensitivity and specificity for the C-20-1 screening procedure. Specificity was 100% for all three methods of evaluating results. Sensitivity was 100% for advanced glaucomatous visual field loss using all three evaluation methods. For moderate glaucomatous visual field loss, sensitivity was 100% for a single abnormal location, 89% for two abnormal locations, and 83% for two clustered abnormal locations. Early glaucomatous visual field loss was detected with a sensitivity of 84% for a single abnormal location, 64% for two abnormal locations, and 60% for two clustered abnormal locations.

The lower graph in Figure 1 presents sensitivity and specificity for the C-20-5 screening procedure. Specificity was 89% for a single abnormal location, 93% for two abnormal locations, and 95% for two clustered abnormal locations. All three evaluation methods demonstrated 100% sensitivity for advanced glaucomatous visual field loss. For moderate glaucomatous visual field loss, one or two abnormal locations had a sensitivity of 100%, and two clustered abnormal locations had a sensitivity of 94%. Sensitivity for detecting early glaucomatous visual field loss was 96% for a single abnormal location, 92% for two abnormal locations, and 88% for two clustered abnormal locations. Both screening test procedures and all three evaluation methods exhibited very good sensitivity and specificity.
Differences among these procedures represented minor trade-offs between sensitivity and specificity.

The upper graph in Figure 2 shows the average test time for the normal subjects and the three patient groups. For a normal visual field, both test procedures take less than 45 seconds per eye on average. For early and moderate glaucomatous visual field loss, the C-20-5 test procedure took slightly longer than the C-20-1 screening test. With increasing severity of visual field loss, there was also an increase in test time of about 60-80 seconds for early glaucoma, 80-100 seconds for moderate glaucoma, and about 125 seconds for advanced glaucoma. The differences in testing time between screening tests and among dif-

Fig. 1. Top: Sensitivity and specificity of the C-20-1 screening test procedure for FDT perimetry. Bottom: Sensitivity and specificity of the C-20-5 screening test procedure for FDT perimetry.
Two screening tests for frequency doubling technology perimetry

Different patient groups appears to be related to the number of abnormal test points and their severity. This is shown in the lower graph of Figure 2, which presents the average number of abnormal points for the two screening tests in the four subject groups. The results are strikingly similar to the findings for testing time. This was expected because the test algorithms are designed to continue testing until a stimulus is detected or the maximum contrast has been presented, in order to provide information about the severity of visual field loss in addition to detecting abnormalities.

Figure 3 presents the result for a representative patient with early glaucomatous visual
field loss. To the left, the Humphrey Field Analyzer gray scale and total deviation plots are presented. The next plot shows the N-30 full threshold results for FDT perimetry. The next two plots to the right present the results for the C-20-1 FDT screening test and the C-20-5 FDT screening test, respectively. Note that there is good correlation between the two screening tests. The C-20-1 screening test shows only those points that were not detected at the \( p < 1\% \) probability level. The C-20-5 test also shows these points, as well as those points that were not detected at the 2% and 5% probability levels. Both screening tests correlate well with the N-30 full threshold FDT test, as well as the Humphrey Field Analyzer results.

**Discussion**

These findings indicate that both the C-20-5 and C-20-1 screening procedures for FDT perimetry have very good sensitivity and specificity characteristics for detection of glaucomatous visual field loss. In addition, both procedures have high efficiency. Testing times average less than 45 seconds per eye for normal visual fields, and range between one and two minutes per eye for abnormal visual fields, depending on the number of affected visual field locations.

Our current findings are quite consistent with a recent report by Quigley, who found a 91% sensitivity and a 94% specificity for FDT perimetry using the C-20-1 screening strategy in a group of glaucoma patients and ocular hypertensives with normal visual fields. The results from our study and those reported by Quigley indicate that the ability of FDT perimetry to detect glaucomatous visual field loss is equal to or better than conventional perimetric techniques with considerably longer testing times.
Based on our results, we recommend that the C-20-1 test procedure be used for large population-based screening applications. This technique is designed to optimize the specificity of test results and minimize the number of false positive results (patients with normal visual fields incorrectly classified as having visual field loss). Although our results indicate that even a single stimulus presented at the age-adjusted 1% normal probability level is rarely missed by normal subjects, we recommend that a second confirming test be performed when only a single test location or two unclustered test locations are abnormal for the C-20-1 test. Ideally, this confirming test should be a full threshold procedure (which takes approximately four minutes per eye), but a repeat screening examination could be performed as well.

For visual field screening in a clinical ophthalmic setting, there is a greater emphasis on the ability to detect early signs of pathology. Therefore, a test that emphasizes sensitivity is appropriate. We thus recommend that, in these circumstances, the C-20-5 screening test be used for these purposes. To maintain a reasonably high specificity with this approach, we suggest using the two clustered abnormal points scoring strategy. If only one point or two unclustered points are abnormal at the 5% probability level, then a confirming repeat test should be performed, preferably a full threshold test procedure.

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References