Purposes. To determine whether the spatial structure of the frequency doubling technology (FDT) perimetry stimulus is visible at detection-contrast threshold in normal observers and those with glaucoma and to assess its perceived spatial frequency at threshold and suprathreshold contrast.

Methods. Three subject groups were assessed: 10 young normal observers (aged <40 years), 10 older normal observers (aged >50 years), and 10 subjects with glaucoma. Detection thresholds for centrally and eccentrically presented 10° squares, 0.25 c/deg, 25-Hz counterphase flicker sine-wave gratings were obtained by using a yes-no staircase procedure. Eccentric locations were in areas of loss of FDT sensitivity (≤21°) in subjects with glaucoma, or at 7° or 21° inferonasally in normal observers. Resolution-contrast thresholds were determined by a two-alternative, forced-choice staircase procedure in which subjects selected the orientation of the grating stimulus tilted at ±45°. Perceived spatial frequency was determined by having subjects alter the spatial frequency of a temporally interleaved stationary sine-wave grating to match the FDT stimulus.

Results. No significant difference was found between detection- and resolution-contrast thresholds, implying that spatial structure was visible at detection threshold. In general, subjects perceived the spatial structure to have a spatial frequency closer to doubled than to veridical, although the young normal subjects reported a lower apparent spatial frequency than older individuals.

Conclusions. When instructed as for clinical testing, subjects respond to the presence of the structure of the grating, and perceive the FDT stimulus to have a spatial frequency greater than its true spatial frequency. These findings were consistent across both normal observers and those with glaucoma, at both central and eccentric test locations. (Invest Ophthalmol Vis Sci. 2003;44:1111-1116) DOI:10.1167/iovs.01-1251

Frequency doubling technology (FDT) perimetry is a recently developed method of visual field assessment.1,2 It uses low-spatial-frequency sinusoidal grating targets that flicker rapidly in counterphase. This combination of spatiotemporal parameters can result in the percept of frequency doubling, in which the apparent spatial frequency of the grating is approximately twice the actual spatial frequency.3-4 For the frequency doubling effect to occur, the grating must have a low spatial frequency (<4 c/deg) and be counterphased at a high temporal rate (greater than 15 Hz). The commercially available FDT perimeter (Humphrey Systems, Dublin, CA, and Welch Allyn, Skaneateles, NY) determines contrast sensitivity for the detection of sinusoidal gratings of 0.25 c/deg undergoing counterphase flicker at 25 Hz. FDT perimetry has been shown to compare favorably with standard automated perimetry in normal observers, patients with glaucomatous visual field loss, and patients with neuro-ophthalmic disorders.5-7 Also, FDT perimetry has reduced test-retest variability compared with that obtained with conventional perimetry, which may be advantageous for the detection of progression of visual field deficits.6,8

Although FDT perimetry is named after the frequency doubling phenomenon, the thresholds measured are contrast-detection thresholds, that is, no direct measure of the presence or absence of doubling is made. Indeed, it is unclear what percept patients are responding to when detection thresholds are assessed with FDT perimetry. Previous studies of the frequency doubling phenomenon are not conclusive regarding whether the stimulus appears to be frequency doubled at contrast threshold. Kelly9 suggests that the percept of frequency doubling exists at contrast threshold, but others suggest that the grating may appear close to its actual spatial frequency10 or as a zone of amorphous flicker.11-13 It is also not clear whether, within a clinical setting, patients respond to the presence of flicker or to the presence of spatial form. Flood and Flanagan14 report that normal observers are approximately 6 dB less sensitive to the clinical FDT stimuli when specifically instructed to respond to the presence of the spatial structure of the grating, rather than to the perception of flicker. Furthermore, they found that sensitivity measures using a criterion of spatial structure were outside the normal age-matched reference data of the perimeter. This finding illustrates the importance of patient instruction for the FDT perimeter task and implies that patients contributing to the normative database of the commercial instrument were not instructed to respond when they could reliably see the striped pattern of the stimulus. A better understanding of what patients are responding to when performing FDT perimetry may aid in optimizing the test procedure for the detection of visual field loss.

The purposes of the experiments described in this study were twofold. The first was to determine whether spatial form is visible at detection threshold for the FDT stimulus. More specifically, we were interested in whether observers representative of clinical patients, tested with a yes/no methodology and instructed as is usual for clinical FDT perimetric assessment, set their criterion at a level where they can detect the spatial structure of the grating. The second purpose was to assess the apparent spatial frequency of the clinical FDT stimulus to determine whether it appears to be frequency doubled. Apparent spatial frequency was determined at both suprathreshold and threshold contrast. To determine whether differences in performance arise in areas of glaucomatous visual field loss, we compared the performance of subjects with glaucoma with that of age-matched control subjects. A group of younger subjects with normal vision was also tested to explore the effects of normal aging.
METHODS

Subjects

Three subject groups participated: 10 younger normal observers (mean age, 35 ± 4.1 years), 10 older normal observers (mean age, 66 ± 6.9 years), and 10 subjects with glaucoma (mean age, 73 ± 5.8 years). The sample size of 10 subjects in each group was determined by power calculation: a sample of 10 subjects’ results at a power of 0.80 for detecting a 3-dB difference between the mean threshold for detection of the stimulus and detection of its spatial structure, assuming the standard deviation of the measurements to be 3 dB. A difference of 3 dB is approximately equal to the 6-dB difference reported by Flood and Flanagan, given the proprietary scaling factor used in the commercial FDT perimeter.

To be included in the young normal group, subjects were required to be aged less than 40 years and to have visual acuity of 20/30 or better, refractive errors of less than 6 D of sphere and 3 D of astigmatism, normal findings on an eye examination, no systemic disorder known to affect visual function, and normal visual fields returned by the screening program (C-20-1 test) of the FDT perimeter (Humphrey Systems, Dublin, CA, and Welch Allyn, Skaneateles, NY). Identical inclusion criteria were used for the older normal observers, with the exception that subjects were required to be aged more than 50 years.

Patients with glaucoma were required to have a clinical diagnosis of open-angle glaucoma, as determined by a fellowship-trained glaucoma specialist, and were not permitted to be taking any medications known to affect visual field sensitivity or contrast sensitivity (including miotics). Other general and ocular inclusion criteria were the same as for the older normal group. Subjects with glaucoma were required to have at least one nonfoveal location of abnormal visual field sensitivity measured with the full-threshold program (C-20 test pattern) of the FDT perimeter.

Before testing, all subjects provided written informed consent in accordance with a protocol approved by the Legacy Health Systems Institutional Review Board and in accordance with the tenets of the Declaration of Helsinki.

Stimuli

FDT perimeter stimuli were generated with a video board (Cambridge Visual Stimulus Generator ([VSG] 2/4; Cambridge Research Systems, Kent, UK) and were displayed on a gamma-corrected 21-inch color monitor (frame rate 100 Hz, mean luminance 50 cd/m2; Trinitron GDM-500PS; Sony, Tokyo, Japan). Subjects were optically corrected for the 33-cm viewing distance, and thresholds were measured for one eye only.

The spatial and temporal properties of the stimuli were designed to mimic as closely as possible those of the commercially available FDT perimeter. Stimuli were presented within 17 locations, being four per visual field quadrant plus one in the central macular region (C-20 test pattern, see Fig. 1, top). Each stimulus was a 10° × 10° patch of 0.25 cyc/deg sinusoidal grating undergoing 25-Hz counterphase flicker. The total stimulus duration was 720 ms and included a 160-ms interval in which the stimulus contrast was ramped up to the test contrast, a 400-ms period at the test contrast, and a 160-ms ramp down to zero contrast.

The sinusoidal gratings were oriented at either 45° or 135°, as illustrated in Figure 1, bottom. This is a departure from the vertically oriented sine-wave stimuli of the commercial instrumentation. We chose to use oblique orientations, because significant asymmetries in peripheral spatial frequency resolution acuity and detection acuity exist between horizontal and vertical gratings, which may affect performance when gratings of vertical and horizontal orientations are interleaved. It should be noted that horizontal and vertical gratings are more easily detectable than oblique gratings (for review see Ref. 15); however, because we were not interested in raw thresholds but rather in comparisons between detection and resolution thresholds within subjects, these differences in raw thresholds were not important for the outcomes of the study.

All sensitivities are presented in terms of contrast sensitivity in dB—that is, contrast sensitivity = [log (1/contrast threshold) × 10], with contrast measured as a percentage, which results in contrast sensitivities being within a 0- to 20-dB range. This differs from the commercial FDT perimeter, which reports contrast sensitivities that have been scaled by eccentricity-dependent weighting factors to more closely correspond to the values obtained for full-threshold testing of standard automated perimetry (Humphrey Field Analyzer; Humphrey Instruments). The commercial FDT perimeter decibel values are 2.0 to 2.4 times higher (depending on location) than those reported in this article.

Detection-Contrast Thresholds

Detection thresholds were measured with a yes/no procedure combined with a three-up, one-down staircase that converged at the 79% correct level. Staircases began with the stimulus being presented at 10 dB. This was sometimes modified for areas of field loss. Step size was initially 3 dB and was halved at the first two reversals. Staircases were run for a total of four reversals, with the contrast at the final two reversals being averaged to obtain the threshold estimate. Subjects were instructed to respond, by means of a button press, to the presence of “flickering, shimmering or striped” targets. For the patients with glaucoma, detection thresholds were measured foveally and at an eccentric location of decreased sensitivity, as identified with the threshold program of the commercial FDT perimeter. Five of the subjects with glaucoma were tested at locations within the inner ring of the FDT perimetry test pattern, and five were tested at locations within the outer ring (Fig. 1, top). Normal observers were also tested at two locations: foveally and in the peripheral inferonasal field. Half of the subjects in each normal group were tested at 7° eccentricity (inner ring of FDT perimetry stimuli) and half at 21° eccentricity (outer ring of FDT perimetry stimuli). Staircases were performed for two stimulus orientations (45° and 135°) and two eccentricities, in a single, interleaved run. The final threshold for each test location was determined as the mean of the thresholds for each stimulus orientation.

Orientation Resolution-Contrast Thresholds

Resolution-contrast thresholds were obtained by using a two-alternative forced choice (2AFC) paradigm combined with a three-up, one-
down staircase. The contrast of the stimuli was adjusted by using the same staircase procedure as for the detection task, and stimuli were presented at the same eccentricities. The three-up, one-down staircase procedure converged at the 79% correct level, which is the same as for the detection thresholds. It should be noted that the convergence level is a property of the staircase and is not dependent on whether a 2AFC or yes/no paradigm is used. Subjects were required to indicate, by means of a button press, whether the stimulus was oriented at 45° (tilted to the right) or 135° (tilted to the left). Two staircases were measured for each eccentricity, and both foveal and eccentric stimuli were interleaved within a single run. The final threshold for each test location was determined as the mean of the results of the two staircases.

Apparent Spatial Frequency Determination

Apparent spatial frequency was determined using a method of adjustment procedure, in which the subjects were required to match the periodicity of a stationary sinusoidal grating to that of the frequency doubling stimulus. The stationary sine wave and frequency doubling grating were temporally interleaved, each stimulus being presented for 720 ms with a 1-second interstimulus interval. Grating orientation was either 45° or 135° and was varied at random, but the orientations for a given pair of stationary and frequency-doubling gratings were always identical. After each pair of gratings was presented, the subject was instructed to either increase or decrease the apparent coarseness or fineness of the stationary grating, by pressing a button, to try to match that of the counterphasing stimulus. Presentations continued until the subject reported satisfaction with the match. The stationary sinusoidal grating was always presented at 8 dB above the subject’s resolution-contrast threshold for the frequency doubling stimulus and was always clearly visible. Matches were obtained for frequency doubling stimuli presented at resolution-contrast threshold, 2.5 dB above resolution-contrast threshold and 5 dB above resolution-contrast threshold. For each stimulus condition, two matches were made, one where the initial spatial frequency of the stationary grating was greater than twice the actual spatial frequency of the frequency doubling patch (a descending run) and one where the initial spatial frequency of the stationary grating was less than the actual spatial frequency (an ascending run). Step size for the adjustment procedure was 0.05 c/deg.

Apparent spatial frequency was determined at both foveal and eccentric locations in a noninterleaved fashion. The eccentric location was the same as that tested using the detection and resolution paradigms. For eccentric testing, both the reference and test stimulus were presented at the same eccentricity.

RESULTS

The visual acuities and the global indices measured using the full-threshold program (C-20 test pattern) of the commercial FDT perimeter are shown for each of the subjects with glaucoma in Table 1. Each of the subjects with glaucoma is identified by a unique symbol that can be used to identify individual performance in the figures.

Figure 2 shows the repeatability of the detection and resolution threshold measures for each subject group at both foveal and eccentric locations. The difference between the two-staircase threshold estimates determined for each subject is plotted with young normal, older normal, and glaucoma groups in the top, middle, and bottom panels, respectively. Each of the 10 subjects in each group (young normal subjects, older normal subjects, and glaucoma) is represented by a unique symbol. These symbols are retained in subsequent figures so that performance of individuals can be identified. Subjects tested at 7° are represented by unfilled symbols and subjects tested at 21° are represented by filled symbols. The foveal data represents all 10 observers in each group, whereas the eccentric data show the data of 5 observers only (as half of each group was tested at each location). For the data from the glaucoma group, it was assumed that the inner and outer rings of the FDT stimulus (Fig. 1, top) approximated eccentricities of 7° and 21°, respectively. A two-way repeated-measures ANOVA on the difference

<table>
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<th>PSD</th>
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Including the denominator of their visual acuity, the mean deviation (MD) and pattern standard deviation (PSD) indices measured using the C-20 threshold program of the FDT perimeter.
between the results of the two staircases (test–retest) was performed to determine whether the staircases were less repeatable for specific subject groups or locations (central versus periphery). For the detection and resolution tasks, no significant differences were found between groups (detection, \( P = 0.82 \); resolution, \( P = 0.46 \)) nor locations (detection, \( P = 0.72 \); resolution, \( P = 0.57 \)) and no significant interaction was found between group and location (detection, \( P = 0.94 \); resolution, \( P = 0.13 \)). Pooling the data resulted in a mean SD difference between the two staircases of 0.03 SD for the detection task and 0.13 SD for the resolution task. This level of repeatability compares favorably with test–retest variability reported previously for FDT perimetry, as does the observation that repeatability does not vary with deficit depth or eccentricity.

To determine whether the spatial structure of the FDT perimetry stimulus was visible at detection threshold, we compared performance on the detection and resolution-contrast threshold tasks. Detection- and resolution-contrast sensitivities are presented in Figure 3 for the young normal, older normal, and glaucoma groups in the upper, middle, and lower panels respectively. Inspection of Figure 3 reveals that in all three groups, detection sensitivity approximately matched resolution sensitivity. A two-way ANOVA on the difference data (resolution sensitivity minus detection sensitivity) showed no effect of group (\( P = 0.40 \)) or eccentricity (\( P = 0.72 \)), and so the data were pooled. No significant difference existed between the detection and resolution thresholds (95% confidence intervals for the mean of the pooled difference data, averaged for each observer \([df = 29]\) = \(-0.55 \pm 0.23\)). This result implies that in all three subject groups, at both foveal and eccentric locations, the spatial structure of the frequency doubling grating was visible at the contrast threshold measured using the detection paradigm. The next question was whether the spatial form appeared frequency doubled. Figure 4 presents the apparent spatial frequency at the three different contrast levels tested for each of the subject groups. The left panels show data for the patch presented foveally, and the right panels, for the eccentric location. Apparent spatial frequency is displayed as a percentage of the true spatial frequency; hence, 100% represents veridical perception (that is, the grating appears to be its true spatial frequency), and 200% represents frequency doubling. Several subjects reported that they could not confidently see the stripes at resolution-contrast threshold. This observation was expected, because the staircase procedure used to determine threshold converged at the 79% correct level. Matches were not obtained if after repeated attempts subjects were unable to make a match. Inspection of the middle and lower panels reveals that most of the older normal subjects and patients with glaucoma viewed the stimulus as closer to doubled (200%) than veridical (100%); however, there is considerable variation between subjects in the perceived spatial frequency with some subjects matching at frequencies greater than doubled. It should be noted that in general, individual subjects demonstrated similar trends of matching across all conditions.

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Frequency Doubling Stimulus Appearance

contrast levels. The low level of intraobserver variability on the task suggests that subjects were able to reliably perform the task at both central and peripheral locations. There was no significant difference in apparent spatial frequency between older normal subjects and patients with glaucoma at either eccentricity (two-way repeated-measures ANOVA: fovea, \(P = 0.81\); eccentric, \(P = 0.95\)). Appearance of the FDT stimulus was also not altered in areas of glaucomatous visual field loss (foveal versus eccentric matches at 5 dB above resolution threshold in the glaucoma group, paired \(t\)-test; \(P = 0.64\)).

Comparison of the upper and middle panels of Figure 4 reveals differences in the apparent spatial frequency observed by younger normal subjects and older normal subjects. The apparent spatial frequency was significantly lower in the young normal group than the old normal group at both eccentricities (two-way repeated measures ANOVA: difference between groups for central condition, \(P = 0.015\); for the peripheral condition, \(P < 0.001\)).

**Discussion**

In this study, no significant difference was found between detection sensitivity and resolution-contrast sensitivity for the FDT perimetric stimulus. This finding was robust to differences in subject age and eccentricity of presentation and was present in locations of normal sensitivity and those with depressed sensitivity due to glaucomatous visual field loss. Detection thresholds were determined using a yes/no technique similar to that used when measuring clinical FDT thresholds, and subjects were provided with instructions considered typical of clinical FDT assessment. This finding implies that when performing a yes/no detection FDT perimetry task, subjects set their criterion for a yes response at a contrast level at which they can just determine the spatial structure of the grating. Our findings also imply that subjects set this criterion for a yes response consistently, regardless of eccentricity, age, or loss of sensitivity. Our finding of equivalence between the detection and resolution sensitivity measures conducted in this study does not necessarily disprove the existence of a zone of veridical perception where the grating appears at its true spatial frequency or a zone of uniform flicker at reduced contrasts (see the introduction); however, it does demonstrate that the criterion set by patients to elicit a yes response for the clinical detection task includes the perception of grating structure.

Because it has been reported that the instructions given to patients can significantly affect perimetric thresholds, we verified the appropriateness of our verbal instructions by providing the same set of instructions (respond to the presence of ‘flickering, shimmering, or striped targets’) before the subjects’ baseline FDT perimetric measurements (C-20 test; Welch Allyn and Humphrey Systems). With these instructions all the screening tests of control subjects in this study yielded normal results on the commercial instrument; hence, the criterion set by the patients was appropriate to the normative database of the instrument. We assume the same criterion was used for the subsequent detection task, because subjects were provided with the same instructions.

Our findings may initially seem to differ substantially from those of previous investigators who report a difference between detection and resolution thresholds for FDT perimetric stimuli. Flood and Flanagan\(^{13}\) report an average sensitivity difference of 6 dB between FDT perimetry results when subjects were specifically instructed to respond to either the presence of flicker (detection) or the presence of lines (resolution). The 6-dB difference reported when the commercial instrument is used is equivalent to approximately 3 dB when using our decibel scale. Similar methodology has also been used by Bosworth et al.\(^{10}\) who similarly report a difference between detection and resolution thresholds for frequency doubling stimuli. These findings may be reconciled by considering methodological differences between the studies. The detection task for the previous two studies shared essentially the same methodology as ours; however, the methodology for the resolution tasks differed between the studies. Flood and Flanagan\(^{13}\) measured resolution sensitivity using a yes/no paradigm in which subjects were asked to respond to the presence of lines within the target. It is possible that these instructions will encourage subjects to set conservative criteria; hence, they may not respond until they are sure that they can see the lines. In contrast, we used a 2AFC procedure in which subjects were required to choose the orientation of the grating, even when they were not certain that they could see the grating. The staircase procedure converged at the 79% correct performance level for both the detection and resolution tasks. By definition, at the 79% correct level, subjects are not certain about the stimulus, and because no difference was found between detection and resolution thresholds, it is implied that at threshold contrast the subjects are not certain about either the presence of the stimulus or of its spatial structure. This is illustrated in the data of Figure 3, in which several patients were unable to make a spatial frequency match at their resolution threshold contrast because they could not reliably see the grating.

It is well established that a large number of factors influence perceived spatial frequency. These include stimulus orientation,\(^ {19,20}\) contrast,\(^ {19,20}\) and eccentricity when compared with a foveal reference.\(^ {19,21}\) We controlled for the effects of eccentricity and orientation by matching the reference and test stimulus for these parameters. The reference stimulus was always of higher contrast than the test stimulus, which is preferred to increase the perceived spatial frequency of the low-contrast test stimulus by approximately 10%.\(^ {20}\) It is important to mention that all subjects were measured at the same equivalent apparent contrast (relative to their own contrast threshold), and therefore any fractional increase of perceived spatial frequency due to the higher contrast of the reference stimulus should have been consistent across all observers.

The data in Figure 4 demonstrate that although there were substantial between-subject differences in perceived spatial frequency, in the main, individual subjects were consistent in their matching. For example, those subjects who perceived the stimulus as more than doubled did so in both central and eccentric viewing conditions, across all contrast levels. We found no significant difference between the apparent spatial frequency matches reported by the observers with glaucoma and those from the age-matched controls. This finding implies that the apparent spatial frequency of the frequency doubling stimulus remains unchanged in areas of reduced sensitivity due to glaucoma. It remains possible that changes in apparent spatial frequency may arise in areas of severe field loss; however, inspection of Figure 4 shows no trend in those with glaucoma with the worst FDT results (see Table 1) to produce the most aberrant matches. It is also possible that smaller targets may reveal differences in performance; however, no such differences were identified when using stimuli representative of those in the commercially available FDT instrument.

Several subjects consistently matched the frequency doubling stimulus with a stimulus of spatial frequency greater than double the veridical frequency. One possible explanation of this finding is a floor effect. The veridical spatial frequency is low; hence, the range of possible matching frequencies below the veridical frequency is limited (in our case, only five steps of 0.05 cyc/deg were possible below the true frequency of 0.25 cyc/deg). If subjects are uncertain, then judgments greater than the veridical frequency are more likely to result.
We identified a significant difference in spatial frequency percept between the younger and older normal groups where, on average, the younger subjects matched the FDT stimulus at somewhat less than doubled. It seems unlikely that the differences manifest due to different levels of psychophysical experience between the groups. Two of the subjects in the young normal group (Fig. 4; unfilled circle and filled square) and one of the older normal subjects (Fig. 4; filled circle) were experienced psychophysical observers who were aware of the experimental purpose. If a floor effect influenced results, then this may imply that the older observers were less certain of their matches, because guessing is more likely to generate matches greater than veridical. However, in the main, individual subjects were consistent with their matches across all contrast conditions and at both central and eccentric locations.

There was not a trend for higher-spatial-frequency matches at lower contrast, or in the periphery, where subjects are likely to be less certain. Previous studies of spatial frequency matching for grating stimuli have generally used, at most, three observers aged less than 40 years.3,9,11,22,23 Nevertheless, individual variability in spatial frequency matching has been reported,22 as has the observation of fractional doubling.9,11,12,22 To our knowledge, our study is the first to measure apparent spatial frequency in a larger number of subjects stratified by age, in areas of normal and reduced sensitivity.

References