Frequency-Doubling Technology Perimetry and Optical Defocus

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Purpose. The frequency-doubling technology (FDT) perimeter has no provision for introducing corrective lenses, save for the patient's spectacles, and so patients are sometimes tested in the presence of moderate levels of defocus. The effect of defocus on frequency-doubling (FD) sensitivity was determined for both the commercially available instrument and for smaller targets that may be useful in spatially localizing visual field defects. In addition, whether stimulus artifacts may be detectable in the presence of defocus was assessed.

Methods. Detection and resolution thresholds for FD stimuli, along with detection thresholds for spatially uniform flickering stimuli, were measured in normal observers in the presence of up to +6 D of defocus. In addition, the effect of defocus on the summary indices (mean deviation [MD], and pattern standard deviation [PSD]) of both the commercial FDT perimeter and a customized perimeter with smaller, higher spatial frequency targets was determined.

Results. Thresholds for conventional FD targets (0.25 cyc/deg, 25 Hz) increased 0.1 log unit with +6 D defocus, whereas thresholds for smaller, higher spatial frequency (0.5 cyc/deg) targets increased 0.4 log unit. Despite the presence of a luminance artifact in the FD stimuli, detection, and resolution thresholds remained coincident at maximum defocus, suggesting that the artifact was not detectable. MD was significantly affected by defocus for the customized FD perimeter only, and PSD was not altered for either the conventional or customized test.

Conclusions. In normal observers, optical defocus has little effect on FDT perimetry sensitivity and does not make low spatial frequency artifacts detectable. Improving the spatial resolution of FDT perimetry decreases its robustness to defocus. (*Invest Ophthalmol Vis Sci.* 2003;44:4147–4152) DOI:10.1167/iovs.02-1076

The frequency-doubling (FD) phenomenon was first described by Kelly,[1] who observed that a low-spatial-frequency sine-wave grating appeared to double in spatial frequency when its contrast was counterphase flickered at high rates. Because contrast sensitivity to FD stimuli is reduced in glaucoma,[2–5] FD stimuli have been used in the frequency-doubling technology (FDT) perimeter (Welch Allyn, Skaneateles Falls, NY, and Carl Zeiss Meditec, Inc., Dublin, CA). In this article, we refer to the targets used by the FDT perimeter (FDT stimuli) separately from the general class of flickering gratings (FD stimuli) that can be used to demonstrate the FD effect.

Determining the effects of defocus is important for FDT perimetry, because the perimeter has no provision for the introduction of corrective lenses, except for the patient's spectacles. There is anecdotal evidence that refractive errors up to 6 D do not affect FDT perimetry,[2] and this limit is recommended by the manufacturers. Preliminary work suggests that refractive errors of this magnitude result in a significant reduction in sensitivity, however (Nicolela MT, et al. *IOVS* 2002;43: ARVO E-Abstract 2147). Because the targets used in FDT perimetry are of low spatial frequency (0.25 cyc/deg), sensitivity may be expected to be robust to optical defocus.[6] Even small amounts of defocus can, however, cause prominent "notches" in the contrast sensitivity function when it is measured at suitably narrow intervals of spatial frequency.[7,8] The location of these notches shift to lower spatial frequencies as the amount of defocus increases,[9] and so could significantly reduce FD sensitivity, even if contrast sensitivity to higher and lower spatial frequency targets is relatively unaffected.

The influence of optical defocus on the response criterion adopted by the patient is unclear. We have shown that simple detection strategies for FDT perimetry isolate the same visual mechanisms as when subjects use a criterion based on spatial form (i.e., the appearance of a striped pattern).[10] It is possible, however, that this equivalence between strategies is not maintained when optical defocus is high. The square window in which the FDT targets appear creates very low spatial frequency artifacts that may be more robust to defocus and eventually become important for detection at high levels of defocus. One potentially significant artifact is a change in the average luminance that modulates at 25 Hz, because there is not an integer of cycles present in the FDT target.

Recent work has shown that decreasing the target size increases both the spatial resolution and the ability to detect visual field defects in FDT perimetry[11] without adversely affecting test variability,[12] and so future generations of FDT tests may be more useful if target size is decreased. To offset the loss of contrast sensitivity caused by decreasing the target size, Johnson et al.[11] decreased the temporal frequency and increased the spatial frequency of the target, however. It would be expected that the tolerance to defocus diminishes with smaller, higher spatial frequency targets. Loss of flicker sensitivity has been shown to be a sensitive test for age-related maculopathy[13–16] and central serous chorioretinopathy,[17] suggesting that targets even smaller than the 4 deg^2 targets investigated by Johnson et al.[11] may be useful for spatially localizing visual field deficits in the macula.

In this study, we investigated the effect of optical defocus on sensitivity to FDT perimetry targets, both for the large targets currently incorporated in the commercial device and for smaller targets that may improve spatial localization of visual field defects. In addition, we wanted to establish whether optical defocus had the same effect on sensitivity when a criterion based on spatial form (resolution) was used, given the presence of low-spatial-frequency artifacts in FDT stimuli.

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Materials and Methods

Apparatus and Procedure

We presented stimuli on a calibrated video monitor system (VSG 2/4 graphics card; Cambridge Research Systems Ltd., Kent, UK, and CPD-G500 monitor, frame rate 100 Hz; Sony, Tokyo, Japan). The monitor subtended 11° × 8.4° (width × height) at the 1-m viewing distance and had an average luminance of 50 cd/m^2. Ambient room illumination was approximately 4 cd/m^2.

Three sinusoidally flickered sine-wave gratings were used: a 10-deg^2, 0.25-cyc/deg grating flickering at 25 Hz; a 5-deg^2, 0.5-cyc/deg grating flickering at 18 Hz; and a 2-deg^2, 0.5-cyc/deg grating flickering at 12.5 Hz. Respectively, these targets were designed to approximate the conventional FDT targets, those used in the 24-2 pattern FD test (described later),[11] and those that may be useful for assessing macular sensitivity. All three stimuli were within the spatiotemporal domain that gives spatial-frequency doubling, as reported by Kelly.[1] Stimulus contrasts were specified as Michelson contrasts and were presented in a raised cosine window of 1000 ms. The minimum time between the offset of one stimulus and the onset of another was 500 ms. All grating stimuli were oriented at 90°, except in the orientation discrimination task outlined later, in which the grating was oriented at either 45° or 135°. The spatial phase was randomized for each presentation, and all stimuli were presented foveally.

Experiment 1: Effect of Defocus on FD Sensitivity

We determined both detection and resolution (orientation discrimination) thresholds for the grating stimuli. For the detection thresholds, subjects were permitted to respond to any attribute of the FD stimulus and pushed a button whenever they believed a stimulus had been presented. For the resolution thresholds, subjects were forced to chose whether the FD stimulus was oriented at 45° or 135° by pushing one of two response buttons. Comparison of the results from these two paradigms allows the effect of detection versus pattern resolution criteria on the mechanisms isolated by the FD stimulus to be determined.[10] It should be noted, however, that this technique does not determine whether the pattern appears to double in spatial frequency at the pattern threshold. Although it has been suggested that gratings appear at their true spatial frequency at threshold,[18] recent work suggests that both normal observers and those with glaucoma see the gratings as being close to being doubled in spatial frequency at their clinically determined contrast thresholds.[19]

Detection thresholds were measured with a yes/no paradigm of eight trials, with contrast manipulated by a zippy estimation by sequential testing (ZEST) procedure[20] that converged at the 78% correct level. Resolution thresholds were measured using a two-alternative forced-choice paradigm of 30 trials, with the ZEST procedure converging at the 81% correct level. We selected convergence levels that optimized the efficiency of the ZEST procedure.[20] Thresholds from each subject were the geometric mean of four measurements for detection data and of two measurements for resolution data. Data for each paradigm (detection or resolution) and level of defocus were collected in a randomly interleaved manner.

To assess the effect of defocus on the luminance artifact present in the FD stimuli (see the introduction), we measured thresholds for spatially uniform patches of the same sizes and temporal frequencies as the grating targets.

We measured each subject's refraction with an autorefractor (Humphrey Automatic Refractor Model 530; Carl Zeiss Meditec), with the spherical component of the refraction subsequently adjusted so that an additional +0.50 D reduced the subject's distance acuity by one line on the acuity chart.[21] During testing, subjects wore their refractive corrections, adjusted for the 1-m working distance, in a trial frame. We produced optical defocus by introducing positive spherical trial lenses of 1, 2, 3, 4, and 6 D.

Experiment 2: Effect of Defocus on FD Visual Field Indices

In addition to the main experiment just described, we investigated the effect of spherical defocus on the conventional FDT perimeter and on a 24-2 FD perimeter that has been described previously.[11] The latter test uses 4-deg^2 0.5-cyc/deg sine-wave targets that counterphase flicker at 18 Hz, with a square-wave temporal envelope. Fifty-four targets are arranged in a spatial pattern identical with the 24-2 test on the Humphrey Field Analyzer II (Carl Zeiss Meditec). The test has a normative database from which global indices for the visual field (mean defect [MD]) and pattern SD [PSD]) are calculated. Since it was described in the literature, the test has been conducted with the ZEST threshold algorithm.[20] The perimeter's lens holder can accommodate a maximum of two lenses, and so we adjusted the nominal lens value by no more than 0.25 D for high defocus levels when the exact dioptric value was not available in the trial lens set.

When performing conventional FDT perimetry, subjects wore their habitual spectacle corrections and held a spherical trial lens between their spectacles and the FDT eyepiece. We verified that the addition of +0.50 D of defocus was sufficient to decrease each subject's habitual visual acuity by one line.

Subjects

Nine psychophysically experienced subjects, aged 19 to 43 years (average, 32) and with corrected visual acuities in their right eyes of better than 6/6, participated in the main experiment. Each subject viewed the monitor monocularly with the right eye and natural pupil (average diameter, 4.6 mm; range, 3.5–6 mm) and fixated a small, dark marker in the center of the monitor when defocus was minimal, or simply in the center of the screen when high amounts of defocus made the fixation point invisible. No subject reported any difficulty localizing the test targets. All subjects had normal screening test results on the FDT perimeter (C-20-5 test, software version 3.00.1; Carl Zeiss Meditec) for their right eyes. The study complied with the tenets of the Declaration of Helsinki and was approved by our institutional review board, with all subjects giving informed consent before participating.

Analysis

Linear regression lines were used to fit the individual data. The mean values from the individual coefficients were used to fit the average data, consistent with the mean coefficient technique described by Anastasi et al.[22] The suitability of a linear model was established by a Q statistic,[23] with $Q > 0.01$ taken to indicate acceptable models. Slopes were compared with a one-way repeated-measures (RM) ANOVA, with a Tukey all pair-wise multiple comparison procedure used to isolate individual differences. The criterion for significance was $P \leq 0.05$. A one-way RM ANOVA on ranks was performed on one data set that failed the test for normality ($P \leq 0.05$). Statistical testing was performed on computer (SigmaStat, ver. 2.0; SPSS Sciences, Chicago, IL).

Results

Experiment 1: Effect of Defocus on FD Sensitivity

Figure 1 shows the effect of optical defocus on sensitivity to the three grating targets, with the parameters of the regression lines given in Table 1. Although the slopes for the detection sensitivity regression lines for the two smaller targets (middle and lower panels) were not significantly different, the slope of the detection values for the 10° FD target (Fig. 1A) was significantly shallower (RM ANOVA, $P < 0.001$). In all cases, the slopes of the lines for the detection and resolution paradigms were not significantly different (paired *t*-tests). Six diopters of defocus altered FD sensitivity by approximately 0.1 log unit for the large target, and by 0.4 log unit for the smaller targets.

Figure 2 shows how optical defocus affected the detection of a spatially uniform flickering patch of the same sizes and

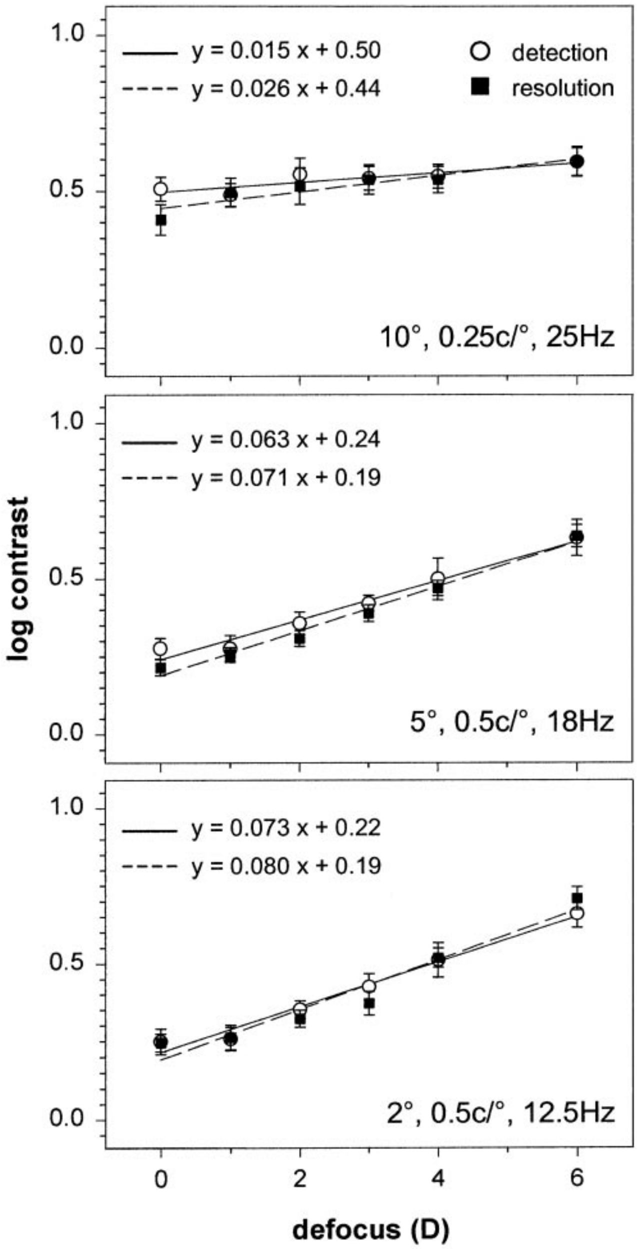

FIGURE 1. Effect of defocus (abscissa) on contrast threshold (ordinate: log percentage contrast) for three target configurations (**A–C**), showing the yes/no detection thresholds and the two-alternative, forced choice resolution thresholds. Data points are the average from nine observers (±SEM). Parameters for the regression lines are shown in Table 1.

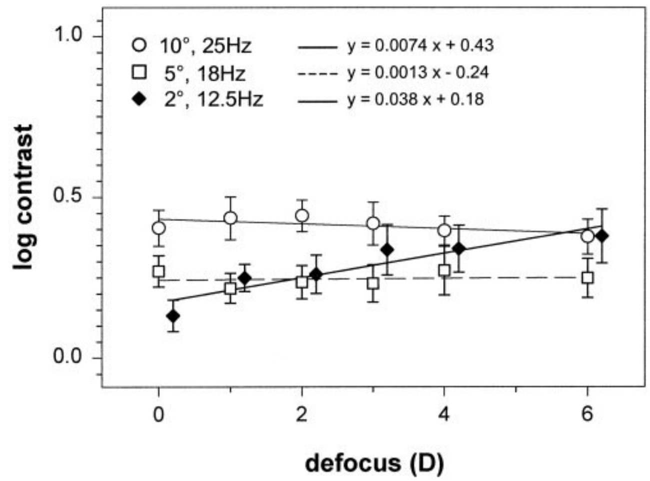

FIGURE 2. Effect of defocus (abscissa) on contrast threshold (ordinate) for spatially uniform flicker. Data points are the average of seven observers (±SEM). Parameters (±SD) for the fitted lines are: (○) m (slope) = 0.0074 ± 0.012, c (intercept) = 0.43 ± 0.16), Q = 1.00; (□) m = 0.0013 ± 0.022, c = −0.24 ± 0.12, Q = 1.00; (◆), m = 0.038 ± 0.031, c = 0.18 ± 0.10, Q = 0.99.

temporal frequencies as the grating patches in Figure 1. For a given target size, the slopes of the curves in Figure 2 were shallower than both the detection and resolution curves in Figure 1 (RM ANOVA, $n = 7$: 10° target, $P = 0.002$; 5° target, $P < 0.001$; 2° target, $P = 0.01$), indicating that defocus raised thresholds for the grating target at a faster rate than for a luminance artifact of the same size. With no defocus, thresholds for the uniform flickering patches were significantly smaller than detection thresholds for grating patches of the same size for both the 10° and 2° targets (paired t-test: $P = 0.01$ and 0.04, respectively) but not for the 5° targets ($P = 0.69$).

Experiment 2: Effect of Defocus on FD Visual Field Indices

Figure 3 shows the effect of optical defocus on the MD and PSD summary indices of the FDT perimeter. Neither index correlated significantly with defocus, and no subject returned abnormal (MD and/or PSD $P < 0.5\%$) field results. Because of the proprietary scaling used for the output of the FDT instrument,[24] quantitative comparison between these results and for the single target in experiment 1 could not be performed.

Figure 4 shows the same analysis as for Figure 3, but for the 24-2 version of the FD test. Optical defocus had no significant effect on PSD, but decreased MD (lower solid line) at a rate that was not significantly different from that predicted from the single-target data obtained in experiment 1 (Fig. 4, dashed line). Two of four subjects returned abnormal ($P < 0.5\%$) MD

TABLE 1. Parameters for the Fitted Lines in Figure 1

	m (slope)	*c* (intercept)	*Q*
0.25 cyc/deg, 25 Hz, 10° wide			
Detection	0.015 ± 0.011	0.50 ± 0.12	1.00
Resolution	0.026 ± 0.015	0.44 ± 0.13	1.00
0.5 cyc/deg, 18 Hz, 5° wide			
Detection	0.063 ± 0.024	0.24 ± 0.10	0.99
Resolution	0.071 ± 0.014	0.19 ± 0.063	0.99
0.5 cyc/deg, 12 Hz, 2° wide			
Detection	0.073 ± 0.025	0.22 ± 0.11	1.00
Resolution	0.080 ± 0.018	0.19 ± 0.077	0.92

Data are the mean ± SEM.

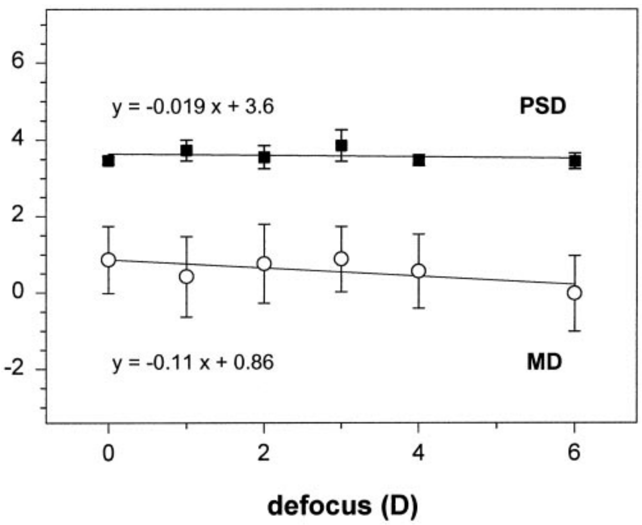

FIGURE 3. Effect of defocus (abscissa) on MD and PSD indices for FDT perimetry. Data points are averaged from five observers (±SEM). Parameters (±SD) for the *top solid line* are $m = -0.019 \pm 0.094$, $c = 3.6 \pm 0.37$, $Q = 0.94$, and for the *bottom solid* line $m = -0.11 \pm 0.11$, $c = 0.86 \pm 2.1$, $Q = 1.0$.

indices with 3 D of defocus, with all subjects returning abnormal MD indices with 6 D of defocus. Individual PSD indices were always normal.

DISCUSSION

Our results show that conventional FDT perimetry is robust to the effects of optical defocus, with 6 D of defocus reducing sensitivity by 0.1 log unit only (Fig. 1). Defocus failed to cause a significant decrease in either the PSD or MD index (Fig. 3). The shallow, significant slope of approximately 0.23 dB/D, found by Nicolela et al. (Nicolela MT, et al. *IOVS* 2002;43: ARVO E-Abstract 2147) for the index MD, provides an acceptable fit for our data ($Q = 1.0$). We measured refractive errors centrally, and not for each peripheral location tested, and so it may be thought that the flat curves in Figure 3 could result from the defocusing lens reducing peripheral defocus in some subjects, while increasing it in others, resulting in little average effect. If this were true, however, the error-bars on the graph would systematically widen as the power of the defocusing lens increased. There is evidence that peripheral retinal contrast sensitivity is more robust to defocus, even once peripheral refractive errors have been corrected,[25] and so it is likely that our foveally measured results represent the maximum effect of defocus for a given retinal location.

Direct comparisons between these results and previous reports investigating the effect of defocus on white-on-white perimetry is difficult, however, because FDT and white-on-white perimetry use different contrast metrics (Michelson versus Weberian contrast, respectively). It has been reported that sensitivity to a conventional size III (0.43°) perimetric target decreases by approximately 0.8 log unit with 6 D of defocus.[26] Given that intersubject variability is only 50% (0.3 log unit) greater for white-on-white perimetry than for FD thresholds,[27] it may be estimated that, relative to normal test variability, white-on-white perimetry is three times (0.5 log unit) more susceptible to the effects of defocus than the commercially available FDT perimeter.

Because there is a noninteger of grating cycles (2.5) used in conventional FDT targets, there is a change in average luminance that modulates at 25 Hz. This luminance artifact arises from the unpaired half cycle and is equal to $2/(5\pi)$ of the grating's peak luminance, thereby making the contrast of the luminance artifact 0.9 log unit below the contrast of the grating. (A half-cycle of a sine-wave grating produces a luminance increase equal to $2/\pi$ of the grating's peak luminance. Averaged over an area of 2.5 cycles [or, 5 half-cycles] in the FDT stimulus, this luminance increase is reduced to $2/[5\pi]$ of the grating's peak luminance.) Contrast thresholds for this artifact alone (Fig. 2, circles, no defocus) were approximately 0.1 log unit less than for the FDT grating target (Fig. 1A, circles, no defocus), and so defocus would need raise grating thresholds approximately 0.8 log unit (0.9 minus 0.1) more than artifact thresholds before the artifact became more detectable than the grating. Although defocus raised grating thresholds at a significantly faster rate than artifact thresholds, the difference was insufficient to make the artifact detectable at the levels of defocus we investigated. Further evidence against the detectability of such an artifact is that detection and resolution thresholds remain comparable at the greatest level of defocus (Fig. 1A). Because the luminance artifact does not give information about grating orientation, a divergence in these two thresholds should occur if the artifact was used for stimulus detection. Similar to the conventional FDT targets, the 5° diameter, 0.5 cyc/deg target in this study contained a noninteger of grating cycles and so contained a change in average luminance that modulated at 18 Hz. The differential effect of defocus on the luminance artifact (Fig 2., squares) versus the grating target (Fig. 1B) was greater than for conventional FDT targets, but was still less than that necessary to make the artifact visible. If reductions in contrast sensitivity are roughly uniform at low spatial frequencies, artifacts should remain invisible in areas of visual field loss caused by disease. Recent work[19] showing that absolute detection thresholds and pattern resolution thresholds are increased by comparable amounts in glaucoma provides evidence that luminance artifacts do not become detectable in areas of visual field damage.

We found that thresholds for higher spatial frequency targets (0.5 cyc/deg), as may be useful in more finely spaced FD test strategies, were more susceptible to defocus than conven-

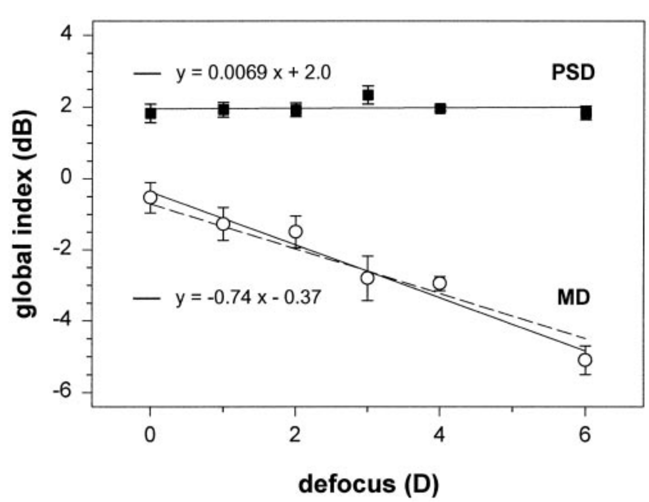

FIGURE 4. Effect of defocus (abscissa) on MD and PSD indices, for a 24-2 FD test. Data points are averaged from four observers (±SEM). Parameters (±SD) for the *top solid line* are $m = 0.0069 \pm 0.047$, $c = 2.0 \pm 0.18$, $Q = 0.94$, and for the *bottom solid line*, $m = -0.74 \pm 0.044$, $c = -0.37 \pm 0.79$, $Q = 0.85$. *Dashed line*: gradient at the detection data in Figure 1B, but scaled to decibels of sensitivity ($m = -0.63$) and to intercept the solid line at 3 D; the 95% confidence intervals for the gradients of these two lines overlap. At 4 D of defocus, three subjects returned abnormal ($P < 5\%$) MD indices.

tional FD perimetry targets (Fig. 1). The slopes of the curves relating threshold to defocus were indistinguishable for the 5° and 2° targets, suggesting that it was the spatial frequency of the grating and not the size of the grating that governed this relationship. When higher spatial frequency targets were used in a perimetric test, the MD index became abnormal at high levels of defocus (Fig. 4). In our database for the 24-2 FD test, the 5% limit for normality is −2.6 dB (OD), and it would be expected that the average MD would reach this value with 3.5 D of defocus. It should be remembered, however, that defocus less than this amount results in abnormal indices in patients who have MDs less than average, being approximately half of the normal population. Despite the effect on MD, we found no evidence that defocus affects the PSD index in normal subjects, which suggests that defocus results in generalized depression of the visual field. A similar result has been reported for white-on-white perimetry.[28] It may be, however, that defocus affects the PSD in patients with abnormal visual fields, as defocus may make the borders of focal defects less distinct. Studies have found that PSD deteriorates in patients with glaucoma after cataract extraction, despite an improvement in MD,[29,30] which suggests that the reduced image quality in cataract partially masks localized visual field defects. Similarly, the PSD index of abnormal fields is reduced in visual field test strategies that incorporate spatial averaging techniques.[31-33]

We performed our study on subjects that were younger than those on whom FDT perimetry would typically be conducted, and so it is reasonable to consider how the subject's age may affect our results. Because pupil diameter decreases with age,[34] this may increase depth of focus for low spatial frequencies,[6] although large intersubject variations in depth of focus effects can occur.[8] Media changes in the eye with age may also ameliorate the effects of defocus, irrespective of pupil size.[35] Overall, older subjects may be less affected by optical defocus than our young test group and so our results probably indicate the maximum effect of defocus on FD perimetry.

In conclusion, we found that the current FDT test is robust to optical defocus, and that defocus does not make low spatial frequency artifacts in the FDT targets visible. With higher spatial frequency targets, as may be useful in test patterns of greater spatial resolution, tolerance to optical defocus is reduced.

References

1. Kelly DH. Frequency doubling in visual responses. *J Opt Soc Am*. 1966;56:1628–1633.
2. Johnson CA, Samuels SJ. Screening for glaucomatous visual field loss with frequency-doubling perimetry. *Invest Ophthalmol Vis Sci*. 1997;38:413–425.
3. Johnson CA, Cioffi GA, Van Buskirk EM. Evaluation of two screening tests for frequency doubling technology perimetry. In: Wall M, Wild JM, eds. *Perimetry Update 1998/1999. Proceedings of the XIIIth International Perimetric Society Meeting*, Gardone Riviera (BS), Italy, September 6–9, 1998. The Hague, The Netherlands: Kugler Publications; 1999:103–109.
4. Maddess T, Goldberg I, Dobinson J, Wine S, Welsh AH, James AC. Testing for glaucoma with the spatial frequency doubling illusion. *Vision Res*. 1999;39:4258–4273.
5. Maddess T, Severt WL. Testing for glaucoma with the frequency-doubling illusion in the whole, macular and eccentric visual fields. *Aust N Z J Ophthalmol*. 1999;27:194–196.
6. Green DG, Campbell FW. Effect of focus on the visual response to a sinusoidally modulated spatial stimulus. *J Opt Soc Am*. 1965;55:1154–1157.
7. Atchison DA, Woods RL, Bradley A. Predicting the effects of optical defocus on human contrast sensitivity. *J Opt Soc Am A*. 1998;15:2536–2544.
8. Strang NC, Atchison DA, Woods RL. Effects of defocus and pupil size on human contrast sensitivity. *Ophthalmic Physiol Opt*. 1999;19:415–426.
9. Woods RL, Strang NC, Atchison DA. Measuring contrast sensitivity with inappropriate optical correction. *Ophthalmic Physiol Opt*. 2000;20:442–451.
10. Anderson AJ, Johnson CA. Mechanisms isolated by frequency-doubling technology perimetry. *Invest Ophthalmol Vis Sci*. 2002;43:398–401.
11. Johnson CA, Cioffi GA, Van Buskirk EM. Frequency doubling technology perimetry using a 24-2 stimulus presentation pattern. *Optom Vis Sci*. 1999;76:571–581.
12. Spry PG, Johnson CA. Within-test variability of frequency-doubling perimetry using a 24-2 test pattern. *J Glaucoma*. 2002;11:315–320.
13. Mayer MJ, Spiegler SJ, Ward B, Glucs A, Kim CBY. Preliminary evaluation of flicker sensitivity as a predictive test for exudative age-related maculopathy. *Invest Ophthalmol Vis Sci*. 1992;33:3150–3155.
14. Mayer MJ, Spiegler SJ, Ward B, Glucs A, Kim CBY. Foveal flicker sensitivity discriminates ARM-risk from healthy eyes. *Invest Ophthalmol Vis Sci*. 1992;33:3143–3149.
15. Mayer MJ, Spiegler SJ, Ward B, Glucs A, Kim CBY. Mid-frequency loss of foveal flicker sensitivity in early stages of age-related maculopathy. *Invest Ophthalmol Vis Sci*. 1992;33:3136–3142.
16. Phipps JA, Guymer RH, Vingrys AJ. Temporal sensitivity deficits in patients with high-risk drusen. *Aust N Z J Ophthalmol*. 1999;27:265–267.
17. Vingrys AJ, Pesudovs K. Localized scotomata detected with temporal modulation perimetry in central serous chorioretinopathy. *Aust N Z J Ophthalmol*. 1999;27:109–116.
18. Parker A. The effects of temporal modulation on the perceived spatial structure of sine-wave gratings. *Perception*. 1983;12:663–682.
19. McKendrick AM, Anderson AJ, Johnson CA, Fortune B. Appearance of the frequency doubling stimulus at threshold, in normals and glaucoma patients. *Invest Ophthalmol Vis Sci.* 2003;44:1111–1116.
20. King-Smith PE, Grigsby SS, Vingrys AJ, Benes SC, Supowit A. Efficient and unbiased modifications of the QUEST threshold method: theory, simulations, experimental evaluation and practical implementation. *Vision Res*. 1994;34:885–912.
21. Bailey IL, Lovie JE. New design principles for visual acuity letter charts. *Am J Optom Physiol Opt*. 1976;53:740–745.
22. Anastasi M, Brai M, Lauricella M, Geracitano R. Methodological aspects of the application of the Naka-Rushton equation to clinical electroretinogram. *Ophthalmic Res*. 1993;25:145–156.
23. Press WH, Teukolsky SA, Vetterling WT, Flannery BP. *Numerical Recipes in C. The Art of Scientific Computing.* 2nd ed. Cambridge, UK: Cambridge University Press; 1992:659–661.
24. Kogure S, Membrey WL, Fitzke FW, Tsukahara S. Effect of decreased retinal illumination on frequency doubling technology. *Jpn J Ophthalmol*. 2000;44:489–493.
25. Anderson RS, McDowell DR, Ennis FA. Effect of localized defocus on detection thresholds for different sized targets in the fovea and periphery. *Acta Ophthalmol Scand*. 2001;79:60–63.
26. Heuer DK, Anderson DR, Feuer WJ, Gressel MG. The influence of refraction accuracy on automated perimetric threshold measurements. *Ophthalmology*. 1987;94:1550–1553.
27. Spry PGD, Johnson CA, McKendrick AM, Turpin A. Variability components of standard automated perimetry and frequency-doubling technology perimetry. *Invest Ophthalmol Vis Sci*. 2001;42:1404–1410.
28. Goldstick BJ, Weinreb RN. The effect of refractive error on automated global analysis program G-1. *Am J Ophthalmol*. 1987;104:229–232.
29. Smith SD, Katz J, Quigley HA. Effect of cataract extraction on the results of automated perimetry in glaucoma. *Arch Ophthalmol*. 1997;115:1515–1519.
30. Gillies WE, Brooks AM. Effect of lens opacity on the glaucomatous field of vision. *Aust N Z J Ophthalmol*. 1998;26:S19–S21.

31. Morales J, Weitzman ML, González de la Rosa M. Comparison between Tendency-Oriented Perimetry (TOP) and Octopus threshold perimetry. *Ophthalmology*. 2000;107:134–142.
32. Maeda H, Nakuara M, Negi A. New perimetric threshold test algorithm with dynamic strategy and tendency oriented perimetry (TOP) in glaucomatous eyes. *Eye*. 2000;14:747–751.
33. González de la Rosa M, Mesa F, Arteaga V, González-Hernández M. Second generation of the Tendency Oriented Perimetry algorithm: TOP plus. In: Wall M, Mills RP, eds. *Perimetry Update 2000/2001. Proceedings of the XIVth International Perimetric Society Meeting.* Halifax (NS), Canada, September 6–9, 2000. The Hague, The Netherlands: Kugler Publications; 2001:155–159.
34. Winn B, Whitaker D, Elliot DB, Phillips NJ. Factors affecting light-adapted pupil size in normal human subjects. *Invest Ophthalmol Vis Sci*. 1994;35:1132–1137.
35. Nio YK, Jansonius NM, Fidler V, Geraghty E, Norrby S, Kooijman AC. Age-related changes of defocus-specific contrast sensitivity in healthy subjects. *Ophthalmic Physiol Opt*. 2000;20:323–334.