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ORIGINAL ARTICLE

Development of a Critical Flicker/Fusion Frequency Test for Potential Vision Testing in Media Opacities

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ABSTRACT: *Purpose.* To determine whether critical flicker/fusion (CFF) thresholds fulfill the criteria for a potential vision test (PVT) by being unaffected by media opacity yet affected by retinal disease. *Methods.* CFF thresholds for three different stimulus sizes (0.5, 1.0, and 1.5°) were measured in 72 patients (mean age, 78.43 ± 7.07 years) comprising 31 subjects with media opacity, 21 with macular disease, and 20 with pseudophakia. *Results.* There were no statistically significant differences between CFF values from the media opacity and the pseudophakia groups for any target size ($p > 0.10$). However, CFF values were significantly lower in patients with macular disease for all the target sizes ($p < 0.05$). Analysis of a subset of six subjects with media opacity and seven subjects with macular disease and visual acuity of 20/200 or worse showed the media opacity group still had similar CFF values as the pseudophakia group and had significantly higher CFF than the macular disease group. *Conclusions.* CFF testing is shown to fulfill the requirements for a PVT and may prove to be particularly useful for patients with dense media opacity. (Optom Vis Sci 2004;81:905–910)

Key Words: critical flicker/fusion frequency, media opacity, age-related macular degeneration (ARMD), potential vision test

Cataract is the most common cause of visual impairment in the elderly population.[1] Improved visual acuity (VA), functional vision, and quality of life are achieved in most cases with modern cataract surgery and intraocular lens implantation.[2, 3] However, when associated with comorbid eye disease, particularly age-related macular degeneration (ARMD), poor visual outcome and patient disappointment may occur postoperatively.[4] Patients with cataract and comorbid eye disease can provide the clinician with a difficult decision as to whether to recommend cataract surgery when the contribution of each disease to the patient's visual disability is not clear. Moreover, some controversy exists as to the benefits of cataract surgery among such patients.[4–9] Potential vision tests (PVT's) have been developed to predict visual function behind cataracts and other media opacity. However, a major review by the Agency for Health Care Policy and Research (AHCPR) concluded that the usefulness of existing PVT's was limited and that they were particularly poor at predicting the outcome of cataract surgery in eyes with dense opacity and acuity of 20/200 [1.0 logarithm of the minimum angle of resolution (logMAR) equivalent] or worse or when macular disease is present but the posterior pole cannot be observed.[10]

The purpose of the present study was to investigate the possibility of critical flicker/fusion frequency (CFF) being used as a PVT. Measurements of flicker/fusion for the diagnosis of eye disease have been reported for more than a century. Braunstein[11] was one of the first to investigate CFF in cases of optic atrophy, optic neuritis, amblyopia, glaucoma, and chorioretinitis. Since then, flicker measurements have been shown to be sensitive to the presence of retinal or optic nerve diseases when other clinical tests remain unaffected.[12–16] Similar measurements of flicker sensitivity, such as flicker sensitivity in electroretinographic measurements,[17] contrast sensitivity function (or de Lange curve),[18] and flicker perimetry,[19, 20] have also been shown to be sensitive to retinal disease. Havener and Henderson[21] and Simonson and Wohlrabe[14] measured CFF data in patients with cataract to determine whether the CFF was sensitive to cataract and could be used as a measure of its development. Although CFF, measured with a low luminance target, was found to be depressed with dense lens

opacities, no difference in CFF was found between a group of 238 normal patients and 18 patients with early cataract as long as the luminance of the CFF target was relatively high.[14] Other workers found that flicker perimetry appears to be independent of the presence of media opacities such as cataracts,[19, 22] and CFF measurements with most target sizes were found to be resistant to optical blur.[19, 23, 24] However, although the CFF has been shown to be somewhat resistant to the effects of media opacity and refractive blur and yet sensitive to retinal/neural disease, it has never previously been proposed as a PVT.

Several factors have previously been shown to increase the CFF; these include increased mean luminance, increased target size, and increased luminance contrast.[25] We chose stimulus conditions likely to be resistant to optical blur to help distinguish between visual loss caused by media opacities and neural disease. To maximize penetration of media opacities, the stimulus luminance was increased to its brightest available value, and a red stimulus was selected to minimize the effect of short wavelength absorption from the aging crystalline lens and nuclear cataract.[26]

It has previously been shown that the sensitivity to flicker varies with retinal location (i.e., depending on the retinal elements stimulated), and this in turn depends on the luminance and the area of the stimuli used.[27] Granit and Harper[28] suggested that to ensure that CFF with central fixation is higher than CFF with peripheral fixation, the stimuli size should be limited to 2° visual angle. Thus, small targets giving visual angles of 0.5, 1.0, and 1.5° were chosen to specifically test foveal function (i.e., foveal flicker fusion). The 0.5° stimulus was used to measure the foveal response because it represents the only totally rod-free region in the retina.[29] Douthwaite et al.[30] found that this target size produced a CFF maximum at the fovea, whereas a bright target larger than about 2° will produce its highest CFF values about 10 to 15° from fixation. Thus, although larger target sizes will produce an increase in the CFF threshold, the CFF maximum will shift to the mid-periphery, and the use of too large a target size should be avoided because any local foveal defect could be masked by an unaffected surrounding retina.

METHODS

Subjects

Subjects were recruited from the Eye Unit at the Leeds General Infirmary, Leeds, U.K. The study was approved by the Hospital Ethical Committee and followed the Declaration of Helsinki for research involving human subjects. Inclusion criteria were age $\geq$60 years, pseudophakia with otherwise normal healthy eyes and VA better than 0.2 logMAR (about 20/30 Snellen), or media opacity (either cataract or corneal opacity) with otherwise normal healthy eyes and VA worse than 0.2 logMAR, or macular disease (ARMD or other) with clear media and VA worse than 0.2 logMAR. Exclusion criteria included subjects with a combination of media opacities and macular disease, the inability to speak English sufficiently to be instructed to perform the tests, insufficient mental ability to perform the tests, being unable to see any of the three target sizes, and any physical disability that would make it arduous to perform the tests (e.g., wheelchair user).

Seventy-two subjects (37 women) were included in the study (mean age, 78.43 $\pm$ 7.07 years). Five patients with macular degeneration were excluded from the study because they were unable to see any of the three CFF targets (VA's were 0.78, 1.34, 1.42, 1.60, and 1.60 logMAR; Snellen, about 20/120 to 20/800). Twenty-one subjects had macular disease (19 ARMD, 1 myopic degeneration, and 1 macular hole); 31 had media opacity (26 cataract, 3 cataract plus Fuchs' dystrophy with corneal decompensation, and 2 pseudophakic bullous keratopathy); and 20 had pseudophakia with normal VA (0.05 $\pm$ 0.08 logMAR; Snellen, 20/22). In patients with both eyes that fitted the inclusion and exclusion criteria, the eye with worst VA was chosen. The three groups were similar for age [$F(2,70) = 0.845$; $p > 0.10$]: macular disease (79.0 $\pm$ 8.7 years), media opacity (79.0 $\pm$ 6.0 years), and pseudophakia (77.0 $\pm$ 6.3 years). There was also no significant difference in VA between the media opacity (0.64 $\pm$ 0.44 logMAR; Snellen, 20/87) and macular disease groups (0.81 $\pm$ 0.41 logMAR; Snellen, 20/129; $p > 0.10$).

Procedure

The stimulus consisted of a red, light-emitting diode (LED) of peak wavelength 625 nm capable of emitting a frequency range from 1 to 86 Hz. The circular stimulus was 10 mm in diameter and subtended visual angles of 0.5, 1.0, and 1.5° at viewing distances of 114.6 cm, 57.3 cm, and 38.2 cm, respectively. The LED mean luminance was 513 cd/m^2 (the brightest available at the time to aid penetration of media opacities), and the average luminance of the surrounding screen was 94 cd/m^2. The function generator produced a sine wave with an equal light/dark phase and a modulation depth of 98%. The LED source was mounted at the center of a matte white rectangular screen (50 $\times$ 50 cm). Two diagonal red lines, which crossed at the LED, were fixed to the screen and were used to help observers, particularly those with macular disease, maintain central fixation. The stimulus could be presented either continuously or as a 2-s presentation. The continuous mode was used for demonstration purposes, and the 2-s presentation was used for the CFF measurement. The CFF apparatus was calibrated using a light cell and an oscilloscope to construct a calibration table in steps of 1 Hz. Measurements were taken monocularly on one eye of each subject, with any refractive error corrected and using natural pupils. The observer was asked to look directly at the center of the red light. To familiarize the subject with the appearance of the target, an obviously flickering stimulus (10 to 20 Hz depending on the subject's VA) was initially presented to illustrate the appearance of flicker. The frequency of flicker was then increased until the frequency was high enough to produce the appearance of a steady light (about 60 Hz). The transition point where the intermittent light source appears to be a steady light or the steady light appears to flicker is the CFF threshold.

All the CFF thresholds were obtained using a 2-s presentation stimulus to avoid local adaptation to the flicker.[25, 31, 32] A staircase method collecting three ascending and three descending presentations (with 2-Hz steps) in an alternating order was used to find the thresholds. The fusion threshold was recorded for the ascending runs with the flicker threshold recorded for the descending runs. The mean of the six recordings thus gave the flicker/fusion threshold. The procedure was randomly repeated for the three stimulus sizes analyzed (0.5, 1.0, and 1.5° visual angle). Additional working distance lenses were provided for the three test distances (+0.75

DS, +1.50 DS, and +2.25 DS, respectively). The testing duration was about 10 min to minimize fatigue.[30] Before CFF testing, VA was measured using the Bailey-Lovie logMAR chart at a mean luminance of 160 cd/m^2 using a by-letter scoring system.[33] The diagnoses were established by ophthalmologic examination.

The CFF for the groups were compared by analysis of variance with *post hoc* (Fisher) testing. Optimal target size for differentiation between the opacity and the subjects with macular disease was determined by means of a receiver-operating characteristic (ROC) analysis using MedCalc software (Mariakerke, Belgium). The relationship between VA and CFF was explored using linear regression analysis. All the statistical analyses were performed on Statview 5.0.1 (SAS Institute, Cary, NC).

The intrasubject repeatability of the flicker/fusion threshold for the 1.5° stimulus was obtained by comparison of the first and third reading in the ascending and descending runs on a single flicker/fusion measurement.

The effects of pupil dilation were investigated in a separate study in which CFF thresholds were measured before and after pupil dilation with 1% tropicamide and 2.5% phenylephrine using a 1.5° stimulus. Twenty-seven subjects with cataract only or cataract associated with some degree of macular disease were included in the dilation study (mean age, 75.5 ± 8.4 years; mean VA, 0.43 ± 0.30 logMAR).

RESULTS

Two subjects with macular disease could not see the 0.5° target, and one could not see the 1.5° target. One subject with cataract was unable to see the 0.5° target. Their data were not included in any of the analyses. Fig. 1 plots mean ± 1 SD CFF threshold against target size for the three groups. There was a statistically significant difference between groups in the CFF thresholds for the 0.5° [$F(2,66) = 4.54$; $p < 0.02$], 1.0° [$F(2,69) = 9.77$; $p < 0.005$], and 1.5° [$F(2,68) = 10.93$; $p < 0.0001$] targets. *Post hoc* analysis indicated that there were no significant differences in the CFF thresholds between the media opacity group and the pseudophakia group for any of the three target sizes ($p > 0.10$). However, significant differences existed between the macular disease group and the pseudophakia and the media opacity groups for all the target sizes (all $p < 0.05$).

A significant correlation between CFF and VA was found in the subjects with macular disease ($p < 0.01$) for all the target sizes, with coefficients of determination (r^2) of 0.33 (0.5°), 0.36 (1.0°), and 0.36 (1.5°). However, the coefficients of determination between the CFF and VA in the opacity group were only 0.03, 0.09, and 0.04 for the 0.5°, 1.0°, and 1.5° targets (all $p > 0.10$). The relationship between CFF and VA for the media opacity group is shown in Fig. 2A and for the macular disease group in Fig. 2B.

The above analysis indicated that CFF measurements were unaffected by media opacity and yet were sensitive to changes in VA caused by macular disease. However, this only established significant differences between the macular disease and media opacity group means. The analysis did not indicate the usefulness of this test paradigm as a PVT for individual subjects. To assess the ability of the CFF to discriminate between media opacity and macular disease on an individual basis, a ROC curve was plotted for the three target sizes (Fig. 3). Sensitivity (the proportion of true positives) was determined as the proportion of CFF values below the cutoff value among the subjects with macular disease, and specificity (the proportion of true negatives) was determined as the pro-

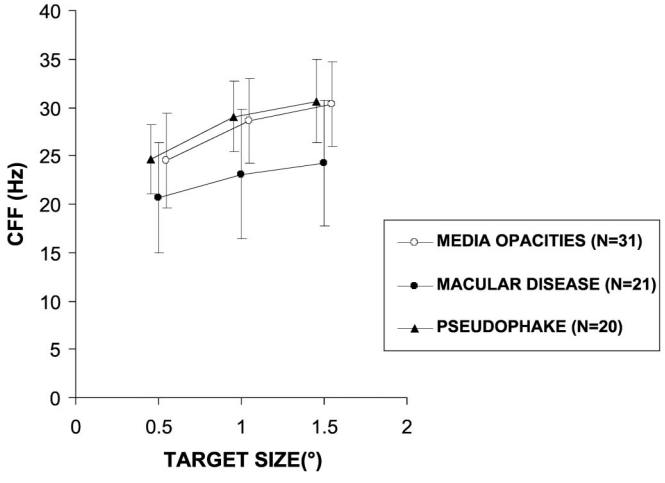

FIGURE 1.
Critical flicker fusion (CFF) threshold means (±1 SD) plotted for three target sizes from groups of subjects with media opacity, macular disease, and pseudophakia. The target size values are offset to avoid overlap of error bars.

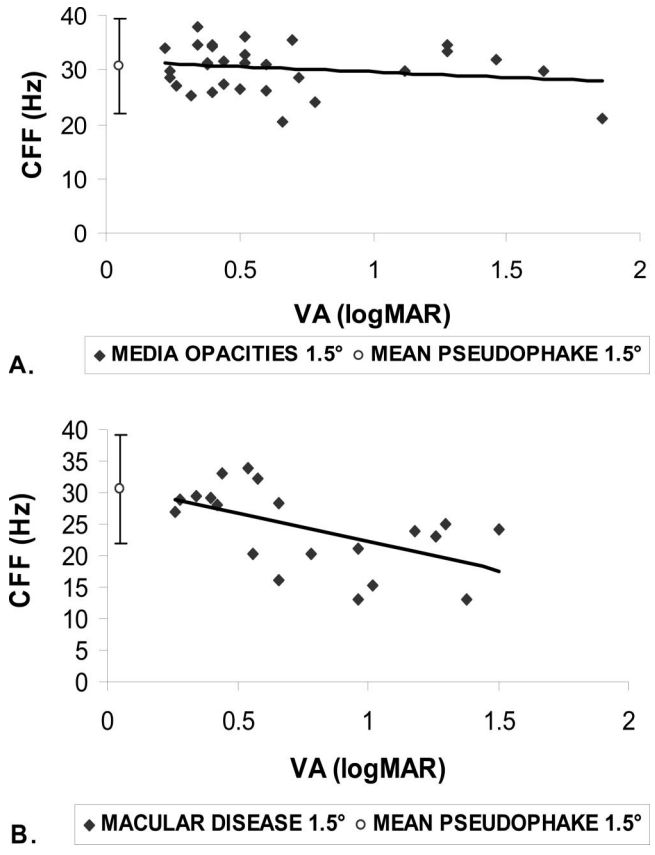

FIGURE 2.
Scatterplot showing linear regression of critical flicker/fusion (CFF) against visual acuity (VA) in the media opacity group (1.5° visual angle; A) and in the macular disease group (1.5° visual angle; B). For comparison purposes, the mean ±2 SD from the pseudophakia group is provided.

portion of CFF values above the cutoff value among the media opacity group. The points in the top left corner of the graph would represent the highest sensitivity and specificity and therefore represented the best criteria to differentiate between macular dysfunction and media opacity subjects. Fig. 3 suggests that the 1.5° target size showed the highest sensitivity and specificity.

ROC plots offer an excellent visual comparison of discriminative ability, and this can be quantified using the area under the curve (AUC) for each of the target size. The AUC was 0.79 for the 1.5° target size [95% confidence interval (CI), 0.66 to 0.90] compared with 0.75 for the 1.0° target size (95% CI, 0.61 to 0.86) and 0.70 for the 0.5° target size (95% CI, 0.56 to 0.82). All the target sizes were shown to be statistically significantly different than random level performance (i.e., where AUC = 0.50). In addition, pair-wise comparisons showed that the 0.5° target size curve was significantly different to the 1.5° target size curve ($p < 0.05$), but no other significant differences were found. On this basis, for further investigations, we decided to use the 1.5° target size because it showed the greatest AUC.

The intrasubject repeatability of the flicker/fusion threshold was evaluated for the 1.5° target size by comparing the first and last readings of three ascending and three descending measurements. The intrasubject repeatability was assessed in terms of coefficient of repeatability, which represents the 95% CI for any discrepancy between test and retest data.[34] For normally distributed data, the coefficient of repeatability is obtained by calculating the SD of the difference between the repeated measures and multiplying this by 1.96. The coefficient of repeatability was ±2.92 Hz for the macular disease group, ±3.23 Hz for the pseudophakia group, and ±1.78 Hz for the media opacity group.

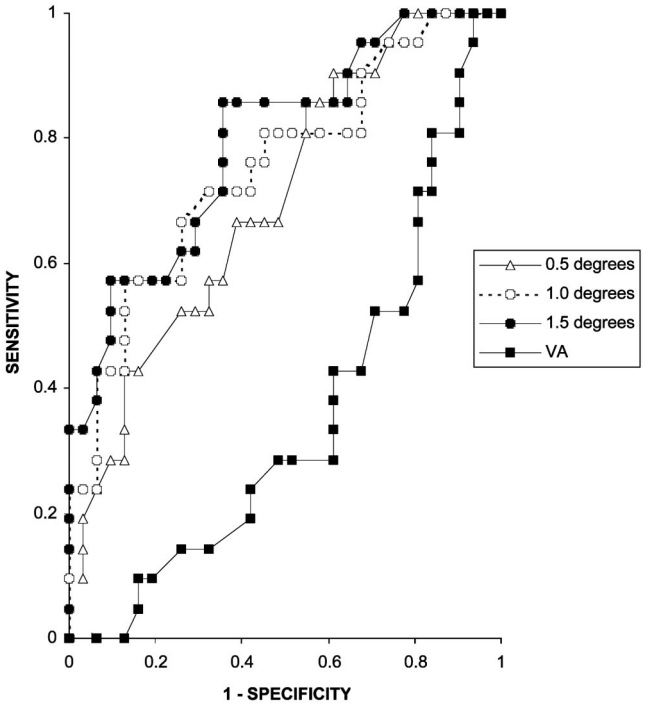

FIGURE 3.

Receiver-operating characteristic (ROC curve) of sensitivity vs. (1-specificity) for 31 subjects with media opacity and 22 subjects with macular disease for critical flicker fusion (CFF) thresholds at three target sizes. The ROC curve for visual acuity (VA) is shown for comparison purposes.

The findings from the separate study in which we investigated the effects of pupil dilation on CFF measurement indicated that CFF thresholds increased only by an average of 3.2 Hz with the increased pupil size (38.1 ± 3.7 Hz undilated vs. 41.3 ± 3.8 Hz dilated). Thus, pupil dilation achieves only a modest increase in the CFF.

The AHCPR concluded that existing PVT's could predict postoperative outcome reasonably well in eyes with a preoperative vision of better than 20/200 (1.0 logMAR equivalent), but none of them provided an accurate estimate of visual outcome when preoperative vision was 20/200 or worse.[10] For this reason, we assessed the 1.5° CFF results from a small subgroup of subjects with VA worse than 20/200. There were six subjects with media opacities (mean VA, 1.44 ± 0.27 logMAR; Snellen, 20/550; mean age, 77.3 ± 7.17 years) and seven subjects with macular disease (mean VA, 1.30 ± 0.17 logMAR; Snellen, 20/400; mean age, 78 ± 7.7 years). There was no statistically significant difference between the CFF values from the subjects with pseudophakia and the six subjects with dense media opacities ($p > 0.10$). However, a highly statistically significant difference was found between the macular disease group and the media opacity and the pseudophakia group [$F(2,29) = 11.1$; $p < 0.001$] as seen in Fig. 4.

DISCUSSION

Higher CFF results were found with increased target size for all the subject groups. Moreover, there were no significant differences in CFF thresholds between the media opacity group and the pseudophakia group for any of the three target sizes (Fig. 1), and there was no obvious effect on CFF when media opacities induced a reduction in VA (Fig. 2A). This confirms previous findings that the CFF is unaffected by early cataracts[14] and extends this finding for a high luminance target to include dense cataracts and corneal opacities. The macular disease group had significantly lower thresholds than either the pseudophakia or the media opacity

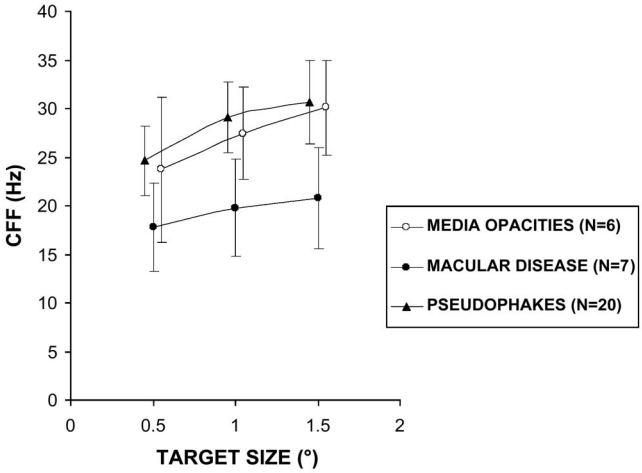

FIGURE 4.

Critical flicker fusion (CFF) threshold means (±1 SD) plotted for three target sizes from groups of subjects with media opacity and macular disease and visual acuity of 20/200 or worse. Data from the subjects with pseudophakia and good visual acuity are shown for comparison. The target size values are offset to avoid overlap of error bars.

groups (Fig. 1), and the CFF data from the macular disease group displayed a trend that demonstrated a reduction of CFF with a reduction of VA (Fig. 2B). This confirms previous findings of reduced CFF in macular disease.[11, 14–16] These results are also similar to the findings with flicker perimetry in which temporal contrast sensitivity measurements are shown to be independent of lens opacities and yet useful in the detection of retinal disease.[22]

Although the present investigation does not include any subject with both media opacities and macular disease, these results predict that decreased flicker/fusion thresholds in such subjects may be caused by the presence of macular disease because the CFF measurement appears to be unaffected by the presence of media opacities (up to 1.6 logMAR). In such cases, the decrease in the CFF measurement would be proportional to the severity of macular disease. This hypothesis will be investigated in future studies.

For all three target sizes, CFF testing discriminates between the media opacity and macular disease shown by the ROC analysis (Fig. 3), and the AUC analysis indicates that the 1.5° target size best discriminates between subjects with media opacity and macular disease. Given this, and that larger flickering sources are more resistant to refractive defocus than smaller ones,[35] we recommend the use of the 1.5° visual angle target size for PVT. Although the data show significant group differences in CFF between the media opacities and macular disease groups, there is a degree of overlap between the two groups (Fig. 1). This suggests that our prototype CFF PVT had moderate predictive ability regarding potential vision in early and moderate cataract. The data are much more promising for dense media opacities. All the subjects with media opacity were able to see the 1.5° CFF target. This included a subject with bullous keratopathy who had the worst VA in the study (1.86 logMAR; about 20/1450). The CFF's of the subjects with dense media opacity were high (mean, 31.9 ± 2.2 Hz, excluding the subject with bullous keratopathy and 1.86 logMAR VA who had a CFF of 21 Hz). All the CFF's of the seven subjects with macular disease with VA worse than 1.0 logMAR (20/200) who could see the target were below the 95% confidence limits of the media opacity data (range, 13 to 24.2 Hz).

We suggest that differences in stimulus size, stimulus luminance, adaptation, and stimulus generation may account for the discrepancy found between this study and previous investigations that found reductions in CFF with dense cataract.[14, 21] In subsequent studies, we intend to use even higher LED luminance levels to improve penetration of dense opacities. Earlier investigations using the standard PVT's, the potential acuity meter and laser interferometer, have shown a somewhat limited clinical applicability mainly because of the high rate of false-negative (i.e., underestimate of postoperative visual outcome) results[10] caused by the limited capability of the standard techniques to bypass dense media opacities. Thus, the results of the present investigation appear to overcome previous limitations by showing a good penetration of dense media opacities, although increased numbers of subjects with dense media opacities are required to validate the suitability of this technique.

Another advantage of CFF measurement over some of the standard PVT's is that pupil dilation is not required. Pupil dilation was found to produce only a slight increase in the CFF threshold in agreement with previous investigations.[36] Therefore, we recommend that the flicker/fusion measurement described in this investigation is made without pupil dilation. Because of the slight increase in CFF with dilation, it is advisable to avoid comparison between dilated and undilated measurements.

One of the limitations of the proposed test is the examiner's inability to monitor fixation during data collection, especially when a retinal condition is present. Therefore, its successful implementation relies on the careful instruction before its measurement and the use of two diagonal lines to assist steady fixation in subjects with a central scotoma.

We acknowledge that the present findings only represent the first step toward the development of flicker/fusion as a PVT, and further investigation is required to verify predictive ability as compared with the standard PVT techniques. The promising results have encouraged us to conduct further experiments on its suitability as a PVT before and after cataract removal compared with other standard PVT's, and this research is ongoing.

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