

Original

Frequency Doubling Technology Perimetry in Age-related Macular Degeneration

Shwu-Jiuan Sheu^{1,3}
Ying-Ying Chen¹
Li-Chen Chou¹
Tsung-Tien Wu¹
Kwok-Kei Cheng²

¹Department of Ophthalmology,

²Department of Surgery, Kaohsiung Veterans
General Hospital, Kaohsiung; and

³National Yang-Ming University School of
Medicine, Taipei, Taiwan, R.O.C.

Key Words

age-related macular degeneration;
frequency doubling technology
perimetry;
macula;
visual acuity

Background. The role of frequency doubling technology perimetry (FDT) in glaucoma has been promising in terms of speed and simplicity as well as in its high sensitivity and specificity compared to conventional automatic perimetry. In this study, we investigated the possible role of FDT in exudative type age-related macular degeneration (ARMD).

Methods. FDT using full-threshold C-20 mode was performed in patients with ARMD. The macula was classified into 3 zones by the distance from the fovea center (zone I: central 1°, zone II: central 3° except zone I, zone III: central 5° except zones I & II). The lesion was scored into 3 ranks by the area ratio of involvement in each zone. The retinal scores, visual acuity and dis ease du ration were compared with the FDT scores of the central target, which was graded into 5 ranks according to the probability level of abnormal points on total deviation plots using Spearsman's rank correlation method.

Results. Measurements from 32 eyes (30 patients) with exudative ARMD were collected. The FDT scores of the central target correlated significantly with the lesion scores in zone III ($p = 0.033$), but not with the lesion scores in central 3° (zone I: $p = 0.383$, zone II: $p = 0.077$). Visual acuity was weakly correlated with the FDT scores of the central target ($p = 0.022$), and the lesion scores in zone III ($p = 0.038$), but strongly correlated with the lesion scores in zone I and zone II ($p < 0.001$). The FDT scores of the central target were within normal limit in 20 eyes.

Conclusions. Our results suggest that FDT using full-threshold C-20 mode is not sensitive enough for the detection of small macular lesions in ARMD. Therefore, it might not be a useful functional evaluation in ARMD. Further modification of the central target of FDT is necessary to detect small macular lesions in ARMD.

[Chin Med J (Taipei) 2002;65:435-440]

Age-related macular degeneration (ARMD) is one of the leading cause of blindness in developed countries, and is getting more and more important as the ratio of aged people in the general population is growing.¹⁻¹¹ In the treatment of ARMD, quantitative functional assessment of the visual field defect caused by ARMD is critical. Conventional automated perimetry

and scanning laser ophthalmoscope fundus perimetry are currently used for functional assessment before and after treatment.¹²⁻¹⁶ However, there are several disadvantages that limit their wide spread and routine use. The disadvantages include time-consuming procedures, high cost of equipment, complex set-up and operation, patient fatigue and lack of transportability.

Received: September 21, 2001. Accepted: April 29, 2002.

Correspondence to: Shwu-Jiuan Sheu, MD, Department of Ophthalmology, Kaohsiung Veterans General Hospital, 386, Ta-Chung 1st Road, Kaohsiung 813, Taiwan. Fax: +886-7-346-8216; E-mail: sjsheu@isca.vghks.gov.tw

Frequency doubling technology perimetry (FDT) is based upon a unique and innovative advance in visual field stimulus technology called Frequency Doubling.¹⁷⁻²³ It is outstanding in speed and simplicity, which makes perimetry less intimidating for patients. Reports had shown that it can detect glaucomatous visual field loss with high sensitivity and specificity compared to conventional automated perimetry.^{24,25} Its potential in quantifying pathologic change looks quite promising as well.^{26,27} Will it be helpful in the field of ARMD in which visual field defect is also regarded as an important pathognomic sign? In our previous study, which scored the fundus according to the area ratio of lesion alone, we concluded the FDT might be a useful and simple technique for functional evaluation in rhegmatogenous retinal detachment, but had limited value in ARMD.²⁸ The purpose of this study was to re-evaluate the role of FDT in exudative type ARMD, which is the target of treatment in ARMD, with a different scoring system according to the distance from the fovea center. Other possible relating factors, including visual acuity and disease duration, were also analyzed.

Methods

FDT using full threshold C-20 mode was performed in patients with exudative ARMD, confirmed by fundus fluorescein angiogram. Those who had significant cataract which was expected to interfere with the visual field (nuclear sclerosis: ++ or more, posterior subcapsular opacity: prominent, 2 mm in diameter or more, partial, 4 mm in diameter or more), history of glaucoma, diabetes and other ocular diseases, were excluded. All patients received detailed ophthalmological examination, including visual acuity, slit lamp biomicroscopy, intraocular pressure, indirect ophthalmoscopy, contact lens biomicroscopy, and fundus fluorescein angiogram.

The FDT perimeter was a prototype of Welch Allyn (Skaneateles, NY)/Humphrey Systems FDT perimeter (Humphrey Systems, Dublin, CA; FDP/Vfver: 2.60/1.00). Patients tested with the

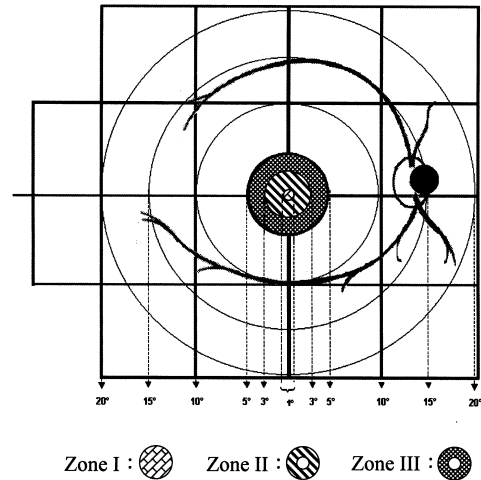


Fig. 1. Correlation of the retinal topographic construction and the total deviation plots in frequency doubling technology perimetry.

FDT perimeter (full-threshold test C-20 mode) were presented with 16 targets arranged in a 4-by-4 grid, plus 1 target in the macula. Each peripheral square is 10 degrees \times 10 degrees, and the central stimulus is a 5-degree circle. The FDT for threshold test is performed by determining the contrast threshold for each of the target locations in the display. A 0.25 cyc/deg sinusoidal grating undergoing 25 Hz counterphase flicker (contrast reversal of light and dark bars, 50 times/sec) was generated on the monitor for all stimuli, except for the central 10° pattern, which used a 0.5 cyc/deg sinusoidal grating with 25 Hz counterphase flicker. The visual field indices mean deviation and pattern standard deviation, and their significance, are included along with a raw data plot in decibels. Other reliability data, such as fixation errors, false positives and negatives, are also provided. According to the correlation of the retinal topographic construction and the total deviation plots in FDT, the macula was classified by the distance from the fovea center (Fig. 1). Zone I represented central 1°, zone II represented central 3° except zone I, and zone III represented central 5° except zone I & II. The lesion on fluorescein angiogram was scored into 3 ranks by the area ratio of involvement in each zone (1: free of lesion, 2: less than half, 3: more than half). As the

threshold level on FDT presents as decibels (dB), but not actually the difference in the age-matched groups, probability is more reliable data to compare between different individuals. Our previous experience showed that a probability between 2% and 5% could be normal variation in an aged group.²⁹ We graded the FDT scores of the central target into five ranks according to the probability level of abnormal points on total deviation plots in FDT full threshold C-20 mode (1: >2%, 2: <2%, 3: <1%, 4: <0.5%, 5: max). The visual acuity was scored into 4 ranks (rank 1 ≥ 6/12, 6/12 > rank 2 ≥ 6/20, 6/20 > rank 3 ≥ 6/60, rank 4 < 6/60). The retinal scores, visual acuity and disease duration were compared with the FDT scores of the central target using Spearman's rank correlation method.

Results

Measurements from 32 eyes (30 patients) with exudative ARMD were collected., including 27 men and 3 women. The 30 patients had a mean (± SD) age of 70.83 ± 7.69 years, with a range from 50 to 85 years. The diagnosis was made by fluorescein angiography. The initial visual acuity ranged from 1/200 to 20/20. The disease duration was eligible in 30 eyes (1-108 months). The FDT scores of the central target correlated significantly with the presence of macular lesions in zone III ($r = 0.329, p = 0.033$), but not with the presence of lesions in central 3° (zone I, $r = 0.055, p = 0.383$; zone II, $r = 0.259, p = 0.077$) (Fig. 2). Visual acuity weakly correlated with the FDT scores of the central target ($r = 0.360, p = 0.022$), and the lesion scores in zone III ($r = 0.319, p = 0.038$), but strongly correlated with the lesion scores in zone I and zone II ($p < 0.001$) (Fig. 3).

No significant correlation was found between disease duration and central visual field defect on FDT ($r = -0.060, p = 0.376$), yet correlation existed between disease duration and best corrected visual acuity ($r = -0.472, p = 0.004$). The FDT scores of the central target were within normal limit in 20 eyes. Take for example, Case 8, he had a small central macular lesion in his right eye, whose lesion score was zone I:3, zone

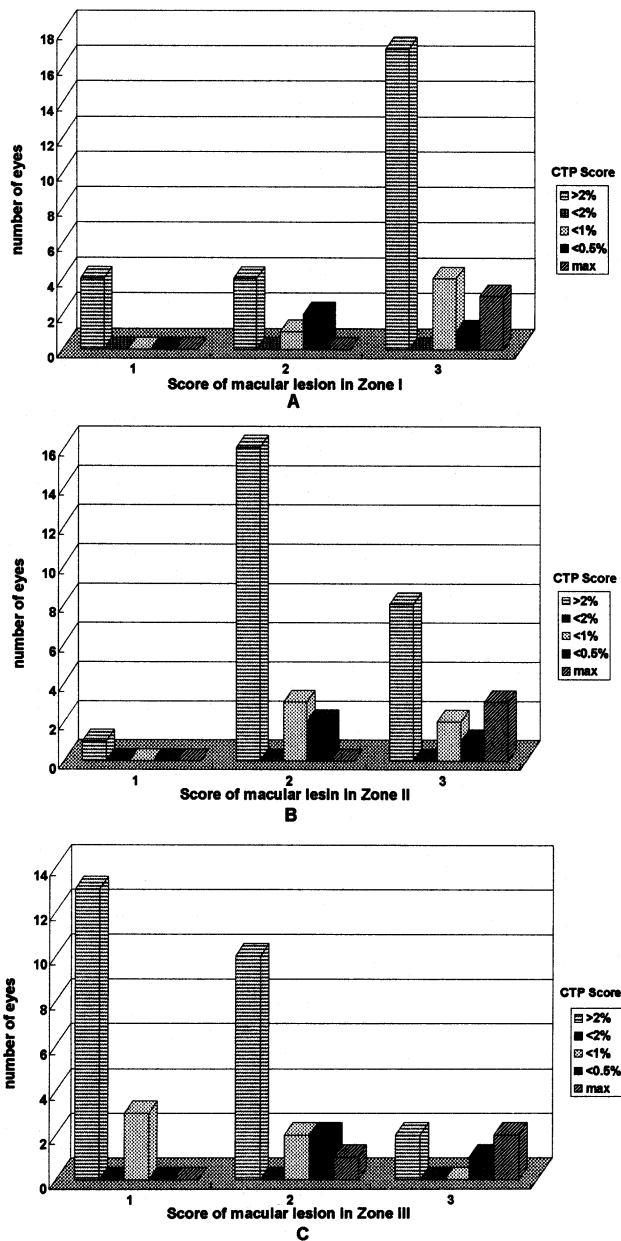


Fig. 2. Correlation between FDT score on central target (CTP) and the score of macular lesion in different zones. A. zone I, $p = 0.383$; B. zone II, $p = 0.077$; C. zone III, $p = 0.033$. The FDT scores of the central target correlated significantly with the presence of lesions in zone III, but not with the presence of lesions in central 3°. Fig. 2A shows that although zone I was involved over 50%, the CTP scores were still normal in over two-thirds of the eyes.

II:2, zone III:1, yet there was no abnormal point on FDT in spite of 6/60 vision (Fig. 4).

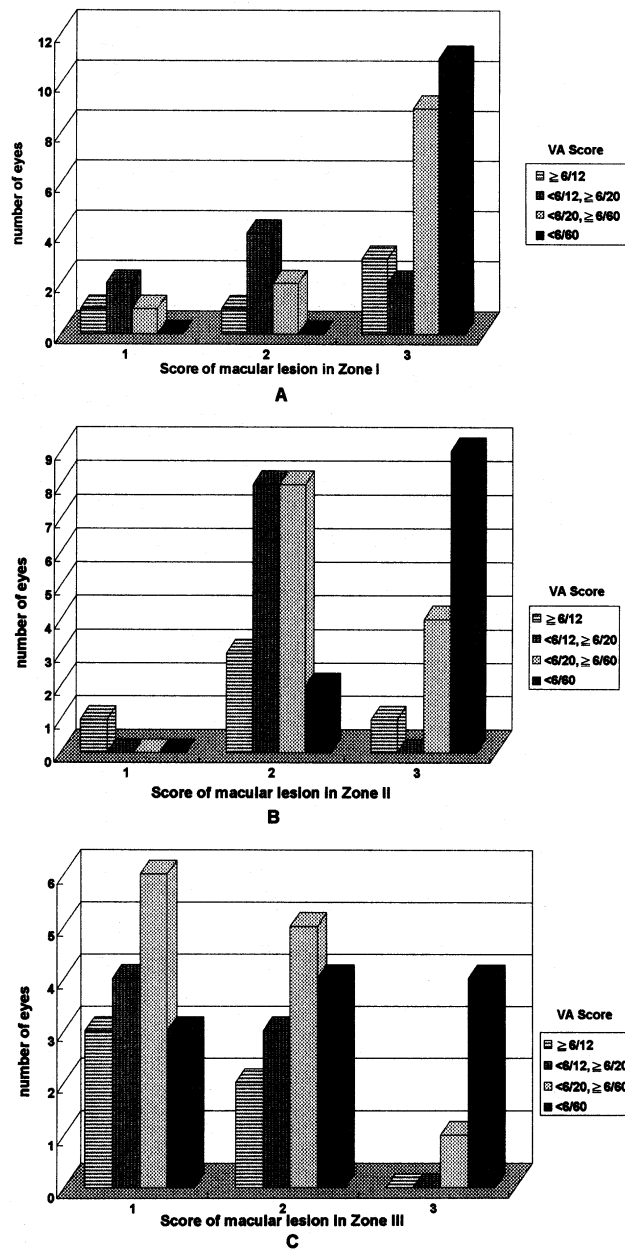


Fig. 3. Correlation between visual acuity (VA) and the lesion scores in different zones. A. zone I, $p < 0.001$; B. zone II, $p < 0.001$; C. zone III, $p = 0.038$. The visual acuity correlated strongly with the scores of lesions in central 3° , but not so in zone III.

Discussion

With its rapid testing speed and convenience of use, FDT scores high on its “creature comforts”.¹⁷⁻²³ Moreover, it showed high sensitivity and high specifi-

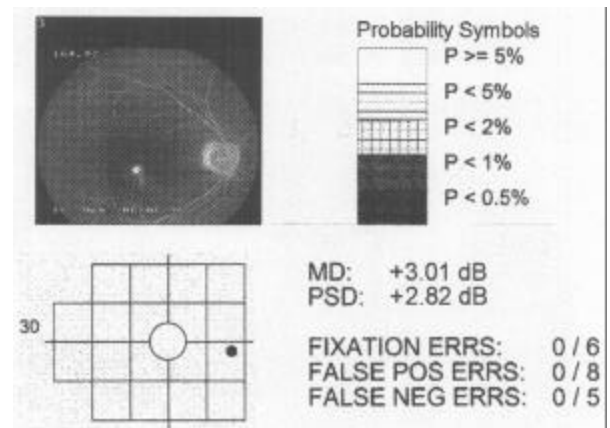


Fig. 4. A 70-year-old man had a small central macular lesion with visual acuity of 6/60 in his right eye. The lesion score was zone I:3, zone II:2, zone III:1. Nevertheless, there was no abnormal point on the total deviation plots in FDT in spite of the poor vision and central scotoma on the Amsler grid chart.

city in patients with glaucoma.²⁴⁻²⁷ It will be great if it can be used as a functional evaluation tool in ARMD patients, who usually be have worse during conventional automated perimetry.

In our previous study, visual field defect correlated strongly with the extent of retinal involvement in patients with rhegmatogenous retinal detachment, but was limited in patients with ARMD.²⁸ Our speculation was that the scoring system according to the area ratio of involvement in whole macula alone did not fully reflect the intensity of macular disease. Other factors, such as distance from the fovea center, disease duration, and type of ARMD might be related to the visual field change as well. As exudative type ARMD is the main cause of significant visual loss and is the target of treatment in ARMD, we excluded the dry type ARMD in this study and tried to use a different scoring system according to the distance from the fovea center and analyze other possible factors. The idea of our scoring system came from the fact that the distribution of photoreceptors varies in a concentric pattern away from the fovea. With this new scoring system, the central visual field defect correlated significantly with the lesion scores in zone III, but not with the lesion scores in central 3° (zone I and II). The results suggested that FDT using full-threshold C-20 mode is not sensitive enough for the detection of small

macular lesions (within central 3°) in patients with ARMD. As the FDT full-threshold C-20 mode presents with 16 targets, arranged in a 4-by-4 grid, plus 1 target in the macula. The targets correspond to the retina within 20 degrees of visual angle, including the whole posterior pole and limited nasal retina. The macular area was evaluated by 1 target only, which consisted of the central 5-degree radius. This might explain why central visual field in FDT full-threshold C-20 mode would not be abnormal unless the lesion was large enough to involve up to zone III to be detected. The visual acuity correlated significantly with the lesion scores in zone I, II and III, especially zone I and zone II. As we know, central 3° visual angle is determinant for central visual acuity, and exudative type ARMD has the tendency to grow into the fovea center. It is quite natural that visual acuity correlate strongly with zone I and II (central 3° visual angle). The fact that the central visual field defect in FDT full-threshold C-20 mode correlated with lesions in zone III only, which was less correlated with visual acuity further support that FDT full-threshold C-20 mode is not sensitive enough to detect small lesions in ARMD, and therefore might not be a useful functional evaluation in ARMD, even under this scoring system. Further modification of the central target of FDT is needed to detect small macular lesions in ARMD.

Acknowledgements

This study was supported in part by grants No. VTY-90-P3-20 and VGHKS-90-74 from Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan.

References

1. Leibowitz HM, Krueger DE, Maun der LR, Mil ton RC, Kini MM, Kahn HA, *et al.* The Framingham Eye Study [Monograph] *Surv Ophthalmol* 1980;24(suppl):335-610.
2. Ferris FL III. Senile macular degeneration: review of epidemiologic features. *Am J Epidemiol* 1983;118:132-51.
3. Pauleikhoff D, Barondes MJ, Minassian D, Chisholm IH, Bird AC. Drusen as risk factors in age-related macular disease. *Am J Ophthalmol* 1990;109:38-43.
4. Klein R, Klein BEK, Lin ton KLP. Prevalence of age-related maculopathy: the Beaver Dam Eye Study. *Ophthalmology* 1992;99:933-43.
5. Vingerling JR, Dielemans I, Hofman A, Grobbee DE, Hijmering M, Kramer CF, de Jong PT. The prevalence of age-related maculopathy in the Rotterdam Study. *Ophthalmology* 1995;102:205-10.
6. Macular Photocoagulation Study Group. Argon laser photocoagulation for senile macular degeneration: results of a randomized clinical trial. *Arch Ophthalmol* 1982;100:912-8.
7. Macular Photocoagulation Study Group. Argon laser photocoagulation for neovascular maculopathy: three-year results from randomized clinical trial. *Arch Ophthalmol* 1986;104:694-701.
8. Macular Photocoagulation Study Group. Argon laser photocoagulation for neovascular maculopathy: five-year results from randomized clinical trial. *Arch Ophthalmol* 1991;109:1109-14.
9. Macular Photocoagulation Study Group. Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration: results of a randomized clinical trial. *Arch Ophthalmol* 1991;109:1220-31.
10. Macular Photocoagulation Study Group. Subfoveal neovascular lesions in age-related macular degeneration: guidelines for evaluation and treatment in the Macular Photocoagulation Study Group. *Arch Ophthalmol* 1991;109:1242-57.
11. Macular Photocoagulation Study Group. Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration: findings from two clinical trials. *Arch Ophthalmol* 1993;111:1200-9.
12. Schuchard RA. Validity and interpretation of Amsler grid reports. *Arch Ophthalmol* 1993;111:776-80.
13. Fine AM, Elman MJ, Ebert JE, Prestia PA, Starr JS, Fine SL. Earliest symptoms caused by neovascular membranes in the macula. *Arch Ophthalmol* 1986;104:513-4.
14. Timberlake G, Mainster M, Webb R, Hughes GW, Trempe CL. Retinal localization of scotomata by scanning laser ophthalmoscopy. *Invest Ophthalmol Vis Sci* 1982;22:91-7.
15. Sunness JS, Schuchard RA, Shen N, Rubin GS, Dagnelie G, Haselwood DM. Landmark-driven fundus perimetry using the scanning laser ophthalmoscope. *Invest Ophthalmol Vis Sci* 1995;36:1863-74.
16. Midena E, Angeli CD, Blarmino MC, Valenti M, Segato T. Macular function impairment in eyes with early age-related macular degeneration. *Invest Ophthalmol Vis Sci* 1997;38:469-77.
17. Kelly DH. Frequency doubling in visual response. *J Opt Soc Am* 1966;56:1628-33.
18. Kelly DH. Nonlinear visual responses to flickering sinusoidal gratings. *J Opt Soc Am* 1981;71:1051-5.
19. Richards W, Felton TB. Spatial frequency doubling: retinal or central? *Vision Res* 1973;13:2129-37.

20. Tyler CW. Observations on spatial frequency doubling. *Perception* 1974;3:81-6.
21. Virsu V, Nyman G, Lehtio PK. Di phas ic and polyphas ic temporal mod u la tions mul ti ply ap par ent spa tial fre quency. *Perception* 1974;3:323-6.
22. Tolhurst DJ. Il lu sory shifts in spa tial fre quency caused by temporal mod u la tion. *Perception* 1975;4:331-5.
23. Virsu V, Laurinen P. Long-lasting af ter im ages caused by neural ad ap ta tion. *Vision Res* 1977;17:853-60.
24. Johnson CA, Samuels SJ. Screening for glau co ma tous vi sual field loss with fre quency-doubling pe rimetry. *Invest Ophthalmol Vis Sci* 1997;38:413-25.
25. Yamada N, Chen PP, Mills RP, Leen MM, Lieberman MF, Stamper RL, Stan ford DC. Screening for glau coma with fre quency-doubling tech nol ogy and Damato Campimetry. *Arch Ophthalmol* 1999;117:1479-84.
26. Cbauban BC, Johnson CA. Test-retest variability of fre quency-doubling pe rimetry and con ven tional pe rimerty in glau coma pa tients and nor mal sub jects. *Invest Ophthalmol Vis Sci* 1999;40:648-56.
27. Sponsel WE, Arango S, Cot YT, Trigo Y, Mensah J. Clin i cal clas si fi ca tions of glau comatous vi sual field loss by fre quency dou bling pe rimetry. *Am J Ophthalmol* 1998;125:830-6.
28. Sheu SJ, Chen YY, Lin HC, Chen HL, Wu TT. Fre quency dou bling tech nol ogy pe rimetry in re ti nal dis eases: pre li mi nary re port. *Kaoshiung J Med Sci* 2001;17:25-8.
29. Chen YY, Sheu SJ. Eval u a tion of the dif fer ent modes of fre quency dou bling tech nol ogy and the Oc to pus pe rimetry in pri mary an gle-closure glau coma. *Invest Ophthalmol Vis Sci* 2000;41(suppl):293.