

Review Article

Recent progress in macular function self-assessment

Richard Trevino

Evansville VA Outpatient Clinic, 500 East Walnut Street, Evansville, IN 47713-2438, USA

Abstract

Background: Patients that are deemed to be at risk for the development of choroidal neovascularization are frequently instructed to self-monitor their vision for symptoms that may signal the presence of choroidal neovascularization. Traditionally, the Amsler grid has been used for this purpose, but recent technological innovations have resulted in a number of potential alternatives that offer important advantages, including greater sensitivity, the ability to differentiate exudative from non-exudative disease, and quantitative analysis of test results.

Methods: The following technologies that could be employed for patient self-assessment of macular function in a home setting are reviewed: computerized Amsler grid, preferential hyperacuity perimetry, macular mapping test and noise-field campimetry.

Conclusions: A number of technologies are currently available that could significantly improve the ability of patients at risk for the development of choroidal neovascularization to self-monitor their central visual field.

Keywords: age-related macular degeneration, Amsler grid, computerized Amsler grid, macular mapping test, noise-field campimetry, preferential hyperacuity perimetry

Progress in the medical and surgical management of choroidal neovascularization (CNV) has led to renewed interest in the field of macular function self-assessment. Earlier intervention, when CNV lesion size is smaller and visual acuity is better, improves the patient's visual outcome following any of the currently employed treatments for neovascular age-related macular degeneration (AMD) (The Macular Photocoagulation Study Group, 1994; The Treatment of Age-related Macular Degeneration with Photodynamic Therapy Study Group, 2003; The VEGF Inhibition Study in Ocular Neovascularization Clinical Trial Group, 2005; The MARINA Study Group, 2007b). Since it was first introduced around 1950, the Amsler grid has been the primary method of patient self-assessment of the central visual field (Marmor, 2000). However, the sensitivity of the Amsler grid in detecting vision defects has been

documented to be approximately 50%, suggesting that approximately half of the scotomas that may be present are not detected (Schuchard, 1993). This had led to a search for more sensitive means for patients to evaluate their central vision for changes associated with choroidal neovascularization. Recently, a number of promising new technologies have emerged that may be employed by patients to monitor their macular function.

The importance of early detection

Anti-angiogenic therapy has revolutionized the treatment of CNV. Today, many patients undergoing treatment for neovascular AMD will experience improvement in their vision. Ranibizumab (Lucentis) was the first Food and Drug Administration (FDA)-approved drug for the treatment of CNV secondary to AMD. It is an antibody fragment that inhibits the activity of vascular endothelial growth factor (VEGF). When injected intravitreally, ranibizumab is associated with arrested growth of, and leakage from, CNV (The MARINA Study Group, 2006). In the MARINA study, a randomized double-masked study of the effectiveness of ranibizumab in AMD, both mean visual acuity (The MARINA Study Group, 2006) and mean visual function scores (The

Received: 2 January 2008

Revised form: 3 February 2008

Accepted: 7 February 2008

Correspondence and reprint requests to: Richard Trevino.

Tel.: +812 465 6247; Fax: +812 465 6287.

E-mail address: rtrevino1@yahoo.com

MARINA Study Group, 2007a) showed improvement at 12 and 24 months. Similar improvements have been reported from the VISION study for pegaptanib sodium (Macugen) (The VEGF Inhibition Study in Ocular Neovascularization Clinical Trial Group 2004), the other FDA-approved anti-VEGF medication. A recent systematic review of the literature found no statistically significant difference in the effectiveness of the two medications in halting the progression of neovascular AMD (Takeda *et al.*, 2007). A third VEGF inhibitor, bevacizumab (Avastin), is widely used off-label to treat neovascular AMD. There are currently no published randomized controlled trials documenting its effectiveness; however, numerous small case series with limited follow-up have been published. The currently available evidence suggests that Avastin is at least as effective as the other two drugs (Nagpal *et al.*, 2007).

Earlier intervention, when neovascular lesion size is smaller and visual acuity is better, will generally improve the final visual outcome of therapy. A recent subgroup analysis of 24-month data from the MARINA study found that the two important predictors of final visual acuity were initial visual acuity and CNV lesion size (The MARINA Study Group, 2007a). Similar analysis of the VISION data found earlier detection and treatment improved the visual outcome of Macugen-treated patients (The VEGF Inhibition Study in Ocular Neovascularization Clinical Trial Group, 2005). Treatment of neovascular AMD patients earlier in the course of their disease with anti-angiogenic agents results in greater vision recovery and, ultimately, less permanent vision loss. The earlier in the disease process that a patient presents for care, the greater the odds of avoiding severe vision loss.

Challenges of self-assessment

The availability of highly effective therapies that can not only stabilize neovascular AMD, but can improve vision, has made it more important than ever to have patients with treatable lesions present for care as early in the disease process as possible, when vision is least affected. It has long been recognized that patient self-assessment of their vision on a daily basis offers the best hope of detecting disease progression in a timely manner (The Macular Photocoagulation Study Group, 1985). Yet, many patients with documented disease progression fail to detect changes while self-monitoring their vision with the Amsler grid (Fine *et al.*, 1986; Zaidi *et al.*, 2004). This has led to a call for making the development of a cost-effective self-assessment tool for patients with macular degeneration a research priority (Crossland and Rubin, 2007).

There appear to be two primary reasons why home monitoring protocols utilizing the Amsler grid fail to

detect disease progression: non-compliance and the subjective nature of the test (Zaidi *et al.*, 2004). Non-compliance is frequently encountered with any health care regimen that patients are instructed to follow for prolonged periods of time, although the clinician can take steps that may maximize patient adherence and persistence (Rosner, 2006). Objective tests of macular integrity, such as optical coherence tomography, require little or no patient input and could, at least in theory, be devised in such a way as to screen for the presence of CNV (Sandhu and Talks, 2005). However, objective tests generally entail expensive instrumentation, making such tests impractical for patients to use at home. Subjective tests, such as the Amsler grid, are generally limited by the user's ability to understand the test, interpret their findings and reliably report the results. The Amsler grid is an especially challenging test for patients because it requires the patient to delineate, on the chart, the perception of their vision defects, while fixating elsewhere (Achard *et al.*, 1995). When compared with a gold standard of microperimetry performed with the scanning laser ophthalmoscope, the Amsler grid fails to detect approximately half of the scotomas that are present (Schuchard, 1993). Yet, because the Amsler grid test is inexpensive, conceptually easy to understand and rapid to perform, it is the most commonly employed method of macular function self-assessment (Achard *et al.*, 1995; Zaidi *et al.*, 2004).

A patient's subjective appreciation of their vision defects is influenced by a number of factors, including eccentric fixation (Crossland *et al.*, 2005), crowding effects (Parkes *et al.*, 2001) and the perceptual completion phenomena (Schuchard, 1993; Achard *et al.*, 1995). Perceptual completion is a psychophysical phenomenon wherein scotomas are filled-in with visual information from the rest of the visual field, thereby inhibiting subjective awareness of the vision defect (Ramachandran and Gregory, 1991). Perceptual completion is often imperfect, especially across larger scotomas, and may result in the perceived distortion of filled-in patterns, simulating metamorphopsia (Schuchard, 1993). Metamorphopsia is a distortion in the perceived size and shape of objects, and is usually associated with displacement of retinal photoreceptors. Loewenstein *et al.* (2003) hypothesized that the change in photoreceptor location that occurs following pigment epithelial detachment is the anatomical basis of metamorphopsia in AMD. Perceptual completion limits our ability to evaluate scotomas and metamorphopsia psychophysically. For example, perceived distortions on the Amsler grid may arise from imperfect filling-in across scotomas or, equally likely, reflect metamorphopsia because of shifts in photoreceptor position.

A number of alternatives have been developed in an effort to either improve or replace the Amsler grid

(Table 1). The Amsler grid has been modified in a variety of ways to improve its sensitivity, including red-on-black grids (Almony *et al.*, 2005), low contrast grids (Cheng and Vingrys, 1993) and computerized grids (Fink and Sadun, 2003, 2004; Nazemi *et al.*, 2005). Alternatives to the grid test include preferential hyperacuity perimetry (Loewenstein *et al.*, 2003; The Preferential Hyperacuity Perimeter Research Group, 2005a,b, Kampmeier *et al.*, 2006), macular mapping test (Trauzettel-Klosinski *et al.*, 2003; Bartlett *et al.*, 2005) and noise-field campimetry (Freeman *et al.*, 2004; Crossland *et al.*, 2007). Some of the most promising developments in the search for a self-assessment tool for patients with macular degeneration are summarized below.

Computerized Amsler grid

The sensitivity of the Amsler grid can be increased by decreasing its contrast, either with low-contrast printed charts (Cheng and Vingrys, 1993) or with cross-polar-

izing lenses (Wall and Sadun, 1986; Almony *et al.*, 2005). As chart contrast is decreased, scotomas tend to grow in size and additional defects may appear. Traditionally, the threshold Amsler grid test has involved performing the test using cross-polarizing lenses adjusted such that the Amsler grid is barely perceptible (Wall and Sadun, 1986; Almony *et al.*, 2005).

Fink and Sadun (2003, 2004) have developed a novel three-dimensional computer-automated version of the threshold Amsler grid test. Patients are instructed to map their visual field defects using a standard Amsler grid displayed on a touchscreen computer monitor. The patient uses their finger to outline the margins of their vision defects on the touchscreen at each of five contrast levels (100%, 80%, 60%, 40% and 20%). Each eye requires approximately 5 min to be tested. The results are then analysed to produce a three-dimensional depiction of visual field defects that can be analysed in terms of their slope, location, shape and depth (Figure 1).

Table 1. Alternative self-assessment tools for patients at-risk for choroidal neovascularization

Tool	Status	Comment
Computerized Amsler grid	Pending	Actively studied as a research tool, but not currently available to the public
Home PHP device	Pending	Currently undergoing FDA review. Expected to be commercially available in Fall 2008.
Macular mapping test	Available	Computer software program. Available at http://www.ski.org/Rehab/MacKeben/General/MMTest-webpage.html
MyVisionTest	Available	Online entoptic perimetry program. Available at http://www.myvisiontest.com
Television static	Available	Noise-field campimetry using static from a non-transmitting television station

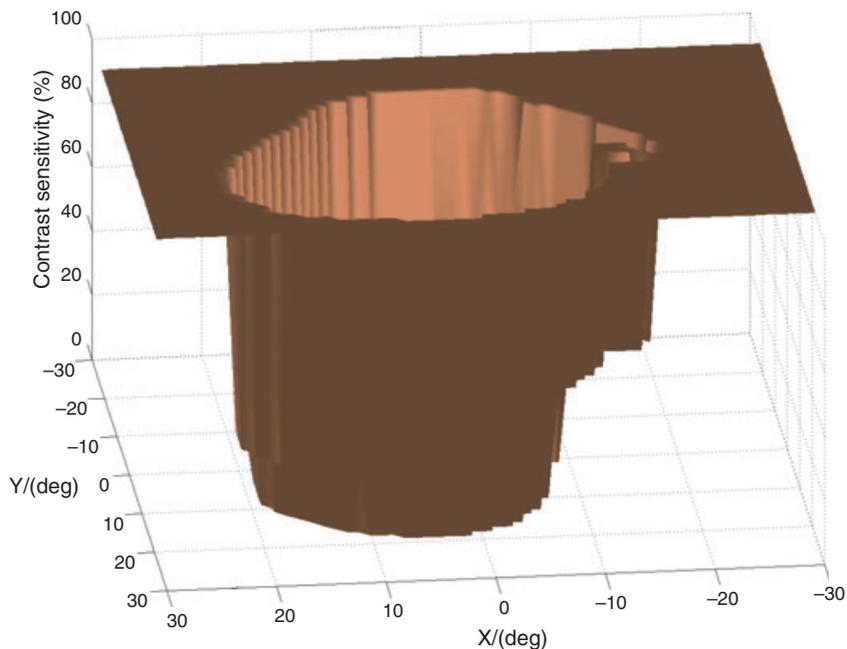


Figure 1. Computerized Amsler grid results. 3-D display of a scotoma in a patient with macular degeneration recorded by the computer-automated threshold Amsler grid test. The x-y axis denotes the horizontal and vertical coordinates of the visual field in degrees with (0,0) being the center of fixation. The z-axis denotes the contrast sensitivity of the retina expressed in percent. (Image courtesy of Wolfgang Fink; http://autonomy.caltech.edu/biomedicine/3d_computer_automated.html).

Nazemi *et al.* (2005) reported the results of a pilot study conducted with the computerized Amsler grid test, consisting of 41 eyes from 25 patients with age-related macular degeneration. The three-dimensional scotoma depictions consistently demonstrated 'scallop'-shaped borders and step-like patterns, with either steep slopes or a combination of steep and shallow slopes. The investigators reported that visual field defects in patients with non-exudative AMD were found to have steep-sloping margins while patients with the exudative form of the disease tended to have scotomas with shallow-sloping margins; however, sensitivity and specificity data for this finding were not reported. Test-retest variability was not investigated. The authors concluded that this device is an effective tool in accurately evaluating, characterizing and monitoring scotomas in patients with AMD. More recently, this device has also been employed to screen for glaucoma (Nazemi *et al.*, 2007).

The computerized Amsler grid would appear to have potential as a self-assessment tool. Nazemi *et al.* (2005) specifically suggested that the computerized Amsler grid test may be a useful tool for monitoring patients with macular degeneration for the development of choroidal neovascularization over the Internet, although to our knowledge it is not currently deployed in this fashion. An important advantage of this technology is the fact that most macular degeneration patients are already familiar with the use of the Amsler grid; therefore, they may more easily adapt to the computerized version of this test. The ability to differentiate exudative from non-exudative disease is a very exciting finding but requires further investigation. The shortcomings of the conventional grid test, including crowding effects and filling-in, may continue to limit the sensitivity of this test.

Preferential hyperacuity perimetry

Loewenstein and colleagues have developed the preferential hyperacuity perimeter (PHP) (Loewenstein *et al.*, 2003; The Preferential Hyperacuity Perimeter Research Group, 2005a,b). This device may assist in the early detection of neovascular AMD.

The test procedure analyses the central 14° of the visual field by presenting the patient with a series of dotted lines on a touchscreen video monitor (The Preferential Hyperacuity Perimeter Research Group, 2005b) (*Figure 2*). Each line that is presented to the patient contains one dot out of alignment with the others (an artificial distortion). Each dotted line appears for only 160 ms, then the patient, fixating a central point, touches the screen with a stylus at the perceived location of the misaligned dot. The artificial distortion serves as a competitive stimulus to any pathological distortion that might appear on the presented pattern. When a CNV lesion is present, attention competition between the artificial distortion and the pathological distortion takes place in the patient's brain (Loewenstein, 2007). In general, the brain ignores smaller stimuli when there is a larger one. This phenomenon is exploited in PHP testing to assess the magnitude of the pathological distortion: varying sizes of artificial distortion are presented, allowing quantification of the pathological distortion by analyzing the patient's responses. Based upon these responses, a visual field map is constructed, analysed and compared with normative data, thereby determining the likelihood of a defect being the result of CNV. The test samples 500 data points in each eye and takes about 5 min per eye to complete.

The PHP has been shown to be more sensitive than the conventional Amsler grid in detecting visual changes



Figure 2. The Foresee Preferential Hyperacuity Perimeter (Foresee PHP™). The patient is positioned on a chin rest and directs their gaze at a central fixation target. A stylus is used to record on a touchscreen video monitor the location of the perceived distortion of a dotted line stimulus. (Image courtesy of Notal Vision, Tel Aviv, Israel: <http://www.notalvision.com>).

associated with AMD. The Preferential Hyperacuity Perimeter Research Group (2005b) reports on a multicenter study of 150 patients that underwent both conventional Amsler grid testing and PHP. Fundus photographs and fluorescein angiograms read by investigators masked to both the PHP and Amsler results were used to establish the presence and type of macular degeneration. This study found that 68% of all patients with AMD had a positive PHP, while 26% had positive results on Amsler grid examination ($p < 0.001$). Of those patients with neovascular AMD, 100% were positive on the PHP and 53% on the Amsler grid. However, 18% of patients without AMD had a positive PHP. Thus, although the PHP was found to be more sensitive than the Amsler grid in detecting AMD, it had a relatively high rate of false positives.

The Preferential Hyperacuity Perimetry Research Group (2005a) reports on another study of the PHP after making adjustments to the algorithm to decrease the number of false positives. A total of 122 participants with either intermediate stage AMD or presumed recent-onset (within 60 days) neovascular AMD underwent PHP testing. Photographs and angiograms were evaluated by graders masked to the PHP results to establish the stage of the macular degeneration. The investigators found that the sensitivity of PHP to detect newly diagnosed CNV was 82% and the specificity to differentiate newly diagnosed CNV from the intermediate stage of AMD was 88%. Furthermore, PHP results were not influenced by lesion size or location; lesions that did not extend under the center of the macula as well as lesions with a small size (< 2 disc areas) were detected with a sensitivity similar to that for the entire cohort. Test-retest variability was not investigated. The authors conclude that PHP is able to differentiate recent-onset neovascular AMD from intermediate stage AMD with high sensitivity and specificity.

Kampmeier *et al.* (2006) report on 140 patients with AMD that underwent testing with both the PHP and conventional Amsler grid and found little difference in the sensitivity of the two tests. The stages of AMD were independently graded in a masked fashion by fundus photographs and fluorescein angiography. Of 50 patients with advanced non-neovascular AMD, the Amsler was marginally more sensitive than the PHP; 23 (46%) tested positive with the PHP test and 26 (52%) were positive on the Amsler grid. Of 45 patients with neovascular AMD, the PHP was marginally more sensitive than the Amsler; 38 (84%) had a positive PHP test and 36 (80%) a positive Amsler grid test. Surprisingly, there were more false positives with the Amsler grid than the PHP; one of 34 normal controls (3%) had a positive PHP test and five (15%) had a positive Amsler grid test. The authors conclude that both tests are useful for detecting AMD, but that the

PHP may be more sensitive in patients with neovascular AMD.

The utility of the PHP as a device for self-monitoring at home has been investigated. A portable version of the PHP referred to as the 'ForeseeHome AMD Monitor' has been developed for this purpose (Notal Vision Inc, Tel Aviv, Israel). Loewenstein *et al.* (2007) reported on a validation study using the home PHP device involving 62 patients with AMD, 46 with intermediate-stage AMD and 16 with neovascular AMD. All patients underwent supervised examinations using the home PHP device, then 32 of the patients with intermediate-stage AMD continued using the device at their homes twice a week for 6 weeks to assess performance reliability in a home environment. During the supervised examinations, 11 of 13 patients with CNV and reliable test performance were found to have a significant defect using the home PHP device (sensitivity of 83%), and 30 of 36 patients with intermediate-stage AMD and reliable test performance did not demonstrate a significant defect (specificity of 83%). All of the patients tested at home performed the test reliably and managed to operate the device independently. The authors conclude that the concept of patients with intermediate-stage AMD self-monitoring their vision at home using the ForeseeHome AMD Monitor was validated successfully.

An important advantage of using a device such as the ForeseeHome AMD Monitor for self-assessment of macular function is that the instrument could achieve a standardized presentation of the test stimuli. Variables associated with differences in computer hardware, such as size and quality of the video display, are avoided. The ability of PHP to differentiate early onset neovascular AMD from intermediate stage AMD is of major clinical significance. An important disadvantage of the home PHP device would be the cost barrier associated with patients acquiring the device. As a potential alternative to having patients purchase a PHP device, the Preferential Hyperacuity Perimetry Research Group (2005a) suggested that clinicians could use in-office PHP to periodically monitor individuals that have intermediate-stage AMD in between regular examinations in an effort to identify recent-onset CNV.

Macular mapping test

The macular mapping test (MMT) was designed primarily for quick assessment of residual vision in patients with maculopathies (MacKeben, 2007). However, it may also be employed as a tool for monitoring disease progression (Trauzettel-Klosinski *et al.*, 2003; Bartlett *et al.*, 2005).

The MMT is a computer software program used in conjunction with a personal computer. The test screen displays a constant background pattern throughout the

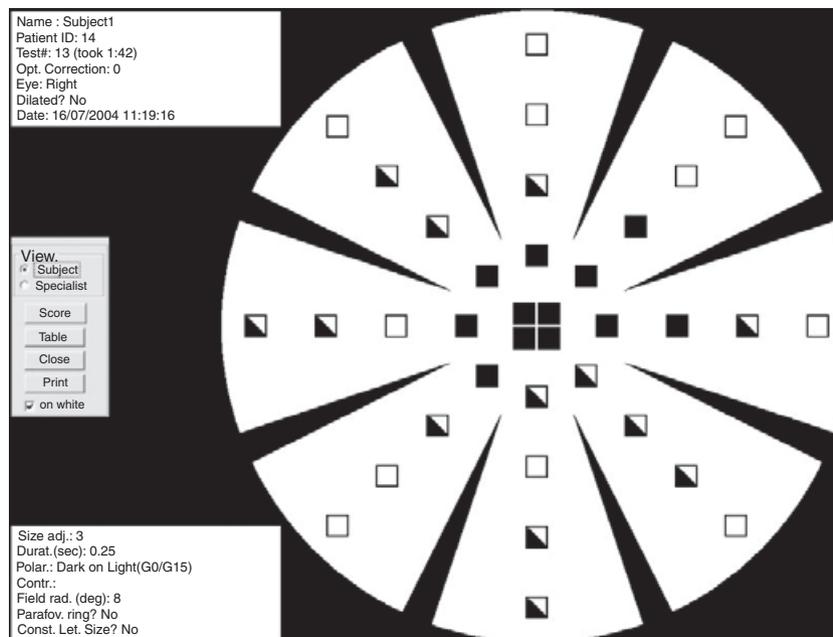


Figure 3. Subject view of the MMT results. Black squares indicate letters that were not seen, half-shaded squares indicate those that were seen but not correctly identified, and white squares indicate letters that were correctly identified. (Source: Bartlett, H., et al. 2005. Reprinted in accordance with the BioMed Central Open Access License.)

test, that resembles a 'wagon wheel' subtending the central 18° of the visual field (Figure 3). Eight spokes point inwards but do not reach the center of the display area. This pattern is designed to aid the patient with maintaining fixation at the center of the display area during the vision test. Test stimuli are uppercase letters drawn from the modern Latin alphabet that appear for 234 ms, unpredictably, in one of 36 locations on the test screen. The letters are five pixels high in the center of the screen and become progressively larger toward the periphery. During the test, the patient fixates the center of the test screen and is asked to identify each letter after it has appeared. There are three possible categories of response: (i) target not detected, (ii) target detected but not recognized (including incorrect responses) and (iii) target correctly recognized. The final score is calculated using the following system: target not detected, 0; target detected but not recognized, 1; target correctly recognized, 2. The final score is displayed at the end of the test along with a 'map' of the areas that are seen and unseen. The test takes approximately 3 min per eye.

Trauzettel-Klosinski *et al.* (2003) have compared the results of MMT with those of manual perimetry using the Tübingen perimeter in 50 patients with a variety of disorders that produce a central scotoma, including AMD, Stargardt's disease and diabetic maculopathy. To allow direct comparison of the two tests, the investigators divided the central 10° of visual field into 32 sectors, according to the stimulation grid of the MMT. The results of corresponding locations of the tests were compared. Only absolute field defects were analysed.

For perimetry, only the brightest stimulus, and for MMT only 'not detected' responses were counted as deficits. Using this approach, the investigators found that correspondence between the two tests was 87.5%, suggesting that there is little difference in the ability of the two tests to detect and delineate dense scotomas. The authors concluded that there was a good agreement between MMT and manual perimetry and that MMT is well suited to screen for, and monitor the course of, central vision loss in patients with macular disease.

Bartlett *et al.* (2005) have investigated the test-retest variability of the MMT. Thirty-one healthy eyes of 31 normal subjects underwent the test. MMT readings were also taken from 17 eyes of 17 patients with soft drusen and 12 eyes of 12 patients with geographic atrophy secondary to AMD. The study was designed to assess reproducibility (variability between different examiners) and repeatability (variability with the same examiner). Test-retest repeatability of MMT scores was analysed by calculating the coefficient of repeatability, which yields the 95% confidence limits for the amount of difference between two sets of results. The average MMT score for the 12 eyes with AMD was 61.9 ± 23.8 , and for 16 age-matched controls, it was 94.5 ± 4.8 ($p < 0.001$). The MMT scores of patients with soft drusen were not significantly different to those of normal age-matched controls. The intraexaminer coefficient of repeatability was ± 6.70 and ± 7.40 for the two examiners in this study. Between examiners, the coefficients ranged between ± 4.3 and ± 7.24 . Based upon these results, the investigators determined that the MMT score has to

change by more than 14 points for the change to be considered clinically significant. They conclude that despite considerable variability, the MMT score could be useful for monitoring progression of AMD.

The MMT is a potential self-assessment tool for patients with AMD. It is easy to understand, rapid to perform and yields a quantitative score that can be tracked over time. The software appears to be as sensitive as manual perimetry in delineating dense scotomas caused by macular degeneration, but whether this holds true for more subtle defects is unknown. One important disadvantage is the cost of the software (\$325 USD at the time of writing – personal communication, Manfred MacKeben) which could be prohibitively expensive for many patients with AMD. Another disadvantage would be the aforementioned test–retest variability, such that a loss of 7 test points (scored at 2 points each) is required before disease progression can be confirmed.

Noise-field campimetry

The filling-in phenomena that normally prevents the subjective perception of scotomas can, in some instances, be overcome by gazing at random visual noise, such as video static (Aulhorn and Köst, 1988). Patients with an acquired scotoma secondary to a retinal or optic nerve lesion may perceive an inhomogeneous region within the noise pattern that corresponds to their scotoma. Once the scotoma is perceived, it may be possible to map the vision defect, a procedure referred to as entoptic perimetry. Variations of this technique have been successfully used to screen for vision defects caused by a variety of pre-chiasmal eye diseases, including AMD, diabetic retinopathy and glaucoma (Adachi and Shirato, 1994; Brown *et al.*, 2000; Plummer *et al.*, 2000). Noise-field campimetry is not very effective in eliciting scotomas caused by post-chiasmal lesions (Schiefer *et al.*, 1998) or the physiological blindspot.

Freeman *et al.* (2004) determined the sensitivity and specificity of entoptic perimetry in patients with AMD. In this study, the noise field was generated by a computer software program and was delivered to the patient via a scanning laser virtual retinal display. The patient traced out their scotomas on a touch-sensitive pad that fed the virtual drawings into the computer and they then appeared within the virtual display. This procedure was performed on 171 eyes of 91 patients with AMD and 43 eyes of 24 healthy age-matched control subjects. The presence and severity of AMD was determined by masked readings of fundus photographs. The entoptic perimetry findings were read by an investigator masked to the ophthalmological findings. The sensitivity of entoptic perimetry was assessed for each of eight grades of severity of AMD. Sensitivity measurements ranged from a low of 70% for patients

with mild drusen to a high of 100% for patients with untreated CNV. Overall, the mean sensitivity was 82% and the specificity was 1.00. The authors conclude that scanning laser entoptic perimetry is a specific and sensitive test for detecting AMD, even at the earliest stages when patients are typically asymptomatic.

Crossland *et al.* (2007) employed the twinkle after-effect (TwAE) to further enhance scotoma perception during entoptic perimetry. The TwAE is an illusion that can be elicited following adaptation to a random noise stimulus. If the noise pattern does not stimulate a circumscribed region within the visual field, i.e. a scotoma, that area will appear to ‘twinkle’ when the noise pattern is suddenly replaced with a uniform field (Ramachandran and Gregory, 1991). Eight subjects, seven with bilateral advanced AMD and one with unilateral traumatic maculopathy, viewed video static on a computer monitor for 15 s (adaptation phase) followed by an isoluminant grey screen for 15 s (test phase) (Figure 4). This cycle was repeated five times (total test time: 2.5 min) for each eye that was tested. During the test phase, if the subject perceived a TwAE, they were asked to outline it using a stylus on a touchscreen that recorded their drawing. Half of the subjects experienced perceptual filling-in of their vision defects during the adaptation phase, in other words, four (50%) of the eight subjects did not perceive their scotomas while viewing the video static. Six (75%) of eight subjects experienced the TwAE during the test phase and could easily trace around its perimeter. Of the four subjects who experienced filling-in, three experienced the TwAE. Therefore, seven (87.5%) of eight subjects perceived their scotomas either via the noise field or via the TwAE. The investigators report that they were unable to identify any distinguishing characteristics of the one subject that was unable to perceive his scotomas during either the adaptation or test phase of the experiment. The researchers compared the accuracy of the defects recorded by patients using the TwAE and those recorded with microperimetry. There was excellent agreement between both measures. The authors conclude that the TwAE is a quick and accurate technique for investigating scotomas.

Noise-field campimetry is a promising tool for self-assessment of macular function in patients with macular degeneration. Viewing video static, most patients are able to subjectively perceive their defects, either directly or with the assistance of the TwAE, and accurately map their scotomas. Another advantage is that the test takes very little time to perform, which may improve compliance with daily self-assessment. An important disadvantage of noise-field campimetry is that subjective appreciation of scotomas is completely foreign to most people, making it potentially difficult for some patients to understand and perform the test in an unsupervised home setting. It also seems clear that not all patients are

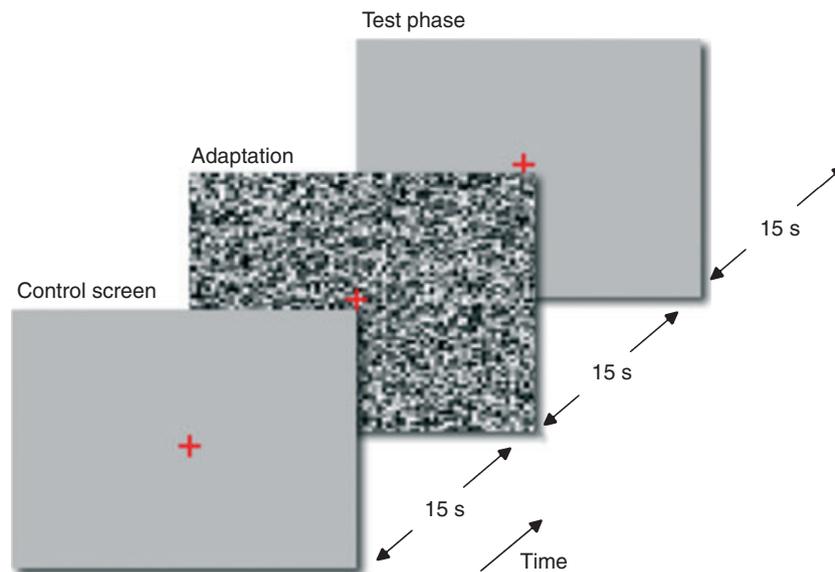


Figure 4. Noise-field stimulus presentation. The control screen was an isoluminant grey screen presented for 15 seconds to determine whether subjects could trace their scotoma boundary against a regular background. The adaptation phase was a dynamic field of random grayscale noise presented for 15 seconds. The test phase was a further insolominant grey screen presented for 15 seconds. A red cross was present throughout to guide fixation. Adaptation and test phase were repeated to a total of five times. (Source: Crossland et al. 2007. Reprinted in accordance with the Creative Commons Attribution License.)

capable of perceiving their scotomas using currently available noise-field campimetry techniques.

Conclusion

A number of emerging technologies hold promise as potential self-monitoring tools for patients at-risk for choroidal neovascularization. Each technology is associated with a distinct set of advantages and disadvantages. The technologies reviewed in this paper are superior to the current practice of using a printed Amsler grid chart in that they offer one or more of the following: (i) the ability to detect more subtle defects, (ii) to differentiate exudative from non-exudative disease and (iii) quantitative analysis of test results. A workable approach to incorporating these new tools into clinical practice may be to introduce patients to a variety of methods of assessing their vision and allow them to find one that works best for them.

References

- Achard, O. A., Safran, A. B., Duret, F. C. and Ragama, E. (1995) Role of the completion phenomenon in the evaluation of Amsler grid results. *Am. J. Ophthalmol.* **120**, 322–329.
- Adachi, M. and Shirato, S. (1994) The usefulness of the noise-field test as a screening method for visual field defects. *Jpn. J. Ophthalmol.* **38**, 392–399.
- Almony, A., Garg, S., Peters, R. K., Mamet, R., Tsong, J., Shibuya, B., Kitridou, R. and Sadun, A. A. (2005) Threshold Amsler grid as a screening tool for asymptomatic patients on hydroxychloroquine therapy. *Br. J. Ophthalmol.* **89**, 569–574.
- Aulhorn, E. and Köst, G. (1988) Rauschfeldkampimetrie: eine perimetrische Untersuchungsweise. *Klin. Monatsbl. Augenheilkd.* **192**, 284–288.
- Bartlett, H., Davies, L. and Eperjesi, F. (2005) The macular mapping test: a reliability study. *BMC Ophthalmol.* **5**, 18.
- Brown, J. C., Kylstra, J. A. and Mah, M. L. (2000) Entoptic perimetry screening for central diabetic scotomas and macular edema. *Ophthalmology* **107**, 755–759.
- Cheng, A. S. and Vingrys, A. J. (1993) Visual losses in early age-related maculopathy. *Optom. Vis. Sci.* **70**, 89–96.
- Crossland, M. and Rubin, G. (2007) The Amsler chart: absence of evidence is not evidence of absence. *Br. J. Ophthalmol.* **91**, 391–393.
- Crossland, M. D., Culham, L. E., Kabanarou, S. A. and Rubin, G. S. (2005) Preferred retinal locus development in patients with macular disease. *Ophthalmology* **112**, 1579–1585.
- Crossland, M. D., Dakin, S. C. and Bex, P. J. (2007) Illusory stimuli can be used to identify retinal blind spots. *PLoS ONE* **2**, e1060, viewed 31 December 2007, doi:10.1371/journal.pone.0001060
- Fine, A. M., Elman, M. J., Ebert, J. E., Prestia, P. A., Starr, J. S. and Fine, S. L. (1986) Earliest symptoms caused by neovascular membranes in the macula. *Arch. Ophthalmol.* **104**, 513–514.
- Fink, W. and Sadun, A. (2003) Novel 3D computerized threshold Amsler grid test, *Perimetry Update 2002/2003*. Kugler, Amsterdam, pp. 207–212.
- Fink, W. and Sadun, A. (2004) Three-dimensional computer-automated threshold Amsler grid test. *J. Biomed. Opt.* **9**, 149–153.

- Freeman, W. R., El-Brady, M. and Plummer, D. J. (2004) Scanning laser entoptic perimetry for the detection of age-related macular degeneration. *Arch. Ophthalmol.* **122**, 1647–1651.
- Kampmeier, J., Zorn, M. M., Lang, G. K., Botros, Y. T. and Lang, G. E. (2006) Vergleich des preferential-hyperacuity-perimeter (PHP)-tests mit dem Amsler-netz-test bei der diagnose verschiedener stadien der altersbezogenen makuladegeneration. *Klin. Monatsbl. Augenheilkd.* **223**, 752–756.
- Loewenstein, A. (2007) The significance of early detection of age-related macular degeneration. *Retina* **27**, 873–878.
- Loewenstein, A., Malach, R., Goldstein, M., Leibovitch, I., Barak, A., Baruch, E., Alster, Y., Rafaeli, O., Avni, I. and Yassur, Y. (2003) Replacing the Amsler grid: a new method for monitoring patients with age-related macular degeneration. *Ophthalmology* **110**, 966–970.
- Loewenstein, A., Ferencz, J. R., Lang, Y., Yeshurun, I., Pollack, A. and Springer, A. (2007) 'Can We Help Patients Diagnose their CNV Early at Home? A New Home-use Macular Perimeter', Poster Presented to the Twenty-fifth Annual Meeting of the American Society of Retina Specialists. American Society of Retina Specialists, Indian Wells, CA, 4 December.
- MacKeben, M. (2007) *Macular Mapping Test*. Smith-Kettlewell Eye Research Institute, San Francisco, viewed 31 December 2007. Available at: <http://www.ski.org/Rehab/MacKeben/General/MMTest-webpage.html>.
- Marmor, M. F. (2000) A brief history of macular grids: from Thomas Reis to Edvard Munch and Marc Amsler. *Surv. Ophthalmol.* **44**, 343–353.
- Nagpal, M., Nagpal, K. and Nagpal, P. N. (2007) A comparative debate on the various anti-vascular endothelial growth factor drugs: Pegaptanib sodium (Macugen), ranibizumab (Lucentis), bevacizumab (Avastin). *Indian J. Ophthalmol.* **55**, 437–439.
- Nazemi, P. P., Fink, W., Lim, J. I. and Sadun, A. A. (2005) Scotomas of age-related macular degeneration detected and characterized by means of a novel three-dimensional computer-automated visual field test. *Retina* **25**, 446–453.
- Nazemi, P. P., Fink, W., Sadun, A. A., Francis, B. and Minckler, D. (2007) Early detection of glaucoma by means of a novel 3D computer-automated visual field test. *Br. J. Ophthalmol.* **91**, 1331–1336.
- Parkes, L., Lund, J. and Angelucci, A. (2001) Compulsory averaging of crowded orientation signals in human vision. *Nat. Neurosci.* **4**, 739–744.
- Plummer, D. J., Azen, S. P. and Freeman, W. R. (2000) Scanning laser entoptic perimetry for the screening of macular and peripheral retinal disease. *Arch. Ophthalmol.* **118**, 1205–1210.
- Ramachandran, V. S. and Gregory, R. L. (1991) Perceptual filling in of artificially induced scotomas in human vision. *Nature* **350**, 699–702.
- Rosner, F. (2006) Patient noncompliance: causes and solutions. *Mt. Sinai J. Med.* **73**, 553–559.
- Sandhu, S. S. and Talks, S. J. (2005) Correlation of optical coherence tomography, with or without additional colour fundus photography, with stereo fundus fluorescein angiography in diagnosing choroidal neovascular membranes. *Br. J. Ophthalmol.* **89**, 967–970.
- Schiefer, U., Skalej, M., Kolb, M., Dietrich, T. J., Kolb, R., Braun, C. and Petersen, D. (1998) Lesion location influences perception of homonymous scotomata during flickering random dot pattern stimulation. *Vision Res.* **38**, 1303–1312.
- Schuchard, R. A. (1993) Validity and interpretation of Amsler grid reports. *Arch. Ophthalmol.* **111**, 776–780.
- Takeda, A. L., Colquitt, J., Clegg, A. J. and Jones, J. (2007) Pegaptanib and ranibizumab for neovascular age-related macular degeneration: a systematic review. *Br. J. Ophthalmol.* **91**, 1177–1182.
- The Macular Photocoagulation Study Group (1985) Early detection of extrafoveal neovascular membranes by daily central field evaluation. *Ophthalmology* **92**, 603–609.
- The Macular Photocoagulation Study Group (1994) Visual outcome after laser photocoagulation for subfoveal choroidal neovascularization secondary to age-related macular degeneration. *Arch. Ophthalmol.* **112**, 480–488.
- The MARINA Study Group (2006) Ranibizumab for neovascular age-related macular degeneration. *N. Engl. J. Med.* **355**, 1419–1431.
- The MARINA Study Group (2007a) Improved vision-related function after ranibizumab treatment of neovascular age-related macular degeneration: results of a randomized clinical trial. *Arch. Ophthalmol.* **125**, 1460–1469.
- The MARINA Study Group (2007b) Subgroup analysis of the MARINA study of ranibizumab in neovascular age-related macular degeneration. *Ophthalmology* **114**, 246–252.
- The Preferential Hyperacuity Perimeter Research Group (2005b) Results of a multicenter clinical trial to evaluate the preferential hyperacuity perimeter for detection of age-related macular degeneration. *Retina* **25**, 296–303.
- The Preferential Hyperacuity Perimetry Research Group (2005a) Preferential hyperacuity perimeter for detecting choroidal neovascularization study. *Ophthalmology* **112**, 1758–1765.
- The Treatment of Age-related Macular Degeneration with Photodynamic Therapy Study Group (2003) Verteporfin in Photodynamic Therapy study group. Effect of lesion size, visual acuity, and lesion composition on visual acuity change with and without verteporfin therapy for choroidal neovascularization secondary to age-related macular degeneration: TAP and VIP report No. 1. *Am. J. Ophthalmol.* **136**, 407–418.
- The VEGF Inhibition Study in Ocular Neovascularization Clinical Trial Group (2004) Pegaptanib for neovascular age-related macular degeneration. *N. Engl. J. Med.* **351**, 2805–2816.
- The VEGF Inhibition Study in Ocular Neovascularization Clinical Trial Group (2005) Enhanced efficacy associated with early treatment of neovascular age-related macular degeneration with pegaptanib sodium: an exploratory analysis. *Retina* **25**, 815–827.
- Trauzettel-Klosinski, S., Biermann, P., Hahn, G. and Weismann, M. (2003) Assessment of parafoveal function in maculopathy: a comparison between the macular mapping test and kinetic manual perimetry. *Graefes Arch. Clin. Exp. Ophthalmol.* **241**, 988–995.

Wall, M. and Sadun, A. A. (1986) Threshold Amsler grid testing: cross polarizing lenses enhance yield. *Arch. Ophthalmol.* **104**, 520–523.

Zaidi, F. H., Cheong-Leen, R., Gair, E. J., Weir, R., Sharkawi, E., Lee, N. and Gregory-Evans, K. (2004) The Amsler chart

is of doubtful value in retinal screening for early laser therapy of subretinal membranes: the West London Survey. *Eye* **18**, 503–508.