

SCOTOMAS OF AGE-RELATED MACULAR DEGENERATION DETECTED AND CHARACTERIZED BY MEANS OF A NOVEL THREE-DIMENSIONAL COMPUTER-AUTOMATED VISUAL FIELD TEST

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Purpose: We used the recently devised three-dimensional computer-based threshold Amsler grid test to acquire and identify typical patterns of visual field defects (scotomas) caused by age-related macular degeneration (AMD).

Methods: Patients with AMD traced on a computer touch screen the borders of those areas on an Amsler grid that were missing from their field of vision. Scotomas were repeatedly outlined and recorded at different grid contrast levels. The resulting three-dimensional “hole” in the central 25° of the visual field was further characterized by its slope, location, shape, and depth. The results were compared with fundus photographs and fluorescein angiograms.

Results: Twenty-five patients and 41 eyes were examined. The three-dimensional depictions consistently demonstrated central scotomas with “scallop”-shaped borders and steplike patterns, with either steep slopes or a combination of steep and shallow slopes. The steep slopes corresponded to nonexudative AMD, while the shallow slopes indicated exudative AMD.

Conclusion: The three-dimensional computer-automated threshold Amsler grid test may demonstrate characteristic scotoma patterns in patients with AMD that conform to the respective fluorescein angiograms. The test shows promise as an effective tool in accurately evaluating, characterizing, and monitoring scotomas in patients with AMD. It may have the potential as a screening tool for the early diagnosis of AMD.

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Age-related macular degeneration (AMD) is the leading cause of visual impairment in people older than 65 years of age in the Western world.¹ Between 4 and 10 million people in the United States

are estimated to have AMD.^{2–7} The advanced form can be choroidal neovascularization and geographic atrophy. Patients are defined as having the earliest form of nonexudative AMD if an eye has drusen of at least 63 μm in size. In some of these patients and especially in patients with large soft confluent drusen with retinal pigment epithelium mottling, there is a risk for conversion to the exudative (neovascular) form. An estimated 80% of AMD patients have the nonneovascular form; however, the neovascular form may account for almost 90% of the severe visual loss (20/200 or worse in both eyes) due to AMD.⁸

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Despite the uncertainty about the pathogenesis of AMD, beneficial treatment exists, such as the use of verteporfin in patients with predominantly classic subfoveal choroidal neovascularization.⁹ With several treatment possibilities for neovascular AMD, early detection and diagnosis may improve treatment outcome. To address this possibility of a screening method for the early detection of AMD, we first set out to characterize the visual field defects caused by macular degeneration.

Visual field testing has advanced greatly since the development of the Amsler grid by Mark Amsler in the 1920s. Testing for macular degeneration did not become routine until the dissemination of the Amsler grid in the middle of the 20th century. The Amsler grid was designed to specifically test visual field defects in the central 10°. ^{10,11} An inexpensive and rapid method, the Amsler grid test utilizes a suprathreshold target to analyze the central 10°. It is good for detecting metamorphopsia but is not sensitive for the detection of relative scotomas. ¹¹ The detection of relative scotomas was advanced by the development of the threshold Amsler grid test by Wall and Sadun ¹¹ and Wall and May. ¹² By using cross-polarizing filters to vary perceived luminance, threshold Amsler grid testing significantly increases the yield of scotoma detection in the central 10°. Accordingly, it was found to be much more sensitive for shallow scotoma detection in patients with maculopathies and optic neuropathies. ^{11,12} Threshold Amsler grid testing of the central 25° or more can now be easily and rapidly accomplished with the recently introduced three-dimensional computer-automated threshold Amsler grid test. ^{13–16} This psychophysical test may be used to rapidly identify and monitor patients with a variety of visual field defects. It has been shown to provide several advantages over conventional perimetry, primarily by adding a third (*z*) dimension in terms of contrast sensitivity to the *x* and *y* coordinates of the visual fields and in characterizing and distinguishing optic neuropathies.

The purpose of our study was thus to first retrieve typical signature patterns of AMD and then to establish the size, shape, slope, and extent of the visual field defects using this three-dimensional computer-automated visual field test. This study also aimed to further distinguish the visual field defects of AMD patients with respect to exudative (i.e., neovascular) versus nonexudative (i.e., drusen or geographic atrophy) forms of macular degeneration.

Patients and Methods

We recruited 25 patients from the Doheny Eye Institute at the Keck School of Medicine of the University of Southern California (Los Angeles). Patients

were recruited from the retina clinic directly or contacted and scheduled to participate in the study. Institutional review board approval was obtained. There was no minimum requirement for visual acuity. A total of 41 eyes were tested using the three-dimensional computer-automated visual field test. The examination employed the equipment introduced by Fink et al ¹³ and Fahimi et al ¹⁴ and was performed in a designated examination room. We utilized an IBM compatible Pentium II PC running Windows 98 in conjunction with a 17-inch touch-sensitive computer monitor. The brightness level was well defined and graded systematically throughout each study and between the separate trials. The monitor was not recalibrated but was kept at the same brightness and contrast settings both throughout each study and between separate trials for consistency. Each patient was positioned in front of the computer monitor. The angle of the visual field was determined by seating the patient at the fixed distance of 12 inches from the central fixation marker on the computer screen (0° horizontally and 0° vertically from fixation). An eye cover was used to occlude the eye that was not being examined. Refractive correction was used with the patient's eyeglasses when necessary. The patients utilized their spectacle (bifocal) correction during the test when appropriate, and additional corrective lenses were not used.

An Amsler grid at a preselected gray scale (i.e., contrast) level and preselected angular resolution was displayed by the computerized test program. The preselected angular resolution for all patients was determined by the distance between the monitor and the patient and the Amsler grid spacing on the monitor. It was consistently set to 1° (standard Amsler grid) between lines for each patient and study. This expanded to represent 60° × 44° for the entire visual field test. The patient was first asked to focus on a changing fixation marker at the center of the grid. The fixation marker did not change in brightness, independent from the gray scale level of the Amsler grid. To suppress the central Troxler effect and keep the patient's attention, the shape of the fixation marker was regularly changed. Given the instability of fixation in patients with central scotomas, the patient was instructed to use the four corners of the rectangular monitor as an additional reference frame for fixation. The patient was asked to mark the areas on the Amsler grid that were missing from his or her field of vision by tracing the border of this region with their finger on the touch screen while maintaining fixation. The patient's response was recorded by the computer program.

After completion of a particular gray scale level, the contrast/gray scale level of the Amsler grid was changed, and the patient had to perform the same task as outlined above. This procedure was repeated for a total of five different contrast levels, with one level being the standard Amsler grid, in our case a white grid on a black background (i.e., 100% contrast difference with respect to the background of the computer screen). The gray scale levels were presented in an ascending order. Areas of 0% contrast sensitivity were then defined as the inability of a patient to recognize an Amsler grid displayed at 100% contrast difference in those areas. Areas of 100% contrast sensitivity were defined as the ability of a patient to recognize an Amsler grid displayed at the lowest preset contrast (i.e., the darkest grid). By changing the contrast at which the Amsler grid was presented, horizontal “cuts” through the hill-of-vision at various “heights” (i.e., contrast sensitivity levels) were performed, which, in combination, resulted in an instantaneous three-dimensional depiction of the hill-of-vision (thus the name of the novel test).

Increasing degrees of contrast were simulated by repeating this procedure at different preselected gray scale levels. The results were recorded and later displayed as topographic contour rings by the computerized test program after each recording. A three-dimensional depiction of the central 25° of the visual field was attained using these results, which could also be displayed as color shaded depictions in three dimensions that could be viewed or rotated to any perspective. The results were then used to establish the location, extent, slope, depth, and shape of the scotomas in the AMD patients. Each eye required a total of ≈5 minutes to be tested.

Description of the Slope Measurement Method

The ratio between the loss of contrast sensitivity over degrees of visual field taken perpendicularly to the closest contour rings expressed as a grade (%/degree) was initially computed to determine the steepest slope of the scotoma. In the second method, the ratio between the loss of contrast sensitivity over degrees of visual field taken perpendicularly to the least compacted contour rings expressed as a grade (%/degree) was considered as a measure of the least steep (shallowest) side of the three-dimensional “hole.” In addition, the scotomas were characterized using the ratio of the area of the scotoma at the highest and lowest contrast levels. This was expressed as a scotoma area ratio (SAR), defined as the area of the scotoma at the highest contrast level divided by the area of the scotoma at the lowest contrast level. Sco-

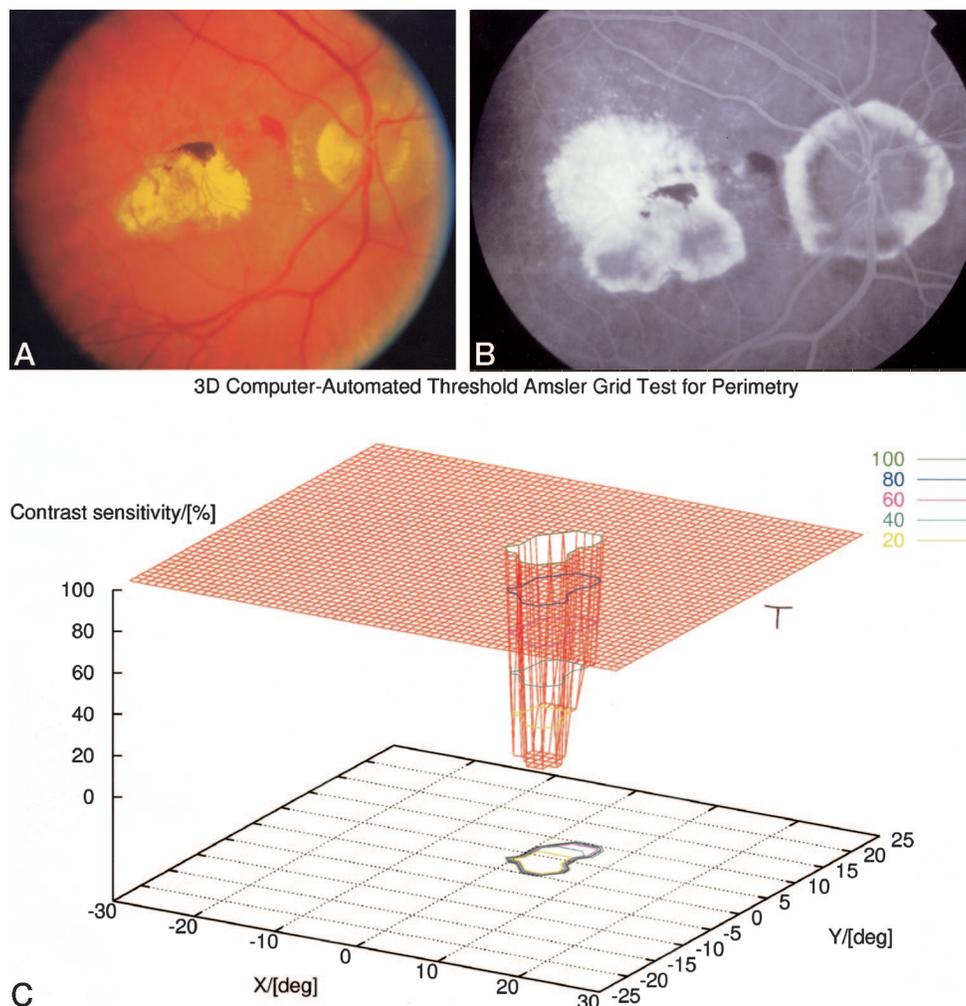
tomas with relatively steep slopes are characterized by SARs close to 1, whereas scotomas with predominantly shallow slopes are characterized by lower SARs.

Results

Forty-one eyes of 25 patients (17 women and 8 men) with AMD underwent examination with the three-dimensional computer-automated visual field test. Visual acuities ranged from 20/60 to 20/200. The nonexudative group included patients with focal hyperpigmentation along with >5 drusen and confluence of the soft large (>63 μm) drusen, and geographic atrophy. The three-dimensional depictions of visual field loss associated with macular degeneration consistently demonstrated large central scotomas with “scallop”-shaped borders characterized by many changes in the radius of curvature of the borders. All of these patients demonstrated absolute scotomas on the three-dimensional computer-automated visual field test. The patterns revealed a characteristic steplike pattern, with steep slopes or a combination of steep and shallow slopes (Figs. 1–3). The outlined scotoma boundaries for each tested contrast level (total of 5 gray scale levels) were concentrically arranged, and the lines were overlapping and not crossing. The mean of the steepest slope (%/degrees of visual field) for the 41 eyes was 73.2%/degree (range, 16%/degree to 80%/degree). The mean of the shallowest slope was 30.0%/degree (range, 5.6%/degree to 80%/degree). All of the scotomas were absolute to the highest gray scale Amsler grid (100% contrast difference).

The steep slopes determined by the three-dimensional Amsler grid test corresponded to nonexudative AMD, as determined by the fundus photographs and fluorescein angiograms. The shallow slopes were seen in patients with exudative AMD. Further, the area of shallow slopes often corresponded to the area of neovascularization on the fundus color photographs and fluorescein angiograms. Figure 1 demonstrates an absolute central scotoma with a steplike pattern and combination of steep and shallow slopes of the right eye. The area of laser photocoagulation in the subfoveal region corresponds with the steepest slope on the three-dimensional Amsler grid test (80%/degree). Subretinal fluid and adjacent subretinal blood are seen nasal and superior to the laser scar, with a corresponding shallow slope (20%/degree). The marked scotoma area measured 57 degree² at the lowest tested grid to 24 degree² at the highest tested grid. The SAR measured 0.42. An active membrane in the right eye of a patient with classic AMD is seen in Figure 2. The shal-

Fig. 1. **A**, Fundus photograph of the right eye shows an area of laser photocoagulation in the subfoveal region. Nasal and superior to this is subretinal fluid with some adjacent subretinal blood. **B**, Laminar-phase fluorescein angiogram shows hyperfluorescence corresponding to a laser scar with deeper choroidal vessels visible. Superior to this are areas of speckled hyperfluorescence that show leakage on late frames of the angiogram (not shown). Nasally, there is blocked fluorescence due to hemorrhage. **C**, Gridlike depiction of three-dimensional visual field in a patient with age-related macular degeneration that was recorded by the three-dimensional computer-automated threshold Amsler grid test. The x-axis and y-axis denote the horizontal and vertical coordinates of the visual field, respectively, in degrees with (0,0) being the center of fixation. The z-axis denotes the contrast sensitivity of the visual field expressed in percent: 0% contrast sensitivity corresponds to the standard (brightest) Amsler grid, and 100% contrast sensitivity corresponds to the Amsler grid displayed at the lowest preset contrast (i.e., the darkest grid). T, temporal.



lowest slope (8%/degree) seen temporally on the three-dimensional Amsler grid corresponds to the slightly nasal location of the choroidal neovascular classic component on the fundus photograph. The area of the scotoma measured 1,388 degree² and 852 degree² at the area of the lowest and highest tested grids, respectively, and the SAR was 0.61. Early- and late-phase angiograms in Figure 3 show leakage corresponding to choroidal neovascularization in the subfoveal region of the left eye. A corresponding three-dimensional Amsler grid test reveals a shallow slope (8%/degree) and a steepest slope of 80%/degree. The area of the scotoma was 594 degree² for the area at the lowest tested grid and 274 degree² for the area at the highest tested grid. The SAR measured 0.46.

Discussion

AMD is the leading cause of visual impairment in the elderly and the most common cause of permanent blindness in the developed world. As such, it repre-

sents a major public health problem. The usefulness of automated perimetry in the differential diagnosis of patients with macular disease has been confirmed.¹⁷ However, automated visual field testing often is not regularly performed on macular degeneration patients due to a lack of resolution and fixation. There is a paucity of literature with detailed description of visual field defects caused by macular degeneration. Unlike conventional perimetry and campimetry that provide information pertaining to the borderline between seeing and nonseeing areas but do not provide the additional information inherent in a region of visual depression, the computerized three-dimensional test displays the area of depression on the z-axis in regards to changes in visual contrast sensitivity in addition to the area of depression in the x-axis and y-axis (relative to visual fixation). The three-dimensional information permits further distinctions between certain visual disorders. Other important advantages of this technique over conventional perimetry have already been described.¹³⁻¹⁶

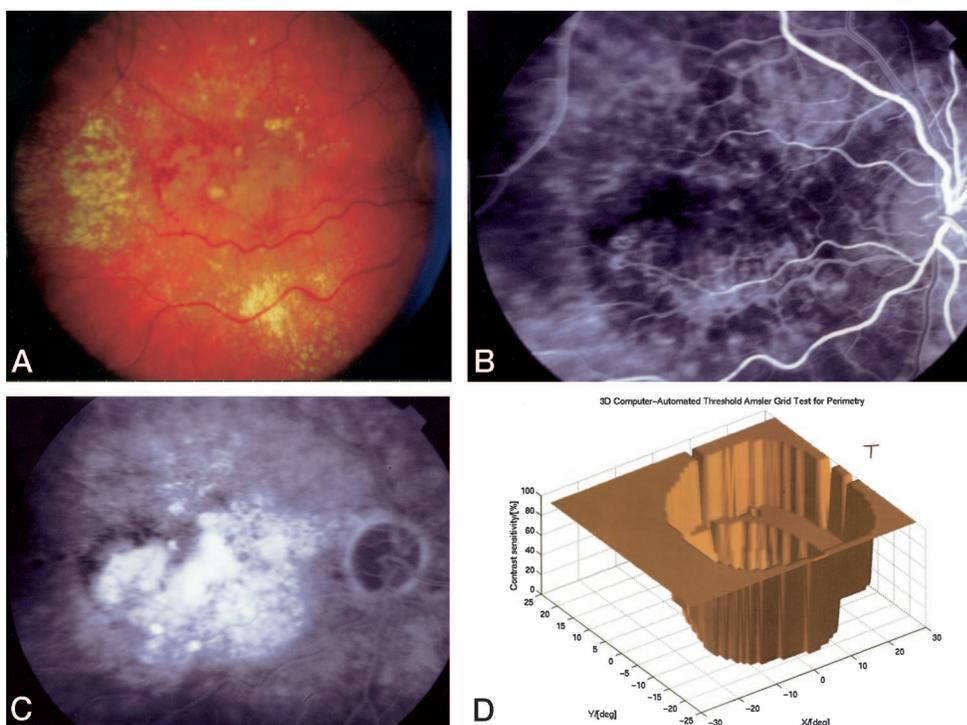


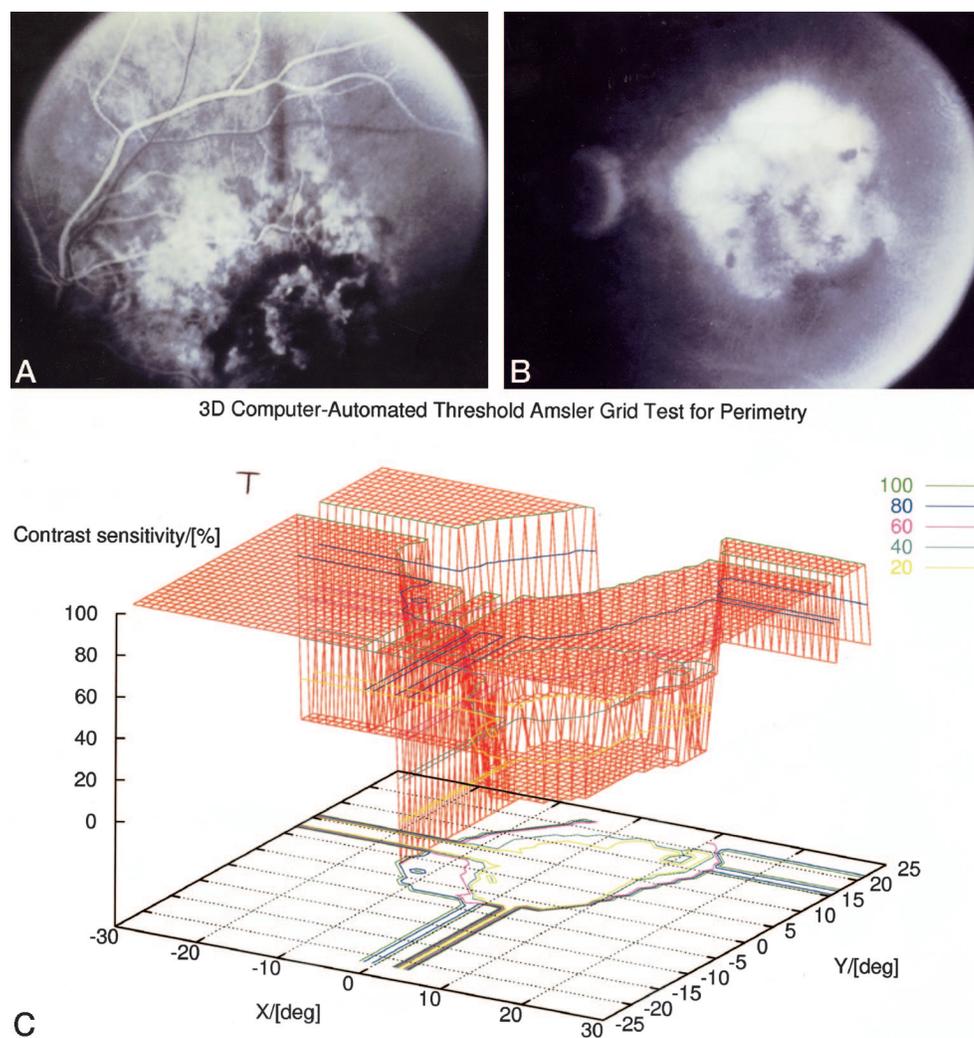
Fig. 2. **A**, Fundus photograph of the right eye shows subfoveal subretinal fluid, hard exudates, and drusen. Areas of subretinal hemorrhage are present. An area of choroidal neovascularization is visible as grayish green discoloration in the subfoveal region. The scotoma involves central fixation. **B**, Early laminar-phase angiogram shows an area of subfoveal choroidal hyperfluorescence with some blocked fluorescence corresponding to blood. **C**, Late-phase angiogram of the right eye shows areas of hyperfluorescence as well as leakage in the subfoveal space. There are still some areas of blocked fluorescence corresponding to the blood in the right eye. **D**, Fully shaded depiction—equivalent to the gridlike display—of the three-dimensional visual field in a patient with age-related macular degeneration that was recorded by the three-dimensional computer-automated threshold Amsler grid test (for explanation of axes, see Fig. 1C). The scotoma involves fixation. The temporal field to the center correlates with the slightly nasal location of the choroidal neovascular classic component. T, temporal.

In our study, we set out to use three-dimensional computer-based threshold Amsler grid test technology to characterize the visual field defects caused by macular degeneration. Most forms of automated perimetry have proven most useful in the detection of glaucoma and other types of optic neuropathies. Improvements in resolution and reliability have made computer-based testing increasingly more common as a useful diagnostic tool for detecting retinal disease. For example, scanning laser entoptic perimetry has recently been shown to be an effective and inexpensive test for screening retinal disease in visually asymptomatic patients and glaucoma patients.^{18,19} Because the early diagnosis of exudative AMD may be more critical for effective treatment, we tested the additional benefits of greater sensitivity, higher resolution, better reliability, and additional information made possible by computation and consideration of the third dimension.

The present study was undertaken to first obtain and identify distinctive signature patterns for defects caused by AMD. Patients with previously known diagnoses of AMD were evaluated. The results of the test were as expected in terms of revealing a centrally

located, circular shaped visual field defect. Patients with very variable fixation might outline different areas at different contrast levels and may produce variable findings from session to session. The patients in this study had difficulty identifying the central fixation marker and were instructed to use the four corners of the monitor as a reference frame for fixation. The success of this arrangement is demonstrated by the finding that the outlined scotoma boundaries for each tested contrast level (total of 5 gray scale levels) were concentrically arranged and the lines were overlapping and not crossing. This implies that the patients were able to maintain adequate fixation. However, repeated testing within each of the five contrast levels was not performed. This will be necessary to determine the variability of the test within subjects. The depth, shape, and slope of the field defects were then calculated. The patterns of visual field defects in patients with AMD demonstrated a combination of steep slopes interrupted by stepwise shallow slopes. The patients in our study had later stages of AMD and demonstrated absolute scotomas on the three-dimensional computer-automated visual field test. Patients

Fig. 3. **A**, Early laminar-phase fluorescein angiogram shows a subfoveal area of choroidal neovascularization with surrounding blocked fluorescence corresponding to blood and occult hyperfluorescence beyond the blood. **B**, Late-phase angiogram showing leakage corresponding to choroidal neovascularization in the subfoveal region of the left eye. **C**, Gridlike depiction of the three-dimensional visual field in a patient with age-related macular degeneration that was recorded by the three-dimensional computer-automated threshold Amsler grid test (for explanation of axes, see Fig. 1C). Horizontal and vertical lines extending to the periphery represent artifacts. T, temporal.



with earlier stages would more likely have shown no scotoma at all or a relative scotoma. Such visual field deficits may escape detection altogether by the standard Amsler grid. So far, it appears that the shape and slope patterns of the scotomas in AMD are unique for this disease. However, in the absence of comparison of these patterns with other macular diseases as well as in the absence of testing across a larger sample, more studies may be called for to better characterize the pattern of visual field loss in AMD patients. The steep slopes indicated nonexudative AMD, whereas the shallow areas often pointed to areas of neovascularization as confirmed by color photographs and fluorescein angiograms. Areas of steep slopes were also seen in exudative cases. In Figure 2, the slight nasal location of the choroidal neovascularization on the fundus photograph demonstrates a corresponding shallow slope located (8%/degree) on the three-dimensional Amsler grid test. However, the choroidal neovascularization also extends temporally as seen on

the fluorescein angiogram but has a steep border (80%/degree). A possible reason for this finding, which has not yet been clarified, is that the area of grayish green discoloration, seen nasally on the fundus photograph, may represent a more long-standing lesion, whereas the area extending temporally represents a new lesion that has not caused pigmentary changes.

The SARs were also calculated to better characterize the scotomas. For example, both Figures 2 and 3 demonstrate a shallow slope of 8%/degree and a steepest slope of 80%/degree. However, there is a difference in the relative frequency of occurrence of both shallowest and steepest slopes in both figures, as demonstrated by their respective SARs. On the basis of these findings, it seems reasonable to suggest that the three-dimensional computer-automated threshold Amsler grid test may be used to frequently monitor patients with nonexudative AMD for the development of choroidal neovascularization. The early diagnosis

of exudative AMD and its prompt treatment may be useful in mitigating further damage to the retina with resultant visual field loss. Clearly, this is a pilot study, and thorough longitudinal follow-up studies are required to assess this hypothesis.

Our 21 patients were also tested with standard Amsler grid methodology, and the two tests were compared for their ability to characterize absolute visual field defects. Amsler grid testing did not accurately indicate the shape and extent of the scotoma. A possible reason for this is that with standard Amsler grid testing, the patient may have difficulty maintaining fixation or charting the changes that may often be confusing. In contrast, patient motivation and participation in the three-dimensional computer-based threshold Amsler grid test is higher due to the peripheral help with fixation and clear changes in boundaries that occur at different contrast depths. This may result in a more precise depiction of the visual field defect. Of course, the standard Amsler grid test serves only to detect the presence of an absolute scotoma, without any further information such as depth or slope. In addition, it is well known that Amsler grids may underestimate both the extent and the degree of scotomas as compared with SLO perimetry.²⁰ However, this study did not compare the three-dimensional computer-based threshold Amsler grid test with conventional computerized visual field testing for several reasons. First, we wished to determine whether the three-dimensional Amsler grid test could help to refine the scotoma determination as compared with the standard Amsler grid. Second, we wished to determine functional correlates that may have been implicated by any features of the test that were specific to certain fundus findings. Hence, we sought to correlate the three-dimensional Amsler grid test findings with the topographic correlates on the fundus examination for each patient. As we found, the steepness of the slope does seem to correlate with the fundus finding, unlike the more nonspecific standard Amsler grid changes. Conventional computerized visual field testing is not very reliable, such as for problems with fixation. Future studies could be performed comparing our method with microperimetry. Furthermore, our method is also relatively fast (<5 minutes/eye) and offers additional information through three-dimensional depiction of scotomas and potential worldwide accessibility over the Internet, as compared with microperimetry mapping of the macular field and scotomas.

The visual field defects in patients with AMD usually begin as relative scotomas and may progress to become absolute in the center over time. This is in contrast to the visual field defects in optic neuritis,

which often start out as areas of absolute scotoma that over time often resolve to patches of relative scotoma. Therefore, AMD may be a more important disease with which to look for relative scotomas in the early detection of potentially treatable forms that may be important for the prevention of severe visual loss.

The three-dimensional computer-automated threshold Amsler grid test may also have the potential as a screening tool for the early detection of AMD in general. This was demonstrated as a relative scotoma in a 43-year-old patient with a family history of AMD in both parents who presented with metamorphopsia and no previous diagnosis of macular degeneration. As expected, given that the three-dimensional visual field test was a more sensitive measure, a relative scotoma was detected that was not identified by the standard Amsler grid. The scotoma was characteristic of our family of macular degeneration scotomas. Specifically, the patient's visual field examination demonstrated a centrally located relative scotoma with "scallop"-shaped borders, steplike pattern, and a steep slope (80%/degree). The three-dimensional depiction of the visual field loss in this patient may be suggestive of an early stage of nonexudative AMD. Hence, we believe that this computerized psychophysical test may be an effective tool in the early diagnosis of AMD. Its clinical utility will become even more apparent with the development of further treatments for AMD. The capability of the three-dimensional Amsler grid test to detect shallow or relative scotomas in addition to absolute scotomas, combined with the characteristic pattern of visual field defects in AMD patients, may enable the earlier detection of AMD. However, this study did not evaluate the use of the test as a screening tool, and further studies will be needed to address this possibility.

The three-dimensional computer-automated visual field test shows promise as an effective tool in accurately evaluating, characterizing, and monitoring the visual field defects in patients with AMD. Further, it may have the potential as a screening tool for the early diagnosis of AMD.

Key words: three-dimensional computer-based threshold Amsler grid test, age-related macular degeneration (AMD), Amsler grid, contrast sensitivity, exudative AMD, nonexudative AMD, perimetry, scotomas, visual fields, visual field testing.

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