IMPORTANCE  To our knowledge, there is no reliable screening method for glaucomatous eyes with myopic tilted discs.

OBJECTIVE  To evaluate the diagnostic ability of a novel screening modality, the crescent moon (CM) sign, defined as the discontinuity between the superior or inferior optic rim margin and the temporal optic rim margin, for the detection of glaucomatous eyes with myopic tilted discs.

DESIGN, SETTING, AND PARTICIPANTS  The study was cross-sectional and conducted in a hospital setting from November 1, 2011, to November 1, 2013. Seventy eyes of 70 individuals with early open-angle glaucoma (mean deviation greater than −6 dB) and 70 eyes of 70 normal control participants who had myopic tilted discs were recruited. Another independent group consisting of 60 eyes of 60 individuals with early glaucoma and 60 eyes of 60 normal control participants was enrolled. Two masked glaucoma specialists independently assessed the optic disc on stereoscopic disc photography. The diagnostic performance of the CM sign was evaluated in comparison with violation of the ISNT rule (inferior ≥ superior ≥ nasal ≥ temporal order of configuration for disc rim thickness in normal eyes) and the modified ISNT rule (application of the ISNT rule based on the long axis of the disc).

MAIN OUTCOMES AND MEASURES  Sensitivity and specificity of the CM sign.

RESULTS  The CM sign was more frequently observed in the inferotemporal optic rim margin than in the superotemporal optic rim margin. In a comparative evaluation of the glaucoma diagnostic sensitivity and specificity, the CM sign showed higher sensitivities (90.0%-91.4%) than the ISNT rule (73.3%-75.7%) or the modified ISNT rule (68.6%-70.0%). The CM sign also showed higher specificities (82.9%-83.3%) than the ISNT rule (68.3%-71.4%) or the modified ISNT rule (76.6%-80.0%). Furthermore, the CM sign was shown to be associated with the occurrence of visual field defects in the corresponding hemifield (P < .001).

CONCLUSIONS AND RELEVANCE  The CM sign can be a useful screening tool for the detection of early glaucoma with myopic tilted discs.
Glaucoma is a progressive optic neuropathy characterized by excavation of the optic nerve head and the corresponding visual field defect. Because open-angle glaucoma is usually asymptomatic until the advanced stage, it is important to establish an effective screening tool for the detection of glaucoma. Although various imaging devices including optical coherence tomography and confocal scanning laser ophthalmoscopy are widely used for the diagnosis of glaucoma, careful examination of the optic nerve head remains indispensable.1

The structural changes of glaucomatous optic neuropathy include generalized enlargement or vertical elongation of the optic disc cup, localized notching or narrowing of the optic disc rim, and violation of the ISNT rule (the thickness of disc rims beginning with the inferior rim followed by the superior rim, the nasal rim, and the temporal rim).2 In myopic eyes, however, early detection of glaucomatous optic disc changes is difficult because myopic discs have large diameters, a larger cup-disc ratio, shallow and concentric disc cupping, and a high frequency of disc tilting.3,4

To overcome these limitations, we propose a novel diagnostic sign, the crescent moon (CM) sign, for glaucoma screening in the myopic tilted disc. This sign is defined as discontinuity in the inner margin of the optic rim between the superior or inferior quadrant and the temporal quadrant. In this study, we evaluated the diagnostic ability of the CM sign for detection of early glaucoma in the myopic tilted disc.

Methods

Study Participants

The study protocol was approved by the institutional review board of Seoul National University Boramae Hospital. All of the study procedures adhered to the tenets laid out in the Declaration of Helsinki. Participants did not provide written or verbal consent owing to the retrospective nature of this study.

Participants with myopic tilted discs (group 1) meeting the eligibility criteria were consecutively enrolled from the Glaucoma Clinic of Seoul National University Boramae Hospital and the Armed Forces Capital Hospital in Korea from November 1, 2011, to November 1, 2012. To validate the diagnostic accuracy and the generalizability of the CM sign, a second independent group of individuals with myopic tilted discs (group 2) was consecutively enrolled from the same institutes between December 1, 2012, and November 1, 2013.

The tilted optic disc was defined as a tilt index (ie, the ratio of the minimum to the maximum optic disc diameter) less than 0.85 and myopia was defined as a spherical equivalent equal to or less than −0.50 D or axial lengths equal to or greater than 24.0 mm. In cases where both eyes of a participant were eligible for the study, 1 eye was randomly enrolled.

All of the participants had a best-corrected visual acuity of 20/40 or better and an open anterior chamber angle. Eyes with a history of other ocular diseases, amblyopia, intraocular surgery (except uncomplicated cataract operation), or systemic diseases affecting the visual fields were excluded. All participants included in the study were familiar with the standard automated perimetry test from earlier experiences of at least 2 visual field examinations. The results of the Humphrey visual field test with the Swedish interactive threshold algorithm 24-2 standard in this study were reliable in all cases (ie, fixation loss was less than 20% and false-positive and false-negative rates were less than 33%).

The glaucomatous eyes enrolled for the study had retinal nerve fiber layer (RNFL) defects on red-free RNFL photography and corresponding mild glaucomatous visual field loss (mean deviation greater than −6 dB), regardless of the optic nerve appearance as to avoid selection bias in the optic nerve head evaluation. The glaucomatous visual field loss was defined as a pattern standard deviation beyond the 95% normal limits, glaucoma hemifield test results outside the normal limits, and/or a cluster of at least 3 points with a P value of <.05 on a pattern deviation plot, one of each with P < .01 affecting the same hemifield; moreover, the cluster could not be contiguous with the blind spot and could not cross the horizontal midline on 2 consecutive visual field tests. All participants with glaucoma were required to show progression of either an RNFL defect or visual field defects during follow-up.

Normal control eyes were defined as those having an intraocular pressure 21 mm Hg or less with no history of increased intraocular pressure, no visible RNFL defect on red-free RNFL photography masked for the optic nerve head, and a normal standard automated perimetry result. The normal control eyes mainly included participants who had been referred as having glaucoma by general ophthalmologists during routine eye checkups or refractive surgery evaluations but whose eyes subsequently were confirmed as nonglaucomatous by glaucoma specialists based on complete ophthalmic examinations. Spherical equivalent-matched normal control eyes without any progressive changes on either the RNFL or visual field for at least 3 years’ follow-up before enrollment were selected.

Ophthalmologic Examination

All of the participants underwent a comprehensive ophthalmic examination including a medical history review, measurement of best-corrected visual acuity, slitlamp biomicroscopy, Goldmann applanation tonometry, gonioscopy, dilated fundoscopic examination with a 90-diopter lens, stereoscopic disc photography, red-free RNFL photography, and standard automated perimetry (Humphrey Field Analyzer II; Carl Zeiss Meditec). The axial length was measured by partial coherence interferometry (IOLMaster; Carl Zeiss Meditec).

Two masked glaucoma specialists independently evaluated the optic disc on stereoscopic disc photography; discrepancies between the 2 observers were resolved either by discussion or by adjudication of a third glaucoma specialist. The optic disc assessment was performed without knowledge of the corresponding clinical information (eg, the visual field test result).

Optic nerve neuroretinal rim thickness was evaluated for the inferior, superior, nasal, and temporal locations. The ISNT rule was considered to be observed if the inferior rim thickness was greater than or equal to the superior rim thickness, the superior rim thickness was greater than or equal to the na-
sal rim thickness, and the nasal rim thickness was greater than or equal to the temporal rim thickness order was followed. As for the modified ISNT rule, it was deemed to be observed in the rotated (torted) optic disc if this order was followed, based on the long axis of the disc (considered to be the central vertical axis).

**CM Sign**

We established a new glaucoma-screening protocol for the myopic tilted disc named the CM sign. It is defined as discontinuity in the inner margin of the optic rim between the superior or inferior quadrant and the temporal quadrant. The presence or absence of the CM sign can be assessed intuitively. That is, if the optic disc rim of the superior or inferior quadrant is not connected curvilinearly to that of the temporal quadrant, we can consider it to be a positive CM sign without schematization. When the CM sign is present between the temporal rim and the superior or inferior rim, the superior-nasal-inferior optic disc rim is shaped like a crescent moon. Hence, the name of this new sign (Figure 1 and eFigure 1 in the Supplement).

The CM sign is explained with the aid of the images in eFigure 2 in the Supplement. On stereoscopic disc photography, a reference point is determined where the inner margin of the optic disc rim meets the disc border. At this point, a line tangential to the inner curvature of the optic disc rim margin is drawn. When the tangential line extends in the direction opposite to the macula, the CM sign is present (eFigure 2A in the Supplement). Contrastingly, when the tangential line is extended to the macula, the CM sign is absent (eFigure 2B in the Supplement).

**Statistical Analysis**

Statistical analyses were performed using SPSS version 18.0 software (SPSS Inc) and MedCalc 12.3.0 (MedCalc Software). The t test, χ² test, and Fisher exact tests were used to compare both groups. The sensitivities and specificities of the ISNT rule, the modified ISNT rule, and the CM sign were compared using the McNemar test. The topographic correlation between the CM sign and visual field defect was analyzed by the χ² test. The CM sign’s interobserver agreement was assessed with reference to the Cohen κ value.

**Results**

This study initially involved 140 eyes of 140 participants (70 eyes of 70 individuals with early glaucoma and 70 eyes of 70 normal control individuals) and were defined as group 1 (test group). Subsequently, 120 eyes of 120 individuals (60 eyes of 60 individuals with early glaucoma and 60 eyes of 60 normal control individuals) were enrolled and were defined as group 2 (validation group). The participants’ demographic and background characteristics are listed in eTable 1 in the Supplement. Age, sex, refractive error, axial length, and tilt index were similar between the normal and the glaucomatous eyes; however, the 2 groups differed in regards to the standard automated perimetry result (P < .001, t test).

Table 1 shows that the CM sign was more frequently observed in glaucomatous eyes than in normal control eyes (P < .001, χ² test). Of the 70 glaucomatous eyes in group 1, 26 eyes showed the CM sign in the superotemporal rim and 55 showed the CM sign in the inferotemporal rim. Of the 60 glaucomatous eyes in group 2, 22 showed the CM sign in the superotemporal rim and 47 showed the CM sign in the inferotemporal rim.

The sensitivities and specificities of the ISNT rule, modified ISNT rule, and CM sign for detection of glaucoma in the myopic tilted disc are provided in Table 2. The sensitivity and specificity of the ISNT rule were 73.3% to 75.7% and 68.3% to 71.4%, respectively. The sensitivity and specificity of the modified ISNT rule were 68.6% to 70.0% and 76.6% to 80.0%, respectively. For the CM sign, the sensitivities in groups 1 and 2 were 91.4% and 90.0%, respectively, which were higher than...
the ISNT rule \( (P = .01 \text{ in group } 1, P = .006 \text{ in group } 2) \) and the modified ISNT rule \( (P = .002 \text{ in group } 1, P = .008 \text{ in group } 2) \). The specificities of the CM sign in groups 1 and 2 were 82.9% and 83.3%, respectively, which also were higher than the ISNT rule \( (P = .13 \text{ in group } 1, P = .05 \text{ in group } 2) \) and the modified ISNT rule \( (P = .82 \text{ in group } 1, P = .45 \text{ in group } 2) \).

In both superior and inferior hemifields, the CM sign was related to the occurrence of corresponding visual field defect (all \( P < .001, \chi^2 \text{ test} \)) (Table 3). In groups 1 and 2, the specificities of the CM sign for detection of visual field defect in the corresponding hemifield were 87.3% and 93.0%, respectively, for the superior hemifield and 70.0% and 63.0%, respectively, for the inferior hemifield. Meanwhile, the specificities of the CM sign for detection of corresponding hemifield defect were 82.4% and 83.1%, respectively, for the superior hemifield and 90.0% and 90.3%, respectively, for the inferior hemifield. The representative cases are shown in Figure 2.

The agreement between the 2 observers in judging the presence or absence of the CM sign according to the schematic definition was found to be excellent (\( \kappa \text{ values} = 0.825-0.867, \text{ eTable 2 in the Supplement} \)).

### Discussion

Multiple large population-based studies have shown that myopia is significantly associated with primary open-angle glaucoma.\(^{6-9}\) Therefore, it is important to evaluate the presence of glaucoma in myopic eyes. However, it might be difficult to detect a glaucomatous optic disc change in cases of the myopic tilted disc, owing to several morphological characteristics that can mask early glaucomatous structural change.\(^{3-4,10}\) These characteristics are oblique positioning of the optic disc resulting in tilt and torsion, a larger and shallower cup, and a larger zone beta of parapapillary atrophy compared with non-myopic eyes.\(^{11,12}\) Because there has been no single effective screening method developed for glaucoma with a myopic tilted disc, it is essential for accurate glaucoma diagnostics to iden-

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### Table 1. Topographic Frequency of Crescent Moon Sign in Normal Individuals and Individuals With Glaucoma

<table>
<thead>
<tr>
<th>Crescent Moon Sign Location</th>
<th>No. (%)</th>
<th>Value (95% CI)</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (70 Eyes)</td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>Glaucoma (70 Eyes)</td>
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<tr>
<td>Superior temporal CM sign</td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>5 (7.14)</td>
<td>26 (37.1)</td>
<td>.001</td>
<td>.001</td>
<td>4 (6.67)</td>
<td>22 (36.7)</td>
<td>.001</td>
<td>.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>9 (12.9)</td>
<td>55 (78.8)</td>
<td>.001</td>
<td>.001</td>
<td>6 (10.0)</td>
<td>47 (78.3)</td>
<td>.001</td>
<td>.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferotemporal CM sign</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td>Positive</td>
<td>58 (82.9)</td>
<td>6 (8.6)</td>
<td>.001</td>
<td>.001</td>
<td>50 (83.3)</td>
<td>6 (10.0)</td>
<td>.001</td>
<td>.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td></td>
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</tbody>
</table>

Abbreviations: CM, crescent moon; ISNT, the thickness of disc rims beginning with the inferior rim followed by the superior rim, the nasal rim, and the temporal rim; modified ISNT rule, application of the ISNT rule based on the long axis of the disc.

### Table 2. Sensitivities and Specificities of the CM Sign, ISNT Rule, and Modified ISNT Rule in Discriminating Glaucoumatoses Eyes From Normal Eyes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Positive ( ^{a} )</th>
<th>Negative ( ^{a} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>CM sign</td>
<td>91.4 (81.6-96.5)</td>
<td>82.9 (71.6-90.5)</td>
<td>.001</td>
<td>.001</td>
</tr>
<tr>
<td>ISNT rule</td>
<td>75.7 (63.7-84.8)</td>
<td>71.4 (59.2-81.3)</td>
<td>.001</td>
<td>.001</td>
</tr>
<tr>
<td>Modified ISNT rule</td>
<td>68.6 (56.2-78.9)</td>
<td>76.6 (64.7-86.2)</td>
<td>.001</td>
<td>.001</td>
</tr>
</tbody>
</table>

Abbreviations: CM, crescent moon; ISNT, the thickness of disc rims beginning with the inferior rim followed by the superior rim, the nasal rim, and the temporal rim; modified ISNT rule, application of the ISNT rule based on the long axis of the disc.

### Table 3. Topographic Relationship Between the CM Sign and Corresponding Visual Field Defect

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 Visual Field Defect</th>
<th>Group 2 Visual Field Defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior hemifield defect,</td>
<td>Positive (63)</td>
<td>Positive (53)</td>
</tr>
<tr>
<td>Inferotemporal CM sign</td>
<td>Negative (77)</td>
<td>Negative (67)</td>
</tr>
<tr>
<td>Positive</td>
<td>48</td>
<td>40</td>
</tr>
<tr>
<td>Negative</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Inferior hemifield defect,</td>
<td>Positive (32)</td>
<td>Positive (26)</td>
</tr>
<tr>
<td>Superotemporal CM sign</td>
<td>Negative (108)</td>
<td>Negative (94)</td>
</tr>
<tr>
<td>Positive</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td>Negative</td>
<td>9</td>
<td>10</td>
</tr>
</tbody>
</table>

Abbreviation: CM, crescent moon.

\( ^{a} \) \( \chi^2 \) Test.
tify the morphological hallmarks of glaucomatous optic neuropathy in the myopic tilted disc. In the present study, we established the novel diagnostic CM sign on the stereoscopic view and determined that it offered good diagnostic performance in detecting early glaucomatous eyes with myopic tilted discs.

The ISNT rule introduced by Jonas et al.13 has been the standard screening tool in glaucomatous optic neuropathy. If the order of the ISNT rule is violated, glaucomatous damage to the optic disc rim is implicated.14 As far as we know, the usefulness of the ISNT rule in the myopic tilted disc has yet to be evaluated. Furthermore, the morphological characteristics of the myopic disc, specifically tilt and torsion, make the application of the ISNT rule problematic. Therefore, we applied a modified version of the ISNT rule in consideration of the rotation of the optic disc. That is, instead of the original central vertical axis connecting the 6- and 12-o’clock positions, the longest axis of the optic disc was used. Consequently, as the vertical axis of the optic disc was rotated, the rim configuration also was rotated. In any case, whereas the specificity of glaucoma detection was enhanced slightly by this modification, the sensitivity of glaucoma detection was slightly reduced, which remains unsatisfactory for precision glaucoma diagnostics. In the present study, the CM sign, compared with both the ISNT and modified ISNT rules, showed superior diagnostic sensitivity and specificity in identifying glaucomatous optic nerve damage. These present findings strongly suggested that the CM sign plays an important role as a screening tool in glaucomatous optic neuropathy with a myopic tilted disc. The good interobserver reliability shown in the assessment of the CM sign also supported the clinical applicability of the CM sign.

Because the optic disc is tilted temporally, the temporal slope decreases and the vertical ovality of optic cup increases.15-17 Therefore, the temporal rim of a normal myopic tilted disc is generally thin or absent. Instead, there are smooth connections between the inferior and temporal rim or between the superior and temporal rim. With the progression of localized glaucomatous damage, focal loss of neural rim tissue known as an optic disc notch develops.18,19 In the case of a myopic tilted disc, as glaucoma develops the optic disc notch can look like a disconnection between the inferior or the superior and the temporal rim margin, which represents the CM sign. That is, in the myopic tilted disc, the CM sign can be considered another form of glaucomatous neuroretinal rim loss. For example, in this study of glaucomatous eyes, the CM sign was more frequently observed in the inferior rim margin than in the superior rim margin. We attributed this to the fact that in the early stage, glaucomatous neuroretinal rim loss most frequently occurs in the inferotemporal region of the optic disc.20

In the myopic tilted disc, the optic cup is relatively larger than in eyes with normal refractive errors. Consequently, for accurate discrimination of glaucomatous and normal optic discs, depending solely on the cup-disc ratio is inadequate. In the present study, the area under the receiver operating characteristic curves of the cup-disc ratio for detection of glaucoma was 0.790 (data not shown).

The sensitivity of the CM sign for detection of a visual field defect in the corresponding hemifield was higher for the superior hemifield (87.3%-93.0%) than for the inferior hemifield (63.0%-70.0%). This might be explained by the fact that the optic disc tilt is most commonly associated with torsion in the inferotemporal direction21 and that even a small extent of inferior neuroretinal rim loss can be more easily detected as a CM sign in the early stage of glaucoma. On the other hand, superior neuroretinal rim loss can be relatively less obtrusive because it presents as a CM sign in the relatively advanced stage of glaucoma.

Recently, numerous computerized imaging devices such as optical coherence tomography and confocal scanning laser ophthalmoscopy have been used for the diagnosis of glaucoma. However, they are not suitable for glaucoma screening because they require expensive instruments and time-consuming processes. Moreover, optical coherence tomography seems not to offer the requisite sensitivity for glaucoma.
Research Original Investigation

myopic discs. This study validated the simple and intuitive CM sign as a prospectively more suitable mode of glaucoma diagnostic screening for cases of myopic tilted discs.

This study has several limitations. First, the sample size was relatively small. However, we enrolled another independent group for the validation whereby we were able to confirm the clinical utility of the CM sign. To verify the diagnostic ability, reliability, and validity of the CM sign as a widely applicable diagnostic tool for glaucoma, further studies that include large numbers of participants are essential. Second, the age distribution of the glaucoma group was relatively younger compared with those of other previous studies. We suppose that this was owing to the significant number of participants with myopic tilted discs that had been admitted to the glaucoma clinic for abnormal findings in their preoperative examination for refractive surgery. Because refractive surgery is performed mainly on young myopic patients, most of the individuals who were recruited in the present study were young. The mean age of individuals with myopic tilted disc with or without glaucoma is low, relative to the general glaucoma population. Therefore, in future studies, it would be prudent to validate the clinical utility of the CM sign with older individuals with myopic–tilted discs. Third, the control eyes were selected among individuals who had been referred as having glaucoma by general ophthalmologists but whose eyes subsequently were judged to be nonglaucomatous by glaucoma specialists; furthermore, these eyes did not show any glaucomatous progression for at least 3 years. Therefore, it is likely that they did not have glaucoma at the time of their inclusion. Nevertheless, we do not think that the CM sign can predict future development of glaucoma. Rather, we believe that in cases where the normal myopic tilted disc progresses to a glaucomatous disc, the CM sign will be evident.

Even considering these limitations, this study carries significance for its introduction of a new morphological hallmark (the CM sign) of glaucomatous optic neuropathy in the myopic tilted disc, as well as for its assessment of the sign’s diagnostic ability compared with the ISNT rule.

Conclusions

The present study suggests that the presence of discontinuity between the superior or inferior optic rim margin and the temporal optic rim margin (the CM sign) provides an important diagnostic indication of glaucomatous optic neuropathy with a myopic tilted disc. Compared with the ISNT rule, the CM sign demonstrated both superior diagnostic sensitivity and higher predictive strength relating to the occurrence of glaucoma with myopic tilted discs.

ARTICLE INFORMATION


Author Contributions: Dr S. H. Kim had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: M. J. Kim, S. H. Kim, Hwang, D. M. Kim. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: M. J. Kim, S. J. Kim, D. M. Kim. Critical revision of the manuscript for important intellectual content: M. J. Kim, Hwang, Park, T-W, Kim. Statistical analysis: M. J. Kim, S. H. Kim. Administrative, technical, or material support: T-W Kim. Study supervision: Hwang, Park, D. M. Kim.

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Correction: This article was corrected on August 26, 2014, for a typographical error in the Abstract.

REFERENCES


I See a Seashell in My Right Eye

Ehsan Rahimy, MD; James Vander, MD

A 43-year-old man with a known history of macular telangiectasia type II presented with acute onset of a scalloped-shaped scotoma, which he described as “seeing a seashell” in his right eye. Ophthalmoscopy revealed intraretinal and subretinal macular hemorrhage, and fluorescein angiography demonstrated perifoveal leakage consistent with subretinal neovascularization. The scalloped nature of the blood was due to its accumulation within the Henle layer, as confirmed by optical coherence tomography.