Photoreceptor Inner/Outer Segment Defect Imaging by Spectral Domain OCT and Visual Prognosis after Macular Hole Surgery

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PURPOSE. To evaluate photoreceptor inner/outer segment (IS/OS) defect parameters by using spectral domain-optical coherence tomography (SD-OCT) for correlation with visual outcomes in macular hole surgery (MHS).

METHODS. This study was an interventional, retrospective case series. Twenty-three eyes (23 patients) were examined by SD-OCT before and after (median, 2.3 months) anatomically successful MHS. Two formats of OCT were analyzed: linear (raster) and composite (partial fundus image). Factors that may have confounded IS/OS measurements were controlled by using weighting and normalization of data. The main outcome measures were diameter and area of the IS/OS defect, weighted area of the IS/OS defect, macular density ratio (MDR), healing pattern of the macular hole, and preoperative and postoperative best corrected visual acuity (BCVA).

RESULTS. Poorer preoperative BCVA correlated with larger preoperative diameter of the IS/OS defect (P = 0.005). A greater improvement in BCVA correlated with a larger preoperative area of IS/OS defect (P = 0.038) and smaller MDR (P = 0.012). Poorer postoperative BCVA correlated with a larger postoperative diameter of the IS/OS defect (P = 0.010), larger weighted postoperative area of IS/OS defect calculated by raster scan (P = 0.015), larger postoperative area of IS/OS defect measured from the partial fundus image (P = 0.003), and apparent glial sealing pattern on SD-OCT (P = 0.0005). The shape of the IS/OS defect area was round and regular before surgery, but irregular afterward.

CONCLUSIONS. BCVA after MHS correlates with objectively ascertainable SD-OCT measurements of IS/OS defects and other features. The postoperative area of the IS/OS defect, when directly measured, correlates more strongly with BCVA than do linear-based measurements, perhaps because of the irregular shape of the IS/OS defect after surgery. (Invest Ophthalmol Vis Sci. 2010;51:1651–1658) DOI:10.1167/iovs.09-4420

The prognostic relationships between preoperative clinical features of macular holes such as size, preoperative best corrected visual acuity (BCVA), duration and stage and postoperative visual outcome have long been established.1–3 Optical coherence tomography (OCT) has revolutionized macular imaging and also allows quantitative measurements of many anatomic parameters in vivo. A first generation of such quantitative capabilities from time domain (TD-OCT) yielded measurements in macular hole cases, such as basal diameter, macular hole index (MHI), and hole form factor,4,5 which have recently been shown to correlate with visual prognosis.6,7 An initial theme has been that photoreceptor reflectivity more closely correlates with postoperative visual acuity than with inner foveal morphology.9

The inner segment/outer segment (IS/OS) junction is a more specific representation of photoreceptor integrity, and although it can be resolved with TD-OCT,10 it is better resolved by using spectral domain OCT (SD-OCT) imaging.10 It has been identified as a key component influencing visual acuity in eyes with epiretinal membranes,9,11 retinal detachment,12,13 macular holes, and myopic tractional maculopathy.14,15 The SD-OCT methodology yields a wealth of digital data for analysis and three-dimensional reconstruction imaging.10,16

It seems rational that the integrity of the IS/OS junction should be a surrogate for photoreceptor function. Although, early studies with TD-OCT suggested that photoreceptor cell thickness correlates with visual prognosis,8,9 there are some conflicting reports regarding IS/OS correlation with visual prognosis.17–24 A fundamental, but overlooked issue has been the lack of standardized criteria for measuring the IS/OS defect; hitherto, it has been visually defined from the image, which involves an element of subjectivity when judging margins.

The purpose of this study was to standardize measurements of the IS/OS and to investigate the relationship of the IS/OS defect to visual acuity outcomes in patients before and after macular hole surgery (MHS). A specific question was whether the area of the IS/OS defect correlates better than linear measures.

METHODS

The study design was that of a consecutive, retrospective case review. The protocol was approved by the Human Subjects Committee of the University of Miami Miller School of Medicine and was conducted in accordance with the Declaration of Helsinki for research in human subjects. Between April 2006 and August 2008, 26 patients undergoing surgery for idiopathic macular hole at the Bascom Palmer Eye Institute by two surgeons (WES, HWF) were imaged before and after surgery with an SD-OCT system (Cirrus; Carl Zeiss Meditec, Inc., Dublin, CA) and the results included in this study. This system utilizes a superluminescent diode with a bandwidth of 50 nm centered at 840 nm. Three patients were excluded because of conditions that might confound
visual potential, including advanced glaucoma (one case), failed closure of a macular hole (one case), or a reopened hole after previously successful surgery (one case).

The patients underwent a complete ophthalmic examination, including BCVA measurement and SD-OCT before and after surgery. ETDRS (Early Treatment of Diabetic Retinopathy Study) charts were not used, but calibrated, projected Snellen charts were used to provide a manifest refraction at the specified time point. Three sets of SD-OCT protocols were acquired for each eye at each sitting: one 5-line raster pattern and two cube patterns centered around the fovea. The 5-line raster data sets consisted of five horizontal B-scans, each of which covered a horizontal distance of 6 mm and comprised 4096 A-scans; each B-scan was spaced 250 μm apart. Two SD-OCT cube protocols, which yielded the composite (partial fundus image) were used: one with a 512 × 128 cube and the other using a 200 × 200 cube, where the first number denotes the number of horizontal B-scans acquired, and the second indicates the number of A-scans within each B-scan. Both cube scans covered a retinal area of 6 mm². One of each cube scan protocol was acquired as part of the imaging protocol.

Pars plana vitrectomy (20-gauge) was performed using regional anesthesia and monitored anesthesia care. The inner limiting membrane (ILM) was removed for 360° around the edge of the macular hole in all eyes. No ILM staining was used in 19 (83%) eyes; indocyanine green staining was performed in 3 (13%) eyes, and triamcinolone was used in 1 (4%) eye. Gas tamponade with 16% perfluoropropane in 22 (96%) eyes or 20% sulfur hexafluoride in 1 (4%) eye was followed by green staining in 3 (13%) eyes, and triamcinolone was used in 1 (4%) eye. Gas tamponade with 16% perfluoropropane in 22 (96%) eyes or 20% sulfur hexafluoride in 1 (4%) eye was followed by green staining in 3 (13%) eyes, and triamcinolone was used in 1 (4%) eye. Gas tamponade with 16% perfluoropropane in 22 (96%) eyes or 20% sulfur hexafluoride in 1 (4%) eye was followed by green staining in 3 (13%) eyes, and triamcinolone was used in 1 (4%) eye. Gas tamponade with 16% perfluoropropane in 22 (96%) eyes or 20% sulfur hexafluoride in 1 (4%) eye was followed by green staining in 3 (13%) eyes, and triamcinolone was used in 1 (4%) eye. The inner limiting membrane was removed for 360° around the edge of the macular hole.

Measuring the IS/OS Defect in Horizontal Cross-sectional Images

The central B-scan in the 5-line raster image was exported as a bitmap file and processed to an image by using Image J. Linear distances of the diameter of the IS/OS defect, the horizontal basal diameter of the macular hole, the minimum hole diameter, and hole height were measured. The MHI was calculated as macular hole height/basal diameter.

The reflectivity of the IS/OS was measured from within a 40-μm-thick slab located 20 μm above the retinal pigment epithelium (RPE) to incorporate the IS/OS junction line in Image J, by using the plot profile function of a line with the fixed width of 6 pixels (Fig. 1). This function accounted for variations in the curvature and orientation of the image. Since visually determining the margin of the IS/OS defect involves some subjectivity, its border was defined as the point on the gray-scale image at which IS/OS reflectivity had diminished by 2 SD from the normalized central mean IS/OS reflectivity. The normalized central mean IS/OS reflectivity was calculated by multiplying the mean of the reflectivities of the IS/OS of the unaffected peripheral macula between 2 and 3 mm from the foveal center (both sides) by the ratio of central-to-peripheral reflectivity from 12 normal fellow (control) eyes, to control for possible general signal attenuation defects in the image. The defect was measured 10 times in each patient, and the 80% trimmed mean was used for analysis; the coefficient of variance in each patient ranged from 0.003 to 0.049 (mean, 0.014).

Within the defect area margins as defined, there were some non-contiguous zones where the reflectivity exceeded the 2-SD lower threshold definition. This finding varied among cases, but might represent areas subserving some level of visual function, albeit subnormal. To capture this potential anatomic correlate of visual function, we analyzed these zones by using a weighting factor, the defect reflectivity ratio (DRR), defined as [(normalized central mean IS/OS reflectivity − mean reflectivity of the IS/OS defect)/(normalized central mean IS/OS reflectivity)]. The weighted IS/OS area defect was calculated by assuming that the area of the defect was circular: DRR × π × (the defect diameter/2)².

Measuring the IS/OS Defect Area in the Partial Fundus Image

The partial fundus image was obtained from the cube scan by using the advanced visualization setting in the system software (Cirrus, 3.0; Carl Zeiss Meditec). Using the technique described earlier, we selected an RPE-based, 40-μm-thick slab, positioned 20 μm above the RPE for each B scan. This method displayed the SD-OCT data located between two surfaces parallel to the RPE, but displaced anteriorly. Each B-scan was viewed individually, to confirm that the IS/OS junction line stayed within the RPE-based slab. This partial fundus image was processed to a gray-scale image with Image J. A threshold adjustment was performed to segment the gray-scale image into features of interest (IS/OS defect) and background (normal IS/OS). The threshold level was set at 1 SD from the mean of the reflectivity from the histogram of the image. The resultant area was measured by using the wand tool to trace the boundary on the image, containing the red components of the original. This raw area measurement was used to calculate the weighted IS/OS defect area from the partial fundus image. The largest horizontal diameter of the IS/OS defect was measured from the partial fundus image and compared to values from the raster scan for validation. The IS/OS defect area was measurable directly from the partial fundus image of the IS/OS in 18 preoperative eyes and 18 postoperative eyes (Fig. 2), but was not
measurable in the other eyes, because early software limitations limited movement of the RPE-based slab within the image.

**Macular Density Ratio**

The possibility that signal strengths of IS/OS reflectivity is stronger due to less attenuation by optically clearer retinal tissue anterior to it, such as might occur with macular edema spaces, was compensated for by defining a macular density ratio (MDR). This quantitative factor varied inversely with the proportion of macular edema (i.e., the more cystic spaces, the lower the MDR) and was used to normalize the IS/OS reflectivity measurement. Image J was used to measure the mean reflectivity from the center of the macula out to 1.5 mm, excluding the hole and subretinal space area, from just above the retinal pigment epithelium (RPE) to the inner retinal border (ILM) in the line raster scan. Similar to the normalization technique for DRR, the mean reflectivity of the retina in the normal (nonedematous) peripheral macula between 2 and 3 mm from the center of the same eye was measured as a control value for the SD-OCT image. Each parameter was measured 10 times in each patient, and the 80% trimmed mean was used for analysis. The MDR was defined as the ratio of the reflectivity of the central sample of the macula to the control (peripheral) value.

**Macular Hole Healing Pattern**

The pattern of the closed macular hole after surgery was categorized according to the presence or absence of apparent glial sealing (markedly disordered reflectivity) as imaged on the line raster scan. Glial sealing was defined as a hyper-reflective lesion that replaced normal foveal retinal layers, including the external limiting membrane and the IS/OS junction (Fig. 3). The patterns were very disparate, and a distinction was never equivocal between two independent observers.

**Statistical Analysis of Anatomic–Visual Acuity Correlations**

The SD-OCT measurements were compared to pre- and postoperative BCVA corresponding to the date the scan was obtained, best postoperative BCVA, and change in BCVA. The patients who were observed for less than 3 months after surgery were excluded from best postoperative BCVA correlations. BCVA, visual prognosis, and IS/OS defect relationships were statistically analyzed (SPSS, ver. 12.0; SPSS Inc., Chicago, IL). Visual acuities were converted to logarithm of the minimal angle of resolution (logMAR) units before statistical analysis. The Wilcoxon’s signed-ranks test was used to compare the change between pre- and postoperative measurements. Correlations between SD-OCT parameters and visual acuity were analyzed with Spearman’s ranked correlation or multiple linear regressions. Differences in measurements between healing patterns were analyzed with the Mann-Whitney U test. A Bland-Altman plot of the difference of the IS/OS defect between the horizontal cross-sectional image and the partial fundus image was drawn to assess the agreement between the two methods, since it is more appropriate (but less familiar) for correlation between different methods of measure.27 Correlations between MDR and IS/OS defect parameters when controlling the difference of basal hole diameter were analyzed with Spearman’s partial correlation (SAS, ver. 9.13; SAS Inc., Cary, NC).

**RESULTS**

**Clinical Features**

The study cohort comprised 23 eyes of 23 patients. There were 7 (30%) male patients and 16 (70%) female patients (Table 1).
The median age was 64 years; 18 (79%) were phakic and 5 (21%) were pseudophakic before surgery. The median interval between onset of visual symptoms and MHS was 3 months. Five eyes had a stage 2 macular hole, 15 eyes stage 3, and 3 eyes stage 4. Preoperative SD-OCT was obtained a median of 6 days before surgery. The median interval until SD-OCT imaging after surgery was 2.3 months. The median interval between MHS and last follow-up examination was 3 months. The median preoperative BCVA was 20/80 and improved to 20/40 at the time of postoperative SD-OCT imaging.

### SD-OCT Features in Normal Eyes

SD-OCT parameters including IS/OS reflectivity and MDR were measured in 12 normal fellow eyes of the present study patients who underwent SD-OCT. Their median age was 59 years (range, 42–71). Eight patients were women. The measured IS/OS reflectivity in the central and peripheral macula followed a Gaussian distribution. The mean IS/OS reflectivity in decibels of the central macula was 95.7% ± 0.02% of the reflectivity of the peripheral macula. The mean MDR of normal eyes was 0.94 ± 0.02.

### Preoperative SD-OCT Features

#### Horizontal Cross-sectional Image

The median basal hole diameter was 602 μm (range, 104–998). The mean preoperative IS/OS junction defect linear dimension was 1389 μm (range, 600–2432). A larger preoperative IS/OS defect diameter correlated with a larger basal hole diameter ($P = 0.001$, correlation coefficient $r = 0.667$), greater hole height ($P < 0.001$), lower MDR ($P < 0.001$), and older age ($P = 0.043$), but not symptom duration. Multiple linear regression analysis including age, basal diameter, hole height, and MDR also showed that a larger preoperative diameter of the IS/OS defect correlated with a larger hole height ($P = 0.012$) and lower MDR ($P = 0.043$), but not with basal diameter or age.

#### Partial Fundus Image for IS/OS

The median basal hole diameter from the partial fundus image for IS/OS was 664 μm (range, 90–957). The median preoperative IS/OS junction defect diameter was 1474 μm (range, 480–2070). The median basal hole area and IS/OS defect area were 0.325 (range, 0.007–0.760) and 1.408 (0.072–3.257) mm², respectively.

### Postoperative SD-OCT Features

#### Horizontal Cross-sectional Image: 5-line Raster

The median postoperative horizontal IS/OS defect diameter was reduced to 720 μm (range, 0–1702 μm) from the raster scan, compared with preoperative values ($P < 0.001$). Larger postoperative IS/OS defect diameter correlated with larger preoperative basal hole diameter ($P = 0.040$, $r = 0.432$) and with smaller preoperative MHI ($P = 0.003$, $r = -0.588$), but not with preoperative diameter of the IS/OS defect, age, or symptom duration. A larger decrease in the IS/OS defect diameter correlated with a lower preoperative MDR ($P = 0.023$, $r = -0.473$), even when controlling for the difference in basal hole diameter ($P = 0.003$, $r = -0.599$, Spearman’s partial correlation). Postoperative MDR did not correlate with IS/OS defect diameter, area, or weighted defect.

#### Partial Fundus Image for IS/OS

The median postoperative diameter and area of the IS/OS defect were reduced to 708 μm (range, 0–1490) and 0.210 mm² (0.11–1.132), respectively ($P < 0.001$).

The preoperative (slope = 0.924; $r = 0.861$) and postoperative (slope = 1.028; $r = 0.898$) diameters of the IS/OS defect in the 5-line raster scan correlated closely (92%) with the partial fundus image measurement (Figs. 4A, 4B). The preoperative (slope = 1.049; $r = 0.880$) IS/OS defect area calculated by using the linear diameter measured from the 5-line raster scan was similar to that measured from the preoperative partial fundus image of the cube scan (Fig. 4C), but the postoperative area (slope = 1.264; $r = 0.677$) was not (Fig. 4D). The preoperative area of the IS/OS defect, as it appeared in the partial fundus image, was relatively round and regular, but the postoperative area of the IS/OS defect was irregularly shaped (Fig. 5).

### Correlation between Anatomic Features and BCVA

Poorer pre- ($P = 0.002$) and postoperative BCVA correlated with larger horizontal macular hole basal diameter from the horizontal cross-sectional image ($P = 0.013$; Table 2). Poorer preoperative BCVA correlated with larger preoperative diameter of the IS/OS defect from the 5-line raster scan ($P = 0.005$) and with larger hole height ($P = 0.043$). Poorer pre ($P = 0.047$) and postoperative ($P = 0.027$) BCVA, but not change in BCVA, correlated with smaller MHI. Improvement in BCVA correlated with lower preoperative MDR ($P = 0.012$).

Poorer post ($P = 0.042$) and postoperative BCVA ($P = 0.042$) correlated with larger horizontal macular hole basal diameter from the partial fundus image. Poorer preoperative BCVA correlated with larger preoperative IS/OS defect diameter from the partial fundus image ($P = 0.045$) and with larger basal hole area ($P = 0.007$) and preoperative IS/OS defect area ($P = 0.009$), but more improvement in BCVA correlated only with larger preoperative IS/OS defect area ($P = 0.038$).

Poorer postoperative BCVA correlated with larger postoperative IS/OS defect diameter ($P = 0.010$), calculated IS/OS defect area ($P = 0.010$), and weighted calculated IS/OS defect area ($P = 0.013$) on the horizontal cross-sectional image (5-line raster). Postoperative BCVA did not correlate with postoperative MDR (Table 3). Poorer postoperative BCVA also correlated with IS/OS defect diameter ($P = 0.008$), IS/OS defect area ($P = 0.003$), and weighted IS/OS defect area ($P = 0.003$), when measured on the partial fundus image of the cube scan.

### Recovery Pattern of IS/OS Defect

An apparent glial sealing pattern of the macular hole was seen in 5 of the 23 eyes. The basal hole diameter (mean ± SD, 945 ± 64 μm) was larger in eyes with glial sealing than in eyes without (548 ± 221 μm; Mann-Whitney U test, $P = 0.001$, $U = 0.000$; Fig. 6, top left). The preoperative IS/OS defect diameter on the 5-line raster scan was not different between sealing patterns. The eyes with glial sealing had a lower ratio of IS/OS defect diameter to basal hole diameter (1.44 ± 0.34, Mann-Whitney U test $P = 0.001$, $U = 0.000$) and lower MHI (0.40 ± 0.05, Mann-Whitney U test, $P = 0.001$, $U = 0.000$) than did the eyes without glial sealing (2.80 ± 1.48, 0.79 ± 0.52).

The preoperative BCVA was not different between sealing patterns, but best postoperative BCVA (0.49 logMAR) was poorer in the eyes with apparent glial sealing than in patients without it (0.17 logMAR, Mann-Whitney U test, $P = 0.005$, Mann-Whitney U = 0.500).

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**TABLE 1.** Patient Characteristics

<table>
<thead>
<tr>
<th>Patients, n</th>
<th>23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>43-84 years (median, 64)</td>
</tr>
<tr>
<td>Sex</td>
<td>Female 16 (70%)</td>
</tr>
<tr>
<td>Symptoms duration, mo</td>
<td>1-17 (median, 5)</td>
</tr>
<tr>
<td>Lens status, phakic</td>
<td>18 (78%)</td>
</tr>
<tr>
<td>Preoperative BCVA</td>
<td>20/20-20/400 (median, 20/80)</td>
</tr>
<tr>
<td>Postoperative BCVA</td>
<td>20/20-20/400 (median, 20/40)</td>
</tr>
<tr>
<td>Best postoperative BCVA</td>
<td>20/20-20/80 (median, 20/30)</td>
</tr>
<tr>
<td>Time of preop SD-OCT imaging, d</td>
<td>1-29 (median, 6)</td>
</tr>
<tr>
<td>Time of postop SD-OCT imaging, mo</td>
<td>0.5-6 (median, 2.3)</td>
</tr>
<tr>
<td>Postop follow-up, mo</td>
<td>0.5-16 (median, 3.0)</td>
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</table>
DISCUSSION

Photoreceptors are a critical determinant of macular function. The IS/OS junction represents one aspect of photoreceptor integrity and probably also reflects its function. SD-OCT not only allows a better subjective image, but yields data for more detailed analysis of IS/OS defects and other features. Previous studies have reported a poorer visual prognosis in eyes with larger IS/OS defect. Larger volumes and diameters of photoreceptor defect correlated with poorer postoperative BCVA.
Correlation between Preoperative SD-OCT Parameters and Best-Corrected Visual Acuity

<table>
<thead>
<tr>
<th>Pre. SD-OCT parameters</th>
<th>Median (Range)</th>
<th>Pre. BCVA Correlation</th>
<th>Pre. BCVA P*</th>
<th>Best Post. BCVA Correlation</th>
<th>Best Post. BCVA P*</th>
<th>Change in BCVA Correlation</th>
<th>Change in BCVA P*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Preoperative SD-OCT Parameters</td>
<td>Median (Range)</td>
<td>Correlation</td>
<td>P*</td>
<td>Correlation</td>
<td>P*</td>
</tr>
<tr>
<td>From horizontal cross-sectional image</td>
<td></td>
<td>Basal hole diameter</td>
<td>602 μm (104–998)</td>
<td>−0.608</td>
<td>0.002</td>
<td>−0.644</td>
<td>0.013</td>
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<td></td>
<td></td>
<td>IS/OS defect diameter</td>
<td>1389 μm (600–2432)</td>
<td>−0.564</td>
<td>0.005</td>
<td>−0.130</td>
<td>0.658</td>
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<tr>
<td></td>
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<td>Hole height</td>
<td>354 μm (152–509)</td>
<td>−0.427</td>
<td>0.042</td>
<td>−0.049</td>
<td>0.867</td>
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<tr>
<td></td>
<td></td>
<td>MHI</td>
<td>0.6 (0.4–2.8)</td>
<td>0.418</td>
<td>0.047</td>
<td>0.588</td>
<td>0.027</td>
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<tr>
<td></td>
<td></td>
<td>MDR†</td>
<td>0.80 (0.61–0.96)</td>
<td>0.376</td>
<td>0.077</td>
<td>0.038</td>
<td>0.897</td>
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<tr>
<td>From partial fundus image for IS/OS</td>
<td></td>
<td>Basal diameter</td>
<td>664 μm (90–957)</td>
<td>−0.483</td>
<td>0.042</td>
<td>−0.619</td>
<td>0.042</td>
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<td></td>
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<td>IS/OS defect diameter</td>
<td>1474 μm (80–2070)</td>
<td>−0.477</td>
<td>0.045</td>
<td>−0.088</td>
<td>0.797</td>
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<tr>
<td></td>
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<td>Basal hole area</td>
<td>0.325 mm² (0.007–0.760)</td>
<td>−0.615</td>
<td>0.007</td>
<td>−0.531</td>
<td>0.093</td>
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<tr>
<td></td>
<td></td>
<td>IS/OS defect area</td>
<td>1.408 mm² (0.072–3.257)</td>
<td>−0.594</td>
<td>0.009</td>
<td>−0.120</td>
<td>0.724</td>
</tr>
</tbody>
</table>

Pre., preoperative; Post., postoperative; BCVA, best corrected visual acuity; IS/OS, inner/outer segment; MHI, macular hole index; MDR, macular density ratio.

* Spearman’s ranked correlation, bold type indicates P < 0.05.
† The mean reflectivity of the center of the macula to 1.5 mm/the mean reflectivity of the peripheral macula 2 to 3 mm from the center.

Table 3. Correlation between Postoperative SD-OCT Tomography Parameters and Postoperative BCVA

<table>
<thead>
<tr>
<th>Postoperative SD-OCT Parameters</th>
<th>Median (Range)</th>
<th>Correlation</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>From horizontal cross-sectional image</td>
<td></td>
<td>IS/OS defect diameter</td>
<td>720 μm (0.1–1.702)</td>
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<tr>
<td></td>
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<td>Calculated IS/OS defect area†</td>
<td>0.407 mm² (0.2–2.27)</td>
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<td></td>
<td></td>
<td>Weighted calculated IS/OS defect area</td>
<td>0.143 (0.723)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Macular density ratio‡</td>
<td>0.84 (0.56–0.96)</td>
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<tr>
<td>From partial fundus image for IS/OS§</td>
<td></td>
<td>IS/OS defect diameter</td>
<td>708 μm (0.1–1.900)</td>
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<tr>
<td></td>
<td></td>
<td>Measured IS/OS defect area</td>
<td>0.210 mm² (0.1–1.132)</td>
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<tr>
<td></td>
<td></td>
<td>Weighted measured IS/OS defect area</td>
<td>0.069 (0.4–7.5)</td>
</tr>
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</table>

BCVA, best corrected visual acuity; IS/OS, inner/outer segment.
* Spearman’s ranked correlation (in the 18 eyes with both five-line raster and partial fundus image calculations), bold type indicates P < 0.05.
† Calculated by assuming that the area of the defect was circular using \( \pi \times (\text{defect diameter})^2 \).
‡ Macular density ratio, the mean reflectivity of the central 3 mm of the macula/the mean reflectivity of the peripheral macula.
§ Calculable in 18 of the eyes with available partial fundus image, using the defective reflectivity ratio from raster scan.
introduced no more than a 6% variation from assuming no function central to the defect border.

The present study also used the MDR, under a principle similar to that reported elsewhere, to evaluate the possibility that inner retinal abnormalities such as macular edema may affect the amount of reflectivity from deeper tissues and confound IS/OS defect correlations. Although more improvement in BCVA correlated with a lower MDR (more edema), perhaps by being a reversible feature, it did not confound other postoperative correlations, probably because there are few or no intraretinal cystic spaces in closed macular holes.

The normalization factors and the automated measurement techniques described in this study reduced subjective errors to a level that seems to be below clinical significance, but image interpretation involves some manual steps. Furthermore, other factors (e.g., duration, initial BCVA) may confound even the most accurate measurements of the most important parameters, and so caution is necessary in applying these results to clinical practice.

A limitation of the present study is that the interval to postoperative SD-OCT imaging was not the same for each patient. The defect area is likely to decrease for several months after surgery and may account for the sustained improvements in visual acuity that have been reported in many cases. To minimize this effect, we used the BCVA measured at the time of SD-OCT examination for analysis of BCVA. Two patients underwent an SD-OCT at least twice after surgery. In one, the IS/OS defect and BCVA improved (Fig. 3), but both parameters were unchanged in the other patient. This result should be studied further.

Morphology may reflect function, but also with some qualifications. Previous studies have or have not found inner retina morphology to correlate with visual function. Ko et al. sorted SD-OCT imaging features after MHS into five categories, of which might relate to an IS/OS defect and account for prognostic value. In the present study, an apparent glial sealing–type (disordered reflectivity) healing pattern, apparently correlated with the histopathologic appearance, which correlated with poorer postoperative BCVA and IS/OS defect size, but also larger preoperative macular hole size. Whether glial closure is a consequence of larger macular holes or an impediment to better healing of the IS/OS defect requires further study.

In conclusion, we used SD-OCT with rigorously defined metrics and control factors to measure IS/OS defect parameters in a cohort of eyes that underwent MHS. Linear measures of IS/OS defects clearly correlated with visual function parameters and prognosis, but the irregular shape of the IS/OS defect area helped explain why visual function results correlate more significantly with measured area. Other factors such as macular edema and glial sealing morphology may also be important factors influencing outcome and must be considered in context.

References