Wide-Field En Face Swept-Source Optical Coherence Tomography Features of Extrafoveal Retinoschisis in Highly Myopic Eyes

Wei Xiao,1 Zhuoting Zhu,1 Capucine Odouard,1 Ou Xiao,1 Xinxing Guo,1 and Mingguang He1,2

1State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China
2Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, Melbourne, Victoria, Australia

PURPOSE. To evaluate the features of extrafoveal retinoschisis (EFRS) in highly myopic eyes detected by swept-source optical coherence tomography (SS-OCT).

METHODS. In this retrospective case series, 89 eyes of 65 patients with high myopia and coexisting EFRS were included. The participants underwent a comprehensive ophthalmologic examination, including visual acuity, ocular biometry, refraction, and perimetry. Three-dimensional wide-field scans were obtained with SS-OCT, and en face images were reconstructed with custom software. En face OCT features of EFRS were determined by two ophthalmologists masked to clinical characteristics. The associations of EFRS subtypes with ocular biometry and other OCT features were compared. The sample was divided into subgroups according to specific features of EFRS subtypes.

RESULTS. In wide-field SS-OCT scans, EFRS was classified into three different types, the inner limiting membrane detachment and inner and outer EFRS, according to the specific layer of the splitting. All these three types were most frequently distributed in the inferotemporal quadrant (71.2% for ILM detachment, 59.5% for inner EFRS, and 75.0% for outer EFRS). Inner limiting membrane detachment and inner EFRS were often adjacent to peripapillary atrophy. Outer EFRS tends to coexist with inner EFRS, as we did not observe any case with standalone outer EFRS or with coexisting with ILM detachment. Eyes with all three types combined had the longest axial length (29.1 ± 1.26 mm, P = 0.003) and the greatest refractive error (−13.0 ± 2.86 diopters [D], P = 0.014). The incidence of retinal microfolds and breaks among subgroups was significantly different (P = 0.012 and 0.003, respectively). Staphyloma was associated with outer EFRS (30.6% with versus 7.6% without outer EFRS).

CONCLUSIONS. Wide-field SS-OCT reveals the spatial distribution of retinoschisis outside the fovea, and associations with retinal vessels and other retinal landmark structures. Further observations on the longitudinal changes and functional damage would help lead to a better understanding of its mechanism and prognosis.

Keywords: extrafoveal retinoschisis, optical coherence tomography, en face, high myopia

High myopia is associated with a progressive elongation of the eyeball, which can cause a variety of retinal complications including lacquer cracks in the Bruch's membrane, diffuse and focal chorioretinal atrophy, and myopic macular holes.1 With the emergence of optical coherence tomography (OCT), several types of retinal abnormalities barely visible in slit-lamp microscope have become documentable in highly myopic eyes, for example, foveal and extrafoveal retinoschisis2,3 and a series of paravascular vascular abnormalities (i.e., paravascular cysts, microfolds, paravascular lamellar holes, and paravascular retinoschisis).3 Previous studies have largely concentrated on documenting the OCT characteristics of foveoschisis (i.e., foveal retinoschisis), and its correlation with developing severe sight-threatening conditions such macular hole or retinal detachment.5,6 Evidence also indicates that paravascular retinoschisis and lamellar holes are associated with the formation of foveoschisis.4,7 As the potential precursors of foveoschisis,4,7 retinoschisis outside the fovea (extrafoveal retinoschisis) and paravascular abnormalities are less described in terms of OCT features and links with biometry and other OCT findings. Moreover, most previous observations were dependent on single or several cross-sectional OCT B-scans, so they could not provide an adequate view of the retinoschisis, especially that outside the fovea.

A new technique called swept-source OCT (SS-OCT), which uses a frequency-swept (tunable) laser and a dual-balanced photo detector, offers potential advantages compared to the spectral-domain OCT (SD-OCT).8 Commercial devices, for example, the DRI OCT-I system (Atlantis; Topcon, Tokyo, Japan), has an image acquisition speed of 100,000 A-scans per second. The ability of high-speed imaging has overcome eye motion artifact in routine examinations and also made it possible to observe larger areas (e.g., 12 × 6 mm for DRI-OCT versus 6 × 6 mm for three-dimensional [3D] OCT) and enable 3D reconstructions of the entire posterior pole. Further, by combining this high-speed imaging with en face technique, it produces simultaneous longitudinal and transverse images of the macular area with high pixel-to-pixel correspondence. This technique has enabled new detailed characterization of retinal diseases such as neovascular age-related macular degeneration,9...
chronic central serous chorioretinopathy,\textsuperscript{10} and polypoidal choroidal vasculopathy.\textsuperscript{11,12} Novel information on these conditions has provided us with information on the underlying pathogenesis of these conditions.

With the novel features of the SS-OCT, we sought to elucidate the en face features and their spatial distribution of extrafoveal retinoschisis (EFRS) in a wide-field scanning range in highly myopic eyes. The features identified were correlated with ocular biometry and other OCT abnormalities. Our goal was to use this analysis to understand the exact clinical features of EFRS and its association with the complications of high myopia. Myopic macular retinoschisis is generally classified as inner limiting membrane (ILM) detachment and inner and outer schisis.\textsuperscript{13,14} However, there was no study investigating the classification of EFRS. Therefore our study also sought to classify myopic EFRS and to link this classification with pathological changes such as staphyloma.

**METHODS**

All participants with high myopia (spherical dioptr [D] \(\leq 6\) in both eyes) and EFRS confirmed by OCT B-scans were selected from a High Myopia Registry study, a prospective study on the natural history of high myopia and related complications. This study adhered to the tenets of the Declaration of Helsinki. All procedures were prospectively approved by the Institutional Review Board of Zhongshan Ophthalmic Center. Written informed consent was obtained before ophthalmic examination.

All subjects received a complete ophthalmic examination, including best-corrected visual acuity test (BCVA), ocular biometry, intraocular pressure, retinal photographs, and a dilated fundus examination by a skilled ophthalmologist. Axial lengths were obtained from optical low-coherence reflectometry (Lenstar LS-900; Haag-Streit AG, Gartenstadstrasse, Koeniz, Switzerland). Refraction was measured with an autorefractor (Topcon KR-8800; Topcon) after cycloplegia. Retinal images were taken from a nonmydriatic fundus camera (Canon CX-1; Tokyo, Japan). Posterior staphyloma was independently assessed by two investigators (OX and XG) from retinal photographs according to the International Photographic Classification and Grading System for Myopic Maculopathy.\textsuperscript{15} Briefly, posterior staphyloma was graded into four groups: none, macula involved, macula not involved, and others. Macula-involved staphyloma was further divided into wide, narrow, and inferior subtypes, while macula not involved was divided into peripapillary, nasal, and inferior subtypes.

Patients were examined with a single SS-OCT system (DRI-OCT1; Topcon). The center wavelength of the probe beam was 1060 nm, and the axial resolution was 8 \(\mu\)m. The diopter compensation was set as needed. Twelve-line radial scans centered through both the optic disc and the fovea were used for confirming the presence of EFRS. A 12 \(\times\) 9-mm-wide 3D volumetric scan with 512 \(\times\) 256 A-scans was taken for both eyes and used for en face reconstruction subsequently. Subjects with the following conditions were excluded: (1) poor-quality scan, which was defined as the image quality value provided by the system less than 45; (2) any associated or concomitant retinopathy that could confound the retinal interpretation of OCT images; (3) a history of surgical treatment for retinal detachment, macular hole, epiretinal membrane, or foveoschisis; (4) a history of intravitreal administration of agents (e.g., triamcinolone, anti-vascular endothelial growth factor) or retinal photocoagulation.

En face images were generated from the 12 \(\times\) 9-mm-wide 3D volumetric scan with an intensity- and gradient-based prototype software (EnView, ver.1.0.1.31385; Topcon). The investigators could choose any of the three layers as reference surface for en face display: the Bruch’s membrane (BM), the inner plexiform layer/inner nuclear layer (IPL/INL), or the ILM. By automatically aligning and flattening the reference surface, the concavity and irregularity of the retina were corrected to provide a better quality of en face images. En face images of EFRS were evaluated and extracted at varying depth when the optimal reference surface was set. Generally, for ILM detachment and inner EFRS assessment, we set ILM as the reference surface, while we set BM as the reference plane to assess outer EFRS. The EnView software also allowed point-to-point correlation between en face images and B-scans. Paravascular abnormalities, including paravascular microfolds, vitreoretinal adhesion, and retinal break, were assessed from the same volumetric through viewing B-scans. Brightness and contrast of both en face and B-scan image were set as needed. To increase the en face image quality, the averaging ratio of the software was set to 2.6 times. All images were read by two ophthalmologists (WX and ZZ) masked to the patient’s information.

According to the layers affected by EFRS, we divided all enrolled eyes into five mutually exclusive subgroups: (1) ILM detachment only, (2) inner EFRS only, (3) ILM detachment plus inner EFRS, (4) inner plus outer EFRS, and (5) all subtypes combined. We did not observe any case with only outer EFRS or a combination of ILM detachment and outer EFRS, so there was no subgroup with outer EFRS only or outer EFRS plus ILM detachment. To investigate the spatial distribution of EFRS, we divided the 12 \(\times\) 9-mm rectangle scanning area into four quadrants, namely, supranasal, supratemporal, inferonasal, and inferotemporal zones in the schematic diagrams. The spatial distribution of each type of EFRS across in the posterior pole was analyzed the areas affected by each subtype.

All data were expressed as mean \(\pm\) standard deviation. Statistical analyses were performed using the Fisher exact probability test, \(\chi^2\) test, and Mann-Whitney \(U\) test. All analyses were performed by using STATA software version 12.0 (StatCorp, College Station, TX, USA). A \(P\) value of < 0.05 was accepted as statistically significant.

**RESULTS**

From the High Myopia Registry, we initially included 122 eyes of 82 subjects with apparent EFRS on B-scan in the analysis. Of these, 33 eyes (27.0%) were excluded because of poor quality of en face images (12 eyes, 9.8%), confounding retinopathies, for example, epiretinal membrane, macular hole (18 eyes, 14.8%), and history of intraocular surgery (3 eyes, 2.5%), thus yielding 89 eyes of 65 patients for the present analysis. Epiretinal membrane (ERM) and macular holes (MH) are common complications in high myopia. It was reported that 11.2% of eyes with spherical dioptr greater than \(-8\) D had ERM.\textsuperscript{16} In the present study, we aimed to describe the features of retinoschisis secondary to the elongation and deformation of eyeballs rather than the internal traction by ERM or MH. Accordingly, we ruled out 18 eyes with these complications. The age of the included patients ranged from 9.4 to 66.8 years (median 21.1 years). Thirty-three subjects (50.8%) were male and 32 (49.2%) were female. For the enrolled 89 eyes, the mean spherical equivalent (SE) was \(-1.45\) mm with a range of 24.6 to 31.5 mm. The mean BCVA was 0.73 \(\pm\) 0.24 (decimal scale, range, 0.2 – 1.0). Of the 65 patients, 41 (63.1%) were unilaterally affected by EFRS. The EnView software also allowed point-to-point correlation between en face images and B-scans. Paravascular abnormalities, including paravascular microfolds, vitreoretinal adhesion, and retinal break, were assessed from the same volumetric through viewing B-scans. Brightness and contrast of both en face and B-scan image were set as needed. To increase the en face image quality, the averaging ratio of the software was set to 2.6 times. All images were read by two ophthalmologists (WX and ZZ) masked to the patient’s information.

According to the layers affected by EFRS, we divided all enrolled eyes into five mutually exclusive subgroups: (1) ILM detachment only, (2) inner EFRS only, (3) ILM detachment plus inner EFRS, (4) inner plus outer EFRS, and (5) all subtypes combined. We did not observe any case with only outer EFRS or a combination of ILM detachment and outer EFRS, so there was no subgroup with outer EFRS only or outer EFRS plus ILM detachment. To investigate the spatial distribution of EFRS, we divided the 12 \(\times\) 9-mm rectangle scanning area into four quadrants, namely, supranasal, supratemporal, inferonasal, and inferotemporal zones in the schematic diagrams. The spatial distribution of each type of EFRS across in the posterior pole was analyzed the areas affected by each subtype.

All data were expressed as mean \(\pm\) standard deviation. Statistical analyses were performed using the Fisher exact probability test, \(\chi^2\) test, and Mann-Whitney \(U\) test. All analyses were performed by using STATA software version 12.0 (StatCorp, College Station, TX, USA). A \(P\) value of < 0.05 was accepted as statistically significant.
ly greater SE ($-10.8 \pm 3.54$ vs. $-10.4 \pm 3.44$ D, $P = 0.420$), longer AL (28.1 ± 1.60 vs. 27.8 ± 1.69 mm, $P = 0.412$), and poorer BCVA (0.71 ± 0.25 vs. 0.74 ± 0.25, $P = 0.558$) than the fellow eyes, but the differences were not statistically significant (paired $t$-test, Table 1). The differences of SE, AL, and BCVA between the right and left eye in bilaterally affected patients were also not significant (paired $t$-test, data not shown).

Characteristically, retinoschisis presented as hyporeflective spaces within the neurosensory retina on B-scan. From the wide-field scans, we found EFRS occurring within or between various retinal layers. However, the predominant subtypes were splitting within the retinal nerve fiber layer (ILM detachment), inner retina (beneath retinal nerve fiber layer [RNFL]), and outer retina (within or beneath plexiform layer [OPL], Fig. 1). In en face images, EFRS subtypes showed varied features. Of the 89 eyes, 52 eyes (58.4%) showed splitting between ILM and RNFL (ILM detachment). En face SS-OCT imaging revealed these lesions as heterogeneously hyporeflective areas extending along the RNFL. Generally, their upper and lower margins were well circumscribed, but the temporal and nasal borders were ill defined. Retinal nerve fibers through the affected areas presented as individual short hyperreflective arcs within a black background that followed an arcuate pattern across the retina (Fig. 1C). These hyperreflective arcs corresponded to the bridging tissues in retinoschisis space in B-scans (Fig. 1B). We observed 84 (94.4%) and 36 (40.5%) eyes with inner and outer EFRS,
respectively. Compared to ILM detachment, splitting beneath RNFL and intra-OPL showed homogeneously hyporeflective space in B-scans (Figs. 1E, 1H). In en face images, they also manifested as hyporelectivity with an irregular shape and poorly demarcated borders (Figs. 1E, 1H). Inner EFRS was manifested as hyporeflectivity with an irregular shape and space in B-scans (Figs. 1E, 1H). In en face images, they also showed homogeneously hyporeflective RNFL and intra-OPL respectively. Compared to ILM detachment, splitting beneath outer retina showed a different spatial distribution and was more likely to affect the inferonasal (38.9%) and supranasal (27.8%) quadrants.

We compared the clinical characteristics among eyes with different subtypes and combinations. The majority of the eyes (n = 56, 62.9%) were affected by two or more subtypes of EFRS. As summarized in Table 2, the difference of refractive error, AL, and BCVA was significant across the five subgroups (Kruskal-Wallis test, P = 0.014, 0.003, and 0.039, respectively). A trend was noted between the extent of refractive error, AL, and BCVA and the type of retinoschisis seen. Eyes with a combination of all three subtypes had the greatest refractive error (−13.0 ± 2.86 D), the longest AL (29.1 ± 1.26 mm), and the worst BCVA (0.65 ± 0.23), which was followed by that of eyes with both inner and outer EFRS (Table 2).

All three subtypes of EFRS could be detected in all quadrants; however, most cases affected the inferotemporal zone (71.2% for ILM detachment, 59.5% for inner EFRS, and 75.0% for outer EFRS), followed by the supratemporal (50.0% for ILM detachment and 53.6% for inner EFRS) and inferonasal (48.1% for ILM detachment and 39.3% for inner EFRS) quadrants. However, splitting within outer retina showed a different spatial distribution and was more likely to affect the inferonasal (38.9%) and supranasal (27.8%) quadrants before affecting the inferotemporal zone (Fig. 2).

We then analyzed the relationship of EFRS and paravascular abnormalities. The prevalence of vitreoretinal adhesion, paravascular microfolds, and paravascular holes/breaks was 22.5%, 68.5%, and 37.1% in our studied eyes, respectively. In en face images, the posterior vitreous membrane was frequently adhered to the retinal surface adjacent to major vessels (Fig. 1) or peripapillary areas forming a hyporeflective circle (Fig. 3D). Paravascular lamellar holes or retinal breaks were located along the retinal vessel contour and presented as regular paravascular hyporeflective column-like areas in en face images (Figs. 4E, 4H). We did not find any full-thickness retinal holes in our study, but in some cases retinoschisis spaces were shown to communicate with each other or with the vitreous cavity through multilayer breaks (Figs. 4C, 4F).

### Table 2. Comparison of Clinical Characteristics Among Eyes With Different Subtypes of Extrafoveal Retinoschisis

<table>
<thead>
<tr>
<th>Subtype</th>
<th>N</th>
<th>Refractive Error, D</th>
<th>P</th>
<th>Axial Length, mm</th>
<th>P</th>
<th>BCVA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILM detachment only</td>
<td>5</td>
<td>−8.45 ± 2.29 (−11.25 to −6.25)</td>
<td>0.014</td>
<td>26.5 ± 0.56 (25.6–27.0)</td>
<td>0.003</td>
<td>1.02 ± 0.11 (0.9–1.2)</td>
<td>0.039</td>
</tr>
<tr>
<td>Inner EFRS only</td>
<td>28</td>
<td>−11.0 ± 3.07 (−18.0 to −6)</td>
<td></td>
<td>28.2 ± 1.56 (24.6–31.4)</td>
<td>0.73</td>
<td>0.24 (0.3–1.0)</td>
<td></td>
</tr>
<tr>
<td>ILM detachment</td>
<td>20</td>
<td>−10.7 ± 2.95 (−18.75 to −6)</td>
<td>0.003</td>
<td>28.5 ± 1.22 (26.5–30.9)</td>
<td>0.75</td>
<td>0.26 (0.3–1.0)</td>
<td></td>
</tr>
<tr>
<td>+ inner EFRS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inner + outer EFRS</td>
<td>10</td>
<td>−11.5 ± 3.39 (−19 to −8)</td>
<td></td>
<td>28.8 ± 1.36 (27.5–31.5)</td>
<td>0.75</td>
<td>0.18 (0.5–1.0)</td>
<td></td>
</tr>
<tr>
<td>Three types combined</td>
<td>26</td>
<td>−13.0 ± 2.86 (−18.75 to −9)</td>
<td>0.003</td>
<td>29.1 ± 1.26 (26.7–30.9)</td>
<td>0.65</td>
<td>0.23 (0.2–1.0)</td>
<td></td>
</tr>
</tbody>
</table>

* Kruskal-Wallis test.

Overall, eyes with all three types of EFRS had the highest percentage of vascular microfolds (80.8%) and paravascular breaks (57.7%), whereas eyes with a combination of ILM detachment and inner EFRS were accompanied by the highest prevalence of vitreoretinal adhesion (40.0%, Supplementary Table S1). Eyes with only ILM detachment (subgroup A) were never associated with vascular microfolds or paravascular lamellar holes. We found that staphyloma was concomitantly present in 11/36 eyes (30.6%) with outer EFRS, but only in 4/55 without outer EFRS (7.6%, Fisher’s exact P = 0.008). The rates between eyes with versus without ILM detachment or with versus without inner EFRS were not statistically significant (P > 0.05). When eyes with EFRS were divided into five subgroups, the presence of staphyloma was not associated with each subtype (Fisher’s exact P = 0.09, Supplementary Table S1); and the presence of EFRS was not associated with the subtypes of posterior staphyloma either (P > 0.05, data not shown).

We analyzed the association between EFRS and optic disc from en face imaging. Inner EFRS in 55 of 84 eyes (65.5%) terminated at the border of peripapillary atrophy (PPA), therefore separated from the disc margin. Only 10 out of 52 eyes (19.2%) with ILM detachment extended to the PPA margin. We did not detect any cases of ILM detachment and inner EFRS directly connecting to the optic disc. The percentage for outer EFRS directly linking the PPA was 47.2% (17 of 36 eyes). Notably, we found three cases (8.3%) in which EFRS connected to the optic disc directly or through peripapillary retinal detachment within the PPA (Figs. 5H, 5I).

Finally, we report four cases (4.5% of 89 eyes) with quadrate maculopathy bundles (Figs. 5). The subjects were aged from 13.8 to 17.7 years, and two were male. Their refractive error ranged from −6.25 to −15 D, and AL ranged from 25.6 to 29.4 mm. Best-corrected visual acuity was from 0.3 to 1.0, and intraocular pressure was within normal limits. Humphrey central 24-2 threshold perimetry showed mean defect (MD) from −4.47 to −0.81 dB with pattern standard deviation (PSD) from 1.59 to 4.51 dB (Table 3). Color fundus photography demonstrated three eyes with peripapillary crescent (myopic conus) and one with multiple localized areas of chorioretinal atrophy. Sectional scans showed mild splitting under the ILM. Among the four eyes, one had vitreoretinal adhesion, but none had vascular

### Table 3. Clinical Characteristics of the Four Eyes With Retinoschisis in Papillomacular Bundles

<table>
<thead>
<tr>
<th>ID</th>
<th>Age, y</th>
<th>Sex</th>
<th>Eye</th>
<th>SE, D</th>
<th>AL, mm</th>
<th>BCVA</th>
<th>MD, dB</th>
<th>PSD, dB</th>
<th>IOP, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>270</td>
<td>17.7</td>
<td>F</td>
<td>OS</td>
<td>−11.25</td>
<td>26.8</td>
<td>1.0</td>
<td>−4.47</td>
<td>4.51</td>
<td>22</td>
</tr>
<tr>
<td>934</td>
<td>15.1</td>
<td>M</td>
<td>OS</td>
<td>−6.75</td>
<td>26.4</td>
<td>1.0</td>
<td>−0.81</td>
<td>2.65</td>
<td>12</td>
</tr>
<tr>
<td>955</td>
<td>13.8</td>
<td>F</td>
<td>OS</td>
<td>−6.25</td>
<td>25.6</td>
<td>0.9</td>
<td>−2.01</td>
<td>1.59</td>
<td>17</td>
</tr>
<tr>
<td>996</td>
<td>14.4</td>
<td>M</td>
<td>OS</td>
<td>−15.00</td>
<td>29.4</td>
<td>0.3</td>
<td>−4.12</td>
<td>3.45</td>
<td>12</td>
</tr>
</tbody>
</table>

IOP, intraocular pressure.
microfolds or paravascular retinal breaks. Outer EFRS did not concurrently exist in any of the four cases either. En face images revealed the lesions adjacent to the optic disc and with similar features to ILM detachment seen in other cases (Fig. 5).

DISCUSSION
Wide-field SS-OCT can be used in diagnosing EFRS in highly myopic eyes, especially when lesions are beyond the current range of scanning (typically 6 × 6 mm). When combined with en face reconstruction, it could comprehensively delineate the spatial distribution of EFRS and describe the spatial correlation with other lesions (e.g., peripapillary retinal detachment and paravascular abnormalities). In this study, we described the en face features of three subtypes of EFRS in 89 eyes and established the relationship with clinical characteristics (i.e., AL, refractive error, and visual acuity). To our best knowledge, our study is the first of its kind to report features of retinoschisis outside the fovea using this technique. In addition, we report a distinct kind of inner EFRS occurring exclusively in the papillomacular bundles. Further cases are warranted to replicate these findings.

Retinoschisis may occur at central and peripheral retina in highly myopic eyes. Macular retinoschisis or foveoschisis was first described by Takano and Kishi using time-domain OCT. Extensive foveoschisis could naturally progress into macular detachment, resulting in severe vision impairment. Extrafoveal retinoschisis, including paravascular retinoschisis, was just recently reported in high myopia. In eyes with EFRS, separation between retinal layers could involve only the region beyond the fovea (extrafoveal). It is thought that EFRS reflects increased intra- and extracocular forces, and it is reported to be a precursor of foveoschisis. Identification of EFRS might be valuable in preventing foveoschisis through early intervention and traction release from the vitreoretinal interface.

Foveoschisis in highly myopic eyes is generally classified as inner and outer foveoschisis. However, there are no studies describing the classification of EFRS. Similar to observations of foveoschisis, we detected retinal splitting at a variety of different levels, and the main classifications were ILM detachment, inner EFRS, and outer EFRS. Unlike outer retinoschisis as the most common subtype of foveoschisis, inner EFRS was the predominant subtype in our study. The explanation for such discrepancy is not clear. One possible factor is that the retina near the central fovea is avascular. Major retinal vessels, which undergo extensive traction force from the vitreous body, anatomically lie in the nerve fiber and ganglion cell layers. These are exactly the levels where inner EFRS occurs. Such a hypothesis could also be supported by evidence that paravascular abnormalities including paravascular cysts, breaks, and microfolds in high myopic eyes are often concurrently present with paravascular retinoschisis.

Splitting in multiple intraretinal layers may develop sequentially. Eyes with outer EFRS, or all three types combined, tended to be more myopic and had longer AL and higher frequency of posterior staphyloma. This is in combination with the fact that outer EFRS did not present alone but always developed with coexisting inner EFRS. We speculate that with the extreme elongation of the globe, the splitting may start from the inner retina, followed by the outer layer when the further elongation develops. Longitudinal studies would help to confirm our hypothesis.

We mapped the distribution of each EFRS subtype over the wide-field en face images. All three subtypes consistently showed the highest percentage in the inferotemporal quadrant, which is consistent with previous data on the distribution of paravascular abnormalities. Intriguingly, ILM detachment and inner EFRS were rarely connected to the margin of the optic disc but frequently terminated at the border of the PPA. This may be explained by the anatomy, where the retinal nerve fibers slope at the conus edge. Atrophy and thinning of the outer retina at the conus may increase the tightness of nerve bundles, and seal the fissure beneath/within the RNFL.
FIGURE 3. The topographic association of EFRS and the optic disc. ILM detachment and inner EFRS in the left eye of a 38-year-old female with axial length of 28 mm and refractive error of $-11.375$ D. Peripapillary atrophy (A, E, F) (red dashed line) can be seen surrounding the optic disc. ILM detachment and inner EFRS present separate from the optic disc (C) and terminate at the edge of peripapillary atrophy (B). Such structural correlation with the optic disc and PPA is clearly demonstrated by en face images ([E, F] for ILM detachment and inner EFRS, respectively). Of note, this eye also has posterior vitreous cortex adhering to retinal vessels and peripapillary retina (D) (red arrowhead). Outer EFRS in a 19-year-old male is shown in the bottom row. Peripapillary detachment is detected within the inferior PPA (H) (yellow arrowhead). The en face photograph illustrates that widespread intra-OPL EFRS is connected with the optic disc through extension and peripapillary detachment (I) (yellow arrowhead).

FIGURE 4. Paravascular abnormalities associated with EFRS. A multilayer EFRS can be seen in the left eye of a 39-year-old man. The eye’s axial length was 29.2 mm, refractive error was $-11.375$ D, and best-corrected visual acuity was 1.0 decimal. Color fundus photograph (A) and red-free image (B) show no apparent anomalies. Wide horizontal scans reveal both inner and outer EFRS in the upper retina adjacent to the optic disc. Vascular microfolds (C, F) (asterisk), vitreoretinal adhesion (G) (red arrowhead), and multiple retinal breaks (C, F) (yellow arrow and arrowhead) near retinal major vessels are noted. En face images show paravascular retinal breaks as columnar hyporeflectivity along retinal vessels (E, H). The reference planes were set as the inner limiting membrane (D) and Bruch’s membrane (G).
Vitreoretinal traction has been suggested as a trigger for the development of retinoschisis in highly myopic eyes. The posterior vitreous cortex at the site of the retinal vessels might pull on major vessels to form retinal cysts and vascular microfolds. Such anteroposterior traction may further facilitate the liquefied vitreous fluid entering into intraretinal layers, thus extending preexisting lesions. In the present study, we observed a relatively high prevalence of vitreoretinal traction and retinal break, and a much higher percentage of vascular microfolds of 68.5% versus the 44.1% reported by Shimada et al. We cannot fully understand the clinical significance of such findings, but confluence of multilayer defect might to some extent increase the risk of vision-threatening conditions, such as retinal detachment.

In the present study, we report a distinct type of retinoschisis involving the inner portion of papillomacular bundles. It showed subtle dehiscence at the nerve fiber layer in sectional OCT scans, but the affected area was dramatically larger than expected from an en face view. Recent studies showed that peripapillary retinoschisis was occasionally detected in glaucomatous eyes, but all our subjects denied history of glaucoma. Intraocular pressure and perimetry test were within normal range. It is suggested that papillomacular retinoschisis in myopic eyes might be a distinct entity from that in glaucomatous eyes.

Our study has several limitations. Firstly, as a case series study, it is mostly descriptive. Secondly, all subjects did not undergo follow-up, so for now we cannot provide the longitudinal changes over time or direct evidence of the sequential development of multilayer EFRS. Thirdly, none of the patients had foveoschisis; thus we cannot establish the correlation between extrafoveal and foveal retinoschisis. This might be due to the relatively young age (median age 21.1 years) and short AL (28.5 ± 1.45 mm) of enrolled subjects.

In conclusion, we have described the clinical features of different types of EFRS in highly myopic eyes using wide-field en face SS-OCT. To the best of our knowledge, this was the first use of this novel imaging technique in high myopia. Detailing the characteristics of retinoschisis will help to advance understanding of the underlying pathogenesis and its relation with other myopia-related complications. Further observations on the longitudinal changes and functional damage of the included eyes are warranted to create a better understanding of the progress, prognosis, and natural history of EFRS.

Acknowledgments

Supported by Fundamental Research Funds of the State Key Laboratory in Ophthalmology, National Natural Science Foundation of China 81125007, 81271037, and 81420108008. Centre for Eye Research Australia (CERA) receives operational infrastructure support from the Victorian Government.

Disclosure: W. Xiao, None; Z. Zhu, None; C. Odouard, None; O. Xiao, None; X. Guo, None; M. He, None

References


