Govetto and associates used optical coherence tomography and a mathematical model of mechanical force transmission to study the Z-shaped Muller cells in myopic foveolar schisis and foveolar schisis associated with tractional lamellar macular holes. They modeled the parafoveal Z-shaped Muller cells as consisting of three rigid segments of different lengths (Figure 1).

They conceptualized the middle segment to be horizontal and joining the first and third segments by flexible hinges that allowed rotation only of the second segment. The third segment was vertically oriented and considered fastened at the external limiting membrane. The first segment was also vertically oriented but could not rotate and was localized at the inner limiting membrane. The angle subtended between the second segment and the vertically oriented first and third segment was described as angle θ. They documented a reduction of the subtended angle θ between the parafoveal Z-shaped Muller cells (angle θ) towards the foveal center (increasing farther from the center of the fovea). However, in myopic traction maculopathy, there was no such difference, and the angles were more vertically oriented (angle θ closer to zero degrees).

The investigators documented a significant association with reduced visual acuity and a lower subtended angle θ by the parafoveal Z-shaped Muller cells at 200 microns temporal and nasal from the fovea.

Three cases of non-high myopic foveolar schisis are presented. We document and illustrate structural similarities among the parafoveal Z-shaped Muller cells to those represented in the literature. Current concepts attributing to Muller cell involvement in foveolar schisis formation are concisely discussed.

Case Reports
Case 1. A 67-year-old Asian female presented with a one-week onset of floaters. The patient denied other symptoms of retinal detachment. She was taking Viread (tenofovir disoproxil fumarate) 300 mg once a day for the management of Hepatitis B. Her refraction was +0.75-0.75x090 in the right eye, +0.75-0.75x070 in the left eye with a best corrected visual acuity of 20/20 in each eye. Preliminary findings and slit lamp exam were unremarkable in both eyes. Goldmann applanation tensions were 12 mm Hg in both eyes. Dilated fundus exam
revealed normal findings with a cup/disc ratio of 0.65 and healthy rim tissue and color in the right eye. The cup/disc ratio in the left eye was 0.8, healthy rim tissue and color. An epiretinal membrane was observed in the left eye. Spectral domain optical coherence tomography confirmed the presence of the epiretinal membrane and the presence of a foveolar schisis in the left eye. The angle subtended by the parafoveal Z-shaped Muller cells appeared to be reduced as it approached the foveal center, (increasing farther from the foveal center). Muller cells conceptualized as composed of three segments (R1, R2, R3) of different lengths (L1, L2, L3). The photoreceptor and outer retina remain intact.  

Case 2. A 60-year-old Hispanic female presented with sudden decreased vision in the right eye 2 weeks earlier. With a correction of -1.00-2.00x069 in the right eye and +0.50-0.75x109 in the left eye, her BVA was 20/30 and 20/20, respectively. Goldmann applanation tensions were 16 mm Hg in each eye. Dilated fundus exam revealed a full thickness macular hole in the right eye. Spectral domain optical coherence tomography of the right eye confirmed the presence of a macular hole with a complete posterior vitreous detachment attached to an operculum. The foveolar schisis demonstrated localized areas in which the parafoveal Z-shaped Muller cells had a reduced subtended angle as it approached the central fovea (increasing farther from the foveal center), the photoreceptor and outer retinal layers in this area were intact (Figure 3). The patient was referred to a retinal specialist and underwent macular hole surgical repair. Approximately two years and eight months from her initial visit, she returned to clinic. At that visit she reported having macular surgery and cataract surgery in the right eye. With a correction of -0.25-0.75x085 in the right eye and +0.75-0.75x110 in each eye, her BVA was 20/20 in each eye. A posterior chamber intra-ocular lens was present in the right eye. Dilated fundus exam revealed an attached macula in the right eye. Other findings were unchanged from her initial visit. Spectral domain optical coherence tomography confirmed the macula was re-attached following surgical repair (Figure 4). 

Case 3. A 52-year-old Hispanic female presented for a routine eye examination complaining of blurred vision. She reported unremarkable health and not taking any medications. With a correction of +0.75-0.25x074 in the right eye and +1.25-0.50x115 in each eye, her best corrected visual acuity was 20/20 in each eye. Goldmann applanation tensions were 12 mm Hg in each eye. Dilated fundus exam revealed isolated posterior pole chorio-retinal scars in both eyes and cup/dic ratios of 0.45/0.45 in the right eye, 0.35/0.35 in the left eye with healthy rim and tissue color both eyes. A radiating foveolar schisis was present in the macula of OS. Spectral domain optical coherence tomography confirmed the foveolar schisis, with the parafoveal Z-shaped Muller cells conformation having a reduced
of three rigid segments of different lengths (Figure 1). As described in the introduction of this paper, they conceptualized the middle segment to be horizontal and joining the first and third segment by flexible hinges that allowed rotation only of the second segment. The third segment was vertically oriented and considered fastened at the external limiting membrane. The first segment was also vertically oriented but could not rotate and was conceived to be localized at the inner limiting membrane. The angle subtended between the second segment and the vertically oriented first and third segment was described as angle \( \theta \). Govetto and associates then described that in tractional lamellar holes, the angle \( \theta \) was significantly smaller or reduced as it approached the foveal center, as opposed to myopic retinoschisis where there was no significant change with the three segments (angle \( \theta \) closer to zero degrees or more vertically oriented). Lower angles (angles closer to zero degrees or more vertically oriented) at 200 microns nasal and temporal to the fovea center were significantly associated with reduced visual acuity. At angle \( \theta = 0 \) parafoveal Muller cells has the same configuration as foveal Muller cells. They indicated that as the angle \( \theta \) became smaller, the rigidity and firmness of the parafoveal Muller cells increased, consequently angle \( \theta \) was a predictive of the Muller cells’ firmness. As the angle \( \theta \) increases, the Z-shaped Muller cells are less rigid and more flexible thus providing structural support by mitigating tractional stress. They suggested that reduction of tractional stress at Henle’s layer may prevent or minimize damage to the integrity of photoreceptor axons complexes and preserve their function in foveolar schisis.

In two of our three cases, best corrected visual acuities were 20/20 in both eyes. After undergoing macular hole surgical repair, the patient in the second case recovered to 20/20. In all the cases spectral domain optical coherence tomography illustrated a similar arrangement by the parafoveal Z-shaped Muller cells with a reduction of the subtended angle as it approached the foveal center. The parafoveal Z-shaped Muller cells therefore, had a less vertical orientation or larger magnitude subtended angle away from the foveal center.

Discussion
Alterations of Muller cell structural support have been documented to contribute to the formation of foveal schisis in a variety of ocular conditions. A genetic defect of the retinoshisin gene that affects the formation of the foveoschisin protein is thought to interfere with the retinal adhesion provided by the Muller cells and results in the characteristic stellate foveolar retinoschisis observed in X-linked foveolar retinoschisis. Traction by an epiretinal membrane may also cause Muller cells to deteriorate and affect the inner and outer retinal plexus circulation. This will similarly contribute to the impairment of its functions and eventually result in the development of a foveolar schisis. Stellate nonhereditary idiopathic foveomacular retinoschisis represents a new variety of stellate retinoschisis but lacks the abnormality of the retinoschisin gene. Other conditions such as congenital or acquired optic nerve head pits, myotonic dystrophy, autosomal dominant retinoschisis, niacin and medications that contain derivatives of taxane have also been implicated in presentations resembling foveal schisis. In these conditions damage to the Muller cells may be a contributing factor to the development of foveal schisis. Disruption of potassium homeostasis regulation and its accumulation within Muller cells in diabetes and diabetic macular edema, has been documented to cause Muller cell swelling and dysfunction with subsequent retinal fluid removal and exacerbation of macular edema. Diabetes may also affect the production and release of growth factors and cytokines by the Muller cells. Consequently, Muller cells may contribute to retinal angiogenesis and the related aggravated complications of diabetic retinopathy.

Understanding what characteristics of Muller cell disruption may lead to reduced visual acuity or otherwise preserve it in foveal schisis is clinically important. A recent study by Govetto and associates may help provide some clarification. Their model of the parafoveal Z-shaped Muller cells consisted
We previously documented a case of foveolar schisis secondary to optic nerve pit that at approximately ten years from initial presentation best corrected visual acuity remained 20/20 and the visual fields remained normal. Although we did not systematically use the methodology to analyze the spectral domain optical coherence tomography foveal schisis structure asGovetto and associates did, an analogous configuration to those described by these investigators was apparent in all our cases and the case of the optic pit related foveoschisis. We suggest that the parafoveal Z-shaped arrangement in all these cases may have protected the photoreceptors axon junctional complexes from further damage and contribute to the visual acuity preservation.

In conclusion, our cases support the suggestion that in foveolar schisis, a larger angle subtended by Z-shaped Muller cells at the parafoveal region, may help mitigate tractional stress at the Henle's layer, and preserve the junctional complexes of the photoreceptor’s axons and subsequently visual function. As exemplified by the post-surgical recovery of vision in our case with the macular hole, pre-surgical spectral domain optical coherence tomography imaging of para-foveal Z-shaped Muller cells may help in the evaluation of candidates for macular hole surgery.

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References