

Restoration of ELM Reflection Line Crucial for Visual Recovery in Surgically Closed MH

New SD-OCT imaging insights related to the reconstruction of photoreceptor layer and visual outcomes after macular hole repair.

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Since Kelly and Wendel first reported the successful closure of idiopathic macular holes (MHs) by pars plana vitrectomy in 1991,¹ several advances in surgical techniques and instrumentation have been made to improve the anatomic and visual success rates of MH surgery during the past two decades. With the introduction of internal limiting membrane (ILM) peeling, anatomic success rates have been increased to approximately 85% to 100%, and visual improvement rates have improved to approximately 85% to 95%.^{2,3} Poor visual recovery, however, is still observed in some patients despite anatomically successful closure of the MH. In those cases, possible mechanisms accounting for the visual disturbance, such as microstructural abnormalities at the macula, have been difficult to identify with conventional examination using slit-lamp biomicroscopy or indirect ophthalmoscopy. The recent advent of high-resolution spectral-domain optical coherence tomography (SD-OCT) has enabled improved visualization of intraretinal morphology and has provided new insight related to the foveal microstructural changes in a variety of macular diseases including MH. Several studies have reported a possible association between the integrity of the photoreceptor inner and outer segment (IS/OS) junction and postoperative visual acuity after successful MH repair.⁴⁻⁶ However, we have often encountered cases of patients with favorable visual recovery soon after surgery but who still have a disruption of IS/OS at the fovea (Figure 1). There is a question whether the integrity of IS/OS essentially reflects the visual recovery after successful MH surgery.⁷ Theoretically, the structural integrity of the IS/OS line may simply enhance the status of the photoreceptor OS at the time of examination but not fully reflect the photoreceptor

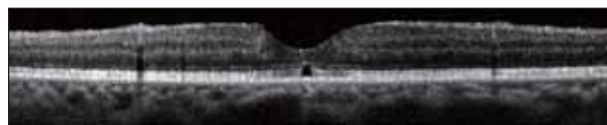


Figure 1. An SD-OCT image obtained 1 month after successful MH repair. Despite a focal disruption of the photoreceptor IS/OS line, the foveal ELM line is well reconstructed. The visual acuity is 20/20.

cell survival, which seems to be more critical for predicting postoperative visual prognosis.

In normal subjects, cross-sectional SD-OCT images through the fovea clearly shows a distinct back-reflection line corresponding to the IS/OS junction and a thin back-reflection line above the IS/OS corresponding to the external limiting membrane (ELM; Figure 1). The ELM is physiologically not a membrane structure but is thought to be an alignment of structures representing the border between the outermost aspect of the outer nuclear layer and the photoreceptor inner segment myoid portion. Because the location of the ELM is close to the photoreceptor cell bodies, we hypothesized that the integrity of the ELM line may more directly reflect the integrity of the photoreceptor cells or the misalignment of the photoreceptor layer as compared with that of the IS/OS. In eyes with surgically closed MHs, the integrity of the ELM line can be accurately illustrated using SD-OCT because the reflective signal from the ELM will not be attenuated or obscured by the inner-retinal abnormalities often seen in exudative macular pathologies such as age-related macular degeneration, retinal vein occlusion, or diabetic retinopathy. Therefore, the ELM may be another good parameter

All images taken with the RTVue SD OCT (Optovue, Fremont, CA).

for assessing the degree of microstructural changes in the photoreceptor layer in closed MHs.

CRITICAL SD-OCT FINDINGS PREDICTING VISUAL RECOVERY

The major variations of structural abnormalities in surgically closed MHs have been reported in detail by Ko and associates⁸ using ultrahigh-resolution (UHR) OCT: foveal hyperreflective lesions (Figure 2), foveal detachment, nerve fiber layer defects, and disruption of the photoreceptor layer. Of these, the integrity of the foveal photoreceptor layer is the only SD-OCT finding critically associated with postoperative visual acuity, according to our recent retrospective analysis from a consecutive series of 40 surgically closed MHs.⁹ We subsequently studied the relation between the reconstructive pattern of the photoreceptor layer and visual recovery in 40 eyes with closed MHs. The reconstructive pattern of the photoreceptor layer can be assigned into three groups based on the integrity of IS/OS and ELM line reflections (Figure 2): restoration of both the IS/OS and ELM lines at the fovea (group A), disruption of the IS/OS but with an intact ELM line (group B), and disruption of both the IS/OS and ELM lines at the fovea (group C).

When comparing the visual acuity at 3 months after surgery among groups, the mean visual acuity of groups A and B, both of which had a well-reconstructed ELM regardless of the restoration of the IS/OS, were significantly better than group C (Figure 3). In contrast, the differences in the mean visual acuity between groups A and B were not statistically significant. These results suggest that the integrity of the ELM at the fovea is more critical than that of the IS/OS for predicting the early postoperative visual acuity after successful MH repair.

It is notable that the disruption in photoreceptor IS/OS and/or ELM lines at the fovea in the early postoperative days will often be reconstructed over time. At the 12-month postoperative follow-up, several eyes assigned to the group B at the 3-month postoperative examination had a nicely reconstructed IS/OS line at the fovea and could be reassigned to group A (Figure 4). Similarly, some eyes in group C at the 3-month examination showed intact ELM lines and could be reassigned to group B at 12 months. After reassigning the 40 eyes based on the 12-month postoperative SD-OCT images, it is of interest that a similar tendency of visual significance was found among the three groups (Figure 5). This result again highlights the importance of reconstruction of the ELM for predicting better postoperative visual acuity in closed MHs.

If we combine groups B and C together as one group to focus only on the integrity of the IS/OS line regardless of the integrity of the ELM, the mean visual acuity in group A is in actuality significantly superior to that in the com-

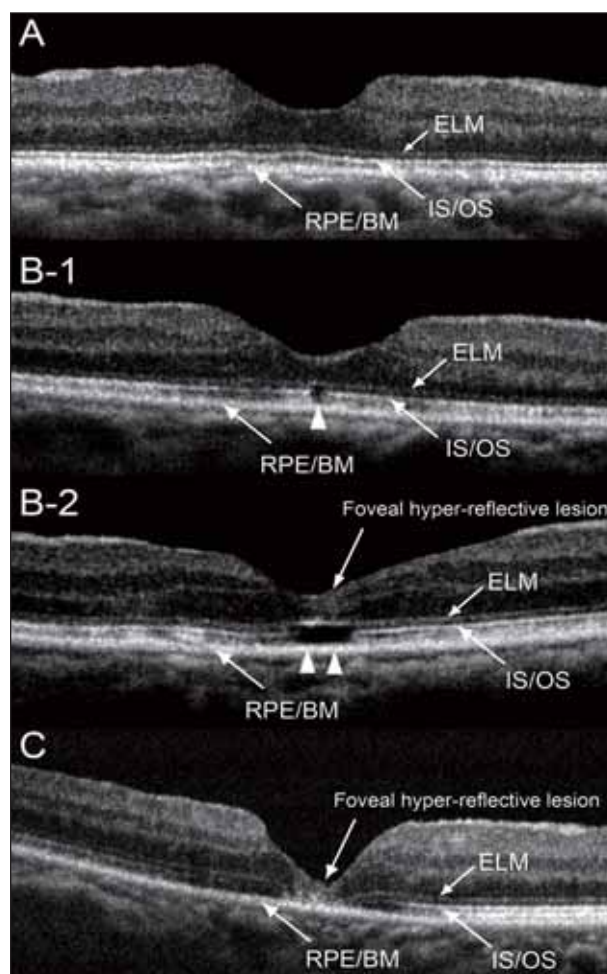


Figure 2. The reconstructive patterns of foveal photoreceptor layer obtained by SD-OCT after MH repair. The restoration of both the ELM and photoreceptor IS/OS junction (A). The disruption of the IS/OS line but restored ELM with (B-1) or without (B-2) the foveal hyper-reflective lesion located in the inner retina above the intact ELM line (B). The disruption of both the IS/OS and the ELM (C). The foveal hyper-reflective lesion replaces whole intraretinal layers. ELM = external limiting membrane; IS/OS = inner segment/outer segment; RPE/BM = retinal pigment epithelium/Bruch membrane.

bined group. This may account for the reason that the reconstruction of IS/OS at the fovea was suggested to be associated with visual recovery in previous studies.⁴⁻⁶ However, because we often encounter cases conflicting to this proposal as shown in Figure 1, although the identification of an intact ELM line can clearly explain the reason why visual acuity recovered favorably in such cases, we propose that the integrity of the ELM line at fovea may be more crucial than that of the IS/OS to predict visual recovery in surgically closed MHs.

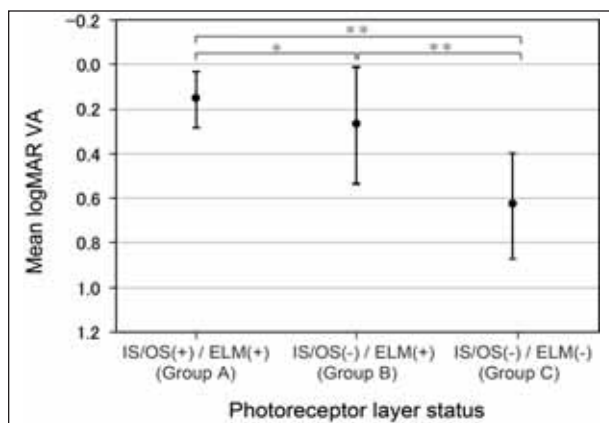


Figure 3. The graph demonstrates the mean of logMAR visual acuity (VA) at 3 months in each group. The mean visual acuity in groups A (six eyes) and B (26 eyes) are significantly better than in group C (eight eyes). However, the difference in the mean visual acuity between groups A and B was not statistically significant.

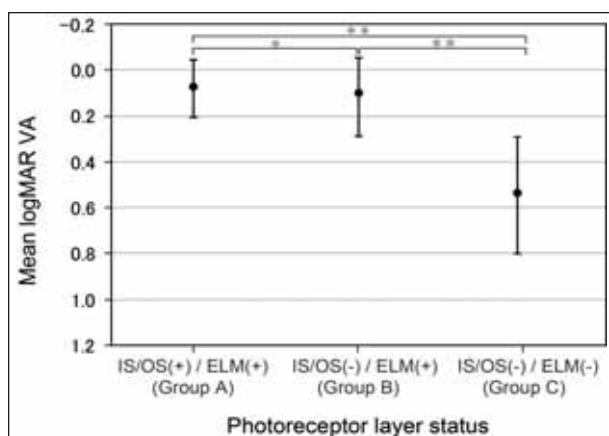


Figure 5. The graph shows the mean of logMAR VA based on reassignment of the foveal photoreceptor status at 12 months. Similar to the data obtained at 3 months postoperatively, the mean VA in the reassigned groups A (20 eyes) and B (15 eyes) are significantly better than the reassigned group C (five eyes). However, the difference in the mean visual acuity between groups A and B was not statistically significant.

RECONSTRUCTIVE PATTERN OF THE FOVEAL PHOTORECEPTOR LAYER

In our study, no eyes with a disrupted ELM line had an intact IS/OS line at the fovea. In addition, there were no eyes showing an intact IS/OS line without reconstruction of the ELM throughout the postoperative follow-up. These findings suggest that foveal reconstruction in surgically closed MHs may be initiated by centripetal bridging of the ELM followed by the regeneration and realignment of the IS/OS.

Another noteworthy finding in the surgically closed MHs is the presence of foveal hyperreflective lesions. This finding

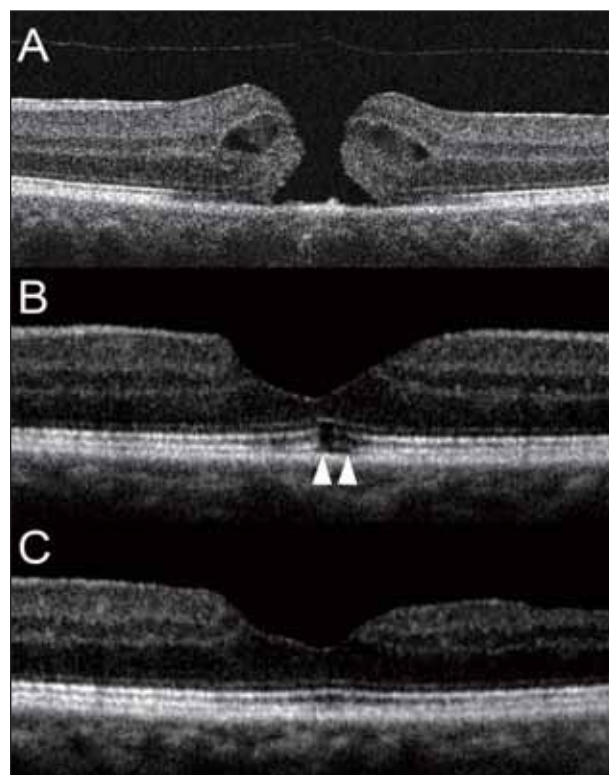


Figure 4. The over-time reconstructive changes in the photoreceptor IS/OS after MH repair. Preoperative SD-OCT image shows a full-thickness MH. The visual acuity is 20/100 (A). The SD-OCT image obtained 3 months after surgery shows a disrupted IS/OS (arrowheads) with a well restored ELM. The visual acuity is 20/40 (B). The SD-OCT image obtained 12 months after surgery shows an intact IS/OS line at the fovea. Visual acuity is 20/25 (C).

is considered to represent glial cell proliferative events at the foveal defect during MH closure.^{8,10,11} Although the presence of foveal hyperreflective lesion was not directly associated with postoperative visual acuity in our series, this finding is significantly more often seen in eyes with a longer symptom duration and a larger hole size. In our series, all study eyes in group C with poorer visual recovery had a hyperreflective lesion replacing whole intraretinal layers at the fovea. In contrast, among eyes in groups A and B, the reflective lesion was localized at the inner retina just above the ELM line or was absent. The balance between the proliferating glial cells filling the foveal defect and the bridging of the ELM with subsequent reapproximation of the normal photoreceptors to the central fovea during MH closure may determine the early fate of visual recovery in surgically closed MHs and may also account for the reason why MHs with larger hole size before surgery often have poorer visual prognosis, as seen in group C, despite clinically successful MH repair.^{12,13}

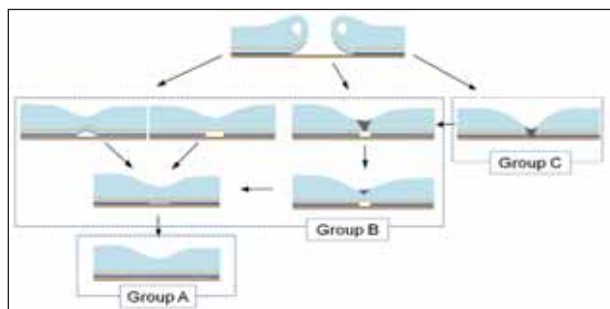


Figure 6. Schematic diagram illustrates the reconstructive patterns of the foveal photoreceptor layer and the potential changes of its microstructures over time after successful MH repair. Group A includes eyes with both intact ELM and IS/OS lines, potentially having good visual recovery immediately after surgery. In group B with disrupted IS/OS but a restored ELM, the integrity of IS/OS at the fovea will be highly restored along with the intact ELM line during postoperative follow-up. Group C includes eyes with MH filled by proliferating glial cells, resulting in loss of both IS/OS and ELM reconstructions at the fovea. Nevertheless, some eyes in this group may have the chance to obtain gradual ELM reconstruction with visual recovery along with postoperative follow-up. The brown, blue, and orange lines represent retinal pigment epithelium, IS/OS, and ELM, respectively. The gray area indicates hyper-reflective lesions representing glial cell proliferation at the fovea.

A schematic diagram (Figure 6) summarizes the proposed reconstructive patterns of the foveal photoreceptor layer and its association with visual prognosis in surgically closed MHs. If postoperative centripetal re-approximation of the ELM occurs with normal inner neuroretinal tissues forming a foveal depression, or the centripetal bridging of the ELM proceeds faster than glial cell proliferation into the foveal defect, the ELM reflection line will be well seen in SD-OCT images, as in groups A and B. In these cases, the visual acuity likely improves well from early postoperative days regardless of the integrity of the IS/OS. In contrast, if the foveal defect is filled by proliferating glial cells that replace the normal intraretinal layer, it may result in loss of the bridging of the ELM at the fovea and prevent subsequent reapproximation of the normal photoreceptor cells. This finding is seen in eyes with larger hole size preoperatively in group C, in which a large hyper-reflective lesion replaced the whole intraretinal foveal layer; the eyes generally have poorer visual recovery soon after surgery compared with the other two groups. Nevertheless, it is interesting to note that some eyes in group C may have the chance to obtain a gradual ELM reconstruction with visual recovery along with postoperative follow-up. As expected, eyes in group B will have a higher chance of regeneration of the IS/OS following the centripetal reapproximation of the ELM and visual improvement.

SUMMARY

The current SD-OCT survey in surgically closed MHs, despite its retrospective nature with a relatively small number of eyes, newly identified that early postoperative reconstruction of the ELM line is important for morphologic and functional recovery of the foveal photoreceptor layer in surgically closed MHs. Whether the initial closure of the hole (foveal defect) is achieved by the bridging of the ELM or by proliferating glial cells seems to be crucial for early visual recovery in patients after MH repair. Because there are currently no surgical techniques that can ensure the perfect restoration of the photoreceptor IS/OS and ELM in surgically closed MHs, the current SD-OCT findings provide only a better understanding of the foveal microstructural changes and a possible reason for the differences in visual recovery after successful MH repair. However, this information is expected to be helpful for developing novel therapeutic strategies to retain the normal retinal microstructures after successful MH repair in the future. ■

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