• Clinical Research •

Fundus autofluorescence patterns in highly myopic eyes received macular buckling surgery for myopic maculoschisis with macular detachment

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Abstract

● **AIM:** To investigate the changes of fundus autofluorescence (FAF) patterns in myopic maculoschisis eyes with macular detachment (MD) following macular buckling (MB) surgery.

● **METHODS:** Patients who received MB surgery for myopic maculoschisis with MD between August 2018 and August 2020 were reviewed. All participants underwent comprehensive preoperative and postoperative ophthalmic evaluations. Autofluorescence (AF) imaging was conducted using a Spectralis HRA+optical coherence tomography (OCT) device.

● **RESULTS:** A total of 49 eyes (from 49 patients) were included. The mean age of participants was 55.02±11.21y (range: 31–77y), with 33 females (67.35%, F:M=2.1:1). The duration of postoperative follow-up was 32.61±16.00mo, with a range of 12 to 69mo. Three different preoperative AF patterns at the macula were identified: unremarkable AF (20 eyes, 40.8%), patchy hyper-AF (15 eyes, 30.6%), and diffuse hypo-AF (14 eyes, 28.6%). Compared with preoperative visual acuity, the mean visual improvement at final visit was 9.84±6.04, 16.60±6.87, and 12.27±5.61 (P<0.05) letters in the eyes with unremarkable AF, patchy hyper-AF, and diffuse hypo-AF, respectively. Early postoperative FAF imaging captured at 1mo after surgery revealed two different AF patterns in 36 eyes: unremarkable AF (10 eyes, 27.8%) and round-like hyper-AF (26 eyes, 72.2%). Furthermore, the above 26 eyes with round-like hyper-AF all evolved into unremarkable AF gradually during the following observation period. Particularly, a total of 13 eyes (26.5%) displayed retinal pigment epithelium (RPE) atrophy at the edge of buckle, which were first detected after a mean follow-up of 14.73±6.21mo.

● **CONCLUSION:** FAF patterns in myopic maculoschisis eyes with MD show potential as biomarkers for evaluating MB surgery. Postoperative RPE atrophy at the edge of buckle deserves vigilant clinical attention.

● **KEYWORDS:** fundus autofluorescence; myopic maculoschisis; macular detachment; macular buckling; retinal pigment epithelium

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INTRODUCTION

Myopic traction maculopathy (MTM), represented by myopic maculoschisis, has attracted growing concern among ophthalmologists worldwide because this condition is not only prevalent among individuals with high myopia but also closely associated with severe vision damage[1-5]. Although the clinical application of fundus optical coherence tomography (OCT) has made the diagnosis of MTM no longer challenging, the understanding to its pathogenesis and treatment approaches remain to be further study[6-8].

Physiologically, retinal pigment epithelium (RPE) cells phagocytize the fallen outer segments of photoreceptor, producing lipofuscin. Moreover, lipofuscin exhibits fluorescence with the stimulation by specific external wavelengths, which is a significant property[9-10]. Currently, fundus autofluorescence (FAF) imaging stands as the sole non-invasive technique capable of mapping lipofuscin deposits within living RPE cells, which is an irreplaceable tool in clinic for assessing RPE metabolic activity and functional integrity[11-14].

Macular buckling (MB) surgery is an episcleral procedure targeting the macular region. Its surgical principle involves

placing an implant posterior to the eyeball to elevate the macula, relieving preexisting excessive traction to neural retina of macula[15-16]. Multiple studies published in recent years have demonstrated amazing efficacy of MB surgery in treating MTM, including improvements in both visual acuity and structure of macula on OCT imaging[17-18]. However, whether this operation has effects on RPE, another critically affected layer in myopic maculopathy, remains unclear.

In this study, we analyzed alterations in patterns of FAF imaging in macular area following MB surgery in myopic maculoschisis eyes with macular detachment (MD), aiming to investigate potential correlations between RPE and MB surgery.

PARTICIPANTS AND METHODS

Ethical Approval Approval for this retrospective study was granted by the Ethics Committee of Zhongshan Ophthalmic Center, Sun Yat-sen University (ethics number: 2022KYPJ247). All procedures were conducted in strict accordance with the tenets of the Declaration of Helsinki. The medical records of patients who received MB surgery alone for myopic maculoschisis with MD at Zhongshan Ophthalmic Center from August 2018 to August 2020 were screened. We obtained informed consent from all participants prior to their enrollment in this study.

All participants underwent comprehensive preoperative and postoperative ophthalmic evaluations. Autofluorescence (AF) imaging was conducted using a Spectralis HRA+OCT device (Heidelberg Engineering, Heidelberg, Germany). The details for all ophthalmic examinations including FAF have been described in our prior publication[19]. The inclusion criteria were defined as follows: 1) the presence of maculoschisis with MD on OCT; 2) axial length (AL)≥26.5 mm; 3) a minimum 12mo postoperative follow-up, accompanied by confirmed macular reattachment on OCT; 4) FAF imaging was obtained preoperatively and on at least two separate occasions postoperatively. The exclusion criteria included: 1) a combination of pars plana vitrectomy; 2) patchy chorioretinal atrophy or macular atrophy; 3) full-thickness macular hole; 4) active or inactive myopic choroidal neovascularization; 5) a history of corneal refractive surgery or intraocular surgery; 6) co-existing nonmyopia-related eye diseases, including remarkable opacities of the refractive media, glaucoma and other fundus diseases.

MTM Classification of Included Eyes Recently, an MTM staging system that incorporates both macular retinal status and foveal status has been proposed and widely used in clinical practice[6]. This system enumerates all OCT-visible clinical manifestations of MTM and outlines the overall progression of each MTM subtype, facilitating a better understanding of clinical prognosis and management in MTM patients. It classifies MTM into four retinal stages: Stage 1, inner/outer maculoschisis; Stage 2, predominantly outer maculoschisis; Stage 3, concurrent maculoschisis and MD; and Stage 4, MD without maculoschisis, as well as three foveal stages: Stage a, intact fovea; Stage b, inner lamellar macular hole; and Stage c, full-thickness macular hole.

Identification of FAF Patterns in Macular Area In the macular area of a normal eye, FAF signal exhibits significant attenuation at the fovea because of absorption by luteal pigment, and the signal intensity progressively increased with greater distance from the fovea[9]. In this study, FAF pattern of included eyes which is in accordance with above characteristics was defined as unremarkable AF.

Hypoautofluorescence (hypo-AF) and hyperautofluorescence (hyper-AF) denote regions exhibiting reduced or elevated autofluorescence, respectively, relative to adjacent unaffected retina. The morphological description of FAF pattern depended on observed phenotypic features. Specifically, hypo-AF or hyper-AF pattern with well-defined irregular lesions were classified as patchy hypo-AF/hyper-AF pattern, while those with poorly-defined boundaries were categorized as diffuse hypo-AF/hyper-AF patterns. Compound AF was characterized by the concurrent presence of both hypo-AF and hyper-AF. Preoperative FAF imaging was achieved within 7d prior to surgical intervention. In addition, FAF imaging acquired at the 1mo postoperative visit were designated as early postoperative FAF.

Two independent researchers (Li J and Chen C) performed duplicate assessments of all fundus images, encompassing both OCT and FAF. Any disagreement underwent adjudication by Lu L, a senior retinal specialist.

Surgical Procedures Following a 360° limbal peritomy of the conjunctiva and Tenon's capsule, a T-shaped buckling implant was positioned at the posterior pole and secured *via* episcleral suturing. Final buckle placement was confirmed by the use of a binocular ophthalmoscope. Our previous study comprehensively documented both the buckle manufacturing process and the standardized MB operative technique. Notably, the buckle's central component consists of a round-like drum-shaped silicone sponge, which directly elevates macula upon surgical implantation[20].

Statistical Analysis Data were analyzed using SPSS Statistics version 22 (IBM Corp., Armonk, NY). Continuous data are expressed as means with standard deviations (SD), while categorical variables are presented as counts and proportions (%). Continuous variables across three preoperative FAF pattern groups were analyzed using one-way analysis of variance (ANOVA). For comparisons between two early postoperative FAF pattern groups, independent samples *t*-tests were employed. Categorical variables were analyzed using Chi-square tests. Statistical significance was defined as $P<0.05$.

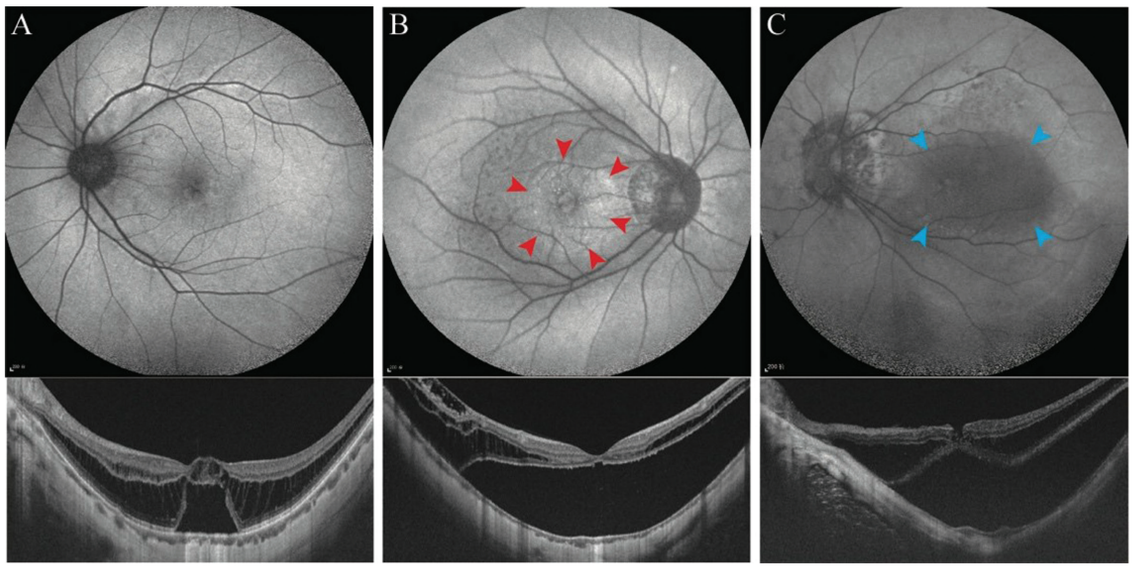


Figure 1 Representative images of three distinct fundus autofluorescence patterns in myopic maculoschisis eyes with macular detachment A: Left eye of a 48-year-old woman with high myopia. Fundus autofluorescence (FAF) imaging revealed no remarkable abnormality, consistent with a classification of unremarkable autofluorescence (AF) pattern. Optical coherence tomography (OCT) showed outer maculoschisis and localized macular detachment (MD). Visual acuity (VA) was 20/100. B: Right eye of a 38-year-old female patient with high myopia showed patchy hyper-autofluorescence (hyper-AF) at macula. A well-demarcated irregular hyper-AF lesion is indicated by red arrowheads. Corresponding OCT revealed concurrent inner and outer maculoschisis with extensive MD. VA was 20/200. C: Left eye of a 54-year-old man with high myopia showed diffuse hypo-AF at macula. A hypo-AF lesion with poorly-defined boundary was detected on FAF imaging (blue arrowheads). Outer maculoschisis and extensive MD was found on OCT. VA was 20/1000.

RESULTS

Demographic Information A total of 49 eyes (from 49 patients) with myopic maculoschisis and MD were included. The mean age of participants was 55.02±11.21y (range: 31–77y), with 33 females (67.35%) and 16 males (32.65%; F:M=2.1:1). Among all eyes, mean preoperative best-corrected visual acuity (BCVA) was 0.94±0.49 logarithm of the minimum angle of resolution (logMAR), and mean AL was 29.61±1.95 mm. The duration of postoperative follow-up was 32.61±16.00mo, with a range of 12 to 69mo. Among the 49 included eyes, 35 (71.43%) eyes had intact fovea (Stage 3a), and 14 (28.57%) eyes had inner lamellar macular hole (Stage 3b).

Autofluorescence Patterns: Correlation with Postoperative Visual Acuity Improvement Three distinct AF patterns were observed in the macula across all included eyes: 1) unremarkable AF, a pattern with no significant abnormality, was found in 20 (40.8%) eyes; 2) patchy hyper-AF, a pattern of hyper-AF with well-defined district, present in 15 (30.6%) eyes; 3) diffuse hypo-AF, a pattern of hypo-AF with poorly-defined boundary, detected in 14 (28.6%) eyes (Figure 1).

A significant difference was detected in the baseline BCVA, with logMAR values of 0.71±0.29, 1.13±0.57, and 0.91±0.43 for the unremarkable AF pattern, patchy hyper-AF pattern, and diffuse hypo-AF, respectively (P=0.025). Particularly, the eyes with unremarkable AF pattern is of better visual acuity than the eyes of the other two AF patterns (P<0.05). However, no differences were observed in other ocular characteristics among the three AF pattern groups, including age (P=0.732), AL (P=0.963), gender distribution (P=0.543), and myopic atrophy maculopathy (MAM) severity (P=0.711). Although follow-up durations were comparable across the three AF pattern groups, eyes with patchy hyper-AF demonstrated significantly greater BCVA improvement at final follow-up compared to other AF patterns (P<0.05; Table 1; Figure 2).

Early Postoperative FAF Patterns and Longitudinal Evolution At the 1mo postoperative visit, FAF imaging was obtained in 36 patients (73.5% of the cohort). Two distinct patterns were identified: unremarkable AF (10 eyes, 27.8%) and round-like hyper-AF (26 eyes, 72.2%; Figure 3). Baseline characteristics showed no significant differences between the two early postoperative FAF pattern groups, including age (P=0.845), AL (P=0.164), BCVA (P=0.243), and follow-up durations (P=0.151). At final follow-up, eyes with unremarkable AF demonstrated greater BCVA improvement than those with round-like hyper-AF (15.56±7.00 letters *vs* 11.52±7.57 letters), though this difference did not reach statistical significance (P=0.155; Table 2).

Eyes exhibiting unremarkable AF in the early postoperative period maintained stable AF patterns throughout follow-up. In contrast, eyes with initially round-like hyper-AF demonstrated ultimate progression to unremarkable AF patterns over time (Figure 4). Among the latter group, 84.6% of eyes (22/26) first

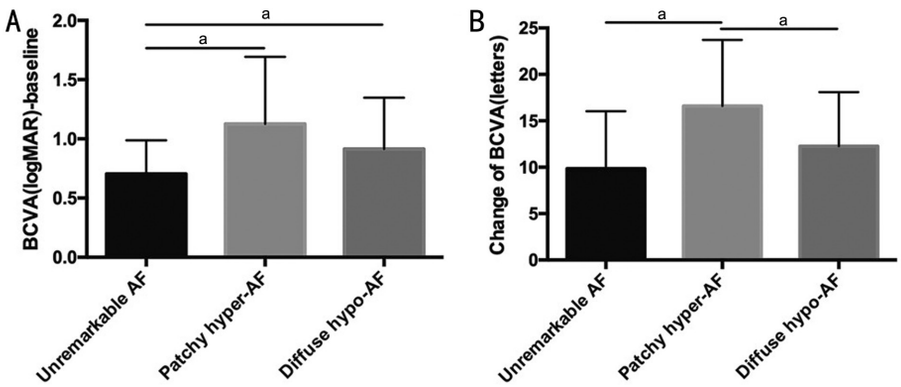


Figure 2 Post-hoc multiple comparisons were performed following significant repeated-measures analysis of variance (ANOVA) to analyze differences among the three fundus autofluorescence patterns in myopic maculoschisis eyes with macular detachment A: Post-hoc multiple comparisons in preoperative visual acuity among three fundus autofluorescence (FAF) patterns. Eyes with unremarkable autofluorescence (AF) demonstrated significantly better best-corrected visual acuity (BCVA; lower logMAR values) than those with patchy hyper-AF or diffuse hypo-AF patterns. B: Post-hoc multiple comparisons in improvement of BCVA following macular buckling (MB) surgery among three FAF patterns. Eyes with patchy hyper-AF showed significantly greater BCVA improvement versus unremarkable AF or diffuse hypo-AF groups. [a]*P*<0.05.

Table 1 Demographic and baseline characteristics for 49 included myopic maculoschisis eyes with different preoperative autofluorescence patterns mean±SD

Parameters	Total (*n*=49)	Unremarkable AF (*n*=20)	Patchy hyper-AF (*n*=15)	Diffuse hypo-AF (*n*=14)	*P*
Age (y)	55.02±11.21	56.15±11.16	53.13±10.91	55.43±12.16	0.732
Baseline BCVA (logMAR)	0.94±0.49	0.71±0.29	1.13±0.57	0.91±0.43	0.025
AL (mm)	29.61±1.95	29.66±2.07	29.49±1.96	29.66±1.91	0.963
Postoperative follow-up (mo)	32.61±16.00	28.30±13.89	27.77±14.64	36.25±14.85	0.078
Total improvement of BCVA (ETDRS letters)	11.82±8.33	9.84±6.04	16.60±6.87	12.27±5.61	0.045
Gender, *n* (%)					0.543
Male	16 (32.65)	7 (35.00)	6 (40.00)	3 (21.43)	
Female	33 (67.35)	13 (65.00)	9 (60.00)	11 (78.57)	
Severity of MAM, *n* (%)					0.711
C1	17 (34.69)	8 (40.00)	4 (26.67)	5 (35.71)	
C2	32 (65.31)	12 (60.00)	11 (73.33)	9 (64.29)	

SD: Standard deviation; logMAR: Logarithm of minimum angle of resolution; BCVA: Best-corrected visual acuity; AL: Axial length; ETDRS: Early Treatment Diabetic Retinopathy Study; MAM: Myopic atrophy maculopathy; AF: Autofluorescence.

Table 2 Comparison between two groups eyes with different early postoperative autofluorescence patterns mean±SD

Parameters	Unremarkable AF (*n*=10)	Round-like hyper-AF (*n*=26)	*P*
Age (y)	55.00±3.43	54.46±12.74	0.845
AL (mm)	30.59±2.02	29.57±1.89	0.164
Baseline BCVA (logMAR)	0.78±0.27	0.93±0.49	0.243
Postoperative follow-up (mo)	38.80±17.13	30.00±15.71	0.151
Total improvement of BCVA (ETDRS letters)	15.56±7.00	11.52±7.57	0.155

AL: Axial length; logMAR: Logarithm of minimum angle of resolution; BCVA: Best-corrected visual acuity; ETDRS: Early Treatment Diabetic Retinopathy Study; AF: Autofluorescence; SD: Standard deviation.

demonstrated conversion to unremarkable AF patterns at ≥1y postoperatively.

Autofluorescence Alterations at the Buckle Edge Interestingly, 13 eyes presented patchy compound AF lesions along the buckle edge in this study after a mean period of 14.73±6.21mo follow-up, accounting for 26.5% of the all included participants. Moreover, all these lesions demonstrated a uniform morphological configuration characterized by hyper-AF peripheries and hypo-AF cores. During longitudinal follow-up, the peripheral hyper-AF progressively faded, while the central hypo-AF areas expanded (Figure 5).

DISCUSSION

Recently, studies have revealed the superiority of MB surgery in treating MTM[20-21]. Its main therapeutic mechanism was

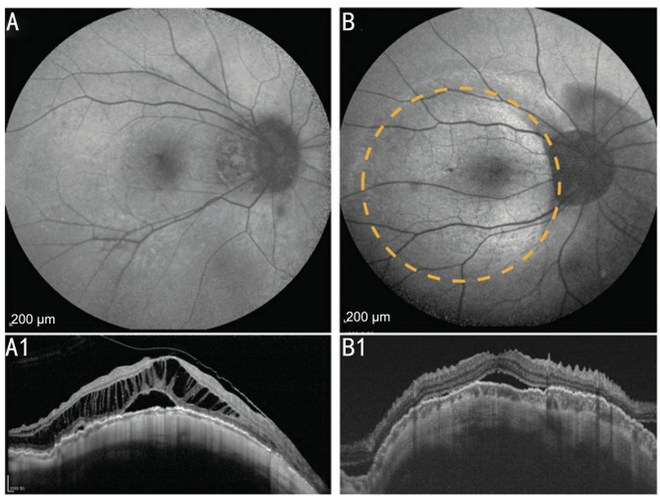


Figure 3 Early postoperative fundus autofluorescence patterns A: Fundus autofluorescence (FAF) imaging at 1mo post-macular buckling surgery: right eye of a 62-year-old woman, and its characteristics were consistent with unremarkable autofluorescence (AF) pattern. A1: Concurrent optical coherence tomography (OCT) showed posterior scleral elevation by the buckling element with alleviated macular detachment (MD) and maculoschisis. Visual acuity (VA) was 20/50. B: A 1mo postoperative FAF image from a 51-year-old man presented round-like hyper-AF (yellow dashed circle) exhibiting morphological congruence with the buckle contour. B1: Elevated posterior sclera and limited MD were displayed on OCT. VA was 20/100.

relieving the existence of posterior staphyloma, greatly weakening both inner and outer traction to macular neuro-retina[22]. RPE, essential for functional integrity of photoreceptor, is a primarily affected layer in myopic maculopathy[23-24]. This study employed FAF imaging to analyze preoperative and postoperative FAF patterns, evaluating the potential correlations between RPE and MB surgery.

MAM represents the primary condition in myopic maculopathy[25-26]. Given that severe MAM induces obvious RPE damage and aberrant FAF patterns[19], this study excluded eyes exhibiting patchy chorioretinal atrophy or macular atrophy.

Preoperative FAF imaging presented three distinct patterns in the study cohort, including unremarkable AF. The appearance of this pattern suggests relatively normal function of RPE. Furthermore, the eyes with unremarkable AF exhibited localized neurosensory detachment on OCT, indicating a shorter duration of MD. We believe all the above are the main reason why unremarkable AF is of optimal visual acuity in the three AF patterns in our data. Patchy hyper-AF, another preoperative AF pattern, demonstrated the most remarkable visual acuity improvement following surgery. In myopic maculoschisis eyes with MD, increased FAF signal signifies coexisting excessive fallen outer segments of photoreceptor and RPE with relatively normal function[9,27], consequently driving increased lipofuscin accumulation. In such circumstances, photoreceptor-RPE reattachment, the consequence of MB surgery, enables significant visual recovery. Preoperative diffuse hypo-AF was associated with limited improvement of postoperative visual acuity. The reduced FAF signal indicates RPE cells loss or atrophy[9], which reflect severe RPE damage secondary to long-term MD.

Parolini *et al*[28] revealed RPE damage progression of eyes with MTM in the natural course of the disease was worse than that of eyes with MTM received MB surgery, although the difference was not of statistical significance. Two distinct early postoperative FAF patterns were detected in this study. Round-like hyper-AF, demonstrating morphological congruence with the scleral buckle contour. Particularly, we propose this pattern arises from activated RPE in a compensatory physiological state, wherein mechanical support from the buckle enhances metabolic activity, generating intensified autofluorescence. With extended postoperative follow-up, this intensified autofluorescence progressively diminished and ultimately transitioned to an unremarkable pattern. This evolution suggests that neurosensory-RPE reattachment following MB surgery promotes normalization of RPE metabolic activity and lipofuscin production. However, there was no significant difference in final postoperative visual improvement between eyes presenting with two distinct early-postoperative FAF patterns.

Follow-up assessments revealed patchy compound AF at the buckle margin in 26.5% of eyes. This pattern's morphological characteristics and progressive evolution signified ongoing RPE atrophy within these lesions. The edge of posterior scleral staphylomas represents a well-established predilection site for MAM[28-29]. We hold the opinion that RPE atrophy at the buckle margin arises from surgically induced staphyloma-like deformation, wherein the sclera external to the buckle margin forms a steep, localized outpouching relative to the supported internal sclera. A novel scleral buckle design featuring a smoothly contoured edge profile may relieve this complication.

Previous studies have indicated that pars plana vitrectomy, currently the primary surgical intervention for MTM worldwide, can aggravate RPE atrophy[30]. In the present research, BCVA significantly improved at the final follow-up compared with baseline (0.70±0.46 *vs* 0.94±0.49 logMAR, $P<0.01$). Moreover, our findings suggest that MB surgery may be of protective effect on the RPE. We believe this study provides evidence from a novel perspective, further supporting the superiority of MB over pars plana vitrectomy in the treatment of MTM[31].

This study has several limitations. First, as a tertiary retinal referral center, selection biases might be unavoidable in our cohort. Second, quantitative analysis of FAF spatial distribution or intensity was not performed. Third, the retrospective design

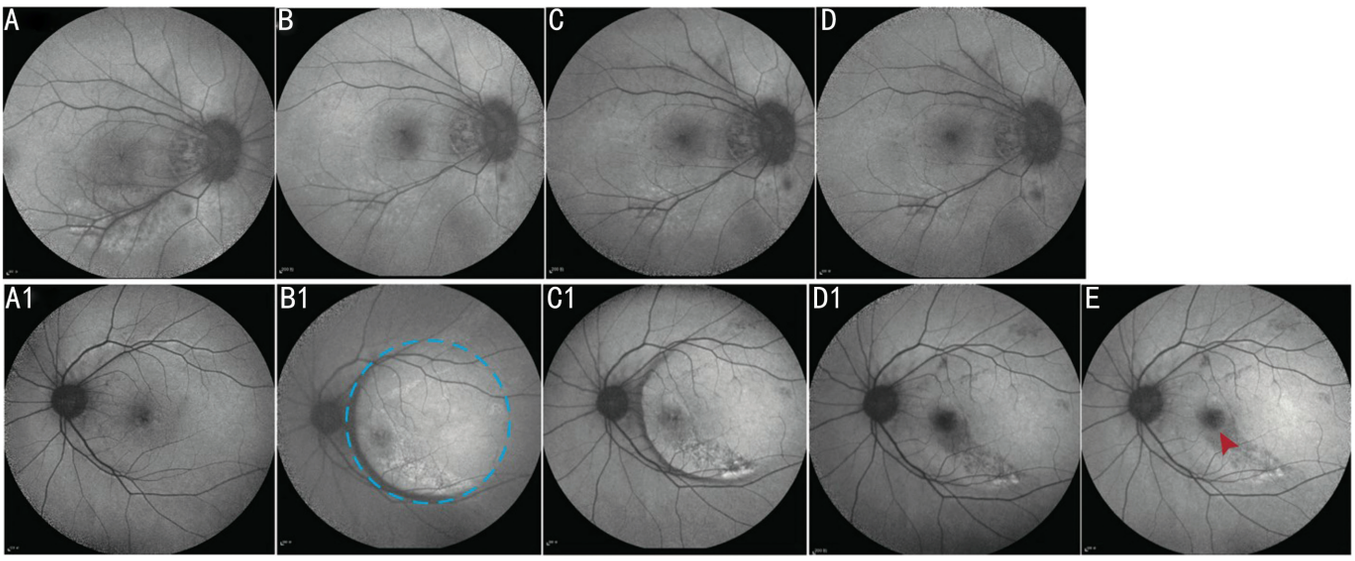


Figure 4 Representative cases of longitudinal evolution of early postoperative fundus autofluorescence patterns Fundus autofluorescence (FAF) images of the right eye at preoperation (A), 1mo (B), 12mo (C), and 24mo (D) following macular buckling (MB) surgery in a 62-year-old patient. Best-corrected visual acuity (BCVA) measured 20/50, 20/32, and 20/32 at the three postoperative follow-up visits. Unremarkable autofluorescence (AF) pattern was observed at the 1-mo postoperative assessment and remained stable throughout the follow-up period. Longitudinal FAF images analyses of the left eye in a 46-year-old patient before and after MB surgery: preoperative unremarkable AF pattern (A1); round-like hyper-AF without foveal attenuation at 1mo (blue dashed circle; B1); progressive signal reduction with emerging foveal attenuation at 6mo (C1); complete transition to unremarkable AF by 12mo (D1); sustained physiological foveal attenuation (red arrowhead) at 36mo (E). BCVA measured 20/40, 20/32, 20/32, and 20/28 at the above four times visit.

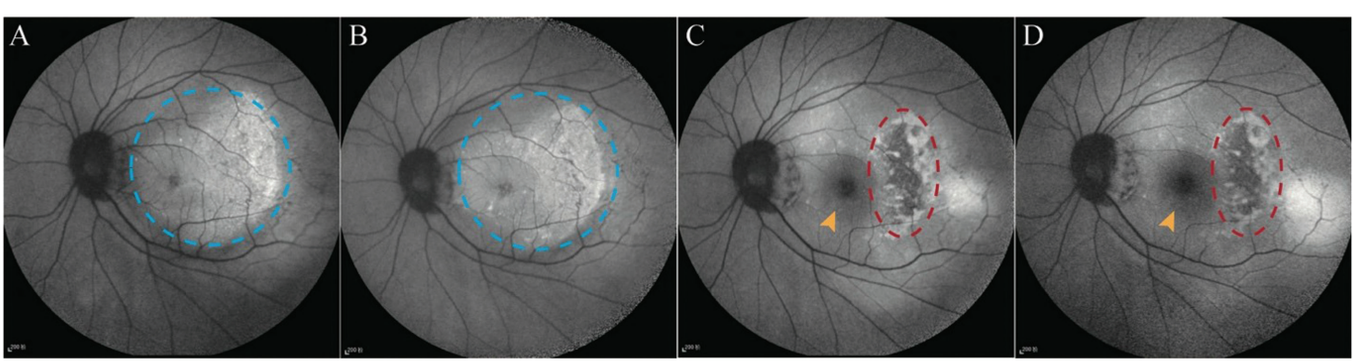


Figure 5 Representative case with autofluorescence alterations at the edge of buckle Longitudinal fundus autofluorescence (FAF) evolution of the left eye in a 38-year-old male patient after macular buckling (MB) surgery. A: Longitudinal FAF analyses demonstrated round-like hyperautofluorescence (hyper-AF) with mild foveal attenuation at 1mo postoperatively (blue dashed circle); B: Progressive reduction in hyperautofluorescent area was observed by 6mo (blue dashed circle); C: At 15mo, a pattern of compound AF at the edge of buckle emerged—characterized by hyperautofluorescent peripheries and hypoautofluorescent cores (red dashed ellipse)—concurrently with resolution of the round-like hyper-AF and restoration of physiological foveal attenuation (yellow arrowhead); D: By 24mo, expansion of hypoautofluorescent cores occurred alongside weakening hyperautofluorescent peripheral density (red dashed ellipse). BCVA measured 20/100, 20/63, 20/63, and 20/50 at the above four times visit.

precluded control for potential confounders that prospective studies could address.

To summarize, as far as we are concerned, this represents the first systematic investigation of FAF patterns evolution in myopic maculoschisis eyes with MD before and after MB surgery. Our findings demonstrate that FAF patterns might be potential biomarkers for evaluating surgical effects. Additionally, postoperative RPE atrophy at the buckle margin deserves vigilant clinical monitoring.

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Authors' Contributions: Li J performed the conceptualization, the data analysis and wrote the manuscript. Chen C performed the methodology and the validation. Huang X and Chen SD performed the investigation. Lu L performed the supervision and review of the writing.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author, Lin Lu, upon reasonable request.

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Conflicts of Interest: Li J, None; **Chen C,** None; **Huang X,** None; **Chen SD,** None; **Lu L,** None.

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