

Distinct Morphological Progression Patterns in Primary Versus Recurrent Pterygium: Vertical Attenuation Versus Deep Stromal Invasion

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Purpose: To compare progression patterns between primary and recurrent pterygium using quantitative imaging.

Methods: This retrospective cohort study included 114 primary and 24 recurrent pterygium eyes. Clinical severity was assessed via T grade, V grade, and loss of vertical length of plica semilunaris (LPS). Morphological parameters, including horizontal invasion length (HIL), height, thickness, and the residual corneal thickness to central corneal thickness (RCT/CCT) ratio, were measured using anterior segment swept-source optical coherence tomography. Clinical severity and HIL-adjusted morphological parameters were compared, and correlation analyses assessed structural progression.

Results: Recurrent pterygia exhibited higher clinical severity (T3 and V3 grades, $P < 0.001$) and greater LPS ($P < 0.001$). After adjusting for HIL, recurrent cases showed lower height ($P = 0.048$) and thickness ($P = 0.012$) compared to primary cases. In primary pterygium, HIL negatively correlated with height ($r = -0.478$, $P < 0.001$), thickness ($r = -0.191$, $P = 0.042$), and the RCT/CCT ratio ($r = -0.483$, $P < 0.001$), suggesting a pattern of "vertical attenuation." Conversely, in recurrent pterygium, HIL demonstrated a much stronger negative correlation with the RCT/CCT ratio ($r = -0.704$, $P < 0.001$) but no correlation with height, indicating a pattern of "deep stromal invasion."

Conclusions: Primary pterygium demonstrates an association consistent with vertical attenuation, whereas recurrent pterygium exhibits a structural pattern consistent with deep stromal invasion while maintaining its vertical bulk.

Translational Relevance: Characterizing the distinct pathways provides an objective basis for tailored surgical planning and optimized patient care strategies.

Introduction

Pterygium is characterized by a triangular-shaped, abnormal fibrovascular growth of epithelial and subepithelial tissue that invades the cornea, eventually leading to ocular surface irritation, chronic inflammation, foreign body sensation, and cosmetic concerns.¹ While traditionally viewed as a simple fibrovascular proliferative condition, contemporary understanding emphasizes it as a stem cell disorder. Ultraviolet (UV) radiation-induced damage to

limbal epithelial stem cells leads to their dysfunction, loss of barrier function, and subsequent epithelial-mesenchymal transition (EMT), which facilitates the invasion of conjunctival tissue onto the cornea.² The prevalence of pterygium is significant, with an epidemiological study reporting a prevalence of 3.8% in individuals aged 40 years and older and even higher rates among those over 60.³ Given its progressive nature and age-dependent prevalence,³ the morphological characteristics of pterygium likely vary according to the duration of the disease.

Although UV radiation is a well-established primary cause of pterygium,⁴ numerous studies have investigated to identify various other etiologic and contributing factors influencing the occurrence and progression of pterygium.^{5–7} Furthermore, because high recurrence has historically remained one of the most significant clinical challenges,⁸ substantial research has focused on reducing recurrence rates through the development of advanced surgical techniques.^{9,10} Notably, recent advancements in surgical methods, particularly limbal-conjunctival autograft reconstruction as popularized by Hirst¹¹ and further validated by Lee et al.,¹² have demonstrated the potential to reduce recurrence rates to as low as 0–1.7%. However, research exploring morphological features and how they contribute to the symptoms and signs of pterygium remains limited. Interestingly, our recent study demonstrated that protruded pterygia, characterized by increased height, induced higher tear secretion and ocular surface staining scores, likely because of mechanical friction and reflex tearing.¹³ These findings suggest that the morphological analysis of pterygium extends beyond mere structural characterization, potentially reflecting the functional impairment experienced by patients.

It is generally recognized that primary pterygium is a chronic, slow-progressing condition originating from the limbal microenvironment. In this process, altered epithelial stem cells gradually lose their barrier function due to long-term, cumulative ultraviolet radiation, leading to the insidious conjunctivalization of the corneal surface that often spans years or even decades.^{2,14} In contrast, recurrence represents an accelerated breakdown of the limbal barrier. It arises from the abnormal surgical bed where the physically compromised limbal niche fails to maintain the border between the cornea and the conjunctiva, facilitating the rapid repopulation of altered progenitor cells and hyperplastic scarring. This results in a much more rapid progression, typically within weeks or months after surgery, compared to the slow chronic evolution of primary cases.^{1,2,15} In this regard, the patterns of morphological progression may differ significantly between primary and recurrent cases. Delineating these distinct progression patterns could help clinicians predict the specific discomfort patients may experience and anticipate future disease progression in both primary and recurrent scenarios.

We recently used anterior segment swept-source optical coherence tomography (AS SS-OCT) to develop quantitative morphological parameters including horizontal invasion length, vertical width, and thickness of pterygium, and reported their significance in determining the optimal timing for surgical intervention.¹⁶ Since the corneal invasion length of

the pterygium head is a widely recognized indicator of disease progression,¹⁷ the present study analyzed changes in various AS SS-OCT-based morphological parameters relative to this invasion length. Through this approach, we aimed to characterize and compare the distinct progression patterns between primary and recurrent pterygium.

Material and Methods

This retrospective single-center cohort study, conducted through medical chart review, adhered to the principles outlined in the Declaration of Helsinki. Approval for the research protocol was granted by the Institutional Review Board of Chung-Ang University Hospital (Approval No. 2307-001-19478). Given the retrospective nature of the study, the necessity for informed consent was waived by the Institutional Review Board of Chung-Ang University Hospital.

Subjects

The study included individuals diagnosed with primary or recurrent pterygium at our institution who were scheduled for excision surgery and had undergone AS SS-OCT (Anterior, Heidelberg, Germany) examinations between September 2021 and June 2023. Only patients with pterygium located in the nasal area were included. Patients with a history of corneal refractive surgery were excluded.

Study Protocol

The study was conducted according to the following protocol:

1. Evaluation of clinical severity: T grade, V grade, and loss of vertical length of plica semilunaris (LPS) grade.¹⁸
2. Measurement of morphological parameters: Horizontal invasion length (HIL), pterygium height and thickness, and the residual corneal thickness (RCT) to central corneal thickness (CCT) ratio (RCT/CCT ratio) using AS SS-OCT (Anterior).
3. Comparison of clinical severity and HIL-adjusted morphological parameters between primary and recurrent pterygium groups.
4. Correlation analysis of HIL with height, thickness, and the RCT/CCT ratio in both groups.

Clinical Severity Grading of Pterygium

All eyes were assessed using anterior segment photographs based on three established grading crite-

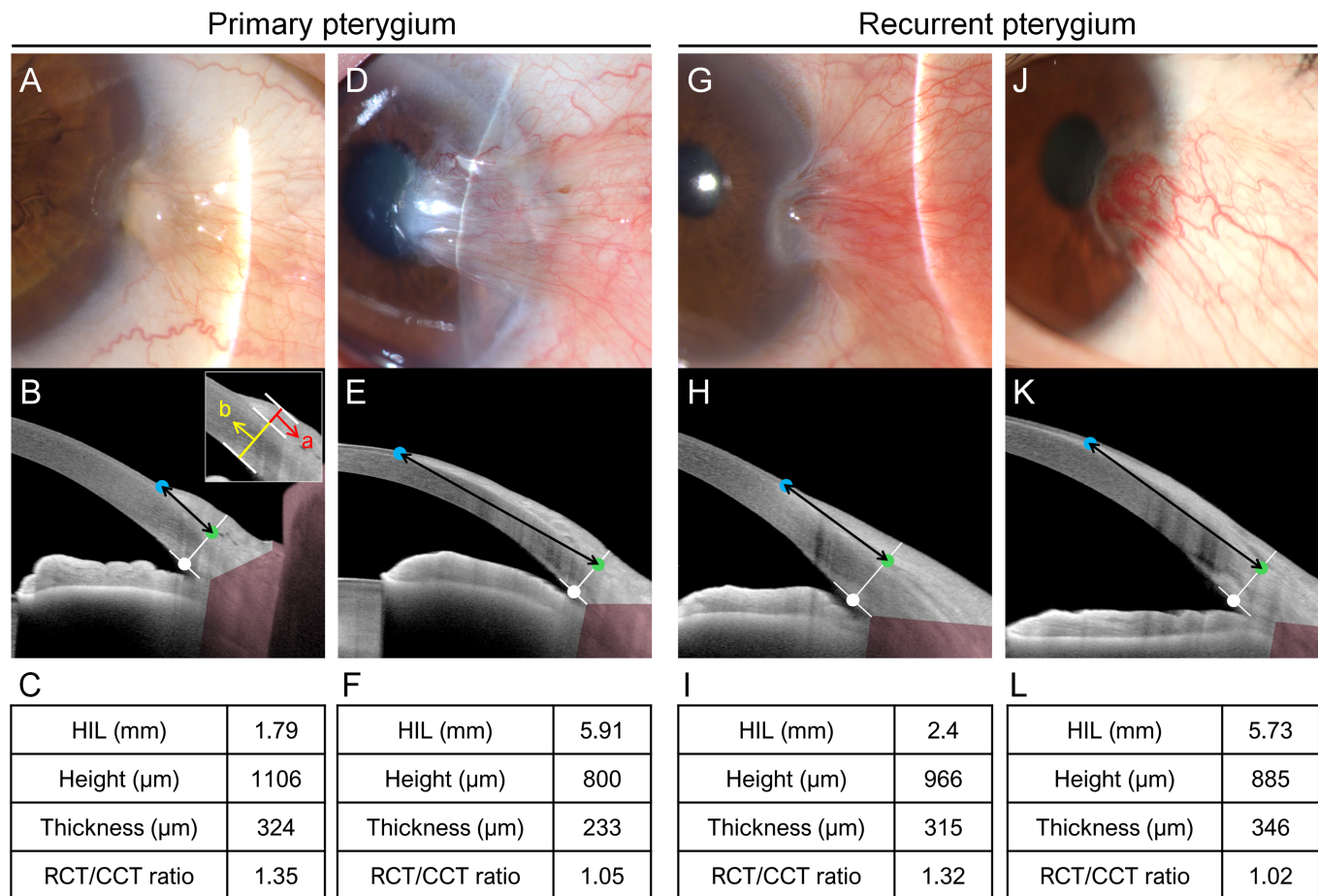


Figure 1. Quantitative morphological analysis of primary and recurrent pterygium using anterior segment swept-source optical coherence tomography (AS SS-OCT). (A–F) Representative cases of primary pterygium and (G–L) recurrent pterygium. Anterior segment photographs (A, D, G, J) and the corresponding AS SS-OCT images (B, E, H, K) and morphological parameter values for each case (C, F, I, L) are shown. In the AS SS-OCT images, a tangent line was drawn along the corneal endothelium passing through the scleral spurs (white dots), with a perpendicular reference line constructed from this tangent at the spur level. The green dot represents the point of deepest pterygium depth on this reference line, whereas the blue dot indicates the most distal tip of the pterygium head. The black double-headed arrow defines the horizontal invasion length (HIL), measured as the distance between the green and blue dots. As shown in the magnified view in (B), at the midpoint of the HIL, the length of the red line (a) indicates the pterygium thickness (depth of invasion), and the yellow line (b) indicates the residual corneal thickness (RCT). The sum of thickness (a) and RCT (b) represents the total pterygium height at that point.

ria: the transparency of the pterygium body stroma (i.e., T grade), the degree of vascularity (i.e., V grade), and the extent of LPS. A single experienced investigator performed all assessments to ensure consistency.

Briefly, the T grading system categorized pterygia as follows: T1 (clearly visible underlying episcleral vessels), T2 (partially obscured episcleral vessels), and T3 (completely obscured episcleral vessels).¹⁹ Vascularity was graded as V1 (minimal), V2 (moderate), or V3 (marked), characterized by unidirectional and enlarged vessels.²⁰ LPS was assessed using digital photographs (10 × magnification) captured via a slit-lamp imaging system during lateral gaze, with and without a yellow barrier filter. The extent of LPS (%) was calculated as the ratio of the length of the plica semilunaris

within the plica to its total length, following previously described methods.¹⁸

Pterygial Morphological Parameters via AS SS-OCT

Morphological parameters of the pterygium, including HIL, height, thickness, and the RCT/CCT ratio, were measured using AS SS-OCT (Anterior) imaging. These measurements were based on methods that we previously reported^{13,16} with the following modifications (Fig. 1). First, a tangent line was drawn along the corneal endothelium passing through the scleral spur, and a line perpendicular to this tangent (i.e., scleral spur reference line) was constructed. HIL was defined as the length (mm) of the line connecting

the point of deepest pterygium depth on this the scleral spur reference line to the most distal tip of the pterygium head. At the midpoint of the HIL, another line perpendicular to the endothelial tangent was drawn to define the thickness (μm) and RCT (μm). The depth of pterygium invasion along this perpendicular line was defined as thickness, while the remaining distance from the deepest point of invasion to the endothelium was defined as the RCT. The sum of thickness and RCT was defined as pterygium height (μm). CCT (μm) values were obtained using the device's built-in metrics application. Because RCT was measured at the midpoint of the HIL rather than at the corneal center, the RCT/CCT ratio may exceed 1 in some cases.

Statistical Analysis

Statistical analyses were performed using GraphPad Prism (GraphPad Software, La Jolla, CA, USA) and SPSS software (IBM, Chicago, IL, USA). Data normality was assessed to select appropriate parametric or non-parametric tests. Comparisons between

groups were conducted using the unpaired *t*-test, Mann-Whitney U test, χ^2 test, or Fischer's exact test. Correlations were evaluated using Pearson's correlation or Spearman's rank correlation tests. Analysis of covariance (ANCOVA) was used to compare pterygium height, thickness, and the RCT/CCT ratio between the primary and recurrent groups while adjusting for HIL as a covariate. Data are presented as mean $\pm$ standard deviation (SD), and statistical significance was defined as $P < 0.05$.

Results

Demographics, Clinical Severity Grades, and Morphological Profiles of Pterygium

This study included 114 eyes from 114 primary pterygium patients as well as 24 eyes from 24 recurrent pterygium patients. Demographic information, clinical severity grades, and morphological profiles of pterygium in both groups are presented in [Table 1](#).

Table 1. Demographics, Clinical Severity Grades, and Morphological Profiles of Pterygium in Primary and Recurrent Pterygium Groups

Variables	Group		P Value
	Primary Pterygium	Recurrent Pterygium	
Total no. of subjects (eyes)	114 (114 eyes)	24 (24 eyes)	—
Age (yrs) ^a	57.5 $\pm$ 12.5	57.2 $\pm$ 10.5	0.896
% Female (M:F) ^b	44.7% (63:51)	41.5% (15:9)	0.516
Clinical severity grades			
T grade			
T1 ^c	25 eyes (21.9%)	1 eye (4.2%)	0.046*
T2 ^c	72 eyes (63.2%)	1 eye (4.2%)	<0.001*
T3 ^c	17 eyes (14.9%)	22 eyes (91.7%)	<0.001*
V grade			
V1 ^c	15 eyes (13.2%)	2 eyes (8.3%)	0.737
V2 ^c	75 eyes (65.8%)	2 eyes (8.3%)	<0.001*
V3 ^c	24 eyes (21.1%)	20 eyes (83.3%)	<0.001*
Extent of LPS (%) ^d	56.32 $\pm$ 29.79	92.08 $\pm$ 21.87	<0.001*
Morphological profiles			
HIL (mm) ^a	4.09 $\pm$ 1.28	4.17 $\pm$ 1.24	0.771
Height (μm) ^a	982.5 $\pm$ 132.2	926.0 $\pm$ 114.2	0.054
Thickness (μm) ^d	389.9 $\pm$ 115.2	325.5 $\pm$ 96.3	0.027*
RCT/CCT ratio ^a	1.10 $\pm$ 0.15	1.11 $\pm$ 0.13	0.896

CCT, central corneal thickness; RCT, residual corneal thickness.

* $P < 0.05$, ANCOVA.

^aUnpaired *t*-test.

^b χ^2 test.

^cFisher's exact test.

^dMann-Whitney U test.

Table 2. Comparison of Pterygium Height Between Primary and Recurrent Pterygium With Adjustment for HIL

Group	Pterygium Height (μm)			
	Estimated Marginal Mean $\pm$ SE	F	P value	Partial η^2
Primary pterygium	981.84 $\pm$ 11.04	4.00	0.048*	0.029
Recurrent pterygium	928.90 $\pm$ 24.06			

* $P < 0.05$, ANCOVA.**Table 3.** Comparison of Pterygium Thickness Between Primary and Recurrent Pterygium With Adjustment for HIL

Group	Pterygium Thickness (μm)			
	Estimated Marginal Mean $\pm$ SE	F	P Value	Partial η^2
Primary pterygium	389.72 $\pm$ 10.38	6.44	0.012*	0.046
Recurrent pterygium	326.52 $\pm$ 22.64			

* $P < 0.05$, ANCOVA.**Table 4.** Comparison of RCT to CCT Ratio Between Primary and Recurrent Pterygium With Adjustment for HIL

Group	RCT/CCT Ratio			
	Estimated Marginal Mean $\pm$ SE	F	P Value	Partial η^2
Primary pterygium	1.10 $\pm$ 0.01	0.107	0.744	0.001
Recurrent pterygium	1.11 $\pm$ 0.03			

* $P < 0.05$, ANCOVA.

The primary pterygium group consisted of 51 females (44.7%) and 63 males (55.3%), with an average age of 57.5 ± 12.5 years (SD). The recurrent pterygium group included 9 females (41.5%) and 15 males (58.5%), with an average age of 57.2 ± 10.5 years (SD). No significant differences were observed between the two groups regarding age ($P = 0.896$) or sex distribution ($P = 0.516$).

Regarding clinical severity and morphological profiles, the recurrent pterygium group showed a significantly higher proportion of T3 ($P < 0.001$) and V3 grades ($P < 0.001$), along with a greater extent of LPS ($P < 0.001$) compared to the primary pterygium group. Although HIL, height, and the RCT/CCT ratio did not differ significantly between the two groups, the recurrent group exhibited significantly lower thickness ($P = 0.027$) compared to the primary group.

Comparison of Morphological Parameters Adjusted for HIL Between the Primary and Recurrent Pterygium Groups

To evaluate how morphological characteristics differ between primary and recurrent pterygium at a comparable degree of corneal involvement, an ANCOVA was

performed using HIL as a covariate. The estimated marginal mean of pterygium height was significantly lower in the recurrent group ($928.90 \pm 24.06 \mu\text{m}$) compared to the primary group ($981.84 \pm 11.04 \mu\text{m}$; $P = 0.048$, Table 2). Similarly, the adjusted mean thickness was significantly reduced in the recurrent group ($326.52 \pm 22.64 \mu\text{m}$) relative to the primary group ($389.72 \pm 10.38 \mu\text{m}$; $P = 0.012$, Table 3). In contrast, the RCT/CCT ratio showed no significant difference between the two groups after adjusting for HIL, as the primary (1.10 ± 0.01) and recurrent (1.11 ± 0.03) groups yielded comparable adjusted means ($P = 0.744$, Table 4). These findings collectively indicate that for a given HIL, recurrent pterygium exhibits a flatter vertical profile characterized by lower height and thickness, while maintaining a similar relative involvement of the underlying corneal bed as primary pterygium.

Correlation of HIL With Morphological Parameters of Pterygium

The correlation analysis between HIL and various morphological parameters is summarized in Table 5. In the primary pterygium group, HIL exhibited a significant negative correlation with height ($r = -0.478$,

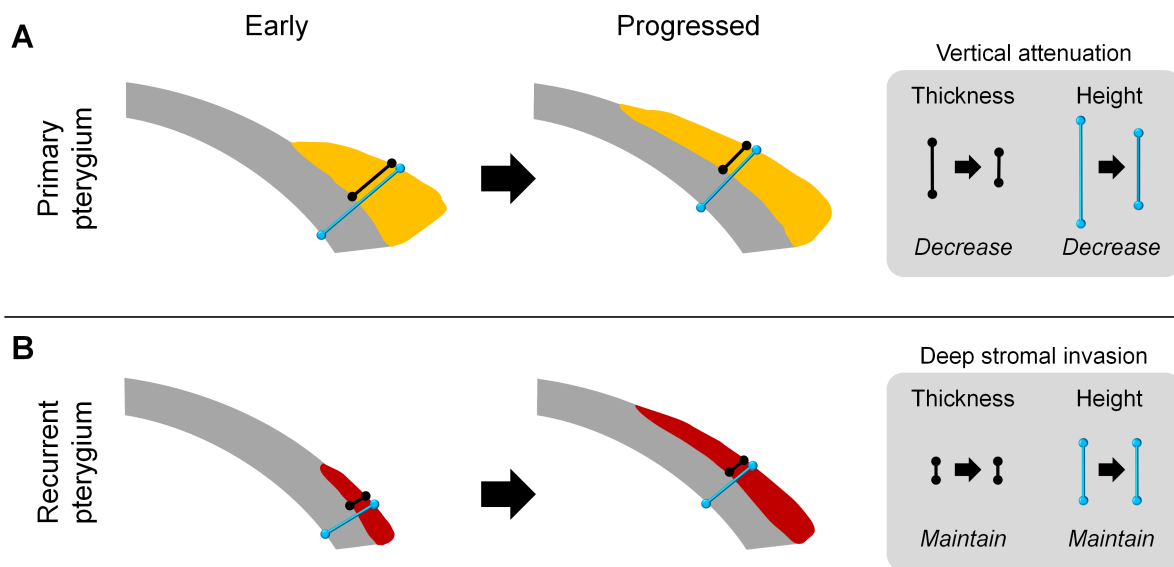
Table 5. Correlation of HIL With Height, Thickness, and the RCT to CCT Ratio of Pterygium in Primary and Recurrent Pterygium

Group	Correlation vs. HIL	Height	Thickness	RCT/CCT Ratio
Primary pterygium	<i>r</i>	−0.478 ^a	−0.191 ^a	−0.483 ^b
	<i>P</i> value	<0.001 [*]	0.042 [*]	<0.001 [*]
Recurrent pterygium	<i>r</i>	−0.103 ^b	0.272 ^b	−0.704 ^b
	<i>P</i> value	0.632	0.199	<0.001 [*]

^{*} $P < 0.05$, ANCOVA.

^aSpearman's rank correlation test.

^bPearson correlation test.

**Figure 2.** Schematic representation of the two distinct morphological patterns. (A) Primary pterygium is characterized by vertical attenuation, where the lesion height decreases and flattens against the corneal surface as it extends horizontally. (B) Recurrent pterygium is characterized by deep stromal invasion, where the lesion maintains its vertical bulk while aggressively penetrating deeper into the corneal stroma as it extends horizontally. The thickness and height of the pterygium are indicated by the *black* and *light blue* lines, respectively.

$P < 0.001$), thickness ($r = -0.191$, $P = 0.042$), and the RCT/CCT ratio ($r = -0.483$, $P < 0.001$). These findings suggest that primary pterygia demonstrate an association consistent with vertical attenuation with increasing horizontal involvement. In this progression pattern, the lesion progressively loses its vertical profile and flattens against the ocular surface while simultaneously sinking into the deeper corneal stroma (Fig. 2A).

In contrast, within the recurrent pterygium group, HIL demonstrated a strong negative correlation only with the RCT/CCT ratio ($r = -0.704$, $P < 0.001$). Notably, HIL showed no significant association with either height ($r = -0.103$, $P = 0.632$) or thickness ($r = 0.272$, $P = 0.199$) in recurrent cases. This indicates that the structural characteristics of recurrent pterygium are predominantly defined by deep stromal

invasion (Fig. 2B). Unlike primary cases, recurrent lesions do not follow a pattern of vertical attenuation. Instead, they maintain their vertical bulk while exhibiting aggressive stromal involvement at greater horizontal invasion lengths.

Discussion

Pterygium is a progressive fibrovascular overgrowth that represents significant clinical challenges due to ocular surface irritation and its high recurrence rate.^{4,13} Although previous research has focused heavily on surgical techniques and molecular markers,^{1,9} morphological differences during the progression of primary versus recurrent cases have remained poorly under-

stood. This study used AS SS-OCT to delineate two distinct progression patterns: vertical attenuation in primary pterygium and deep stromal invasion in recurrent pterygium. By investigating these patterns, we sought to provide a morphological basis for the differing clinical behaviors and patient symptoms observed in these two forms of the disease.

In primary pterygium, we observed that an increase in HIL was significantly correlated with a reduction in height, thickness, and the RCT/CCT ratio. These findings suggest a pattern of vertical attenuation, where the lesion effectively exhibits a flattened profile against the corneal surface at more advanced horizontal stages. Pathophysiologically, this aligns with the nature of primary pterygium as a chronic, degenerative condition initiated by UV-induced epithelial damage.^{4,7} The proliferation of fibroblasts and subsequent fibrotic remodeling may lead to the compaction of anterior stromal tissue, explaining the observed reduction in RCT beneath the advancing lesion.

We hypothesize that the clinical significance of vertical attenuation in primary pterygium may be related to its impact on ocular surface tribology. Specifically, as the lesion's height decreases in advanced stages, the mechanical friction between the eyelid and the pterygium surface similar to those in lid-parallel conjunctival folds may be potentially alleviated.^{21,22} This provides a potential morphological explanation for why some patients with long-standing primary lesions report a paradoxical stabilization or even an improvement in irritation symptoms, despite continued horizontal growth, as previously reported.¹³ Furthermore, a lower profile may interfere less with the dynamics of blinking and the distribution of the tear film. Understanding this vertical attenuation pattern, alongside the structural modeling of pterygium shapes, enables clinicians to better communicate with patients regarding the evolution of their symptoms and the long-term functional impact of the disease.¹⁴

In contrast, recurrent pterygium followed a distinctly different progression pathway. Because the ANCOVA analysis, adjusting the HIL, revealed that recurrent pterygia exhibited significantly lower pterygium height compared to primary cases, the deep stromal invasion progression pattern of the recurrent pterygium is likely due to the fact that recurrent growth originates from a previously flattened surgical bed rather than the naturally bulky conjunctival tissue.¹ From a clinical perspective, this lower height suggests that recurrent lesions may initially induce less mechanical friction and eyelid irritation than early-stage primary pterygium.

However, the morphological nature is more aggressive in the recurrent pterygium. Although the height

of primary pterygia significantly decreases as they lengthen, the height of recurrent pterygia remains relatively constant regardless of horizontal growth as shown in Table 5. Most importantly, recurrent pterygium demonstrated a much stronger negative correlation between HIL and the RCT/CCT ratio compared to primary cases. These data indicate that the morphological pattern of recurrent pterygium is characterized by deep stromal invasion rather than vertical attenuation. Instead of sinking and flattening out like primary lesions, recurrent pterygia aggressively dive into the stromal bed while the lesion height remains relatively constant. These findings of distinct morphological patterns in primary and recurrent pterygia may be closely linked to the degree of limbal stem cell (LSC) alteration. The deep stromal invasion observed in recurrent cases could reflect a more profound loss of LSC barrier function and aggressive EMT processes. Consistent with this observation, recurrent lesions are known to exhibit pronounced fibroblastic proliferation and neovascularization, which is driven by inflammatory mediators such as VEGF and COX-2.^{23,24} The robust inflammatory nature of recurrent lesions serves as a primary driver for their aggressive penetrative growth, distinguishing them from the slow degenerative changes of primary lesions. For the clinician, this implies that while the patient's discomfort from lid friction may not worsen or improve over time, the risk of permanent corneal scarring and structural thinning is notably higher in cases with greater horizontal invasion. This deeper stromal invasion significantly elevates the technical difficulty of subsequent salvage surgeries and the likelihood of irreversible visual impairment.

Several limitations of this study should be considered. Primarily, the cross-sectional design, which evaluated different patients at various stages rather than following a single cohort longitudinally, may limit the ability to fully capture longitudinal morphological changes of pterygium over time. Future longitudinal studies are warranted to confirm the observed associations of vertical attenuation and deep stromal invasion as the disease advances. Nevertheless, this study is significant as the first to characterize these two distinct progression pathways in primary and recurrent pterygium using AS SS-OCT, providing a novel model for understanding their differing clinical behaviors. Another limitation of this study is the relatively small sample size of the recurrent pterygium group ($n = 24$) compared to the primary group ($n = 114$). This imbalance in sample size, which reflects the natural difference in prevalence between the two conditions in clinical settings, may reduce the statistical power of our findings. Furthermore, prior surgical techniques and

the time interval since the last surgery could confound the morphological features of recurrent pterygium. However, because our retrospective cohort included patients referred from various clinics, precise surgical histories were unavailable for covariate analysis. While this cross-sectional design limits inferring dynamic growth trajectories, the distinct morphological patterns observed still provide meaningful structural insights that warrant future longitudinal validation. Future prospective studies with longitudinal follow-up are required to validate these progression models.

In conclusion, this study proposes two distinct morphological progression patterns: vertical attenuation for primary pterygium and deep stromal invasion for recurrent pterygium. These findings provide clinicians with objective evidence to explain symptom variability in primary patients and to anticipate the aggressive stromal involvement in recurrent cases. By characterizing these distinct pathways, this research supports more tailored surgical planning and improved patient care strategies.

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* YIY and DHH contributed equally to this study as co-first authors.

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