Research Square

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Mid-Iris Atrophy as a Preoperative Predictor of Impaired Pupillary Dilation and Intraoperative Complications in Cataract Surgery

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Research Article

Keywords: Cataract surgery, Mid-iris atrophy, MIA, Surgical complication, Intraoperative floppy iris syndrome, Iris smoothness index

Posted Date: August 26th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10606073/v1

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Additional Declarations: No competing interests reported.

Abstract

Mid-iris atrophy (MIA) is a slit-lamp clinical sign characterized by mid-peripheral stromal thinning and depigmentation. This prospective observational study evaluated the association between MIA and iris biomechanical properties, pharmacologic dilation, and intraoperative outcomes during phacoemulsification. Forty-eight eyes were enrolled and classified into MIA (n=17) and control (n=31) groups. All eyes underwent preoperative anterior segment optical coherence tomography (AS-OCT) to assess iris thickness at 1, 2, and 3 mm from the pupillary margin, and the Iris Smoothness Index (ISI), a quantitative measure of anterior iris surface irregularity within a 3-mm segment. Baseline demographic and biometric parameters were comparable between groups. Iris thickness was significantly reduced at 2 mm from the pupillary margin in MIA eyes (298 ± 44 μm vs. 337 ± 62 μm; P = 0.047), with no significant differences at 1 or 3 mm or in mean overall thickness. MIA eyes demonstrated significantly higher ISI (0.922 ± 0.017 vs. 0.886 ± 0.052; P = 0.007) and smaller post-dilation pupil diameter (P < 0.001). ISI showed a significant inverse correlation with post-dilation pupil diameter (r = −0.45; P = 0.004). Intraoperative events occurred exclusively in the MIA group (64.7% vs. 0%; OR = 55.0, 95% CI: 5.9–604.8; P < 0.0001), and surgical duration was significantly longer (338.9 ± 72.8 vs. 289.6 ± 54.3 seconds; P = 0.022). These findings suggest that MIA may serve as a clinically recognizable indicator of increased surgical complexity, warranting anticipatory surgical planning in affected eyes.

Key Message

What is known: Structural and pharmacologic factors impairing pupillary dilation are recognized predictors of intraoperative complications during cataract surgery; however, the role of intrinsic iris morphological alterations remains poorly characterized.

What is new: MIA is associated with focal mid-peripheral iris thinning on AS-OCT, increased iris surface smoothness, and impaired pharmacologic dilation. Eyes with MIA demonstrate markedly higher rates of intraoperative events, including IFIS, iris prolapse, and posterior capsule rupture, suggesting MIA as a clinically recognizable indicator of surgical complexity warranting anticipatory management.

Introduction

Cataract surgery is the most frequently performed surgical procedure worldwide, with more than 20 million operations annually, and remains one of the most cost-effective interventions in medicine [1, 2]. Although modern phacoemulsification techniques have achieved high safety and efficacy profiles, intraoperative complications continue to occur and may significantly influence visual outcomes [3–5]. Large clinical series report an overall intraoperative complication rate of approximately 4–5%, with zonular dialysis and posterior capsule rupture among the most common adverse events [6–10]. While severe vision-threatening complications are rare (< 0.03%) [6], even less catastrophic events may prolong surgical time, increase technical difficulty, and compromise postoperative recovery. These risks are

influenced by surgeon experience, patient characteristics, and preoperative anatomical factors [11, 12]. Therefore, identifying subtle anatomical predictors of surgical complexity remains clinically relevant.

Among ocular anatomical determinants, iris configuration and dynamic behavior during surgery have emerged as important but incompletely characterized contributors to operative risk. Adequate pupillary dilation is essential for optimal visualization and safe capsulorhexis creation. Small pupil diameter (≤ 4 mm) has been consistently associated with increased rates of capsular complications, iris trauma, hyphema, and vitreous loss [13–15]. Impaired mydriasis may result from pharmacologic influences—particularly systemic alpha-1 adrenergic antagonists—systemic diseases such as diabetes mellitus, and ocular conditions including pseudoexfoliation syndrome, prior intraocular surgery, trauma, uveitis, and glaucoma [14, 16–21].

Intraoperative Floppy Iris Syndrome (IFIS), can lead to billowing of the iris, progressive intraoperative miosis, and iris prolapse despite pharmacologic dilation [22–24]. IFIS has been linked primarily to systemic alpha-1 antagonist use, yet accumulating evidence suggests that intrinsic iris structural properties also modulate its occurrence and severity [17–19, 25, 26]. Moreover, quantitative anterior segment optical coherence tomography (AS-OCT) studies have demonstrated that iris thickness, volume, convexity, and surface characteristics influence dynamic iris behavior during pharmacologic dilation [27–35]. Variations in stromal composition and fluid dynamics appear to affect both mydriatic response and anterior chamber configuration.

Despite increasing recognition of iris biomechanical variability, structural and morphological features of iris have not been studied well yet. During routine practice, we identified a distinct slit-lamp finding characterized by stromal thinning with localized depigmentation of the mid-peripheral iris. Clinically, eyes exhibiting this feature appeared to be more prone to intraoperative complications during cataract surgery. We therefore propose mid-iris atrophy (MIA) as a novel clinical sign in slit-lamp examination.

Accordingly, this prospective study aimed to determine the association between MIA and AS-OCT–derived quantitative iris structural parameters, and to evaluate the relationship between MIA and intraoperative complications during cataract surgery. We hypothesized that eyes with MIA would demonstrate impaired dilation dynamics and a higher frequency of intraoperative complications compared with controls.

Methods

Study Design and Participants

This prospective observational study was conducted between February 2023 and August 2024. Consecutive patients scheduled for phacoemulsification cataract surgery were recruited. Written informed consent was obtained from all participants. The study adhered to the Declaration of Helsinki and received institutional ethics approval (IR.TUMS.FARABIH.REC.1402.017).

All participants underwent comprehensive ophthalmic examination including corrected distance visual acuity assessment, slit-lamp biomicroscopy, Goldmann applanation tonometry, and dilated fundus examination.

MIA was defined as stromal thinning with depigmentation localized to the mid-peripheral iris, in the zone extending between the pupillary margin and the iris root. Eyes were categorized into two groups according to preoperative slit-lamp biomicroscopic findings, documented using standardized slit-lamp photography: the MIA group comprised eyes in which these changes involved more than 50% of the iris circumference (Fig. 1), while the control group included eyes with normal iris appearance and no clinical evidence of atrophy. A threshold of > 50% circumferential involvement was applied to define MIA as a diffuse structural phenotype, distinguishing it from focal or localized iris changes that may represent incidental or age-related findings rather than a clinically meaningful biomechanical variant.

To reduce confounding factors affecting iris behavior or surgical outcomes, the following were excluded: pseudoexfoliation syndrome [21, 36], long-standing diabetes (> 5 years) or diabetic retinopathy, glaucoma or glaucomatous optic neuropathy, previous ocular trauma or intraocular surgery, use of medications associated with IFIS, including tamsulosin, other alpha-1 antagonists, finasteride, and antipsychotic medications [22, 37].

Imaging Protocol and Quantitative Iris Assessment

Imaging Protocol and Quantitative Iris Assessment
Standardized slit-lamp photographs were obtained for all participants (DC3, Topcon, Tokyo, Japan). Ocular biometric parameters, including axial length, anterior chamber depth, and keratometry values, were measured using optical biometry (IOLMaster 500, Carl Zeiss Meditec, Jena, Germany). Anterior segment optical coherence tomography (AS-OCT; CASIA2, Tomey Corporation, Nagoya, Japan) was performed in a dark room prior to dilation.

AS-OCT scans were obtained along four meridians (0°, 45°, 90°, and 135°). Measurements were obtained from both iris halves of each scan and averaged. Iris thickness was measured at standardized distances of 1,2, and 3 mm from the pupillary margins, as well as the maximum and minimum iris thickness. For each 3-mm segment, the cross-sectional thickness was measured and divided by 3000 μm to calculate the mean iris thickness per segment. Measurements from eight iris halves were averaged to obtain a single value per eye. Due to limited visualization of the posterior pigment epithelium, only the anterior border layer and stromal thickness were analyzed (Fig. 2).

The Iris Smoothness Index (ISI) was calculated as previously described [33–35], defined as the straight-line distance connecting the most peripheral and central points of the anterior iris border divided by the actual curved contour length of that border within the 3-mm segment. Values from all iris halves were averaged for each eye (Fig. 3).

Pharmacologic mydriasis was induced using 1% tropicamide administered three times at 20-minute intervals (Fig. 4). Post-dilation AS-OCT imaging was performed 20 minutes after the final instillation. Pupil diameter was measured before and after pharmacologic dilation.

All measurements were obtained by a masked examiner and independently verified by a second examiner. In cases of discrepancy, a third review was performed to reach consensus. All image analyses were performed manually using ImageJ software (National Institutes of Health, Bethesda, MD, USA).

Surgical technique and Intraoperative events

All surgeries were performed by a single experienced surgeon (SG) using a phacoemulsification system (Stellaris, Bausch & Lomb, Rochester, NY, USA) through a 2.8-mm clear corneal incision following a standard surgical technique.

Intraoperative events including IFIS, iris prolapse, anterior capsule tear, posterior capsule rupture, zonular dialysis and vitreous loss were recorded.

Surgical time was defined as the interval between the first corneal incision and removal of the lid speculum.

Statistical Analysis

Data distribution was assessed using the Shapiro–Wilk test. Continuous variables were reported as mean ± standard deviation (SD) for normally distributed data or median and interquartile range (IQR) for non-normally distributed data. Categorical variables were presented as frequencies and percentages.

Between-group comparisons were performed using the independent-samples t-test for normally distributed continuous variables and the Mann–Whitney U test for non-normally distributed variables. Categorical variables were compared using the chi-square test or Fisher’s exact test when appropriate.

All statistical tests were two-tailed. A p-value < 0.05 was considered statistically significant. Statistical analyses were conducted using GraphPad Prism (version 9.5.1; GraphPad Software, San Diego, CA, USA).

Results

Preoperative Characteristics

A total of 48 eyes from 48 patients undergoing phacoemulsification with posterior chamber intraocular lens implantation were included. Baseline demographic and ocular characteristics are summarized in Table 1.

There were no statistically significant differences in demographic characteristics and baseline biometric parameters between the MIA and control groups (P > 0.05), indicating that the two groups were comparable at baseline (Table 1).

Table 1
Preoperative characteristics

Characteristic/Parameter	**Mid-iris Atrophy Group**	**Control Group**	***P*-value**
Number of eyes	17	31	-
Age (y)	69.1 ± 11.1	63.3 ± 8.7	0.054 [a]
Male gender, n/N (%)	13/17(76.5%)	14/31(45.2%)	0.13 [b]
Diabetes mellitus	5	6	0.42 [b]
Axial length	23.1 ± 0.8	23.2 ± 0.7	0.7 [a]
K1	44.0 ± 1.4	44.1 ± 1.3	0.9 [a]
K2	45.1 ± 1.7	44.9 ± 1.5	0.7 [a]
Anterior chamber depth	3.1 ± 0.3	3.1 ± 0.3	0.9 [a]
Mean ISI (undilated)	0.922 ± 0.017	0.886 ± 0.052	0.007 [a]
Mean undilated pupil diameter (μm)	3374 ± 736	3867 ± 739	0.052 [a]
Mean dilated pupil diameter (μm)	5069 ± 621	5896 ± 624	< 0.001 [a]
Mean IT at 1mm (μm)	425 ± 47	436 ± 89	0.661 [a]
Mean IT at 2mm (μm)	298 ± 44	337 ± 62	0.047 [a]
Mean IT at 3mm (μm)	325 ± 63	346 ± 63	0.338 [a]
Average mean IT (μm)	352 ± 28	367 ± 57	0.382 [a]

K1: flat keratometry, K2: steep keratometry, ISI: iris smoothness index, IT: iris thickness. [a] Independent samples t-test. [b] Chi-square or Fisher's exact test.

Following pharmacologic dilation, the mean pupil diameter was significantly smaller in the MIA group than in the control group (5.07 ± 0.62 mm vs. 5.90 ± 0.62 mm, P < 0.001). (Table 1) (Fig. 4 and Fig. 6A, B).

The mean iris thickness at 2 mm from the pupillary margin was significantly lower in the MIA group than in the control group (298 ± 44 μm vs. 337 ± 62 μm, P = 0.047) (Table 1), supporting the designation of this phenotype as mid-iris atrophy. However, no significant differences were observed between two groups in

iris thickness measurements at 1 and 3 mm from the pupillary margin and in average iris thickness (P > 0.05; Fig. 6C). To provide a spatial visualization of iris thickness distribution, meridian-based iris thickness maps were constructed using AS-OCT measurements at 1, 2, and 3 mm from the pupillary margin across eight meridians in MIA and control groups (Fig. 5). In MIA group, the maps demonstrated consistent relative thinning at the 2-mm mid-peripheral zone across all meridians, visually corroborating the statistically significant reduction observed at this location. Control group displayed a relatively more homogenous mid-peripheral thickness profile compared with MIA group.

Eyes with MIA demonstrated a significantly higher ISI compared with control eyes (0.922 ± 0.017 vs. 0.886 ± 0.052, P = 0.007) (Table 1; Fig. 6E). Post-dilation pupil diameter demonstrated a moderate negative correlation with mean ISI (r = -0.45, P = 0.004; Fig. 6F) which suggests that increasing anterior iris surface smoothness is associated with reduced pupillary dilatory response, resulting in smaller post-dilation pupil diameter.

Intraoperative Events

Intraoperative events of any types occurred in 11 of 17 eyes (64.7%) in the MIA group, compared with none in the control group (P < 0.0001). The presence of MIA was strongly associated with the occurrence of intraoperative events (odds ratio [OR], 55.0; 95% confidence interval [CI], 5.9–604.8). The distribution of intraoperative events across groups is presented in detail in Table 2.

Mean surgical duration was significantly longer in the MIA group compared with controls (338.9 ± 72.8 seconds vs. 289.6 ± 54.3 seconds, P = 0.022; Fig. 6G).

Table 2
Incidence of Surgical Complications in Mid-Iris Atrophy and Control Groups.

Intra-operative Events	**MIA (n = 17)**	**Control (n = 31)**	**Relative Risk (95% CI)**	**Odds Ratio (95% CI)**
Any intraoperative event	11	0	20 (3.8 to 115.6)	55 (5.9 to 604.8)
IFIS	8	0		
Iris Prolapse	2	0		
Post capsule tear	1	0		

MIA: mid-iris atrophy; IFIS: intraoperative floppy iris syndrome; RR: relative risk; OR: odds ratio; CI: confidence interval. RR and OR were calculated for the composite outcome of any intraoperative event using continuity correction. Individual event rates are reported descriptively due to the small number of events and limited statistical power for separate effect estimation.

Discussion

MIA is a morphological feature of the iris characterized by localized stromal thinning and depigmentation in the mid-peripheral zone, sparing the pupillary margin. Although its exact pathophysiology remains incompletely understood, structural remodeling of the iris stroma appears to play a central role[32].

In this prospective study, we demonstrated that eyes with MIA, in the absence of other known risk factors for IFIS, exhibited significantly impaired pharmacologic pupillary dilation, a markedly higher frequency of intraoperative events, and prolonged surgical time during cataract surgery. Baseline demographic and biometric parameters were comparable between the two groups, minimizing the potential for anatomical confounding.

Although average iris thickness did not differ significantly between groups, eyes with MIA demonstrated a significant reduction in iris thickness specifically at the 2-mm location from the pupillary margin, corresponding anatomically to the clinically affected mid-iris region. This localized thinning supports the use of the term “atrophy” and suggests that MIA is characterized by focal rather than diffuse stromal tissue loss. Averaging measurements across multiple iris regions may obscure these localized structural changes, whereas segment-specific analysis appears more sensitive for detecting the characteristic morphologic alterations of MIA. To our knowledge, this is the first study to present a meridian-based iris thickness map derived from AS-OCT, providing a spatial visualization of focal mid-peripheral stromal thinning across multiple meridians. Analogous to epithelial thickness mapping (ETM) in keratoconus screening, this mapping approach offers a clinically intuitive tool for preoperative iris phenotyping and MIA risk stratification. With further validation, AS-OCT–based iris thickness mapping may represent a valuable addition to the preoperative workup in cataract surgery.

ISI was originally developed as a quantitative morphometric parameter to detect subtle anterior iris surface alterations, defined as the ratio of the straight-line distance between two predefined points on the anterior iris border to the actual curved contour length between those points. This index was introduced to replace subjective slit-lamp assessment with an objective measurement capable of identifying early structural changes [33–35]. In our cohort, eyes with MIA demonstrated significantly higher ISI values compared with controls. Since ISI reflects the degree of smoothness of the anterior iris surface, these findings suggest that MIA is associated with flattening and loss of normal surface undulations. Such smoothing of the anterior iris contour may represent localized tissue loss within the affected mid-peripheral iris region. Notably, this difference was observed despite the absence of a significant difference in average iris thickness between groups, indicating that alterations in iris morphology may be more sensitively detected by surface contour analysis than by global thickness measurements alone.

Functionally, these structural alterations appear clinically relevant. Eyes with MIA demonstrated significantly reduced pharmacologic dilation, and higher ISI values were associated with smaller post-dilation pupil diameters. Together, these findings suggest that flattening of the anterior stromal architecture may reflect underlying stromal remodeling that affects the biomechanical behavior of the

iris. Such changes may reduce the ability of the iris to respond to pharmacologic stimulation and could potentially increase susceptibility to iris instability during intraocular surgery.

Poor pupil dilation is a well-established factor contributing to increased surgical difficulty and a higher risk of complications during phacoemulsification [5, 15]. In this study, mean pupil diameters, after pharmacologic dilation, was significantly smaller in the MIA group compared to the control group. This observation suggests that MIA may compromise the iris's ability to dilate adequately, potentially as a result of structural alterations in the iris tissue. Atrophic changes in the iris have been linked to collagen reorganization, loss of stromal integrity, and partial replacement of contractile elements with fibrotic tissue, which may impair the biomechanical properties of the iris. Such remodeling could reduce tissue elasticity and hinder effective force transmission from the dilator muscle, thereby disrupting pharmacologic pupillary dynamics [38].

A particularly notable finding was the high frequency of IFIS in the MIA group despite the absence of systemic α1-antagonist exposure or other established predisposing factors. IFIS is classically associated with tamsulosin and other α1-adrenergic antagonists [39]. However, cases have also been reported in association with other medications [40] and even in patients without identifiable pharmacologic exposure. In addition, smaller preoperative dilated pupil diameter has been identified as an independent predictor of IFIS [37]. We propose that iris instability — whether pharmacologically induced or structurally mediated — may represent a shared final pathway underlying the hallmark intraoperative manifestations of IFIS, including iris fluttering, progressive miosis, and iris prolapse. In this framework, α1-antagonists and structural atrophy such as MIA may act through distinct but converging mechanisms: the former by impairing neurogenic dilator tone, and the latter by reducing stromal rigidity and biomechanical resilience, both ultimately compromising the iris's ability to resist the fluid dynamics generated during phacoemulsification. Previous studies have identified structural iris alterations in IFIS, including dilator muscle thinning and persistent anatomical changes that may contribute to iris floppiness independent of pharmacologic exposure [23]. In line with these findings, the occurrence of characteristic IFIS features in our cohort supports MIA as a potential anatomical susceptibility phenotype and suggests that IFIS may arise through both structural and pharmacologic pathways.

Intraoperative events—including iris prolapse and posterior capsule rupture with vitreous loss—occurred exclusively in the MIA group, and surgical duration was significantly longer in these eyes. Poor pupillary dilation and abnormal iris behavior are recognized risk factors for intraoperative complications, as they impair visualization, limit surgical maneuverability, and increase the risk of capsular or zonular injury [24, 41, 42]. Therefore, preoperative recognition of MIA may be valuable for surgical planning. In eyes with suspected MIA, prophylactic measures such as modified corneal incision construction, intracameral epinephrine or atropine, reduced fluidics settings, and early use of mechanical pupil expansion devices may improve intraoperative stability and reduce complication risk [22]. Such anticipatory, rather than reactive, management may help reduce surgical stress and facilitate safer phacoemulsification. Given the higher rate of intraoperative events observed in our cohort, involvement of an experienced cataract surgeon may be considered in selected cases.

Importantly, prolonged operative time is not merely a marker of technical difficulty but may itself contribute to worse surgical outcomes. Longer phacoemulsification duration has been associated with greater corneal endothelial stress, increased postoperative inflammation, and higher rates of intraoperative complications [12, 43, 44]. Collectively, our findings suggest that MIA may serve as a clinically recognizable indicator of increased surgical complexity, warranting anticipatory surgical planning.

This study is strengthened by its prospective design, standardized imaging protocol, and masked outcome assessment. However, the relatively small sample size resulted in wide confidence intervals for some estimates, and the single-center design may limit external validity. Additionally, MIA was classified without a formal severity grading scale. Whether a dose-response relationship exists between the extent of atrophy and surgical outcomes remains to be explored in future studies. Inter-observer reliability statistics for MIA classification and ISI measurements were not formally assessed, which represents a further limitation; future studies should include reproducibility analyses to establish the reliability of these parameters. The etiology of MIA remains incompletely understood, and possible contributing mechanisms were not directly investigated in the present study. Future studies are needed to elucidate the pathophysiological basis of MIA and its relationship to systemic or ocular comorbidities.

In conclusion, MIA represents a distinct structural remodeling phenotype of the iris, characterized by focal mid-iris thinning and increased anterior surface smoothness despite preserved overall iris thickness. By providing objective AS-OCT evidence corroborating this clinical sign and demonstrating its tangible consequences on surgical outcomes, this study highlights the importance of recognizing MIA during preoperative assessment. The combination of higher ISI, impaired pharmacologic dilation, and increased intraoperative instability suggests that MIA may serve as a clinically meaningful marker of cataract surgery complexity and intraoperative risk, while laying the groundwork for future investigation into its underlying mechanisms and broader clinical implications.

The authors express their gratitude to Farabi Hospital and everyone who contributed to this investigation.

Declarations

The authors express their gratitude to Farabi Hospital and everyone who contributed to this investigation.

Author contributions: A.G collected the data. S.G designed the study, H.F analyzed the data. H.F, A.G, S.G and M.P wrote the manuscript. All authors critically reviewed the final manuscript.

Competing interests: The authors declare no competing interests.

Additional Information: Additional data or materials related to this study can be provided to researchers upon reasonable request.

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

Ethics approval: This study was approved by the Ethics Committee of Tehran University of Medical Sciences (Ethics code: IR.TUMS.FARABIH.REC.1402.017). All procedures were performed in accordance with the Declaration of Helsinki.

Consent to Participate: Written informed consent was obtained from all participants.

Consent to Publish: Not applicable.

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Figures

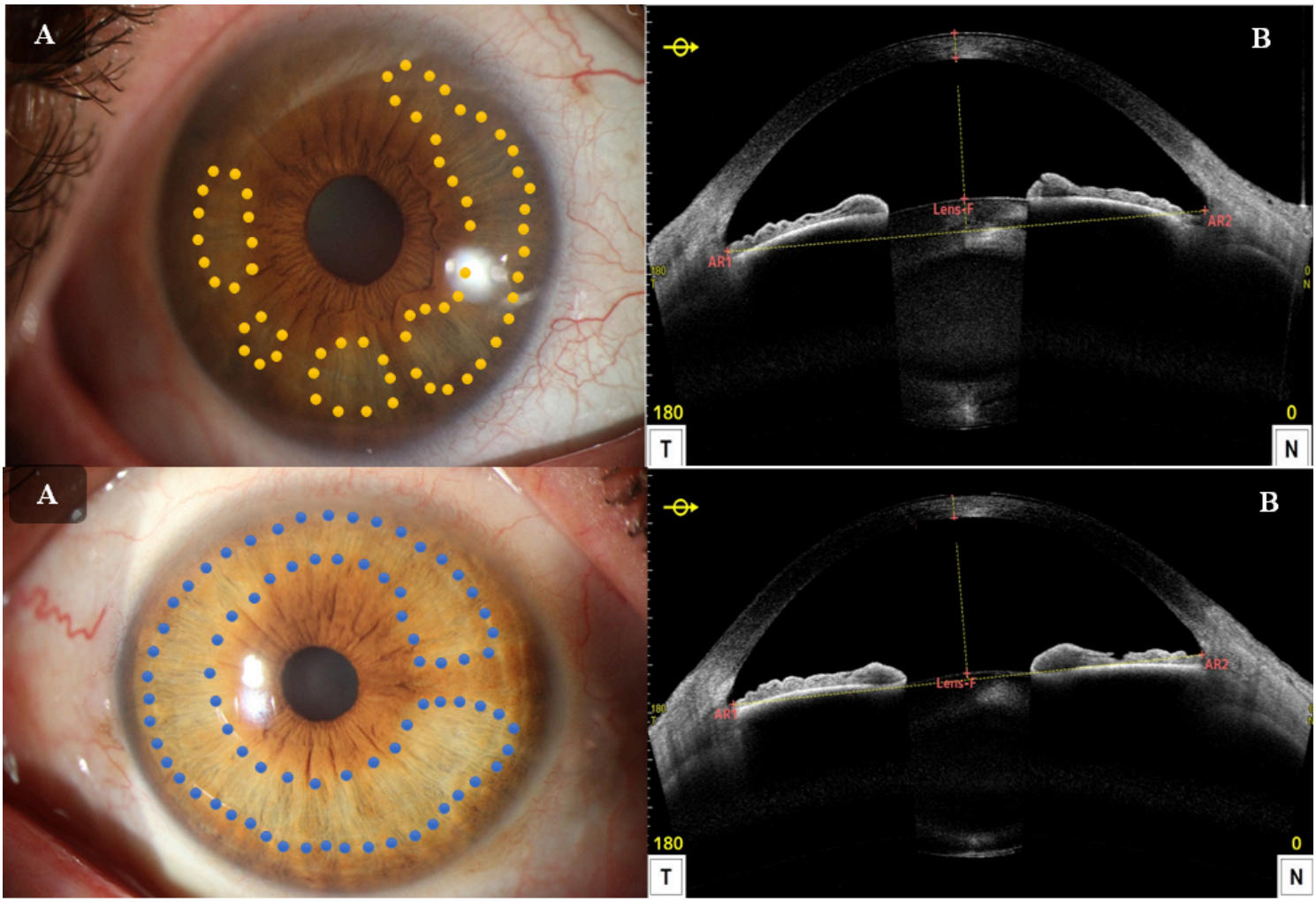


Figure 1

Slit-lamp photograph demonstrating the area of MIA (dotted outline) with the corresponding AS-OCT image.

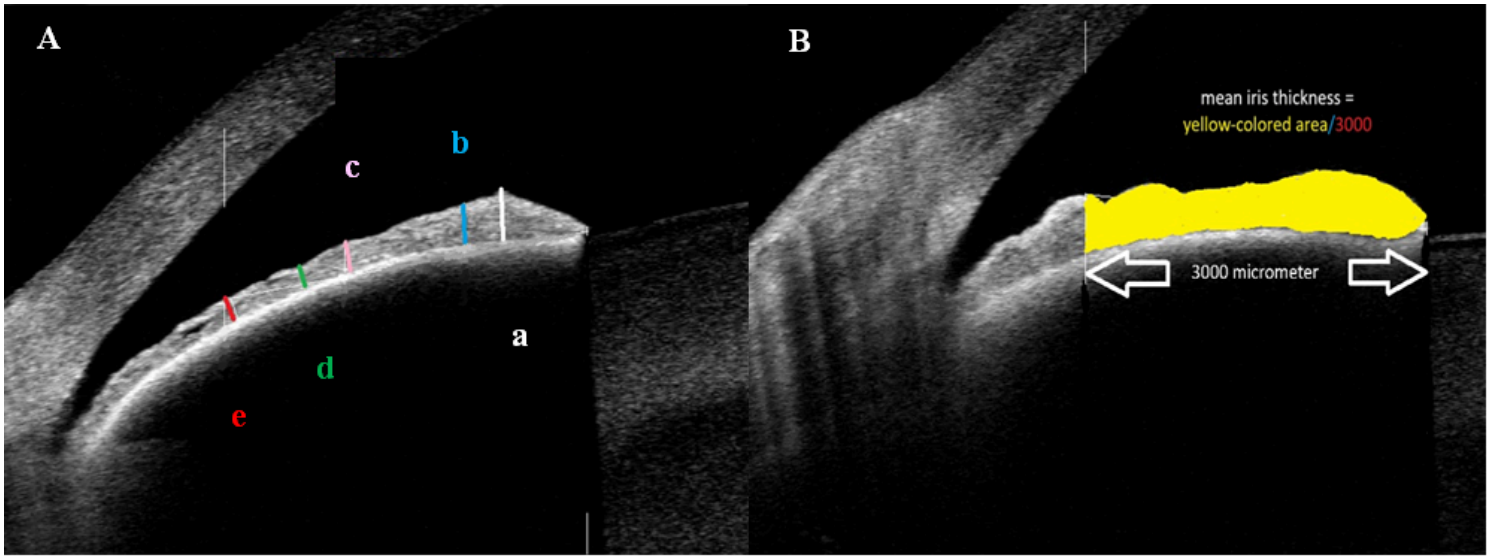


Figure 2

Iris Thickness measurements at 1mm, 2mm, and 3mm distance from pupil margin. a: Maximum iris thickness, b: Iris thickness in 1mm, c: Iris thickness in 2mm, d: Minimum iris thickness, e: Iris thickness in 3mm (A). Calculation of the mean iris thickness per segment (B).

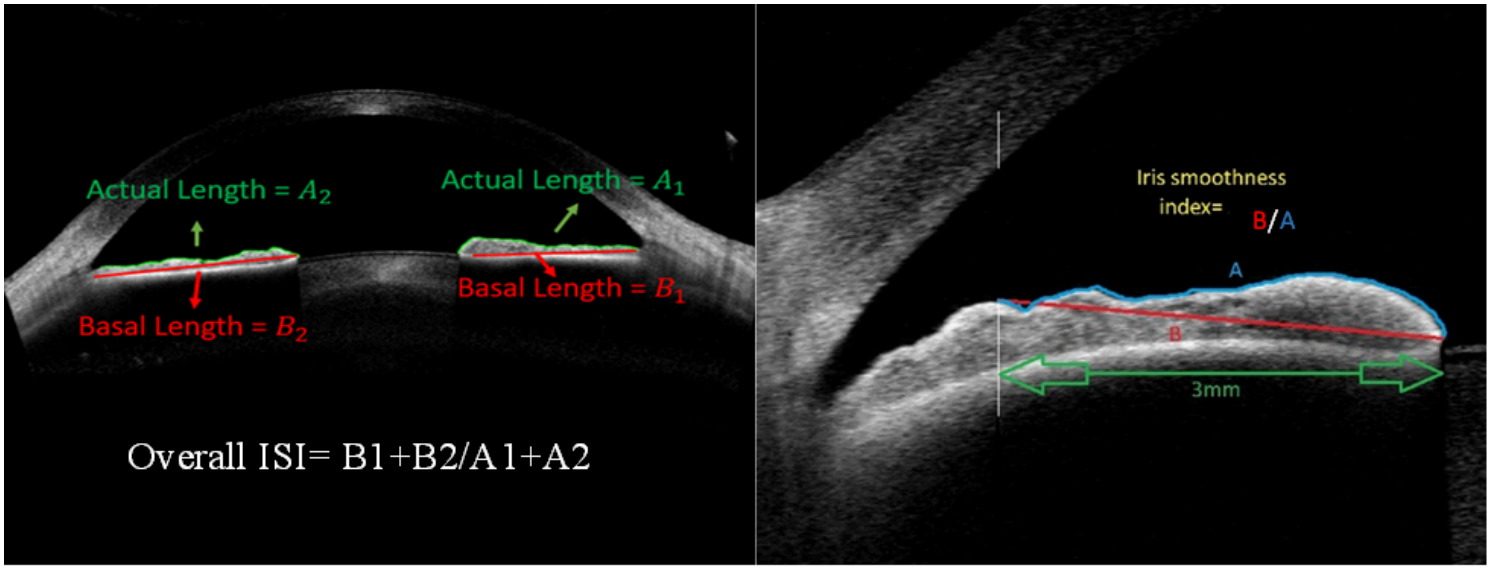


Figure 3

(A) Schematic illustration of the overall iris smoothness index (ISI), defined as the ratio of the basal line to the actual iris surface contour (adapted from Fakhredin et al) [35]. **(B)**Measurement of the ISI at 3 mm from the pupillary margin according to present study.

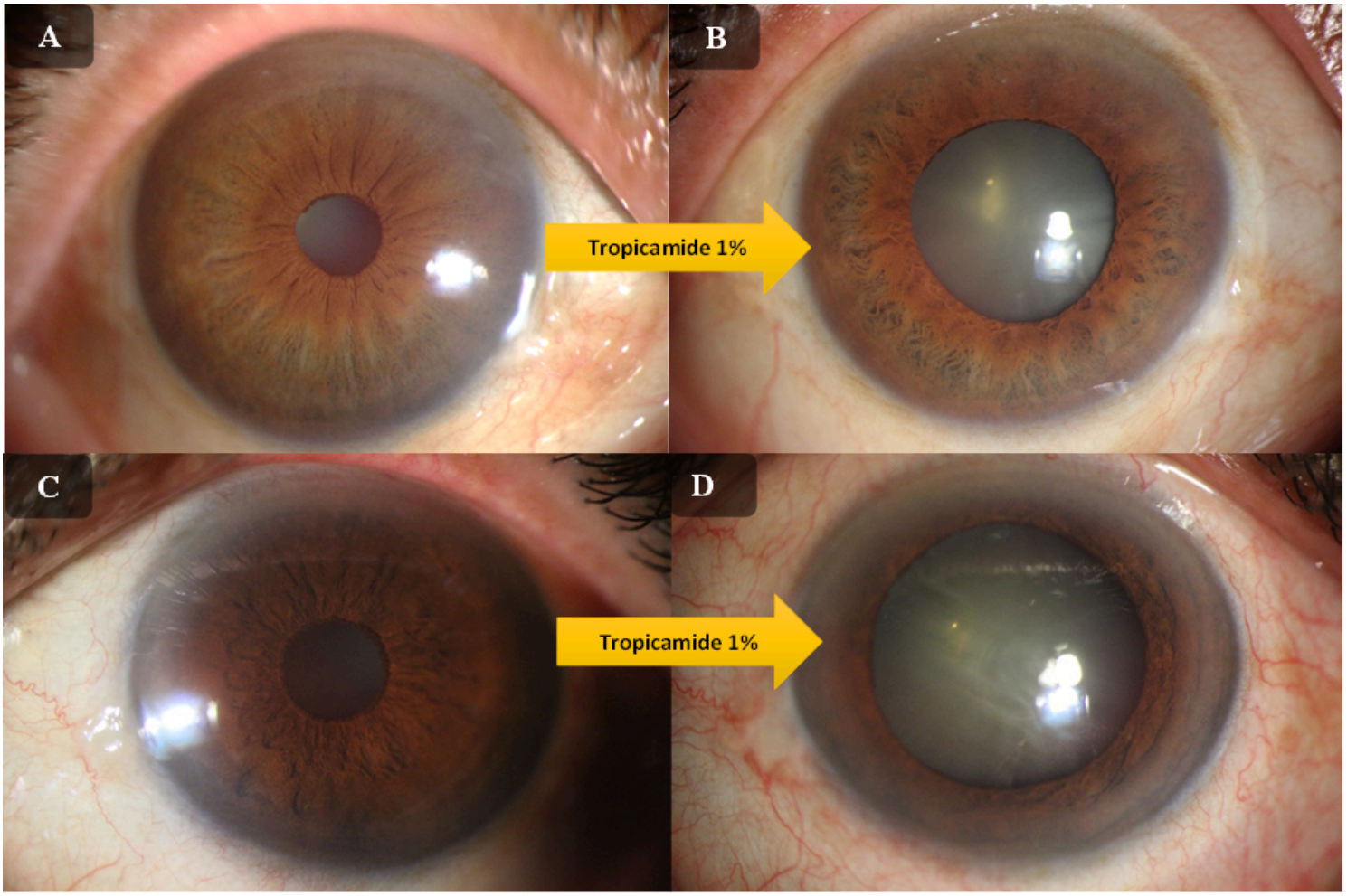


Figure 4

Slit-lamp photographs of an MIA eye before **(A)** and after **(B)** pharmacologic dilation, and a normal control eye before **(C)**and after **(D)** dilation. Pupillary dilation was induced using 1% tropicamide administered in three doses at 20-minute intervals. Compared with the normal control eye, the MIA eye demonstrates poor pupillary dilation and persistent pupillary irregularity after dilation.

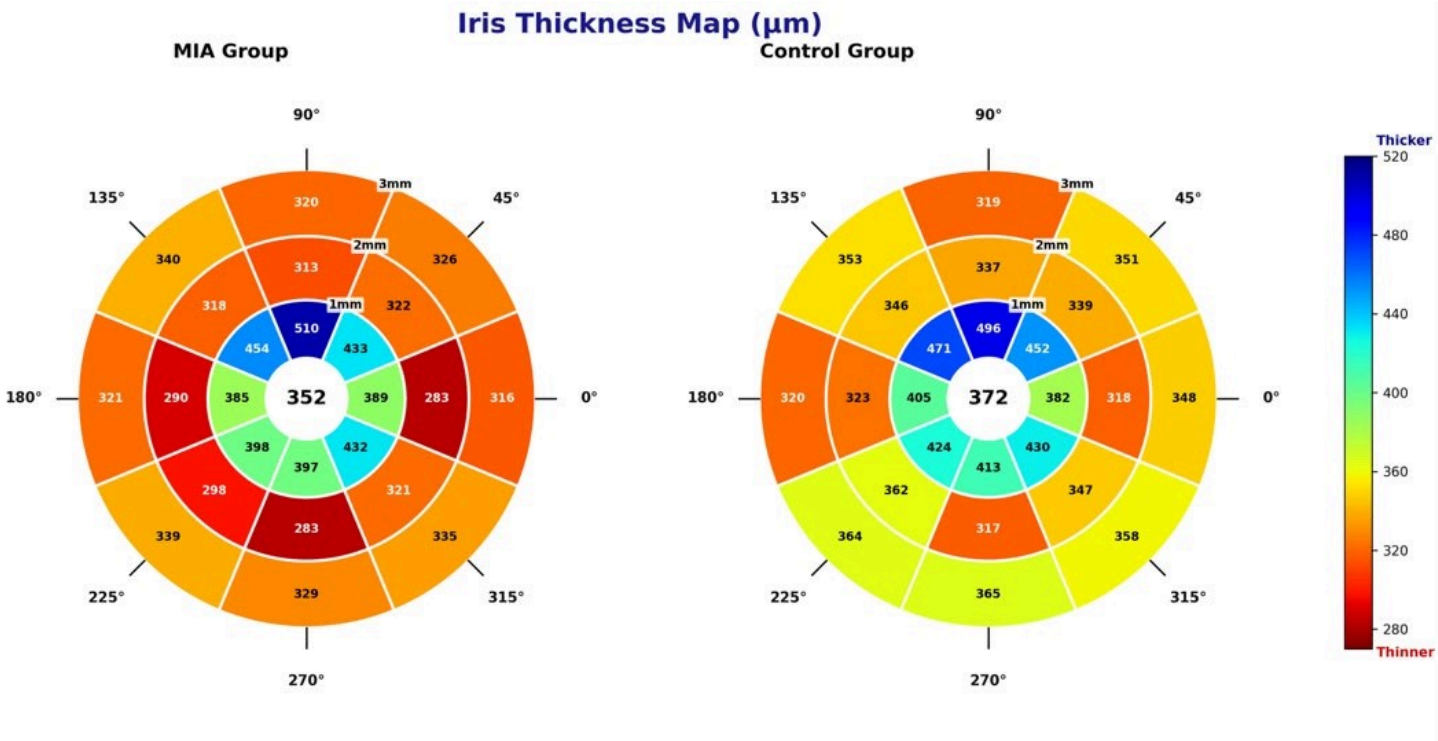


Figure 5

Meridian-based iris thickness map derived from AS-OCT in MIA and control eyes. Mean iris thickness (µm) is displayed at 1, 2, and 3 mm from the pupillary margin across eight meridians (0°, 45°, 90°, 135°, 180°, 225°, 270°, and 315°). Color coding reflects thickness values as indicated by the scale bar; red indicates thinner and blue indicates thicker iris tissue. The 2-mm mid-peripheral zone demonstrates consistently thinner tissue in MIA eyes compared with controls. Each 45° sector represents measurements obtained at the corresponding meridian.

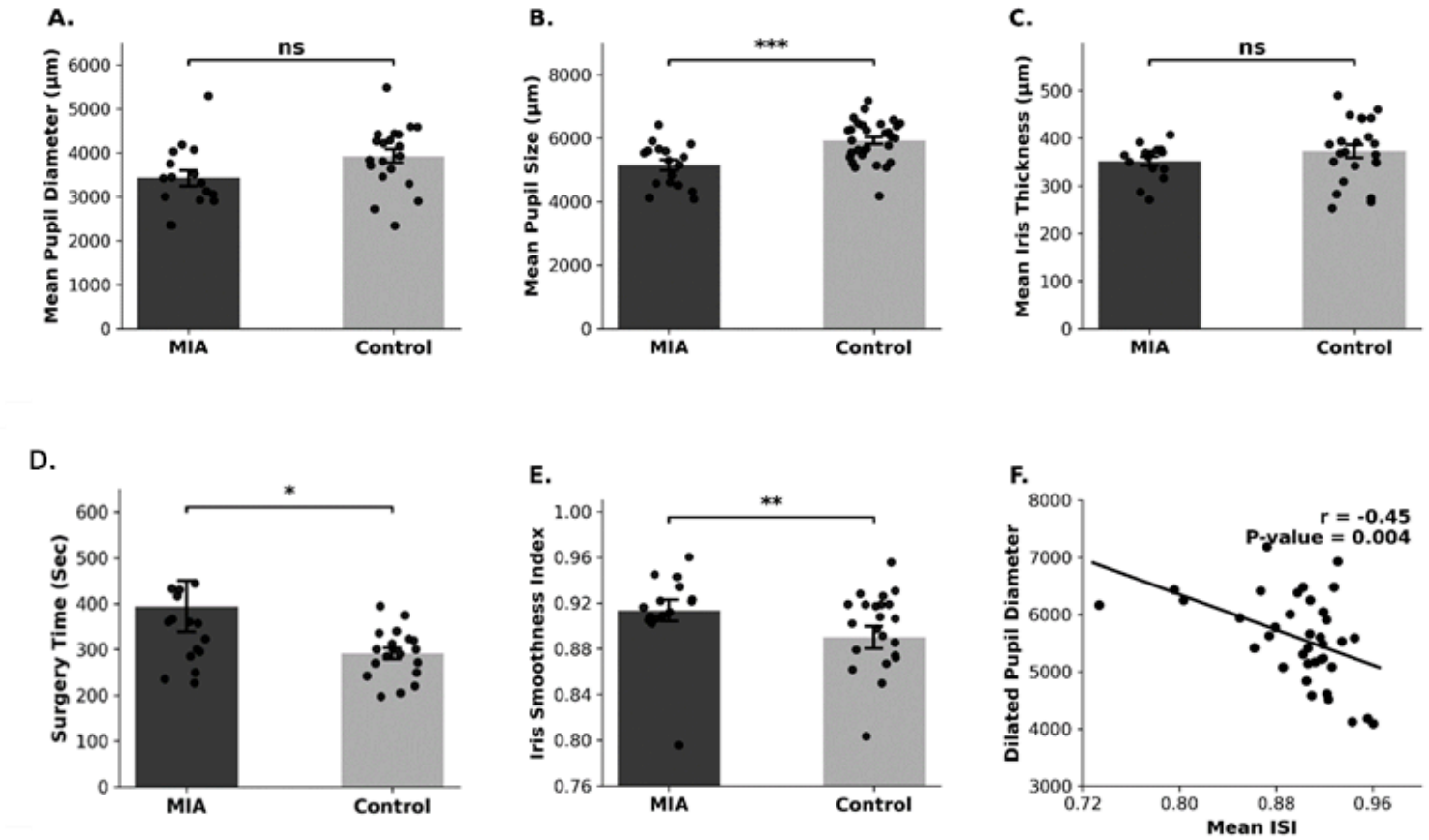


Figure 6

Preoperative measurements. The analysis of the differences in mean pupil diameters between the mid-iris atrophy group and control group after dilation **(A, B).** The analysis of the differences in mean iris thickness **(C)**, Surgery time differences between the mid-iris atrophy group and the control group **(D)**, mean iris smoothness index **(E)** between the mid-iris atrophy group and the control group. Pearson correlation analysis between Mean ISI and Dilated pupil diameter in all patients **(F)**. *: P-value < 0.05; **: P-value < 0.01; ***: P-value < 0.001; ****: P-value < 0.0001; ns: non-significant.