

Comparison of Extraocular Muscles in Patients with Exotropia and Healthy Participants Using Anterior Segment Optical Coherence Tomography

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To analyze and characterize the medial and lateral rectus muscles in patients with exotropia using anterior segment optical coherence tomography (AS-OCT). This study included 24 patients with exotropia (48 eyes) and 25 healthy individuals (50 eyes). Anterior segment optical coherence tomography was used to construct the en face images. The anterior chamber angle to the extraocular muscle insertion distance, muscle width, and muscle fiber angle from the muscle insertion sites were compared between the exotropia and the control groups. The correlation between these parameters and age or angle of deviation was evaluated. The mean ages were 13.2 ± 4.1 years for the exotropia group and 17.6 ± 7.2 years for the control group. The lateral rectus angle was significantly more inwardly rotated in the exotropia group than in the control group ($1.6 \pm 6.3^\circ$, $-1.4 \pm 4.0^\circ$, $p=0.014$). With increasing angle of deviation, the width of the lateral rectus increased ($p=0.002$). Our results indicate that the lateral rectus angle is significantly more inwardly rotated in patients with exotropia. These findings should contribute to a deeper understanding of the extraocular muscles in patients with this condition.

Key words: exotropia, AS-OCT, anterior chamber angle to extraocular muscle insertion distance, muscle width, muscle fiber angle

The reported success rates of surgery for exotropia (XT) vary widely, from 18% to 92%, among the different surgical modalities used [1]. In addition to the surgical method, factors contributing to the wide range of postsurgical outcomes include the age of patients and the length of the follow-up period. Another contributing factor may be the impact of structural abnormalities in the extraocular muscles on ocular alignment in patients with XT, which suggests that clarifying the characteristics of the extraocular muscles in patients with XT could help improve the surgical success rate.

Accordingly, several studies have investigated the

characteristics of extraocular muscles in patients with XT during autopsy or surgery [2-5]. However, the accuracy of these studies was limited by their research methods. Tissue shrinkage occurs during autopsy and can affect the measurements [2]. Studies that use surgical calipers have issues with imprecise measurements owing to the analog nature and unclear measurement boundaries of the instrument [3-5]. One study compared patients with XT to a control group comprising patients with retinal detachment [5]. Due to advances in optical coherence tomography (OCT), anterior segment OCT (AS-OCT) has become available as a means of measuring the extraocular muscles; AS-OCT has

already been used to evaluate extraocular muscles preoperatively and after recession, resection, or plication [6-12]. However, due to variations in the location of the extraocular muscles and the imaging angles, it can be challenging to obtain consistent information from these images.

We previously developed a method for examining the shape of the extraocular muscles in healthy participants by measuring the muscle insertion and direction of the muscle fibers [13]. This method involves creating en face images by superimposing tomographic images and flattening the shape of the eyeball based on the conjunctival surface (using a fluttering technique). In this study, we used this method to investigate the characteristics of the medial rectus (MR) and lateral rectus (LR) muscles in patients with XT.

Materials and Methods

This retrospective study was conducted on 24 patients with XT (48 eyes) and 25 healthy participants (50 eyes), all under the age of 30 years, at our hospital between July 2019 and June 2022. Data were collected from all patients before surgery. No cycloplegic refraction was performed. The angle of deviation (in degrees) was converted from the prism diopter value obtained during the preoperative examination using a prism adaptation test. Exclusion criteria were previous strabismus surgeries, vertical deviation (>5 prism diopters), subjective cyclodeviation during the preoperative examination, A and V pattern strabismus, or other diseases that could affect ocular alignment, such as thyroid ophthalmopathy, myasthenia gravis, internuclear ophthalmoplegia, high-grade (pathologic) myopia (>6 diopters), amblyopia, or paralytic strabismus. Wider extraocular muscles were excluded because their edges were easily blocked by the eyelids. This study was not conducted in a masked manner.

All participants provided informed consent before participation. The study protocol adhered to the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of our hospital.

Preoperative AS-OCT measurement method.

Each patient underwent AS-OCT measurements in both eyes using a CASIA2 OCT system (Tomey, Nagoya, Japan), and MR and LR images were obtained. To minimize positional changes in the head during examination, the patient's head was centrally positioned in a

chin rest device in alignment with the horizontal angle of the camera. The chin and forehead were firmly fixed to the device. The head position was confirmed, and tilting was avoided by verifying that the horizontal head axis (an imaginary line connecting both ears) was parallel to the horizontal border of the AS-OCT table [14]. During the measurement, patients were instructed to gaze at the tip of their index finger, which was positioned along the horizontal meridian of the eye to maximize the lateral gaze during MR or LR scanning. The examiner then adjusted the fingertip position, and the patient was instructed to gaze laterally as much as possible. The patients were asked to turn their right and left eyes horizontally toward their ears and nose, respectively. Using the stereoscopic imaging function of the CASIA2 OCT, a series of 256 consecutive MR and LR tomographic images were captured. These images covered a range of 12 mm from the corneal limbus toward the target rectus muscle and spanned a width of 16 mm. Subsequently, we applied a fluttering technique based on the conjunctival surface of the tomographic images using the CASIA2 built-in software and constructed en face MR and LR images (Fig. 1).

Analysis of en face images. Images that were unclear or in which the muscle edges were obscured by the eyelids were excluded from the analysis. The following measurements were made using ImageJ software (version 1.52a; Wayne Rasband, National Institutes of Health, MD, USA): i) the minimum distance from point (A), which is on an arc indicating the corneal angle, to the center (I) of the insertion site of the extraocular muscle (anterior chamber angle to extraocular muscle insertion distance [AID]); ii) the muscle width at the insertion sites; and iii) the muscle fiber angles (defined as a horizontal angle of 0° , internal rotation as positive, and external rotation as negative) (Fig. 2). Point (A) was the same as the rim of the anterior chamber angle reported by Shibata *et al.* [13].

Statistical analysis. The AID, muscle widths, and muscle fiber angles of MR and LR were compared between the XT and control groups. In this study, we used data from both eyes of each participant. To account for the potential correlation between measurements from the right and left eyes, Generalized Estimating Equations (GEE) were used for statistical analysis. We conducted a comparative study to evaluate intergroup differences in AID, muscle width, and muscle fiber angle of the MR and LR, considering the eye

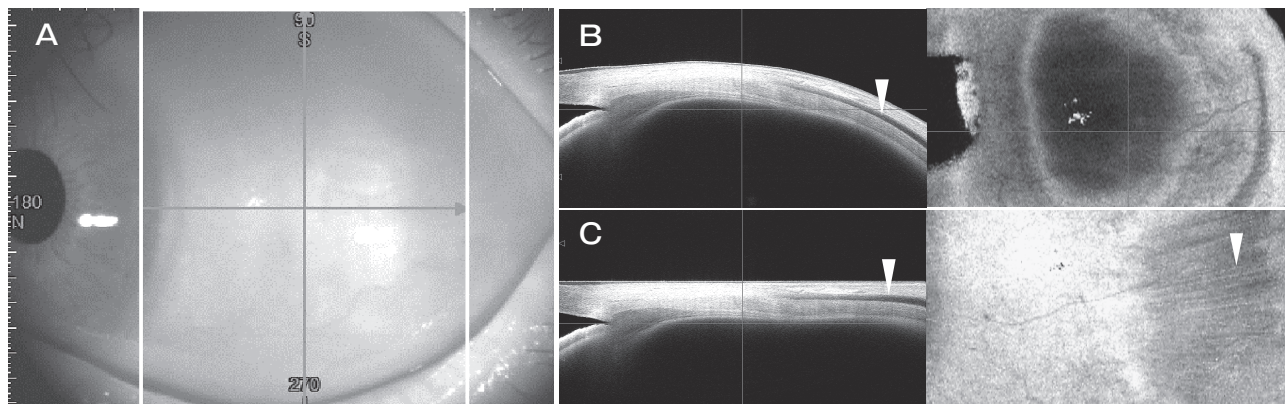


Fig. 1 Analysis of en face images using anterior segment optical coherence tomography (AS-OCT). **A**, Anterior segment images rendered using AS-OCT; **B**, Before the fluttering technique (left: tomographic image; right: en face images parallel to the frontal plane constructed from tomographic images); **C**, After fluttering (left: image based on the conjunctival surface; right: en face image showing an outlined lateral rectus [LR]). White arrowhead: LR.

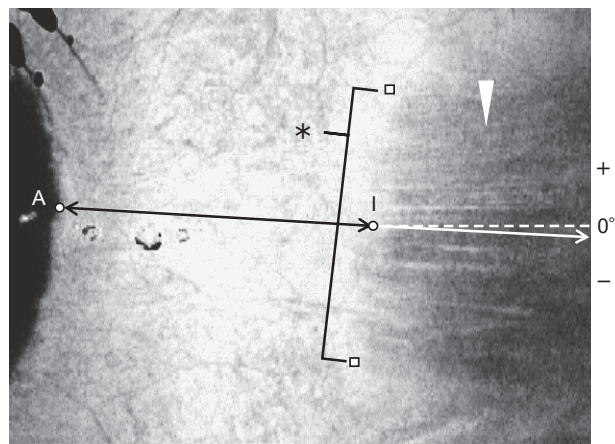


Fig. 2 Area to be measured in en face images. Point A: located on an arc indicating the corneal angle, at the minimum distance from point I. Black double-ended arrows from point A to midpoint I of the muscle width: anterior chamber angle to the extraocular muscle insertion distance (AID). Square: superior and inferior margins of the muscle insertion site. Asterisk: muscle width. White arrow: muscle fiber angle. Horizontal dashed line: 0° angle. +: Internal rotation. -: External rotation. White arrowhead: lateral rectus.

(right and left) as a within-subject factor. In the subsequent analysis, GEE was applied to evaluate the correlations between age and angle of deviation as covariates and the outcome variables, which included AID, muscle width, and muscle fiber angle of the MR and LR. The analyses were conducted using IBM SPSS Statistics for Windows (version 22.0; IBM Corp., Armonk, NY,

USA). Statistical significance was set at $p < 0.05$. Descriptive statistics are reported as mean $\pm$ standard deviation.

Ethics statement. All participants provided informed consent before participation. The study protocol adhered to the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Okayama University Hospital (K1901-006).

Results

The clinical parameters of the XT and control groups are summarized in Table 1. The mean age was 13.2 ± 4.1 years (range: 6-24) in the XT group and 17.6 ± 7.2 years (range: 8-30) in the control group, with male/female distributions of 7/17 and 14/11, respectively. The mean deviation in the XT group was 17.8 ± 6.7 angle degrees (range: 9.6-38.1). Patient age was significantly lower in the XT group than the control group ($p = 0.008$). The mean equivalent spherical values were -1.1 ± 1.7 D (range: -5.00 to $+1.25$) in the XT group and -1.4 ± 3.2 D (range: -5.50 to $+8.50$) in the control group, with no significant difference ($p = 0.741$). We evaluated 21 MRs and 45 LRs in the XT group and 23 MRs and 45 LRs in the control group. We then used multiple regression analysis to estimate the correlation between the XT and control groups. The image analysis parameters for the XT and control groups are listed in Table 2.

The mean AID of MR was 5.2 ± 1.0 mm (range: 3.2-7.0) in the XT group and 5.8 ± 1.0 mm (range: 3.6-7.5)

in the control group ($p=0.053$). The mean AID of LR was 5.7 ± 0.7 mm (range: 4.2-7.2) in the XT group and 5.7 ± 0.7 mm (range: 4.2-7.4) in the control group, with no significant difference ($p=0.913$). The widths of MR and LR were 8.6 ± 1.2 mm and 6.3 ± 1.1 mm in the XT group and 8.5 ± 1.2 mm and 6.2 ± 0.9 mm in the control group, respectively; neither width was significantly different between groups ($p=0.894$ for MR and $p=0.636$ for LR). The mean muscle fiber angle in the LR was $1.6 \pm 6.3^\circ$ (range: -11.6 to 19.3) in the XT group and $-1.4 \pm 4.0^\circ$ (range: -12.3 to 8.2) in the control group ($p=0.014$) (Fig. 3). The XT group exhibited a significantly greater inward rotation of the LR muscle fiber angle compared to the control group. No significant difference between groups was observed for the MR muscle fiber angle (-1.6 ± 5.3 and 0.4 ± 6.3 , respectively, $p=0.297$).

Next, we examined the correlations between these factors and age or angle of deviation within the XT group (Table 3). No significant correlation was observed

between age and AID for either MR or LR ($p=0.107$ and $p=0.708$, respectively). Moreover, no significant correlations were found between age and muscle width ($p=0.703$ for MR; $p=0.960$ for LR) or between age and muscle fiber angles ($p=0.577$ for MR; $p=0.102$ for LR). However, the width of the LR muscle was significantly positively correlated with the angle of deviation ($p=0.002$). For MR, no significant correlation was observed between the angle of deviation and the muscle width ($p=0.730$). Furthermore, no significant correlation was observed between the angle of deviation and the AID or muscle fiber angles for either MR or LR (MR: $p=0.228$ and $p=0.055$, LR: $p=0.177$ and $p=0.320$, respectively).

Discussion

In this study, the LR angle exhibited significantly greater inward rotation in the XT group than in the control group. Our results may demonstrate structural abnormalities of the LR in patients with XT. For example, sagging eye syndrome causes inferior displacement of the LR pulley with progressive elongation and rupture of the LR-superior rectus band ligament, leading to external rotation of the eye [15]. Disorders in the stability of the pulley can lead to strabismus. In the XT group, the LR was lifted upward against gravity,

Table 1 Comparison of clinical parameters between the XT and control groups

	Control	XT	P-value
Age (years)	17.6 ± 7.2	13.2 ± 4.1	0.008*
Angle of deviation ($^\circ$)	NA	17.8 ± 6.7	NA
Equivalent spherical value (diopter)	-1.4 ± 3.2	-1.1 ± 1.7	0.741

AID, anterior chamber angle to extraocular muscle insertion distance; LR, lateral rectus muscle; MR, medial rectus muscle; XT, exotropia. Values are presented as mean $\pm$ standard deviation.

* $p < 0.05$, determined by Generalized Estimating Equations.

Table 2 Comparison of image analysis parameters between the XT and control groups

		Control	XT	P-value
AID (mm)	MR	5.8 ± 1.0	5.2 ± 1.0	0.053
	LR	5.7 ± 0.7	5.7 ± 0.7	0.913
Muscle width (mm)	MR	8.5 ± 1.2	8.6 ± 1.2	0.894
	LR	6.2 ± 0.9	6.3 ± 1.1	0.636
Muscle fiber angle ($^\circ$)	MR	0.4 ± 6.3	-1.6 ± 5.3	0.297
	LR	-1.4 ± 4.0	1.6 ± 6.3	0.014*

AID, anterior chamber angle to extraocular muscle insertion distance; LR, lateral rectus muscle; MR, medial rectus muscle; XT, exotropia. Values are presented as mean $\pm$ standard deviation.

* $p < 0.05$, determined by Generalized Estimating Equations.

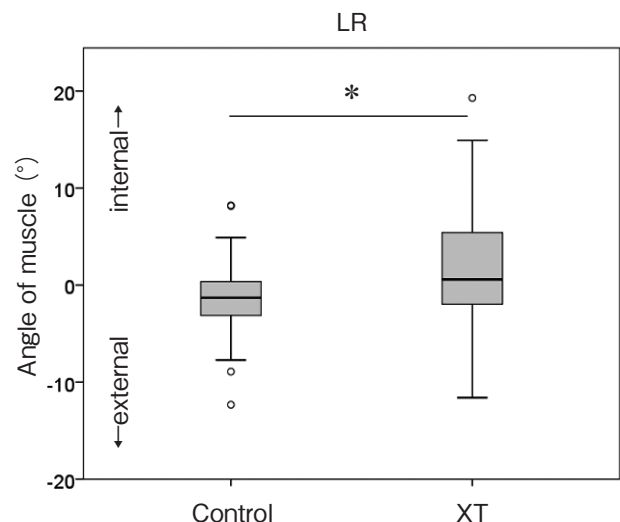


Fig. 3 Comparison of muscle fiber angles between the XT and control groups. The box-and-whisker plot shows the minimum value, first quartile, median, third quartile, and maximum value. White circle: outlier. * $p < 0.05$. LR, lateral rectus; XT, exotropia.

Table 3 Correlations with age or angle of deviation

		Age		Angle of deviation	
		Correlation coefficient	P-value	Correlation coefficient	P-value
AID	MR	0.068	0.107	-0.066	0.228
	LR	-0.013	0.708	-0.018	0.177
Muscle width	MR	0.022	0.703	0.026	0.730
	LR	0.002	0.960	0.073	0.002*
Muscle fiber angle	MR	0.302	0.577	0.324	0.055
	LR	0.538	0.102	-0.137	0.320

AID, anterior chamber angle to extraocular muscle insertion distance; LR, lateral rectus muscle; MR, medial rectus muscle.

* $p < 0.05$, determined by Generalized Estimating Equations.

increasing muscle tension and possibly causing medial rotation; however, further investigations will be needed to confirm this mechanism. In addition, when measuring LR, the eyes are turned inward, and they may turn inward more easily in patients with XT.

We expected that a longer AID of the MR would be associated with XT. However, no significant differences were observed between the two groups in this study. Shibata *et al.* investigated the correlations between the AID of the MR and age in healthy participants and found that the AID of the MR lengthens between the ages of 8 and 36.3 years [13]. In this study, no correlation was observed between the AID of the MR and age between 6 and 16 years in patients with XT, suggesting that the AID does not extend over time in these patients. Shibata *et al.* also reported that the AID was elongated in MR and shortened in LR as the axial length was elongated in healthy participants. In this study, the almost equal AID of MR and LR in healthy participants was likely due to the difference in axial length, but no correlation was found between the AID and equivalent spherical values of MR and LR. These discrepancies might be related to the limited number of patients.

Factors affecting the angle of deviation in patients with XT include visual acuity, accommodative convergence, refractive errors, and axial length [16-19]. Niyaz *et al.* reported that the width of the LR is not correlated with the angle of deviation in XT [5]. However, in this study we found that wider LR values were correlated with greater angles of deviation, suggesting that the LR width contributes to the angle of deviation in XT. Although there was no significant difference in muscle width between the XT and control groups, it is possible that the structural abnormalities of

LR, including with respect to the pulley, led to differences in the angle of deviation.

This study has some limitations. Both groups had a small number of patients and a narrow age range. In addition, both eyes were used for the sample, and eyes with wider extraocular muscles were excluded. The AID and muscle width were measured to be shorter than the actual distances on the spherical surface because of flattening of the eyeball's spherical surface during measurement. Finally, the evaluation was based on an equivalent spherical value, instead of the axial length.

In conclusion, shape analysis of the extraocular muscles in patients with XT and healthy participants using AS-OCT en face images revealed statistically significant differences in the muscle fiber angle of the LR between the XT and control groups. Moreover, the width of the LR was significantly correlated with the angle of deviation. Our findings will contribute to a deeper understanding of the characteristics of the extraocular muscles in patients with XT.

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