Quantitative Analysis of Translatory Movements in Patients With Horizontal Strabismus

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PURPOSE. To investigate translatory movement during the lateral gaze in patients with horizontal strabismus using magnetic resonance imaging.

METHODS. Patients with esotropia or exotropia and normal controls underwent orbital magnetic resonance imaging during the central gaze and lateral gaze at 40°. The position of the static tissues was superimposed three-dimensionally for all gazes using a self-developed software, allowing the analysis of the net eyeball movement. Then, the eyeball centroid coordinates were extracted for each gaze, and the distance and direction of centroid movement from the central to lateral gaze were calculated.

RESULTS. The mean distance ± standard deviation of the centroid movement was 1.0 ± 0.5 mm during abduction in the exotropia group, which was significantly longer than that in the esotropia (0.6 ± 0.3 mm; $P = 0.003$) and control (0.7 ± 0.2 mm; $P = 0.002$) groups. Conversely, the centroid moved farther in the esotropia group (0.9 ± 0.3 mm) than the exotropia (0.6 ± 0.3 mm; $P = 0.005$) and control (0.7 ± 0.2 mm; $P = 0.023$) groups during adduction. Posterior translation during abduction was longer in the exotropia group (−0.8 ± 0.3 mm) compared with the esotropia (−0.5 ± 0.3 mm; $P = 0.017$) and control (−0.4 ± 0.3 mm; $P = 0.001$) groups, whereas that during adduction was longer in the esotropia group (−0.4 ± 0.4 mm) than the exotropia (−0.1 ± 0.2 mm; $P = 0.033$) and control (−0.1 ± 0.2 mm; $P = 0.026$) groups.

CONCLUSIONS. During abduction, more translatory movement occurred in the exotropia group, whereas the centroid moved farther in the esotropia group during adduction. The translatory movement difference between both strabismus groups implies that there is a difference in biomechanics among the types of strabismus.

Keywords: translatory movement, translation, eyeball movement, three-dimensional magnetic resonance imaging, exotropia, esotropia

Magnetic resonance imaging (MRI) is one of the objective methods used for the analysis of eye movements, and recent technical advancements in MRI have enabled the noninvasive and in-depth study of eye movements in living subjects. Previously, several studies on translatory eye movement have been performed using high-resolution MRI.[1–3] Although the major eye movement is rotation, translation, the positional change of the eyeball itself, can occur within orbit during rotation, which indicates that the globes do not rotate about their geographic center. Furthermore, this eccentricity of the rotation axis induces a difference in the lever arm of the extraocular muscles during horizontal gazes, resulting in a change in the torques of the extraocular muscles. Therefore, the analysis of translation can help in understanding the physiology of eye movements and the biomechanics of strabismus.[4,5] It can also contribute to the development of eye-gaze tracking technologies.

We conducted studies in the past to investigate and characterize the translatory movements during horizontal and vertical gazing in normal individuals using three-dimensional (3D) MRI.[6,7] However, these studies involved healthy individuals, and we cannot directly apply their results to patients with strabismus. Therefore, in this study, we aimed to investigate the positional changes of the eyeball during the horizontal gaze in patients with horizontal strabismus and compare eye movements between patients with esotropia and exotropia.

METHODS

This study was approved by the Institutional Review Board of Hanyang University Hospital and followed the tenets of the Declaration of Helsinki for biomedical research. The study was fully explained to all participants, and informed consent was obtained prior to their inclusion in the study. We obtained consent from the parents or guardians of patients aged less than 18 years.

Study Subjects

We prospectively studied patients with esotropia ($n = 16$) or exotropia ($n = 29$) between July 2016 and December 2020. The exclusion criteria were as follows: (1) previous strabismus or intraocular surgery, (2) significant ocular disease affecting visual acuity, (3) a history of systemic or neurologic disorders affecting eye movement, and (4) significant A- or V-pattern exotropia. A comprehensive ophthalmologic examination, including best-corrected visual acuity measurement, tonometry, refraction testing, slit-lamp examination, funduscopic examination, prism and alternate cover test, and ocular motility testing, was performed in all patients. Additionally, data from normal controls ($n = 16$) were obtained to compare the translatory movement in patients with strabismus to those in normal subjects.

Magnetic Resonance Image Acquisition

MRI acquisition and 3D processing procedures were performed as described in our previous study.[7] In brief, each participant underwent high-resolution, T2-weighted orbital MRI (repetition time = 2500 ms; echo time = 248 ms; flip angle = 90°; section thickness = 0.6 mm; field of view = 180 × 180 mm; matrix = 256 × 256; and voxel size = 0.7 × 0.7 × 0.6) using a 3.0 T whole-body scanner (Achieva 3.0T; Philips Medical Systems, Best, the Netherlands) with a 32-channel head coil. Their heads were stabilized, and they gazed at targets through an opening in the head coil mask above their eyes. The diameter of the bore was 60 cm, and fixation targets were placed inside the scanner bore. The target for central gaze was positioned in the exact midline of the scanner bore, and the participant's head was aligned in the midline of the bed. Fixation targets for assessing horizontal eye movement were positioned at a 40° angle of the gaze. Before each scan, we confirmed that the positions of the participant's head and targets were appropriate in every case.

Scanning for normal controls was performed when the participants were looking at the target for the central, right, and left gaze, providing three MR imaging sets. Meanwhile, during the scanning for the patients with strabismus, one eye that was not fixated on a target was occluded with a thin patch to secure the monofixation and manifest deviation in each scan. Scanning was repeated when patients were looking at the appropriate fixation target for each gaze—central/left gaze with left eye fixation and central/right gaze with right eye fixation. Finally, four MR imaging sets were obtained for each patient with strabismus.

First, a low-resolution triplanar scan was performed to determine the localization of subsequent imaging. Then, sets of 67 contiguous, 0.6-mm-thick quasitransverse images were obtained, occupying a 40.2-mm field of view. For all orbital MRI scans in this study, the same imaging design, quasitransverse imaging planes, fixation targets, and gaze directions were used.

Three-Dimensional MRI Processing Procedures

Acquired digital MR images were converted into a DICOM file format and processed using custom analysis programs written in Visual C++ using Visual Studio Community software (Version 2015; Microsoft, Redmond, WA). All MR images were reconstructed three-dimensionally and superimposed based on the position of the static tissues, such as the brain and skull, to evaluate the net movement of the eyeball. It should be noted that the MR images become left–right inverted compared with the original MR images after the processing procedure. Two authors (Y. M. and H. W. L.) independently checked all MR images to see whether any structures other than the eyeball showed movement among the images in each gaze.

Image Analysis

To evaluate the translatory movement, we used the eyeball "centroid." The eyeball centroid is the arithmetic mean position of all the points in the eyeball on the axial MR image; therefore, the centroid represents the eyeball position unless the shape of the eye changes. The extraction procedure of the centroid coordinate using ImageJ (National Institutes of Health, Bethesda, MD) was also described in our previous article.[7] All procedures were automatically conducted, yielding x and y coordinates in the axial plane (X–Y plane) images, which had the largest cross section of the eyeball. The x-axis indicated the mediolateral axis, and the y-axis represented the anteroposterior axis. We investigated the change in the x and y coordinates of the centroid during lateral gaze to analyze mediolateral and anteroposterior movement, separately. In the horizontal gaze, adduction or abduction of the right and left eyes was symmetric about the y-axis. Thus, the x coordinate shift of the centroid measured in the right eye was multiplied by -1 to match the left eye measurement.

We calculated the distance and direction of the centroid movement between the central and lateral gazes. In the image analysis of the patients with strabismus, the MR image in central gaze with the left eye fixation was used as a reference image for positional changes in the left eye. Then, we compared the MR image in the left gaze to the reference image for abduction, and that in the right gaze for adduction. Similarly, for positional change in the right eye, the MR image in the central gaze with the right eye fixation was used as a reference image. Then, we compared the MR image in the right gaze with the reference image for abduction and that in the left gaze for adduction. Thus, it should be noted that the contralateral eye was fixated during adduction (Fig. 1).

The distance of the centroid movement was calculated using a distance formula, and the movement direction of the centroid was calculated using an arctangent formula, yielding angles in degree units, as follows:

$$\text{Distance formula d (mm)} = \sqrt{(x2 - x1)^2 + \left(y2 - y1\right)^2}$$

$$\text{Arc} - \text{tangent formula } \theta\ (^\circ) \frac{\tan^{-1}\{(y2-y1)/(x2-x1)\}}{\pi} \times 180$$

where d is the distance between centroid positions in central and horizontal gaze, θ is the angle of the direction of movement of the centroid from central to horizontal gaze, $x1$ and $y1$ are the x and y coordinates of the centroid position in the central gaze, and $x2$ and $y2$ are the x and y coordinates of the centroid position in the lateral gaze.

In the horizontal gaze, adduction or abduction of the right and left eyes was symmetrical about the y-axis. Thus, the x

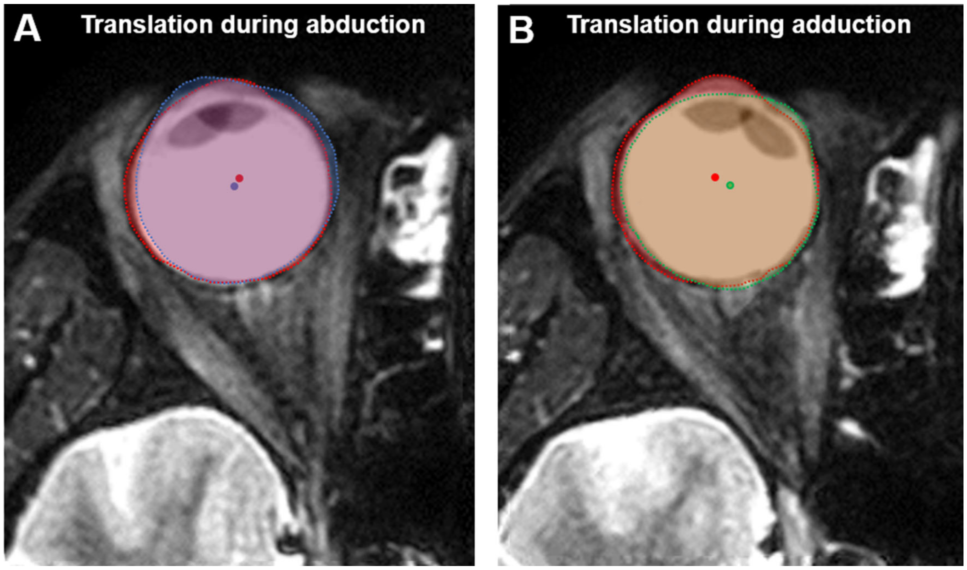


Figure 1. Extraction and evaluation of the centroid movement of the eyeball. After MR image processing, the MR images become right–left inverted compared with the original MR images. (**A**) The extracted outline of the left eyeball is marked with a *red dotted line* and the centroid of the left eye with a *red dot* in the central gaze. The eyeball outline is marked with *blue dotted lines* and the centroid with a *blue dot* in the left gaze. The superimposed image, which is adjusted based on the positions of static tissues, shows the difference in centroid position between two MR images. (**B**) The extracted outline of the left eyeball is marked with a green dotted line and the centroid with a green dot in right gaze.

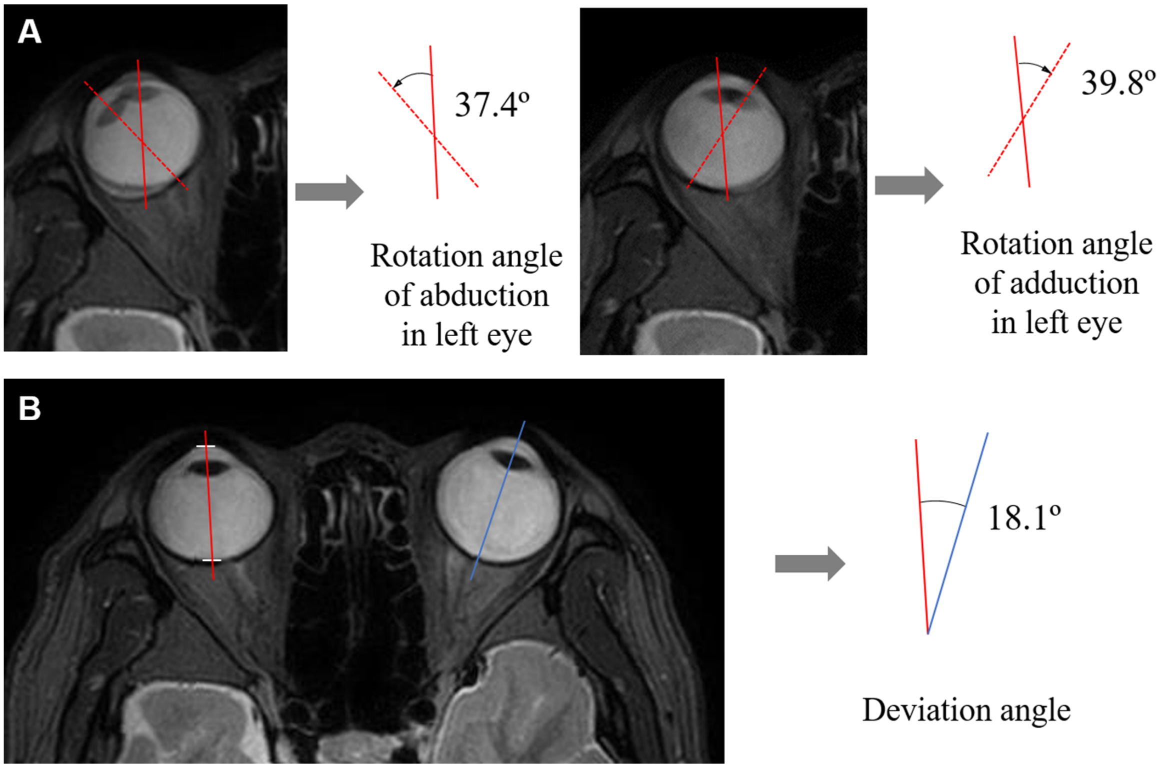


Figure 2. Various measurements in MR images. (**A**) In the superimposed MR image, the visual axes of the left eye are marked with red lines; the solid lines indicate the visual axes in the central gaze, and the dotted lines indicate the visual axis in lateral gazes. The visual axis was defined as a perpendicular line to the lens connecting the corneal vertex and fovea. The angle between two visual axes is the rotation angle of abduction (up) and adduction (down). (**B**) Deviation angle is the angle between visual axes of both eyes (the *red line* in the fixating eye and the *blue line* in the deviating eye) in MR images in which the study eye (left eye in this case) is fixated at the central target. The axial length was also measured as the distance between two short white lines, which indicate the corneal vertex and the fovea on the visual axis when the eye was fixated at the central target.

coordinate shift of the centroid measured in the right eye ($x2 - x1$) was multiplied by -1 and used in the arc-tangent formula to match the left eye measurement. Finally, all analyses were based on the left eye's orientation and medial was defined as 0°, anterior as 90°, lateral as 180°, and posterior as 270° counterclockwise in the axial plane.

In this study, the rotation angle during abduction or adduction was measured using axial MR images. First, the visual axis of each eye was defined as the line perpendicular to the lens connecting the corneal vertex and the fovea. The rotation angle was measured as the angle between the visual axis of the eye in the central gaze and that in the lateral gaze. Similar to the measurement of the centroid, for the measurement of rotation angle in the left eye, the MR image in the central gaze with the left eye fixation was used as a reference image. Then, we compared the MR image in the left gaze with the reference image for abduction and that in the right gaze for adduction. Similarly, for the rotation angle in the right eye, the MR image in the central gaze with the right eye fixation was used as a reference image. Then, we compared the MR image in the right gaze to the reference image for abduction, and that in the left gaze for adduction. When the actual rotation angle was less than 15°, the data on translation from the eye were excluded for the final analysis. We also measured the deviation angle of strabismus as the angle between the visual axes of both eyes in MR images, which were acquired as the study eye fixated on the central target. The axial length was defined as the length between the corneal vertex and the fovea on the visual axis, and it was measured on the MR image obtained when the eye gazed at the central target (Fig. 2).

Statistical Analyses

One eye from each participant was randomly selected for the statistical analysis. SPSS (version 23.0; SPSS Inc., Chicago, IL) was used for all analyses. The Kruskal–Wallis H test, Mann–Whitney *U* test, χ^2 test, and Fisher's exact test were used for comparisons among the three groups. Statistical significance was set at a *P* value of 0.05 or less. All data are presented as mean ± standard deviation.

RESULTS

The baseline demographics and clinical information of the participants are summarized in Table 1. The deviation angle was significantly larger in the exotropia group than in the esotropia group. The rotation angle of abduction during the horizontal gaze showed no significant differences among the three groups. However, the participants only fixated on the left target with their left eye and the right target with their right eye with the other eye occluded. Hence, the rotation of the eye for adduction did not correspond to the actual target displacement, resulting in smaller adduction in the exotropia group compared with the other two groups (35.2 ± 7.5° in the esotropia group, 26.4 ± 12.7° in the exotropia group, and 36.0 ± 8.3° in the control group; $P = 0.011$).

The distance and direction of centroid movements according to horizontal eye movement in the three groups are presented in Figure 3. In the Mann–Whitney *U* test, the mean distance of centroid movement during abduction was longer in the exotropia group than in the esotropia and control groups ($P = 0.003$ and $P = 0.002$, respectively). Conversely, the centroid moved farther in the esotropia group than the exotropia and control groups during adduction ($P = 0.005$ and $P = 0.023$, respectively). However, it should be noted that the rotation angle of adduction was smaller in the exotropia group.

We separately analyzed the mediolateral and anteroposterior movements according to the rotation angle (Fig. 4 and Table 2). During abduction, the centroid of the esotropia group moved less laterally compared with the exotropia and control groups, however the difference in mediolateral movement between the esotropia and control groups did not reach statistical significance. The centroid moved more posteriorly in the exotropia than in the esotropia and control groups ($P = 0.017$ and $P = 0.001$, respectively).

For the analysis of the centroid movement during adduction, we selected subjects whose adduction angle was between 25° and 45° to match the amount of rotation (14 eyes in the esotropia group, 15 eyes in the exotropia group, and 10 eyes in the control group). There were no significant differences in mediolateral movement among the three groups. However, the esotropia group showed longer posterior translation compared with the exotropia and control groups ($P = 0.033$ and $P = 0.026$, respectively).

DISCUSSION

In this study, we investigated the translatory movement during lateral gaze in patients with horizontal strabismus using the coordinates of the centroid of the eyeball in 3D reconstructed MR images. Our study showed different patterns of positional change of the eyeball during horizontal movement in the esotropia and exotropia groups. In patients with horizontal strabismus, the translatory move-

TABLE 1. Baseline Demographic and Clinical Characteristics of the Study Population

	Esotropia Group ($n = 16$)	Exotropia Group ($n = 29$)	Control Group ($n = 16$)	*P* Value
Age (years)	31.3 ± 16.4	33.4 ± 18.2	32.0 ± 7.6	0.791
Sex (M : F)*	10 : 6	17 : 12	10 : 6	0.953
Right eye : left eye	8 : 8	12 : 17	9 : 7	0.617
Axial length (mm)	25.4 ± 1.3	24.8 ± 1.3	25.3 ± 1.4	0.164
Angle of deviation at distance (PD)	36.6 ± 12.1	48.1 ± 15.6	N/A	**0.005**
Angle of deviation at near (PD)	38.1 ± 14.1	46.9 ± 15.2	N/A	**0.049**
Angle of deviation in MR image (°)	15.7 ± 8.7	22.0 ± 8.7	N/A	**0.018**
Rotation angle of abduction (°)	38.3 ± 6.1	37.9 ± 9.7	37.1 ± 6.4	0.769
Rotation angle of adduction (°)	35.2 ± 7.5	26.4 ± 12.7	36.0 ± 8.3	**0.011**

* Values are presented as the ratio of the number of patients.
Numbers in bold indicate statistically significant differences.
F, female; D, diopter; M, male.

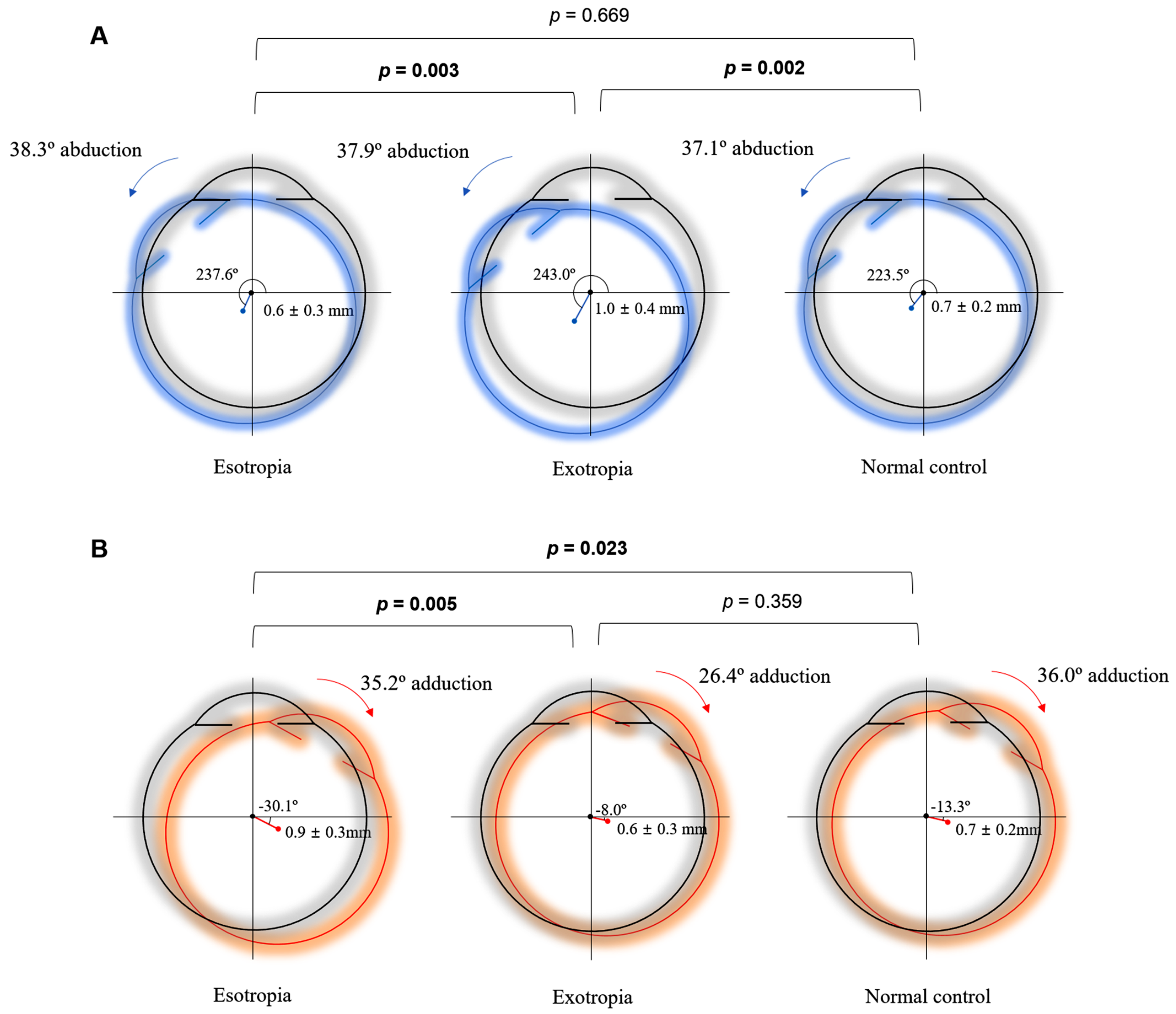


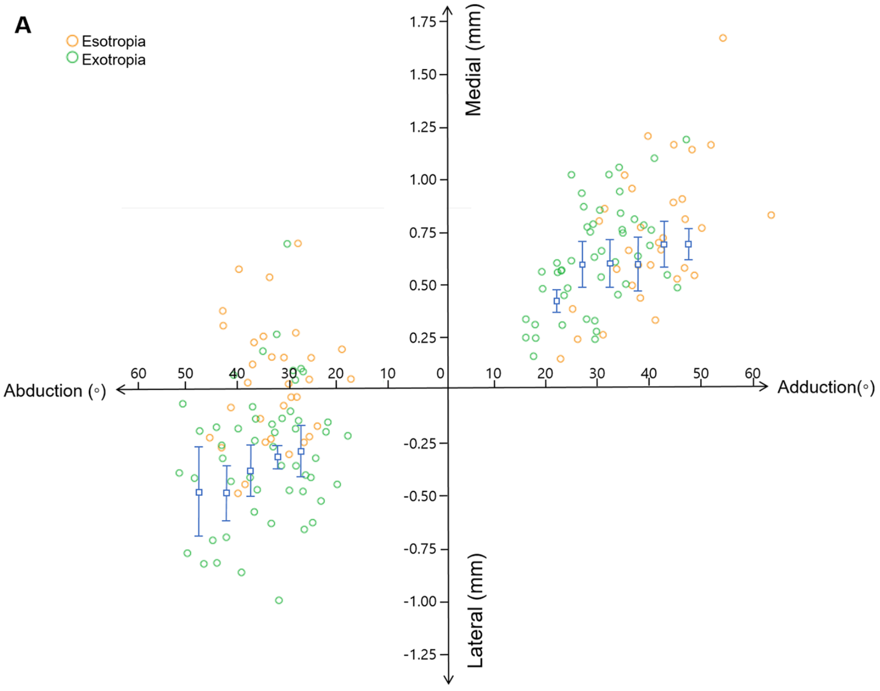
FIGURE 3. Centroid movement of three groups during (**A**) abduction and (**B**) adduction. Origin on the graph indicates the position of the centroid in the central gaze.

ment is more marked when the eye turns in the direction of horizontal deviation. During abduction, the centroid moved more posterior in the exotropia group than in the esotropia and control groups. The centroid moved farther in the posterior direction in the esotropia group during adduction compared with that in the exotropia and control groups. In contrast, healthy individuals showed a similar distance of centroid movement during abduction and adduction as reported in our previous study.[7]

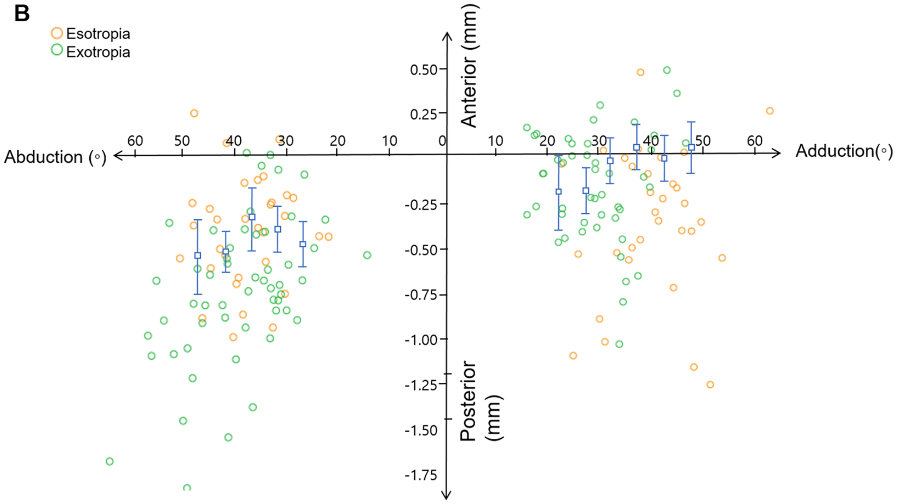
Eye movements consist of rotation and translation, which implies that the centroid of the eyeball cannot be the axis of rotation. Any eccentricity of the rotation axis would change the relative lever arm lengths for the rectus muscles. During abduction, the eccentricity of the rotation axis would shorten the lateral rectus lever arm while lengthening the medial rectus lever arm. In contrast, during adduction, the eccentricity of the rotation axis shortens the medial rectus lever arm and lengthens the lateral rectus lever arm.[3] This change would be large in the exotropia group during abduction and in the esotropia group during adduction, inducing an imbalance between the agonist and the antagonist of horizontal gaze. The cause of the change in the eccentricity of the rotation axis may be due to nervous or muscular factors, or both. Regardless, the change in eccentricity would be associated with the pathogenesis of comitant horizontal strabismus. Further study of eccentric rotation in strabismus patients may help to understand the ocular mechanics in strabismus.

The mechanism of the translatory movement is not understood fully. One of the candidate actuators for translation is the orbital layers of the rectus muscle, and the other is the smooth muscle present in the pulley suspensions.[8,9] A previous study reported a difference in the location of the pulley of the medial rectus muscle between esotropia and exotropia under general anesthesia.[10] The smooth muscles around the pulley receive rich innervation, suggesting complex excitatory and inhibitory control.[11] Considering the dynamic role of the pulley in ocular motility, it likely contributes to horizontal strabismus, at least partially, and induces a change in translatory movement.

In addition to this active force, structural factors should also be considered. Unfortunately, we were not able to obtain data regarding the duration of the disease in all participants. However, some reported having strabismus for more than 10 years. The long-standing eccentric deviation



Movement of x coordinate according to rotation angle



Movement of y coordinate according to rotation angle

Figure 4. The plots showing (**A**) the mediolateral and (**B**) the anteroposterior translation according to the rotation angle during horizontal gazes. In these plots, total data from both eyes of 16 patients with esotropia, 29 patients of exotropia, and 16 normal controls are presented. The origin on the graph indicates the position of the centroid in the central gaze and blue error bar indicates mean ± standard error of translation in normal controls.

of the eyeball, by itself, causes structural changes in the extraocular muscles and soft tissues of the orbit.[12] The material properties of the extraocular muscles and other soft tissues affect the amount of translatory movement because the eye is suspended with the extraocular muscles in the orbit surrounded by soft tissues.

Recently, eye-tracking systems have become easier to integrate into research and clinical practice. However, most eye tracking techniques assume that the eye only has rotational movement, which induces intrinsic errors because real eye movement is composed of both rotation and translation.[13–15] Furthermore, patients with horizontal strabismus show asymmetric translation during horizontal eye movement. Therefore, errors could be exacerbated when using eye-tracking systems to evaluate eye movements in patients with strabismus. Although translation comprises a smaller portion than rotation, it should be addressed, especially for eye movement evaluation in patients with strabismus.

This study had several limitations. First, we only included patients who were able to undergo MRI, and only five patients were children less than 15 years of age. Thus, selection bias should be considered when interpreting our results. Second, we evaluated the eye movements in a fixed experimental setting. The subjects only fixated on the left target

Table 2. Distance of the Centroid Movement According to the Horizontal Eye Movement (Mean ± Standard Deviation)

				***P* Value**[†]		
	Esotropia (E)	**Exotropia (X)**	**Control (C)**	**E vs X**	**E vs C**	**X vs C**
During abduction						
Mediolateral movement (mm)	−0.2 ± 0.3	−0.5 ± 0.4	−0.4 ± 0.3	**0.024**	0.067	0.740
Anteroposterior movement (mm)	−0.5 ± 0.3	−0.8 ± 0.3	−0.4 ± 0.3	**0.017**	0.724	**0.001**
During adduction[*]						
Mediolateral movement (mm)	0.7 ± 0.2	0.6 ± 0.2	0.6 ± 0.2	0.310	0.259	0.892
Anteroposterior movement (mm)	−0.4 ± 0.4	−0.1 ± 0.2	−0.1 ± 0.2	**0.033**	**0.026**	0.807

[*] The subjects whose adduction angle was between 25° and 45° were included in this analysis (14 eyes in the esotropia group, 15 eyes in the exotropia group, and 10 eyes in the control group).

[†] *P* value obtained from Mann–Whitney *U* test.

Medial and anterior movements are positive.

Numbers in bold indicate statistically significant differences.

with their left eye and the right target with their right eye, with the other eye occluded. Hence, the rotation of the eye for adduction did not correspond to the actual target displacement, resulting in smaller adduction in the exotropia group and larger adduction in the esotropia group. The eye movements in this study were also limited to the conjugate version, and vergence, such as convergence and divergence, was not evaluated in this study. Third, the individual subject parameters, such as pupillary distance and head diameter, were not considered fully in this experimental setting. Although the real rotation angle was not exactly 40° owing to various individual properties, the three groups had no significant difference in rotation angles. Therefore, the error induced by the individual properties might not have had significant effects on the results. Finally, owing to the small sample size in each group, we were not able to analyze the associated factors other than the type of strabismus. Further studies with larger sample sizes are needed to identify the clinical factors associated with translatory movement. Despite these limitations, to our knowledge based on the PubMed (Medline) databases search for "strabismus" and "translation," this study is the first to evaluating eye movements in patients with strabismus that focused on translation. This study was able to assess physiological eye movement using 3D reconstructed MRI, which was one of the strengths of this study.

In conclusion, translatory movement was more prominent when the eye was rotated in the direction of horizontal deviation in patients with horizontal strabismus. The evaluation of translatory movement may help to better understand the eye movements and biokinetics of strabismus.

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