Local Deformation of Extraocular Muscles during Eye Movement

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PURPOSE. To study extraocular muscle (EOM) function, the local physiologic contraction and elongation (deformation) along human horizontal EOMs were quantified by using motion-encoded magnetic resonance imaging (MRI).

METHODS. Eleven subjects (healthy right eye) gazed at a target that moved horizontally in a sinusoidal fashion (period, 2 seconds; amplitude, ±20°), during MRI with an optimized protocol. In addition, EOM longitudinal deformation in two patients with Duane’s syndrome type I was analyzed. The horizontal EOMs and the optic nerve were tracked through 15 time frames, and their local deformation was calculated. Eight segments were separated along the EOMs and left-to-right and right-to-left eye movements were compared.

RESULTS. In healthy subjects, the maximum EOM deformation was situated at approximately two thirds of the muscle lengths from the scleral insertions. The EOM deformations were similar for the entire movement range as well as in both movement directions. In the two patients with Duane’s syndrome type I, the abnormal innervation of lateral rectus muscle affected specific EOM segments only. The posterior muscle segments contracted and the anterior muscle segments relaxed during adduction.

CONCLUSIONS. Motion-encoded MRI is a useful technique for advancing the understanding of the physiology and pathophysiology of EOMs in humans during eye movement. (Invest Ophthal Vis Sci. 2009;50:5189–5196) DOI:10.1167/iovs.08-3182

To better understand the etiologies of ocular misalignment, the mechanics of the human orbit, especially those of the extraocular muscles (EOMs), have been extensively studied. The anatomy of the complex system of orbital connective tissues, which was carefully investigated by Koornneef, has also been described by means of magnetic resonance imaging (MRI) coronal sections. Different eye positions have been imaged by computed tomography, x-ray, and MRI. Miller showed that the path of the rectus muscles is stable relative to the orbit during different gaze directions. Other MRI studies documented EOM atrophy as a consequence of cranial nerve palsies. Also, EOM tissue borders have been observed by using MRI. Gold beads were implanted inside monkey orbits to demonstrate orbital soft tissue deformation. All above-mentioned studies used static gaze positions for their analysis.

To further improve the understanding of EOM properties, force measurements targeted effective EOM activity in alert monkeys. However, the EOMs have been largely inaccessible. Two years ago, tagging of the orbit was used to investigate noninvasively the inhomogeneous local deformation along the EOM’s length during eye movement.

The purpose of this study was to present baseline data on horizontal EOM segments in normal subjects. Moreover, the kinetics of the local physiologic contraction/elongation of the medial rectus muscle (MMR) and the lateral rectus muscle (LRM) for left-to-right movement was compared with right-to-left movement. To demonstrate that tagging can be used to differentiate normal from pathologic movement, physiological patterns in healthy subjects were compared with those in two patients with Duane’s syndrome type I (DSTI). To serve this need, the postprocessing technique was improved to increase the number of segments that could be differentiated along the EOMs. Landmark chains (polylines) along the EOMs were replaced by a two-dimensional tetragonal landmark grid (called mesh) covering the entire EOM’s length. Landmarks are dimensionless locations in the image, tracked through the 15 time frames. They are needed for the tracking algorithms to work.

Materials and Methods

Subjects and Setup

The study was conducted according to the tenets of the Declaration of Helsinki and approved by the ethics committee of the Health Department of the Canton of Zurich, Switzerland. Each subject agreed to participate after the scientific value and possible risks of the study were explained. Eleven healthy right eyes (five women and six men; mean age, 32 years; range, 22–55) were imaged. The left eye of 2 of the 11 subjects (a 25-year-old woman and a 22-year-old man) with DSTI diagnosed in the left eye, were also imaged. The patients showed the clinically classic abduction deficit and globe retraction in adduction. This disease was chosen to investigate the local behavior of the lateral rectus muscle during adduction, when an elongation over the entire length of this muscle is expected. The healthy subjects of the control group were recruited by advertisement; the two patients were invited. Visual acuity of all subjects was sufficient to track the visual stimulus: a horizontal sinusoidally oscillating white square on a black background (target size = 0.4°) with an amplitude of ±20° and a period of 2 seconds (corresponding to a maximum angular eye velocity of 63 deg/s). The stimulus induced smooth pursuit eye movements. For the presentation of the visual stimulus, a computer, projector, projection screen, and commercial software (Presentation; Neurobehavioral Systems, Inc., Albany, CA) were used. A mirror allowed the subjects to gaze out of the bore to the projection screen. Similar setup and stimulus paradigms were used as described in Piccirelli et al. A receive-only surface coil of 47-mm diameter was placed on one eye like a monocle, so that the subject could see the target through it. Foam pads immobilized the subject’s head.

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MRI Sequence

Axial CSPAMM (complementary spatial modulation of magnetization) tagging images\textsuperscript{14} were acquired with a gradient echo sequence acquired on a 1.5-T system (Achieva 1.5T; Philips Healthcare, Best, The Netherlands; Fig. 1). The tagging image plane was defined on a coronal scan (perpendicular to the optic nerve) in straight-ahead gaze and included the orbital apex as well as the scleral insertions of the horizontal EOMs. The 40° right-to-left and left-to-right eye movements were split into 15 time frames of 12-ms duration, separated by 58 ms, resulting in an acquisition of $15 \times 70 = 1050$ ms. The remaining 950 ms of the 2-second periodic eye movement served for signal recovery. Therefore, the two movement directions were acquired separately. As in cardiac motion analysis, images with CSPAMM preparation (twice-a-line tagging pattern) were acquired. The period of the signal modulation is called the tagline distance. In this study, it was set to 2.5 mm. The images with the horizontal and vertical tag lines were multiplied to one image with a grid-tagging pattern. The acquisition flip angle was adapted over the time frames to get homogeneous signal intensity over time. Further details on the CSPAMM technique can be found in the following publication.\textsuperscript{15} Other parameters were identical with those described previously\textsuperscript{15}: field of view, $140 \times 140$ mm$^2$; scan resolution, $1.2 \times 1.2 \times 4.0$ mm; number of signal averages, 8; and reconstruction matrix, $256 \times 256$. The use of an echo planar imaging (EPI) factor of five shortened the acquisition time to 4.5 minutes. The same image plane was measured again without the tagging preparation as a high-resolution anatomic image in straight-ahead gaze direction. Because of the static setup, the scan time was much shorter, even with a higher resolution. This image was used to improve the mesh placement that is described in the next section. The mesh vertices were tracked through the 15 time frames.

Postprocessing

The new postprocessing technique corrects potential polyline crossing (see the animated Fig. 2 in Piccirelli et al.\textsuperscript{13}). Note that multiple polylines drawn on the same EOM path do not yield statistically independent measurements; these are only multiple analyses of the same original digital measurement. The postprocessing software assigns the nearest equivalent tissue point of the next time frame to each tissue point and therefore tracks each mesh vertex (landmark) independently.\textsuperscript{13} If inconsistent tracking of the vertices generated mesh irregularities (crossing of connections), the tracking algorithm regularized the mesh using the information of the neighbors of the mistracked vertices. This does not imply a loss of information, as the cells of the mesh were smaller than the filtered image resolution.\textsuperscript{13}

The $41 \times 11$ two-dimensional tetragonal meshes were manually drawn on the whole length of the optic nerve (ON) and of each EOM on the 10th time frame (approximately gaze straight ahead; Fig. 1). To ascertain that the meshes lay on the tissues, we took additional high-resolution anatomic images as references and realigned the meshes if needed. These meshes divided the tissues length into 40 isometric segments, which were numbered from 1 to 40 beginning at the scleral insertion of the EOMs, respective to the ON. A good knowledge about the orbital anatomy is needed to be able to lay the meshes on the correct tissues; nevertheless, no further training is needed.

For each EOM, the consistency of the mesh lengths between the two datasets was checked. The length of the MRM should be equal at the end of the left-to-right eye movement compared to the beginning of the right-to-left movement, and so should the LRM. Because of possible head movement between two consecutive scans, the length of the EOM lying in the image plane can vary slightly. We attempted to limit this difference to less than 10%. If the limit was not achieved, the
The diameter of the filter corresponded to 2.3 image pixels. A pass filter was applied to extract the harmonic peak in Fourier space. Longitudinal deformation is represented as a function of its position along the LRM, plotting the time-frames-wide averaging kernel. The relative length of each segment deformation over time of each segment was smoothed with a three-segment-wide averaging kernel. Therefore, the deformations of these eight segments are independent from each other. Finally, the deformations of the eight segments for each EOM. These eight segments take the limited imaging data of the 40 segments were condensed into eight independent datasets (Table 1).

Evaluation of the Meshes

For each of the 13 imaged eyes, the length of each of the 40 segments of the EOMs and ON was averaged transversely to the tissue over the 11 parallel connections. For calculation of the relative length change, the segment length at the first time frame (20° right gaze for right-to-left, and 20° left gaze for left-to-right eye movement, respectively) was selected as a reference. The relative length change of each segment was calculated by dividing its length at the actual time frame by its reference length (Fig. 2). The deformations of the 40 segments were then smoothed by a five-segment-wide averaging kernel. Therefore, the deformations of each particular segment can be traced by following the relative length of the segment (as an example, the vertical arrows show the deformation of segment 3). For the left-to-right abducting movement, the segment with the greatest contraction was segment 5, showing a 25% shortening. The anterior half of the EOMs contracted less than the posterior half for the 40° movement range. The shape of deformation profile at the 8th time frame (gaze straight ahead) was similar to the shape of the deformation at the 15th time frame (right gaze).

In healthy subjects, the local deformation along the horizontal EOMs was heterogeneous. Figure 3 summarizes the deformation profiles of all 11 subjects’ healthy right eyes for all 15 time frames. The anterior half of the EOMs deformed less than the posterior half, in accordance with the results of Miller.6 For all time frames, the maximum deformation amplitude was closer to the orbital apex than to the scleral insertion of the muscles. All deformation maxima were situated at approximately two thirds of the muscle lengths from the scleral insertions. For the right eye left-to-right movement (adduction), the maximum local contraction of the LRM was 22%, whereas the MRM elongated locally up to 30%. For movements from right-to-left (adduction), the maximum local elongation of dataset was rejected. As a further consistency check, the length of the LRM mesh had to exceed the length of the MRM mesh and did so for all datasets (Table 1).

The postprocessing software is based on a commercial software (TagTrack 1.5.6; GyroTools Ltd., Zurich, Switzerland) that integrates harmonic phase (HARP)16 with peak combination.17 A circular band pass filter was applied to extract the harmonic peak in Fourier space. The diameter of the filter corresponded to 2.3 image pixels.

RESULTS

A representative contraction profile of a healthy right LRM (subject 9) during 40° horizontal eye movement is shown in Figure 2. The length of each of the eight segments along the LRM is scaled by its length at the first time frame at 20° left gaze (black solid line, first time frame). The length of each segment at the first time frame was set to 1.0. The deformation of each particular segment can be traced by following the relative length of the segment (as an example, the vertical arrows show the deformation of segment 3). For the left-to-right abducting movement, the segment with the greatest contraction was segment 5, showing a 25% shortening. The anterior half of the EOMs contracted less than the posterior half for the 40° movement range. The shape of deformation profile at the 8th time frame (gaze straight ahead) was similar to the shape of the deformation at the 15th time frame (right gaze).

For each subject, the lengths of the EOM meshes are listed separately at the beginning and at the end of the left-to-right movement and of the right-to-left movement.

For each subject, the data were excluded from further analysis, as the anterior part of the LRM was not in the image plane.

† The subject’s eye movements were not accurate enough. Consequently, tracking of the EOMs could not be performed with sufficient accuracy.
the LRM was 26%, whereas the MRM contracted locally by 26%. The maximum local deformations of the LRM (contraction 22%, elongation 26%) were smaller than the maximum local deformations of the MRM (contraction 26%, elongation 30%). This result is expected, as the LRM is longer than the MRM.

Nevertheless, the deformation kinetics were almost homogeneous: nearly no change of profile shape was observed during the eye movement. Furthermore, for each EOM, the difference between abduction and adduction deformation profiles is hardly striking.

The ON deformations were roughly 10 times smaller than the deformation of the EOM segments (Fig. 3A.3, 3A.6). The deformations of the ON segments were also more homogeneous than the deformation of the EOMs. The ON relative segment lengths reached a minimum at the eighth or ninth time frame for both eye movement directions, corresponding approximately to gaze straight ahead. Here, the ON is curled in the orbit most. Since the deformation of the ON could only be reported in the axial image plane, the ON curling out of this plane is misleadingly interpreted as shortening of the ON.

Figure 3B shows the corresponding standard deviations (SDs) among the 11 subjects. Each curve corresponds to a time frame. The SDs increased with time, but stayed below 8% of the normalized segment lengths. The larger SDs of the LRM segments of the (thinner) anterior half compared to the (thicker) posterior half were due to (in plane) partial volume effects that appeared at the interface of tissues with different movements. The average SD at the 15th time frame of the segments 10 to 30 was approximately 0.06. This corresponded to a mean SD increase of $0.06/15 = 0.4\%$ per time frame. If the tissue deformations of all subjects were identical (no biological variation), the average tracking error per time frame could be estimated to be 0.4% of the segment length at that time frame.

Subsequently, the deformation of two DSTI horizontal EOMs were compared to the healthy group. Some segments of the DSTI EOMs deformed inversely to the healthy EOMs (Fig. 4). Patients' data outside the (4 SDs broad) error bar interval differed significantly from normal. In particular, the deformation of the posterior part of the DSTI LRM differed significantly from the healthy group. In Figures 4A.6–4A.8, segments 7 and 8 showed aberrant contraction (see arrows, values below 1.0); segments 5 and 6 showed a smaller elongation than normal, and segments 1, 2, and 3 showed an elongation very similar to normal. In Figure 4A.1, after the pathologic contraction of the posterior LRM segments 7 and 8, there was a small but significant elongation at the beginning of the opposite movement. At the beginning of abduction (Fig. 4A.2) the DSTI LRM contracted. From gaze straight ahead, this contraction did not result in attempted abduction (Figs. 4A.3–4A.4). Conversely, in Figures 4B.2–4B.4, the anterior segments 1 and 2 of the DSTI MRM deformed inversely to the healthy MRM, whereas the DSTI MRM posterior half deformed similarly to the normal MRM. Although, because of a smaller eye movement, the DSTI MRM deformed less than the healthy subjects’ MRM.

The local maximum deformations of the DSTI EOMs were shifted in comparison to the healthy EOMs. In contrast to healthy subjects, the DSTI LRM maximum deformations were located on segment 3, closer to the scleral insertion. (Fig. 4A). The LRM anterior half deformed more than the posterior half. In contrast, the location of the DSTI MRM maximum deforma-
The maximum local contraction of the LRM was 7% for patient 1 and 8% for patient 2, respectively, whereas the MRM relaxed locally up to 17% and 27%, respectively. The LRM maximum local elongation was 11% and 14%, respectively, whereas the MRM contracted locally 12% and 19% at most, respectively.
Analysis of motion-encoded MRI provided new detailed insights into how the horizontal extraocular muscles transformed smooth pursuit commands into eye movements. In healthy subjects, the local muscle deformation was heterogeneous. During the entire 40° horizontal eye movement, the maximum deformation amplitude was located nearer to the orbital apex than to the muscles' scleral insertion. A smaller than 40° eye movement led to a smaller but similarly shaped deformation profile. However, the shape and timing of the deformation profiles were altered in two patients with DSTI: the aberrant innervation of third cranial nerve fibers into the LRM led to a pathologic contraction of the posterior segment of this muscle during adduction. The effect of the pathologic neuronal command could be resolved by analyzing the kinetics of deformation of specific EOM segments. The added knowledge supports the accepted hypothesis of the mechanism of globe retraction in adduction in patients with DSTI.\textsuperscript{18}

Normal Deformation Profiles of Antagonistic EOMs during Smooth Pursuit

For each eye movement direction, the shape of the EOM deformation profiles remained similar over the whole 40° movement range. For example, the amount of deformation at the 8th time frame (gaze straight ahead) was nearly half of the deformation at the 15th time frame (20° horizontal gaze). The
maximum deformation was always located at the same muscle segment during eye movement. Furthermore, the deformation profiles of the two EOMs were similar for the two eye movement directions.

The intersubject variability of the EOM deformation profiles was low, since the SD among the subjects was small in relation to the entire EOM length (4% in average). Yet, the SD is not negligible when it is compared to the observed segmental length changes.

In the present study, the LRM deformed to a lesser extent than the MRM, which is expected as the LRM is longer than the MRM. The peak deformation correlated with the amplitude of the eye movement, but the deformation profiles remained similarly shaped for the whole movement range. Therefore, the profile shapes describe EOM relevant properties. On the other hand, the amplitude of the deformation is dependent on the eye movement range.

The ON segment lengths relative to the first time frame reached a minimum at the 8th or 9th time frame for both eye movement directions. These time frames correspond to gaze straight ahead during which the distance from the ON globe insertion to the orbital apex is shortest. In this position, the ON is curled in the orbit. Since the deformation of the ON could only be reported in the axial image plane, the ON curling out of this plane is misleadingly interpreted as shortening of the ON.

**DIST: Altered EOM Deformation Profile as a Consequence of Aberrant Innervation**

As documented in postmortem dissections, the LRM is not innervated by the sixth cranial nerve (CN6) in most patients with DISTI. The LRM is innervated by an aberrant branch of the oculomotor nerve (CN3) which normally supplies the MRM. Electromyography confirmed the LRM endplate function-ality by the presence of CN3 action potentials into the muscle. MR imaging showed that aberrant CN3 branches connect with the LRM, even or even co-innervation of the LRM by CN3 and CN6 may occur.

Early studies on DISTI argued that globe retraction in adduction may result from contraction of the agonist MRM combined with missing elongation of the antagonist LRM due to fibrotic reorganization. The co-contraction hypothesis arose from first careful histologic examinations and electromyography data. The present study demonstrates that the DISTI LRM posterior quarter (segments 7 and 8) contracted on adduction (Fig. 4) leading to globe retraction. Although the LRM anterior segments relaxed to a greater extent than expected, the reported data showed that the entire elongation of the LRM was smaller than the MRM contraction (Fig. 4) which indeed induced globe retraction. Nevertheless, it is noteworthy that the globe retraction on adduction of the two DISTI patients in our study were relatively small on clinical testing and were recorded in a limited adduction of not more than 20°.

**Postprocessing of Motion-Encoded MRI**

The mesh algorithm takes into account that the shapes of the EOMs and the ON remain smooth and regular, which justifies the correction of the mesh irregularities. Tracking the same meshes without the correction of mesh irregularities induced a much higher sensitivity to image noise. The mesh algorithm improved the stability of the tracking procedure and allowed the characterization of eight independent segments along the horizontal EOMs. Since the mesh vertices were homogeneously spread over the tissue width, a higher precision of the tracking procedure was achieved.

A different manner of connecting polylines was recently described. Pan et al. used meshes for the heart and Liu et al. for the tongue to correlate two dimensional motion-encoded image sets, thereby gaining three dimensional information. Their methods require an additional loop in the tracking algorithm (see Fig. 3 in Ref. 29). Our method separates the tracking from the correction procedure, in order not to assign mechanical properties to the tissues a priori, such as smoothness or elasticity (see §2.3 in Ref. 29), which would be difficult to determine and would change with the activation of the muscular contraction.

**Main Limitations and Future Developments**

Manual positioning of the mesh on the EOMs may be a source of error. Automatic positioning of the meshes would enhance the precision of the methodology. The limited image resolution induced through-slice and in-slice partial volume effects. These effects are accentuated by the fat shift and the manual positioning of the image slice. Use of three dimensional imaging with a slight resolution improvement would reduce these artifacts. The scanner bore length and diameter limited the amplitude of the visual target oscillation and hence the gaze movement range.

In conclusion, motion-encoded MRI of the orbit has a number of potential clinical applications. Our work provided deformation profiles for healthy subjects as reference data for a more detailed understanding of the physiology of the EOMs during eye movement. Moreover, the consequences of aberrant innervation on individual EOM segments were demonstrated in two patients by using this noninvasive technique.

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**References**


