Dynamic Imaging of the Eye, Optic Nerve, and Extraocular Muscles With Golden Angle Radial MRI

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PURPOSE. The eye and its accessory structures, the optic nerve and the extraocular muscles, form a complex dynamic system. In vivo magnetic resonance imaging (MRI) of this system in motion can have substantial benefits in understanding oculomotor functioning in health and disease, but has been restricted to date to imaging of static gazes only. The purpose of this work was to develop a technique to image the eye and its accessory visual structures in motion.

METHODS. Dynamic imaging of the eye was developed on a 3-Tesla MRI scanner, based on a golden angle radial sequence that allows freely selectable frame-rate and temporal-span image reconstructions from the same acquired data set. Retrospective image reconstructions at a chosen frame rate of 57 ms per image yielded high-quality in vivo movies of various eye motion tasks performed in the scanner. Motion analysis was performed for a left–right version task where motion paths, lengths, and strains/globe angle of the medial and lateral extraocular muscles and the optic nerves were estimated.

RESULTS.Offline image reconstructions resulted in dynamic images of bilateral visual structures of healthy adults in only ~15-s imaging time. Qualitative and quantitative analyses of the motion enabled estimation of trajectories, lengths, and strains on the optic nerves and extraocular muscles at very high frame rates of ~18 frames/s.

CONCLUSIONS. This work presents an MRI technique that enables high-frame-rate dynamic imaging of the eyes and orbital structures. The presented sequence has the potential to be used in furthering the understanding of oculomotor mechanics in vivo, both in health and disease.

Keywords: golden angle radial MRI, dynamic MRI, optic nerve, extraocular muscles, strabismus

The eye and orbital visual structures including the optic nerve, extraocular muscles (EOMs), and orbital fat form a highly complex dynamic system with multiple degrees of freedom. The body of work dedicated to measuring and modeling the motion of the eyes and orbital structures spans decades and includes multiple techniques.1–9 Oculomotor measurement techniques including electro-oculograms, search coils, and infrared and video trackers provide excellent eye motion sensitivity and temporal resolution.1 However, these techniques do not provide detailed anatomic insight on the structures of the orbit. Radiological imaging techniques, especially magnetic resonance imaging (MRI) can provide detailed anatomical information, but MRI has been used mostly in the static eye. Most biophysical models of motion of orbital structures have been based on anatomic and mechanical parameters derived from static imaging data.2–9 Also, to our knowledge, none of these models have been fully validated with truly dynamic high-frame-rate in vivo imaging data. Therefore, a technique that combines the temporal resolution of nonimaging methods with the in vivo imaging capabilities of MRI can potentially be useful in validating and fine-tuning models of oculomotor motion.

In vivo diagnostic MRI of the eye, EOMs, and optic nerve has also mostly been restricted to static imaging with fixed gazes.10–12 Motion is generally considered to be a confound rather than the point of interest and therefore clinical MRI is often performed under cued blinking where data are not acquired during periods of rest inserted during the scan. However, imaging of the motion of the eye, EOMs, and optic nerve can be potentially useful in understanding a range of ocular pathologies. For example, detailed analysis of patient-specific EOM motions can be potentially useful in identifying exact etiologies in complex strabismus and help in planning surgical interventions and monitoring rehabilitation.4,13–15 In the evaluation of optic nerve gliomas, dynamic information can be helpful in determining lesion adhesions to peripheral tissue, information that is not gleaned from static MRI.16 Knowledge of optic nerve motion can be helpful in determining altered elastic properties and strain in ocular disease. A technique to noninvasively image the dynamic moving eye, optic nerve, and EOMs can therefore add value in the clinic.

Recent advances in the field of accelerated MRI have included the development of a technique for imaging of freely moving structures with high temporal and spatial resolutions.
The method known as golden angle radial imaging has been used for several dynamic imaging applications, including imaging of the heart, joints, abdominal organs, and even human speech, but has never been applied to survey the orbit in humans. In this sequence, data are acquired continuously in a radial trajectory where the center of $k$ space is sampled by each data profile. Importantly, the data profiles are spaced by a constant radial angle of $111.246^\circ$, which ensures optimal spacing between profiles and most efficient coverage of 2D $k$ space. For an arbitrary number of acquired profiles, a more optimal distribution of samples is generated with this sequence as compared to linearly acquired data where data profiles are stepped by $180/P$ degrees radially ($P$ is usually the profile resolution, commonly 256 or 128). The main strength of this sequence, however, is the flexibility it provides in image reconstruction. In any continuously acquired radial data set (golden or linear angle), images may be reconstructed by grouping together data profiles that are acquired sequentially in time. However, in order for the images to be artifact free, the traditional linear angle radial sequence requires that the $k$ space be fully sampled radially. To achieve this, $P$ data profiles are necessary per reconstructed image, increasing the temporal span per image. In contrast, the unique sampling scheme of a golden angle trajectory enables artifact-free image reconstruction with significantly lower number of profiles per image, improving the temporal span per image. Furthermore, images can be reconstructed by grouping arbitrary sets of data profiles. These sets can be overlapped temporally (Fig. 1), which provides a time series of images of moving anatomy, with a freely adjustable frame rate given by $TR*T_p$, where $TR$ is the repetition time, usually in milliseconds, and $T_p$ is the profile step between reconstructed frames. Together, the freely adjustable image frame rate and temporal span per image lends to high-quality reconstruction of dynamic images of freely moving structures. Figure 1 gives a graphical overview of the golden angle radial sequence.

In this article, we present a proof-of-concept demonstration of the dynamic imaging of the eyes, optic nerve, and EOMs by using the above-introduced golden angle radial technique at a field strength of 3 Tesla. High-frame-rate time series in vivo MRI data are presented from volunteers performing various ocular motions in the scanner. Quantitative analyses of moving structures in the axial plane are presented as examples of potential analyses possible with motion data.

**Methods**

This research followed the tenets of the Declaration of Helsinki. Participants gave written consent for participation in the study. The design of this study was approved by the Vanderbilt University Institutional Review Board (IRB). All participants were scanned after signed informed consent according to the institutional IRB.

**Image Acquisition**

All experiments were performed on a Philips Achieva 3 Tesla human imaging system (Philips Healthcare, Best, The Netherlands) with a 2-channel body transmit/8-channel head receive coil. Eight healthy adult subjects ($31.9 \pm 6.3$ years of age; five male, three female) were scanned in 10 different scan sessions. Two subjects were scanned twice on different days to ensure repeatability of the imaging method. One 8-mm axial, sagittal, or coronal slice was planned on the basis of T2-weighted scout images, such that the eye globes, complete extent of the optic nerve, and the EOMs were captured in the axial, and sagittal slices (Fig. 2). Data were acquired with a golden angle (GA)

**Image Reconstruction**

Complex time series images were reconstructed offline in Python (Anaconda version 3.4.2; Continuum Analytics, Austin, TX, USA) using 128 profiles per reconstructed image ($128 \times 0.0057 = 0.72$-second temporal span) and a frame step of 10 radial profiles (0.057 s/frame, or $\sim 18$ frames/s). GA image reconstruction involved correction for profile $k$-space shifts and sampling density before gridding, 2D fast Fourier transform and roll-off compensation. The reconstruction steps have been presented in more detail earlier. An 8-channel receive coil combination was performed in the image domain by using the method of Walsh et al. to yield final dynamic images. The choice of 128 profiles per image that defined the temporal span, and profile step of 10 profiles that defined the frame rate, was arbitrary and could be adjusted freely if desired. Choices of these parameters influence the spatial and temporal quality of the dynamic images in a competing manner. To illustrate the effect of image temporal span on overall image quality, images from the fixation task were reconstructed at a chosen time point with 4, 16, 32, 64, 96, 128, 192, and 256 number of...
profiles, representing 0.02-, 0.09-, 0.18-, 0.36-, 0.55-, 0.72-, 1.09-, and 1.46-second time span per image frame.

Motion Analysis

An exemplary analysis of motion patterns of the eyes, optic nerve, and EOMs was performed on the levoversion/dextroversion time series image data in all subjects. Specific image landmarks that corresponded to anatomic points of interest were first identified manually in a subset of time series images 0.11 s apart (every 2 frames) and spanning 2.85 seconds (50 frames). The selected segment started with all subjects looking right, followed by sweeping the eyes to look left and sweeping the eyes to return to the original position. Fourteen points, seven per orbit, were landmarked in each time frame: the lens, the points of optic nerve junctions to the globes, the points of the extraocular muscle insertions on the globe, and one point approximately midway in each EOM and optic nerve (see Fig. 2). In addition, one common point of convergence of the optic nerve and the rectus muscles at the Annulus of Zinn (AOZ) was also marked in all images. This common landmark served as the reference in our estimation of muscle and optic nerve lengths over the version cycle.

Motion track data of the bilateral EOMs and the optic nerves were extracted by fitting the landmarked points to a second-order polynomial over the full levoversion/dextroversion cycle. A fit was performed in order to obtain a smooth approximation to the manually chosen points that naturally included some jitter. In addition to the motion tracks of the identified landmark points, the data were also used to calculate several basic parameters to better quantify the observed motions. These included the following:

1. Angles of eye movement over a version cycle: The angle of eye movement was estimated as the acute angle between the segments connecting the lens with the optic nerve head and the optic nerve head with the AOZ (Fig. 2, black and white line segments in the right eye). The angles were positive with the eyes looking left and negative when looking right.

2. Optic nerve lengths over time: The optic nerve length in each image frame was estimated by a second-order polynomial fit over three landmarked points: the optic nerve-globe junction, the midway point, and the AOZ landmark in all images for both eyes. The length of the nerve was calculated by summation of the individual fitted segments.

3. EOM lengths over a version cycle: The EOM lengths over time were estimated as the second-order fit distances from AOZ to the points of insertion of the EOM muscles on the eye globe for both eyes.

4. Strains over a version cycle: The strains induced in the EOMs and the optic nerve over the version cycle were estimated as

\[
\text{Strain} = \frac{l - l_{\text{min}}}{l_{\text{min}}}
\]

where \(l\) was the length of the anatomy at any time point and \(l_{\text{min}}\) was the minimum length during the version cycle. Also, the average strain/globe angle was estimated for all anatomic structures and subjects.

RESULTS

Dynamic time series image results for all subjects and all scans are included as movies in .mp4 format. Only segments of ~5 seconds of data are included in the Supplementary Video files owing to data file size limits. These segments, however, adequately depict the eye motions performed during these scans. These include movies of version tasks in three orientations and rest versus fixation tasks. In the text, selected frames in different orientations with time stamps are presented that cover the range of motions undertaken.

Figure 3 shows axial image frames from the rest (left column) and fixation (right column) tasks in subject 1. The entire orbital anatomy is seen with good contrast between the eye globes, optic nerve, surrounding fat, and the medial and lateral rectus muscles. Two image frames are shown, the top at an initial time of 0.36 second and the bottom at time 2 seconds. Qualitative
observation of the two states reveals that there is involuntary motion of the eye and optic nerve in the resting state even within 2 seconds, which is minimized by fixation. The drifting nature of this motion, especially in the right eye and optic nerve, is seen well in the video file (Supplementary Video S16, Subject 1 Scan 1 Axial Rest.mp4). Although somewhat expected, these data can help improve the design of imaging experiments, particularly where eye motion is a challenge.

Figures 4a and 4b show time frame images 0.5 seconds apart from two subjects performing left–right versions (Supplementary Video S17: Subject 1 Scan 1 Axial LR Motion.mp4; Supplementary Video S21: Subject 2 Scan 1 Axial LR Motion.mp4). Each version cycle was performed in approximately 3 seconds. Abduction/adduction of the medial/lateral rectus muscles is seen to impart large movements of the eyes along with the optic nerves. Muscle widths and the location of the muscle belly are seen to change dynamically with muscle contractions as expected. Another feature of interest is the hyperintense signal inside the globes that is seen to change with motion (see Supplementary Video file). In particular, the hyperintensity originates circumferentially at the end of each eye version and decays transiently thereafter. One hypothesis is that this signal change originates from the swirling flow of vitreous humor with highest velocities at the scleral wall, a pattern that has been predicted by some earlier modeling studies.24–26 Similar signal change patterns were seen in all subjects. Detailed investigation of this transient signal is beyond the scope of this report. The rapid motion of the optic nerve causes some blurring in frames, especially in the middle of a version where the acceleration is highest. This is obvious, for example, in frame 5 of Figure 4a. Strategies to minimize this effect by varying the number of profiles per reconstructed image are pointed out in the discussion. Figures 4c and 4d show second-order polynomial fit motion tracks of the three landmarked points over dextroversion and levoversion, respectively, overlaid on the last frame of each version.

Figure 5 shows the results of quantitative analysis of the motion of the version cycle. The circles represent the lengths estimated from the manually selected points, and the lines represent polynomial fits to the circles. Data from all 10 scans are shown. Figures 5a and 5e, and Figures 5b and 5f show the estimated lengths of the right and left lateral and medial EOMs, respectively, over the complete version cycle (starting from looking right, then looking left, and returning to looking right). The EOM lengths are seen to vary significantly in opposing directions in the two eyes as expected. Also, the lateral and medial EOMs in each eye work in a complementary manner. Table 1 gives the estimated minimum and maximum lengths of the anatomic structures over the version cycle, averaged over the eight subjects. The medial EOM lengths were on average
shorter than the lateral EOMs. The black and gray arrowheads in Figure 5a show two repeated scans from two subjects. The measured lengths match closely, indicating minimal interscan variability. Figures 5c and 5g show optic nerve lengths over half of the 2.85-second period, similar in pattern to the EOM changes. Figures 5d and 5h show the globe angles during the motion. The main observation was that there is a shift in the range of angles swept by the two eye globes and a lag in the angles at any point of time. Also, in general each eye globe was seen to have a larger angle with its optic nerve when gazing in the contralateral side. Also, the variation in the optic nerve and EOM lengths follows the globe angles as expected. Since the motion was not guided by an external source, intersubject variations can be seen in the number of cycles performed within the 2.85 seconds. Subject 10, for example, performed the task at almost double the rate of the others. The strains calculated in all the structures are shown in Supplementary Figure S1. In general larger eye rotations produce larger strains, as expected, and complementary muscles have opposite trends in strains. Table 2 shows the average strains/degree of globe rotation estimated over all subjects.

Figure 6 shows sagittal image frames from two subjects performing up–down versions (Supplementary Video S19: Subject 1 Scan 1 Sagittal UpDown Motion.mp4; Supplementary Video S24: Subject 2 Scan 1 Sagittal UpDown Motion.mp4). Abduction/adduction of the inferior and superior EOM is again observed, as are swirling motions of the vitreous fluid. Figure 7 (Supplementary Video S23: Subject 2 Scan 1 Coronal LR Motion.mp4; Supplementary Video S38: Subject 4 Scan 1 Coronal LR Motion.mp4) shows coronal images of left–right version movements for two subjects. The motion of the four EOMs and the optic nerve within the orbital fat are clearly observed. The inferior and superior EOMs are seen to be

### Table 1. Average Lengths Over a Left–Right Version Cycle for Eight Subjects

<table>
<thead>
<tr>
<th>Anatomy</th>
<th>All Subjects</th>
<th>Without Subject 8</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Min Length, mm</td>
<td>Max Length, mm</td>
</tr>
<tr>
<td>Right lateral EOM</td>
<td>42.4</td>
<td>57.2</td>
</tr>
<tr>
<td>Right medial EOM</td>
<td>36.5</td>
<td>52.2</td>
</tr>
<tr>
<td>Right optic nerve</td>
<td>28.3</td>
<td>43.2</td>
</tr>
<tr>
<td>Left lateral EOM</td>
<td>41.3</td>
<td>54.9</td>
</tr>
<tr>
<td>Left medial EOM</td>
<td>37.5</td>
<td>53.7</td>
</tr>
<tr>
<td>Left optic nerve</td>
<td>29.0</td>
<td>41.3</td>
</tr>
</tbody>
</table>

Max, maximum; Min, minimum.

### Table 2. Absolute Strain/Degree of Globe Angle for All Structures Estimated Over a Left–Right Version

<table>
<thead>
<tr>
<th>Absolute Strain/Degree of Globe Angle, Mean ± SD</th>
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<tbody>
<tr>
<td>Right lateral EOM</td>
</tr>
<tr>
<td>Right medial EOM</td>
</tr>
<tr>
<td>Right optic nerve</td>
</tr>
<tr>
<td>Left lateral EOM</td>
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<tr>
<td>Left medial EOM</td>
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<tr>
<td>Left optic nerve</td>
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largely stationary during the left–right versions. The motion of the bilateral superior oblique muscles can also be observed.

Figure 8 shows the axial image frames reconstructed with a varying number of profiles per image to illustrate the effect of adjusting the temporal span that is uniquely allowed by the golden angle sequence. In general, the fewer the number of profiles used for reconstructing an image, the worse is the image quality, with greater streaking artifacts, low depiction of detail, and lower signal to noise ratio (SNR). While the highest detail can be seen in the image with 256 profiles per image, including fewer profiles per image might be helpful in reducing time-averaged motion effects when imaging fast-moving structures.

**DISCUSSION**

In this article, the proof-of-concept application of a novel in vivo MRI technique was presented that produces high-quality truly dynamic images of the bilateral orbits and the anatomic structures within. The primary benefit of this technique is the flexibility it offers in reconstructing dynamic images at different frame rates and time points. Successive image frames can be generated, if desired, at every repetition time (5.7 ms in this study). Therefore, data regarding positions, orientations, volumes, and strains of specific anatomic structures can be extracted at much higher sampling rates than static MRI, which typically requires at least ~100 to 200 ms per image. Therefore, not only can fast dynamic changes be captured that may be missed by static gaze imaging, but the larger number of sample points can lead to much more well-conditioned fits of parameters. Dynamic data can help better understand, for example, the time-dependent functional forms of the mechanical forces and strains in the eye and how they differ in disease. The sequence can be performed on any scanner without any external eye tracking/guidance aids and hence can be added to standard clinical MR protocols with very little additional time to yield information on patient populations. It can also be combined with non-MR techniques like optical eye tracking that can be performed inside an MR scanner. Both eyes can be imaged at the same time to extract important bilateral functional relationships during eye motion, while at the same time individual anatomic segments may be analyzed for focal diseases.

An area of clinical application of this technique could be the evaluation of strabismus, where dynamic data might aid in pinpointing the exact EOM dysfunctions involved. Patient-specific data can be used for planning surgical interventions as well as evaluation and monitoring of outcomes. Dynamic data can aid in detecting atrophies of EOM not immediately obvious in static images. Furthermore, the imaging plane may be selected to look at any desired structure, including the superior and inferior oblique muscles. Importantly, the golden angle sequence is very robust to bulk motion, making it an excellent candidate for pediatric MRI applications where head motion might be a challenge. This can be seen for example in subject 5 (Supplementary Video S46: Subject 5 Scan 1 Axial LR Motion.mp4) where bulk head motion is noticed along with eye motion. An additional feature is that the neurological anatomy, that is, optic chiasm and the brain, is also imaged along with the moving eye structures, creating the possibility of holistic anatomic and functional imaging. Future work will delve more deeply into characterizing the differences and testing specific hypotheses in cohorts such as different age groups and patient populations.

The main focus of this article was to introduce the application of the golden angle radial sequence to imaging the moving eye. An alternative technique that has been used before this to image the moving eye has been spin-tagging MRI. While this method also yielded dynamic imaging data it has some limitations. First, the technique requires a long...
signal recovery period relative to the actual data acquisition time. Therefore, continuous motion tracking is not possible. Multiple signal averages are generally required to get sufficient quality data. Also, the temporal resolution and the frame duration are not flexible, as in the golden angle method. The spin-tagging sequence also uses echo planar imaging, which is much more susceptible to image distortions, blurring, and other artifacts. Furthermore, the overall acquisition time is significantly higher, even for a local field of view covering one eye. Spin tagging, however, does have the benefit of allowing segmental motion analysis by following the deformation of individual tag lines. Overall, the simplicity and flexibility of the golden angle sequence might allow it to be adopted more rapidly than spin tagging.

A different fast imaging sequence commonly used in imaging moving anatomic structures is the steady-state free precession (SSFP) sequence. The SSFP gives excellent contrast between cerebrospinal fluid (CSF)-filled space, fat, and surrounding tissue. The temporal resolution that can be achieved with SSFP is high, but lower than that of the golden angle technique. In our 3-Tesla system with 80 mT/m and 200 mT/m/s maximum gradients, a single slice 3–3.5 ms 3T8 m m3 SSFP sequence with TR = 3.2 ms required 654 ms per image without parallel imaging, which was also the lowest possible frame rate. In contrast, the golden angle sequence provides a minimum frame rate = TR (minimum TR = ~3.5 ms). The golden angle method gives better contrast than SSFP in the soft tissue of the brain, but poorer CSF–nerve contrast. Also, SSFP is known to be highly vulnerable to off-resonance. Another technique used commonly to image the eye is cued blinking in which periods of rest are interleaved with fixated period of data acquisition. Therefore, it is used for acquiring high-resolution, static images where cueing is used to freeze the motion that can cause artifacts in the images. The golden angle method in contrast images the eye in motion for gathering dynamic information. Therefore, the two are different techniques used to investigate different questions.

The analysis of the motion of the EOMs, optic nerve, and globes presented in this article was presented as an example of the type of quantification that can be performed with this technique. We also observed transient swirling MR signal changes inside the globes that are triggered with motion in all of our subjects. Qualitatively, these patterns look similar to the data in previous work analyzing vitreous motion using spin-tagging MRI and vitreous flow models. However, analysis of this effect is outside the scope of this article. Also, recent studies have shown the presence of the magic angle effect in the corneoscleral shell in MRI, where fibrous microstructure of the sclera is resolved at the magic angle. We did not observe this effect in our images, likely because of the relatively low in-plane and slice resolutions (1 × 1 × 8 mm3) of our scans causing T2* intravoxel dephasing, point spread function (PSF) broadening, as well as partial voluming.

Golden angle imaging is an area of active research in MRI, and our immediate goals are to improve its capabilities in the context of eye imaging. The first goal is to achieve improvements in the image quality and resolution to better view the structures of interest while maintaining the frame rate. Imaging is performed here over a single plane only. A near-term goal is to therefore extend this technique to 3D covering the entire orbit, with minimal compromise on image quality and temporal sampling. Recently developed stack of stars and stack of spirals with compressed sensing reconstructions might allow such fast 3D coverage with reasonable image quality. Other non-Cartesian methods like 3D kooshball and 3D Cones may be used, but these methods are typically best suited for imaging isotropic fields of views. In the orbit, most of the time would be wasted in imaging structures outside the orbit, reducing the temporal efficiency. A second aim is to push the temporal resolution while maintaining modest spatial coverage. Another area of immediate effort is pushing the imaging resolution to submillimeter levels, allowing improved visualization of finer structures such as the optic nerve head and muscle pulleys in motion. We have used a slice thickness of 8 mm for our scans, which can cause partial voluming. The main influence of partial volume effect is the additional noise that is introduced when manually identifying landmarks, owing to reduced image contrast. We have used polynomial fits in our processing to be more robust to these errors. However, partial volume effects may be more of a challenge if automated image analysis methods are used to segment the anatomic structures of the orbit. A third area of development is the extension of this sequence to higher field strength, for example, 7 Tesla. Since SNR roughly scales with field strength, imaging at 7 T will provide a significant boost without a cost to imaging resolution or sampling time. Finally, most of the feature extraction in this article was manual for the sake of simplicity. The goal was to provide examples of the
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types of motion analyses that may be performed on these imaging data. Future work will focus on the development of automated image analysis techniques for processing and analyses of extended time series data as well as more advanced analysis of motion.

The data in this study remain available for public use in postprocessing and modeling studies. In support of IOVS mission of open source and reproducible research, we plan to share our source code and data with the community. The material will be freely available at https://github.com/senguptatasika/IOVS_Dynamic_GA_MRI_of_the_eye.

CONCLUSIONS
This work presents an MRI technique that enables high-frame-rate dynamic imaging of the eyes. The method is generally applicable without the need for any additional non-MRI instrumentation and allows adaptive image reconstruction for visualizing dynamic structures. The presented sequence may be potentially helpful in furthering the understanding of oculomotor mechanics both in health and disease.

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