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Improved measurement of brain deformation during mild head acceleration using a novel tagged MRI sequence

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ABSTRACT

In vivo measurements of human brain deformation during mild acceleration are needed to help validate computational models of traumatic brain injury and to understand the factors that govern the mechanical response of the brain. Tagged magnetic resonance imaging is a powerful, noninvasive technique to track tissue motion in vivo which has been used to quantify brain deformation in live human subjects. However, these prior studies required from 72 to 144 head rotations to generate deformation data for a single image slice, precluding its use to investigate the entire brain in a single subject. Here, a novel method is introduced that significantly reduces temporal variability in the acquisition and improves the accuracy of displacement estimates. Optimization of the acquisition parameters in a gelatin phantom and three human subjects leads to a reduction in the number of rotations from 72 to 144 to as few as 8 for a single image slice. The ability to estimate accurate, well-resolved, fields of displacement and strain in far fewer repetitions will enable comprehensive studies of acceleration-induced deformation throughout the human brain in vivo.

1. Introduction

Traumatic brain injury (TBI) is a major health concern in both civilian and military populations. In the United States, approximately 1.4million TBIs are reported to occur each year (Langlois et al., 2006). The direct physical cause of TBI is the rapid deformation of brain tissue, typically in response to linear or angular acceleration of the skull (Graham et al., 1995). The effects of brain trauma may lead to neurodegenerative diseases—for example, TBI is an established risk factor for Alzheimer's disease, especially in combination with the ε4 allele of apolipoprotein E (Mayeux et al., 1993; Mortimer et al., 1991). Contact sport participants with histories of repeated head impacts appear to have high incidence of memory impairment, depression, and dementia (Baugh et al., 2012). These symptoms have been associated with post-mortem findings of accumulated hyper-phosporylated tau and the disease protein TDP-43 (Baugh et al., 2012). The mechanism of this pathology is poorly understood and the relationship between the magnitudes, locations, directions, numbers, and frequencies of the mechanical insult and the resulting neurodegeneration is almost entirely unknown.

Because experiments measuring brain deformation during injury-level events in humans cannot be performed for ethical reasons, computer simulations of brain biomechanics, e.g., (Zhang et al., 2004), have been used to estimate brain deformation in response to specific loading conditions. Solutions obtained from computer models are highly dependent on the tissue connectivity, boundary conditions, and material properties assigned to different brain regions. Experimental measurements of brain deformation during acceleration of the skull are necessary to validate such computation models of brain injury. Experiments on physical models of brain injury have been performed using gel-filled skulls, e.g., (Margulies et al., 1990; Meaney et al., 1995), and high-speed biplanar x-ray measurement of radio-opaque targets embedded in cadaver brains during skull impact (Hardy et al., 2001). However, these physical models provide only a sparse set of data points and lack many of the features of the living brain (Gefen and Margulies, 2004; Vappou et al., 2008).

Tagged magnetic resonance imaging (MRI) (Axel and Dougherty, 1989; Zerhouni et al., 1988), a noninvasive approach to track the

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motion of biological tissues, has been applied previously to measure brain deformation during mild linear (Bayly et al., 2005; Feng et al., 2010) and angular (Sabet et al., 2008) acceleration of the live human brain. While these studies provide useful quantitative information regarding brain deformation in response to a known loading condition, only a limited region of the brain could be examined because the subject was required to repeat the head motion 72–144 times to acquire a single data slice. A large number of rotations consumes scan time, causes fatigue in the subject, and potentially introduces artifacts caused by variability between each repetition.

This study has two major contributions. First, in imaging studies of a gelatin phantom and three human subjects during mild angular acceleration, the tagged MRI acquisition parameters were optimized to minimize the number of rotations needed to acquire a single image set. Second, a novel double trigger tagged MRI pulse sequence was developed to reduce the temporal variability between rotations during the acquisition, and thus increase the accuracy of estimated displacement fields. These contributions are important steps toward enabling increased coverage and accurate measurement of deformation throughout the human brain.

2. Methods

2.1. Subjects

Three healthy subjects, two male and one female, were consented under an IRB approved protocol and enrolled in this study. MRI scanning was restricted by the protocol to no more than 2 h, and no subject spent more than 90 min in the scanner.

2.2. Head rotation device

In this experiment, a mild angular acceleration was generated after an angular rotation about the inferior-superior axis towards the subject's left shoulder. To generate a standardized and reproducible angular acceleration of the head, a device (Sabet et al., 2008) was used to constrain head motion within the MRI scanner (Fig. 1). The subject lies in the supine position and his or her head is firmly coupled to the device using side bars and a chin strap.

Prior to each rotation, the subject faces forward in the rest position with the device latched at 0° (Fig. 1a and c). The subject voluntarily initiates each head rotation when ready by releasing a latch to allow an active head rotation, assisted by a small counterweight. A rapid deceleration is generated by rotating into a padded stop set at approximately 32° toward the subject's left shoulder (Fig. 1b and d). This rapid deceleration is approximately 10–15% of that experienced routinely by soccer players in heading a soccer ball (Naunheim et al., 2003). The subject then pauses for 1–2 s before turning his or her head back to the rest position. Use of the device in the MRI environment was approved by the institutional MRI safety committee.

2.3. Optimization of Image acquisition

All MR images were acquired using a Siemens 3.0 T mMR Biograph scanner (Siemens, Munich, Germany). A gelatin phantom was used to validate the proposed approach and to optimize the image acquisition parameters. The stiffness of the gelatin phantom was selected to be within the range of reported values for brain tissue. The gelatin phantom was prepared by filling a plexiglass cylindrical container (diameter = 11.4 cm, length = 18.0 cm) with a mixture of 103.7 g of gelatin (Knox) and 1.8 L of water heated to 82 °C. The solution was stirred vigorously and allowed to cool at 4 °C overnight. Prior to the experiment, the phantom was allowed to equilibrate to room temperature for at least 8 h. The response of the gelatin cylinder to mild angular acceleration has previously been characterized using tagged MRI and compared to a numerical simulation (Bayly et al., 2008). Additionally, the gelatin phantom can be imaged for a longer period of time than human subjects.

All tagged MR images were acquired with a SPAMM tagging pulse (Axel and Dougherty, 1989) followed by a segmented cine gradient echo acquisition at the same slice location. Three image sets were acquired with 24 phase encode lines at 18.5 ms temporal resolution to assess the reproducibility of the acquired strain fields in vivo. The number of phase encode lines (spatial resolution) and the number of lines acquired per rotation (inversely proportional to temporal resolution) directly determine the number of rotations needed to acquire a single image set. To assess the effect of spatial resolution on the strain fields, images were acquired with 20, 24, 28, 36, and 44 phase encode lines at 12.4 ms temporal resolution (4 lines/rotation). To assess the effect of temporal resolution on the strain fields, images were acquired with 24 phase encode lines and temporal resolutions of 6.1 ms (2 lines/rotation), 12.2 ms (4 lines/rotation), 18.4 ms (6 lines/rotation), 24.5 ms (8 lines/rotation), and 30.6 ms (10 lines/rotation).

Given the differences between the live human brain and the gelatin phantom, e.g., geometry, boundary conditions, material parameters, a series of 2D tagging experiments were performed in three human subjects on two adjacent axial slices to ensure that the optimized acquisition parameters were appropriate for use in the live human brain. To assess the reproducibility of the strain fields, three image sets were acquired with 24 phase encode lines at 18.5 ms temporal resolution. To assess the effect of temporal resolution on the strain fields, images were acquired with 24 phase encode lines and temporal resolutions of 6.1 ms (2 lines/rotation), 12.2 ms (4 lines/rotation), 18.4 ms (6 lines/rotation), and 24.5 ms (8 lines/rotation).

2.4. Double trigger approach

For cine tagged MRI acquisition, only a portion of the spatial frequency domain ("*k*-space") is acquired during each rotation, so that the rotation must be repeated to fill *k*-space and create a single cine image sequence. Previous experiments required 72–144 rotations, each corresponding to the acquisition of one line in *k*-space, to acquire a single cine sequence (Bayly et al., 2005; Sabet et al., 2008). For those prior experiments, the MRI scanner was triggered when the latch was released at the beginning of the head motion. Variability in the synchronization between motion and imaging can lead to image distortions, e.g., breaks in the tag lines, making the acquired images unusable. The head rotation device constrains the path of the rotation to be consistent; however, the precise temporal trajectory of each rotation is not constrained. Fig. 2 (left column) shows the angular position versus time profiles of 30 rotations in the gelatin phantom and a single human subject. The motion of the gelatin phantom was very consistent between rotations, with a standard deviation to the time of peak angular acceleration of 1.4 ms. The human subject was more variable, with a standard deviation of 18.4 ms. This amount of variability would likely lead to image distortions.

A novel double trigger tagged MRI pulse sequence was designed to dramatically reduce temporal variability in imaging of human head motion. An MRI-compatible angular position sensor (MICRONOR, USA) was attached to the shaft of the head rotation device. The sensor measures the angular position in real-time for each head rotation. Software from MICRONOR additionally computes acceleration versus time measurements for each head rotation.

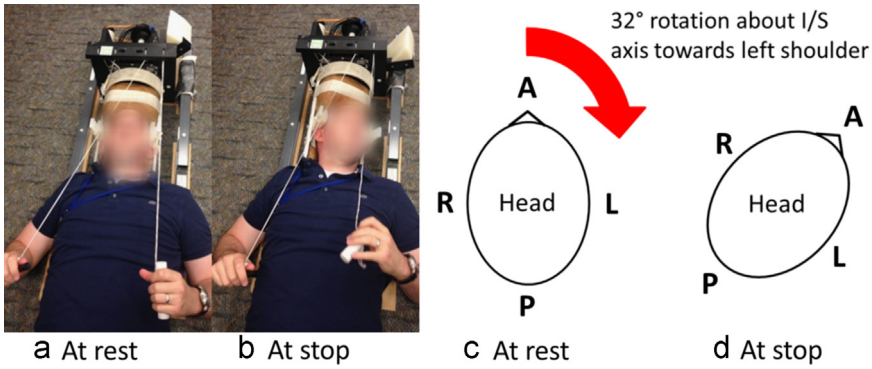

Fig. 1. Photograph of the head rotation device and schematic of head at rest and stop positions: A mild angular acceleration was generated using an MRI-compatible head rotation device. (a) and (c) At rest, the subject lies in the supine position with his or her head facing straight ahead. The subject initiates the motion by releasing a latch, which allows for free rotation about the inferior(I)/superior(S) axis towards his or her left shoulder. (b) and (d) After a 32° rotation, the device encounters a stop, which generates a mild angular acceleration. The subject is instructed to pause for 1–2 s at the stop. The subject then rotates his or her head back to the rest position, and the motion is repeated when the subject is ready.