Imaging two-dimensional displacements and strains in skeletal muscle during joint motion by cine DENSE MR

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Accepted 20 October 2007

Abstract

The objective of this study was to apply cine magnetic resonance imaging (MRI) using displacement encoding with stimulated echoes (DENSE) to measure the dynamic two-dimensional (2D) displacement and Lagrangian strain fields in the biceps brachii muscle. Six healthy volunteers underwent cine DENSE MRI during repeated elbow flexion against the load of gravity. Displacement encoded dynamic images of the upper arm were acquired with spatial and temporal resolutions of 1.9 x 1.9 mm\textsuperscript{2} and 30 ms, respectively. Pixel-wise Lagrangian displacement and strain fields were calculated from the measured images. We extracted the first and second principal strains ($E_1$ and $E_2$) along the centerline and anterior regions of the muscle. $E_1$ and $E_2$ were relatively uniform along the anterior region. However, $E_1$ and $E_2$ were both non-uniform along the centerline region—normalized values for $E_1$ and $E_2$ varied over the ranges of 0.27–1.35, and 0.45–2.36, respectively. The directions of the first and second principal strains varied throughout the muscle and showed that the direction of principal shortening is not necessarily aligned with fascicle direction. This study demonstrates the utility of cine DENSE MRI for analyzing skeletal muscle mechanics and provides data describing the \textit{in vivo} mechanics of muscle tissue to a level of detail that has not been previously possible.

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Keywords: Muscle mechanics; Biceps; Displacement; Strain; DENSE; MRI

1. Introduction

Mathematical models of skeletal muscle are widely used to investigate the causes of movement abnormalities and to analyze surgical treatments. Most models represent muscle properties using simple geometric idealizations that assume that all muscle fibers shorten uniformly (Delp et al., 1990; Zajac, 1989). These simplified models are limited in their ability to accurately represent the \textit{in vivo} behavior of muscles that have complex arrangements of muscle fibers.

Recently, several investigators have developed finite-element models of skeletal muscle that allow for representation of realistic three-dimensional (3D) geometries, incorporate the nonlinear active and passive constitutive properties of muscle tissue, and are able to characterize non-uniform shortening within muscles (Blemker and Delp, 2005; Fernandez et al., 2005; Yucesoy et al., 2002). These models have provided new insights into skeletal muscle mechanics; for example, analysis of a finite-element model of the biceps brachii muscle identified how complex features of muscle architecture could contribute to non-uniform strains along muscle fascicles (Blemker et al., 2005).

In order to broaden the utility of finite-element muscle models, methods to rigorously validate predictions made...
by the models are needed. Dynamic magnetic resonance (MR) imaging techniques have made it possible to characterize in vivo motion and shortening of skeletal muscle tissue during joint movement. For example, cine phase-contrast (cine-PC) MR images taken of the long head of the biceps brachii showed non-uniform shortening along some muscle fascicles during low-load elbow flexion (Pappas et al., 2002). In that study, the displacements of square regions of interest were calculated by integrating the velocity measurements, and one-dimensional strains were determined by calculating the change in length between square regions that were placed along the muscle fascicles. These data provide valuable in vivo measurements to confirm the models’ predictions of non-uniform strains along fascicles. However, in addition to non-uniform shortening along muscle fascicles, finite-element models also predict non-uniform strains transverse to the fascicle direction (Blemker et al., 2005)—results that may have important implications on muscle function, but must be verified with imaging techniques that enable measurements of two-dimensional (2D) strain fields.

MR imaging using displacement encoding with stimulated echoes (DENSE) offers a robust method for quantifying 2D strain fields (Aletras et al., 1999a, b; Aletras and Wen, 2001; Kim et al., 2004). Relative to an initial displacement-encoding time, DENSE directly encodes tissue displacement into the phase of the stimulated echo. A sequence of phase-reconstructed images are obtained using cine DENSE MR imaging to achieve pixel-wise spatial resolution and direct extraction of tissue displacements. Based on the pixel-wise displacement measurement, 2D Lagrangian strain fields can be calculated (Spottiswoode et al., 2007). Using a motion phantom, cine DENSE has previously been shown to be highly accurate (Spottiswoode et al., 2007). Cine DENSE has also been validated in vivo for myocardial function evaluation (Kim et al., 2004; Gilson et al., 2004).

The goal of this study was to apply cine DENSE MR imaging to measure pixel-wise displacement and Lagrangian strain fields of skeletal muscle. With cine DENSE MR imaging, 2D and 3D pixel-wise displacements were measured within the upper arm during active elbow flexion against the load of gravity. To test the technique with existing published results, we extracted one-dimensional strains along the centerline and anterior regions of the muscle and compared these results to cine-PC imaging results, described by Pappas et al. (2002). We then analyzed the 2D strain fields—we determined the values and directions of the first and second principal strains ($E_1$ and $E_2$) along the centerline and anterior regions of the biceps brachii muscle. This study demonstrates the utility of cine DENSE MR imaging for analyzing skeletal muscle mechanics and provides data describing the in vivo mechanics of muscle tissue to a level of detail that has not been previously possible.

2. Methods

2.1. Volunteer imaging

Six healthy subjects (four male and two female, age 24.4 ± 1.14 yr, height 1.81 ± 0.13 m, weight 74.93 ± 12.67 kg) volunteered for participation in this study. Each subject was scanned using a 1.5T Avanto scanner (Siemens Medical solutions, Erlangen, Germany) after informed consent was obtained. All studies were performed in accordance with the general investigational MR imaging/spectroscopy protocol (IRB-HSR #9039) approved by our institutional review board.

The subjects were positioned supine in the MRI bore, allowing them to perform a full range of elbow flexion–extension (Fig. 1). Each subject’s dominant arm was aligned with the longitudinal axis of the scanner, and imaged using a general-purpose flexible radio-frequency receive coil. The subject used the hand of the dominant arm to hold the handle of a
triggering device attached to the table, and performed active elbow flexion against the load of the handle and the weight of the forearm and hand, from nearly full elbow extension to 45–90° of elbow flexion at a rate of 30 cycles/min (i.e. 2 s between each trigger). The subjects were instructed not to bend their wrist joints while performing the elbow flexion. The subject’s upper arm was secured to the table with Velcro straps to ensure that it remained stationary during acquisition. Image acquisition was gated to the onset of elbow flexion using a photodiode circuit. The whole scenario of the study was similar to that described by Pappas et al. (2002). Whenever possible, the imaging parameters were chosen to be the same as those in the study by Pappas et al. (2002), so that a good comparison between these two studies could be made.

2.2. Image acquisition

High-resolution static axial images were acquired using a balanced steady state free precession (SSFP) sequence with the arm in the extended position to serve as the axial imaging plane for the dynamic cine DENSE acquisition, which was defined to be perpendicular to the humerus and to include the biceps, brachialis and triceps with clearly visualized boundaries (Fig. 2B). The axial images were then used to specify an oblique sagittal plane, which was defined to bisect the long head of the biceps brachii muscle and was oriented such that the superior–inferior direction of the image was parallel with the long axis of the distal aponeurosis (Fig. 2A). The imaging parameters for the static images included: field of view = 22 × 22 cm², image matrix = 192 × 144, and slice thickness = 7 mm.

A segmented echo planar cine DENSE sequence that has previously been described for cardiac imaging (Kim et al., 2004; Spottiswoode et al., 2007) was used to acquire displacement encoded dynamic images of the upper arm during elbow flexion. Previous phantom studies have shown that displacement measurements acquired using this technique are accurate to within 0.1 pixels (Spottiswoode et al., 2007). The commencement of elbow flexion triggered the application of displacement-encoding pulses followed by multiphase RF excitation pulses and acquisition of a segment of k-space (Fig. 3). This process was repeated for a series of successive elbow flexions until all of k-space was filled for all dynamic phases. Three multiphase data sets were acquired, one for displacement encoding in each orthogonal direction. Phase reference images without displacement encoding were also acquired. The imaging parameters included: field of view = 24 × 15 cm², slice thickness = 8 mm, flip angle = 15°, TR = 10 ms, TE = 4.8 ms, echo train length = 3, number of phase encoding lines per motion phase per elbow flexion repetition = 9, temporal resolution = 30 ms, motion phases = 50, and displacement-encoding frequency kₑ = 0.05 cycles/mm. The k-space matrix was 128 × 72, and then zero-padded to 128 × 80. Slice following (Fischer et al., 1994; Stuber et al., 1999) was used to obtain true through-plane motion for the axial view. Slice following is a method where an initial slice of muscle is tagged differently, using complimentary positive and negative tagging patterns, in two successive acquisitions. Immediately after tagging, image data are acquired from a relatively large volume containing the tagged slice. By subtracting the second acquired volume from the first, only the initially tagged signal is non-zero and contributes to the image signal intensity. Using this approach, the initially tagged slice is “followed” as it moves and deforms in three dimensions. Twenty-four repeated motion cycles were performed for each of the three orthogonal encoding directions and the phase reference images. Two additional repetitions were employed to eliminate artifacts resulting from imaging during the approach to steady state. Both oblique sagittal and axial cine DENSE data sets were obtained.

2.3. Image reconstruction and data analysis

Reconstruction of phase-corrected phase contrast DENSE images was performed online, and subsequent displacement and strain analysis of these data were performed offline using MATLAB (The Mathworks Inc., Natick, MA, United States) as described previously (Kim et al., 2004;
strains. Each subject, the normalized strain values were interpolated to increments calculated as: (found, where the negative and positive eigenvalues were assigned to the biceps brachii (Pappas et al., 2002), we calculated one-dimensional linear distal biceps tendon, normalized by the biceps muscle length, normalized by the average value across the centerline of the biceps muscle. The normalized strains were expressed as a function of distance from the distal biceps tendon, normalized by the biceps muscle length, \( L_M \). For each subject, the normalized mean strain values were interpolated to increments of 2.5\% of \( L_M \) using cubic splines. The directions of the first and second principal strains were expressed as the angle between the strain vector and the longitudinal axis of the biceps brachii.

3. Results

The phase-reconstructed DENSE images (e.g., Figs. 4 and 5) demonstrate that the displacement measurements are consistent with the muscles’ actions—the antagonistic muscles (biceps brachii and triceps brachii) move in opposite directions during the elbow flexion. The corresponding displacement maps of three motion phases from the elbow extension to the elbow flexion show the extent of the motion recorded by the scans, and illustrate that the peak superior displacement occurs along the centerline of the biceps muscle (Fig. 6).

There was good agreement between the one-dimensional strain distributions extracted from the cine DENSE measurements in our study and previously published cine-PC measurements described by Pappas et al. (2002) in which one-dimensional shortening was estimated along both the centerline and anterior regions of the biceps on a different set of 12 volunteers. Our results showed uniform shortening along the anterior region of the muscle with an average normalized value of 0.99 and non-uniform shortening along the centerline region with a range of normalized values from 0.17 to 1.55 (Fig. 7A). Similarly, the previously published cine-PC results (described by Pappas et al., 2002 and shown in Fig. 7B) also showed uniform shortening along the anterior muscle fascicles (average normalized value was 1.06) and non-uniform shortening along the centerline fascicles (normalized values ranged from 0.60 to 1.71).

The Lagrangian strain maps (e.g., Fig. 8), strain profiles (Fig. 9), and strain values measured by cine DENSE (Table 1) illustrate the 2D complexity of the tissue behavior. The first and second principal strains were both uniform along the anterior region, and the first and second principal strains were non-uniform along the centerline region. The relative values of the first and second principal strains also differed between the anterior and centerline regions (Table 1). Along the anterior region, the first principal strains were larger in magnitude than the second principal strains. By contrast, along the centerline region, the second principal strains were larger in magnitude than the first principal strains. These results indicate that, not only is the shortening non-uniform throughout the muscle, but the nature of the deformation is also substantially different between the centerline and anterior regions.
The principal strain directions were also non-uniform throughout the muscle (Fig. 10). In the proximal half of the centerline region, the first principal strain vectors were oriented at an angle of approximately 25° relative to the centerline. However, a previous ultrasound study (Asakawa et al., 2002b) showed that fascicles in this region are oriented directly along the centerline of the muscle. Our results suggest that the principal direction of shortening varies throughout the muscle and is not necessarily aligned with the muscle fascicle direction.

4. Discussion

The purpose of this study was to apply cine DENSE imaging to characterize strain fields in the long head of the biceps brachii muscle during low-load elbow flexion. The one-dimensional linear strain distributions extracted from the cine DENSE measurements were consistent with previous cine-PC measurements in the same muscle (Pappas et al., 2002). The major finding of the present study is that 2D strains were non-uniform throughout the biceps brachii muscle during low-load elbow flexion. The directions, magnitudes, and relative magnitudes of the first and the second principal Lagrangian strains were non-uniform throughout the muscle. These results describe the in vivo mechanics of skeletal muscle to a level of detail that has not been previously possible and can be used to validate and improve computational models of skeletal muscle (Blemker and Delp, 2005; Fernandez et al., 2005; Yucesoy et al., 2002).

The 2D strains determined in this study illustrate the fact that skeletal muscle contraction involves complex multidimensional deformation. The first principal strain direction results imply that the principal direction of muscle tissue shortening is not necessarily aligned with the muscle...
fiber direction and that contraction involves substantial shearing between fibers. Previous theoretical and computational studies have suggested that muscle tissue undergoes substantial shearing between fibers (Blemker et al., 2005; Huijing, 1999). Characterization of the shearing behavior between fibers is important because it influences the potential for fibers to transmit force laterally via intramuscular connective tissue (Huijing, 1999; Purslow, 2002). Future studies that compare principal strain directions extracted from cine DENSE imaging with detailed...
measurements of fiber directions (from ultrasound or diffusion tensor imaging) will allow for a more in-depth exploration of the precise nature of shearing behavior between fibers.

Other investigators have characterized skeletal muscle tissue motion using cine-PC imaging (Asakawa et al., 2002a; Finni et al., 2003; Pappas et al., 2002; Zhou and Novotny, 2007). Cine-PC imaging encodes pixel velocities into the phase of the image (Pele et al., 1991), and displacements and strains are determined by integrating velocities through space and time. Two of the major limitations of the cine-PC imaging approach are that (i) in order to translate velocity into displacement, the motion is assumed to be linear, and (ii) the strain estimates are sensitive to errors in the calculated displacements that accumulate over time. To account for these errors, velocity measures are generally averaged over several pixels (Zhu et al., 1996), which limits the ability to extract detailed 2D strain fields from cine-PC based estimates of displacements. The strains extracted from cine DENSE images are not based on a linear motion assumption and are not sensitive to error accumulation since the displacements, rather than velocities, are directly encoded into the phase of the image.

Other methods for directly measuring displacement include myocardial tagging (Zerhouni et al., 1988; Axel and Dougherty, 1989), and harmonic phase analysis (HARP) (Osman et al., 1999, 2000; Osman and Prince, 2000). One disadvantage of tagging is the reduced spatial resolution of strain relative to the image spatial resolution. Although it may be interpolated to any desired spatial resolution, the fundamental spatial resolution of strain is nominally determined by the distance between the tag lines, which is typically several pixels. The second disadvantage of tagging is that tag detection typically requires substantial time-consuming manual intervention. HARP obviates tag detection, but the spatial resolution of the resultant strain is not improved over tagging. In contrast to tagging and HARP, cine DENSE provides pixel-wise displacement data and the ability to automatically and quickly extract pixel-wise strain fields.

Several future improvements in the technique will further advance the utility of cine DENSE imaging for studying skeletal muscle. First, the reliability of the displacement measurements is currently dependent on the subjects’ ability to perform repeatable flexion–extension motion. To account for this, we triggered the imaging sequence with the beginning of the motion cycle to minimize effects of non-repeated motion. In the future, higher field strengths, parallel imaging, and artifact reduction strategies that require fewer acquisitions (Zhong et al., 2006), should reduce the required number of repeated motion cycles. Second, not all of our subjects could achieve the same range of motion within the constraints of the MRI bore, which added some variability in the magnitudes of the displacement and strain measurements. To account for this difference, we normalized the strain results to the mean strain for each subject, since our focus was characterizing how strains were distributed throughout the muscle. Usage of large or open-bore systems will allow for a larger range of motion and therefore eliminate the effects of variability.

Fig. 8. Example of the first principal strain $E_1$ (A) and the second principal strain $E_2$ (B) with the bars indicating the direction of strain vectors. Negative strain values represent local tissue element shortening during elbow flexion; and positive strain values represent local tissue element stretching. The centerline and the anterior fascicles can be easily identified in the strain maps.
in range of motion. Third, the need for several repeated motions limited us to a low-load condition in this experiment. Though, interestingly, even in the low load of this experiment, we still observed relatively complex non-uniform strain fields. Implementation of a faster cine DENSE sequence will allow for analyses of mechanics at higher and even maximum loading conditions. Finally, we were limited by imaging in one plane, and therefore could not analyze the full 3D motion of the muscle. To ensure that our measurements were not affected by this limitation, we carefully chose the imaging plane to minimize the through-plane motion. Future developments that allow for 3D measurements of displacements and strains throughout large volumes will further enhance the utility of DENSE for characterizing skeletal muscle motion.

Cine DENSE imaging has the potential to provide the data needed to improve our understanding of muscle contraction mechanics and rigorously evaluate predictions made by muscle models. Muscle pathologies are often manifested by alterations in fibers (Tardieu et al., 1982), connective tissue (Lieber et al., 2003), and passive structures (Shortland et al., 2002). Analyzing skeletal muscle mechanics using cine DENSE imaging in persons with muscle pathology will lead to an advanced understanding of how these alterations affect muscle behavior and function. These results, combined with computational models of muscle, may lead to more accurate and individualized muscle models that can capture effects of

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Table 1
Unnormalized and normalized strain values summarized from six volunteers

<table>
<thead>
<tr>
<th></th>
<th>Average E1</th>
<th>Average E2</th>
<th>Max E1</th>
<th>Max E2</th>
<th>Min E1</th>
<th>Min E2</th>
</tr>
</thead>
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<td>Unnormalized</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Centerline</td>
<td>-0.23 ± 0.07</td>
<td>0.34 ± 0.14</td>
<td>-0.30 ± 0.09</td>
<td>0.54 ± 0.22</td>
<td>-0.07 ± 0.06</td>
<td>0.10 ± 0.05</td>
</tr>
<tr>
<td>Anterior</td>
<td>-0.15 ± 0.07</td>
<td>0.03 ± 0.04</td>
<td>-0.18 ± 0.07</td>
<td>0.09 ± 0.03</td>
<td>-0.09 ± 0.06</td>
<td>-0.02 ± 0.06</td>
</tr>
<tr>
<td>Normalized</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Centerline</td>
<td>1.00 ± 0.00</td>
<td>1.49 ± 0.42</td>
<td>1.35 ± 0.16</td>
<td>2.36 ± 0.74</td>
<td>0.27 ± 0.17</td>
<td>0.45 ± 0.14</td>
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<tr>
<td>Anterior</td>
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<td>0.14 ± 0.20</td>
<td>0.85 ± 0.30</td>
<td>0.44 ± 0.13</td>
<td>0.40 ± 0.23</td>
<td>-0.06 ± 0.30</td>
</tr>
</tbody>
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*The values are reported as means ± SDs.

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![Fig. 9](image1.jpg)

**Fig. 9.** Normalized $E_1$ (A) and $E_2$ (B) along the centerline and the anterior boundary of the biceps brachii at maximal elbow flexion acquired from six normal volunteers. All strains are normalized by the average $E_1$ value along the centerline of the muscle. The normalized strains are plotted as a function of the normalized distance along the biceps muscle. First principal strains ($E_1$) correspond to shortening, and second principal strains ($E_2$) correspond to lengthening. Along the centerline, both first and second principal strains are uniform; however, the second principal strains are larger in magnitude than the first principal strains. By contrast, along the anterior region, both first and second principal strains are uniform; however, the second principal strains are smaller in magnitude than the first principal strains.

![Fig. 10](image2.jpg)

**Fig. 10.** Direction angles of $E_1$ as a function of the normalized distance. The direction is expressed as the angle between the $E_1$ strain vector and the longitudinal axis of the biceps brachii. Data were acquired from six normal volunteers.
pathology and can be used to gain new insights into the causes of movement abnormalities and to simulate novel treatment strategies.

Conflict of interest

None

Acknowledgments

This study was financially supported in part by NIH Grants R01 AR 056201 and R01 EB 001763, the Funds for Excellence in Science and Technology at the University of Virginia, and Siemens Medical Solutions. These sponsors had no involvement in the specific study design and/or analysis. We also gratefully acknowledge George Pappas for sharing previous cine-PC imaging results.

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