Tracking brain motion during the cardiac cycle using spiral cine-DENSE MRI

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Cardiac-synchronized brain motion is well documented, but the accurate measurement of such motion on the pixel-by-pixel basis has been hampered by the lack of proper imaging technique. In this article, the authors present the implementation of an autotracking spiral cine displacement-encoded stimulation echo (DENSE) magnetic resonance imaging (MRI) technique for the measurement of pulsatile brain motion during the cardiac cycle. Displacement-encoded dynamic MR images of three healthy volunteers were acquired throughout the cardiac cycle using the spiral cine-DENSE pulse sequence gated to the R wave of an electrocardiogram. Pixelwise Lagrangian displacement maps were computed, and 2D displacement as a function of time was determined for selected regions of interests. Different intracranial structures exhibited characteristic motion amplitude, direction, and pattern throughout the cardiac cycle. Time-resolved displacement curves revealed the pathway of pulsatile motion from brain stem to peripheral brain lobes. These preliminary results demonstrated that the spiral cine-DENSE MRI technique can be used to measure cardiac-synchronized pulsatile brain motion on the pixel-by-pixel basis with high temporal/spatial resolution and sensitivity. © 2009 American Association of Physicists in Medicine.

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I. INTRODUCTION

It is well documented that brain exhibits cardiac-synchronized pulsatile motion.^{1–11} Transmission of arterial pulse into the cerebrovascular system leads to systolic expansion and motion of the brain and motion propagation into the cerebrospinal fluid (CSF). This motion can potentially affect a variety of physiological behaviors in the brain,¹² as well as the accuracy of imaging studies that attempt to visualize or otherwise derive information about the brain using prior assumption of static anatomy. Developing techniques such as magnetic resonance (MR) thermometry and diffusion imaging are especially sensitive to tissue motion and could therefore be adversely affected by cardiac-synchronized motion. The reported apparent diffusion coefficient (ADC) of the brain is approximately $1 \times 10^{-3} \text{ mm}^2/\text{s}$.^{13,14} This corresponds to a root-mean-squared displacement of roughly 0.1 mm, suggesting that brain motion on the same order may affect the measurement of diffusion. In addition, the pulsatile motion of the brain can be a potential source of error in stereotactic radiosurgery (SRS) treatment of brain disorders, where the basic prerequisite of the high dose per fraction in this technique requires accurate patient positioning, targeting, motion detection, and compensation. The patient setup accuracy for intracranial SRS is reported to be less than 0.3

mm for Gamma Knife and 0.5 mm for dedicated SRS units,¹⁵ indicating that the brain motion on that order can potentially impact the overall treatment accuracy. The ability to accurately measure the cardiac-synchronized brain motion can help increase our understanding of the magnitude of these effects and the development of compensatory techniques.

Several studies have applied velocity-encoded phase contrast magnetic resonance imaging (MRI) techniques to measure pulsatile motion of the brain.^{1,3,8,9} These techniques, however, were restricted to indirect measurement of displacement and to selected regions of interests (ROIs). Tissue tagging methods, which combine complementary spatial modulation of magnetization (CSPAMM) with harmonic phase (HARP) postprocessing, have also been used to measure brain motion.¹⁶ However, the spatial resolution and motion sensitivity of this technique are largely limited by the size of the bandpass filter around the harmonics. Due to these technical limitations, earlier studies failed to obtain sufficient local information to generate pixelwise displacement maps of the brain during the cardiac cycle.

Displacement-encoded stimulation echo (DENSE) MRI, originally developed for assessing myocardial mechanics, is a tissue motion imaging technique where the tissue displacements are encoded into the phase of the stimulated echoes.¹⁷

FIG. 1. Pulse sequence timing diagram for spiral cine-DENSE MR imaging. The displacement-encoding module is played out immediately following the ECG trigger. The spiral k -space imaging sequence modified to include the DENSE encoding and unencoding gradients is used to rapidly sample the displacement-encoded longitudinal magnetization at multiple cardiac phases. The angle notation such as 90°_x means the rotation about the x axis by an angle of 90° in the left-hand convention. The RF pulse of 90°_{-x} is accomplished by setting the phase of the RF pulse of 90°_x to be 180° . α means the rotation about the x axis by a small flip angle of α . k_e is the spatial frequency imparted by the displacement encoding gradient, which is proportional to the area of the gradient and is given by $k_e = (\gamma/2\pi) \int_0^{\tau} G(\tau) d\tau$.

It offers many advantages over phase contrast and tissue tagging techniques, such as high motion sensitivity and high spatial resolution. Cine-DENSE technique was further developed to enable motion measurement at multiple phases during the cardiac cycle.¹⁸ In a recent study Soellinger *et al.* showed the feasibility of using DENSE MRI to measure the pulsatile brain motion during the cardiac cycle.¹⁹ However, their study suffered from limited accuracy in dynamic displacement measurement due to the lack of tissue tracking process. In DENSE, the displacement of each voxel is encoded as a phase shift that accrued since the time t_0 when the displacement encoding was initiated. The vectors in a DENSE displacement field converted directly from the phase at any time all refer to the position of the tissue at time t_0 . The use of these vectors as indicators of tissue motion in dynamic situations is somewhat limited because they provide a net measure of displacement from t_0 (Eulerian displacement) for each pixel at each cardiac phase but not measurements of frame-to-frame motion (Lagrangian displacement). In other words, the pixels at one cardiac phase cannot be directly identified at other cardiac phases. Tissue tracking needs to be used to obtain the frame-to-frame motion trajectories of given tissue pixels.

In this preliminary study we present the implementation of an autotracking spiral cine-DENSE MRI technique for the measurement of brain motion during the cardiac cycle. The autotracking algorithm embedded in this technique makes possible the calculation of motion trajectories for each of the tissue pixels. Spiral k -space trajectories in the pulse sequence increase the signal-to-noise ratio (SNR) efficiency. This technique has previously been used successfully in measuring cardiac motion.²⁰ Our objective in the present study was to investigate the feasibility of using autotracking spiral cine-DENSE MRI to measure the pulsatile brain motion.

II. METHODS AND MATERIALS

II.A. MR imaging

Three healthy volunteers (male; mean age: 34.4 y; range: 29–42) with normal cardiac findings and no history of central nervous disease were enrolled in this study. All study activities were performed after obtaining informed consent and in accordance with the general investigational MR imaging/spectroscopy protocol (IRB-HSR 9039) approved by our center's institutional review board. Each subject was scanned using a 1.5 T whole body scanner (Avanto, Siemens Medical Solutions, Germany). The subjects were positioned supine in the MR scanner without any immobilization devices. A four-channel head coil and single-channel neck coil were used. The subjects were instructed to hold their breath and remain motionless during each scan and to relax and breathe normally between scans.

Rapid scout localization images were first acquired in the sagittal plane. From these images the best location for a mid-line section through the cervical cord and brain stem was then determined. An electrocardiogram (ECG)-gated segmented spiral 2D cine-DENSE sequence,²⁰ as shown in Fig. 1, was applied to acquire displacement-encoded dynamic MR images of the subject's midsagittal plane. After the detection of R wave, the displacement encoding module was immediately performed. The magnetization was put into the transverse plane by the first 90° RF pulse. The spins were dispersed by the displacement encoding gradient with different phase angles according to their positions in the displacement-encoding direction. And then the cosine part of the magnetization was stored back into the longitudinal axis by the second 90° RF pulse. The phase of the second 90° RF pulse of the displacement encoding module was cycled to perform +cosine and –cosine spatial modulations of magne-

tization (SPAMMs), allowing a CSPAMM acquisition to be acquired. The residual transverse magnetization was spoiled after the displacement encoding module. The rest of the sequence repetition time (roughly a cardiac cycle) was then divided into multiple cardiac phases, and in each cardiac phase segmented spiral imaging sequence was performed to sample the k space after a small-flip-angle excitation RF pulse tipped down the magnetization and the displacement unencoding gradient removed phase dispersion according to the spin position in the stimulated echo. Single-shot images with two different echo times were acquired at each cardiac phase to estimate field maps so that linear inhomogeneity correction could be performed for spiral images.²¹ Two multiphase data sets were acquired, one for displacement encoding in each orthogonal direction. Phase reference images without displacement encoding were also acquired to correct the background phase error in DENSE measurements due to field inhomogeneity. Cine-DENSE MR images were also acquired in the coronal plane and in the transverse plane crossing the midbrain. The images were acquired for approximately 700 ms during each cardiac cycle after the R wave of ECG with a total of 18–22 cardiac phases. The total time of cine-DENSE acquisition to encode displacement in two directions was approximately 25 s depending on the individual's heart rate. Imaging parameters include field of view of $230\text{--}320 \times 230\text{--}320$ mm², matrix of 128×128 , slice thickness of 5 mm, temporal resolution of 34 ms, echo time of 1.9 ms, flip angle of 15°, and displacement encoding frequency of 0.4 cycle/mm.

II.B. Data processing

Reconstruction of spiral DENSE images was performed online using gridding and linear inhomogeneity compensation,²¹ and subsequent displacement analysis was performed offline using customized program implemented in MATLAB (The Mathworks, Inc., Natick, MA) as described previously.²² Briefly speaking, complementary raw data sets for each displacement-encoding direction were subtracted as the CSPAMM reconstruction to suppress the T1-relaxation echo. A 2D inverse Fourier transform (2D-IFT) was applied to create complex images. The phase images with displacement encoded in each orthogonal direction were then reconstructed and corrected for background phase error using the phase reference images. A quality-guided path following spatiotemporal (two spatial dimensions and time) phase-unwrapping algorithm²² was applied to the pixels within the boundary of the brain tissue, in which a seed point was selected at the center of the brain tissue on the first cardiac phase assuming no phase wrap occurred at the initial time, and a measure of phase “quality” was then used to guide the path of unwrapping from pixel to pixel. Dividing the unwrapped phase value of each pixel by the displacement encoding frequency then directly yielded the displacement of this pixel relative to the time when the displacement encoding was initiated. The 2D Eulerian displacement of each pixel was computed by means of vector addition of the displacement of the two orthogonal one-dimensionally

displacement-encoded data sets. The pixelwise Lagrangian displacement trajectories were then calculated for all the pixels which were on the first cardiac phase using vector-interpolation tissue tracking.²² To be specific, the vectors in 2D Eulerian displacement field have heads at the centers of the pixels at t_n and tails originating from the positions of these tissue points at t_0 . Considering any point of interest in the tissue at t_0 that we want to track, for a given cardiac phase three vector tails closest to this starting position can be identified. Two-dimensional distance-weighted linear interpolation with these three vectors yielded an estimate of the vector stemming from the selected starting point that we are interested in to the position on this given cardiac phase. A frame-by-frame position trajectory can then be generated using this means. Cine-DENSE displacement measurements at each cardiac phase are independent, which is suited to temporal fitting. The accuracy of the estimate of a point's position can be improved based on its estimated positions at preceding and/or following cardiac phases.²² As a periodic descriptor, Fourier basis function has been suggested for fitting cardiac motion because of its natural periodic behavior.²³ Therefore, the temporal fitting of each pixel was done using the Fourier basis functions²³

$$f_{\text{Fourier}}(t) = \frac{1}{2}h_0 + \sum_{i=1}^{\infty} h_i \cos(i\omega t) + \sum_{i=1}^{\infty} b_i \sin(i\omega t), \quad (1)$$

where h_i and b_i are the Fourier series coefficients, $\omega = 2\pi/T$ is the angular frequency, and T is the cardiac period. In practice, only h_i and b_i ($i=0, \dots, 5$) need to be calculated, since it has been shown that the energy of cardiac motion is largely contained within the first five harmonics.²³ Applying the above tissue tracking and temporal fitting processes to all pixels for all cardiac phases generated the pixelwise Lagrangian displacement trajectories.²² To facilitate the visualization of the small motion of the brain (on the order of submillimeters), color-coded displacement maps were generated in two orthogonal directions.

Quantitative analysis of displacement for selected ROIs was performed only for the sagittal images of each subject. First, absolute 2D displacement (Displacement_{2D}) is calculated pixelwisely as

$$\text{Displacement}_{2D} = \sqrt{\text{Displacement}_{AP}^2 + \text{Displacement}_{CC}^2}, \quad (2)$$

where Displacement_{AP} and Displacement_{CC} are the displacements of the pixel in the anterior-posterior (AP) and cranial-caudal (CC) directions, respectively. Second, the mean 2D displacement of each ROI was calculated and plotted as a function of time, from which the peak 2D displacement and time to peak were determined.

III. RESULTS

Phase-reconstructed DENSE images, as shown in Fig. 2, demonstrate the transition of pulsatile motion from brain stem region to peripheral brain lobes after the R wave of ECG. Figure 3 shows an example of the color-coded La-

FIG. 2. Example of phase-reconstructed DENSE images in a healthy volunteer (subject 1). Left: MR magnitude image. Brain tissue appears white, and CSF appears gray. Right: Phase-reconstructed DENSE images acquired at multiple time points after the R wave. The time interval between two neighboring cardiac phases is 102 ms. Displacement was encoded in the horizontal direction in the top row and in the vertical direction in the bottom row.

grangian displacement maps of the brain, where intracranial structures exhibited characteristic motion amplitude, motion direction, and motion pattern. CSF can be easily identified in the displacement maps as it typically moves in different directions as the surrounded intracranial structures. For example, CSF in the prepontine cistern and interpeduncular cistern moves superiorly while the midbrain moves inferiorly. Small intracranial structures, such as the posterior cerebellomedullary cistern, chiasmatic cistern, fourth ventricle, and confluence of the sinuses, can also be identified in the displacement maps by the characteristic motion patterns of the surrounding CSF. Major brain fissures are clearly visible in these displacement maps presumably (especially in the frontal lobe) because of the high sensitivity of DENSE MRI to the small differences in motion between the cerebrum

and its surrounding CSF. Example motion trajectories of a nine-pixel ROI marked in Fig. 3 within the pons are shown in Fig. 4.

Time-resolved displacement maps illustrate the motion of the brain at multiple cardiac phases after the R wave, as shown in Fig. 5. Changes in displacement magnitude and direction of the intracranial structures throughout the cardiac cycle are evident. It can be seen that the pulsatile motion originates from brain stem and attenuates toward the periphery, in good agreement with the literature.^{9,16} The largest motion in the brain stem occurs approximately 250–300 ms after the R wave, most likely caused by the CSF bulk flow from the third to the fourth ventricle which occurs 200 ms after the R wave.²⁴

FIG. 3. Magnitude image and colored displacement maps of the brain in the middle sagittal plane (top row, from subject 2) and in the coronal plane (bottom row, from subject 3) at 340 ms after the R wave. The directions of the motion are indicated by the arrows. (Square box in the top left image is a nine-pixel region to be shown in Fig. 4.)

FIG. 4. The pixelwise motion trajectories in a nine-pixel region within the pons (corresponds to the square box in the sagittal proton image in Fig. 3). The black dots indicate the initial positions at the first cardiac phase, with the resulting trajectories in lighter black curve. The scale of the motion amplitude with respect to the pixel size is modified for better visualization.

Figure 6 shows the 2D displacement as a function of time after the R wave for the selected ROIs. Table I summarizes the measurements of peak 2D displacement and time to peak of all subjects. Brain motion in the three healthy volunteers is generally small with peak displacement less than 0.3 mm. The largest intracranial motion occurred in the optic chiasm with peak displacement of 0.24 mm, followed by brain stem (midbrain, pons, and medulla) with peak displacements approximately 0.20 mm. The smallest intracranial displacement occurred in the occipital lobe (0.04 mm), followed by cerebellum (0.07 mm) and frontal and parietal lobes (0.09 mm). The measurements of time to peak of different ROIs revealed the propagation of the pulsatile motion through the upper central nervous system. Time to peak is between 250 and 300 ms for the brain stem, approximately 350 ms for the optic chiasm, and 450–500 ms for the peripheral brain lobes. These results are consistent with previous studies that showed the transition of pulsatile motion from brain stem region to peripheral brain lobes.

IV. DISCUSSION

These preliminary results demonstrated that spiral cine-DENSE MRI, in combination with auto-tissue-tracking, can be used for the quantitative assessment of brain motion during the cardiac cycle with high temporal/spatial resolution and sensitivity. The pixelwise dynamic displacement maps clearly revealed the cardiac-synchronized motion of the intracranial structures. Measurements of peak displacement and peak to time for selected ROIs were consistent with previous literature.^{9,19} Brain tissue motion was observed to be generally small (less than 0.1 mm) in healthy volunteers. This magnitude of motion less likely affects diffusion imaging of the brain, which agrees with the observations from earlier studies.^{13,14} The high sensitivity to motion of the spiral cine-DENSE MRI technique makes it a potential powerful tool to measure motion of very small intracranial structures, such as trigeminal nerve, pituitary gland, and optical nerves.

Spiral cine-DENSE MRI can be used to measure the cardiac-synchronized pulsatile motion of the spinal cord, which can be significantly greater than that of the brain. It has been reported that the pulsatile spinal cord velocities go up to 12.40 ± 2.92 mm/s at the cervical and upper thoracic levels, while the brain stem has a maximum velocity of 1.3 ± 0.4 mm/s.^{3,10,11} This suggests that the maximum spinal cord motion can be much greater than that of the brain stem, possibly on the order of five times. Our experience with only a few healthy volunteers (data not shown) revealed that the maximum displacement of the cervical spinal cord is approximately 1.0 mm and at the C5–C7 levels. This magnitude of cord motion can affect the diffusion imaging of the cord, which has been observed by other researchers.^{13,14} DENSE MRI can potentially improve the diffusion imaging of the cord by extracting cardiac-synchronized cord motion information and incorporating it into diffusion imaging. In addition, displacement of the spinal cord on the order of millimeters can be clinically significant in SRS treatment for spinal cord metastases. In a recent study, Chang *et al.* found

FIG. 5. Dynamic displacement maps of the brain of a healthy volunteer (subject 2) at multiple cardiac phases from the R wave of ECG. The time interval between two neighboring cardiac phases is 102 ms. Displacement was encoded in the horizontal direction in the top row and in the vertical direction in the bottom row.

FIG. 6. Example of displacements as a function of time after the R wave for selected ROIs in the midsagittal plane (from subject 2). A total of 18 cardiac phases after the R wave of ECG were acquired in this example.

that a 3 mm positioning error could result in a doubling of the dose to the spinal cord.²⁵ In addition, Uftring *et al.* found that the vascular pulsations tend to cause greater spinal cord movements in the older subjects than in the younger ones using dynamic phase contrast MRI.²⁶ Considering that most of the cancer patients are elderly people, spinal cord motion in this group could be significantly greater than that in healthy subjects.

There are several limitations to this study. First, an immobilization device was not used to minimize the subjects' head motion. Our assumption of no head motion thus largely depends upon the subjects' cooperation level. Future investigations with appropriate head immobilization devices are desired to further improve the accuracy of measurement. Second, the current technique does not have sufficient spatial resolution to resolve accurate motion information of some small intracranial structures because of the partial-volume effect. Spatial/temporal resolution and sensitivity of the spiral cine-DENSE MRI technique can be improved in higher magnetic field which intrinsically provides increased SNR

and longer T1, although the field inhomogeneity in higher magnetic field may pose a challenge, leading to potential image blurring in spiral imaging. The SNR in our current technique is in the range of 5–20 depending on the cardiac phase. An increase of three- to fivefold in SNR will enable us to achieve the spatial resolution of submillimeters with adequate signal to reveal very small intracranial structures such as trigeminal nerve, pituitary gland, and optical nerves. Third, the current study only involved healthy volunteers. Future investigations on patients with brain disorders are desired since the magnitude of displacement can be altered by the patient's age, pathophysiological conditions, presence or absence of prior decompressive surgery, etc. There is a great lack of such information in the literature. In addition, intracranial motion may change dramatically after a decompressive surgery of the head or spine. The magnitude of the spatiotemporal displacements can be potentially significant to the SRS of the central nervous system in such patients. DENSE MRI can be potentially used to improve SRS treatment on these selective patients by providing motion information of the target and sensitive structures. Since MRI scans have already been commonly performed and used in SRS treatment planning to facilitate target delineation, an additional DENSE MRI scan can be added to the protocol without much extra effort.

TABLE I. Measurements of peak 2D displacement and time to peak for selected regions of interest. The results were shown as mean $\pm$ standard deviation (STD).

	Peak 2D displacement (mm)	Time to peak (ms)
Frontal lobe	0.09 $\pm$ 0.05	486 $\pm$ 99
Parietal lobe	0.09 $\pm$ 0.06	476 $\pm$ 144
Occipital lobe	0.04 $\pm$ 0.01	457 $\pm$ 68
Cerebellum	0.07 $\pm$ 0.03	259 $\pm$ 77
Optic chiasm	0.24 $\pm$ 0.04	349 $\pm$ 80
Midbrain	0.17 $\pm$ 0.08	298 $\pm$ 56
Pons	0.15 $\pm$ 0.07	293 $\pm$ 51
Medulla	0.21 $\pm$ 0.06	272 $\pm$ 96

V. CONCLUSIONS

In summary, we have demonstrated that the spiral cine-DENSE MRI technique can be used to measure brain motion during the cardiac cycle on the pixel-by-pixel basis with high temporal/spatial resolution and sensitivity. This technique may lend new insight into the brain motion and provide useful information to improve the SRS treatment of brain disorders.

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