In Vivo Simultaneous Acquisition of Diffusion Tensor Imaging (DTI) and MR Elastography (MRE) in Mouse Brain

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Introduction: MRE and DTI have become very useful in the clinic as noninvasive imaging tools to distinguish normal from diseased tissues via different contrast mechanisms.[1, 2] They represent MRI techniques that involve the application of motion sensitizing and diffusion sensitizing gradients. In MRE, mechanically introduced intravoxel coherent motion is encoded into the phase of the MR signal, which enables assessment of diagnostically relevant tissue stiffness.[3] DTI is sensitive to direction-dependent intravoxel incoherent motion of water molecules, and enables visualization of tissue anisotropy for the diagnostic assessment of conditions, in which anisotropic tissue structure changes. In recent studies, the joint inversion of (separately acquired) DTI and 3D-vector field MRE information allows the assessment of structural anisotropy and viscoelasticity of cerebral tissues.[4, 5] This motivated the development of a technique for concurrent MRE and diffusion acquisition (dMRE),[6] which we extend here as a full 3D-vector field MRE and DTI acquisition implemented in the mouse brain *in vivo*.

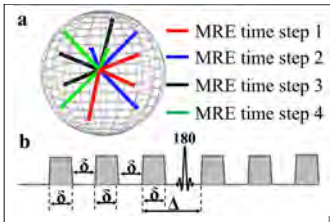

Fig. 1. a) Linking of DTI directions with MRE time steps. b) Advanced gradient waveform applied in the current study.

Methods: *DTI-MRE Gradient Encoding Scheme*: The simultaneous encoding of MRE and diffusion data first requires linking the timing of diffusion/motion-sensitizing gradients (dMSGs) with the diffusion time Δ and the MRE mechanical vibration period T as previously described by Eq. (1): $\Delta = nT + \delta(n = 1,2,3,...)$, where δ is the dMSG lobe duration.[6] The simultaneous encoding of a 3D-vector field MRE and DTI is then achieved by designing a particular gradient encoding scheme with the application of a series of dMSGs in non-collinear and non-coplanar directions. Specifically, N gradient directions are chosen for DTI, which are uniformly distributed in 3D space,[7] and then are clustered into N_{TS} ($N=3N_{TS}$, $N_{TS}\geq 2$) groups according to the criterion given in Eq. (2): $\min \sum_{p=1}^{N_{TS}} \left(\left| e_1^p \cdot e_2^p \right| + \left| e_1^p \cdot e_3^p \right| + \left| e_2^p \cdot e_3^p \right| \right)$ where $\boldsymbol{e}_j^p$ is a unit vector assigned to each direction with j = 1,2,3, and p = 1,2…N_{TS}. N_{TS} is the number of sets of three linear independent gradient vectors that corresponds to the number of MRE time steps. The time offset τ between the mechanical vibration and the start of the dMSG is set to 0, $(1/N_{TS})$T, $(2/N_{TS})$T, …, and $((N_{TS}-1)/N_{TS})$T for the gradients in group 1, 2, …, N_{TS}, respectively. However, this order can be permuted. Figure 1a illustrates one set of suitable gradient vectors (12 directions, N_{TS} = 4) used in this study. *Imaging Acquisition and Processing*: The DTI-MRE method was applied to an adult female C57BL-6 black mouse using a 9.4 T Agilent animal scanner and a 39-mm diameter quadrature coil. A custom-built bite bar shaker was designed to induce the mechanical shear waves inside the brain. FSE-based DTI-MRE acquisition was performed for each of the twelve gradient directions using a triple-trapezoid gradient waveform at a vibration frequency of 800 Hz (Fig. 1b). Images were collected beginning with one reference scan without dMSG (b = 0 s/mm^2) followed by four sets of DTI-MRE with b = 983 s/mm^2. The second repetition was done using a reversed gradient waveform to acquire phase difference images. The acquisition parameters were: TR/TE = 1000/20.6 ms, δ/Δ = 0.625/11.875 ms; dMSG strength= 600 mT/m; FOV = 24 × 24 mm^2, slice thickness = 1 mm, 8 slices, matrix size = 128 × 128; ETL = 4. Using four averages, approximately 54 min of imaging time were required for DTI-MRE measurements. For comparison, conventional MRE and DTI experiments were performed while maintaining the same acquisition parameters except that (1) in MRE, the three gradient vectors at each of the four time steps were oriented the same as in time step 3 of DTI-MRE, and (2) DTI was performed without vibration. The total acquisition time for the two separate acquisitions were 79 min. The fractional anisotropy (FA) maps were calculated by using DTI Studio Software. For MRE analysis, one snapshot of the 3D displacement at each time step (corresponding to a specific group p) was taken from the MR phase images. All displacements were transformed to a Cartesian coordinate system. Complex wave images were calculated from the transformed, temporally resolved displacements. The curl was applied to the noise filtered wave images and subsequently the complex shear modulus was determined by algebraic inversion.[8] Spatial averaged values were calculated within the 2 central slices of the brain ROI and the Spearman correlation coefficient between DTI-MRE and MRE was determined within the whole brain ROI for all components of the complex wave images.[9]

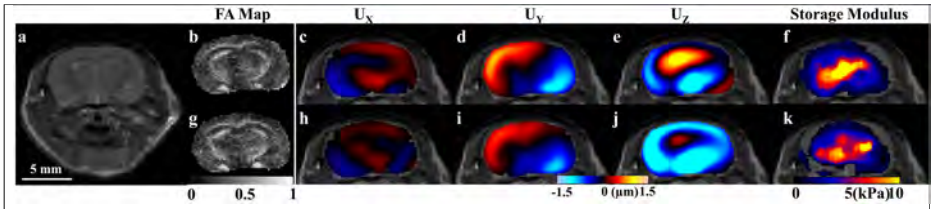

Fig. 2. *In vivo* cerebral DTI-MRE in comparison to conventional acquisitions: (a) Diffusion T2W image acquired from DTI-MRE. FA map acquired from DTI-MRE (b) and from DTI (g). Three components of the complex displacement image (real part) and storage modulus acquired from DTI-MRE (c, d, e, f), and from MRE (h, i, j, k).

Results: Figure 2 shows the comparison of the results acquired from DTI-MRE (top) and conventional DTI and MRE (bottom). FA maps from DTI-MRE and conventional DTI are shown in Figs. 2b and 2g, respectively. The averaged FA values of the corpus callosum based on all pixels within the selected ROIs were (0.66 ± 0.10) and (0.64 ± 0.11) for DTI-MRE and conventional DTI, respectively. The corresponding three components of the complex displacement image acquired from DTI-MRE are shown in Figs. 2c-e, while the displacement images obtained from conventional MRE are displayed in Figs. 2h-j. The spatially averaged values for the storage and loss modulus in MRE (DTI-MRE) were 4.28 (4.36) kPa and 3.07 (3.28) kPa, respectively. The wave images acquired with MRE and DTI-MRE are highly correlated with a Spearman correlation coefficient of 83.5%, 81.2% and 89.8% for the x, y and z-displacement, respectively.

Discussion and Conclusion: DTI-MRE enables the simultaneous acquisition of DTI and MRE data. These *in vivo* results showed a good correspondence between DTI-MRE and the conventional DTI and MRE methods. The simultaneous acquisition can reduce the scan time by up to 50% and allow immediate co-registration of elastogram and diffusion maps, and hence may facilitate the characterization of structural anisotropy and viscoelasticity of biological tissues. While the presented results in *in vivo* mouse brain indicate no interference between MRE and DTI acquisitions, the *in vivo* feasibility of DTI-MRE in human subjects needs to be verified in future studies.

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