New Pulse Sequence Combining Diffusion MRI and MR Elastography (dMRE)

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Target Audience: Clinicians and researchers applying both diffusion-weighed MRI and MR elastography (MRE) for the detection and characterization of pathology in the brain and liver will find this new technique useful for concurrent MRE and diffusion MRI.

Introduction: MRE measures tissue stiffness, which reflects the underlying structural organization of cells, extracellular matrix, and capillaries. Diffusion MRI measures the apparent diffusion coefficient (ADC), which describes the random motion of water molecules in both the intra- and the extra-cellular compartments. Both MRE and diffusion MRI are used for detecting diseases in soft biological tissues such as the brain, liver, and other internal organs.[1-3] Therefore, the combination of MRE and diffusion MRI may provide complementary information on the changes of tissue cellularity and structure associated with pathology. Several studies have shown the potential of combining MRE with diffusion MRI for assessing liver diseases, and for measuring the anisotropic viscoelasticity of gel phantoms and human brains.[4-6] These studies, however, used separate acquisitions of MRE and diffusion that prolong the imaging protocols. Here, we introduce a new pulse sequence, Diffusion-MRE (dMRE), that is capable of encoding diffusion attenuation and MRE wave motion simultaneously.

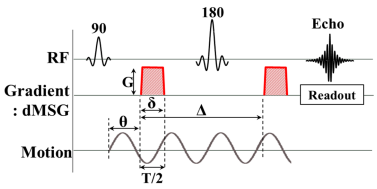

Fig. 1. An example for the arrangement of the dMSGs in dMRE. The dMSGs can be applied along any desired axis, as shown by the shaded regions. The timing parameters are set as described in Eq. (1) to allow the simultaneous encoding.

Methods: ***Theory and sequence development*** The dMRE pulse sequence was developed with two symmetrical diffusion/motion-sensitizing gradients (dMSGs) placed on each side of the 180° refocusing pulse for both motion-sensitization and diffusion encoding. The sequence timing is adjusted so that the bipolar gradients are sensitive to both coherent and incoherent intravoxel motion, i.e. the diffusion time Δ must satisfy a time constraint given by Eq. (1): $\Delta = nT + \delta (n = 1,2,3,...)$. The period of the harmonic motion is denoted with T and δ is the gradient duration. Fig. 1 shows an example for the arrangement of the dMSGs in dMRE. In this scenario, the harmonic motion only causes a phase change of the MR signal while diffusion only leads to the signal attenuation. Thus, in dMRE, shear wave motion and diffusion attenuation can be encoded simultaneously and detected separately in the phase and in the magnitude of the MR signal. In addition, the shape, number, and duration of the dMSG lobes can be adjusted to allow for the flexibility of the encoding efficiency, and thus sensitivity to MRE and diffusion.

Phantom study The dMRE method was validated in a phantom study (n = 3) using a 9.4 T Agilent animal scanner and a 39-mm diameter quadrature coil. The phantoms consist of a gel bead (1.5 cm diameter) embedded in a gel mixture of agarose (0.75% *w/v*) and gelatin (4% *w/v*) in a cylindrical plastic container. The gel-filled container (ID = 30 mm) was mechanically driven by a piezo-actuator with 500 Hz frequency. A 2D SE-based dMRE sequence was used with the following imaging parameters: TR/TE = 1000/42 ms; δ/Δ = 1/31 ms; FOV = 4 cm; axial imaging plane; slice thickness = 2 mm; matrix size = 128×128; 4 time steps; 5 b-values. At each time step, four different gradient amplitudes (218, 312, 509, and 727 mT/m) were employed to achieve four b-values (100, 200, 500, and 1000 s/mm^2). A B_0 image (b = 0) was acquired with zero gradient amplitude. For comparison, conventional MRE and diffusion experiments were performed using a SE-MRE sequence and a SE-diffusion sequence, respectively, while maintaining the same acquisition parameters. The SE-MRE sequence is identical to the dMRE sequence except for that the gradient amplitude was kept constant (400 mT/m) at each of four time steps, corresponding to b = 347 s/mm^2. The SE-diffusion measurement was performed without vibration. In all experiments, the dMSGs were applied along the slice direction, which represents the principle direction of vibration in our experimental setup. The ADC maps were created using a non-negative least squares (NNLS) mono-exponential fit analysis on a pixel-by-pixel basis. Wave images were analyzed with the local frequency estimation algorithm to generate shear stiffness maps.[7] It should be noted that in dMRE, the accumulated MR signal phase was compensated by the different encoding efficiency in each time step. The mean values were reported from ROIs drawn in Fig. 2.

Results: The diffusion-weighted image and the MRE wave image acquired with the dMRE method are shown in Fig. 2a and 2b. The corresponding ADC map and shear stiffness map are shown in Fig. 2c and 2d. The averaged ADC values (n = 3) for selected ROIs in the beads were (1.75 ± 0.16) μm^2/ms and (1.74 ± 0.16) μm^2/ms for SE-diffusion and dMRE methods, respectively. The averaged shear stiffness values (n = 3) in the beads over the same ROIs, were (2.45 ± 0.23) kPa and (2.42 ± 0.20) kPa for SE-MRE and dMRE, respectively. In all dMRE experiments, we observed no interference between the MRE and the diffusion acquisitions.

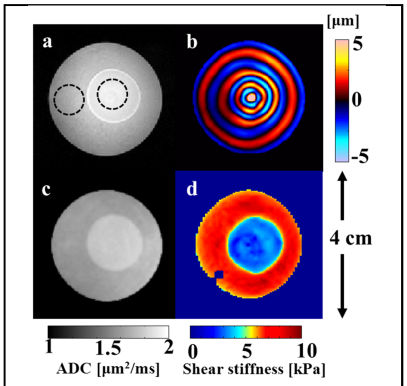

Fig. 2. The results obtained from the dMRE measurement: (a) the diffusion-weighted image (b-value = 500 s/mm^2); (b) the wave image; (c) the ADC map; (d) the shear stiffness map.

Discussion and Conclusion: We introduce a new pulse sequence (dMRE) that provides simultaneous acquisition of MRE and diffusion MRI. The phantom results showed a good correspondence between dMRE and conventional MRE/diffusion methods. The simultaneous acquisition will reduce the scan time and allow immediate co-registration of elastogram and diffusion maps, and hence facilitate combined clinical applications. The time saving factor can be up to 44% depending on the specific pulse sequence design. In addition to the traditional trapezoidal waveform used in the presented study, the dMSGs can be replaced by other waveforms, e.g. an oscillating waveform with one and a half lobes on each side to enhance the MRE encoding efficiency, or a camel-shaped waveform with only two positive lobes to increase the diffusion weighting b-factor. In general, the dMRE approach is not limited to specific directions, frequencies or sequence types. Although we observed no major deleterious interference in phantom experiments, dMRE must be more completely studied, and we are now in the process of implementing it on a human clinical scanner.

References: 1. Glaser KJ, *et al.*, J Magn Reson Imaging. 2012;36:757-74. 2. Horsfield MA, *et al.*, NMR Biomed. 2002;15:570-577. 3. Taouli B, *et al.*, Radiology. 2010;254:47-66. 4. Wang Y, *et al.*, AJR Am J Roentgenol. 2011;196:553-61. 5. Romano A, *et al.*, Magn Reson Med. 2012;68:1410-22. 6. Qin EC, *et al.*, J Magn Reson Imaging. 2013;37:217-26. 7. Knutsson H, *et al.*, Image Processing Proceedings. ICIP-94., IEEE International Conference. 1994.
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