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FREE-BREATHING IN VIVO MAGNETIC RESONANCE ELASTOGRAPHY OF MOUSE LIVER: PROSPECTIVE VS RETROSPECTIVE SYNCHRONIZATION.

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Background: Magnetic Resonance Elastography (MRE) is a recognized non-invasive technique used to measure tissue stiffness, particularly in cases of liver fibrosis[1], [2]. In clinical settings, MRE acquisitions are performed during the expiratory phase of apnea. However, apnea can be challenging for patients, leading to relatively high rates of technical errors thus hindering the development of MRE in clinical practice [3]. Free-breathing techniques [4] have recently been proposed as an alternative to apnea. In the preclinical field, MRE experiments are essential for developing new acquisition methods, such as optimal control MRE [5]. Effective MRE experiments in mice require precise synchronization with their rapid respiratory cycle. Integrating mouse respiration into MRE methods could improve clinical translation and reduce technical failures.

Aims: To compare the performance of a retrospective Intradate© (IG) Gradient Echo (IG FLASH MRE) and a prospective (a triggered FLASH MRE) free-breathing *in vivo* liver MRE acquisition on mouse.

Methods: One healthy female mouse (C57BL/6) was examined following ethical approval and adherence to institutional animal care guidelines. The mouse was anesthetized with 2% isoflurane in an air/oxygen mixture via a nasal cone and its respiratory rate and body temperature were monitored and maintained throughout the experiment. The FLASH MRE sequence is trigger-based, initiating data acquisition in real-time via an external sensor monitoring the animal's breathing cycle. This ensures consistent data acquisition at the desired phase of the respiratory cycle, thereby enhancing image quality and minimizing motion artifacts. The IG FLASH MRE sequence continuously acquires an oversampled k-space and retrospectively sorts the acquired data using the IG navigation signal provided by Bruker. This self-gated sequence results in an increased acquisition time (TA) due to the user-defined oversampling. MRE acquisitions were conducted using a 7T MRI system (Bruker, Germany), with a slice thickness of 1 mm and motion encoding in the slice direction, at frequency acquisitions of 300, 400 and 600Hz, with acquisition parameters detailed in Table 1. For each frequency, 4 equally distributed phase-steps were acquired. Subtraction of phase images and removal of static phase offsets were performed using 2 acquisitions with opposite MEG polarity. Displacement fields were obtained through unwrapping and Fourier transformed to isolate desired frequency information. Directional and spatial filtering techniques were applied for noise reduction. Finally, storage modulus G' maps, representing tissue elasticity, were extracted using the Algebraic Inversion of the Differential Equation (AIDE) algorithm [6].

Results: The magnitude, phase images, and elastograms (Figure 1) were analyzed and compared for all frequencies. Table 1 shows the measured SNR and the mean and standard deviation of G' values in the ROI, placed within the same liver area. The SNR varies slightly with excitation frequency due to differences in TE/TR values, and is possibly also affected by the variability of the mouse's respiratory motions during acquisitions. The G' values were found to be similar regardless of the acquisition technique used.

Conclusions: The obtained results confirm the efficacy of our IG FLASH MRE method in assessing liver stiffness at multiple frequencies. Although the mean G' values are very close for both acquisition methods, IG FLASH MRE acquisitions exhibit lower standard deviations, which is an interesting outcome. Furthermore, multi-frequency acquisitions allowed to observe the dispersive behavior of mouse liver. In parallel, employing a retrospective respiratory synchronization acquisition method like IG FLASH MRE ensures dynamic equilibrium of the magnetization. SNR is satisfactory for both methods. The next step involves validating the IG FLASH MRE method by acquiring data from a cohort of mice and conducting test-retest experiments to evaluate the reproducibility of the developed method.

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References: [1] J. Chen *et al.*, *Alcoholism Clin & Exp Res*, 2021, [2] S. Hoodeshenas *et al.*, *Top. MRI*, 2018, [3] SL Choi *et al.*, *Eur. Radiol*, 2020, [4] M. Shahyari *et al.*, *MRM*, 2021, [5] P. Sango-Solanas *et al.*, *Scientific Rep.*, 2022, [6] Oliphant *et al.*, *MRM*, 2001

Table 1

| MRE Sequence | F _{exc} (Hz) | TR (ms) | TE (ms) | Flip Angle (°) | Matrix (pix ²) | FOV (mm ²) | TA | G' (kPa) ± SD | SNR |
|--------------|-----------------------|---------|---------|----------------|----------------------------|------------------------|-------|---------------|-------|
| FLASH | 300 | 120.16 | 5.82 | 22 | 128 x 128 | 35 x 35 | 2'30" | 2.1 ± 0.43 | 58.92 |
| | 400 | 121.01 | 4.99 | 22 | 128 x 128 | 35 x 35 | 2'30" | 2.47 ± 0.62 | 60.71 |
| | 600 | 78.16 | 5.82 | 22 | 128 x 128 | 35 x 35 | 1'35" | 5.06 ± 0.72 | 57.46 |
| IG FLASH | 300 | 85.34 | 4.82 | 22 | 96 x 96 | 35 x 35 | 7'55" | 2.1 ± 0.38 | 83.24 |
| | 400 | 67.01 | 3.99 | 22 | 96 x 96 | 35 x 35 | 6'20" | 2.33 ± 0.4 | 77.15 |
| | 600 | 50.51 | 4.82 | 22 | 96 x 96 | 35 x 35 | 5'05" | 4.95 ± 0.53 | 76.22 |

Figure 1

