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Tabletop magnetic resonance elastography for the measurement of viscoelastic parameters of small tissue samples

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ABSTRACT

We demonstrate the feasibility of low-cost tabletop MR elastography (MRE) for quantifying the complex shear modulus G^* of small soft biological tissue samples as provided by pathologists. The MRE system was developed based on a tabletop MRI scanner equipped with a 0.5 T permanent magnet and a tissue sample holder mounted to a loudspeaker. A spin echo sequence was enhanced with motion-encoding gradients of 250 mT/m amplitude synchronized to acoustic vibration frequencies. Shear wave images suitable for elastography were acquired between vibration frequencies of 0.5 and 1 kHz in agarose, ultrasound gel, porcine liver, porcine skeletal muscle, and bovine heart with a spatial resolution of 234 μm pixel edge length. The measured frequency dependence of G^* agreed well with previous work based on high-field MR systems. The ratio between loss and storage moduli was highest in liver and ultrasound gel, followed by muscle tissue and agarose gel while ultrasound gel and liver showed similarly low storage moduli compared to the other samples. The shear wave to noise ratio is an important imaging criteria for MRE and was about 4.2 times lower for the preliminary setup of the 0.5 T tabletop system compared to a 7 T animal scanner. In the future, the new tabletop MRE system may serve as a low cost device for preclinical research on the correlation of viscoelastic parameters with histopathology of biological samples.

1. Introduction

Magnetic resonance elastography (MRE) [1,2] is a non-invasive medical imaging modality that depicts the viscoelastic properties of soft body tissue for diagnostic purposes. Various studies have demonstrated the high sensitivity of MRE to diseases including hepatic fibrosis [3–6], heart diseases [7], neurological disorders [8–12], and tumors [13–18].

Sensitivity of viscoelastic constants to pathological tissue alterations arises from the hierarchical organization of mechanical structures in biological tissue. Specifically, the effective shear modulus of biological soft tissue is determined by architectural properties across a continuum of scales from cellular to macroscopic dimensions [19,20]. It has been shown that wideband MRE combining multiple drive frequencies provides similar shear modulus values as compared to oscillatory rheometry which is an established method for studying the topology of viscoelastic networks [21,22]. Nevertheless, it remains a major goal of elastography to identify the relationship between tissue structure and macroscopic viscoelastic parameters towards the analysis of tissue structures by in vivo imaging. Therefore, effort has been invested in performing MRE of tissue samples and animal disease models in order to facilitate a correlation between MRE and histology [23–28]. For example wideband MRE on human liver samples has revealed that fibrogenesis is associated with the replacement of soft and densely linked viscoelastic networks of healthy liver by sparsely cross-linked rigid fibers [29]. Other mechanical test methods for micro samples of biological tissue or single cells such as atomic force microscopy (AFM) or optical stretcher aim at the mechanics based quantification of tumor malignancy [30–32].

Abbreviations: AFM, atomic force microscopy; MEG, motion-encoding gradient; MRE, magnetic resonance elastography; FOV, field of view; ROI, region of interest; SE, spin echo; TE, time to echo; TR, time to repetition.

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So far, MRE of small tissue samples has been conducted using high-field MRI scanners [23–28,33,34]. An alternative MRE setup based on a 0.1 T electromagnet was described in Refs. [35,36], which, however, was not suitable for investigations of small tissue samples of only a few millimeters size. In contrast, a commercially available tabletop MRI device based on a permanent magnet and high-amplitude magnetic field gradients sensitive for small shear wave amplitudes may be used for MRE and could therewith establish an appropriate method for measuring bulk shear properties of small tissue samples.

Therefore, we introduce a tabletop MRE device operated at 0.5 T which is capable of measuring the viscoelastic properties of small biological soft tissue samples at low costs, with little space requirements and a high level of usability. The objectives of this study are (i) to demonstrate the feasibility of the tabletop MRE using small sample volumes typically available from pathology, (ii) to investigate gel samples and tissue specimen in a similar frequency range as previously applied by wideband MRE on a 7 T animal scanner [37], (iii) to give a first assessment of the sensitivity and resolution compared to a 7 T animal scanner, and (iv) to analyze which further developments are needed in order to disseminate tabletop MRE within biophysical and preclinical research labs.

2. Methods

2.1. Sample preparation

Sample preparation is demonstrated in Fig. 1. Bulk pieces of liver and muscle tissue obtained from a local abattoir were cut into cylindrical pieces of 30 mm length and 8 mm diameter. Muscle tissue was dissected carefully in order to assure that the predominant fiber direction was oriented along the cylinder axis leaving the plane of isotropy within the axial images (assuming transverse isotropy) [38]. Finally the samples were carefully transferred into cylindrical glass tubes closed at the bottom (length: 150 mm, inner diameter: 8 mm, outer diameter: 10 mm) using thin rubber sleeves (inner diameter: 0.5 mm, outer diameter: 1 mm) for ventilation. To prevent dehydration, the tissue samples were embedded into ultrasound gel (Sonogel, Bad Camberg, Germany). Pure ultrasound gel was analyzed later along with an agarose gel sample (2% hydrous solution) for their viscoelastic properties in comparison to the biological tissue samples.

2.2. MRE – mechanical stimulation

The glass tubes were connected to a carbon fiber rod by a plastic clamp which allowed the fine adjustment of tube position in the center of the magnet. The other end of the rod was mounted to the vibration coils of a pair of loudspeakers (Visaton, Haan, Germany) which were operated in an alternated position as shown in Fig. 2. Frequency and cycle number of the sinusoidal waveform were controlled by a function generator (Tektronix, Beaverton, OR, USA). The vibration signal was fed into an audio amplifier (Adam Hall, Neu-Anspach, Germany) and transmitted to the loudspeakers. The amplifier output was manually adjusted for each sample and vibration frequencies based on the displacement visible in the phase image of a test scan. The vibration was triggered by the pulse sequence with a transient forerun time corresponding to 20 vibration cycles for approximating stationary vibration conditions.

2.3. MRE – data acquisition

Experiments at low magnetic field were executed using a benchtop MRI scanner (Researchlab, Pure Devices GmbH, Würzburg, Germany) composed of a 0.5 T permanent magnet (MagSpec22 MHz, Pure Devices GmbH, Würzburg, Germany) and controlled by a research console (drivel, Pure Devices GmbH, Würzburg, Germany) exclusively operated with Matlab (Mathworks, Natick, MA, USA). A spin echo sequence implemented in Matlab was sensitized to motion by bipolar trapezoidal motion-encoding gradients (MEG) on both sides of the refocusing RF pulse. The MEG were applied in through-plane direction and synchronized to the vibration frequencies of f = 500, 600, 700, 800, 900 and 1000 Hz with 16, 18, 22, 26, 28, and 32 periods, respectively. The amplitude and slew rate of the MEG were 250 mT/m and 2000 T/m/s. A full wave cycle was captured at eight time points by delaying a trigger pulse by increments of $1/(8f)$ relative to the start of the MEG. Furthermore, the MEG polarity was toggled in each second scan for eliminating static phase offsets by subtracting the phase images with reversed MEG polarity [39] yielding a total of 16 images per frequency. The total scan time was about 8 – 25 min per vibration frequency depending on the repetition time (TR) which varied between 500 and 1500 ms for liver tissue and agarose gel, respectively. Further imaging parameters were: time to echo (TE): 40 ms; matrix size: 64 × 64; field of view

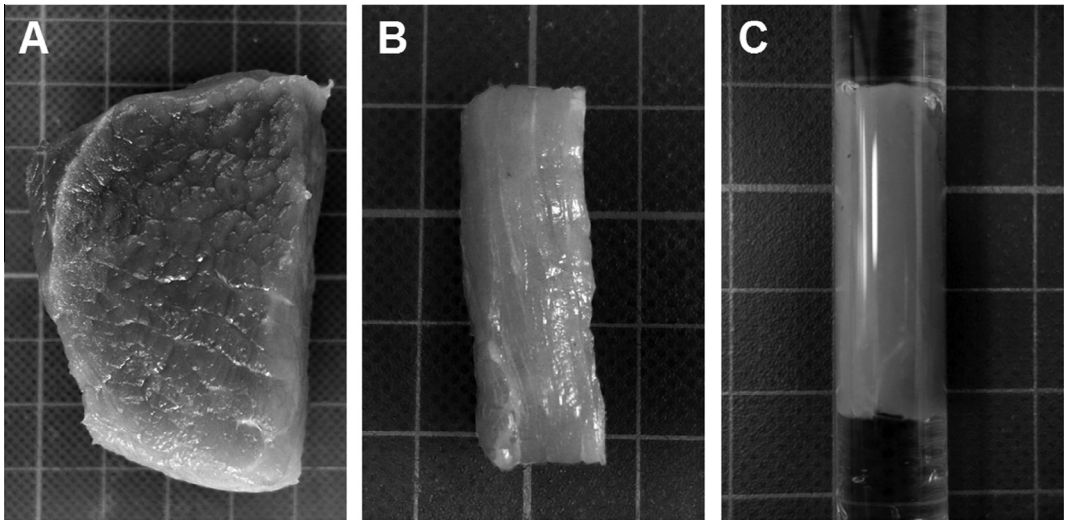

Fig. 1. Demonstration of tissue sample preparation using the example of porcine muscle. Starting from bulk pieces (A) the anisotropic tissue was cut in a way that the fiber direction was oriented parallel to the longitudinal axes of the cylindrical shaped sample (B) and then transferred into a glass tube (C). To prevent dehydration all tissue samples were covered with a layer of ultrasound gel.