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Preclinical multi-organ Magnetic Resonance Elastography (MRE) at 7T: an original piezoelectric actuator design with dedicated sequences

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1. Introduction

Magnetic Resonance Elastography (MRE) allows to non-invasively assess the *in vivo* mechanical response of soft tissues [Muthupillai et al. 1995] and has demonstrated clinical diagnosis effectiveness for cancerous and fibrotic tissues. MRE typically requires 3 elements: (**1**) **Excitation:** non-invasive generation of harmonic shear waves; (**2**) **Imaging:** MRI encoding of the displacement in the phase images; (**3**) **Reconstruction:** estimation of mechanical properties using image processing or inverse problem-solving methods.

The development of small animal MRE poses specific technical issues induced by the sample size (involving higher vibration frequencies) and the limited space available in preclinical systems. To date, very few teams have developed MRE devices for small animals using 3 main approaches: (A) an electromechanical actuator with a fiber rod [Tang et al. 2022]; (B) a piezoelectric actuator with a tooth bar [Clayton et al. 2011]; (C) an electromagnetic coil with a flexure arm, linked to a nut glued to the animal's head [Riek et al. 2012]. Piezoelectric actuators, although difficult to implement in such a small space, prove stable, easy to use and also unobtrusive. We propose a simple flexible original technical solution based on a piezoelectric vibrator with a small footprint for mouse MRE.

Various sequences have been used in the past for small animal imaging synchronized with the mechanical excitation (spin-echo SE [Clayton et al. 2011] but also gradient-echo FLASH [Riek et al. 2010]). To be applicable *in vivo* to a wide range of organs, we present here 2 sequences linked to the original vibration system: a first one relying on echo-planar imaging (EPI) sequence for rapidity purposes, and a second one based on a turbo SE sequence for artefact robustness.

2. Methods

2.1 Design of an original piezoelectric actuator

The pipeline has been developed on a small animal 7T MRI (*Bruker Biospin*, Germany). The vibration setup consists in several subassemblies (Fig 1A): (**1**) **The actuator to generate the vibrations.** The MR-compatible actuator is a multilayer piezoelectric plate (32x7x1mm^3) bender (*CMBP05, CTS* Denmark, red part) with a non-magnetic bender holder. The actuator is powered by an amplified (*NDR6220, CTS* Denmark) sinusoidal signal provided by a function generator triggered by the MRI sequence. (**2**) **The 3D-printed support** links the actuator to the animal bed (yellow, green and orange parts) with 3 degrees of freedom (black arrows in Fig 1A) to be able to accurately position the tip of the piston on a large set of organs in the animal. (**3**) **The piston** transmits actuator motions through a 3D printed transmission system. A volume coil and a 10 mm diameter surface coil positioned around the

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piston were used for MRI excitation and RF signal reception, respectively.

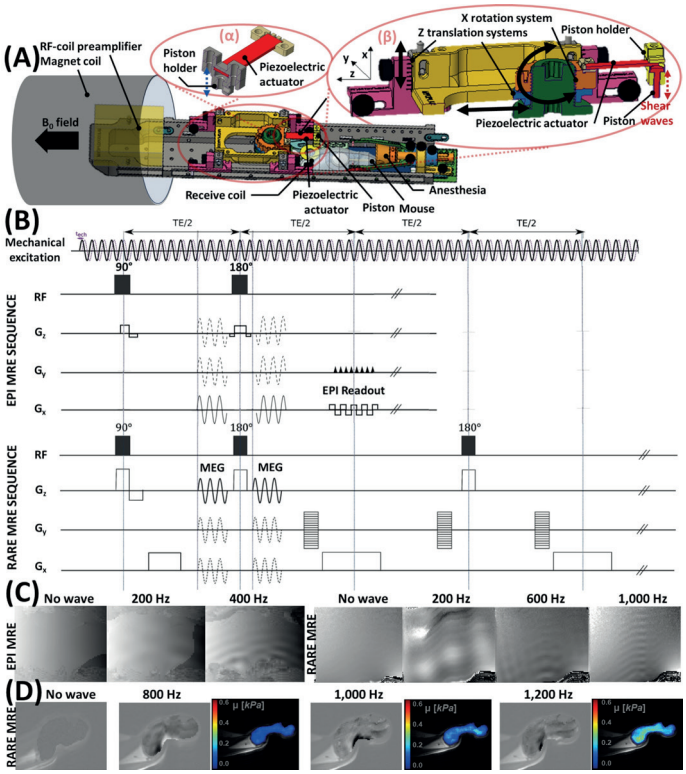

Figure 1. (A) Vibration setup: a multilayer piezoelectric bender with a piston (α) adjustable by a 3D-printed positioning (β). **(B)** Chronogram for the EPI and RARE MRE sequences. **(C)** Examples of post-processed wave images of gelatin phantoms by EPI and RARE sequences **(D)** Phase images and elastograms (shear modulus μ) in a mouse muscle.

Prior to investigation inside the MRI scanner, bench tests were carried out to determine the frequency, amplitude and thermal properties of the actuator as a function of the applied signal with a goal to obtain vibration amplitudes of a few tens of micrometers.

2.2 MRE sequences

Motion Encoding Gradient (MEGs) were added between excitation and signal acquisition in 2 different MRI sequences, detailed below. Then, MRI complex images are obtained and a 2D phase-unwrapping algorithm is then used on the phase images (fast cosine transform completed with a phase correction operation [Zhao et al. 2018]).

To achieve fast acquisitions, a single shot SE EPI sequence was first developed. A 2nd dedicated fast SE RARE (Rapid Acquisition with Relaxation Enhancement) sequence was developed (Fig 1B).

MEGs with sinusoidal or trapezoidal shapes, adjustable frequencies and amplitudes are synchronized with the mechanical excitation. The wave generator is triggered at the very beginning of each TR to achieve a steady-state wave propagation during the MEGs application period. Although requiring longer acquisition times than the EPI, the RARE sequence allows for a larger signal and robustness to physiological movements and susceptibility artefacts to increase the number of organs (*e.g.* skeletal muscles or concerned by physiological movements) targeted by our MRE protocol.

3. Results and discussion

Table 1 summarizes the acquisition parameters for the 2 MRE sequences applied in a 4% gelatin phantom. The wave images are obtained with the new vibrator and the developed chronogram for the RARE and EPI MRE sequences (Fig 1C). As an example, phase images acquisition and mechanical reconstruction using LFE (Local Frequency Estimator) are performed *in vivo* in a mouse skeletal muscle (Fig 1D).

Table 1. Main parameters for the 2 MRE sequences.

	f_0 [Hz]	T_R [s]	T_E [ms]	FOV [mm²]	Matrix
EPI	200-400	1	36.64	30x30	64x64
RARE	200-1200	1	7.75-10.7	23x23	140x140

Concerning the EPI sequence, resolutions of the order of 500μm are achieved with fields of view (FOV) of the order of a few centimeters and acquisition times below 1s. Thus non-invasive *in vivo* biomechanical studies of kinetic evolutions could be analyzed. Our approach is complemented by the RARE sequence, which, at the expense of acquisition time (~30s), enables to scan organs and areas prone to movement and susceptibility.

4. Conclusions

Thanks to this unique and compact device with associated MRE sequences, emphasizing either speed (EPI) or robustness to artefacts (RARE), we propose a powerful biomechanical measurement tool easily adaptable for the preclinical study of many organs, pathologies and mouse models.

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Conflict of Interest Statement

All authors declare that they have no conflicts of interest.

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