Comparison of viscoelastic property characterization of plastisol phantoms with magnetic resonance elastography and high-frequency rheometry

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Abstract— **This study aims at evaluating Magnetic Resonance Elastography (MRE) as a reliable technique for the characterization of viscoelastic properties of soft tissues. Three phantoms with different concentrations of plastisol and softener were prepared in order to mechanically mimic a broad panel of healthy and pathological soft tissues. Once placed in a MRI device, each sample was excited by a homemade external driver, inducing shear waves within the medium. The storage (G') and loss (G'') moduli of each phantom were then reconstructed from MRE acquisitions over a frequency range from 300 to 1,000 Hz, by applying a 2D Helmholtz inversion algorithm. At the same time, mechanical tests were performed on four samples of each phantom with a High-Frequency piezo-Rheometer (HFR) over an overlapping frequency range (from 160 to 630 Hz) with the same test conditions (temperature, ageing). The comparison between both techniques shows a good agreement in the measurement of the storage and loss moduli, underlying the capability of MRE to noninvasively assess the complex shear modulus G* of a medium and its interest for investigating the viscoelastic properties of living tissues. Moreover, the phantoms with varying concentrations of plastisol used in this study show interesting rheological properties, which make them good candidates to simulate the broad variety of viscoelastic behaviors of healthy and pathological soft tissues.**

I. Introduction

Changes in the mechanical properties of biological tissues can reveal the development of a pathology. This consideration has led to the development of elastographic techniques, such as Magnetic Resonance Elastography (MRE) or ultrasound elastography, that are dedicated to the investigation of these mechanical properties in vivo and noninvasively [1]-[2]. In MRE, shear waves are induced in the tissue of interest using an external driver. Tissue motion is encoded in phase images thanks to a motion-sensitive MR imaging sequence and these images are then processed to map and quantify the viscoelastic properties of the examined medium. Magnetic Resonance Elastography remains the object of many studies and is investigated for different organs, such as liver, brain or muscle [3]-[5].

Generally speaking, assessing new imaging methods involves the use of phantoms mimicking the properties of biological tissues. For elastography in particular, various types of phantoms (agarose [1], polyvinyl alcohol cryogel [6], plastisol [7]-[8], copolymer-in-oil [9]…) can be found in the literature, yielding a good range of elastic modulus. Deeper assessment can be performed by comparing the MRE results with either those of other elastographic techniques or with some reference mechanical tests [10]-[13]. However, it is usually quite difficult to compare the techniques in a common frequency range. For example, in Vappou *et al.* (2007) [10], rheometry measurements were performed up to 10 Hz, while MRE data were acquired for frequencies between 80 Hz and 140 Hz. Similarly, Ringleb *et al.* (2005) [12] presented MRE results measured at frequencies between 100 Hz and 200 Hz, complemented with dynamic mechanical analyses from 10 Hz to 50 Hz. The study realized by Okamoto *et al.* (2011) presents yet an overlapping frequency range: from 100 to 400 Hz for MRE and from 20 Hz to 200 Hz for dynamic shear test [13].

Working in a common frequency range allows a direct comparison of results: the purpose of this study is to present MRE and High-Frequency Rheometry (HFR) measurements in a common frequency range. Results are provided for three plastisol phantoms with different softener concentrations. These phantoms have indeed the main interest of presenting a viscoelastic behavior and are therefore good candidates to mimic biological tissues.

II. Materials and Methods

A. Preparation of phantoms

Three homogeneous phantoms were prepared with different concentrations of standard plastisol (which is a suspension of polyvinyl chloride particles in a liquid plasticizer) and softener (which is a di(*2*-ethylhexyl) adipate) (*Plastileurre Standard* and *Assouplissant, Bricoleurre, France*).

The combinations of liquid preparations were: phantom (A) 100% standard plastisol, (B) 75% standard plastisol – 25% softener, and (C) 50% standard plastisol – 50% softener. Each solution was heated to 160°C, poured into cubic molds (35 x 35 x 35 mm) for MRE and on aluminum foil so as to get thin samples as required for rheological tests. They were then cooled until the phantom solidified (about one hour).

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The phantoms were kept at room temperature (22°C). MRE and HFR experiments were performed one week after phantom preparation.

B. Magnetic resonance elastography data acquisition, image processing and data analysis

MRE experiments were run on a Bruker 4.7 T small animal MRI system. Phantoms were placed inside a volume coil for both radiofrequency emission and reception. The MRE sequence developed was a 2D gradient-echo sequence with the following parameters: repetition time = 250 ms, echo time = 20 ms, scan resolution = 128 x 128 pixels, field of view (FOV) = 4 x 4 cm, slice thickness = 3 mm. Four vibration phase offsets were recorded for each excitation frequency.

Shear waves were induced in the phantoms using a non-invasive custom-made device maintaining the medium between two plates, the upper one being fixed while the lower one being activated by a piezoelectric actuator (CEDRAT Technologies), as shown in Fig. 1. This piezoelectric device can cover a large frequency range up to 15 kHz. Acquisitions were conducted at different excitation frequencies, ranging from 300 to 1,200 Hz and at room temperature (around 22°C).

For each excitation frequency, 2D phase images were acquired twice at opposite motion-encoding gradient (MEG) polarity and then subtracted. Four images were obtained, corresponding to the four vibration phase offsets. These resulting images were Fourier transformed (in time domain) and the complex wave image (*U*) was taken at the excitation frequency. Next a band-pass Butterworth filter was applied in order to remove noise and exclude wavelength values that are not in the range of possible values with the considered type of medium. Finally, under common assumptions (linearity, isotropy and local homogeneity), storage (G') and loss (G'') moduli (corresponding to the real and imaginary parts of the complex shear modulus G*) were determined by applying a 2D Helmholtz inversion algorithm, according to the following equation:

$$G^* = -\rho\,\omega^2\, U / \Delta U, \quad (1)$$

ρ being the density of the materials (close to 1000 kg/m^3), ω/2π the excitation frequency, and Δ the Laplacian operator, approximated using a simple central difference scheme.

For each phantom, a Region Of Interest (ROI), excluding the edges of the phantoms, was defined on the obtained elastograms, and G' and G'' mean values as well as standard deviations were extracted from this ROI. The storage modulus G' represents the elasticity of the material whereas the loss modulus G'' is associated to the viscous properties of this material.

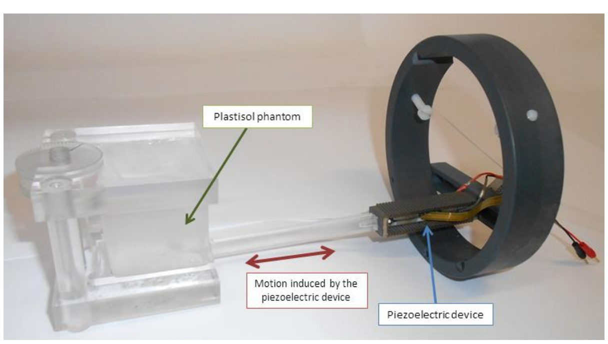


Figure 1. MRE driver used to generate shear waves in the phantoms with a piezoelectric actuator.

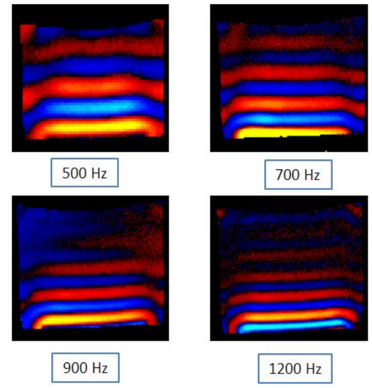


Figure 2. Examples of wave images obtained for phantom (A) at different excitation frequencies: 500, 700, 900 and 1200 Hz.

C. High-frequency rheometry measurements

A high-frequency rheometer [14]-[15] was used for mechanical tests. The sample was contained between two glass plates mounted on piezoelectric. The upper plate was vertically driven by the piezoelectric element in a sinusoidal motion. A squeezing flow was consequently induced in the sample and the stress transmitted to the second plate was measured by the other piezoelectric ceramic. The complex modulus G* was directly deduced from the pressure exerted by the sample on the captor and the amplitude of the motion [16] and was thus rheological model independent. In comparison with standard rheometers whose frequencies are usually up to 10 Hz for very soft materials, this piezo-rheometer is designed to perform measurements in a very large frequency range, from 0.1 Hz to 10 kHz.

For this study, the samples of plastisol phantoms were disc-shaped with a diameter of 15 mm and a thickness between 1 and 2.5 mm. Rheological measurements were realized at 25°C and in the same week than MRE experiments. For each phantom, four samples were tested and the mean and standard deviation were calculated. Results presented hereafter are those obtained at frequencies ranging from 160 to 630 Hz, providing thus an overlapping frequency range with MRE.

III. Results

A. Wave propagation

Fig. 2 shows examples of obtained phase images at different excitation frequencies for phantom (A). It illustrates clearly the wave propagation, and displays the dependence of wavelength and attenuation on frequency. Due to the viscous properties of the phantom, the amplitude of the wave decreases gradually and this is amplified at higher frequencies. As can be expected, the wavelength decreases when the frequency increases.

B. *Reproducibility of the magnetic resonance elastography measurements*

MRE tests were repeated three times on phantom (A). After an initial acquisition, which served as reference, a second acquisition was performed immediately after, the phantom remaining in the same position. The third acquisition (acquisition 3) was recorded ten days later. This last acquisition therefore takes also into account the variability induced by repositioning the phantom. As can be seen from Fig. 3, storage and loss moduli are similar for the three acquisitions.

C. *Magnetic resonance elastography and high-frequency rheometry results*

MRE and HFR results are presented in Fig. 4 for the three different phantoms (A), (B) and (C). Fig. 4a) and b) displays respectively the storage (G') and loss modulus (G''). Results with the two modalities are in quite good agreement for both G' and G''. For example, for phantom (A) at 400 Hz, G' = 33.5 ± 1.9 kPa with MRE technique and G' = 32.7 ± 1.4 kPa with HFR data. The G'' estimation presents significant standard deviations compared to its mean value.

Additionally, different ranges of storage and loss moduli were found for the three studied phantoms: with the MRE results, at 400 Hz, the storage modulus G' for phantom (A), (B) and (C) are respectively 33.5 ± 1.9 kPa, 11.5 ± 1.3 kPa and 3.2 ± 0.5 kPa. Concerning the loss modulus G'', it is respectively equal to 6.7 ± 2.2 kPa, 3.9 ± 1.1 kPa and 1.3 ± 0.5 kPa for each phantom.

IV. DISCUSSION

Results are presented for excitation frequencies varying between 300 Hz (phantom (C)) or 400 Hz (phantoms (A) and (B)) and 1,000 Hz for MRE, and 160 Hz and 630 Hz for HFR. In MRE, frequencies needed to be sufficiently high to be suited to the small-sized media investigated, and sufficiently low to avoid too strong shear waves attenuation. In HFR, although the device used can cover a large range of frequencies (up to 10 kHz), results are provided up to 630 Hz due to inertial effects with the plastisol phantoms at higher frequencies. These frequencies are compatible with biological tissue investigations [18] [19].

Sample thicknesses achieved for HFR were larger (between 1 and 2.5 mm) than the ideal size (less than 1 mm) ensuring an optimal measurement, which can be responsible for less accurate results. Thus, as can be seen for phantom (A), the loss modulus calculated from HFR data has a higher standard deviation than the two other phantoms. (A) had a thickness around 2 mm whereas (B) and (C) had a thickness around 1.5 mm, making these sample dimensions better suited for the measurements performed with the piezorheometer. Despite these difficulties, storage and loss modulus measurements over an overlapping frequency range were obtained, showing good agreement between MRE and HFR.

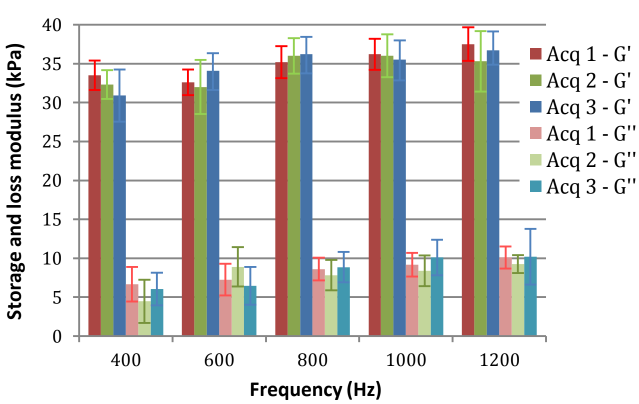
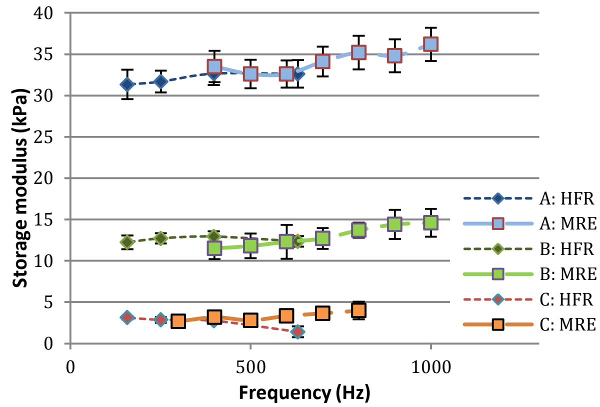


Figure 3. MRE results obtained for phantom A and three different acquisitions: Acquisition 1 is the reference acquisition; acquisition 2 was performed right after 1. Acquisition 3 was recorded ten days later.

a)



b)

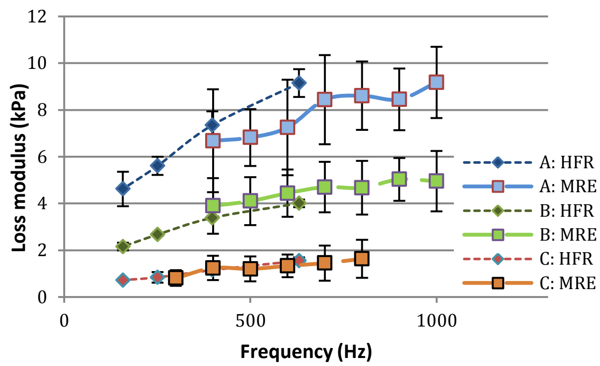


Figure 4. Storage (a) and loss (b) moduli for the three different phantoms and the two techniques, magnetic resonance elastography (dashed lines) and high-frequency rheometry (dotted lines). Results for phantoms (A), (B) and (C) appear in blue, green and orange, respectively.

Acquisitions with both techniques were performed with as close as possible conditions: same phantom preparations, similar temperatures during acquisitions and experiments taking place the same week. However, the size of phantoms remains a main difference between the two techniques: cubic phantoms for MRE experiments and very thin samples for HFR. HFR phantoms need to be regular in thickness whereas plastisol phantoms are difficult to be cut properly, this explains why phantom preparations were poured in cubic molds for MRE, and on an aluminum foil for HFR and then allowed to freely spread out in order to obtain thin layers. These two processes may induce variations in the resulting viscoelastic properties of phantoms, as, for example, the cooling rate is different. A first test was led by considering two phantoms with different sizes (35 x 35 x 35 mm and 35 x 35 x 15 mm) cooled at room temperature, and a second one with three other cubic plastisol phantoms cooled respectively at room temperature (22°C), in a fridge (2°C) and in an oven (at 60°C). Storage and loss moduli were here determined with the MRE technique only. Similar results were obtained for all these five phantoms.

Viscosity property quantification in MRE is quite difficult [17] in particular because G'' estimation is highly affected by noise. Thus the G'' estimations presented here have significant standard deviation compare to their mean values. However, these values are consistent with the ones obtained with HFR, suggesting that MRE is a technique that could give an estimation of the loss modulus G'' and thus of the medium viscosity.

Finally, different ranges of storage and loss moduli were found for the three studied phantoms, depending on the softener concentration. These values are in the storage and loss moduli range of different biological tissues, such as liver, brain or muscle [7]. Porcine white matter storage modulus (measured in vitro) varies from 5 to 10 kPa between 100 and 1,000 Hz and loss modulus from 2 to 6 kPa [14]. The storage modulus in thin rat liver slices was measured with variable fibrosis extent: results ranged between 2.5 and 4.5 kPa, at 600 Hz, depending on the METAVIR score [18]. A fibrotic human liver was found to present a storage modulus varying between 2 to 30 kPa between 100 and 1,000 Hz and a loss modulus varying from 0.2 to 10 kPa [19]. Varying the concentrations in phantoms could be a way to easily mimic elasticity and viscosity of different healthy and pathological tissues.

V. Conclusion

This paper presents a comparison of magnetic resonance elastography and high-frequency rheometry measurements, within an overlapping frequency range and with similar experimental conditions. The quantitative results obtained using these two techniques satisfactorily match, confirming that the complex modulus of a viscoelastic phantom can be reliably assessed using MRE.

Moreover, different ranges of storage and loss moduli were obtained by varying softener concentrations during phantom preparation. These values are in the range of storage and loss moduli for different tissues, such as liver, brain or muscle. Plastisol phantoms could also be helpful to assess new elastographic methods and tools adapted to different soft tissues, as well as to evaluate MRE parameters before in vivo experiments.

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