Non-linear elastic tissue characterization using MR elastography: Preliminary results

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Synopsis

MR elastography (MRE) enables to map tissue elasticities *in vivo*. In dynamic MRE, the elastic coefficients are determined by means of local wavelengths of shear vibrations assuming that the material behaves linear elastic. Here, a method is proposed to measure simultaneously both linear and non-linear elastic tissue characteristics. The technique is based on accumulation of anharmonic vibrations using a balanced steady-state free precision (SSFP) experiment. 2D-wave patterns are captured and temporally filtered for decomposing higher harmonic oscillations. It is shown that the intensity ratio of the 1st and 2nd harmonic is the crucial experimental quantity for deriving a unique and sensitive non-linear elastic parameter that characterizes biological tissues. This non-linear shear modulus (E) was measured in *ex vivo* bovine liver, porcine kidney and porcine calf muscle with E = 20 ± 5, 8 ± 3 and 500 ± 50 kPa, respectively. The results indicate the sensitivity of E for distinguishing different tissue types. Our new approach opens the perspective to employ the non-linear shear modulus for an early detection of pathological changes in living tissue.

Introduction

In MR elastography (MRE), the lengths of shear waves are used as a measure for regional stiffness variations [1]. This approach employs pure harmonic tissue oscillations for characterizing the elasticity of materials. If anharmonic vibrations can be measured by non-linear MRE the very specific non-linear elastic behavior of the material is observable [2]. Thereby, the presence of higher harmonic vibrations is the crucial indicator for estimating the non-linearity of the material. For a quantitative analysis strain wave fields have to be measured along different directions, since the intensity of those higher harmonic vibrations depends on both non-linear elastic coefficients and strain components. In the following a simple theoretical and practical approach to measure a non-linear shear modulus by MRE is demonstrated, which is based on the simulation on experimental 1D-wave profiles.

Theory and Methods

The non-linear quadratic extension of Hooke's law is given by eq.1 ($i,j,k = x,y,z$) [3] using the notation of $\boldsymbol{\sigma}$, $\boldsymbol{\varepsilon}$, $\mathbf{C}^L$ and $\mathbf{C}^N$ for the stress, strain, linear and non-linear elasticity tensors, respectively. Plugging eq.1 into the wave equation (eq.2) yields the non-linear equation of motion of a displacement component $u_z(x,t)$, which is coupled to the displacement component $u_x(x,t)$ (see eq. 3). The two elastic coefficients μ and E denote the tensor components $\mu = C^L_{xzxz}$; $E = C^N_{xzxzxx}$.

$$\sigma_{ij} = C^L_{ijkl}\varepsilon_{kl} + C^N_{ijklmn}\varepsilon_{kl}\varepsilon_{mn} \quad (1) \qquad \rho\frac{\partial^2 u_i}{\partial t^2} = \sum_j \frac{\partial \sigma_{ij}}{\partial x_j} \quad (2) \qquad \rho\frac{\partial^2 u_z}{\partial t^2} = \frac{\partial^2 u_z}{\partial x^2}\left[\mu + 2E\frac{\partial u_x}{\partial x}\right] + 2E\frac{\partial u_z}{\partial x}\frac{\partial^2 u_x}{\partial x^2} \quad (3)$$

Thus, for an evaluation of E it is sufficient to simulate the non-linear wave profile $u_z(x,t)$ incorporating the experimentally determined profile $u_x(x,t)$. Therefore $u_z(x,y,t)$ and $u_x(x,y,t)$ were measured by 2D non-linear MRE in order to extract vertical profiles in A-P direction (defined as our x-axis). Experiments were performed on *ex vivo* bovine liver, porcine kidney and porcine calf muscle using a balanced SSFP acquisition technique with one bipolar gradient before and after the readout gradient (gradient frequency was 108 (liver, muscle) and 200 Hz (kidney)). The wave images were captured at 20 different times and Fourier transformed. The resulting spectral wave patterns were simulated using a finite difference scheme that allows 1D calculations of non-linear wave profiles corresponding to eq.3. The calculated profiles were fitted to the experimental wave profiles $u_z(x,t)$ using $u_x(x,t)$, the previously determined linear shear modulus μ and E, as the variable parameter.

Results: Fig. 1 shows $u_z(x,y)$ after spectral decomposition in fundamental (A) and 2nd harmonic oscillation (B) of bovine liver (I), porcine kidney (II) and porcine muscle (III). Additionally $u_x(x,y)$ is shown. The amplitude ratio of 2nd and 1st harmonic was found to be highest for porcine muscle and lowest for porcine kidney. Correspondingly, the simulation of $u_z(x)$-wave profiles using eq.3 yielded a non-linear shear modulus E that increases in the same order as the amplitude ratios of the specimen (Tab. 1).

	μ [kPa]	E [kPa]
bovine liver	2.3 ± 0.3	20 ± 5
porcine kidney	4.8 ± 0.5	8 ± 3
porcine calf muscle	19.0 ± 0.8	500 ± 50

Tab. 1: Linear shear modulus μ and non-linear shear modulus E of *ex vivo* bovine liver, porcine kidney and porcine calf muscle. μ is derived from wavelengths estimation of the 1st harmonic in $u_z(x,y)$ (Fig.1, col. A). For derivation of E see text.

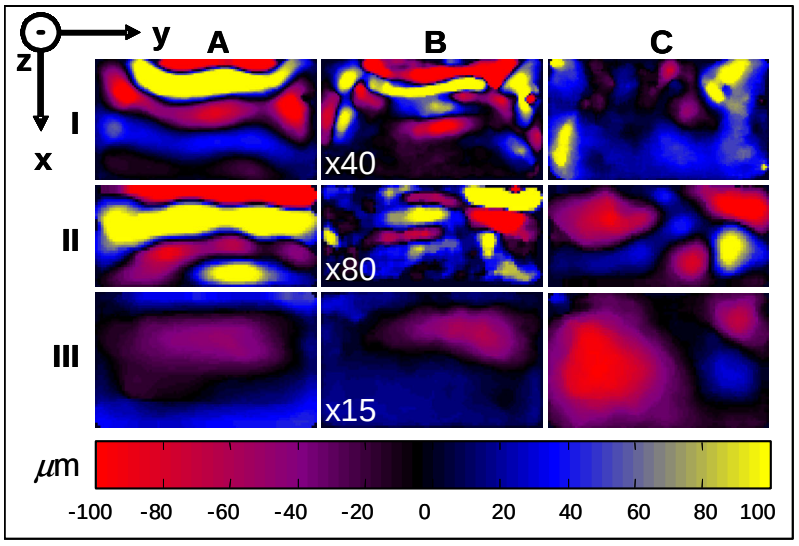

Fig. 1: Non-linear 2D MRE experiments. **I:** bovine liver, excitation frequency f_e= 46 Hz, dim[mm]: 60x110; **II:** porcine kidney, f_e= 74 Hz, dim[mm]: 42x90; **III:** porcine calf muscle, f_e= 46 Hz, dim[mm]: 60x96. **A:** 1st and **B:** 2nd harmonic of $u_z(x,y)$; (wave images of B were scaled with the numbers given on the images); **C:** $u_x(x,y)$

Discussion and Conclusion: Using new SSFP-MRE the measurement of the 1st and 2nd harmonic vibrations in *ex vivo* tissue specimens was simultaneously achieved with temporal resolution and excellent SNR. 1D-calculations of non-linear wave profiles quantified the observation that muscle tissue shows stronger deviations from the linear elastic behavior than liver and kidney. It was demonstrated that the non-linear shear modulus E is a highly sensitive elastic parameter for characterizing different types of biological tissues. Further non-linear MRE studies on pathologic tissue samples may reveal sensitive differences of the elastic behavior between healthy and diseased tissue.

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