Observation of shear wave dispersion using anharmonic MR elastography

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Introduction: MR Elastography (MRE) is capable to test *in vivo* mechanical properties of soft tissue using shear vibrations [1]. Typically, such shear vibrations are excited by harmonically oscillating transducers attached to the body surface resulting in widely monochromatic tissue vibrations. A motion sensitive MR sequence then encodes the prevalent fundamental vibration for calculating the linear shear modulus from the lengths of the captured waves.

Problem: To correctly deduce viscoelastic properties of the examined tissue, knowledge about the wave propagation speed at multiple excitation frequencies is often required. With knowing the dispersion-function of the shear wave speed it is straightforward to calculate the shear modulus and the viscosity using rheological models. However, the repetition of MRE experiments using various monochromatic excitation frequencies is time consuming and therefore often not applicable *in vivo*.

Objective: Here, the use of anharmonic vibrations for an analysis of dispersive waves at multiple frequencies in MR elastography is demonstrated. The bandwidth of the motion sensitive gradient in our MRE sequence was adjusted so that multiple frequencies were encoded simultaneously. In *ex vivo* experiments on porcine liver and kidney, anharmonic vibrations were generated using a ramp-waveform fed into the actuator (fig. 1). Comparison to sinusoidal wave excitation revealed non-linear elastic material properties. Initial *in vivo* studies on the human liver clearly showed 50Hz- and 100Hz-vibrations measured in a single experiment. From these data the viscosity of porcine liver and kidney and human liver were calculated using the dispersion relation of Voigt's body [2].

Methods: All measurements were performed in a 1.5 T scanner (Siemens-Sonata, Germany). The images were acquired using a steady-state free precision (SSFP)-MRE experiment [3] which accesses the signal amplitudes of higher harmonics while their fundamental frequency is simultaneously observed [4]. The propagation of the waves was captured 20 times with an increment of *TR*/20. Motion encoding gradients were applied in the direction of slice selection. Details about the mechanical excitation frequency (f_e), and the frequency (f_G) and cycle number (N) of the motion encoding gradient are given in figure 3. In *ex vivo* experiments both harmonic and anharmonic mechanical excitation was consecutively applied using either a sinusoidal (*HE*) or a ramp-waveform (*AE*), respectively. For *in vivo* human liver measurements a transversal image plane was located near the center of the liver. Shear waves were introduced using a carbon fiber rod connected to a costume-built acoustic actuator. The transducer was attached beneath the right costal arch and vibrated in head-feet direction. The distance between transducer and transverse image plane was about 3-4cm. Since pure sinusoidal vibration of the actuator membrane was not achievable we refer to a mixture of both *HE* and *AE* in table 1 and fig. 3.e.

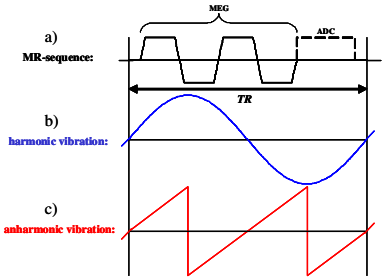

Fig .1: SSFP-MRE experiment. **a:** The sequence enables to detect higher harmonics of the fundamental frequency 1/*TR*. **b:** We used harmonic vibration for analysing frequencies generated because of the material non-linearity. **c:** The mechanical excitation was a ramp function in order to introduce higher harmonics externally.

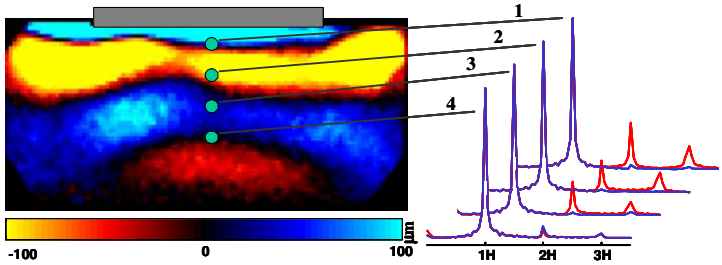

Fig. 2: SSFP-MRE experiment on *ex vivo* porcine liver (*FoV*: 130mm, f_e= 65,5 Hz, f_g = 200 Hz, N = 2).The spectral evolution is displayed at 4 different locations within the tissue for harmonic (blue) and anharmonic (red) mechanical excitation. All spectra are normalized to the value at the fundamental frequency.

Results: Close to the actuator unit (position #1 in fig. 2) the higher frequencies are clearly visible due to an anharmonic excitation whereas a sinusoidal waveform yields a monochromat. With spatial propagation of the shear waves two effects become visible from 1 to 4 in fig.2: i) Higher harmonic frequencies vanish due to viscosity and ii) in opposition to this higher harmonic frequencies are created due to non-linear material properties. Therefore at position #4 the intensity ratios of the fundamentals to their higher harmonics are equal for both actuator modes (*HE* and *AE*). This characteristic of a non-linear viscoelastic material is described by the acoustic Reynolds-number [5]. Both higher harmonics, originated by external vibrations or generated due to non-linear material properties show clear wave speed dispersion (fig.3 a-d). Therefore, the origin of the 2nd harmonic, observed in the human liver was not further considered. Also there, a dispersion of the wave speeds was found (fig.3e). The quantitative results are summarized in table 1.

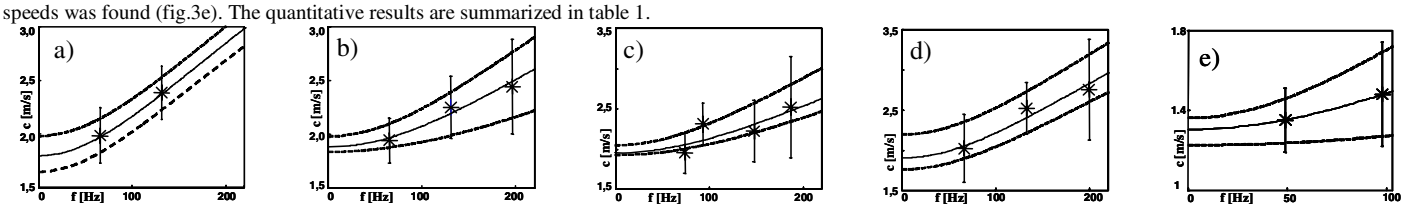

Fig. 3: Dispersion relation for *ex vivo* porcine liver (a, b), kidney (c, d) and *in vivo* human liver (e). Harmonic (a, c) mechanical excitation in comparison with and anharmonic (b, d) excitation. **a+b:** see fig. 1 for parameters. **c:** 1st exp.: *FoV*: 150mm, f_e= 74 Hz, f_g = 200 Hz, N=2; 2nd exp.: *FoV*: 150mm, f_e= 93,5 Hz, f_g = 280 Hz, N=2. **d:** *FoV*: 140mm, f_e= 66,5 Hz, f_g = 200 Hz, N=2; **e:** *HE/AE* excitation; *FoV*: 300 mm, f_e= 49 Hz, f_g = 119 Hz, N=2

Discussion and Conclusion: SSFP-MRE enables to examine wave speed dispersion at multiple excitation frequencies in one single experiment due to the large bandwidth of short motion encoding gradients. Our findings indicate the feasibility of a localized detection of higher harmonics in non-linear MR elastography due to the high viscosity of biological tissue. Using Voigt's model, dispersive wave speeds could be analyzed in terms of viscoelastic material properties indicating a relative low viscosity of human liver. However, the extremely soft elastic behavior limits the penetration depth of the shear waves into the organ. Therefore low excitation frequencies are required for successfully measuring shear wave dispersion in the liver.

	η [Pas]	$\eta_{\Delta1}$ [Pa s]	$\eta_{\Delta2}$ [Pa s]	μ [kPa]	$\mu_{\Delta1}$ [kPa]	$\mu_{\Delta2}$ [kPa]
ex vivo liver *HE*	4,6	5,1	4,1	3,5	4,3	3,0
ex vivo liver *AE*	3,4	4,3	2,2	3,9	4,3	3,7
ex vivo kidney*HE*	3,4	4,6	2,9	4,2	4,6	4,1
ex vivo kidney *AE*	4,5	5,7	3,8	4,0	5,3	3,4
in vivo liver *HE/AE*	2,0	3,0	0,9	1,9	2,0	1,7

Tab. 1: The determined shear modulus μ and the viscosity η of tissue with harmonic (*HE*) and anharmonic excitation (*AE*). μ and η are the best fit to the Voigt's body dispersion relation (solid curves in fig. 3). $\mu_{\Delta1}$ and $\eta_{\Delta1}$ are the parameters of the upper dashed curves in fig. 3. $\mu_{\Delta2}$ and $\eta_{\Delta2}$ belong to the lower dashed curves respectively.

References: [1] Muthupillai et al., Science 269, 1854 (1995); [2] Kruse et al., Phys. Med. Biol. 45, 1579 (2000); [3] Rump et al., ISMRM 2384 (2005) [4] Klatt et al., ISMRM 2557 (2005) ; [5] Naugolnykh, Nonlinear wave processes in acoustics, Cambridge Univ. Press 98