Measured elasticity and its frequency dependence are sensitive to tissue microarchitecture in MR Elastography

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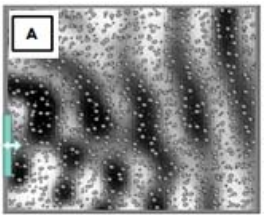
Introduction:

Understanding the effects of micro-obstacles on wave propagation is an essential part when trying to extract micro-structural information from MR-Elastography (MRE) data from tissue abnormalities such as small metastases or neovascularization. To date, the effects of wave scattering on mechanical properties measurements remain poorly understood [1,2]. Nevertheless, scattering plays a major role in linking the architectural properties of a biological tissue to its mechanical properties measured by MRE. In this study, the influence of microparticle size distribution on wave scattering frequency dependence is investigated from a theoretical and numerical approach. Recent preliminary MRE tests on polystyrene microspheres suspensions embedded in agar gel phantoms are used to validate the numerical results presented in this study.

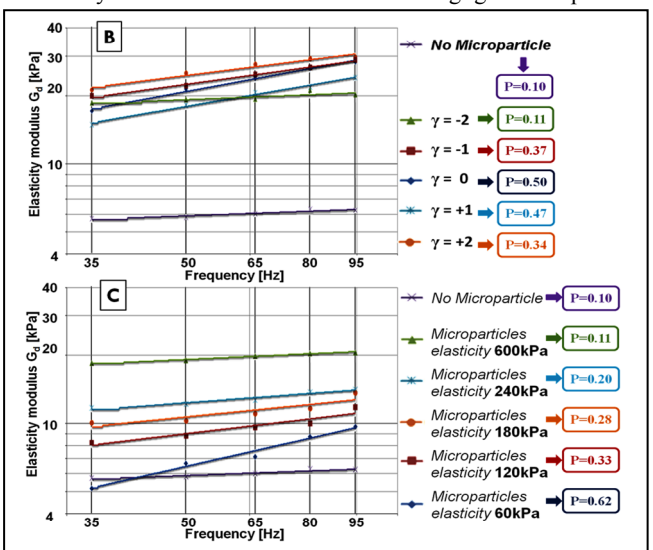
Material and methods:



2D wave propagation has been simulated using Diffpack finite element code [3] in an object of typical macroscopic dimensions (20cm*20cm) with element sizes as small as 390µm, i.e. 512² elements. The simulated high resolution displacement fields were thereafter regridded such as to attain macro-pixels of imaging dimensions, i.e. one macro-pixel constituted the average of 32x32 micro-pixels. Reconstruction of mechanical parameters was performed on the macro-pixels in order to observe the effect of macroscopic shear modulus dispersion caused by changes of the underlying "hidden" microstructure of the material. Stiff micro-particles according to size distributions following power-law ($\#(r)=\alpha.r^{\gamma}$, , r=radius of particle, # = number of occurrence, γ = exponent steering the characteristics of the distribution) were added randomly to the medium with diameters ranging from 1560µm (i.e. the size of four micro-pixels) up to 3.9mm (i.e. one third of a macro-pixel) with a fixed surface fraction of 27% wrt. the background. The random distribution of micro-particles was done in such a way that each macro-pixel contained in the end the same number of micro-particles. **Hence, the material appears on the macro-scale homogeneous in terms of mechanical parameters similar to for instance liver tissue imaged at millimeter resolution.** One of the particle distribution models is shown in Fig. A. Typical in-vivo MRE frequencies were used for the simulation of sinusoidal waves (35 to 95Hz, amplitude 100µm) with attained wavelengths never below 10 macro-pixels in order to assure sufficient precision for the inversion process [4] (waves shown in Fig. A are just for illustration purpose). The following dependencies were studied: i) homogeneous material without micro-spheres having a stiffness of 6kPa, ii) heterogeneous material with very stiff micro-particles (100x stiffer than background) and different particle size distributions (i.e. the exponent γ changed from -2 to 2), and iii) the influence of the impedance rupture between micro-spheres and background for a given particle size distribution. Both background and micro-particles are quasi-incompressible, with 0.48 Poisson's ratio and a density of 1000kg.m^3. Dynamic viscosity is 1Pa.s everywhere and can be considered as negligible compared to the elasticity.

Results:

As expected, the homogeneous case does not show any dispersion with a slope (when considering a power law $G_d(\omega)=\beta.\omega^P$) of P=0.1 which can be considered as the noise floor (Fig.B). Moreover, the expected elasticity of Gd=6kPa is correctly recuperated by the MRE construction algorithm. The addition of stiff micro-particles increases - as expected - the apparent elasticity. Interestingly, when adding basically only one type of particles (case with γ=-2, i.e. many small particles and almost no big ones), no significant dispersion is observed (similar to what happens when water diffuses in a porous medium with constant pore size). This changes dramatically when lowering γ, i.e. attaining for instance a flat particle distribution for γ=0. There, a slope of P=0.5 is measured demonstrating an enormous measurable effect on the dispersion properties of the elasticity. For particle size distributions with a positive γ, i.e. more large particles than small particles, a subsequent reduction of the slope P is noticed (as expected from symmetry). Those theoretical and numerical results have been experimentally confirmed using controlled size distributions of colloidal micro spheres in gels (not shown). Finally, Fig. C shows the dispersion properties for a fixed particle size distribution (γ=-2) as a function of contrast ratio between background and inclusions (from 10 to 100). Apparently, the expected flat frequency response is only obtained once a contrast ratio of 100 is used!



B: Frequency dependence of measured elasticity Gd with respect to microparticles size distributions ($\#(r)=\alpha.r^{\gamma}$ by varying γ value. Results are fitted by a power low $Gd(\omega)=\beta.\omega P$; C: Frequency dependence of measured elasticity Gd with respect to microparticles elasticity (with a constant background elasticity of 6kPa and a microparticles size **distribution** $\#(r)=\alpha.r^2$**.**

Conclusion:

This study shows for the first time the feasibility of linking size distribution and stiffness of micro-particles to the macroscopically observed elasticity.

In diffusion, disordered media can lead to two effects: reduction of the typical diffusion length and/or a mean-square displacement which is not anymore proportional to time but to a fractional power of time not equal to one (so-called anomalous diffusion). Similarly, here classical propagation turns into anomalous propagation due to micro-architectural properties. Hence power-law behavior is observed in frequency domain. This effect might play an important role in understanding the influence of microscopic tissue components on mechanical properties as measured by elastography techniques. It opens the prospect of detecting and describing micro-inclusions, as small metastases or neo-vascularisation, from elastography data, which are not directly detectable by MRE.

[1] O'Doherty RF, Anstey NA, Geophys Prospect 19:430 (1971) [2] Holm S, Sinkus R, J Acoust Soc Am 127:542 (2010)
[3] Langtangen HP, Springer (1999) [4] Sinkus R, Tanter M, et al., Magn Reson Im 23:159 (2005)