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Introduction: Biological tissue exhibits power-law behaviour for the complex shear modulus in the range of 0.01–1000Hz, i.e. $G^* = G_0 + iG_1$ rises with frequency according to $\omega^{2-\gamma}$ [1]. Various rheological models have been developed in order to explain this type of dispersion [2]. Here, we present an entirely new physical approach in order to explain the observed frequency behaviour: it is shown that shear wave propagation is sensitive to the underlying spatial micro-architecture of obstacles which hinder the propagation. This effect is very similar to the well established effect of anomalous diffusion for particles: typically, in a diffusion process, the mean squared displacement (msd) of a particle is a linear function of time, i.e. $R(t) \sim t^{\gamma/2}$ with $\gamma=1$. Anomalous diffusion is used to describe a diffusion process with a non-linear dependence on time which occurs when space is restricted and there is an intimate link between the spatial architecture of the restriction and the exponent γ for the msd [3]. Recently, this anomalous propagation has also been found for light [4] and it is shown for the first time in this work that similar behaviour holds for shear wave propagation.

Methods: 2D simulations of propagating shear waves are carried out with the FEM software package DIFFPACK®. A point source (located at the lower end of the vertical yellow lines in Fig.A,B) generates one period of excitation at 100Hz. The propagation is disturbed with either single-scale (ss) or multi-scale (ms) circles with a strong rupture in acoustic impedance (1000). The ballistic wave front R is traced as a function of time in order to recuperate its temporal behaviour. Transient shear wave propagation experiments in gelatine phantoms are carried out on a 7T Bruker animal system. A CINE FLASH sequence sensitized to 200Hz motion is synchronized to a piston which pushes at 200Hz for one period on the phantom surface (Fig.D). Thereby, the propagation of transient shear waves in different types of phantoms can be studied (i.e. via the addition of glass spheres of one single diameter or of various different diameters to the gelatine). B-scans (Fig.E,F) along the line of wave propagation (red line in Fig.D) allow now to trace the ballistic wave front and to study its temporal behaviour. In-vivo clinical MR-elastography data were obtained from 99 patients that had undergone liver biopsy for suspicion of chronic liver disease [5]. The complex shear modulus of the liver was transformed into the notation of power-law behaviour (Fig.G), i.e. $\alpha = \alpha_0 \omega^y$ with α the attenuation, α_0 a scale parameter and y the exponent of the power-law being related to γ [6]. MRE data from 68 breast lesions were treated equally [6] and studied according to their location in the $y-\alpha_0$ plane.

Results: The 2D simulations clearly show that the shear wave is slowed down due to the presence of the ms obstacles (Fig.B) when compared to the case of ss obstacles (Fig.A, red dashed horizontal line). When tracing the wave front in time (Fig.C) we find that the ss simulation (blue line) yields as exponent $\gamma=2$ (i.e. normal propagation) while the ms simulation (red line) yields $\gamma=1.6$, i.e. anomalous propagation. Thus, the wave is slowed down while propagating. Similar behaviour is found in the phantom experiments. The B-scans (Fig.E=ss and Fig.F=ms) clearly show that the ss case yields a linear behaviour for the ballistic wave front while for the ms case anomalous propagation is observed (curved red line in Fig.F as compared to the straight black line). Liver fibrosis data (Fig.G) show that disease progression is versus lower α_0 values (i.e. versus a stiffening of the liver) but y does not change. Breast cancer data (Fig.H) show an increase in y which correlates with the aggressiveness of the lesion ($y^{\text{benign}}=0.16$, $y^{\text{DCIS}}=0.17$, $y^{\text{G1}}=0.19$, $y^{\text{G2}}=0.25$, $y^{\text{G3}}=0.28$).

Discussion: It is shown that power-law dispersion of shear waves can originate from multi-scattering effects on sub-wavelength structures exhibiting a strong rupture in acoustic impedance (like glass beads in gelatine or blood vessels in case of tissue). Simulations indicate (similar to the effect of anomalous diffusion) a close link between spatial structure of obstacles (for instance their fractal dimension) and the anomalous propagation coefficient γ . Liver fibrosis leads to a stiffening of the organ (and thus a drop of α_0 [5,6]) but no significant change in y . The addition of collagen in case of fibrosis is not sufficient to modulate the scattering process (small rupture in acoustic impedance). In case of breast cancer, where strong neo-vascularization is present in aggressive lesions, we observe a significant change in y because the vessel walls are about 1000x stiffer than the ECM (GPa vs KPa). Thus, anomalous shear wave propagation allows revealing sub-resolution architectural properties of strong scattering objects and might thereby provide unique information about the vascular architecture of tumours at the clinical imaging scale.

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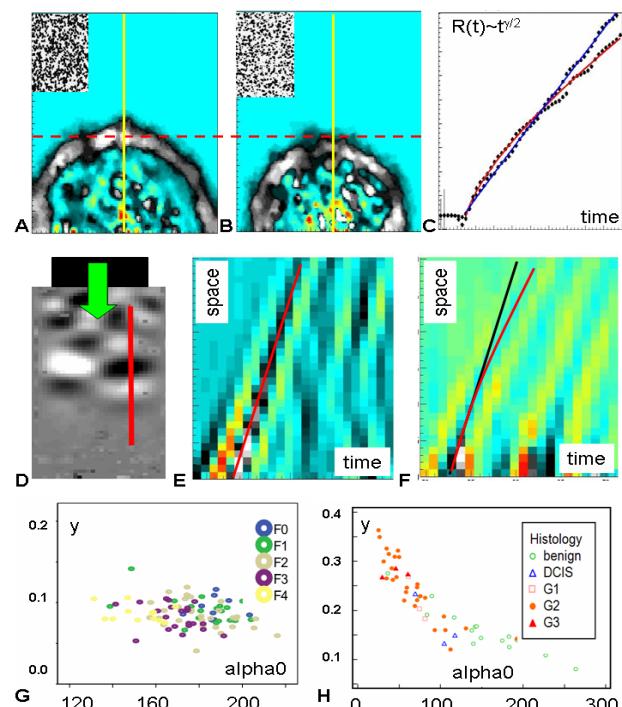
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2D simulation of propagating shear wave at $t=5$ ms in a single-scale (ss) structure (A) and a multi-scale (ms) structure (B). C: Trace of the ballistic wave front $R(t)$ as a function of time for cases A (blue line) and B (red line). D: Transient shear wave image in a ss phantom at 200Hz. B-scans in ss phantom (E) and ms phantom (F). In-vivo data for liver fibrosis (G) and breast lesions (H) in power-law representation, i.e. y versus α_0 .