Breast Cancer exhibits liquid-like mechanical properties – A comparative study between MR-Mammography and MR-Elastography -

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Introduction

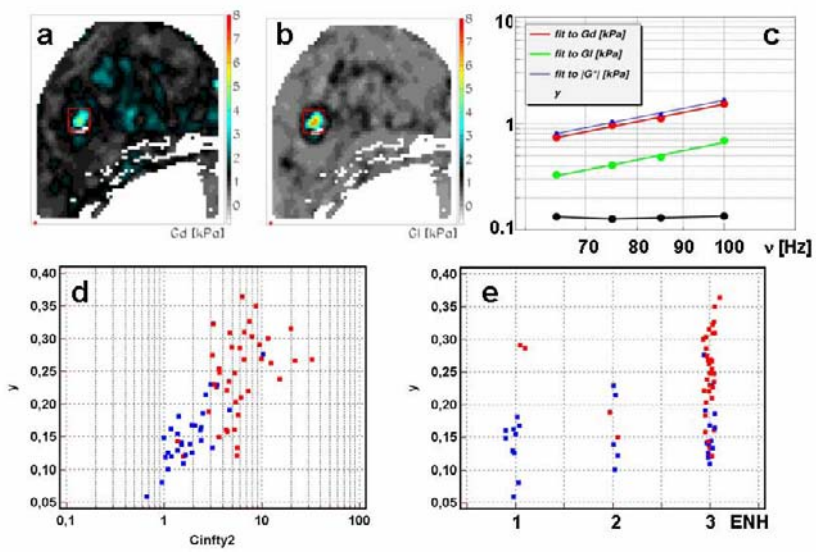
Contrast enhanced MR-mammography (MRM) utilizes temporal MR-signal changes after bolus injection (typically gadopentetate dimeglumine) to characterize lesion properties [1]. Here, malignancy is normally characterized by an initial steep rise followed by a so-called wash-out phase. Benign lesions tend to have a shallow rise which might lead to a plateau or further continuous rise. Those differences in enhancement properties have their origin in architectural differences regarding the vascular system of the lesion. Enhanced leakage into the interstitial medium between arterial and venous system (characteristic for malignant lesions leading to the strong initial signal rise seen in MRI) should lead to clear difference regarding the mechanical properties. Thus, in principle, malignant lesions should behave more liquid-like. Here, we test the hypothesis whether this architectural difference is traceable via MR-elastography (MRE) [2]. Moreover, we consider the relevant question how to interpret the mechanical properties of breast tissue. Therefore, a multi-frequency analysis is performed which demonstrates that the classical mechanical interpretation in terms of the so-called Voigt model (i.e. a spring and a dashpot in parallel) does not hold.

Materials & Methods

The initial signal increase (ENH) is defined from the pre-contrast MRM measurement (using Magnevist® as contrast agent) to the maximum value increase within the first 3 minutes after the administration of contrast media and divided into three groups: 1: ENH<50%, 2: 50%<ENH<100% and 3: ENH>100%. 3D steady-state MR-Elastography is performed after clinical MRM within the same session at 85Hz mechanical excitation frequency with an isotropic resolution of $(2mm)^3$ (acquisition time about 10mins) [3]. MRE at one single frequency provides a complex valued parameter $G^*=Gd+iGl$ which reflects the dynamic properties (Gd) and the loss properties (Gl) of the material at this specific frequency. To properly interpret this information in terms of solid and liquid component, measurements at frequencies between 65 and 100 Hz were performed. The bandwidth was limited by hardware and physical MR limitations (relaxation time with respect to echo time and sensitivity to motion with respect to efficiency of wave penetration).

Results

Typical MRE results for a ductal invasive carcinoma are shown in Fig.a,b). The true location of the tumor is indicated by the red rectangle and agrees very well with the regions of abnormally enhanced values for Gd and Gl. Fig. c) shows the average value of Gd (red line) and Gl (blue line) within the parenchyma of a healthy volunteer for several frequencies. When plotted on a log-log scale it becomes obvious that both, Gd and Gl, follow a frequency power-law with the same power (i.e. $Gd \sim Gl \sim \omega^{1.67}$). This is in harsh contradiction with any classical rheological model for viscoelastic materials (i.e. the Voigt or the Maxwell model). In order to properly interpret the data, we use the fact that dynamic modulus and loss modulus are linked to each other via the Causality principle, i.e. they form a pair of variables which are not independent from each other [4]. Using only the experimental observation that Gd and Gl follow a frequency power-law, it is possible to discover the underlying link between both parameters. The resulting "TRUE" parameters are the exponent of the power-law (y [dimensionless]), the strength of the attenuation (α_0 [1/m]) and the speed of the wave at infinite frequency (C_{infty} [m/s]). Fig. d) shows the scatter-plot of 39 malignant lesions (red markers) and 29 benign lesions (blue markers) in the (y-C_{infty}^2)-plane. A value for y=0.5 represents a purely liquid material. High values for C_{infty}^2 indicate that the material will appear ultimately stiff at high frequencies. It is obvious, that malignant lesions



tend to populate the high y - high C_{infty}^2 region. Fig. e) shows the correlation between the exponent of the power-law and the score for the initial enhancement (ENH) coming from the dynamic MRM measurement. Most malignant lesions show strong initial enhancement (as expected from MRM) AND high values for y, while benign lesions obtain statistically significant lower values of y and for ENH.

Discussion & Conclusions

The disability of classical rheological models to explain the dispersion relation of $G^*(\omega)$ for soft tissue has already been recognized for a long time. Here, we demonstrate that breast tissue does follow a power-law which necessitates much more complex rheological models (typically fractal models) for explanation. The final use of rheological models to gain further insight into materials is rather limited. Therefore we are proposing to interpret the data in an extremely unbiased manner: the experimental fact that Gd and Gl follow a power-law as a function of frequency is used as a starting point to deduce their intrinsic relationship. The only additional law used in this deduction is the Causality principle which is most general and must be obeyed by any means. The intrinsic relations among Gd and Gl allow to deduce the exponent of the power-law from single frequency data. For y=0 we deal with a material which resembles mainly the properties of a classical viscoelastic material. Benign lesions seem to follow this behavior. On the contrary, malignant lesions, which are strongly vascularised and show high values of initial enhancement (ENH=3) obtain high values for the exponent. For y=0.5 we deal with a pure liquid material. As such, we are capable to observe via the viscoelastic material parameters, measured with MRE, the architectural difference between benign and malignant lesions. It is most interesting to notice that those benign lesions which also show strong initial enhancement (see Fig. e, ENH=3) obtain low values for y. Low enhancing benign lesion have –as expected- low values of y. As such, the viscoelastic parameter y is capable to assess properties which go beyond the simple measurement of initial enhancement of a contrast bolus. Future work is devoted to understand which architectural component on the micro-scale accounts for this difference.

References

[1] Kuhl CK, Radiology 211:101-110 (1999).
[2] Sinkus R, Magn Reson Med. 2005 Feb;53(2):372-387.
[3] Xydeas T,Invest Radiol. 2005 Jul;40(7):412-20
[4] Szabo, Acoust. Soc. Am. 107 (5), 2000.