Physical Boundary Conditions Reconstruction: a Novel Method to Determine Viscoelastic Parameters from Magnetic Resonance Elastography Data

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Introduction:
The direct reconstruction of viscoelastic parameters in MR-Elastography (MRE (1)) is based upon measured displacement data and the subsequent estimation of their spatial derivatives (of different orders) to solve the underlying wave equation. Noise in the original displacement data leads to biases in the derived elasticity maps. Moreover, when operating in 3D, inversion of each spatial component of the wave equation leads typically to different estimates for the viscoelastic parameters (2). Here, we are proposing a new approach for estimating the viscoelastic parameters from 3D displacement data: this novel algorithm is designed to better reflect the underlying physics by including physical boundary conditions (PBC) as constraints to the partial differential equation governing the reconstruction process (figure 1; u: displacement, G^*: shear modulus, ρ: density, ω: acoustic frequency). This way, additional stability is added to the inversion process hence reducing the effect of noise. The obtained viscoelastic parameters are now – for the first time – obtained while obeying two major physical constraints: firstly, that tissue is incompressible and secondly, the isotropy condition, i.e. all three spatial components of the wave equation provide the same estimate for the complex shear modulus. Results on analytic simulations demonstrate the proof of concept and in-vivo data for diffuse liver diseases show a significant improvement in separating the different diseases.

Methods:
The classical direct inversion method in MRE involves two steps: firstly, fitting of 3D analytic functions (typically a polynomial) to the 3D volumetric displacement data to recuperate different orders of local spatial derivatives and secondly, utilization of those derivatives in the 3D wave equation to obtain a local estimate of the complex-valued shear modulus G^* (see Fig.1, left). For many in-vivo applications we assume – given a typical spatial MRE resolution of several millimetres – that tissue is mechanically isotropic. Hence, the three different estimates for G^* are simply averaged. Unfortunately, the first order derivatives from step one typically do not satisfy incompressibility, i.e. $\partial_x U_x + \partial_Y U_Y + \par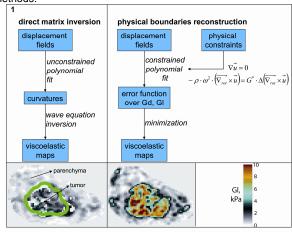tial_Z U_Z \neq 0$. In our new method (Fig.1, right) those two physical constraints of incompressibility and isotropy of the medium were included a priori into the reconstruction process. The constraints were added via lagrange multipliers to the polynomial fit which leads to the presence of terms including G^* within the complex-valued error (χ^2) function. Consequently, the polynomial fit procedure (which is an analytic matrix inversion) was carried out over a range of reasonable G^* values and the combination of $G^*=G'+iG''$ yielding the lowest χ^2 for the fit was taken as solution for that location in space. Validity of the method was demonstrated on analytical solutions of propagating plane waves comprising varying levels of noise. Applicability of the reconstruction process to biomedical problems was demonstrated by reconstructing experimental data acquired with conventional MRE technique (3,4) from a cohort of fibrosis patients.
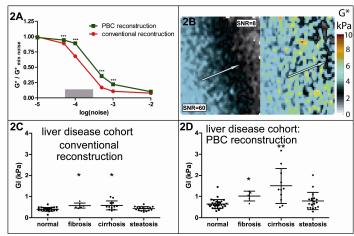
Results:
PBC reconstruction estimates stayed within 10% of the true value for noise levels more than twice those sufficient to fail the conventional method (figure 2A). PBC values from noisy input waves were closer to noise-less estimates than in the case of the conventional method. Consequently noise sensitivity, as seen from a gradual decrease of viscoelastic estimates along the attenuation direction (G^* maps are represented in figure 2B, unit: kPa, arrows: attenuation direction, insets: local signal to noise ratios in the displacement maps simulated with $G^*=6.0$kPa), was more pronounced in conventionally generated maps (fig. 2B, left) than in maps calculated with the physically guided method (figure 2B, right). This result remained valid over several decades of noise magnitude spanning the entire regime of typical experimental noise (2A, hashed box). PBC reconstruction was applied to clinical datasets from a cohort of patients with varying degrees of liver fibrosis or steatosis (fig. 1, 2 ; lower panels). In addition to qualitatively better maps (see for instance the viscosity maps on figure 1, lower panel left: conventional method, lower pane right: PBC reconstruction ; green outline: tumor ; colour scale in kPa), PBC reconstruction detected differences (student t-test) between normal and cirrhotic parenchyma (p<0.01) or between normal and fibrotic components (p<0.05) with higher statistical power than the conventional reconstruction (p<0.05 in both cases ; fig. 2C and 2D). Additionally under ANOVA analysis, the PBC method also distinguished steatotic from cirrhotic livers (p<0.01), whereas these groups could not be differentiated based on results from the analytic inversion method.

Conclusions:
The PBC reconstruction algorithm described herein shows promise as a robust, noise-insensitive method with direct applicability to clinically relevant magnetic resonance elastography data. Inclusion of physics-based criteria at the level of the reconstruction prevents spuriously low viscoelastic parameters to arise by counteracting the deleterious effects of noise on the purely mathematical procedure of polynomial fitting used in conventional methods.

(1) Muthupillai & al., Nat. Med., 1996
(2) Sinkus & al., Phys. Med. Biol. 2000
(3) Huwart & al., Eur. Radiol., 2008
(4) Huwart & al., Radiol., 2007