In vivo quantification of induced liver fibrosis in an animal study using MR-elastography

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Introduction

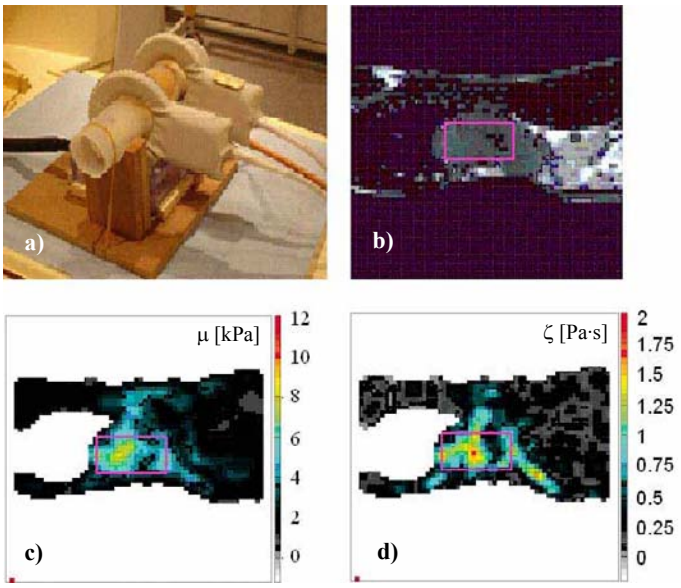
It is known that liver fibrosis is associated with increased liver stiffness [1]. Magnetic Resonance Elastography (MRE) allows the measurement of the mechanical properties of living tissue in a quantitative manner. The aim of this study was to quantify liver fibrosis (expressed in percent) in vivo. Therefore 15 rats (5 normal and 10 fibrotic CCl_4-induced rats) were studied by MR elastography. The shear viscoelastic parameters provided by MRE have been compared to the histological analysis.

Material and methods

Low-frequency (200 Hz) longitudinal mechanical waves were transmitted into the liver via a transducer consisting of a coil driven by a programmable pulse generator. The shear waves are then obtained by mode conversion at interfaces. The transducer was placed on the abdomen of the rat (see Fig.1a) (in prone position). Images were obtained on a 1.5 T Philips Gyroscan Intera whole body imager using a two elements S-Flex coil. The transmitted waves were measured by a phase-locked motion sensitized MR-sequence [2]. Five sagittal slices (SL=1.4 mm) through the liver were acquired. The FOV was 90 mm, matrix size 64^2 leading to an isotropic voxel size of $1.4\times1.4\times1.4$ mm^3. Four dynamics were measured with TE = 40 ms, TR = 250 ms and NSA = 4, leading to an acquisition time of 4 min 18 s for each spatial direction. Five normal rats were first scanned, and then 10 CCl_4-induced rats, scanned at different moments of the injection process. Immediately after the experiment, an autopsy was performed and the liver collected. The histological analysis provided the percentage of fibrosis [3].

The stiffness (Fig.1c) and viscosity (Fig.1d) maps are obtained as described in [2]. The so called Maxwell model (spring and dash-pot in series) was used to reconstruct the elasticity. The viscosity is estimated by the Voigt model (spring and dash pot in parallel). For each case, the largest possible rectangular ROI that fits into the liver (see Fig.1b) was taken to calculate the mean over the ROI for the central slice. The values were then compared with the percentage of fibrosis.

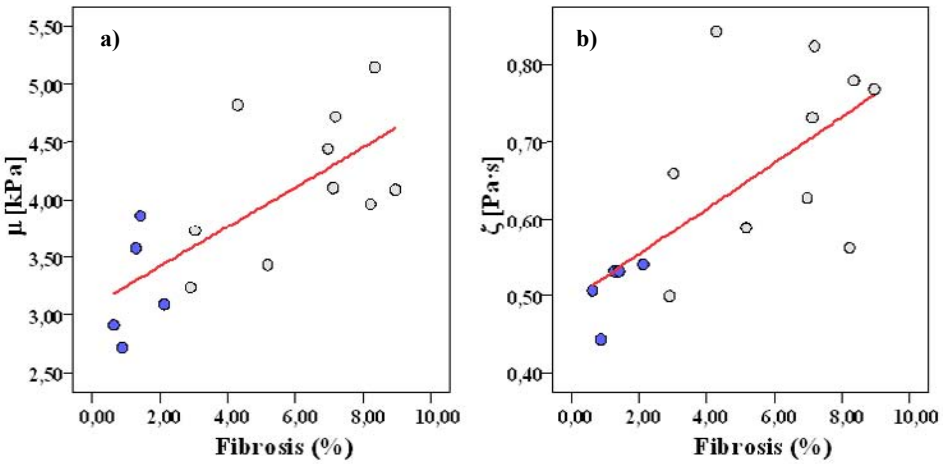
Figure 1: Measurements on rats. The experimental set up is shown on Fig.1a. The magnitude a), elasticity c) and viscosity d) map are reconstructed on a saggital slice. This example corresponds to the data of a fibrotic rat.



Results and Discussion

Figure 1b-d shows one example of the obtained magnitude, shear modulus and viscosity map. Results obtained in this animal study provide a significant correlation between stage of fibrosis and viscoelastic parameters of the liver. The following results are obtained: for shear modulus (Fig.2a) r = 0.76 (Spearman test, p = 0.001) and for shear viscosity (Fig.2b) r = 0.76 (p = 0.001). Note that when comparing these results with those obtained in patients [4], one should realize that the good correlation is easier observed using the percentage scale (linear correlation). On the contrary, for patients, the Metavir score is used which gives rise to a nonlinear (rather exponential) correlation. As a result, the percentage scale facilitates the discrimination of the low grades of fibrosis which is more difficult on patients (Metavir grade from liver biopsy). Moreover, because here a whole slice was analyzed, the histological results are more confident.

Figure 2:
Percentage of fibrosis versus shear modulus and shear viscosity are shown in Figs2a and 2b respectively. The blue markers correspond to the results obtained on normal rats; a small amount of fibrosis is already present. Grey markers represent results obtained with induced fibrosis.



Conclusion

In conclusion, a fairly linear relation between viscoelastic parameters and percentage of fibrosis is observed. Improvements on the precision are expected on data obtained with higher mechanical excitation frequencies, increased number of dynamics (8) and higher spatial resolution.

References

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