BRAIN VISCOELASTICITY MEASURED BY MAGNETIC RESONANCE ELASTOGRAPHY

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ABSTRACT

The knowledge of brain tissue mechanical properties is a critical issue in the head injury biomechanics research field. Due to experimental limitations, brain tissue has been characterized in vitro, whereas its actual in vivo behavior remains poorly known. We propose the use of Magnetic Resonance Elastography as a non invasive, non destructive tool for measuring the viscoelastic properties of brain tissue. The general method and its validation versus rotational rheometry are described, and preliminary results obtained in vivo are presented.

Keywords: Biomechanics, Brains, Soft Tissues, Viscoelasticity

UNDERSTANDING THE MECHANICAL BEHAVIOR OF BRAIN TISSUE is an essential issue in injury biomechanics, especially for the Finite Element Modeling field that requires an accurate and realistic knowledge of tissues properties. Due to obvious experimental reasons, brain tissue has mainly been characterized in vitro, on excised post-mortem brain samples. A few in vivo indentation methods have been proposed (Miller, 2000), but they remain invasive and destructive. Proposing a non invasive and non destructive method that would allow to measure in vivo brain tissue mechanical properties is extremely challenging for this research field.

Magnetic Resonance Elastography (MRE) is a Magnetic Resonance Imaging based method that has been initially developed for the detection of abnormally stiffness differences in soft tissues (Muthupillai, 1995). MRE is based on the detection of propagating shear waves inside the considered medium by using a special motion-sensitizing MRI sequence. Under an externally applied harmonic vibration, displacements resulting form the shear wave propagation are encoded (Lewa, 1991), allowing to retrieve the underlying the mechanical properties of the medium. Most MRE studies assume the medium to be linear elastic. Although this hypothesis is generally sufficient for qualitative stiffness detection, it is very limited for biomechanical purposes. In this work, we present the extension of MRE for determination of linear viscoelasticity. The method is quantitatively compared to rotational rheometry on ex vivo brain tissue. Preliminary results on in vivo brain tissue are then reported.

MATERIAL AND METHODS

MAGNETIC RESONANCE ELASTOGRAPHY

Experiments were performed on two low-field B0=0.1T resistive magnets (Bouhnik SAS, Vélizy-Villacoublay, France), one vertical (Horizontal B0) used for ex vivo studies and one horizontal (Vertical B0) for in vivo studies. Shear waves were generated by a modal exciter EX12 (Prodera, France) driven by a waveform generator. Excitation was transmitted through a non magnetic MR-compatible brass rod. The whole device can be adapted on both magnets. A 2D spin echo sequence with square-shaped motion-sensitizing gradients was used for this study. Motion-sensitizing gradients were synchronized to TTL output of waveform. Typical MR parameters were TR = 600ms-900ms, TE = 60ms, slice thickness= 7mm-10mm, NEX = 16, field of view FOV = 100*100mm^2 with a 128*128 data acquisition matrix, leading to a total acquisition time of 5 to 12 minutes for one image. The whole experimental setup has been described in details in previous studies (Vappou et al, 2006; Vappou et al, 2007).

ROTATIONAL RHEOMETRY

In order to compare the proposed method to mechanical rheometric measurements, reference tests were performed on a AR2000 (TA- instruments, New Castle, DE, USA) rheometer on ex vivo brain tissue samples. Shear frequency sweep tests were performed from 0.1Hz to 10Hz. Experiments were carried out in the linear viscoelastic strain range of the samples (ε=0.5%) and at 25˚C.

EX VIVO BRAIN TISSUE

Both rheometric and MR experiments were performed on normal porcine brains (aged from 6 to 8 months) obtained from slaughterhouse and immediately refrigerated at 4˚C. The total post-mortem time varied between 24 to 48 hours. Experiments were performed on 8 brains, 4 for each method.

For MRE, whole brains were placed inside echographic gels in order to ensure mechanical settling and adequate filling ratio for RF coil. A rectangular thin actuator connected to the exciter was introduced between the two hemispheres.

For rheometric experiments, cylindrical-shaped samples (20 mm in diameter, 4-5 mm high) were excised from white matter in the corona radiata region. A moist chamber was used in order to prevent dehydration and experiments were performed at 25±3˚C. A total of twelve samples were tested.

IN VIVO BRAIN TISSUE

Experiments were performed on 7 Sprague-Dawley male rats aged from 8 to 9 in accordance with french legislation (authorization A6748220). Rats were placed in a MR-compatible technical cell (Minerve SAS, Esternay, France) and were anesthetized with 2% Isoflurane pushed by air. Mechanical excitation was transmitted to rat head through a bite-bar similar to usual bite-bars used on rodents. MRE experiments were performed at 150Hz, 180Hz, and 210Hz in order to investigate dynamic behavior of in vivo brain tissue within this frequency range.

RESULTS

EX VIVO BRAIN

Figure 1 gives an example of shear waves observed in a homogeneous medium and in brain tissue. A wave equation inversion algorithm (Oliphant et al., 2001; Vappou et al. 2007) was developed in order to retrieve locally the values of wave vector k by using the temporal Fourier transforms of the displacement.

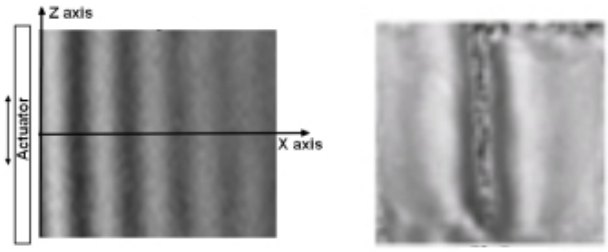

Fig. 1-Shear waves observed in gel (left) and in in vitro porcine brain (right)

The shear storage and loss moduli were then calculated by solving the complex equation $G=\rho\omega^2/k^2$. Figure 2 illustrates an example of spatial distribution of shear storage G' and loss G'' moduli. These values were averaged inside a region of interest ROI corresponding to the corona radiata region, in order to allow comparison with samples tested by rheometry. Figure 3 illustrates the results obtained by MRE compared to those obtained by rheometry. A frequency extrapolation based on previous studies allows to conclude that both methods are in good agreement. As a consequence, the quantitative nature of MRE as a tool for measurement of viscoelasticity was demonstrated.

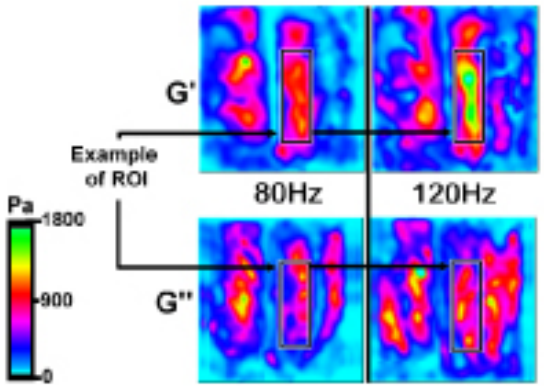

Fig. 2- Distribution maps of shear storage G' and loss G'' moduli (in vitro porcine brain)

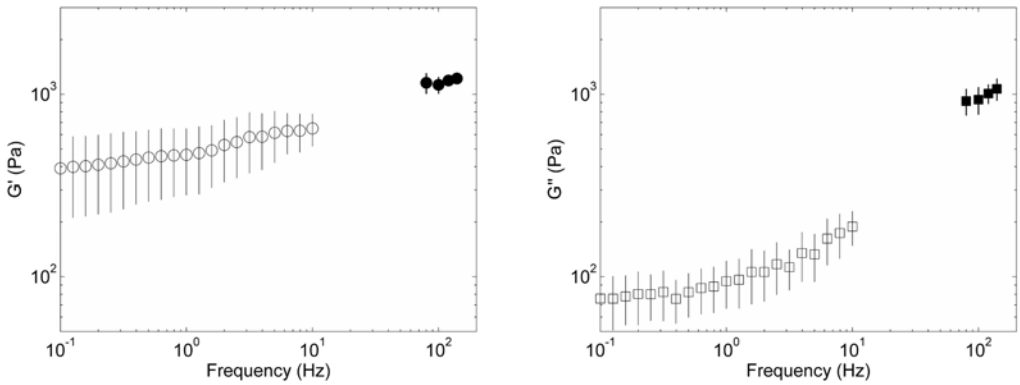

Fig. 3- Shear storage and loss moduli measured by MRE (full) and by rheometry (empty) in in vitro porcine brain

IN VIVO BRAIN

The inverse problem was solved in a similar approach as in ex vivo brain. Figure 4 is an example of spatial distribution of G' and G''. Figure 5 reports the values obtained by averaging among all subjects, showing therefore the in vivo dynamic viscoelastic properties of brain tissue measured by proposed method.

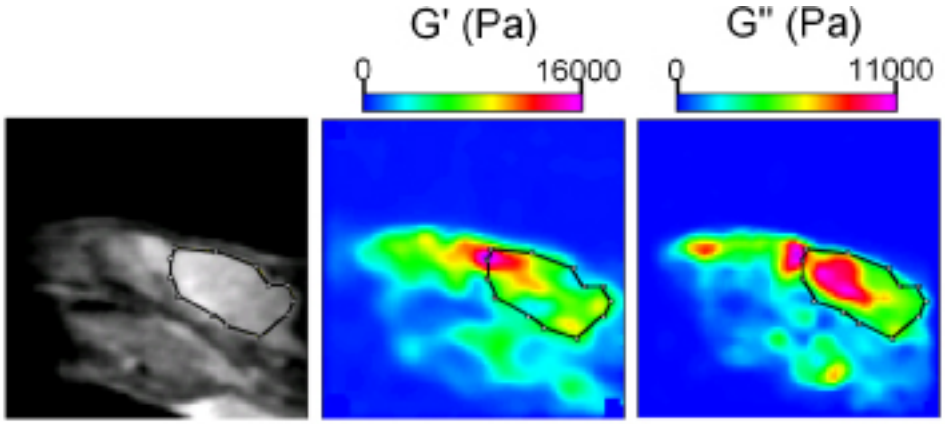

Fig. 4- Magnitude Image (left), and distribution of shear storage and loss moduli inside rat brain in vivo

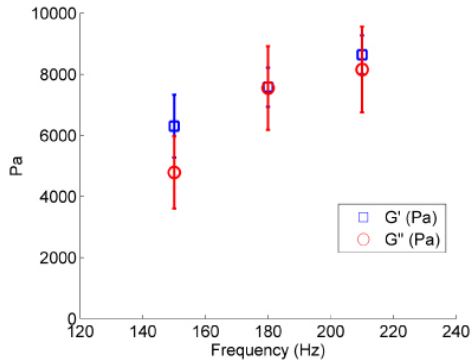

Fig. 5-Shear moduli versus frequency averaged among all subjects (in vivo rat brain)

DISCUSSIONS AND CONCLUSIONS

Several limitations of this method can be mentioned and are discussed in details elsewhere (Vappou, 2006; Vappou, 2007). The most significant limitations concern the inverse algorithm used for the reconstruction of shear moduli, where simplifying physical assumptions were made like the neglection of compression and reflected waves, or the use of a 2D Laplacian operator. However, despite these limitations, this method showed to give results consistent with those found by rheometry on ex vivo tissue.

This method could possibly be very useful for the investigation of many issues related not only to brain biomechanics, but to soft tissues biomechanics in general. As a non invasive tool for soft tissue characterization, many critical questions could be investigated, like their actual in vivo mechanical behavior, the influence of age on their response, and the comparison of living and dead tissue mechanical properties.

References

Lewa, C.J., Magnetic Resonance Imaging in the presence of mechanical waves, Spectroscopy letters, 24:55–67, 1991.

Miller, K., Chinzei, K., Orssengo, G., Bednarz, P., Mechanical properties of brain tissue in-vivo: Experiment and computer simulation. Journal of Biomechanics, 33(11):1369–1376, 2000.

Muthupillai, R., Lomas, D.J., Rossman, P.J., Greenleaf, J.F., Manduca, A., Ehman, R.L. Magnetic resonance elastography by direct visualization of propagating acoustic strain waves. Science, 269(5232):1854–1857, 1995.

Oliphant, T.E. , Manduca, A. , Ehman, R.L., Greenleaf, J.L., Complex-valued stiffness reconstruction for magnetic resonance elastography by algebraic inversion of the differential equation. Magnetic Resonance in Medicine, 45(2):299–310, 2001.

Vappou, J., Willinger, R., Breton, E., Choquet, P., Goetz, C., Constantinesco, A., Dynamic viscoelastic shear properties of soft matter by magnetic resonance elastography using a low-field dedicated system. Journal of Rheology, 50(4):531–541, 2006.

Vappou, J., Breton, E., Choquet, P., Goetz, C., Willinger, R., Constantinesco, A., Magnetic resonance elastography compared with rotational rheometry for in vitro brain tissue viscoelasticity measurement, Magnetic Resonance Materials in Physics, Biology and Medicine, 20, 273-278, 2007.