In vivo helium-3 MR-elastography: Assessment in small animal and human lungs

Roberta Santarelli[1], Marion Tardieu[1], Ralph Sinkus[2], Pierre-Yves Brillet[3], Luc Darrasse[1], and Xavier Maître[1]

[1]IR4M, Université Paris sud-XI, Orsay, Ile de France, France, [2]Centre de Recherches Biomédicales Bichat-Beaujon, Paris, Ile de France, France, [3]3Réponses Cellulaires et Fonctionnelles à l'Hypoxie, Bobigny, Ile de France, France

Introduction

The mechanical properties of lung tissue play a key role in the basic function of the organ. They could be very sensitive pulmonary biomarkers as they are dramatically altered by most lung diseases. Currently available imaging modalities fail to regionally probe them *in-vivo*. Initiated in 1995 [1], MR-elastography was recently implemented on a tracer gas, hyperpolarized helium-3, to explore the viscoelastic properties of the lung. The underlying assumption on gas confinement was asserted on phantoms [2] and the technique was proven to be sensitive to lung inflation [3] and insensitive to pulmonary gas content [4]. This work demonstrates the feasibility *in vivo* of helium-3 MR-elastography in small animal and human lungs.

Materials and methods

Experiments were carried out in a 1.5 T scanner (Achieva, Philips Medical Systems, The Netherlands) at CIERM, Bicêtre Hospital. The rats were lying in a helium-3 double-bracelet Helmholtz coil, in supine position, while shear waves were induced at 290 Hz in the animal lungs by pressure waves, remotely generated by a loudspeaker and guided to the top of the chest. A 30-slice gradient echo sequence was implemented with FOV=(80×80×37.5) mm^3, voxel=(1.25×1.25×1.25) mm^3, TE/TR=5.2/10 ms. The human volunteers were lying, supine, in a prototype helium-3 bird-cage coil (Rapid Biomedical, Würzburg, Germany) while shear waves were induced at 100 Hz throughout the lung volume by a home-built MR-compatible transducer fixed on the chest. A 5-slice gradient echo sequence was implemented with FOV=(350×350×60) mm^3, voxel==(12×11×12) mm^3, TE/TR=15/100 ms. Hyperpolarized helium-3 doses of 10 mL, for the rats, and 600 mL, for the volunteers, were respectively administered and inhaled before 17 s and 12 s apnoeas, as required for the acquisition of each motion-encoded direction. Motion sensitizing gradients along the three spatial directions were synchronized with the mechanical waves at different time offsets with respect to the excitation. As a result, for each spatial direction, eight and four snapshots of the propagating waves were recorded for the rat and human experiments, respectively. In data processing [5], resulting maps were averaged over three consecutive slices and the viscoelastic shear moduli were corrected to account for the lung parenchyma density with 0.42 $g{\cdot}mL^{-1}$, for rats, and 0.12 $g{\cdot}mL^{-1}$, for humans, according to lung X-ray computed tomodensitometry [6].

Results

Figure 1 shows the helium-3 ventilation images and the wavelength, dynamic and loss shear modulus maps for the averaged three central slices for rat and human lungs. As summarized in Table 1, mean shear wavelengths (Figure 1.b) are (4±0.04) mm and (44.8±0.3) mm in the rat and human volunteer's lungs, respectively. Corresponding dynamic shear moduli (Figure 1.c) are (0.72±0.002) kPa and (1.83±0.02) kPa, respectively. Corresponding loss shear moduli (Figure 1**: Helium-3 MR-elastography data set averaged over the three central slices for rat (top row) and human (bottom row) lungs.** a. **Magnitude or helium-3 ventilation images** b. **Shear wavelength maps** c. **Dynamic shear modulus maps** d. **Loss shear modulus maps** 1.d) are (0.16±0.003) kPa and (0.25±0.008) kPa, respectively.

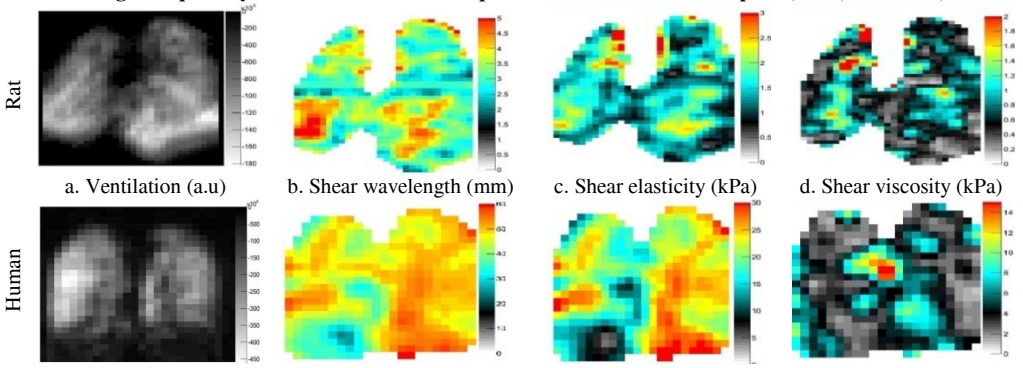

Figure 1: Helium-3 MR-elastography data set averaged over the three central slices for rat (top row) and human (bottom row) lungs. **a.** Magnitude or helium-3 ventilation images **b.** Shear wavelength maps **c.** Dynamic shear modulus maps **d.** Loss shear modulus maps.

Discussion and Conclusion

These results represent the first *in vivo* measurements of shear wave propagation within both rat and human lungs with hyperpolarized helium-3 MR-Elastography. The inferred mean shear dynamic moduli agree fairly well with both stiffness values found *ex vivo* by previous indentation tests [6,7] and density corrected stiffness mean values obtained *in vivo* with dedicated lung parenchyma hydrogen MR-Elastography [8]. Here the structures revealed in the coronal maps of the lung mechanical properties in Figure 1 (b, c, and d) roughly match the expected rat and human organ morphology with a *stiffer* and more *viscous* central bronchial tree. The loss shear modulus (Figure 1.d) is associated with tissue viscosity and it was recently correlated to the inflammation of tissue cells [9,10]. This opens up promising insights into diseased lungs in patients suffering from emphysema, fibrosis, or cancer.

mean ±standard deviation	Dynamic shear modulus(kPa) before correction	Loss shear modulus(kPa) before correction	Density correction ($g\ mL^{-1}$)	Dynamic shear modulus (kPa) after correction	Loss shear modulus (kPa) after correction
Rat	1.8±0.02	0.4±0.008	0.42	0.72±0.002	0.16±0.003
Human	15.3±0.21	2.1±0.07	0.12	1.83±0.02	0.25±0.008

Table 1: Mean viscoelastic moduli for rat and human lungs before and after tissue density correction. The correction factor was inferred from X-ray computed tomodensitometry after conversion of Hounsfield Units (HU) in $g{\cdot}mL^{-1}$: $\rho = (HU+1000)/1000$ with HU_{rat}=-600 and HU_{human}=-880.

Acknowledgements The authors would like to thank Julien Sandeau and Mathieu Sarracanie for their valuable help in data acquisition. This work was supported by European Marie Curie Actions Research Training Network PHeLINet FP6 MRTN-CT-2006-036002

References: 1. Muthupillai *et al.* Science **56**:1854 (1995) **2**. Goss *et al.* Magn Reson Med **56**(5):1060 (2006), Maître *et al.* In: Proceedings of ISMRM Cardiovascular Flow, Function and Tissue Mechanics workshop, Sintra, Portugal, 2009 **3.** Santarelli *et al.* In: Proceedings of Joint Annual Meeting ISMRM-ESMRMB, Stockholm, Sweden, 4613 (2010) **4.** Friese *et al.* In: Proceedings of the Joint Scientific Meeting ISMRM-ESMRMB, Stockholm, Sweden, 3403 (2010) **5**. Sinkus *et al.* Magn Reson Med **53**:372-87 (2005) **6.** Yuan *et al.* Respiratory Research **11**:153 (2010) **6**. Salerno *et al.* J Appl Physiol **86:**66 (1999) **7**. Lai-Fook *et al.* J Appl Physiol **89**: 163 (2000) **8**. Mariappan *et al.* J Magn Reson Imaging **33:**1351 (2011) **) 9.** Salameh *et al.* Radiology, **253**:90 (2009) **10.** Sinkus *et al.* Magn Reson Med **58**:1135 (2007)