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# Titre : *In vivo* liver stiffness assessment in healthy mice by Optimal Control Magnetic Resonance Elastography

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## Summary

Optimal control (OC) and classical multifrequency MR elastography are compared for *in vivo* liver stiffness assessment on mice. OC technique produces higher SNR and accurate G' values for all frequencies, which is of particular interest in cases of fibrosis or iron deposition.

Abstract (/5000 Caractères) : les sous parties sont déjà prévu dans la soumission en ligne

## Introduction

Magnetic Resonance Elastography (MRE) is a non-invasive method employed to quantify tissue stiffness, particularly in conditions like liver fibrosis[1, 2]. Although mice and rats are valuable models for understanding disease physiopathology or monitoring therapy response, only a limited number of studies have addressed liver preclinical MRE.

Main limitations are the design of dedicated drivers for propagating higher frequency waves and shorter transversal relaxations times compared to clinical conditions; imposed by smaller dimension of organs and thus higher magnetic fields of preclinical MRI systems. Recently, Optimal Control (OC) MRE has emerged as a promising alternative, enabling motion encoding at short TE, with improved signal-to-noise ratios (SNR).

In this study, a bench was developed for non-invasive *in vivo* mice MRE liver acquisitions. In order to validate the OC method *in vivo* two MRE sequences were compared at multiple excitation frequencies: a classical Fast Spin Echo (RARE) MRE sequence with motion encoding gradient (MEG) and an OC-based RF pulse RARE sequence [3].

## Methods

Two healthy female mice (mean weight 25g) were examined following ethical approval and adherence to institutional animal care guidelines. Throughout the experiments ran on two separate days, the mice were placed in a prone position and anesthetized using a 2-3% isoflurane in air/oxygen mixture administered via a nose cone while their respiratory rate was continuously monitored and their body temperature regulated with a heating pad.

Classical RARE MRE (MEG RARE MRE) and Optimal Control RARE MRE (OC-RARE MRE) acquisitions were performed and compared. In OC-RARE MRE, RF pulses optimized via OC algorithm were applied simultaneously with a constant gradient G to achieve both slice selection[4], [5] and motion encoding in slice direction. OC-based RF pulses were designed with following optimization input conditions: T2 = 10 ms, gradient amplitude  $G = 211\text{mT/m}$ , motion amplitude  $A = 15\mu\text{m}$ , slice thickness = 1mm, and RF pulse maximal amplitude =  $94\mu\text{T}$  (Acquisition parameters are detailed on **Table 1**).

Technique	FO (Hz)	TR (ms)	TE (ms)	FOV (mm <sup>2</sup> ) / Matrix size (pix)	MEG amplitude (mT/m)	G Amplitude for OC-RARE MRE (mT/m)	Number of MEG's period	Number of Phase Offset	Average / RARE Factor	Number of slices	Slice thickness (mm)
MEG RARE MRE	200	1000	14,83	35*35 / 192*192	211	211	1	4	1 / 4	2	1
MRE	400		8,58				2			1	
OC-RARE MRE	200		10,66				1			2	
MRE	400	1000	8,33	35*35 / 192*192	211	211	2	4	1 / 4	1	1
MRE	600		5,03				1			2	
MRE	300		10,66				2			1	
MEG RARE MRE	500	1000	8,33	35*35 / 192*192	211	211	1	4	1 / 4	2	1
MRE	700		9,77				2			1	
OC-RARE MRE	300		10,66				1			2	
MRE	500	1000	5,03	35*35 / 192*192	211	211	2	4	1 / 4	1	1
MRE	700		9,77				1			2	
MRE	300		10,66				2			1	

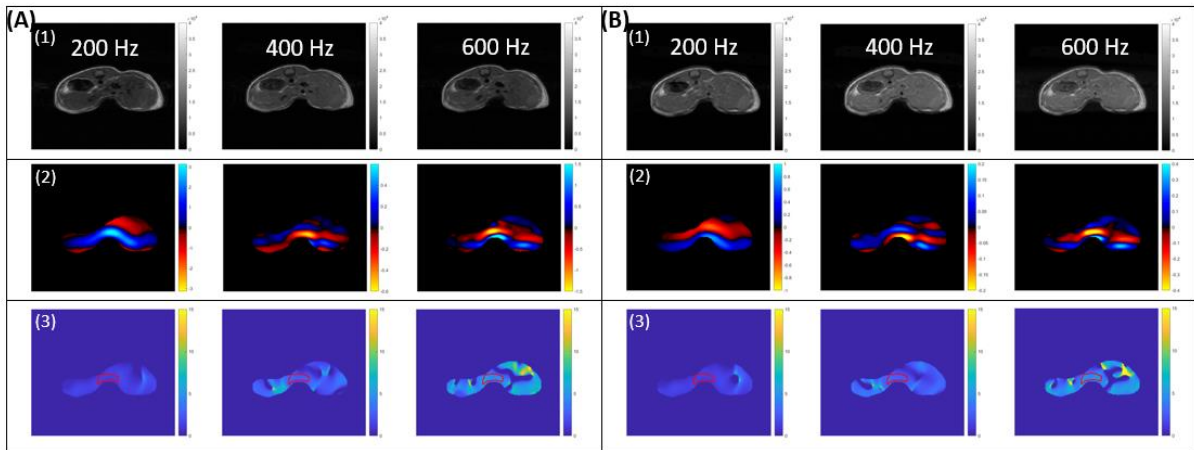
**Table 1:** Acquisition parameters used for both sequences MEG RARE MRE and OC RARE MRE.

MRE acquisitions were conducted on a 7T MRI system (*Bruker, Germany*), with a 40mm quadrature volume coil. Motion was induced by a CEDRAT Technologies piezoelectric actuator at [200, 400, 600] Hz on the first day, and [300, 500, 700] Hz on the second day.

Two acquisitions with opposite MEG polarity in the slice direction were performed with phase image subtraction to remove static phase offsets. Phase images were then unwrapped to obtain displacement fields, which were temporally Fourier transformed along the temporal direction to filter information at the desired frequency. Directional filtering along the wave propagation direction, followed by a 4th order 2D Butterworth spatial bandpass filter, were applied to reduce low and high-frequency noise. Finally, shear modulus ( $G'$ ) were obtained with an Algebraic Inversion of the Differential Equation (AIDE) algorithm[6].

Mean and standard deviations of  $G'$  were calculated manually trace regions of interest (ROI) in the livers of mice for both MEG RARE MRE and OC-RARE MRE sequences. To assess and compare the quality of signal acquisition between the two sequences, the SNR were calculated on the magnitude images, by evaluating the ratio between the average pixel intensity in a manually traced ROI in the liver and the standard deviation of the noise (ROI traced outside the mouse).

## Results



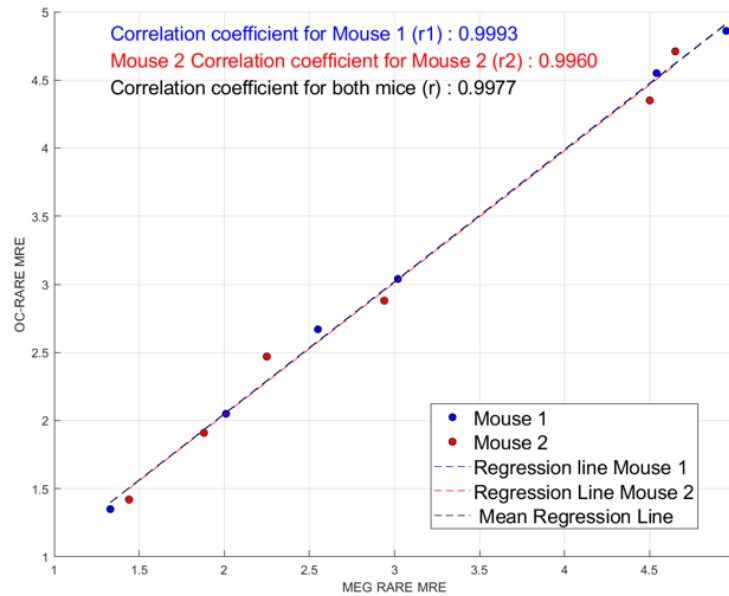
**Figure 1 :** Representative images acquired at day 1 for mouse 1 :  
**Columns :**(A) MEG RARE MRE sequence, (B) OC- RARE MRE sequence  
**Rows :**(1) Magnitude, (2) Phase images and (3) Elastograms

**Figure 1** displays a representative magnitude, phase images, and elastograms that underwent analysis and comparison. **Table 2** presents the measured SNR, mean, and standard deviation of  $G'$  values within the region of interest placed on the liver for the experiments conducted over two days on both mice.

Mice	Frequency (Hz)	G' with SD (kPa)		SNR	
		MEG RARE MRE	OC-RARE MRE	MEG RARE MRE	OC-RARE MRE
1	200	$1,33 \pm 0,11$	$1,35 \pm 0,1$	35,06	98,6
2		$1,44 \pm 0,28$	$1,42 \pm 0,22$	36,56	96,85
1	300	$2,01 \pm 0,27$	$2,05 \pm 0,23$	34,38	92,39
2		$1,88 \pm 0,31$	$1,91 \pm 0,24$	29,45	87,51
1	400	$2,55 \pm 0,24$	$2,67 \pm 0,23$	54,43	107,7
2		$2,25 \pm 0,34$	$2,47 \pm 0,31$	52,56	104,4
1	500	$3,02 \pm 0,34$	$3,04 \pm 0,32$	38,99	91,71
2		$2,94 \pm 0,41$	$2,88 \pm 0,37$	35,18	88,45
1	600	$4,54 \pm 0,43$	$4,55 \pm 0,38$	49,61	105,4
2		$4,5 \pm 0,39$	$4,35 \pm 0,37$	45,53	102,6
1	700	$4,95 \pm 0,62$	$4,86 \pm 0,57$	36,75	93,92
2		$4,65 \pm 0,48$	$4,71 \pm 0,45$	32,64	92,36

**Table 2:** Summary of obtained results ( $G'$  and SNR) for the two mice on days 1 (200-400-600 Hz) and 2 (300-500-700 Hz) based on the acquisition method.

**Figure 2** shows the good correlation of  $G'$  values for each technique and frequency, demonstrating the effectiveness of the OC-RARE MRE sequence on estimating liver stiffness *in vivo*. Moreover, the progressive increase in  $G'$  with frequency observed over the two days, demonstrates the ability to assess the dispersive behavior of liver stiffness *in vivo* as well as the consistency of results obtained across experiments.



**Figure 2:** Scatter plot displaying  $G'$  values (in kPa) for MEG RARE MRE and OC-RARE MRE sequences at various excitation frequencies. Dashed lines represent linear regression lines.  $G'$  values used are summarized in **Table 2**.

SNR variability, due mainly to respiration, is low in OC. However, in classical MRE it is greater, since TEs vary according to MEG frequency. Additionally, the OC-RARE MRE sequence exhibits significantly higher SNR compared to the MEG RARE MRE sequence.

## Discussion & conclusion

The promising findings on healthy mice confirm the ability of OC-RARE MRE to quantify liver stiffness at multiples frequencies, as shown in **Figure 2** with a correlation coefficient  $r$  close to 1. The significant improvement in SNR with the OC-RARE MRE sequence opens up promising prospects, especially for low excitation frequencies applications. This also proves particularly beneficial in tissues with low T2/T2\* values, such as in cases of advanced fibrosis stages or liver iron deposition.

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## References

- [1] S. K. Venkatesh, G. Wang, S. G. Lim, et A. Wee, « Magnetic resonance elastography for the detection and staging of liver fibrosis in chronic hepatitis B », *Eur Radiol*, vol. 24, n° 1, p. 70-78, janv. 2014, doi: 10.1007/s00330-013-2978-8.
- [2] S. Hoodeshenas, M. Yin, et S. K. Venkatesh, « Magnetic Resonance Elastography of Liver: Current Update », *Topics in Magnetic Resonance Imaging*, vol. 27, n° 5, p. 319-333, oct. 2018, doi: 10.1097/RMR.000000000000177.
- [3] P. Sango-Solanas *et al.*, « Short echo time dual-frequency MR Elastography with Optimal Control RF pulses », *Sci Rep*, vol. 12, n° 1, p. 1406, janv. 2022, doi: 10.1038/s41598-022-05262-3.
- [4] E. Van Reeth, H. Ratiney, M. Lapert, S. J. Glaser, et D. Sugny, « Optimal control theory for applications in Magnetic Resonance Imaging », *Pac. J. Math. Ind.*, vol. 9, n° 1, p. 9, déc. 2017, doi: 10.1186/s40736-017-0034-3.
- [5] P. Sango Solanas, K. Tse Ve Koon, H. Ratiney, F. Millioz, C. Caussy, et O. Beuf, « Harmonic wideband simultaneous dual-frequency MR Elastography », *NMR in Biomedicine*, vol. 34, n° 2, févr. 2021, doi: 10.1002/nbm.4442.
- [6] T. E. Opliphant *et al.*, « Complex-Valued Stiffness Reconstruction for Magnetic Resonance Elastography by Algebraic Inversion of the Differential Equation », *Magnetic Resonance in Med*, vol. 45, p.299-310, mars 2001, doi: 10.1002/1522-2594(200102)45:23.O.CO;2-O