Interventional MR Elastography for MRI-Guided Percutaneous Procedures

Nadège Corbin, Jonathan Vappou, Elodie Breton, Quentin Boehler, Laurent Barbe, Pierre Renaud, Michel de Mathelin de Papigny

► To cite this version:

Nadège Corbin, Jonathan Vappou, Elodie Breton, Quentin Boehler, Laurent Barbe, et al.. Interventional MR Elastography for MRI-Guided Percutaneous Procedures. *Magnetic Resonance in Medicine*, 2015, 75 (3), pp.1110-1118. 10.1002/mrm.25694 . hal-02375273

HAL Id: hal-02375273

<https://hal.science/hal-02375273>

Submitted on 28 Nov 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Running Title: Interventional Magnetic Resonance Elastography

Interventional Magnetic Resonance Elastography for MRI-guided percutaneous procedures

Nadège Corbin ¹, Jonathan Vappou ^{1*}, Elodie Breton ¹, Quentin Boehler ¹, Laurent Barbé ¹,
Pierre Renaud ¹ and Michel de Mathelin ¹

¹ ICube, University of Strasbourg, CNRS, IHU Strasbourg, France

(4450 words)

* Jonathan Vappou, Ph.D (Corresponding author)

ICube, University of Strasbourg, CNRS, IHU Strasbourg, France

Mailing address: IRCAD/ICube, 1 place de l'Hôpital, 67000 Strasbourg , France

Telephone: +33 3 88 11 91 32

Email: jvappou@unistra.fr

Abstract.

PURPOSE: MRI-guided thermal ablations require reliable monitoring methods to ensure complete destruction of the diseased tissue while avoiding damages to the surrounding healthy tissue. Based on the fact that thermal ablations result in substantial changes in biomechanical properties, interventional Magnetic Resonance Elastography (MRE) dedicated to the monitoring of MR-guided thermal therapies is proposed here.

METHODS: Interventional MRE consists of a needle MRE driver, a fast and interactive gradient echo pulse sequence with motion encoding, and an inverse problem solver in real-time. This complete protocol was tested in vivo on swine and the ability to monitor elasticity changes in real-time was assessed in phantom.

RESULTS: Thanks to a short repetition time, a reduction of the number of phase-offsets and the use of a sliding window, one refreshed elastogram was provided every 2.56 seconds for an excitation frequency of 100 Hz. In vivo elastograms of swine liver were successfully provided in real-time during one breath-hold. Changes of elasticity were successfully monitored in a phantom during its gelation with the same elastogram frame rate.

CONCLUSION: This study demonstrates the ability of detecting elasticity changes in real-time and providing elastograms in vivo with interventional MRE that could be used for the monitoring of thermal ablations.

Keywords: MR elastography, thermal ablation, therapy monitoring, interventional radiology

Introduction

Thermal therapies and biopsies are increasingly performed using percutaneous approaches under real-time MRI-guidance. Such minimally invasive procedures have been shown to improve the patient comfort and reduce the complication rate (1). Thermal ablation methods include radiofrequency (RF), microwave, laser, high intensity focused ultrasound ablations (HIFU) and cryotherapy (2). All of them consist in inducing tissue destruction through thermal changes (hot or cold).

MRI is a non-ionizing imaging modality, offers good intrinsic contrast in soft tissues and has full 3D imaging capability. The emergence of real-time interactive MR-imaging and MR-compatible surgical tools has allowed the development of interventional MRI (3). Specific MR-pulse sequences have been adapted to interventional radiology by increasing the acquisition speed (4), allowing for frame rate values inferior to one second.

The standard protocol of a thermal therapy consists in several steps: 1/ Planning 2/ Targeting 3/ Monitoring 4/ Controlling and finally 5/ Assessing the treatment response (5). Except for HIFU therapy, all thermal ablation techniques require a percutaneous applicator. MRI-guidance offers the possibility of interactively changing the position and orientation of the image slice without interrupting the acquisition, so that the operator is able to align the slice with the applicator during the whole insertion process. In addition, thermal ablations can be typically monitored by using MR thermometry (6–10). However, MR-thermometry provides only information on an external instantaneous parameter, namely, the temperature, and gives no direct information on intrinsic changes in tissue structure.

Magnetic Resonance Elastography (MRE) is a non-invasive technique that allows measuring the mechanical properties of soft tissues. MRE relies on a mechanical excitation that results in the propagation of a low-frequency (~ 60 Hz) mechanical wave inside the tissue of interest. The displacement induced by the wave is encoded on phase images by a motion-sensitizing MR pulse sequence (11). The propagation speed of the wave depends on mechanical properties; therefore, solving an inverse problem allows to retrieve mechanical properties from the phase images, yielding elastograms or elasticity maps. Several studies have illustrated the capability of MRE to detect tumors in organs such as breast (12, 13) or liver (14, 15), based on the fact that tumors and healthy tissues have different mechanical properties.

Typical MRE acquisition times are currently not suitable for interventional applications that require real-time guidance. Several approaches have been proposed to accelerate the MRE acquisition. For example, motion sensitizing gradients (MSG) have been implemented on fast MR-pulse sequences such as gradient (16) and spin (17) echo sequences with echo-planar imaging. Another interesting approach aiming at reducing MRE acquisition times is the optimization of k-space filling (18) based on the fact that the main information of MRE phase image is located around the center of the k-space. The emergence of fractional

encoding (19) (encoding frequency higher than mechanical excitation frequency) has made possible to reduce the echo time and has led to new acceleration techniques such as multifrequency sequences (20, 21). More recently, multidirectional (22) sequences have been designed to reduce the number of acquisitions. In spite of previously mentioned refinements to accelerate the MRE examination, there are only a few reports of the use of MRE in interventional MRI. To the best of our knowledge, only four publications (23–26) have proposed to use information on elasticity obtained by MRE to assess the treatment response of MR-guided thermal ablations. Among these, only one publication successfully demonstrated the monitoring of thermal ablation in vivo with MRE (23). These publications have some limitations: 2D elastograms or 1D displacement values have not been continuously computed during the thermal ablation, but only before and after, or with a long interval between successive measurements (40 s). In the field of ultrasound elastography, *Mariani et al.* (27) showed that the Young's modulus of the treated liver tumor in swine increases from 6 to 40 kPa approximately during a 5 min-long radiofrequency ablation by providing elastographic information every 30 seconds. The monitoring of thermal ablations with MRE is limited by the number of images required for the reconstruction of one elastogram, while the monitoring of thermal ablations requires a high information update rate. Conventional MRE uses 4, 8 or more phase images with varying phase shifts between mechanical excitation and MSG in order to apply the temporal Fourier transform and to select only the displacement induced by the generated mechanical wave. In addition, conventional MRE external excitation systems typically consist in a large pneumatic exciter placed on the skin that enables a completely non-invasive examination. On one hand, deep-lying regions are difficult to reach because of the wave attenuation through the body. On the other hand, their bulk prevents their use in the very demanding interventional MRI environment where compact and ergonomic tools must be used. In this context, the objective of this work is to develop interventional MRE for the monitoring of percutaneous procedures in order to provide the physician with a refreshed elasticity map during the thermal ablation. The method uses a mechanical exciter specifically adapted to percutaneous procedures, a fast and interactive motion encoding pulse sequence with reduced number of phase-offsets, and an online inverse problem solver with high elastogram update rate.

Methods

Needle MRE driver as mechanical exciter

A minimally-invasive system was used for generating shear waves. *Chan et al.* (28) demonstrated that the longitudinal movement of a needle inside a tissue could be the source of a mechanical wave for MRE. *Zhao et al.* (29) investigated this kind of device to show that deep regions are more accessible with a needle MRE driver than with the surface driver. In the current study, a specific needle MRE driver was designed to

generate the mechanical wave. A piezoelectric actuator (APA^{TM} Cedrat Technologies, Meylan, France) was used to make a needle vibrate inside the tissue directly within the region of interest (Figure 1). This MR-compatible piezoelectric stack driver was chosen for its simplicity of use, its low bulk that was particularly appreciated in the interventional MRI environment, and its reliability and safety in terms of excitation displacement range, intrinsically limited by the actuator. The system was used with an MR-compatible 18 gauge needle, but the needle can easily be replaced by other MR-compatible needles used in interventional procedures. The actuator was powered by a function generator placed in a Faraday shield localized in the MR-room and triggered by the pulse sequence through synchronized optical pulse. The mechanical stimulation of the needle can vary from 50 Hz to 200 Hz. The displacement amplitude depends on the applied voltage and the constraint exerted by the tissue on the needle. The typical displacement is 100 μm in the direction of the needle shaft axis in the absence of any mechanical load.

Interactive motion-encoding pulse sequence

Bipolar motion sensitizing gradients were implemented on the interactive and fast spoiled gradient echo sequence (Beat_IRT, Siemens Healthcare, Germany). The MR-pulse sequence chronogram including MSG is shown in Figure 2. In this work, one cycle of MSG was implemented and its amplitude was set to 20 $\text{mT}\cdot\text{m}^{-1}$. The operator had the possibility of interactively changing the position and the orientation of the acquired slice without interrupting the acquisition. The inter-echo space was equivalent to one mechanical vibration period using a fractional encoding scheme (19). The movement was encoded in only one direction by one cycle of a bipolar motion sensitizing gradient. A phase difference image was reconstructed from two images with opposite MSG polarities in order to cancel the constant noise and increase the motion encoding. MRE experiments reported in the literature use 4, 8 or more phase difference images obtained by changing the shift between the mechanical wave and the MSG. The phase-offsets are regularly spaced across a mechanical period. In the present paper, we propose to use only 3 phase-offsets, in order to reduce the total acquisition time of all phase images that will be used to reconstruct one elastogram. The chosen number of three phase-offsets is the minimum number required by the Nyquist-Shannon sampling theorem to apply the discrete Fourier transform.

Real-time image processing

Every acquired image was transferred to an external computer in real-time through TCP/IP connection. Phase images were processed in Matlab (Mathworks Inc., Natick, MA) in real-time. First, a 2D phase unwrapping algorithm (30) was applied on phase difference images. A temporal fast discrete Fourier transform was implemented on each pixel of a set of unwrapped phase difference images, corresponding to

a complete mechanical excitation cycle, in order to select the frequency of interest. Finally, a Local Frequency Estimation (LFE) -based algorithm (31, 32) was implemented with 10 lognormal quadrature filter pairs spatially oriented in four orthogonal directions and applied in real-time to estimate the local wavelength. LFE aims at measuring the local frequency of a signal which is defined as the derivative of the phase of its analytic signal (33, 34). Under the assumption of a purely linear elastic medium, the shear modulus μ can be related to the wavelength λ by $\mu = \rho(\lambda f)^2$ with ρ being the tissue density and f the excitation frequency.

Let α be the phase shift between the mechanical excitation and the motion sensitizing gradient, $\alpha = 2n\pi/N$, $n=1 \dots N$ with N the number of phase-offsets. Using MRE for interventional MRI requires faster flow of information. The sliding window method proposed here allows the reconstruction of an elastogram with every newly acquired pair of images with opposed MSG polarity (Figure 3). The first elastogram is computed from N phase difference images as in conventional MRE, and then the second one is reconstructed from the $N-1$ previous phase difference images and the most recent one. Hence, one elastogram is reconstructed with every new available phase difference image. As mentioned before, the pulse sequence used here allows to interactively change the position and orientation of slices. If such a change occurs, the algorithm is able to detect this slice pose change and to restart in order to provide the first elastogram for the new slice (as illustrated by slice $n+1$ in Figure 3). Elastograms were displayed on the external computer after median filtering.

Experimental setup

Three different experiments were performed to evaluate interventional MRE in a large bore 1.5T MRI scanner (MAGNETOM Aera, Siemens, Germany).

Exp. 1: Influence of the number of phase-offsets

A preliminary experiment was carried out to evaluate the relevance of computing an elastogram with only 3 phase difference images. Comparison was performed between elastograms reconstructed with the LFE algorithm using 1 phase-offset only (no temporal Fourier transform) or 3, 4, 6 or 12 phase-offsets. A mechanical wave of 120 Hz was generated with an in-house conventional surface pneumatic exciter in a homogeneous phantom made of gelatin (5 %). The designed pulse sequence previously described was used to encode the movement. A set of 240 phase images was collected with 12 phase-offsets evenly spaced across a phase cycle, and 2 images with opposite MSG polarities for each phase-offset. From this set of 240 images, 10 elastograms were reconstructed after subtracting, unwrapping, and filtering of the temporal Fourier transform for the 12 phase-offsets (Figure 4 a). Then, one phase difference image out of two was selected from the entire set in order to simulate an MRE acquisition with 6 phase-offsets, yielding 10 other

elastograms. This decimation was repeated for simulation of MRE acquisition with 4 and 3 phase-offsets, respectively. Finally, 10 other elastograms were reconstructed without applying the temporal Fourier transform using every first difference image out of 12 (Figure 4 *a*). Relevant parameters of acquisition include: excitation frequency 120 Hz, MSG frequency 290 Hz, encoding direction: phase encoding, encoding amplitude 20 mT.m⁻¹, axial slice orthogonal to the surface of the pneumatic exciter, slice thickness 10 mm, FOV 300 mm × 300 mm, acquisition matrix 128 × 128, Repetition Time / Echo Time TR/TE 8.33/5.7 ms, flip angle 10 ° and bandwidth frequency 400 Hz pixel⁻¹. Mean Λ_i^j and standard deviation σ_i^j of wavelength λ were calculated in a large elliptical region of interest (166 mm × 58 mm) on every elastogram j of each data set i . A total of 5 datasets ($i = 1, 3, 4, 6$ and 12 corresponding to the number of phase-offsets) was obtained after appropriate data decimation. For each data set, 10 elastograms ($j = 1$ to 10) were reconstructed. Data analysis was performed on median filtered (kernel of 4 × 4) elastograms, given in terms of wavelength λ [mm].

Exp. 2: In vivo experiment

A feasibility experiment was performed on one porcine subject (35.2 kg) in vivo. The objective was to demonstrate the feasibility of obtaining elastograms in real-time with interventional MRE in vivo and to evaluate the stability of the method. This experiment was approved by the local ethics committee (ICOMETH C2EA - 38). The animal was anesthetized (propofol 3 mg kg⁻¹, pancuronium 0.2 mg kg⁻¹ and isoflurane 2 %) and placed in the large bore 1.5T scanner with a 4-channel flex coil on the abdomen and the spine coil. The needle was inserted by an experienced interventional radiologist inside the liver under MRI-guidance and hand-held during the MRE experiment. MRE scans were performed under one breath hold. Relevant parameters of acquisition include: excitation frequency 100 Hz, MSG frequency 160 Hz, encoding direction: through slice, encoding amplitude 20 mT.m⁻¹, one slice orthogonal to the needle MRE driver (as shown in Figure 5 *a-b*), slice thickness 10 mm, FOV 300 mm × 300 mm, acquisition matrix 128 × 128, TR/TE 10/7.9 ms, flip angle 15°, and bandwidth frequency 795 Hz pixel⁻¹. The total acquisition time for one MR-image was equal to 1280 ms. Six images corresponding to 3 phase-offsets each with 2 opposite MSG polarities were used for the reconstruction of one elastogram. The total acquisition time of the complete data set for one elastogram was equal to 7.68 s. Using the sliding window scheme, elastograms were provided in 2.56 s with every new phase difference image obtained. Elastograms showing the shear modulus μ [Pa] were displayed in real-time on the external computer after median filtering (kernel of 8 × 8).

In order to evaluate the stability of the proposed method, a single breath-held experiment was performed during 85s, during which 31 elastograms were reconstructed. For each elastogram, the shear modulus was averaged within a region of interest of 8 mm in diameter.

Exp. 3: Real-time monitoring of elasticity changes

A third experiment was designed in order to evaluate the capability of observing changes in elasticity in real-time within a region of interest in a gelatin phantom. An approximately 4 cm hole in diameter was scooped out from a homogeneous gelatin phantom (8 %) (Figure 6). The needle was inserted vertically in the phantom and held by a Plexiglas structure in order to avoid gel damage during the experiment. A few minutes before the acquisition, a small volume (200 mL) of gelatin (10 %) was prepared and cooled down. Once the temperature reached 22°C, the liquid was poured in the hole of the phantom and its solidification was monitored using real-time MRE during 30 minutes. Relevant imaging parameters include: excitation frequency 100 Hz, MSG frequency 210 Hz, encoding direction: through slice, encoding amplitude 20 mT.m⁻¹, one slice orthogonal to the needle MRE driver, slice thickness 10 mm, FOV 350 mm × 350 mm, acquisition matrix 128 × 128, TR/TE 10/7 ms, flip angle 15° and bandwidth frequency 380 Hz pixel⁻¹. As in Exp. 2, 3 phase-offsets each with 2 opposite MSG polarities were used. After initial calculation, a new elastogram (μ [Pa]) after median filtering with a kernel of 4 × 4) was provided every 2.56 s with every new phase-offset pair.

Results

Exp. 1: Influence of the number of phase-offsets

Analysis of statistical parameters was performed on computed elastograms in order to evaluate their precision. The average Λ_i of the means and the average σ_i of the standard deviations of each data set i of elastograms ($i = 1, 3, 4, 6$ and 12 corresponding to the number of phase-offsets) are shown in Figure 4 *b-c*. The implementation of the temporal Fourier transform allows for substantial improvement of elastogram reliability as shown by the significantly higher mean standard deviation σ of λ obtained for $i = 1$ compared to $i = 3, 4, 6$ or 12 . Elastograms obtained using the LFE method are stable between $i = 3$ to 12 phase-offsets. Three phase-offsets allow obtaining results close to those obtained with a conventional protocol with four phase-offsets, but with a 25 % reduction in image acquisition time per elastogram.

Exp. 2: In vivo experiment

The needle MRE driver works as a cylindrical source of shear waves: circular wave fronts around the needle shaft were visible on the unwrapped phase difference image (Figure 5 *c*). Elastograms at 100 Hz were reconstructed within a circular region around the needle (85 mm in diameter, Figure 5 *d*). Elastogram reconstruction was not performed within the zone corresponding to the needle artifact. The first elastogram was displayed after 7.68 s and refreshed every 2.56 s using the sliding window elastogram calculation method. Any change of orientation or position of the slice resulted in a waiting time of 7.68 s (i.e. 3 phase-offsets, each one with two opposite MSG) before the next elastogram display. Current online processing

time is 1.2 s per phase difference image, which allows a real-time display of the elastogram with a constant delay of 1.2 s after the last phase image is reconstructed by the scanner. The image transfer time is negligible compared to image acquisition time. The stability of our measurements was investigated over a period of 85 seconds, corresponding to 31 elastograms. Figure 5 *e* illustrates the shear modulus averaged within a ROI of 8 mm in diameter for each one of the 31 elastograms. The shear modulus averaged among the 31 elastograms was found equal to 3.5 kPa, and the standard deviation of the mean was equal to 150 Pa.

Exp. 3: Real-time monitoring of elasticity changes

Phase images acquired at different time steps of the third experiment are shown in Figure 7. The wave pattern at 100 Hz was visible in the inclusion a few minutes after filling the hole with 10 % gelatin. Changes in the wave pattern could be clearly seen over time within the inclusion, corresponding to the cross-linking process of the gelatin, which could also be seen in the corresponding elastograms. Two circular regions of interest were selected, one inside and one outside the inclusion (12 mm in diameter). Means and standard deviations of the shear modulus in the two regions of every computed elastogram are plotted as a function of time for these two regions of interest (Figure 8 and supporting video). As expected, the shear modulus of the surrounding gel was found to be constant around 5 kPa. For a few minutes, the inclusion was liquid and no wave could propagate through it, as illustrated in Figure 8 *a* from 0 to ~200 s. Values obtained for the standard deviation were very high and not repeatable during these first 200 s, as it would be expected because of the absence of shear waves. After 200 s, waves with a small wavelength were observed, corresponding to a dramatic decrease of the standard deviation of μ , and reliable values of shear modulus were obtained. Then, the wavelength in the inclusion increased consistently over time and the interventional MRE method was able to evaluate the variation with a mean standard deviation in the inclusion around 2% of the averaged shear modulus. Significant changes in elasticity could be precisely observed as illustrated by the short temporal window of 2 minutes (Figure 8 *b*).

Discussion

Three experiments were carried out to study the feasibility and the relevance of interventional MRE. A complete MRE system was designed to fulfill the specific requirements for interventional MRE and was tested in phantoms and in vivo.

The needle MRE driver was hand-held by the interventional radiologist for Exp.2 as it would be done in a clinical protocol. The advantage of such internal mechanical exciter is the generation of a localized wave source directly in the region of interest. Hence, the problem of wave attenuation through the tissue located between the mechanical driver and the region of interest is circumvented. This implies that deep-lying

regions of interest can be investigated, and the use of high frequency excitation becomes possible in spite of higher wave attenuation. It is important to note that the excitation frequency can be changed to low values (e.g. 60 Hz) or high values (e.g. 150Hz) depending on the requirements of the application (large coverage or high resolution).

The direction of wave propagation is essentially perpendicular to the needle axis and the displacement is parallel to it, which implies a well-defined cylindrical shear wave pattern. This well-defined shear wave pattern is particularly well-suited to the resolution of the inverse problem. However, the region lying behind the tip of the needle is difficult to investigate because the wave does not propagate correctly further than the needle tip in the needle shaft direction. Further work on this device consists in adapting the mechanical actuator to any percutaneous applicators, including those used for thermal ablations. The same percutaneous instrument may be used for MRE and treatment thus minimizing additional instrumentation.

Interventional MRE includes a fast and interactive MRE sequence based on a spoiled gradient echo pulse sequence. A major advantage of the proposed MRE sequence is its interactivity, which allows changing the monitored image plane dynamically. This is expected to help to the monitoring of thermal therapy. In order to reduce the image acquisition time, the repetition time is equal to only one mechanical excitation cycle thanks to fractional encoding.

In conventional MRE, at least 4 phase-offsets are used to reconstruct the elastogram. As opposed to diagnostic MRE, interventional MRE requires a short acquisition time: acquisition speed of all images necessary for one elastogram must be high enough compared to typical elasticity rate of change. Acquiring several phase offsets enables to apply a temporal Fourier transform and then to select only the displacement induced by the generated shear wave at a given frequency. The first idea would be to remove this step and reduce by 75 % minimum the acquisition time compared to 4 phase-offsets. However, *Exp.1* showed that removing the temporal Fourier transform implies a dramatic decrease of the elastogram quality. A tradeoff was proposed here to improve acquisition times while preserving the quality of elastograms. Only 3 phase-offsets were acquired in order to reduce by 25 % the acquisition time (compared to 4 phase-offsets) without significant loss of the elastogram quality as demonstrated by *Exp.1*.

A conventional surface pneumatic exciter was used in this experiment in order to provide baseline results regarding the influence of the number of phase-offsets. These results are obviously important for interventional MRE, but they are also significant for conventional breath-held diagnostic MRE that could be accelerated in the same manner by decreasing the number of phase-offsets.

In this work, phase difference images were calculated with opposite MSG polarities yielding a total of 6 images for 3 phase-offsets. An alternative is to subtract a single reference phase image without MSG to the following MSG encoded phase images (21). This could potentially reduce to 4 images the total number of

images required to reconstruct one elastogram. However, the motion encoding would be decreased by a factor 2, and using the first image as a reference would result in a higher sensitivity to temperature changes. It is important to emphasize that the proposed method was developed optimally for the monitoring of elasticity changes in interventional radiology, and not particularly for full 3D quantitative biomechanical characterization. Only one excitation frequency and one slice were therefore used. Moreover, as previously mentioned, the needle MRE driver generates a well-defined shear wave pattern. Additional steps of acquisition and processing aiming at removing the longitudinal component (35) are therefore not expected to improve substantially the result of the inverse problem. Motion is thus encoded in only one direction, parallel to the needle shaft axis.

The sliding window scheme was implemented in order to provide an elastogram with every new phase difference image obtained. Thus, the elastogram update rate is as high as the one obtained with the one-phase-offset acquisition protocol but with the benefit of the temporal Fourier transform. Nevertheless, each elastogram is not a totally independent measurement since each wave image is used for three consecutive elastograms. A smoothing effect might therefore be noticed but the accuracy of the measurements is not affected in a different manner as it would be with a classical MRE reconstruction scheme.

The stability of the proposed method was assessed *in vivo*. As illustrated by Figure 5 *e*, the variation of the shear modulus was inferior to 5 % among the 31 elastograms corresponding to a 85 seconds single breath-held experiment. This result illustrates the stability of the proposed method *in vivo*.

It is important to emphasize that acceleration methods for image acquisition, such as partial k-space filling or parallel imaging, were not investigated in this work, which aims at establishing a baseline method for interventional MRE. These acceleration methods should be used in future work for further reduction of the total acquisition time per elastogram.

Exp.3 showed the capability of interventional MRE to monitor the temporal evolution of the elasticity of a phantom during its gelation with good accuracy and high frame rate. Although the kinetics involved in this experiment were slow compared to the change rate of elasticity expected during thermal ablations (27), Exp.3 proved that the method allows to finely monitor elasticity changes. Further experiments are planned to test the protocol for monitoring thermal ablations *in vivo*.

Conclusion

In this work, interventional MRE was developed specifically for MRI-guided percutaneous procedures. Ultimately, this method aims at providing a new biomarker for monitoring thermal ablations in real-time. This dedicated MRE protocol consists of 1/ a needle MRE driver that generates a well-defined shear wave directly in the region of interest regardless of its depth, 2/ an interactive real-time motion sensitizing pulse

sequence that encodes the displacement on phase images in a short acquisition time and 3/ online reconstruction that provides an elastogram with every new phase difference image. Elastograms of swine liver were reconstructed in real-time during one breath-hold and elasticity changes were monitored in real-time in phantom. This additional information on elasticity is expected to help the physician to better assess the treatment response during thermal ablations.

Acknowledgements

The authors would like to thank Dr Fabrice Bing and Pramod Rao from the department of interventional radiology of Strasbourg hospital for his help during the in vivo experiments, as well as Lucile Zorn and Florent Le Bastard for their help in computer assisted design. This work was supported by French state funds managed by the ANR within the Investissements d'Avenir programme for the Labex CAMI (ANR-11-LABX-0004) and the IHU Strasbourg (ANR-10-IAHU-02).

References

1. Gazelle GS, McMahon PM, Beinfeld MT, Halpern EF, Weinstein MC. Metastatic colorectal carcinoma: cost-effectiveness of percutaneous radiofrequency ablation versus that of hepatic resection. *Radiology* 2004;233:729–739. doi: 10.1148/radiol.2333032052.
2. Webb H, Lubner MG, Hinshaw JL. Thermal Ablation. *Semin. Roentgenol.* 2011;46:133–141. doi: 10.1053/j.ro.2010.08.002.
3. Hushek SG, Martin AJ, Steckner M, Bosak E, Debbins J, Kucharzyk W. MR systems for MRI-guided interventions. *J. Magn. Reson. Imaging* 2008;27:253–266. doi: 10.1002/jmri.21269.
4. Yutzy SR, Duerk JL. Pulse sequences and system interfaces for interventional and real-time MRI. *J. Magn. Reson. Imaging* 2008;27:267–275. doi: 10.1002/jmri.21268.
5. Goldberg SN, Charboneau JW, Dodd GD, et al. Image-guided Tumor Ablation: Proposal for Standardization of Terms and Reporting Criteria. *Radiology* 2003;228:335–345. doi: 10.1148/radiol.2282021787.
6. Chen JC, Moriarty JA, Derbyshire JA, et al. Prostate cancer: MR imaging and thermometry during microwave thermal ablation-initial experience. *Radiology* 2000;214:290–297.
7. Seror O, Lepetit-Coiffé M, Bail B, Senneville BD, Trillaud H, Moonen C, Quesson B. Real time monitoring of radiofrequency ablation based on MR thermometry and thermal dose in the pig liver in vivo. *Eur. Radiol.* 2008;18:408–416. doi: 10.1007/s00330-007-0761-4.
8. Arora D, Cooley D, Perry T, Guo J, Richardson A, Moellmer J, Hadley R, Parker D, Skliar M, Roemer RB. MR thermometry-based feedback control of efficacy and safety in minimum-time thermal therapies: Phantom and in-vivo evaluations. *Int. J. Hyperthermia* 2006;22:29–42. doi: 10.1080/02656730500412411.
9. Rieke V, Kinsey AM, Ross AB, Nau WH, Diederich CJ, Sommer G, Pauly KB. Referenceless MR thermometry for monitoring thermal ablation in the prostate. *IEEE Trans. Med. Imaging* 2007;26:813–821. doi: 10.1109/TMI.2007.892647.
10. Baron P, Ries M, Deckers R, de Greef M, Tantt J, Köhler M, Viergever MA, Moonen CTW, Bartels LW. In vivo T2 -based MR thermometry in adipose tissue layers for high-intensity focused ultrasound near-field monitoring. *Magn. Reson. Med. Off. J. Soc. Magn. Reson. Med. Soc. Magn. Reson. Med.* 2014;72:1057–1064. doi: 10.1002/mrm.25025.
11. Muthupillai R, Rossman PJ, Lomas DJ, Greenleaf JF, Riederer SJ, Ehman RL. Magnetic resonance imaging of transverse acoustic strain waves. *Magn. Reson. Med.* 1996;36:266–274.
12. Sinkus R, Lorenzen J, Schrader D, Lorenzen M, Dargatz M, Holz D. High-resolution tensor MR elastography for breast tumour detection. *Phys. Med. Biol.* 2000;45:1649–1664.
13. McKnight AL, Kugel JL, Rossman PJ, Manduca A, Hartmann LC, Ehman RL. MR elastography of breast cancer: Preliminary results. *Am. J. Roentgenol.* 2002;178:1411–1417.

14. Garteiser P, Doblus S, Daire J-L, Wagner M, Leitao H, Vilgrain V, Sinkus R, Van Beers BE. MR elastography of liver tumours: Value of viscoelastic properties for tumour characterisation. *Eur. Radiol.* 2012;22:2169–2177.
15. Venkatesh SK, Yin M, Glockner JF, Takahashi N, Araoz PA, Talwalkar JA, Ehman RL. MR elastography of liver tumors: Preliminary results. *Am. J. Roentgenol.* 2008;190:1534–1540.
16. Maderwald S, Uffmann K, Galbán CJ, de Greiff A, Ladd ME. Accelerating MR elastography: A multiecho phase-contrast gradient-echo sequence. *J. Magn. Reson. Imaging* 2006;23:774–780. doi: 10.1002/jmri.20570.
17. Sack I, Beierbach B, Hamhaber U, Klatt D, Braun J. Non-invasive measurement of brain viscoelasticity using magnetic resonance elastography. *NMR Biomed.* 2008;21:265–271.
18. Murphy MC, Glaser KJ, Manduca A, Felmlee JP, Huston J, Ehman RL. Analysis of time reduction methods for magnetic resonance elastography of the brain. *Magn. Reson. Imaging* 2010;28:1514–1524.
19. Rump J, Klatt D, Braun J, Warmuth C, Sack I. Fractional encoding of harmonic motions in MR elastography. *Magn. Reson. Med.* 2007;57:388–395.
20. Klatt D, Hamhaber U, Asbach P, Braun J, Sack I. Noninvasive assessment of the rheological behavior of human organs using multifrequency MR elastography: A study of brain and liver viscoelasticity. *Phys. Med. Biol.* 2007;52:7281–7294.
21. Garteiser P, Sahebjavaher RS, Ter Beek LC, Salcudean S, Vilgrain V, Van Beers BE, Sinkus R. Rapid acquisition of multifrequency, multislice and multidirectional MR elastography data with a fractionally encoded gradient echo sequence. *NMR Biomed.* 2013;26:1326–1335. doi: 10.1002/nbm.2958.
22. Klatt D, Yasar TK, Royston TJ, Magin RL. Sample interval modulation for the simultaneous acquisition of displacement vector data in magnetic resonance elastography: Theory and application. *Phys. Med. Biol.* 2013;58:8663–8675. doi: 10.1088/0031-9155/58/24/8663.
23. Chen J, Woodrum DA, Glaser KJ, Murphy MC, Gorny K, Ehman R. Assessment of in vivo laser ablation using MR elastography with an inertial driver. *Magn. Reson. Med.* 2014;72:59–67. doi: 10.1002/mrm.24891.
24. Wu T, Felmlee JP, Greenleaf JF, Riederer SJ, Ehman RL. Assessment of thermal tissue ablation with MR elastography. *Magn. Reson. Med.* 2001;45:80–87.
25. Yuan L, Glaser KJ, Rouviere O, Gorny KR, Chen S, Manduca A, Ehman RL, Felmlee JP. Preliminary assessment of one-dimensional MR elastography for use in monitoring focused ultrasound therapy. *Phys. Med. Biol.* 2007;52:5909. doi: 10.1088/0031-9155/52/19/012.
26. Li BN, Shen ZH, Chui CK, Numano T, Washio T, Kobayashi E. Evaluation of Radiofrequency Ablation Using Magnetic Resonance Elastography. In: Long M, editor. *World Congress on Medical Physics and Biomedical Engineering May 26-31, 2012, Beijing, China.* Vol. 39. Berlin, Heidelberg: Springer Berlin Heidelberg; 2013. pp. 2134–2137.
27. Mariani A, Kwiecinski W, Pernot M, Balvay D, Tanter M, Clement O, Cuenod CA, Zinzindohoue F. Real time shear waves elastography monitoring of thermal ablation: in vivo evaluation in pig livers. *J. Surg. Res.* 2014;188:37–43. doi: 10.1016/j.jss.2013.12.024.

28. Chan QCC, Li G, Ehman RL, Grimm RC, Li R, Yang ES. Needle shear wave driver for magnetic resonance elastography. *Magn. Reson. Med.* 2006;55:1175–1179.
29. Zhao XG, Zheng Y, Liang JM, Chan QC, Yang XF, Li G, Yang ES. In vivo tumor detection on rabbit with biopsy needle as MRE driver. *Conf. Proc. Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. IEEE Eng. Med. Biol. Soc. Conf.* 2008;2008:121–124.
30. Goldstein RM, Zebker HA, Werner CL. Satellite radar interferometry: two-dimensional phase unwrapping. *Radio Sci.* 1988;23:713–720.
31. Knutsson H, Westin C-F, Granlund G. Local multiscale frequency and bandwidth estimation. In: *Image Processing, 1994. Proceedings. ICIP-94., IEEE International Conference. Vol. 1. ; 1994. pp. 36–40 vol.1.* doi: 10.1109/ICIP.1994.413270.
32. Manduca A, Oliphant TE, Dresner MA, Mahowald JL, Kruse SA, Amromin E, Felmlee JP, Greenleaf JF, Ehman RL. Magnetic resonance elastography: Non-invasive mapping of tissue elasticity. *Med. Image Anal.* 2001;5:237–254.
33. Boashash B. Estimating and interpreting the instantaneous frequency of a signal. I. Fundamentals. *Proc. IEEE* 1992;80:520–538.
34. Boashash B. Estimating and interpreting the instantaneous frequency of a signal. II. Algorithms and applications. *Proc. IEEE* 1992;80:540–568. doi: 10.1109/5.135378.
35. Sinkus R, Tanter M, Xydeas T, Catheline S, Bercoff J, Fink M. Viscoelastic shear properties of in vivo breast lesions measured by MR elastography. *Magn. Reson. Imaging* 2005;23:159–165. doi: 10.1016/j.mri.2004.11.060.

Figure and video legends

Figure 1: Needle MRE driver and schematic diagram of the interventional MRE system. The piezoelectric actuator is triggered by the MR-pulse sequence. It makes the needle vibrate longitudinally. Elastograms are reconstructed in real-time on an external computer connected to the MRI console.

Figure 2: Chronogram of the motion encoding spoiled gradient-echo sequence. GS, GP, GR are gradients in slice, phase and read direction, respectively. MSG, in dotted line here in GS, can be applied in any direction. f_{MSG} and f_e are encoding and mechanical excitation frequencies, respectively.

Figure 3: Sliding window scheme for the elastogram reconstruction in interventional MRE, here in the case of 3 phase-offsets. One elastogram is obtained by using two previous phase-difference images and the new one. Hence a refreshed elastogram is provided with every new phase-difference image. If a change in slice position or orientation occurs, three new phase-offset difference images are required to provide the new elastogram.

Figure 4: Exp. 1: Impact of the number of phase-offsets on the elastogram quality. a) Decimation scheme used for data analysis. One MRE acquisition protocol with 12 phase-offsets evenly spaced across a mechanical excitation cycle provides 12 phase difference images. Different combinations of them are made to simulate acquisition protocols with i phase-offsets ($i = 1, 3, 4, 6$ or 12). b-c) Standard deviation σ and mean Λ of the wavelength λ in the region of interest of each elastogram (cross) and average of the 10 elastograms (line).

Figure 5: Exp. 2: In vivo experiment in the liver of a swine. a) Coronal and b) axial slices aligned to the needle shaft. MRE imaging plane is represented in red. c) Phase difference image acquired with the motion sensitizing pulse sequence. d) Elastogram reconstructed by the algorithm in real-time overlapped on the magnitude image. Elastogram is displayed only in the region located around the needle (85 mm in diameter). e) Time series of in vivo measurements in a region of interest (8 mm in diameter) during one breath-hold of 85 seconds

Figure 6: a-b) Axial and coronal slice of the homogeneous gelatin phantom showing the ~ 4 cm diameter hole. The needle axis is schematically illustrated as a red line or a cross. c) Coronal slice of the phantom just after filling the hole with the liquid 10 % gelatin.

Figure 7: Evolution of the wave propagation (top row) and corresponding elastograms (bottom row) during the solidification of the gelatin in the inclusion. The gelation process can be clearly seen in both wave images and elastograms.

Figure 8: Evolution of the shear modulus in the inclusion of 10 % gelatin during its gelation (in blue) compared to the surrounding gelatin (in red). The graph on the right is obtained by zooming in the time window represented by the black rectangle. Standard deviations in each ROI are drawn in gray.

Supporting video: Evolution of the wave propagation (left) and corresponding elastograms (middle) during the solidification of the gelatin in the inclusion over 30 minutes. Corresponding shear modulus values (right) in the inclusion (in blue) in comparison to the surrounding gelatin (in red).