

MR guidance, monitoring and control of brain focused ultrasound therapy: in vivo demonstration in rats at 7T

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Objective

In the framework of High Intensity Focused Ultrasound (HIFU) transcranial brain therapy, it is mandatory to develop imaging techniques capable of assessing the focusing quality and location before using therapeutic intensities. Monitoring heat deposition in real time as well as verifying the extension of the treated area are also important steps. The objective of this study was to develop a complete MR-guided HIFU protocol for small animals experiments in a high field MRI scanner. Three complementary MR sequences are proposed to non invasively:

- locate the ultrasonic (US) radiation force induced displacement in tissues and quantify the acoustic pressure at the focus prior to HIFU;
- monitor the temperature rise during HIFU;
- assess the changes in elasticity in the heated area.

Material & Methods

A 7T Bruker scanner was equipped with a stereotactic frame for rats and a single element focused US transducer operating at 1.5MHz. Rats were kept under gas anesthesia (Isoflurane 2% v/v) and their heads were shaved.

A motion sensitized multi-slice spin echo sequence (TE=40ms/TR=1080ms) was optimized to measure the acoustically induced displacements in the brain. The acquisition was synchronized with 3ms US bursts. The imaging resolution was $0.780\mu\text{m} \times 0.780\mu\text{m} \times 2\text{mm}$ with a sensitivity to motion of about $1\mu\text{m}$. Once localized, the maximum displacement was measured and linked to the acoustic pressure at focus. Wave propagation and bioheat equation were simulated using 3D finite differences schemes in order to optimize the HIFU parameters.

During HIFU, a FLASH sequence (TE=3.5ms/TR=15ms/Flip angle=30°) allowed mapping the temperature rise every 518ms in the US focal plane, with a resolution of $0.7 \times 0.7 \times 3\text{mm}^3$. MR-Elastography datasets (TE=26ms/TR=468ms) were acquired at 400Hz before and after HIFU with an isotropic resolution of 0.5mm.

10 rats with injected tumors underwent the protocol. Three different tumor strains were evaluated (C6, 9L and RG2). Tumor growth was followed up in time thanks to T2 and T1+Gd sequences.

The animals are scanned for up to 3 weeks after HIFU and sacrificed for histology.

Results

The proposed protocol was first tested on 5 healthy rats. Before transcranial HIFU heating, the focal spot was localized in vivo at 7T (Figure 1-A and 1-B). MR-acoustic radiation force imaging (MR-ARFI) allowed mapping the distribution of the radiation force at the focus of the array. Comparisons with simulations and pressure curves measured in a water tank confirmed the ability to estimate the acoustic pressure non invasively from the measured MR signal. This pressure estimation in situ allowed to accurately simulate the heat deposition at the focus and to properly plan the heating parameters for the HIFU step (electrical power, duration). The temperature measurements were in good accordance with the predicted curves. Finally, the elasticity maps showed significant changes after treatment, essentially due to the presence of edema. Thermally induced necroses were obtained at the focus as confirmed at histology.

RG2 tumors (Figure 2) were targeted 14 days after injection and partial necrosis of the tumor was obtained.

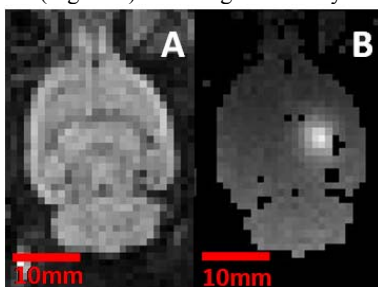


Figure 1: Magnitude (A) and phase (B) coronal images of the MR-ARFI acquisition in the focal plane of the 1.5MHz focused transducer in the rat brain *in vivo*.

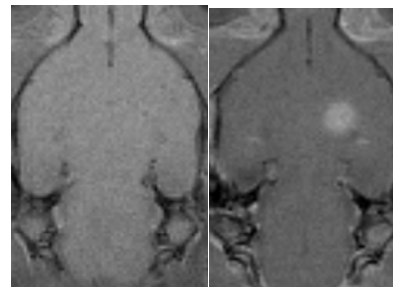


Figure 2: T1 images of the brain of a rat with a RG2 tumor, four days (Left) and nine days (Right) after tumor injection.

Conclusion

Three MR sequences, all based on phase contrast imaging, were validated *in vivo*. Radiation force, temperature and elasticity MR-imaging were combined and successfully implemented in a MR-guided HIFU setup and evaluated on 15 rats. The development of such a small animal setup is key to evaluate the effects of HIFU on healthy and tumor tissues. It is also helpful to test new sequences in the perspective of human brain therapy. Indeed, the fact that MR-ARFI can be quantitative makes it a valuable technique not only for the verification of the focal spot localization but also for the planning of the heating session. Additionally to these two uses, the dependence of the MR-ARFI signal on the viscoelastic properties of the medium may also provide a simple way to assess the thermal necrosis by comparing the signal before and after HIFU.