In vivo detection of pulmonary tumoral nodules in mice lungs by MRI at 7T and 9.4T for the study of tumor evolution during the pathology and vaccination treatment.

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Purpose/Introduction

MRI of normal lung parenchyma is challenging as it suffered of breathing and cardiac pulsation motions artefacts. The high magnetic susceptibilities difference within lungs destroy the MRI signal. However, adapted sequence based on short echo time gradient echo improves the quality of the images (1,2). Moreover, we can benefit from this inconvenient in the case of a pathology generating lesions like edema or nodules.
Our aim was to detect tumoral nodules within mice lungs to characterize B16-F10 metastases appearing in this organ in order to have a model to test the inhibition of the neovascularisation with a vaccination strategy.

Subjects and Methods

We have developed a mouse lung tumoral model by intravenous injection of 0.5 10^6 B16-F10 cells in the tail. Images of the lungs were acquired 16 days after.
The feasibility of the visualisation of lungs lesions by MRI at high field was demonstrated on inflammation models from previous works.
The MRI experiments were carried out on a 7T imaging spectrometer (Varian, Inova, Palo Alto, US) equipped with an 11cm available bore 120mT/m gradient coil and a birdcage custom made probe with 3.6 cm inner diameter. A 9.4T horizontal imaging spectrometer (Bruker, Biospec, Wissembourg, France) equipped with a 20cm bore 950mT/m and a 3.5cm birdcage coil was also used. The mice were anesthetized by 1.4% isoflurane 50/50 O_2/N_20 gas inhalation, and warmed at physiological temperature with the animal care recommendations. At 7T, 2D multislice short TE CINE gradient echo sequence were used with T1 weighting (TR/TE : 0.35s/2.9ms, 45° pulse angle slice thickness of 0.5 mm, FOV = 3.5*3.5cm^2, 512*256 acquisition points, with a shifted echo in the readout dimension) and using an ECG gated system. At 9.4T, similar ECG and respiratory triggered 2D multislice gradient echo experiments (TR/TE : 0.3s/2ms, 30° pulse angle) were performed. The total duration time was about 10min at 7T and 5 min at 9.4T.
Histological studies and image processing were achieved.

Results

T2* high field artefacts were reduced by the use of short TE in the GE sequence (2ms) and a 30% shifted echo during acquisition enabling the recording of MRI with high contrast of lungs lesion to be obtained. At 7T, nodules could be detected preferentially in the lower part. (figure 1). At 9.4T, thanks to the shorter TE and double triggering system, lungs nodules could be detected showing the feasibility of performing lungs lesions detection at high field on mice in vivo (Figure 2). The nodules detection was confirmed by histopathological data.

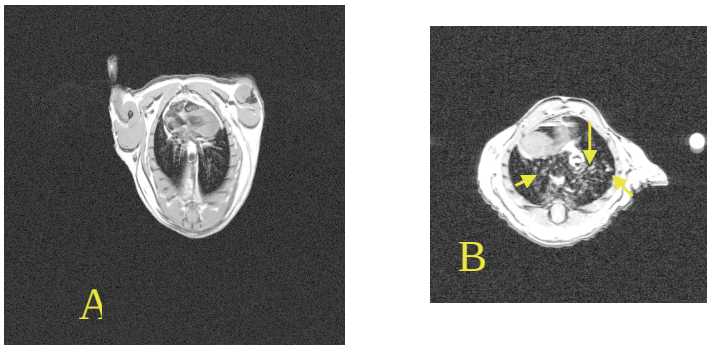

Figure 1 – Mice lungs image at 7T displaying nodules within (additional spots) the tumoral animals (B).

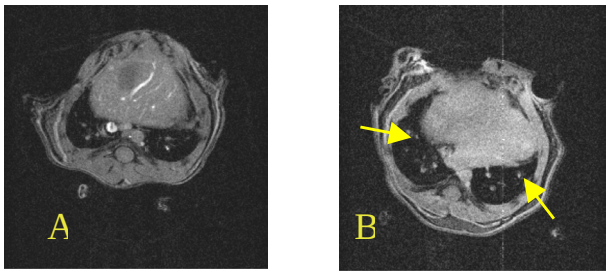

Figure 2 – Mice lungs images at 9.4T with some nodules in the tumoral mouse (B) compared to the control mouse.

Discussion/Conclusion

We have demonstrated the feasibility of detecting pulmonary nodules on mice lungs in vivo by MRI at 7T and 9.4T, showing that, contrarily to the common knowledge, MRI of lungs, even on small animals, is effective and could be very useful. The MRI method will be used to assess a vaccination immunotherapy against the tumoral development whose preliminary biological results were successful. Bioluminescence technique will also be used to compare the methods.

References :

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