Potential of perfusion and diffusion IVIM MRI in a rat brain 9L glioma model

Mami Iima[1,2], Olivier Reynaud[1], Tomokazu Tsurugizawa[1], Luisa Ciobanu[1], Jing-Rebecca Li[1], Françoise Geffroy[1], Boucif Djemai[1], Masaki Umehana[3], and Denis Le Bihan[1]

[1]Neurospin, CEA Saclay, Gif-sur-Yvette, Ile-de-France, France, [2]Diagnostic Imaging and Nuclear Medicine, Kyoto University Graduate School of Medicine, Kyoto, Kyoto, Japan, [3]Kyoto University Faculty of Medicine, Kyoto, Kyoto, Japan

Targeted audience: Scientists and clinicians interested in perfusion and diffusion MRI in tumor model

Background and Purpose: IVIM diffusion MRI[1] is undergoing a striking revival in applications throughout the body, especially to investigate cancer tissues for which vascularity is a key parameter, not only to characterize tumors, but also to predict or monitor therapeutic responses. Indeed, the degree of neovasculization is critical in assessing tumor grade and malignancy, and also in understanding tumor biology. A key feature of IVIM diffusion MRI, as a modality for perfusion MRI, is that it does not involve contrast agents, of interest in patients exposed to the risk of NSF (nephrogenic systemic fibrosis). A theoretical relationship between IVIM parameters and tissue perfusion has been established long ago[1], but this model still remains to be validated, an important step to optimize the imaging acquisition protocols used clinically. Our aim was to investigate diffusion and perfusion MRI parameters in a 9L glioma rat brain tumor model and validate the tissue structure parameters derived from the estimation of the diffusion parameters by histology.

Materials and Methods : The 9L glioma cells were injected intracerebrally to 14 ficher rats (200-350g), and they were imaged at weekly time point on a 17.2 T MRI scanner (Bruker, Germany) using an in-house quadrature ^{1}H coil. The acquisition parameters were set as follows: Resolution 312 x 312 µm², matrix size 64 x 64, field of view 20 x 20 mm^2 , slice thickness 1 mm , TE=21ms, TR=3000 ms, 6 averages, 4 segments. IVIM MRI images were acquired with 72 b values (25 b values from 2 to 160 s/mm², 35 b values from 172.5 to 935 s/mm², and 12 b values from 1150 to 3025 s/mm²). The acquisition time for each b value was 72 seconds, and the total acquisition time was 86 min 24 sec. The signal attenuation, S_{diff}/So, was first fitted using a biexponential diffusion model with a fast and a slow component (fraction f_{slow} and $f_{fast}=1-f_{slow}$, diffusion coefficients D_{fast} and D_{slow}) for the pure diffusion part of the signal (b>500s/mm²):

$$S_{diff}/So=f_{slow}\exp(-bD_{slow}) + (1-f_{slow})\exp(-bDfast) \quad [1]$$

Then, the diffusion component, S_{diff}, was removed from the signal and the remaining signal was fitted using the IVIM model for b <200 s/mm² to get estimates of perfusion fraction, f_{IVIM}, and pseudo-diffusion, D*:

$$(S-S_{diff})/So=f_{IVIM}\exp(-bD^*) \quad [2]$$

f_{IVIM} and D* maps were accordingly generated for each slice on a pixel-by-pixel basis, as well as the diffusion parameters f_{slow} and ADCo, defined as the theoretical ADC extrapolated at very low b value:

$$ADCo=f_{slow}D_{slow} + (1-f_{slow})D_{fast} \quad [3].$$

ROIs were drawn according to the contrast patterns observed on anatomical, IVIM and diffusion images, in order to account for tumor inhomogeneities and best make use of each parameter contrast. IVIM and diffusion model parameters were retrieved for each ROI. All rats were sacrificed and histology (CD31 for vascularity and H&E for cellularity) was obtained and quantitatively assessed for comparison with diffusion parameters.

Results: IVIM maps clearly highlighted areas with high and low fraction perfusion within tumors which were generally heterogeneous, as confirmed by CD31 histology (Fig.1). However, no clear pattern differences in D* could be found, despite the high signal to noise ratio of the data. Within the diffusion parameters, the most differentiating parameter was the slow diffusion fraction, f_{slow}, although a significant negative correlation ($p<0.05$) was also found between tumor cell count (H&E staining) and ADC_0 (Fig.2), in agreement with previous studies[2]. D_{fast} and D_{slow} did not provide usable information on tissue structure.

Discussion and Conclusion: This is the first trial to evaluate the perfusion parameters with IVIM MRI in a rat brain tumor model with a relatively large dataset and high signal to noise ratios reached at 17 T. Perfusion parameters could easily be obtained using a 2 steps processing approach. From the same data sets, diffusion parameters, such as ADCo and f_{slow}, additionally provided information in tissue structure. However, the diffusion parameters estimated from the biexponential model were found to be very sensitive to noise and the initial values used for data fitting. With low signal to noise ratios other models with less degrees of freedom (such as the kurtosis model[3]) could provide more reliable parameter estimates.

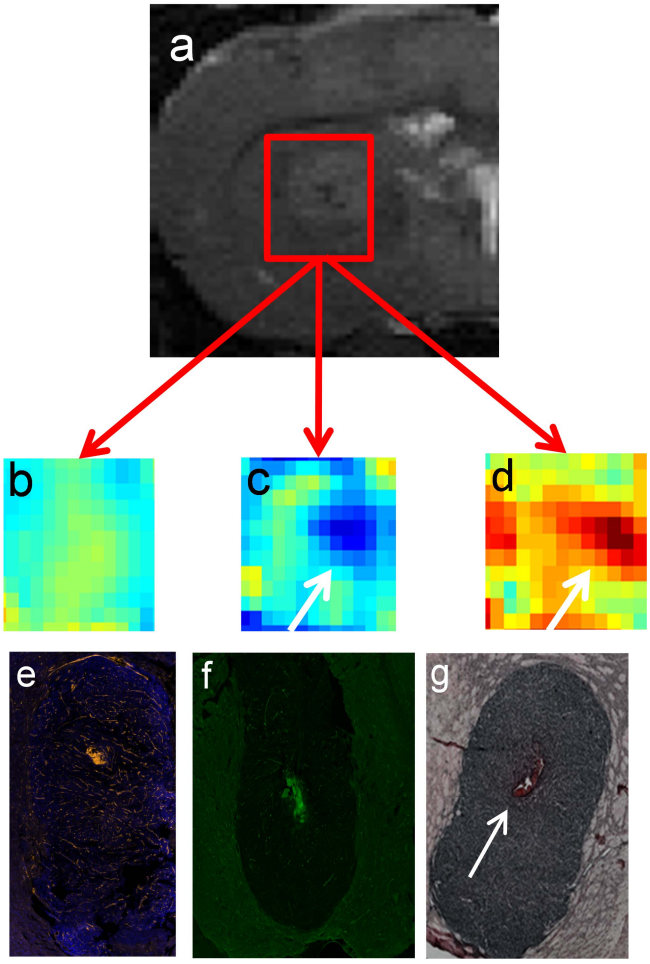

Fig. 1 The anatomical image, fIVIM parameter maps and the histological images of the rat tumor (day7)

The tumor is identified in the left basal ganglia on the anatomical image and suspected of the central necrosis (a). Necrosis is difficult to identify on the ADC map (b), but it can be recognized as low fraction on fIVIM map (c) and high fraction on fslow map (d). Many tumor vessels can be seen on the vWF (e) and the CD31 (f) images, and a hemorrhagic necrosis (arrow) is suspected on the HE image (g) for histology.

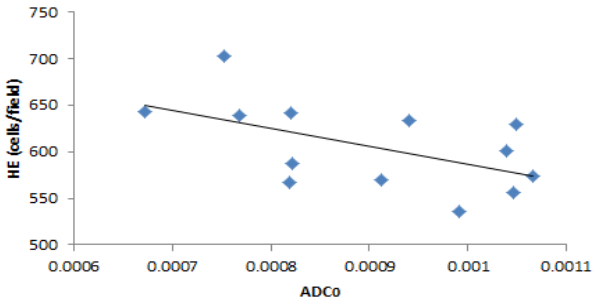

Fig.2 diffusion parameter correlation

Negative correlation between tumor cell count (H&E) and ADCo ($p<0.05$)

References :

1. Le Bihan D, Breton E, Lallemand D, et al. Separation of diffusion and perfusion in intravoxel incoherent motion MR imaging. Radiology. 1988;168(2):497-505.

2. Sugahara T, Korogi Y, Kochi M, et al. Usefulness of diffusion-weighted MRI with echo-planar technique in the evaluation of cellularity in gliomas. J Magn Reson Imaging. 1999;9(1):53-60.

3. Jensen JH, Helpern JA. MRI quantification of non-Gaussian water diffusion by kurtosis analysis. NMR Biomed 2010;23 (7):698–710.