Does the presence of an intravascular contrast agent affect the analysis of DCE-MRI data ?

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Introduction: To characterize the blood brain barrier (BBB) permeability of gliomas, one can use Dynamic Contrast Enhanced MRI (DCE-MRI). However, during the analysis of DCE-MRI data, it can be difficult to distinguish between the contribution of blood volume (BV) and permeability on signal enhancement. To overcome this limitation, an analysis of the first pass of the contrast agent can be performed but, in the case of large BBB permeability value, T_2* and T_1 effects may not be easily distinguished. An alternative approach could be the use of an intravascular contrast agent, which remains intravascular with a disrupted BBB, to determine the BV (1) independently of the DCE-MRI. Thus, the determination of BV would not be affected in case of BBB damage. In this study, we evaluate the impact of the presence of an iron-based contrast agent in the vasculature on DCE-MRI.

Materials and Methods: The C6-glioma model was used as brain tumor model on Wistar rats (10^5 cells, intrastriatal implantation). Six rats were imaged twice a day, 14 days after C6 cell injection: DCE-MRI in the morning, then DCE-MRI preceded by an iron-based contrast agent injection, in the afternoon. 4 hours separate the two imaging sessions allowing the Gd-based contrast agent clearance from the tumor (2). MR imaging was performed on 2.35T scanner.
The iron-based contrast agent injection (Sinerem®, Guerbet SA, 0.2mmol/kg) was performed via the tail vein, as a long bolus.
Anatomical T_1-weighted images were performed with a MDEFT-3D sequence (FOV = 40*40*30mm^3, matrix = 90*90*60), before and after each contrast agent injection.
T_1 map was acquired before the Gd-based contrast agent injection with an IR-spiral sequence (3) (TR/TE = 4400/1.6ms, 5 interleaves, flip angle = 90°, 20 inversion times, slice thickness = 2mm, FOV = 30*30mm², cartesian matrix after gridding = 64*64).
DCE-MRI was performed with spiral imaging during 20min (TR/TE = 600/1.6ms, 5 interleaves, flip angle = 90°, slice thickness = 2mm). Spatial and temporal resolutions were 470µm and 3s/image. After 20 images acquired for the baseline, the Gd-based contrast agent (DOTAREM®) was administered into the tail vein (0.2mmol/kg, 12mL/h).
During DCE-MRI data analysis, [Gd] maps were obtained from T_1 maps, assuming a constant r_1 for the whole brain ($r_1 = 4.02 mM^{-1}.s^{-1}$).

Results: Figure 1 shows T_1-weighted MR images of a transversal slice crossing the tumor. Image (a) is acquired without contrast agent (tumor in hyposignal). After Sinerem® injection, image (b), a dark ring appears around the tumor and large vessels are visible as black holes. Inside the tumor, the mean intensity has not changed with respect to image (a). After the Sinerem® and the DOTAREM® injections, image (c), a remarkable signal enhancement is visible in the tumor and in the temporal muscles. Results from previous experiments (not described) indicate that the decrease of T_1 values in the rat brain after Sinerem® injection is less than 8%.
Figure 2 shows the evolution of the concentrations of Gd in 3 different regions of interest (temporal muscle, cortex, and tumor). The means of the evolutions of [Gd] in the temporal muscle and in the cortex (n=5, Fig. 2a) show variations in amplitude but the curves shapes remain identical between the experiments with and without previous Sinerem® injection. The [Gd] evolutions in the tumors (4 cases shown in Fig. 2b) present differences in amplitude between the two experiments. To compare tumor curves shapes, ratio between the [Gd] data obtained with and without Sinerem® injection was calculated for each time point. After performing a linear fit on each ratio curve between 2 and 20min, we calculated a mean slope of 0.004±0.006 and a mean amplitude of 0.8±0.2.

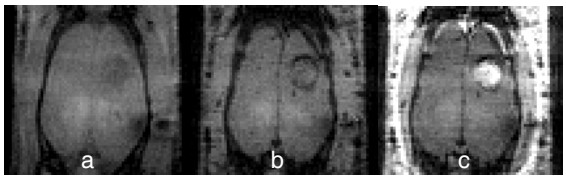

Figure 1: T_1-weighted images acquired (a) without contrast agent, (b) after Sinerem® injection and (c) after Sinerem® and DOTAREM® injections.

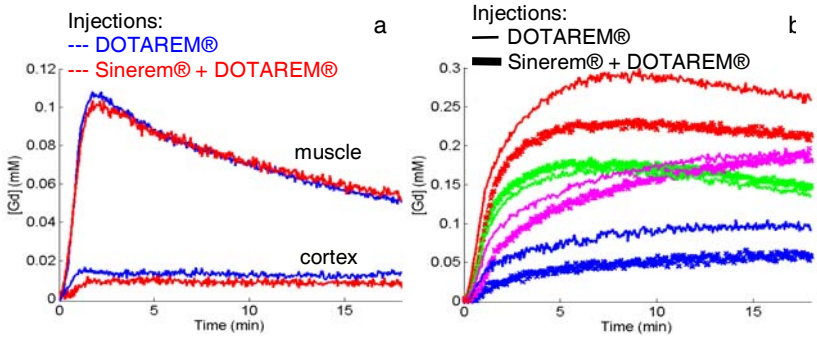

Figure 2: (a) Means (n=5) of the evolutions of [Gd] in the temporal muscle (upper curves) and in the cortex (lower curves) with and without previous Sinerem® injection (red and blue curves respectively). (b) Evolutions of [Gd] in the tumors with and without previous Sinerem® injection (thick and thin curves respectively).

Discussion and Conclusion: The constant ratio of the [Gd] evolutions between the two experiments (slope ≈ 0) indicates that the time constants are unchanged during the extravasation. The amplitude of the curves of the experiments with the Sinerem® injection is decreased (mean ratio amplitude below 1) with respect to the one without Sinerem®. This apparent reduction of Gd concentration could be associated to a diminution of the contribution to the signal of the vascular compartment and surrounding tissue, due to the presence of iron particles in the blood. The results of these DCE-MRI experiments show that the iron-based contrast agent does not seem to affect the evolution of gadolinium concentration in the tissue. A BV determination using iron-based contrast agent can thus be performed prior to the DCE-MRI experiment without consequence on the determination of the permeability value. The next step is the integration of BV information to the quantitative analysis of DCE-MRI data.

References:

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