DCE-MRI using Inversion Recovery TrueFISP for quantitative permeability measurements in rat tumors

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Introduction

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) has been widely used in pre-clinical and clinical research to test anti-angiogenic and anti-vascular drugs. After intravenous injection of a gadolinium based contrast agent (CA), the time course of the T_1 change is measured with fast MRI methods and the tracer kinetics can be calculated. Recently, it was proposed to perform T_1-mapping with the inversion recovery (IR) TrueFISP method (1). IR TrueFISP for DCE-MRI was already tested in patients with liver metastasis on a clinical scanner (2).

In this study, an IR TrueFISP method was developed for DCE-MRI studies in experimental tumor models on a high-field animal scanner. The method was applied to measure a mean vascular input function and to quantify vascular permeability of orthotopic breast tumors in rats.

Methods

Experiments were performed in a 4.7 T Bruker Biospec MR system in anesthetized healthy or orthotopic BN472 breast tumor bearing Brown Norway rats. After automatic, local shimming with FASTMAP, T_1 was measured with an IR TrueFISP sequence with 16 IR delays between 210 and 2500 ms (TE=1.69 ms, TR=3.38 ms, matrix 64 x 48, FOV=60 mm x 45 mm). Temporal resolution was 8 s; 80 scan series were acquired during 12 min. 0.1 mmol Gd/kg of GdDOTA or 0.028 mmol Gd/kg of P792 (both from Guerbet, France) was injected into the tail vein on scan series 8. T_1 maps were calculated for each of the 80 time points using the method described in (3). From the T_1 maps, the CA concentration in the tissue C_m was calculated. Using the tracer kinetics model of Tofts and Kermode (4), vascular permeability (transfer constant K^{trans}) and leakage space v_e were quantified. The input function was measured for the same CA dose in 6 healthy Brown Norway rats in the jugular vein in the neck with the same temporal resolution, but higher spatial resolution (matrix 128 x 96 and FOV 30 mm x 22.5 mm). The plasma Gd concentration curves were calculated and averaged to yield a standard input function $C_p(t)$ used for the Tofts-model. For *in vivo* validation of the method, T_1 was also measured with a segmented IR FLASH sequence (1 k-space line acquired per inversion) in 3 rats with tumors. 11 images were acquired in 70 min with inversion delays between 50 ms and 3500 ms. T_1 was derived from a 3 parameter fit.

Results and Discussion

Comparing the results for pre-CA T_1 in leg muscle and tumor showed that the values derived from IR TrueFISP are up to 15% higher than the values derived from segmented IR FLASH (muscle: 1.77 ± 0.05 s vs. 1.55 ± 0.02 s.; tumor: 2.31 ± 0.04 s vs. 2.04 ± 0.12 s). So IR TrueFISP seems to systematically overestimate T_1 *in vivo*. The mean input function showed a small standard deviation (see Fig. 1). The first pass of the CA bolus could not be resolved in the $C_p(t)$ curve with this time resolution. A biexponential fit of the $C_p(t)$ curve yielded $C_p(t) = 0.511*\exp(-0.0138\ s^{-1}*t) + 0.597*\exp(-0.000812\ s^{-1}*t)$ for GdDOTA and $C_p(t) = 0.168*\exp(-0.00212\ s^{-1}*t) + 0.181*\exp(-0.00213\ s^{-1}*t)$ for P792.

Fig. 2 shows the map of K^{trans} for GdDOTA and P792 in a BN472 tumor. The inhomogeneity is clearly visible. Median value for K^{trans} was 0.090 min^{-1} for GdDOTA, 0.010 min^{-1} for P792. Median value for v_e was 0.12 for GdDOTA, 0.08 for P792. Highest C_m values shortly after injection were 0.4 mM for GdDOTA, 0.06 mM for P792. Results in other animals were similar: the average of the medians (n=12) for K^{trans} was 0.078 ± 0.044 min^{-1} (GdDOTA) and 0.015 ± 0.005 min^{-1} (P792); for v_e it was 0.15 ± 0.04 (GdDOTA) and 0.10 ± 0.03 (P792).

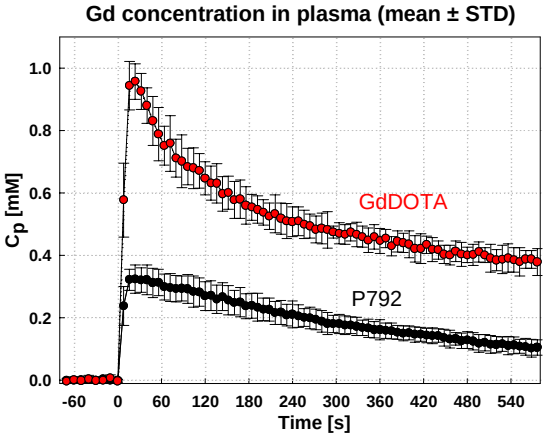

Fig. 1: Input functions measured in the jugular vein of BN rats

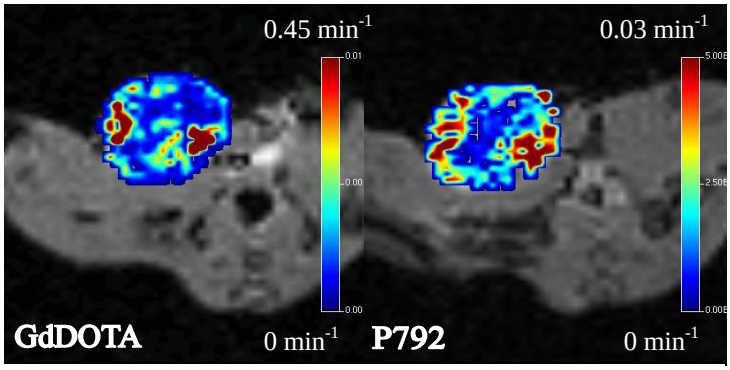

Fig. 2: Color-coded K^{trans} maps (left GdDOTA, right P792) overlaid over TrueFISP-images of BN472 tumor

Conclusion

IR TrueFISP can be applied for quantitative DCE-MRI in rats on an animal scanner. Comparison between GdDOTA and the larger molecule P792 in the same animal model showed the differences in the vascular input function and permeability.

References

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