Evaluation of flow and permeability weighting in the volume transfer constant obtained by DCE-MRI using contrast media with different molecular sizes

Cheng-He Li[1], Fang-Hsin Chen[1], Yu-Shi Lin[2], Ji-Hong Hong[1,3], and Ho-Ling Liu[1]

[1]*Medical Imaging and Radiological Sciences, Chang Gung University, Taoyuan, Taiwan,* [2]*Diagnostic Radiology, Chang Gung Memorial Hospital, Keelung, Taiwan,*

[3]*Radiation Oncology, Chang Gung Memorial Hospital - Linkou, Taoyuan, Taiwan*

Introduction

Dynamic contrast enhanced (DCE) MRI has been widely used for quantifying vascular permeability of neoplastic tumors. The extended Tofts model (ETM) (1) is a commonly applied pharmacokinetic model from which one can obtain volume transfer constant (K^{trans}) along with other physiological parameters that may be important indicators of tumor angiogenesis. In principle, the K^{trans} approximates plasma flow when permeability is relatively large (e.g. with small-size contrast agent) and permeability-surface-area-product (*PS*) when permeability is relatively small (e.g. with large-size contrast agent). Therefore, the K^{trans} obtained from DCE-MRI using clinical contrast agent (e.g. Gd-DTPA) can be heavily flow-weighted. As a result, using contrast agent with larger molecular weight was thought to be more accurate to stand for vascular permeability (2). However, few studies have quantitatively evaluated the flow versus permeability weighting in the K^{trans} obtained using contrast media with different molecular weight by experiments. This study employed the adiabatic approximation to the tissue homogeneity (AATH) model (3) to obtain plasma flow (F_p) and *PS*, and correlated the results with the K^{trans} obtained from two kinds of contrast agents for DCE-MRI of tumors.

Methods

Fourteen seven-eight week old male C57BL/6J mice (syngeneic for TRAMP and B16 tumors) were included for the experiment. For the DCE-MRI, eight mice were injected in a bolus dose of 0.3 mmol/kg of Gd-DTPA (0.9 kD), while the others were injected 0.2 mmol/kg of Gadomer (35 kD) from the tail veins. The arterial input functions (AIFs) were adopted from the previous literatures (4, 5). MR experiments were performed on a 7T animal MRI scanner (Clinscan, Bruker, Ettlingen, Germany). Dynamic scans started 20 s before the injection and lasted for 10 mins. A T1-weighted spoiled gradient-recalled echo (SPGR) sequence was used with the following parameters: TR/TE/FA = 4.9 ms/1.97 ms/20^0, parallel imaging with acceleration factor = 2, matrix size = 128 x 128, number of slice = 3, slice thickness = 1.5 mm, in-plane resolution = 0.25 mm x 0.25 mm. The duration per image sample was approximately 2 s. The concentration time curves were acquired from DCE-MRI data, and the ETM and the AATH models were applied to obtain three parameter maps (K^{trans} from ETM, and F_p and *PS* from AATH). The region of interest enclosing the whole tumor of each mouse was drawn to obtain the mean value from each map.

Results

Table shows the intertumoral result. The mean K^{trans} value obtained by using Gd-DTPA was close to F_p, while that by using Gadomer were close to *PS*, and each had significant correlation. Fig.1 shows the intratumoral scatter plot of K^{trans} versus F_p and *PS*, respectively, from one of the mice with Gd-DTPA (blue) and one with Gadomer (red). The solid lines are linear-regressed results, while dashed lines represent the lines of equality. The K^{trans} results of Gd-DTPA showed better agreement and greater correlation with F_p. On the other hand, data of Gadomer had greater agreement and correlation between K^{trans} and *PS*. Fig.2 shows the examples of three functional maps. The tumor pattern of the K^{trans} map was similar to the F_p map in the upper row derived from using Gd-DTPA. In contrast, the lower row shows that the K^{trans} map from Gadomer is similar to the *PS* map. The patterns are corresponded with the table result and clarify there are different influences when obtaining K^{trans} maps by ETM using two kinds of contrast agent.

Table.

	Gd-DTPA (n=8)	Gadomer (n=6)
ETM		
K^{trans} (min^{-1})	0.20 ± 0.06	0.035 ± 0.011
AATH		
F_p (min^{-1})	0.18 ± 0.06 **	0.20 ± 0.09
PS (min^{-1})	0.56 ± 0.27	0.060 ± 0.033 *

Significantly correlated with K^{trans}: *p<0.05, **p<0.01

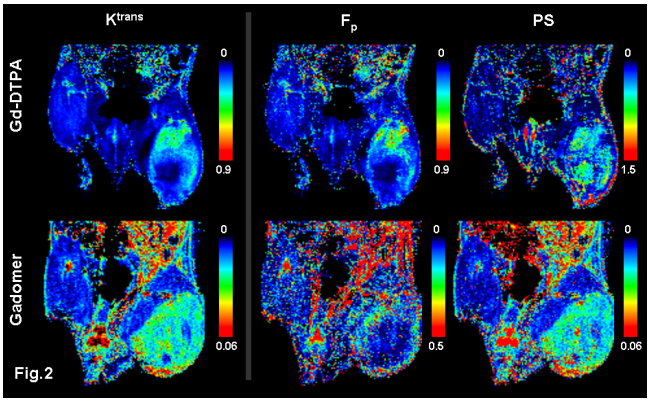

Fig.2

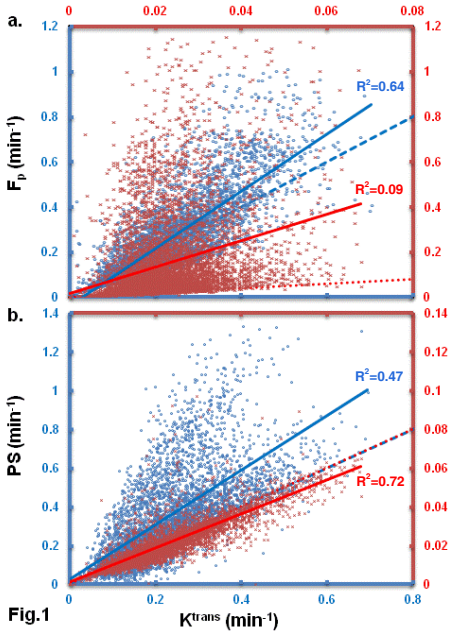

Fig.1

Conclusion

Based on experiments and the use of the AATH model, this study demonstrated that the K^{trans} obtained by DCE-MRI with clinical contrast agent and ETM had more flow-weighting than permeability. The use of more complex models is thus suggested if vessel permeability is the question of interest. Alternatively, this study showed that using contrast agent with larger molecular size was able to yield more permeability-weighted K^{trans} parameter for animal studies.

References

1. Tofts P.S. et al., J Magn Reson Imag, 10:223-232, 1999. **2.** Jaspers K et al., Med Phys, 37:5746-5755, 2010. **3.** St Lawrence K.S. and Lee T.Y., J Cereb Blood Flow Metab, 18:1365-1377, 1998. **4.** Benjaminsen I.C. et al., Magn Reson Med, 52:269-276, 2004. **5.** Verhoye M. et al., Magn Reson Med, 47:305-313, 2002.