Comparison of contrast concentration conversion methods for pharmacokinetic analysis of Dynamic Contrast Enhanced (DCE) MRI in the thin vessel wall: T1 mapping is not worthwhile by introducing more variance

Tingting Wu[1], Jinnan Wang[2], Yan Song[3], Xiaotao Deng[3], Xihai Zhao[1], Rui Li[1], Anqi Li[3], Shuo Chen[1], Chun Yuan[1,4], and Huijun Chen[1]

[1]*Center for Biomedical Imaging Research, Tsinghua University, Beijing, Beijing, China,* [2]*Philips Research North America, Briarcliff Manor, New York, United States,* [3]*Beijing Hospital, Beijing, China,* [4]*Dept. of Radiology, University of Washington, Seattle, Washington, United States*

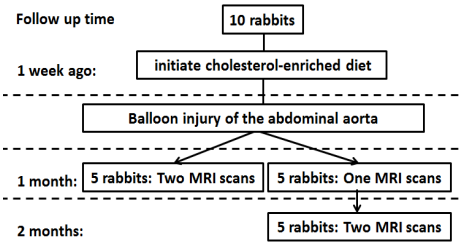
Introduction

Dynamic contrast-enhanced (DCE) MRI of the vessel wall can be an useful tool to quantify atherosclerotic plaque inflammation in vivo. Inflammation is a critial mechanisium for plaque initiaion, progression and even rupture[1]. However, unlike common targets of DCE-MRI, such as brain and tumor, vessel wall DCE usually uses image intensity curves instead of contrast concentration curves for pharmacokinetic analysis by assuming a linear relationship between signal intensity and contrast concentration[2,3]. This approach can potentially introduce bias in kinetic analysis due to the lack of accurate T_1 estimation[4]. The major reason for not using T_1 mapping to perform concentration conversion is that it is challenging to obtain the accurate T_1 map of the small vessel walls, especially for the thin vessel wall (thickness < 1 mm). In this study, we sought to investigate the performance of adding T_1 mapping for contrast concentration conversion in DCE reproducibility assessment on the thin vessel wall. It will be compared with image intensity only curves and contrast concentration curves generated from assumed T_1 values.

Methods

Experimental Animal model: After institutional review board approval, atherosclerotic plaques were induced in the aorta of 10 New Zealand white male rabbits (mean weight = 2.3 ± 0.2 kg). Rabbits were fed with high cholesterol diet (1% cholesterol, 5% lard and 1% egg yolk) beginning one week prior to the surgical balloon injury, which was performed from the rabbit's aortic arch to the iliac bifurcation with a Fogarty balloon catheter introduced through the femoral artery. After the balloon injury, all rabbits remained on the cholesterol-enriched diet. An illustration of the experimental design is shown in Fig. 1. All the repeated scans were used to evaluate reproducibility.

Fig. 1 An illustration of the experimental design.



Imaging Protocol: All MR imaging experiments were performed with a 3.0T MR system (Philips Achieva TX, R3.21, the Netherlands) using an 8-channel knee coil. A T_1 weighted double-inversion-recovery black blood[5] and a T_2 weighted fast spin echo sequence were used to locate atherosclerotic plaques. The per-contrast T_1 mapping was acquired by a SPGR based variable flip angle (VFA) method[6] with three flip angles: $4°, 10°, 20°$. B_1 field mapping[7] was performed to correct the B_1 field inhomogeneity of VFA using AFI method[8] with TR_i = 25 ms, 125 ms. DCE-MR images were acquired by 2D quadruple inversion-recovery[9] (QIR) pulse sequence (TI_1/TI_2 = 323/126 ms, field-of-view = 80mm × 90 mm, matrix = 160 × 170, TR/TE = 650/9 ms, echo train length = 18, slice thickness = 3 mm, and totally 2 slices, scan time for each frame = 13s). 0.17 mmol/kg of contrast (Gd-DTPA) was injected coincident with the third acquisition of total 15 acquisitions at a rate of 2ml/s following with 15ml saline solution.

Fig. 2 a~c: T_1-weighted images with variable flip angle ($\alpha = 4°, 10°, 20°$). d: A representative pre-T_1 map.

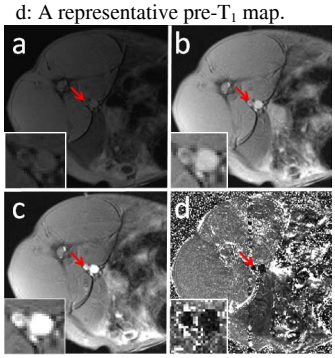


Image analysis: The pre-T_1 maps (Fig. 2) were acquired by fitting the signal equation at the flip angle α_i: $S_i = M_0 \sin\alpha_i (1 - \exp(-TR/T_1))/(1 - \exp(-TR/T_1)\cos\alpha_i)$, where $\alpha_i = 4°, 10°, 20°$ and α_i would have a flip angle correction[7] with B1 field map in this study. In the T_1 maps and DCE images, the vessel wall and reference region (psoas muscle) contours were manually drawn by an expert reader using a customized image analysis software[10] to calculate the average pre-T_1 values and the average DCE signal curves. Signal of vessel wall and muscle derived from the QIR pulse sequence should be expressed as: $S = M_0(1 - e^{-TR/T_1})$. Based on the measured average pre-T_1 value and average signal in the first DCE frame, the equilibrium value (M_0) can be acquired. Next, the changing T_1 values of other frames were obtained from the signal curves of vessel wall and muscle. According to the relationship between concentration and T_1 value[11] ($r[Gd] = 1/T_1 - 1/T_{1,0}$, r = 3.3 L mmol^{-1} s^{-1}), the concentration curves were calculated. As a comparison, other two methods were tested: (1) Calculate the concentration curves by assuming that the vessel wall and muscle both have the fixed pre-T_1 values (pre- $T_1^{\text{vessel wall}}$ = 1150 ms, and pre-T_1^{muscle} = 1150 ms)[12]; (2) Directly use normalized average signal curve ((SI(t)-SI(0))/SI(0), where SI(t) is the intensity at time t. Then, the reference-region method based Patlak model[13] was used to generate pharmacokinetic parameter (the transfer constant K^{trans}) for each method.

Table 1 The CV and ICC of K^{trans} values derived from 3 different methods.

Methods	CV (%)	ICC
Concentration curves with a T_1 mapping	55.38	0.237
Concentration curves with assumed T_1 values	32.97	0.618
Normalized Signal curves	25.80	0.558

Table 2 The CV and ICC of pre-T_1 values of the vessel wall and muscle.

vessel wall		Muscle	
CV (%)	ICC	CV (%)	ICC
16.29	0.418	15.61	0.464

Data analysis: The reproducibility of estimated K^{trans} was evaluated by coefficient of variance (CV) and intra-class correlation (ICC) between the repeated scans for three contrast concentration conversion methods: (1) concentration conversion with pre-T_1 mapping; (2) concentration conversion with assumed pre-T_1. (3) normalized intensity curve. The CV and ICC between two repeated scans of pre-T_1 obtained by T_1 mapping were also calculated.

Results

As shown in Table 1, the concentration conversion using pre-T_1 mapping had the lowest ICC (0.237) and highest CV(55.38%) for K^{trans} estimation; the concentration conversion using assumed pre-T_1 values exhibited highest ICC (0.618); directly utilizing normalized signal curves generated lowest CV (25.8%). The CV and ICC of the pre-T_1 values of the vessel wall and muscle acquired from T_1 mapping were larger than 15% and smaller than 0.5, respectively. Notably, the maximum thickness of aorta from histology analysis of all rabbits was 0.69 ± 0.16mm, indicating early lesions.

Discussion and Conclusion

In this study, we evaluated the reproducibility of pharmacokinetic measurement by using contrast concentration conversion with pre-T_1 mapping in DCE MRI of experimental thin vessel wall (thickness < 1mm). We found that concentration conversion with pre-T_1 mapping has poorest reproducibility, compared with normalized intensity curves and contrast concentration conversion with fixed pre-T_1. The pre-T_1 of thin vessel wall measured by T_1 mapping have poor reproducibility, which may be due to the large additional variance introduced by T_1 mapping based concentration conversion. Thus, adding pre-T_1 mapping for concentration conversion in the analysis of DCE-MRI is not worthwhile on thin vessel wall imaging. Both concentration conversion with assumed pre-T_1 or directly using the normalized signal curves are more preferable.

Reference

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