Use of cardiac output to improve measurement of tracer input function in dynamic contrast-enhanced MRI

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Introduction

Dynamic contrast-enhanced MRI (DCE-MRI) measures the transit of a tracer to estimate physiologic parameters. Applications include estimates of tumor angiogenesis and organ function such as kidney glomerular filtration rate (GFR). Accurate quantitative analysis of DCE-MRI data requires reliably measured arterial input function (AIF). Tracer concentration $C(t)$ can be estimated by measuring the change in longitudinal relaxation time T_1 due to T_1-shortening effect of the tracer. This approach (termed direct conversion) is applicable to solid tissues, but is significantly less accurate in the aorta or other major arteries, because MR signal from these arteries can be distorted by several artifacts, such as inflow effect, dephasing, B_1 inhomogeneity, partial volume effect. These signal errors are amplified in direct conversion. To minimize the adverse effect of the distortions, Parker et al. [1] proposed to average AIFs obtained from a group of controls, and to apply this averaged AIF for data analysis. However, this method may not be able to correct for systematic artifacts such as inflow and partial volume effect, and by disregarding differences between patients, additional sources of errors can be introduced.

This study presents a new method to compute AIF using a constrained conversion that takes into account the subject's cardiac output (Q). We compared the proposed method with conventional methods in simulation studies for measurements of (a) tumor perfusion and (b) renal function, and in MR renography for volunteers.

Methods and Materials

The new approach utilizes the indicator dilution principle [2] to constrain the area under AIF. The principle states that D = Q×AUC, where AUC is the area under the "first pass" component of AIF, D is the mass of the injected tracer, and Q is the cardiac output. Q can be measured using velocity-encoded phase contrast MRI with less than 10% error. With known Q and D, AUC can be predicted. To utilize this AUC for accurately converting arterial signal curve $S(t)$ to AIF, we propose the following steps: (1) Fit $S(t)$ by gamma variate function to obtain the first-pass signal curve S_{fp} (i.e. eliminate recirculation); (2) adjust the pre-contrast signal of S_{fp} to a new value so that the converted concentration has the expected AUC, i.e. D/Q; (3) shift $S(t)$ to the new baseline, and convert it to concentration using direct conversion.

Monte Carlo simulations were performed to compare the proposed method with the conventional methods. The ideal AIF was generated by a compartmental model proposed by Bae et al. [3]. The simulated signal curve $S(t)$ was constructed from ideal AIF using flip angle (FA) 9º and pre-contrast T_1 ($T_1(0)$) 1200 ms. Random noise with SD 10% of $S(0)$ was added to each signal point. The signal curve was also shifted vertically with a shift randomly chosen within ±30% range of $S(0)$, reflecting the various MR artifacts. Three methods were used to convert the simulated signal curve to AIF: direct conversion, the proposed method, and the averaged input function (constructed using Bae's model separately). In direct conversion, FA was randomly chosen within ±1° range of true value, and 5% random noise was added to $T_1(0)$. In the proposed method, 10% random noise was added to Q to reflect its measurement error. For tumor simulation, a model by Tofts et al [4] with K^{trans} and v_e was employed to convolve with the ideal AIF to obtain tissue data. For kidney simulation, a three-compartment renal model [5] with GFR and RPF was used. Deconvolution of the tissue data and the converted AIF resulted in the parameter estimates. Random simulations were repeated 2000 times, to obtain 2000 estimates for each parameter. Two-sampled F-test was used to compare standard deviation (SD) of the estimates from different methods.

In patient study, coronal 3D MR renography was repeated on three separate days for each of the 4 healthy volunteers: TR 2.3 ms, TE 0.8 ms, flip angle 9º, field of view 309 mm × 450 mm, slice thickness 3.0 mm, 32 slices, acquisition time 3 s. After a bolus injection of 4 ml Gd-DTPA, the acquisitions were repeated over 10 min. Image registration and segmentation was done to obtain signal versus time curves for aorta, renal cortex and medulla [6]. The signal curves for the renal tissues were converted to concentration by direct conversion. The aortic signal intensity curves were converted to concentration using the same three methods as in simulation. GFR and RPF were estimated by a 3-compartment model [5].

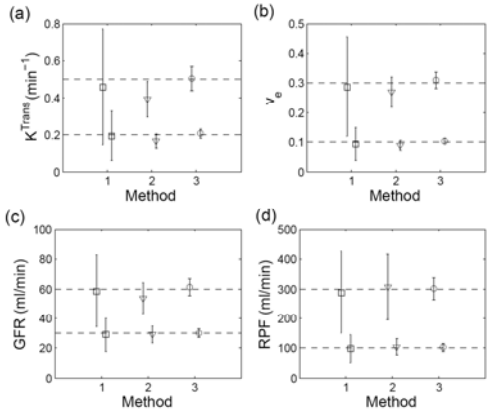

Figure 1. Parameter estimates by the different input methods in simulation. Method '1': direct conversion; '2': averaged input; '3': the proposed method.

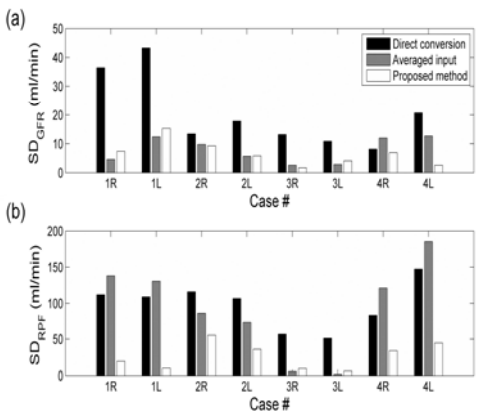

Figure 2. Standard deviations (SD) of three estimates for (a) GFR and (b) RPF from three independent scans in four patients (R, right kidney, and L, left kidney).

Results and discussion

In simulation, the proposed method improved the precisions for all the parameters by at least a factor of three compared with the direct method (Figure 1). For example, in the high-perfusion tumor simulation (nominal value K^{trans} = 0.5 min^{-1}), the SD of K^{trans} was 0.08 min^{-1} using the constrained AIF versus 0.31 min^{-1} using the conventional direct conversion method. The averaged AIF was associated with a systematic deviation of computed parameters. For example, the systematic bias for high-perfusion K^{trans} was -41% and for v_e was -8%, whereas, the estimates by the proposed method showed minimal deviation from their true values: -4.6% for K^{trans}, -0.8% for v_e. In patient study, SD of GFR by the proposed method, 6.4±4.4 ml/min, was significantly lower than that by direct conversion, 20.5±12.7 ml/min, and also significantly lower than that by the averaged input approach, 7.8±4.4 ml/min (Figure 2 (a)). The SD of RPF estimates by the proposed method, 27.4±17.8 ml/min, was lower than that by direction conversion, 97.8±32.1 ml/min, or by averaged input approach, 92.7±64.5 ml/min (Figure 2(b)).

Several features of the proposed method make it advantageous over the previous methods. First, AIF is calibrated using the area under the first-pass curve, which is calculated for each individual patient. Second, more than one source of artifacts can be corrected. Because of its ability to improve reproducibility, the proposed method should be of value in applications where repeated measurements are compared, for example in the monitoring of tumor response to therapy, or pharmacologic challenge such as angiotensin-converting enzyme inhibitor-enhanced renography. We note that in these applications, the measurement of cardiac output is not absolutely necessary, provided that cardiac output change across serial DCE-MRI exams can be neglected.

1. Parker GJ et al MRM 2006 56(5): 993-1000 2. Zieler KL Circ Res 1965 16: 309-321 3. Bae KT et al Radiology 1998 207(3): 657-662 4. Tofts PS JMRI 1997 7(1): 91-101 5. Zhang JL et al MRM2008 59(2): 278-288 6. Rusinek H et al MRM 2007 57(6): 1159-1167