ASSESSING THE EFFECTS OF DECREASING TEMPORAL RESOLUTION ON PHARMACOKINETIC ANALYSIS USING A LOCAL VASCULAR INPUT FINCTION

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Introduction: Dynamic contrast enhanced (DCE)-MRI combined with Pharmacokinetic (PK) modeling of the tissue provides information about its perfusion and vascular permeability that related to prognostic factors of tumors[1,2]. Contrast enhancement of the intravascular space has to be fed to PK models to calculated quantitative parameters. However this signal is mixed with signal of the extravascular space due to low resolution of images and also partial volume effect and cannot be separated. An arterial input function[3] (measured in an artery) is used instead assuming it represents the vascular enhancement.
The contrast enhancement of the artery has a narrow first pass due to high blood flow in the artery and no exchange of contrast agent with the extravascular space. Capturing this narrow enhancement requires high temporal resolution imaging resulting in low spatial resolution. Moreover, high concentration in the artery causes signal saturation leading to error in subsequence PK analyses. However, in the tissue (e.g. prostate) the intravascular enhancement curve is dispersed due to low blood flow in small vessels and arrival of blood in the tissue through different passes with different delays. Calculating this dispersed signal does not require high temporal resolution and also does not suffer from signal saturation as the concentration is any voxel is usually small.
We have developed an adaptive complex independent component analysis (AC-ICA) algorithm[4] to calculate the contrast enhancement curve in the tissue of interest, called local vascular input function (VIF), that was validated using phantoms and in-vivo DCE-MRI data. This paper analyzes sensitivity of PK parameters in prostate calculated using the proposed VIF to decreasing temporal resolution compared to those calculated using an AIF and assesses possibility of using low resolution data in PK analysis. Lowering temporal resolution allows increasing spatial resolution which increases accuracy of PK analysis.

Methods: AC-ICA: Having Z, a linear mixture of source signals S that are mixed with weight coefficients A ($Z = AS$), ICA tries to identify the sources S and weights A, assuming that the sources are independent. AC-ICA algorithm assumes intravascular and extravascular MR signals are spatial independent. It also assumes the distribution of the MRI signal can be approximated with a linear combination of 3 to 5 generalized Gaussian distributions (GGD) given by: $p_y(y) = \frac{\beta}{2\alpha\Gamma(1/\beta)} exp\left(-\frac{|y|^\beta}{\alpha^\beta}\right)$ where $\Gamma(\cdot)$ is the Gamma function. ACICA calculates model parameters (α, β) of the intravascular space through an expectation maximization framework at each iteration of the ICA. The ICA non-linearity is then derived from this distribution and intravascular signal is separated[4].
Pharmacokinetic modeling: The two compartmental extended Tofts model[5] was used to analyze DCE-MRI data in every voxel in the prostate. The model equations are: $v_e \frac{dc_e}{dt} = K^{trans}\left(c_p(t-\omega) - c_e(t)\right)$, & $c_t = v_e c_e + v_p c_p$, where c_t, c_e and c_p are the contrast agent concentrations in tissue, EES and plasma space respectively. ω is delay, v_e and v_p are the EES and plasma fractions and K^{trans} is volume transfer coefficient representing perfusion and permeability.
Acquisition: 8 patients with biopsy proven prostate cancers were scanned using T_2W-MRI, DW-MRI and DCE-MRI on a 3T Achieva MRI scanner (Philips Healthcare) under IRB approved protocols, using a DCE sequence (3D SPGR: TR/TE=3.91/1.81 ms, FA=8°, FOV 20x20 cm, Matrix 112x112x20, slice thickness 3.5 mm) and VFA imaging with FA=5,15° for T_1-mapping prior to routine dynamic contrast enhanced imaging.

Analysis: To study the effects of decreasing temporal resolution we used the full DCE-MRI data of the prostate patients as our high resolution data. The low resolution DCE-MRI data was constructed by removing every other slice in the DCE sequence which results in a dataset with half the temporal resolution. AC-ICA was applied to both high and low resolution prostate datasets and the intravascular signal was separated. This signal was then converted to contrast concentration and was used in PK analysis to calculate the K^{trans} parameter. For comparison the femoral artery was identified in the imaging FOV (at the centre slice of 3D volume to minimize inflow effects) and its contrast enhancement was used as AIF in PK analysis in both high and low resolution datasets.

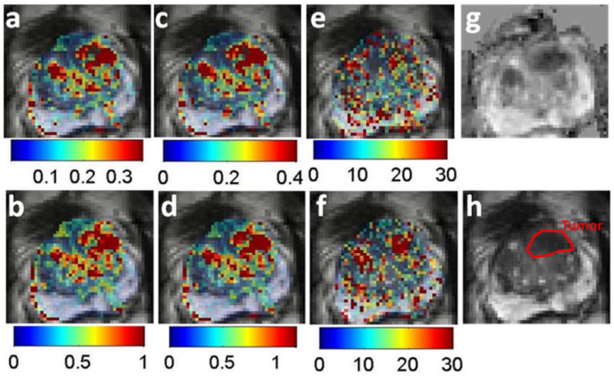

Fig. 1 the K^{trans} map of a sample prostate slice calculated for a) VIF and high resolution data, b) AIF and high resolution data, c) VIF and low resolution data and, d) AIF and low resolution data. Difference between high and low resolution maps for d) VIF and e) AIF. g) ADC map, h) T_2w image of prostate showing tumor ROI.

	VIF		AIF	
Patient	Tumor	Prostate	Tumor	Prostate
P1	10±14	7±13	22±41	16±54
P2	4±4	5±7	10±7	12±7
P3	5±6	6±10	30±34	24±22
P4	7±7	9±13	21±26	20±26
P5	7±5	8±11	22±27	19±25
P6	7±8	7±11	21±25	13±19
P7	7±12	8±11	21±30	14±22
P8	5±7	5±9	14±17	14±18

Table 1 The percentage change (mean and standard deviation) in K^{trans} parameter due to decreasing temporal resolution by factor of 2, for the tumor and entire prostate gland (calculated for all 8 prostate cancer patients).

Results: The K^{trans} values for each voxel of the high and low resolution datasets were compared for the tumor region and also for the entire prostate gland. Fig.1 a, c and e show the VIF-based K^{trans} maps for a sample slice of one of the patients for high and low resolution datasets and the percentage difference between these two maps respectively. Fig.1 b, d and f show the AIF-based K^{trans} maps for high and low resolution datasets and their percentage difference respectively. T_2w MR image (showing the tumor) and ADC map are shown also in Fig1 g and h. Table1 reports mean and standard deviation of the average percentage difference between the K^{trans} maps of high and low resolution datasets for the tumor and prostate gland for both VIF- and AIF-based analyses.

Conclusions: The results in Table1 and Fig.1 show the VIF-based analysis is less sensitive to decreasing the temporal resolution of DCE-MR imaging. Also, AIF-based analyses show the highest change in the tumor region while in VIF-based analyses the change in tumor K^{trans} is similar to the entire gland. Table1 shows that changes due to decreasing temporal resolution in AIF-based PK parameters of tumor region were on average about 3 times higher than the VIF-based analyses. Thus, the temporal resolution of could be reduced if the proposed VIF-based analysis was used which enables imaging with higher spatial resolution. Increasing the spatial resolution, in addition to providing more accurate PK parameters, will also increase the accuracy of AC-ICA algorithm.

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