Blind Multi-Channel Estimation of Arterial Input Function in Dynamic Contrast-Enhanced MRI

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Abstract. This paper studies dynamic contrast-enhanced magnetic resonance imaging, a technique to estimate maps of physiological parameters describing tissue perfusion at the capillary level. One of the most challenging problems of this imaging method is the measurement of the arterial input function. One possibility to estimate the arterial input function is based on multi-channel blind deconvolution applied to signals measured in several tissue regions. An extension to the published methods is presented. A new regularization term is introduced and a more complex model of the tissue residual function is used. Tests on synthetic and clinical data demonstrate the reliability of the method.

1 Introduction

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is an imaging modality used for estimation of tissue perfusion parameters at the capillary level, such as fractional blood volume, fractional volume of the extracellular extravascular space, blood flow, permeability-surface area, etc. [1]. These parameters are important in diagnosis and therapy-monitoring, especially in cancer imaging, but also imaging of other diseases changing vascular physiology can benefit from such a close insight into functional status of tissues. DCE-MRI is currently widely used in research and very likely just one step before clinical use.

In DCE-MRI, image data from an area of interest are acquired for several minutes following application of a contrast agent bolus. For each region of interest (ROI, ideally a voxel), a time-curve of the contrast agent concentration is then derived from the image data and analyzed to estimate the perfusion parameters. For quantitative perfusion analysis, the contrast agent concentration time course in a feeding artery, the so called arterial input function (AIF), has to be derived from the image data too. This is one of the main problems for reliability and reproducibility of the method, mainly due to partial volume effect, flow artifacts, dispersion of the AIF between the measurement site and the tissue-ROI site and due to nonlinearity between the measured quantity (1/T1) and the contrast agent concentration for higher concentrations [1].

One possibility to solve this problem is to estimate the AIF from the tissue curves (contrast agent concentration in the tissue ROI versus time) of several ROIs in tissues adjacent to areas of interest. Each tissue curve can be modeled as a convolution of the tissue impulse response, $R(\Phi,t)$, (a model-based tissue specific function of perfusion parameters Φ and time t) and the AIF, $C_a(t)$, which is assumed to be the same for all ROIs. This leads to a multi-channel blind deconvolution where $C_a(t)$ is estimated simultaneously with the perfusion parameters Φ. This contribution is an extension of the approaches in [2, 3]. A new regularization term is included in the deconvolution to provide better robustness with respect to the measurement noise. In addition, a more complex model of $R(\Phi,t)$, distributed-capillary adiabatic tissue homogeneity (DCATH) model [4], is used instead of the simple widely used Tofts model [1].

This allows more degrees of freedom of $R(\Phi,t)$ and may lead to a more accurate AIF estimates.

2 Methods

The proposed multi-channel blind deconvolution is formulated as minimization of the following function with respect to $C_a[n]$ and Φ_r:

$$\sum_r \sum_n \left[C_t(r,n) - C_a(n) * R(\Phi_r,n)\right]^2 + \lambda \sum_n \left|D(n) * C_a(n)\right|, \quad (1)$$

where, r is the ROI index, n is the time index, $*$ is convolution, $C_t(r,n)$ is the contrast-agent concentration curve in the r-th tissue ROI, $C_a(n)$ is the AIF, $R(\Phi_r,n)$ is the impulse response of the r-th ROI, Φ_r is a vector of perfusion parameters for the r-th ROI, λ is the regularization weight and $D(n)$ is the 2nd-order difference operator impulse response. While the first term represents the fidelity of the measured signal to the model, the second term is a new regularization term, imposing piece-wise linear shape to the AIF estimate (inducing sparse character of the 2nd-order difference). The regularization term prevents amplification of noise typical for maximum-likelihood deconvolution (optimization of the 1st term of Eq. (1) only) and, at the same time, allows steep edges of the AIF curve.

In blind deconvolution, the multiplicative factors of the functions in convolution can not be estimated without further contraints. Hence, the integral of the AIF was set to a fixed value. For synthetic data this value was known from the reference AIF and for clinical data the value was set to the integral of the measured AIF. The optimization was implemented as alternating between optimization with respect to $C_a(n)$ and Φ_r, using the Active Set Algorithm (Matlab Optimization Toolbox). Although convergence to the global optimum is not theoretically guaranteed, the simulation results indicate a good convergence.

3 Results

3.1 Simulated data

For simulated data, AIF was measured from a clinical recording of heart as the mean pixel value within a ROI inside the left ventricle. The first-pass part of the AIF was low compared to a typical AIF shape due to flow artifacts and nonlinearity of the relationship between R1 and the contrast agent concentration. Hence, the measured AIF was squared to approach a more realistic shape (Fig. 2). Then, this AIF was convolved with impulse response functions $R(\Phi_r,n)$, $r = 1,2,3,$ to produce three tissue curves. The perfusion parameter sets Φ_r were set to physiologically valid tissue parameters. Finally, white Gaussian noise was added to each tissue curve. The signal-to-noise ratio (SNR) was 30dB which approximately corresponds to the SNR for ROIs in our clinical recordings. An example of three synthetic tissue curves simulating three ROIs in different tissues is given in Fig. 1.

The proposed AIF estimation method was applied to the synthetic data 50 times, for different noise realizations. The estimated AIF in terms of mean ± standard deviation are given in Fig. 2. The achieved relative error was 13,8 %. The same procedure was tested with other regularization terms, used mainly in image restoration: Tikhonov [5] and total variance [6] regularization terms. The corresponding relative errors were 16.7 % and 14.6 %, respectively. The main deviation from the reference AIF was in the oversmoothed first-pass part of the AIF. This part was sharpest for the proposed regularization. The regularization weight factor was chosen experimentally for all regularization types.

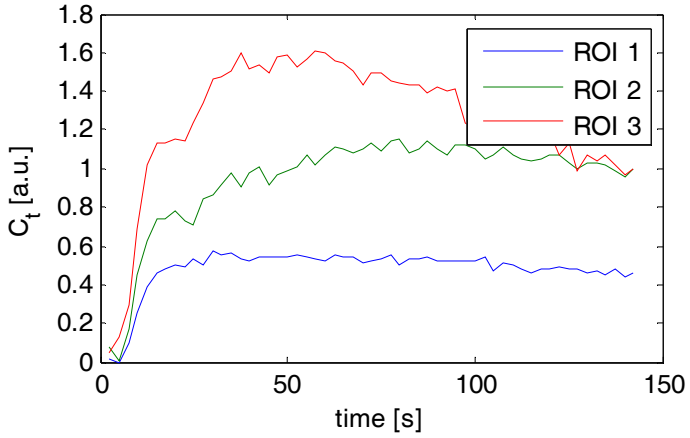

Fig 1. Example synthetic contrast-agent concentration curves for three tissue ROIs.

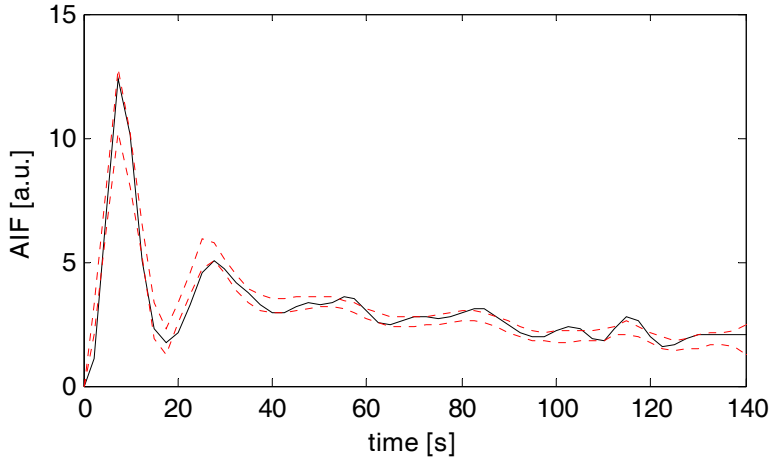

Fig 2.Synthetic data reference AIF (black solid) and mean estimated AIF ± standard deviation (red dotted) for 50 AIF estimations for various random noise realizations.

3.2 Clinical data

The procedure of AIF estimation was also tested on clinical recordings and compared with the measured AIFs. Fig. 3 shows an AIF measured from a clinical recording (solid line) and estimated from 3 ROIs in the same recording (dotted line). A 1.5T MRI Siemens Avanto scanner was used with a 2D FLASH sequence, TR/TE = 6.4/2.7 ms. All legal issues were fulfilled, including a written consent of the patients and the ethical-committee approval. An example coronal-section image of abdomen (Fig. 4a) shows a kidney cancer metastasis in the left lumbar quadrate muscle (circular-shape structure in the right image portion). The AIF estimated by the proposed method, using three tissue ROIs, had a sharper first-pass peak compared to the AIF measured in the left-side lumbar artery presumably feeding the tumor, which illustrates the artifacts in the AIF measurements. The regularization weighting factor λ was chosen experimentally.

Examples of the perfusion-parameter maps obtained from the same patient using deconvolution and the DCATH model of the tissue impulse response (complete procedure described in [7]) are given in Fig. 4. The increased blood plasma flow, Fplasma, and blood plasma volume, v_p, in the tumor rim correlate with highly vascularized proliferating tumor tissue. The increased volume of the extracellular extravascular space, v_e, inside the tumor and also in the adjacent muscle correlate probably with central necrosis and reactive edema. These observations show, that the method provides clinically relevant and expected data which indicates the correctness of this approach.

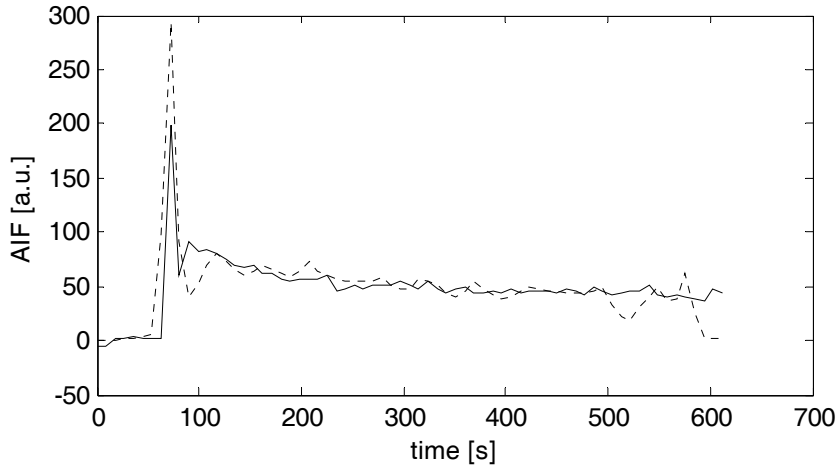

Fig 3. Measured (solid) and estimated (dotted) AIF based on clinical data.

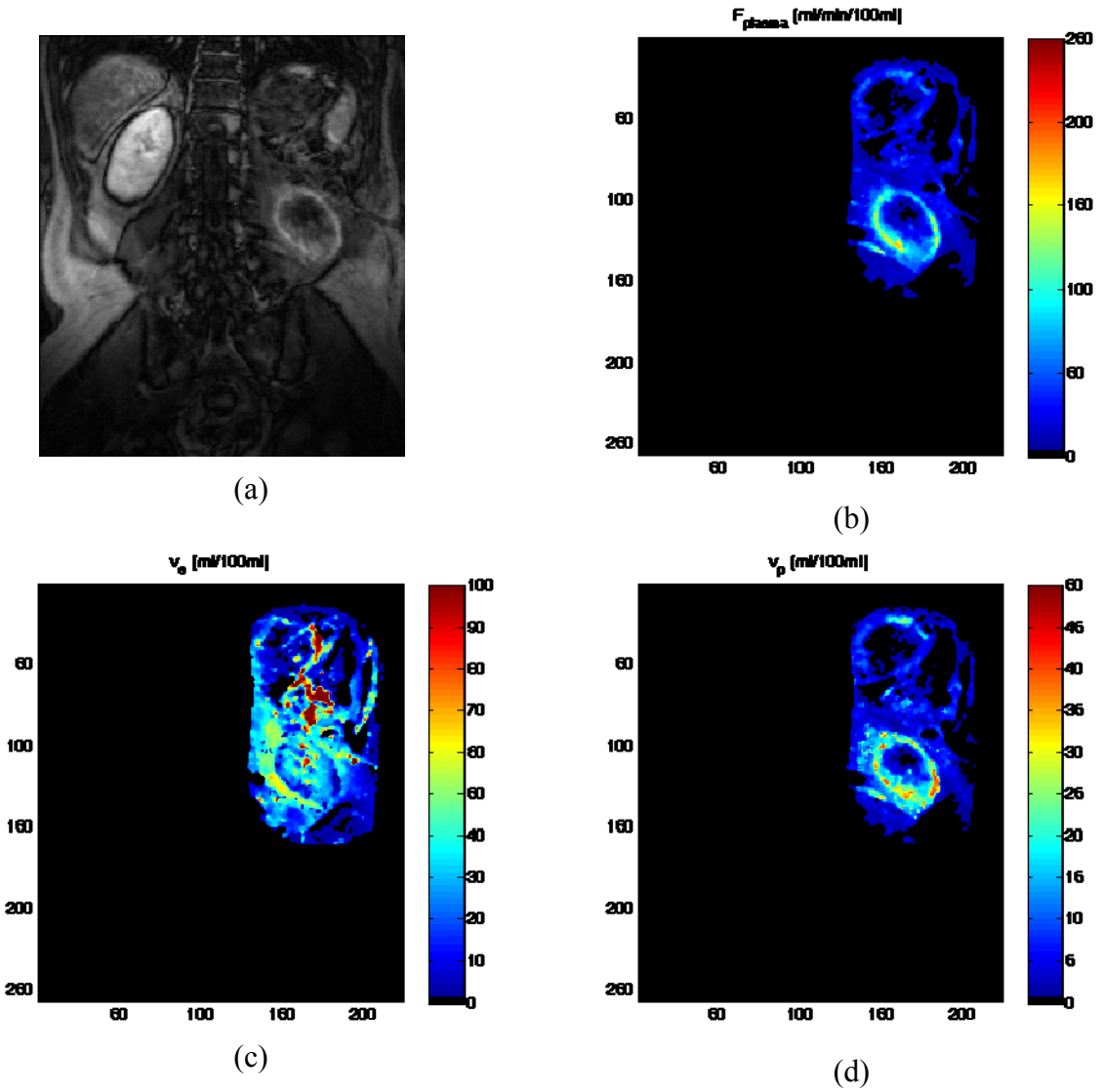

Fig 4. Clinical data. (a) Coronal section abdominal image with kidney cancer metastasis. (b) Map of blood plasma flow. (c) Map of extracellular-extravascular volume. (d) Map of blood plasma volume.

4 Discussion and Conclusions

An extension to available methods for blind multi-channel AIF estimation is presented. It enables perfusion imaging in experiments where the AIF is not measurable. In a clinical setting this situation is very common especially in non-brain applications. The lack of a reliable AIF measurement has been a serious barrier to wider use of clinical DCE-MRI imaging. Fairly good fit was achieved for tests on synthetic and clinical data. However, requirements for estimation accuracy still need to be specified.

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