Robust estimation of MRI myocardial perfusion parameters

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Myocardial perfusion imaging by first-pass contrast-enhanced magnetic resonance allows to asses the viability of a tissue by the study of the contrast agent transit through the cardiac chambers and myocardium. Since visual inspection is difficult and may left aside critical temporal information, the need of automatic quantitative analysis arises. We propose two robust estimators of the parameters that quantify the perfusion according to a prior pharmacokinetic model. The estimators are based on the concentration of the contrast agent inside the tissue and the blood.

Pharmacokinetic modeling of myocardial perfusion

The two-compartment modeling (blood plasma and extravascular/extracellular space) is assumed. The relation between the arterial and tissue concentration is given by the following equation:

$$\frac{dc(t)}{dt} = K_T\, c_a(t) - K_e c(t) \Rightarrow c(t) = c_a(t) * r(t) \tag{1}$$

- $c_a(t)$: concentration of the contrast agent in blood (AIF, arterial input function).
- $c(t)$: concentration of the contrast agent in tissue.
- K_T: kinetic rate constant from vasculature into extravascular/extracellular space.
- K_e: kinetic rate into the myocardial vasculature.

K_T and K_e are related by the fractional volume $v_e = \frac{K_T}{K_e}$

- $r(t)$ impulse response of the tissue given by

$$r(t) = K_T e^{-K_e t} u(t) \tag{2}$$

In the Fourier domain:

$$C(\omega) = C_a(\omega) R(\omega) = C_a(\omega) \frac{K_T}{j\omega + K_e} \tag{3}$$

All this modeling implies initial rest for signals $c_a(t)$ and $c(t)$.

Estimation of Fractional Volume v_e

From eq. (3) the Fourier Transform at the origin:

$$C(0) = C_a(0) \frac{K_T}{0 + K_e} \tag{4}$$

and then

$$v_e = \frac{K_T}{K_e} = \left[\frac{C(\omega)}{C_a(\omega)}\right]_{\omega=0} = \frac{\int_0^\infty c(t)dt}{\int_0^\infty c_a(t)dt} \approx \frac{\sum_{n=1}^{N} c[n]}{\sum_{n=1}^{N} c_a[n]} \tag{5}$$

The volume v_e can be calculated as a ratio between the area below curves of concentration in tissue and in blood. Since the area below the AIF is the same for all the pixels in the image, the denominator can be seen as a constant for all tissues. An error in the measure of the AIF will proportionally affect all the tissues in the same way and the ratio of v_e between tissues will remain constant.

Estimation of parameter K_e

For a robust estimation of parameter K_e, we integrate the convolution in eq. (1):

$$\int_{-\infty}^{t} c(\tau)d\tau = \int_{-\infty}^{t} c_a(\tau) * r(\tau)d\tau = c_a(t) * \int_{-\infty}^{t} r(\tau)d\tau. \tag{6}$$

Since we assume initial rest for all the signals, the lower limits can be changed to zero.

$$\int_{-\infty}^{t} r(\tau)d\tau = \int_{0}^{t} K_T e^{-K_e\tau} u(\tau)d\tau = \frac{K_T}{K_e}u(t) - \frac{K_T}{K_e} e^{-K_e t} u(t)$$
$$= \frac{K_T}{K_e}u(t) - \frac{1}{K_e} r(t)$$

and then

$$\int_{-\infty}^{t} c(\tau)d\tau = c_a(t) * \left(\frac{K_T}{K_e}u(t) - \frac{1}{K_e} r(t)\right) = c_a(t) * \frac{K_T}{K_e}u(t) - \frac{1}{K_e}\underbrace{c_a(t) * r(t)}_{c(t)}$$
$$= \frac{K_T}{K_e}\int_0^t c_a(\tau)d\tau \cdot u(t) - \frac{1}{K_e} c(t)$$

For the sake of robustness we estimate it as

$$\widehat{K_e} = \arg\min \int_0^\infty |f(t; K_e)|^2 dt$$

with

$$f(t; K_e) = \int_{-\infty}^{t} c(\tau)d\tau - v_e \left[\int_0^t c_a(\tau)d\tau\right] + \frac{1}{K_e} c(t)$$

and after some algebra:

$$\widehat{K_e} = \frac{\int_0^\infty c^2(t)dt}{\int_0^\infty c(t)\left[v_e \int_0^t c_a(\tau)d\tau - \int_0^t c(\tau)d\tau\right]dt} \tag{7}$$

Experiments and results

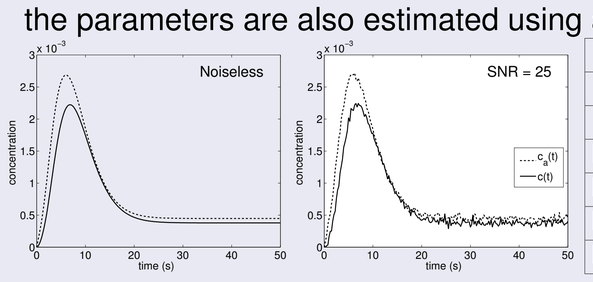
Synthetic experiment: A continuous theoretical model is considered, with AIF:

$$c_a(t) = M_1 \cdot \frac{t^{a-1} e^{-t/b}}{\Gamma(a) b^2} u(t) + M_2 \cdot \left(1 - e^{-t/d}\right) u(t).$$

In order to obtain $c(t)$, the analytical convolution with $r(t)$ is calculated:

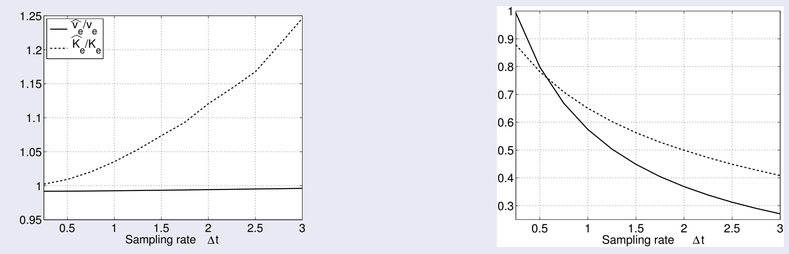
$$c(t) = M_1 \cdot r(t) \cdot \frac{\gamma_i\left(a, t\left(\frac{1}{b} - K_e\right)\right)}{(1 - K_e \cdot b)^a)} + M_2 \cdot K_t \cdot \left(\frac{1 - e^{-K_e t}}{K_e} - \frac{e^{-t} - e^{-K_e t}}{K_e - 1}\right)$$

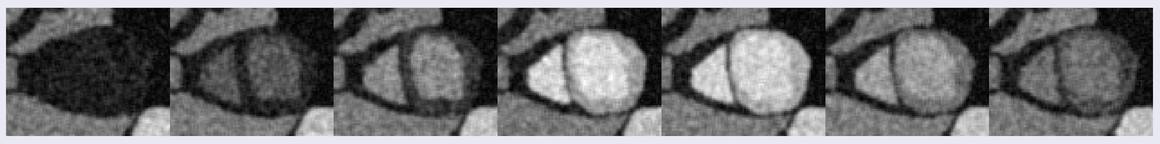
$K_e = 1.3$, $K_T = 1.1$, $\Delta t = [0.25; 1]s$, $t = 50$s. Additive Gaussian noise is added. Parameters v_e and K_e are estimated using the proposed methods. For comparison, the parameters are also estimated using a standard Least Squares (LS) fitting:



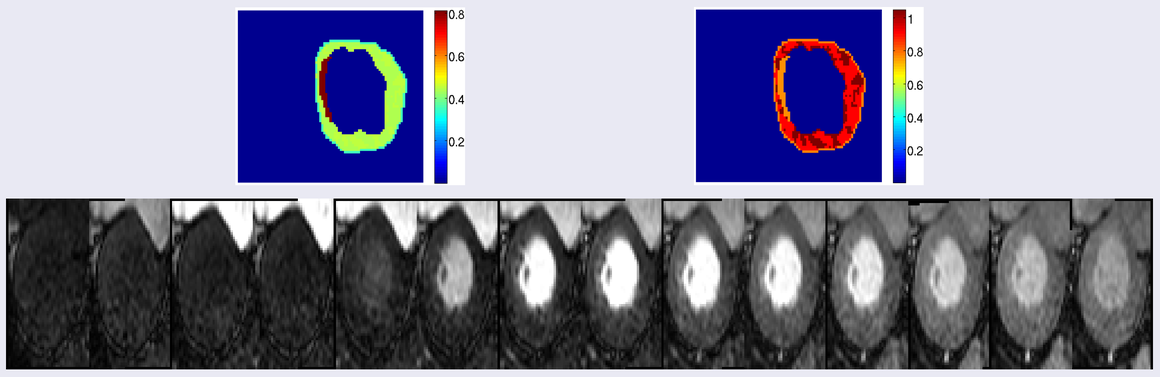
	Proposed				LS	
	$\Delta t = 0.25$		$\Delta t = 1$		$\Delta t = 0.25$	
	v_e	K_e	v_e	K_e	v_e	K_e
Real	0.84	1.30	0.84	1.30	0.84	1.30
Est. (Noiseless)	0.84	1.30	0.84	1.34	0.73	1.14
Est. (SNR=25)	0.84	1.42	0.84	1.53	0.71	1.01
Est. (SNR=10)	0.85	1.11	0.83	1.38	0.74	1.14

The estimation of parameter v_e, is robust to noise and aliasing, due to the integral formulation. The second estimator is more sensitive to the artifacts, due to the more complex formulation and the difference of two related functions in the denominator. In both cases the estimation is more accurate than the one carried out by LS.
Both estimators are depicted for a wide range of sampling rates (from 0.25s to 3s):

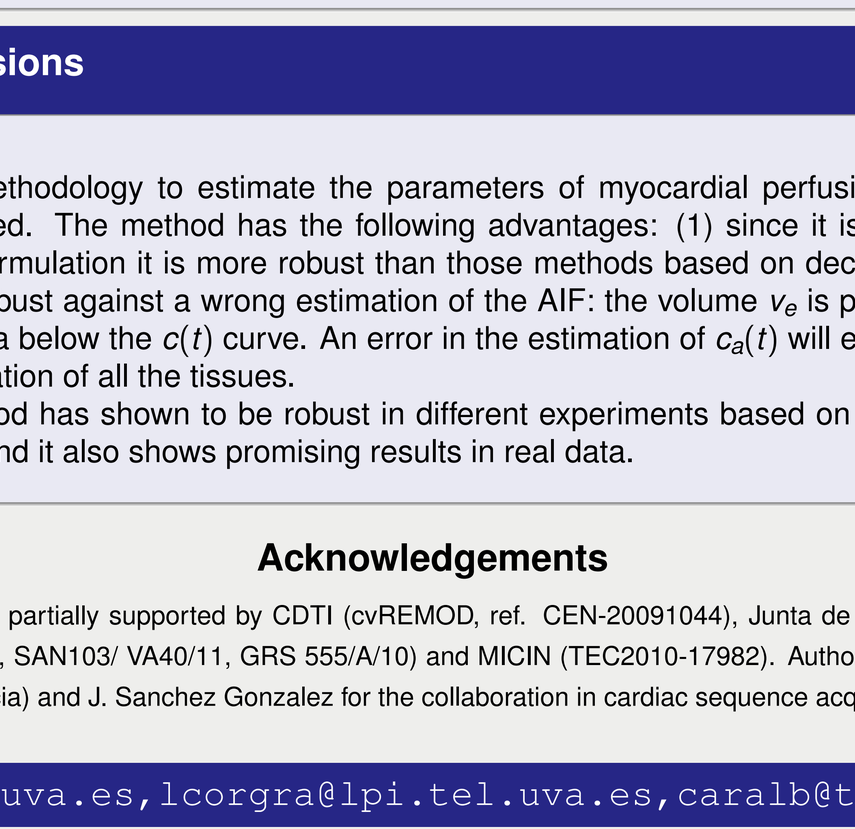




Perfusion phantom: A single coil sequence is simulated with correlated Rician noise ($\sigma_n = 15$), partial volume effect (PVE), $r_1 = 4.5$, TR=2.7290 ms, $\Delta t = 0.75$ s, 50 samples, $K_T = 0.4$, $K_e = 0.9$ for the tissue and $K_T = 0.5$, $K_e = 0.6$ for the scar. Fractional volume estimation, $\widehat{v_e}$ and parameter K_e using a 4-class clustering:



Real Data: An MR myocardial perfusion sequence is considered, with $\Delta t = 0.5$, 3 slices of 10mm and 76 temporal samples, acquired in a Philips Intera 1.5T scanner using fast field echo MAG. Intensity curves for the myocardial perfusion sequence after a 4-class clustering and Fractional volume estimation:



Conclusions

A new methodology to estimate the parameters of myocardial perfusion images is proposed. The method has the following advantages: (1) since it is based on integral formulation it is more robust than those methods based on deconvolution; (2) It is robust against a wrong estimation of the AIF: the volume v_e is proportional to the area below the $c(t)$ curve. An error in the estimation of $c_a(t)$ will equally bias the estimation of all the tissues.
The method has shown to be robust in different experiments based on theoretical models, and it also shows promising results in real data.

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