# Investigation of Weighted Fits applied to Compartment Models of Dynamic Contrast Enhanced Magnetic Resonance Imaging

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## Purpose

Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) in conjunction with pharmacokinetic modelling can be used to assess physiological parameters like perfusion and permeability. The model parameters are found by minimizing the root mean square deviation between model fit and observed signal. By using e.g. two-compartment models, the perfusion and the permeability can be fitted simultaneously. When recording DCE-MRI data continuously over a long time period the first pass is just a fraction of the data supporting the permeability part of the signal (see Fig. 1c). The aim of this study was to investigate the effect of weighted fits applied to DCE-MRI data, using both simulated and measured samples, and the overall goal was to quantify if weighting leads to a better fit performance.

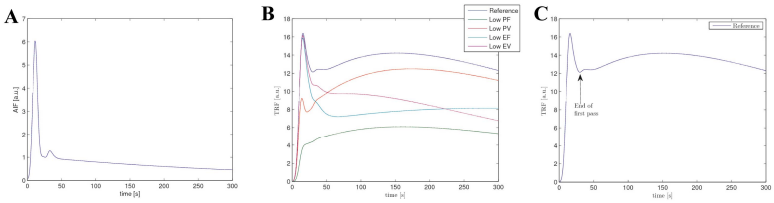


***Fig. 1: Simulated curves. A) arterial input function derived from [2], B) five tissue curves derived from [1], C) depicts the end of the first pass which is used as offset for the weighting.***

## Material and Methods

For simulation studies, five tissues were created using data taken from Luypaert et al [1]. These were labelled to be a reference tissue and four limit tissues. Furthermore, an experimentally derived arterial input function (AIF) [2] was used to simulate the concentration of the contrast agent in the artery (Fig. 1). As pharmacokinetic models, a two compartment exchange model (2CXM) and a two compartment filtration model (2CFM) described by Sourbron et al. [3] were selected. The 2CXM is defined by

$$TRF(t) = PF \cdot [(1 - E_+)e^{-t/T^-} + E_+ e^{-t/T^+}] \otimes AIF(t)$$

with free parameters PF, $E_+$,$T^-$,$T^+$. A conversion of these model parameters into physiological parameters is given in [3]. The minimization of the fit was modified to incorporate weights $\omega_i$:

$$\min \left| \sum_i \varpi_i \bullet TRF(x) - y_{data} \right|$$

with TRF the tissue response function of the pharmacokinetic model and $y_{data}$ the measured data. Two weighting scheme were investigated, linear weighting and an exponential weighting function (see Fig. 2). In this study, the weighting was only employed on the second part of the signal curve, i.e. an offset was defined manually at the end of the first pass. The simulated tissue and AIF curves were superimposed by noise and fitting was repeated 1500 times. Model fitting was performed using MATLAB (Matlab 2012a, The MathWorks, Natick, USA).

To transfer the results obtained by simulation to real world data, a DCE-MRI exam of the rat kidney was used [4]. Briefly, image acquisition was performed using a using a 3D time-resolved angiography with stochastic trajectories (TWIST) sequence with the following parameters: TR/TE/FA=3.4 ms/1.4 ms/20°, matrix = 192 x 84, FOV = 114 x 50 mm², a GRAPPA factor of 2 and 28 slices. The nominal temporal resolution was 0.9 s per volume. Images were continuously acquired for 6 minutes resulting in 400 volumes. After the 15th volume, 0.05 ml of contrast agent (Dotarem, Guerbet, France) was manually administered in the femoral vein, followed by a 1.0 ml saline flush. Tissue signal curve and AIF were derived by placing a region of interest into the renal cortex and abdominal aorta.

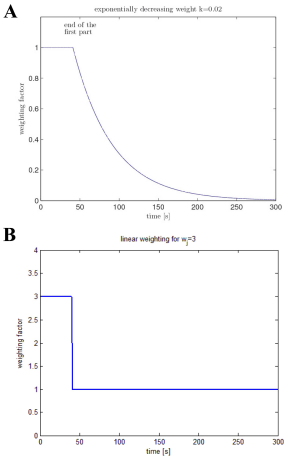


***Fig. 2 Weighting function employed in this study. The first pass is preserved by applying a constant weight of 1. A) exponential weighting with weighting factor k=0.02, B) linear weighting factor with w=3.***

## Results

Simulated data were analysed with both models. For brevity, only the results of the 2CXM are presented. Tab. 1 presents the results obtained for the reference, low PF and low PV tissue. Similar results are obtained also for the other remaining tissues. Only for $T^+$ no reduction could be achieved, all other parameters show a reduction in fit error. However, the linear weighting produces better results compared to the exponential weighting. Both weighting schemes seem to fail for the low PF and low EF tissue as the errors for $T^-$ and $T^+$ are high, however, also the unweighted fit performed similar for these two parameters in the respective tissues.

Applying the weighted fits to the rat data set revealed similar results. Table 2 summarizes the results using unweighted and linear weighted fitting with a factor of 4 and a 2CFM.

| Tissue | weight | mean error PF | ratio % | mean error $E_+$ | ratio % | mean error $T^-$ | ratio % | mean error $T^+$ | ratio % |
|---|---|---|---|---|---|---|---|---|---|
| Ref | 1 | 0.0081 | 1.00 | 0.0048 | 1.00 | 0.260 | 1.00 | 1.99 | 1.00 |
| | 6 | 0.0042 | 0.52 | 0.0033 | 0.70 | 0.154 | 0.60 | 2.17 | 1.09 |
| | 0.2 | 0.0043 | 0.53 | 0.0034 | 0.72 | 0.160 | 0.62 | 3.37 | 1.54 |
| Low PF | 1 | 0.0050 | 1.00 | 0.0605 | 1.00 | 8719.0 | 1.00 | 6.55 | 1.00 |
| | 5 | 0.0036 | 0.71 | 0.0562 | 0.93 | 33836.2 | 3.99 | 7.11 | 1.09 |
| | 0.01 | 0.0040 | 0.78 | 0.0580 | 0.96 | 18723.2 | 2.22 | 8.03 | 1.23 |
| Low PV | 1 | 0.0254 | 1.00 | 0.0158 | 1.00 | 0.208 | 1.00 | 1.41 | 1.00 |
| | 8 | 0.0140 | 0.51 | 0.0071 | 0.49 | 0.097 | 0.53 | 1.61 | 1.13 |
| | 0.04 | 0.0130 | 0.47 | 0.0065 | 0.45 | 0.091 | 0.50 | 4.35 | 3.05 |

***Table 1: Results of fitting the simulated tissue data. For each tissue and parameter of the 2CXM, the unweighted (1), linear weighted, and exponentially weighted fit results are given in terms of the mean error and the ratio of the fit error compared to the unweighted fit. PF has units of ml/min/100ml, $T^+/T^-$ has units of sec and $E_+$ is dimensionless.***

| Fit type | PF (ml/100ml/min) | PV (ml/100ml) | EF (ml/100ml/min) | EV (ml/100ml) |
|---|---|---|---|---|
| Linear, factor 4 | 451 ± 7 | 50 ± 1 | 18 ± 12 | 63 ± 40 |
| unweighted | 446 ± 10 | 51 ± 1 | 18 ± 14 | 64 ± 45 |

***Table 2: Results of weighted and unweighted fitting of DCE-MRI data of the rat kidney.***

## Discussion

It could be shown that in most of the studied tissues the errors of the fit parameters PF, $E_+$, and $T^-$ decreased when linear weights were applied. Initial results of the *in vivo* data of the rat shown made clear that weighting has a small but positive effect on the fit performance in living tissue. Repeating this analysis in more data sets might reveal if weighted fitting has a significant effect on the fit results.

## References:

[1] Luypaert R et al , MRM 65:1491-1497, 2011
[2] Parker, G et al, MRM 56: 993-1000, 2006
[3] Sourbron SP et al, NMR Biomed 26:1004-1027, 2013
[4] Zimmer F et al., PloS ONE 8: e53849, 2013