Comparing the relative effect of input parameter errors on the accuracy of the pharmacokinetic parameters in Tofts' model.

Cristina Lavini[1]

[1]*Department of Radiology, Academic Medical Center, Amsterdam, Netherlands*

Purpose:

The accuracy of Tofts' Pharmacokinetic Modelling (PKM) parameters in Dynamic Contrast Enhanced MRI is dependent on the errors of the model input, i.e. the Arterial Input Function (AIF), and the tissue concentration. Not all the errors, however, will affect the PKM parameters (v_e, K^{trans}, $K_{ep}=K^{trans}/v_e$) to the same degree. In this study we compare the effect of errors on 6 different input parameters, *i.e.* the native tissue T_1, the flip angle of the GRE dynamic sequence, and the four parameters describing the AIF on the PKM parameters.

Methods

Concentration-time data were simulated by assuming that that the tissue concentrations $C_t(t)$ would ideally follow Tofts' model $C_t(t) = v_i C_p(t) + K_{trans} \cdot C_p(t) \otimes e^{-\frac{K^{trans}}{v_e} \cdot t}$ [1] (using standard values of K^{trans} and v_e), that the DCE-MRI data were acquired with a T1-w GRE sequence, for which the relation between the MRI measured signal S and contrast agent (Gd) Concentration is given by $C_{Gd}(t) = \frac{1}{\Re_1}\left\{-\frac{1}{TR}\log\left[\frac{\Xi\cdot\left(e^{-\frac{TR}{T_{10}}}-1\right)+e^{-\frac{TR}{T_{10}}}(1-\cos\alpha)}{1+\cos\alpha\cdot\left(\Xi\left(e^{-\frac{TR}{T_{10}}}-1\right)\right)}\right]-\frac{1}{T_{10}}\right\}$ [2], where $\Xi = \frac{S(t)-S(0)}{S(0)}$, $\Re_1$ is the relaxivity and α the flip angle, and that the AIF was described by $C_p(t) = \beta\left(\chi \cdot t \cdot e^{-mb\cdot t} - e^{-mb\cdot t} + e^{-ma\cdot t}\right)$ [3]. An error was then added to the 6 parameters T_1, α,β,χ, ma,mb (one at a time), in a range of ± 20%, and the errors on the resulting PKM parameters v_e, K^{trans} and K_{ep} calculated.

Results

Errors on the six input parameters impact the three PKM parameters quite differently. Errors on *ma*, representing the slow decay of the AIF, have the smallest impact on all PKM parameters. Conversely errors on T_1 have the largest impact on v_e and K^{trans}, whereas *mb* has a large impact on all of them (Figure 1). Errors on the estimated flip angle α and on the initial AIF peak relative amplitude χ also represent an important source of errors on all the PKM parameters. Errors on the parameter β, representing the amplitude of the AIF (which also represent the miscalculation of the scaling between $C_p(t)$ and $C_t(t)$), affect K^{trans} and v_e, but do not affect K_{ep}.

Discussion

The inputs of Tofts' PK model $C_p(t)$ and $C_t(t)$ are difficult to accurately measure, and errors in the parameters describing these inputs will propagate into the final PKM parameters. We show that the input parameters that most affect the final results are those describing the initial peak of the the AIF (χ and *mb*). This fact points out the fact that an accurate knowledge of the initial part of the AIF is essential for the accurate measurement of PKM parameters. Because the slow decay of the AIF *ma* has he least effect on all PKM parameters, improvements of this part of the AIF will not in significant improvement in the PKM parameters. Whereas *Kep* is insensitive to errors on the factor β (scaling the C_p and C_t), K^{trans} and v_e will strongly depend on them as well as on T_1 errors. In order to obtain reliable estimates of the K^{trans} and v_e, accurate measures of T_1 and of the scaling factor β should therefore be made. These results strengthen the opinion that the AIF should be individually measured in order to obtain the correct initial AIF peak, and that approximating the tissue concentrations results in significant errors on the PKM parameters.

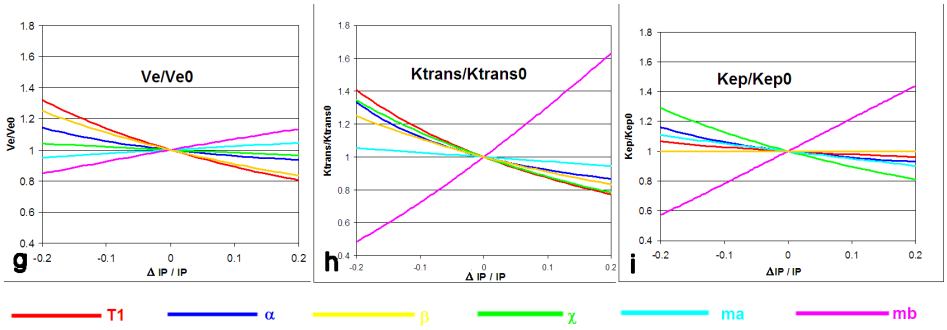

Figure 1. PKM parameter change vs relative IP error. **IP**= input parameter (respectively $T_1,\alpha,\beta,\chi,ma,mb$). Native v_e =0.4, K^{trans} =1.6, v_i=0.05.

References:

1. Tofts PS, et al. J Magn Reson Imaging 1999; 10:223-32.
2. Schabel MC and Parker DL. Phys Med Biol. 2008; 53:2345-73.
3. Orton MR et al. Phys Med Biol. 2008; 53:1225–39.