DCE-MRI using a three compartment Leaky Tracer Kinetic Model (LTKM) for whole body applications

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Introduction: In a recent DCE-MRI analysis of gliomas of different grades using two compartment generalized tracer kinetic model (GTKM) [1]-[3]

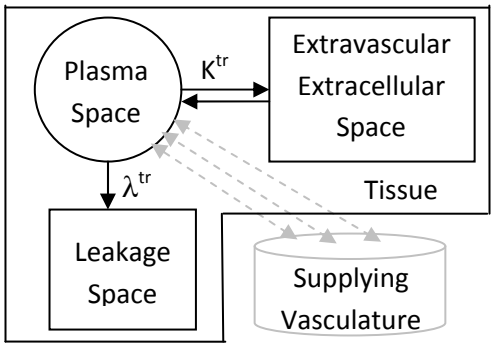

Figure 1: Three Compartment Leaky Tracer Kinetic Model (LTKM)

$$C(t) = C_{PS}(t) + C_{EES}(t) = v_p C_p(t) + k^{trans} \int_0^t C_p(u) e^{-k_{ep}(t-u)} du \ ,$$

where C(t) is the total tissue contrast concentration and $C_{PS}(t)$ and $C_{EES}(t)$ are the concentrations in the vascular and the extravascular extracellular spce, respectively, it was observed that at a number of locations the pharmacokinetic parameters v_p, k^{trans}, k_{ep}, and $v_e = k^{trans}/k_{ep}$ showed a monotone non-constant behaviour with respect to the number of time points used in their calculation. This aroused a suspicion that the EES, which is in dynamic equilibrium with the plasma space of the tissue, may not be fully explaining the breaking of the blood brain barrier and that there is an additional leak $C_L(t)$ which remains uncleared by the vasculature at least during the observational time of a few minutes. Taking the additional leak in to account we arrive at a three compartmental model seen applicable to the whole body.

Material and Methods: The DCE-MRI in different body parts was done on a 3 Tesla scanner (Signa HDxt, General Electric, Milwaukee, USA) through appropriate body coils using a three dimensional spoiled gradient recalled echo (3D-SPGR) sequence [TR/TE/flip angle/ slice thickness/matrix size=5.0ms/ 2.1ms/ 10º/6mm/256×256mm]. At the fourth acquisition, Gd-DTPA-BMA (Omniscan, GE Healthcare, USA) was administered intravenously through a power injector at 5ml/sec, followed by 30ml saline flush. A series of 384 images in 32 time points for 12 slices were acquired (Temporal resolution: 6.03sec). The standard voxel wise precontrast tissue parameter T_{10} was calculated and used to converted the signal intensity time curve S(t) to the concentration time curve(C(t)) [3].

Theory: The leaked concentration $C_L(t)$ of contrast is governed by $dC_L(t)/dt = \lambda^{trans} C_p(t)$, $C_L(0) = 0$, where the rate constant λ^{trans} is the fraction of leaking plasma volume flow per unit time (i.e., minute^{-1}). incorporating which the leaky tracer kinetic model (LTKM) becomes (Fig. 1):

$$C(t) = C_{PS}(t) + C_{EES}(t) + C_L(t) = v_p C_p(t) + k^{trans} \int_0^t C_p(u) e^{-k_{ep}(t-u)} du + \lambda^{tr} \int_0^t C_p(u) du \ .$$

An implicit knowledge of the structure of $C_p(t)$ utilizing a separate measurement of the arterial input function (AIF) from a major volume supplying vasculature is very crucial here, i.e., a simultaneous determination of the parameters v_p, k^{trans}, k_{ep} as well as the function $C_p(t)$ from the equation is an ill-conditioned problem (e.g., the obviously funny solution v_p arbitrary and $C_p(t) = C(t)/v_p$). To our great relief, fortunately, the indicator dilution or the linear control theory, following [2], is applicable and we can estimate the vasular plasma concentration $C_p(t)$ at the tissue location by utilizing

$$C_p(t) = \int_0^T R(u) C_v(t-u) du \ , \ \int_0^T R(u) du = 1 \ ,$$

where T does not exceed the maximum bolus arrival time in the volume imaged, R(u) denotes the tissue position dependent response function and $C_v(t)$ denotes the concentration of contrast in the supplying vasculature, known as the arterial input function (AIF).

The general applicability of the three compartment LTKM to the whole body follows from the premise that a tracer which does not permeate into the cells has to be confined to the vasculature, to the EES reciprocating to the vasculature, or to the non-reciprocating EES which must then be the leakage space. It must, further, be noted that if such a leakage space does not exist at a tissue location the fit ought to give an insignificant value to λ^{tr}. Conversely, a large λ^{tr} signifies a leakage, rupture or a kidney type function.

A discretization of the interval [0, T] using three or four time points and the corresponding R(u) values at them was found to be sufficient for our computational purposes where a determination of $C_v(t)$ followed [4]. The discretized R(u) values and the parameters v_p, k^{trans}, k_{ep} and λ^{tr} get well determined by the least-squares fitting as the accompanying graphs of the fit show.

Results: The self explanatory graphs of fits and their components are shown in Fig. 2. The diverse results show the applicability of LKTM with obvious interpretations.

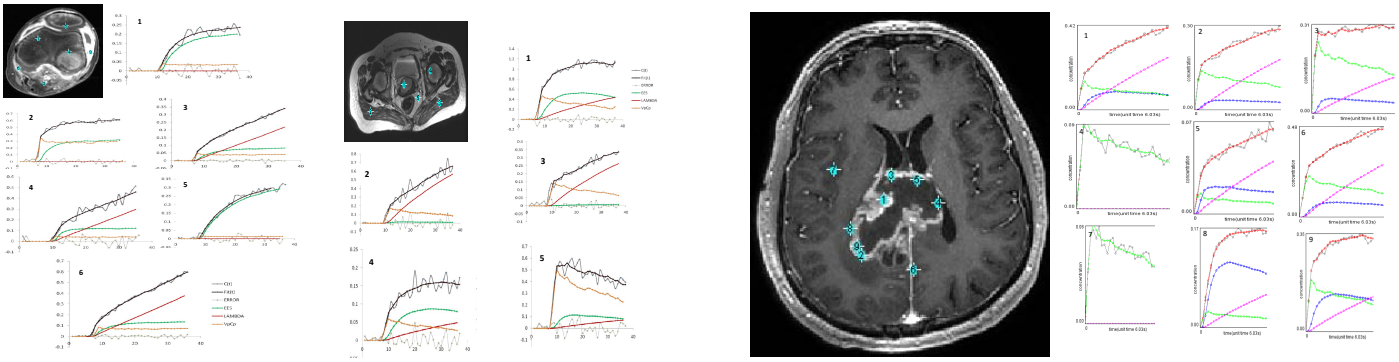

Figure 2: (i) *Left panel graphs shows concentration time profile of different compartments at selected ROIs in knee, (ii) the middle panel that in pelvic imaging and (iii) the right panel corresponds to brain imaging. Note the presence of leakage in (i) 3, 4 , 6, (ii) 1-5, & (iii) 1-3, 5-6, 8-9.*

Conclusion: The three compartmental LKTM model seems to be a promising tool for estimating the perfusion parameters in the whole body DCE-MRI.

References: [1] Tofts et al. *MRM*.1991;17:375-67.[2] Ostergaard et al. *MRM*.1996;36:751-25.[3] Singh et al. *JMRI*.2009;29:166-76.[4] Singh et al. *J Magn Reson Imaging*.2007;26:871-80.[5] Rathore et al. *ISMRM* 2011(Abstract no:539).