Flow and permeability estimation from DCE data: 2-compartment exchange and Tofts models comparison

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Target Audience:

Scientists and clinicians with an interest in DCE perfusion imaging and signal processing algorithms.

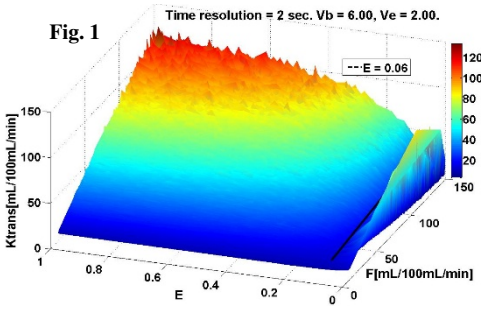
Purpose:

Recently, it was shown[1,2] that perfusion (Flow - F) can be estimated using Dynamic Contrast Enhanced (DCE) MRI .
In order to extract this parameter, a 2-compartment exchange model (2CXM) is needed[3,4] instead of a 1-compartment exchange model (such as the standard Extended Tofts Model (ETM)).
The aim of this study was to demonstrate the interpretation of F as permeability (K^{trans}) in ETM, using simulations and real data.

Methods:

Simulation: Arterial input function (AIF) and tissue concentration time curves (CTCs) were simulated using a 2CXM model which includes perfusion, as described in Larsson et al. [2]. Average population AIF[5] was used. CTCs were created by filtering the AIF through a 2CXM Impulse Response Function (IRF) and a Gaussian noise was added. SNR was set to 15 (mean AIF/noise standard deviation) which is typical to real data. A time resolution of 2 seconds, acceptable for perfusion estimation[2], was used. Blood volume (Vb) and extra vascular (Ve) volumes were set to 2 and 6 [mL/100mL] respectively, simulating small blood volume in which ETM is valid[3]. 100,000 CTCs were simulated using varying F and Extraction (E) values (according to 2CXM) uniformly distributed in 10-150 [mL/100mL/Min] and 0-1 range, respectively. ETM parameters were estimated using a linear method[6] and were used as initial parameters in a non-linear curve fitting, performed with Levenberg-Marquardt (LM) algorithm[6]. To visually describe the misinterpretation of F as permeability when using ETM, we focused on the case of E=0.

Fig. 1

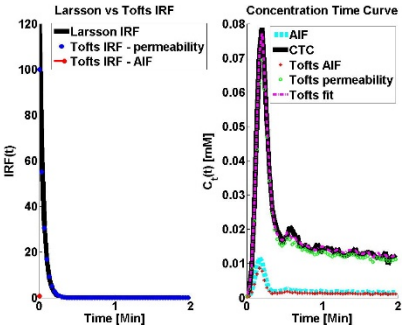


Real Data: DCE with a time resolution of 2.2 seconds was acquired from a patient with primary high grade brain tumor. Model parameters for both ETM and 2CXM were calculated. For F estimation, Tikhonov regularization was used[2].

Results and Discussion:

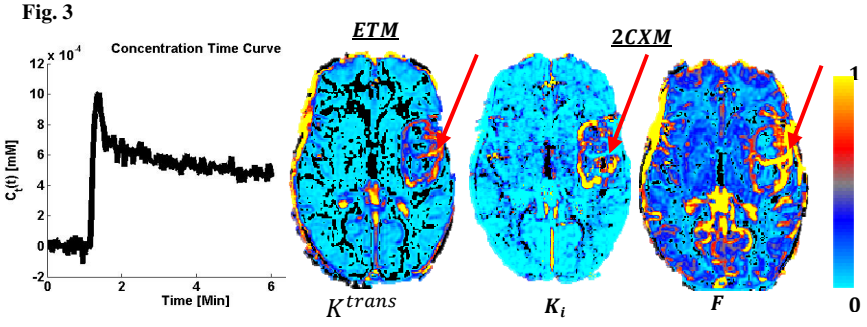
Simulation results: As seen in Figure 1 (K^{trans} as a function of E and F), in cases with low permeability ($E \to 0$), F is misinterpreted as permeability using ETM. According to simulation, E ≈ 0.06 is a lower limit from which we get high artificial K^{trans} estimation. To demonstrate the problem, we separated the ETM's fit to two parts: **1.** Tofts AIF (blood plasma concentration) - $\boldsymbol{V_p \cdot AIF(nT)}$. **2.** Tofts Permeability (extra-vascular extra-cellular space concentration) - $\boldsymbol{K^{\text{trans}} e^{-k_{ep} nT} * AIF(nT)}$, where $*$ stands for convolution. The fit to the CTC (Tofts fit) is the summation of those two parts.

Fig. 2



In Figure 2, the problem of fitting ETM to a CTC, which encounters delay and dispersion due to F, is evident. On the left, the original Larsson IRF vs. the two fitted parts of the ETM's IRF[3] ($AIF - \boldsymbol{V_p \cdot \delta(t)}, Permeability - \boldsymbol{K^{trans} e^{-k_{ep} t}}$) is displayed. On the right, it can be seen that to compensate for F, ETM must use its permeability part (K^{trans}).

Fig. 3



Real Data results: Model parameters were estimated using 2CXM and ETM. As seen in Figure 3 (normalized maps, in black – ignored pixels), the usage of a 2CXM is better in areas with high F. For example, deep veins, known to have high perfusion[7] show high F and low permeability (*Ki*) in the 2CXM model, but high permeability (K^{trans}) using ETM. Most importantly, an ROI next to the tumor (red arrow), which is non-permeable tissue as seen from its CTC (left), shows high F with no permeability using the 2CXM model while ETM shows high permeability.

Conclusion:

This study shows the importance of F in DCE analysis. When using ETM, care should be taken when interpreting permeability maps. The delay and dispersion of bolus peak due to F, cannot be explained in ETM without using misinterpreted permeability. When temporal resolution allows, the 2CXM provides a better model and fit and should be used.

References: [1]Sourbron et al., MRM 2009; [2]Larsson et al., MRM. 2009; [3] Sourbron et al., MRM 2011. [4] Zwick et al. S, *Eur Radiol* 2010 [5] Parker et al. ,MRM 2006 [6]T S Ahearn et al., Phys. Med. Biol 2005, [7] Artzi et al., NeuroImage. 2011.