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An Attempt to Integrate Diffusion Weighted and Dynamic Contrast Enhanced MRI

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ABSTRACT

Diffusion Weighted MRI (DWI) and Dynamic Contrast Enhanced MRI (DCE-MRI) are increasingly used for cancer assessment. Both modalities require adequate post-processing to extract useful information. DWI can be analyzed using the Intra-Voxel Incoherent Motion (IVIM) model while DCE-MRI can be analyzed using the Extended Tofts and Kermode (ETK) model. Both models have some parameters that can be estimated *via* numerical data-fitting procedures. The two mentioned models are typically fitted independently from each other. However, noise superimposed on images can affect the reliability of estimated parameters. In this feasibility study, we propose to exploit the link between the two models in order to possibly improve the quality of fitting. Preliminary results suggest that IVIM fitting can be improved when both ETK and IVIM are performed.

KEYWORDS: Diffusion weighted MRI; Dynamic contrast enhanced MRI; Intra-Voxel Incoherent Motion model; Extended Tofts-Kermode model; Simultaneous fitting.

INTRODUCTION

In cancer studies of several organs (e.g. breast, prostate, liver, etc…) functional imaging can give useful information for better quantify the staging. In particular, Diffusion Weighted Imaging (DWI) and Dynamic Contrast Enhanced (DCE) MRI are becoming increasingly adopted in clinical practice.

DWI can give information about the microstructure organisation of the tissue. In fact, tumors have an increased cellularity leading to reduced water diffusion.[1] Isotropic diffusion can be modeled using Intra-Voxel Incoherent Motion (IVIM)[2] which depends on a few parameters: perfusion fraction f (fraction of plasma vessels), 'slow' diffusion D_s (conventional diffusion), 'fast' diffusion D_f *(diffusion in randomly oriented vessel)*. Diffusion constants are measured in mm^2/s.

DCE provides information on the capillary wall permeability. This latter increases in cancer because of leaky vessels associated to the fast grow induced by VEGF (vascular endothelial growing factor).[3] One of the most commonly employed models is the Extended Tofts-Kety (ETK) model[4] includes the following parameters: vascular plasma fraction (v_p), transfer constant from plasma to extra-vascular-extra-cellular space (EES) K^{trans}, transfer constant from EES to plasma k_{ep}. Transfer constant are mesured in min^{-1}.

Both models parameters are typically estimated from measured DCE and DWI data. Due to noise the estimated parameters can inaccurate and imprecise.

Following the suggestion by LeBihan et al.[5] in this study we hypothesized that perfusion fraction (f) in IVIM and plasma volume fraction (v_p) should be equal and might be

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used for improving the estimation of parameters attainable with DWI and DCE.

In particular, we performed a Monte Carlo simulation in order to evaluate how the IVIM and ETK fitting can be performed simultaneously and if the simultaneous fitting can produce better performance than separate fitting.

METHODS

Intra-Voxel Incoherent Motion (IVIM) Modeling

The IVIM model has been proposed by Le Bihan et al[2] according to this model the signal intensity of the diffusion weighted images is given by: $S_{IVIM}(b) = S_0 \cdot [(1-f) \cdot \exp(-b \cdot D_s) + f \cdot \exp(-b \cdot D_f)]$. where S0 is the signal intensity with no diffusion gradient, f is the perfusion fraction, D_s is the slow diffusion coefficient of water and D_f is the 'fast' diffusion coefficient, b is the b-value that is related to the pulse magnetic gradient intensity and duration.

Extended Tofts And Kermode (ETK) Modeling

Tofts and Kermode proposed a model for the capillary flow.[4] According to this model the concentration of contrast agent within a voxel is given by: $S_{ETK}(t) = v_p \cdot C_p(t) + C_p(t) \star K^{trans} \cdot e^{-k_{ep}t}$ where t is time, K^{trans} min^{-1}. is the transfer constant across the capillary wall from the plasma to the Ees, k_{ep} is the reverse constant from EES to plasma, v_p is the plasma volume fraction.

Simultaneous Fitting Of IVIM And ETK

Le Bihan et al[5] suggested that the perfusion fraction within the IVIM model should be interpreted as the vessel fraction within a voxel. This hypothesis, might be used to improve the numerical estimation of model parameters (DWI and DCE) performing simultaneous fitting of both data.

In order to take advantage of the link between IVIM and ETK models we need to perform a simultaneous fit of the data. In this study we propose to perform minimization of an appropriate cost function. Under the hypothesis that $f=v_p$ the cost function can be written:

$$C(f, D_s, D_f, K^{trans}, k_{ep}) = \sum_b (S_{IVIM}(b, f, D_s, D_f) - S_{DWI}(b))^2 + \sum_t (S_{ETK}(t, f, K^{trans}, k_{ep}) - S_{DCE}(t))^2$$

where $S_{DWI}(b)$ is the signal acquired during DWI and $S_{DCE}(t)$ is the signal acquired during DCE-MRI.

SIMULATIONS

We simulated one ETK curve with K^{trans}=0.046 min^{-1}. and k_{ep}=0.148 min^{-1}. and v_p=0.0074. The parker model for the arterial input function has been used.[6] Time sampling was simulated as in fast TWIST (Time-resolved angiography With Interleaved Stochastic Trajectories) pulse sequences with an image every 3 sec. Noise was superimposed having a standard deviation of 0.1 mMol.

Further we simulated a IVIM curve using $f=v_p$=0.0074, D_s=0.001 mm^2/s, D_f=0.01 mm^2/s and b-values (0, 50, 100, 150, 200, 500, 600, 700, 800, 900, 1000, s/mm^2). Noise was simulated having standard deviation 0.05 normalised units.

Simultaneous fitting using the cost function proposed in the previous section has been performed. Starting values were: K^{trans}=1, k_{ep}=0.5, v_p=f=0.5, D_s=1e-3, D_f=10e-3. The Levenberg-Marquardt algorithm in Matlab has been used.

Monte Carlo simulation on 10 repetitions has been performed on the same noisy data but with different starting points chosen randomly within 10% of the starting values reported in the previous paragraph.

RESULTS

Figures 1 and 2 report the simulated curves with superimposed

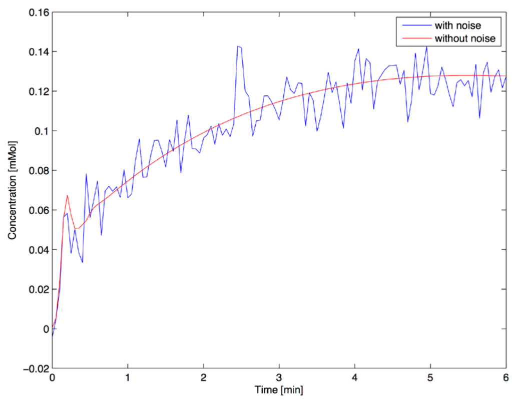

Figure 1: DCE simulated data without and with noise superimposed. It is assumed that a fast pulse sequence is used (e.g. such as TWIST[7]) capable to acquire an image every 3 seconds. The noise level (std) has been fixed to 0.01 mMol. Noise distribution was assumed zero-mean Gaussian.

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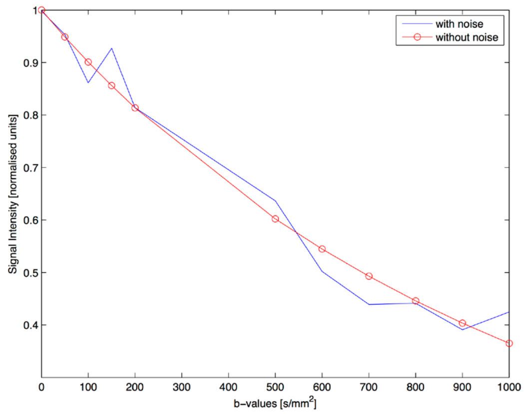

Figure 2: DWI simulated data without and with noise superimposed. It is assumed that a typical range of b-values has been used (0, 50, 100, 150, 200, 500, 600, 700, 800, 900, 1000, s/mm^2). The noise level (std) has been assumed 0.05 normalized units. Noise distribution has been assumed zero-mean Gaussian.

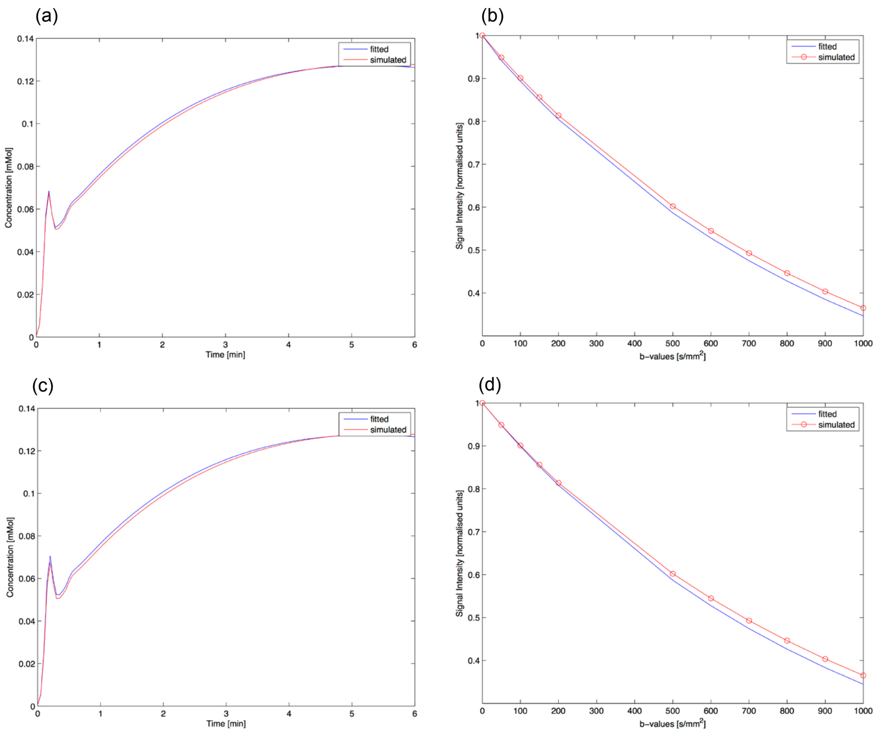

Figure 3: (a) and (b) fitting using the cost function proposed combining DCE and DWI. (c) and (d) fitting separately DCE and DWI.

noise. Figure 3 report the result of fitting using the proposed cost-function (Figures a and b) , and separately fitting the data (Figures c and d).

When using simultaneous cost-function, mean relative error (expressed in percentage %) on parameters were: K^{trans}=-7.20%, k_{ep}=11.54 %, v_p=f=21.01%, D_s=-5.1132%, D_f= -99.9850%. When the fitting were performed separately mean percentage errors were: K^{trans} = -3.75 %, k_{ep}=6.37% v_p=4.25% for the ETK model and f=6*10^6%, D_s=6.13%, D_f= 347%.

DISCUSSION

In this study we explored the possibility to perform simultaneous fitting of DCE and DWI data under the hypothesis that plasma fraction and perfusion fraction are the same as suggested by Le Bihan et al.[5] We performed Monte Carlo simulations with noisy DCE and DWI data. Simulated data were fitted separately and in combination.

Results suggest that DCE fitting can lead to better

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results when performed alone. However, DWI data fitting can lead to huge errors in parameter estimates that might be attenuated when fitted simultaneously with DCE data.

Although results seems promising, we must underline the limits of this study. In our study we did not evaluate the impact of different curve fitting algorithms, the influence of the noise level, the influence of the number of b-values used.

It seems reasonable that a larger number of b-values might improve DWI fitting alone and consequently also the combined fitting.

CONFLICTS OF INTEREST: None.

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