A Finite Element Based Optimization Algorithm to Include Diffusion into the Analysis of DCE-MRI

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Abstract

DCE-MRI is a widly used technique to obtain a quantitative description of the tumour vasculature. Contrast agent diffusion has a great impact on the extraction of this descriptors. This work presents a new approach based on the FEM to account for this phenomenon. The proposed model outperforms the state-of-art models.

Introduction

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a well-stablished method to get an insight on tissues vascularization (specially in cancer). To obtain physiological information, pharmacokinetic (PK) models are fitted to concentration-time curves of the injected Contrast Agent (CA) on each voxel in the tissue. The most common PK models in clinical practice are the Standard Tofts model (STM) [1] and the extended Tofts model (ETM) [2]. Some authors have proposed updated versions of these models [3, 4] to consider passive delivery of CA. Despite improving previous models, these updated works were limited by either the computational cost or the range of application due to simplifications.

This work presents a new approach based on the Finite Element Method (FEM) to include this diffusive phenomenon into the models used in clinical practice.

Methods

Formulation and implementation

Starting from the original formulation of the ETM, a term to account for CA diffusion was included in the equation. Given the similarity between CA diffusion in biological tissues and substance diffusion in porous media, the formulation of the diffusive term is based on the concept of effective diffusivity (D_{eff}).

Equation (1) is the constitutive equation for the proposed diffusion-corrected ETM (D-ETM) model:

$$\frac{\partial C_t(\boldsymbol{x},t)}{\partial t} = \nabla \cdot \left(D_{eff} \nabla C_t(\boldsymbol{x},t)\right) + \frac{K^{Trans}}{v_e}(\boldsymbol{x}) \left(C_p(t)\left(v_e(\boldsymbol{x}) + v_p(\boldsymbol{x})\right) - C_t(\boldsymbol{x},t)\right) + v_p(\boldsymbol{x}) \frac{dC_p(t)}{dt} \quad (1)$$

Where K^{Trans}, v_e and v_p are the nodal parameters that describe vascular properties; C_p is the CA concentration in blood and C_t is the CA concentration averaged in the reference volume of the tissue.

Equation (1) is then implemented in ANSYS using the mass transport module. The last terms of the right-hand side (extravasation term and blood volume contribution) are introduced as mass generation sources.

Optimization algorithm

Once the forward FE model is implemented, an optimization method to fit Equation (1) to the curves obtained from DCE-MRI sequences needs to be defined. To do so, the algorithm chosen is based on the Least-Squares Method. Being a gradient-based method, the Jacobian matrix needs to be computed. This matrix, which defines the influence of each parameter on the global solution, is usually obtained numerically (Finite Differences Method). To avoid the computational bottleneck due to the number of simulations needed for this numerical approach, a new analytical method based on the discrete form of equation (1) is defined. By doing so, the number of simulations needed is reduced from millions to just a few.

For more information, this work has been published in *Eng. Comput.* [5].

Results

Following the validation process described in previous works [3,4], the model and the algorithm were first tested on a benchmark problem. This problem was defined on a 2D circular geometry, where there were defined two different zones: a necrotic core, where there was almost no vascularization; and a well perfused rim. The D-ETM showed an improved accuracy with respect to the ETM (Figure 2a), specially in the necrotic core, where diffusion plays a key role.

Once validated, the D-ETM was then applied to a second *in silico* case corresponding to a real tumour geometry. Results show that the D-ETM outperforms the ETM, accurately depicting the heterogeneity in the distributions. The ETM, however, tend to average and homogeneize the parameters distribution (Figure 2b).

Discussion

The described D-ETM is the first diffusion-corrected PK model to be implemented using the FE method. By embracing the concept of effective diffusivity, it avoids the inclusion of additional variables to the model and provides a more accurate formulation of the diffusive process. The analytical method formulated to compute the Jacobian matrix greatly reduces the computational cost and opens the door for further gradient-based optimization methods for FE-based PK models.

The results obtained are promising, since the model has accurately retrieved the true values, outperforming the ETM. Future works should test this model on real clinical or experimental data.

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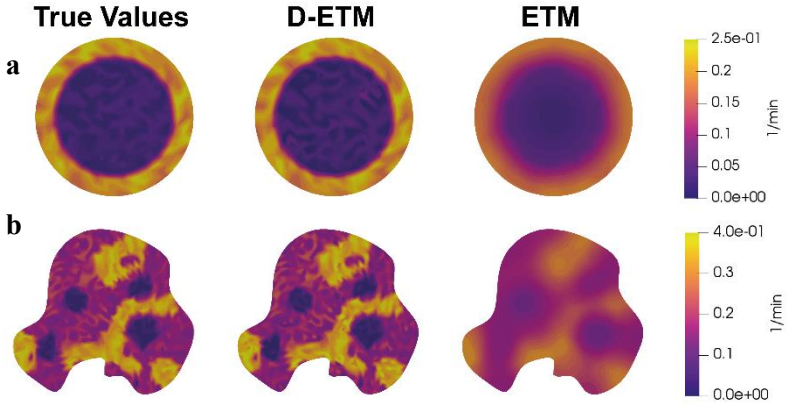

Figure 1. K^{Trans} distributions (True values, D-ETM fitting and ETM fitting) for the two different in silico cases analyzed.