

## Modeling the Effect of Diffusion on the Assessment of $K^{trans}$ and $v_e$ in DCE-MRI

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### INTRODUCTION

Dynamic contrast enhanced (DCE) MRI allows for the estimation of tumor tissue parameters by modeling contrast agent (CA) kinetics within a region of interest (ROI). The standard model of analysis considers the ROI as two fully mixed compartments representing the intravascular volume (plasma) and the extravascular extracellular volume ( $v_e$ ) [1]. While this approach can successfully describe many situations, cases exist in which the analysis results in parameter values that are not physically relevant (e.g.,  $v_e > 1$ ). It has been hypothesized that the reason for failure of parameter estimation in these cases is due to passive diffusion of the contrast agent that occurs in poorly perfused tissues, a phenomena not accounted for in the standard model [2]. In order to investigate the possible effect of this deficiency, we developed a 2-dimensional finite element model (FEM) of CA concentration in the tissue as described by diffusion and CA delivery through a centralized vessel.

### METHODS

The standard model uses a differential equation to describe the concentration change within the two compartments:

$$\frac{dC_t}{dt} = K^{trans} C_p - \frac{K^{trans}}{v_e} C_t, \quad (1)$$

where  $C_t$  is the CA concentration in the tissue compartment,  $C_p$  is the CA concentration in the plasma (the so-called arterial input function, or AIF),  $v_e$  is the extravascular extracellular volume fraction and  $K^{trans}$  is the volume transfer constant. In most cases,  $K^{trans}$  and  $v_e$  are estimated by fitting Eq. (1) to the measured  $C_t$  and  $C_p$  time-courses. To further this model, and to evaluate the effect of diffusion on the optimized parameter assignment, we employed the standard diffusion equation,

$$\frac{dC_t}{dt} = \nabla D \nabla C_t, \quad (2)$$

to describe the 2D domain representing a tissue region of interest, and the standard model as the boundary condition between the tissue and the vessel. The mesh of the domain consisted of triangular elements (Fig 1), and the FEM was developed using the Galerkin approach with the standard Lagrange polynomial interpolants. A forward evaluation of this model with prescribed  $K^{trans}$  and  $v_e$  values and a defined population AIF generates a concentration distribution over time for the representative domain. The concentration versus time curve can then be retrofitted by the standard model, resulting in assigned  $K^{trans}$  and  $v_e$  values. The diffusion coefficient of the domain can be varied in order to analyze the effect of diffusion on the parameter assessment; comparison of the estimated  $K^{trans}$  and  $v_e$  values to the known input values allows for a direct evaluation of the error associated with ignoring diffusion in the standard model.

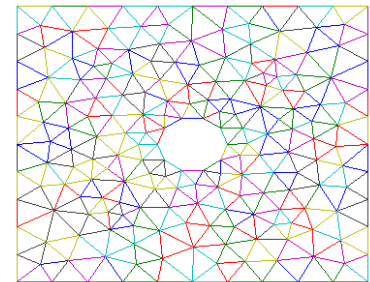


Figure 1. Representative triangular mesh of the tissue domain.

### RESULTS

To verify the model, we first ran the simulation with a coefficient of diffusion ( $D$ ) equal to zero. This represents the limiting case for which the standard model would be able to accurately evaluate  $K^{trans}$  and  $v_e$ . Our model proved successful in generating the expected concentration profile, and the error between the input parameters and the optimized parameters was minimal (<1% in most cases). We subsequently incrementally increased the diffusion coefficient and the results indicate that, as expected, diffusion within a tissue region has an effect on the parameter assessment by the standard model. The coefficient of diffusion was incremented on a scale relative to the scale of the tissue domain. Initially, at low values of  $D$ , the standard model is able to assign the appropriate parameter values. However, with increasing  $D$ , the accuracy of the standard model falters. Specifically, with increasing  $D$ ,  $K^{trans}$  is increasingly underestimated by the standard model, with  $v_e$  is increasingly overestimated. Additionally, we were able to replicate the situation in which the standard model assigned physically irrelevant values of  $v_e$  (i.e.  $v_e > 1$ ); in these situations, the input  $v_e$  was less than 1 and the (substantial) diffusion within the tissue accounted for the misrepresentation by the standard model.

Table 1. Standard model optimized parameters and percent error over range of D values.

Model values:  $K^{trans}=1.0$ ,  $v_e=0.5$

D	$K^{trans}$	Error	$v_e$	Error
0	1.004	0.4%	0.500	0.0%
1.0E-05	1.001	0.1%	0.502	0.4%
2.5E-05	0.997	-0.3%	0.504	0.9%
5.0E-05	0.989	-1.1%	0.509	1.8%
1.0E-04	0.974	-2.6%	0.517	3.4%
2.5E-04	0.929	-7.0%	0.540	8.1%
5.0E-04	0.859	-14.1%	0.574	14.9%
1.0E-03	0.732	-26.9%	0.631	26.2%
2.5E-03	0.500	-50.0%	0.760	52.1%
5.0E-03	0.406	-59.4%	0.903	80.6%
1.0E-02	0.369	-63.1%	1.085	116.9%
1.0E-01	0.321	-67.9%	2.508	401.6%

### CONCLUSION

It has been previously hypothesized that inaccuracies in the parameter estimates in DCE by the standard model may be due to the effect of passive diffusion within the tissue. With our FEM model of active vessel CA delivery and passive diffusion within a tissue segment, we were able to show that diffusion may have a significant effect on the parameters assigned by the standard model. We were also able to show that cases in which the standard model assigns physically irrelevant values of  $v_e$  can be accounted for by diffusion. This work serves as a preliminary investigation of the effect of diffusion in parameter assessment of DCE, and the results indicate that diffusion may need to be considered in the quantitative evaluation of such data.

**REFERENCES** [1] Tofts et al; *J Magn Reson Imaging* 1999;10:223-32, [2] Pellerin et al; *Mag Res in Med* 2007;58:1124-1134.

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