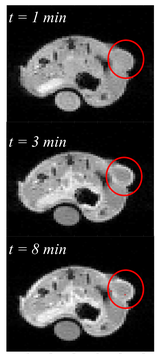
Comparison of cellular- and tissue-scale models of dynamic contrast-enhanced MRI

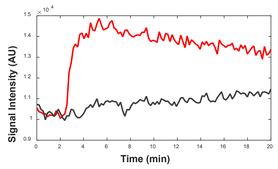
Ryan T Woodall[1,3], Stephanie L. Barnes[3], David A. Hormuth II[3], Anna G. Sorace[2], C.Chad Quarles[5], Thomas E Yankeelov[1-4]

Department of Biomedical Engineering[1], Dell Medical School[2], Institute for Computational Engineering Sciences[3], Livestrong Cancer Institutes[4], Barro Neurological Institute[5]

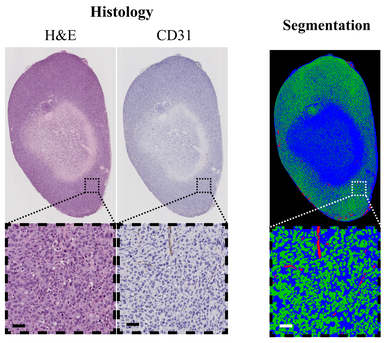
Background

- Dynamic contrast enhanced MRI (DCE-MRI)
- Used to evaluate vascular and cellular properties of tissue in cancer
- Utilizes contrast agents with well-known magnetic properties
- Rapidly-aquired T_1-weighted images measure dynamic signal
- Resulting time course for each voxel can be fit to a family of pharmacokinetic models.
- Curve fitting results in estimations of perfusion, permability, tissue volume fractions [1].
- Standard models assume instantaeous equilibration of CA within the domains.
- They do not account for leaking of contrast agent between voxels, or unevem distribution of contrast agent within the voxel [3].
- *Hypothesis*: The Standard Model of DCE-MRI does not accurately capture CA dynamics of a slowly diffusing CA





Cellular-scale FEM Model



Compartment Model:

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

2D Transient diffusion equation

$$\frac{dC(x,y,t)}{dt} = \nabla \cdot D\nabla C(x,y,t)$$

$$< \nabla^2 C, \phi_i > = \oint \nabla C \cdot \hat{n}, \phi_i ds - < \nabla C \cdot \nabla \phi_i >$$

Boundary Conditions:

$$\nabla C \cdot \hat{n} = P\left(C_p(t) - C(t)\right)$$

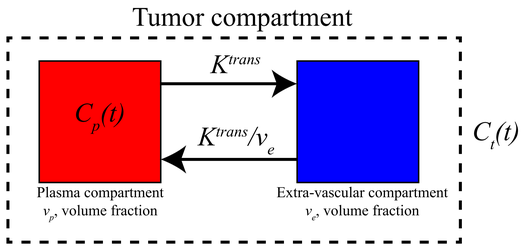
$$P = \frac{K^{trans}V}{S}$$

Definition of terms:
C_t, concentration of tracer in tissue
K^{trans}, transfer coefficient from plasma to extra-vascular compartment
$C_p(t)$, population arterial input function
v_e, extra-vascular extra-cellular volume fraction
D, molecular coefficient of diffusion

P, vessel permeability
V, imaging voxel volume
S, vascular surface area

Scale bars: 50 microns

Tissue-scale Model



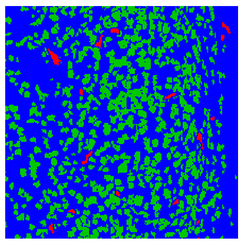
1st order ODE:

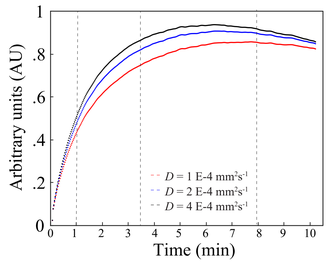
$$\frac{dC_t(t)}{dt} = K^{trans}C_p(t) - \frac{K^{trans}}{v_e}C_t(t)$$

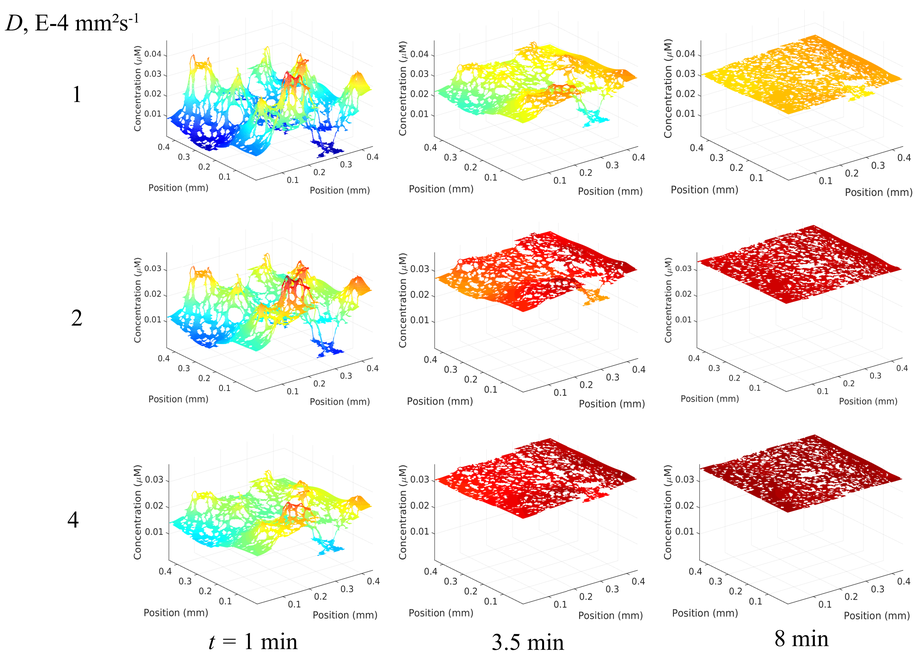
Solution with known $C_p(t)$ [2]:

$$C_t(t) = K^{trans}\int_0^t C_p(u)exp\left(\frac{K^{trans}}{v_e}(t-u)\right)du + v_p C_p(t)$$

Single Voxel Results

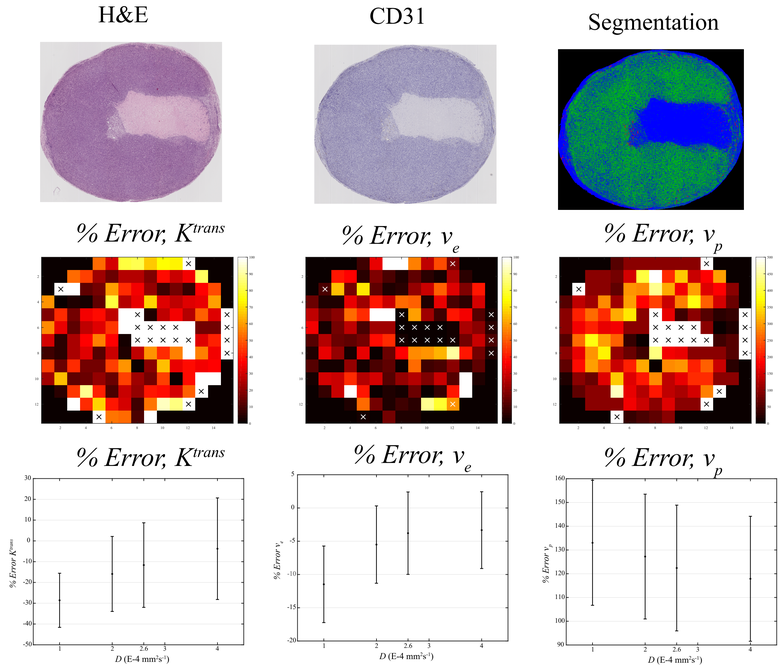






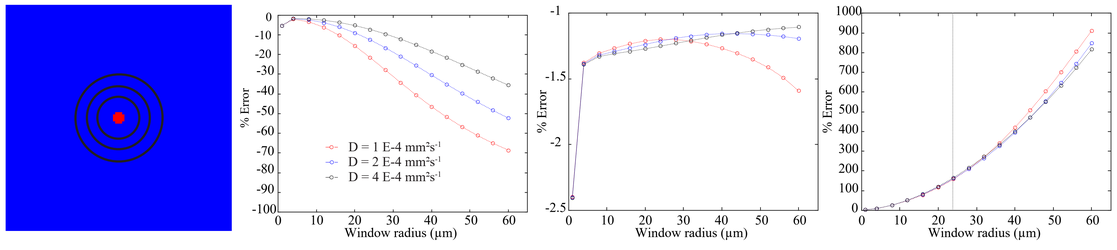
An example voxel time course demonstrated for 3 different values of molecular diffusivity, D. The amount of contrast agent within the domain at a given time point is demonstrated by the 3D plots of the FEM mesh. These time points are then converted to an aggregate signal intensity for the entire voxel domain. As the diffsivity increases, the total signal enhancement in the voxel increases. This is due to a bottle-neck at the vessel boundary caused by slow diffuion of the contrast agent. As the diffusivity of the contrast agent increases, the domain fills more evenly and in a shorter amount of time. A higher diffusivity corresponds to a quicker equilibration of contrast agent within then voxel, and a corresponsing decrease in parameterization error, shown in the column on the far right.

Whole-Tumor Results



FEM simulation of contrast agent entering the tumor domain was performed for the entire tumor at 4 different values of D. The middle row demonstrates the estimated error of a DCE-MRI curve fit of the Standard Model where $D = 2.6$. This is the molecular diffsivity of Magnevist (Bayer), a commonly used DCE-MRI contrast agent. Simulated DCE-MRI resolution is 438 microns in X and Y.

Single Vessel Results



Analysis of this domain was performed using windows of increasing radii around the central vessel. As window size increases, parameter estimation becomes less accurate. Contrast agents with higher diffusivity fill the domain more quickly, and therefore continue to approximate the parameters of the standard model better than slower diffusing contrast agents.

Conclusions

Error in the standard analysis of DCE-MRI data can be attributed to the slow diffusion of contrast agent within the tissue domain, which contributes to the uneven distribution of contrast agent within the tumor domain. In order to improve the accuracy of the standard model, we propose the inclusion of a diffusion term which corrects for physiological levels of contrast agent diffusivity. The ability to determine the arrangement of cells and vessels at the sub-voxel scale will be important in improving the model.

Acknowledgements

We thank the Cancer Prevention Research Institute of Texas (CPRIT) for funding through RR160005, the National Cancer Institute for funding through U01CA174706 and R01CA186193, and the National Institute of Health (NIH) for funding through EB007507. The authors acknowledge the Texas Advanced Computing Center (TACC) at The University of Texas at Austin for providing high-performance computing resources that have contributed to the research results reported within this paper. URL: http://www.tacc.utexas.edu

Contact Information

rwoodall@utexas.edu

https://www.ices.utexas.edu/research/centers-groups/cco

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