Tracer-kinetic field analysis in DCE-MRI and DSC-MRI: theory and examples

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TARGET AUDIENCE: Physicists

INTRODUCTION: The classic analysis of DSC- and DCE-MRI assumes that all voxels are isolated systems supplied by the same arterial concentration [1]. This leads to fundamental errors [2,3], but also fails to exploit the structure encoded in the spatial concentration gradients [4]. Steps have been taken towards resolving this problem [5-8], but further progress requires a more general tracer-kinetic theory that models the spatial as well as the temporal variation in concentration.

METHODS: A tracer-kinetic field theory is developed where the measured concentration $C(\mathbf{r},t)$ (mmol/ml) depends on position $\mathbf{r}$ and time *t*, and where all tissue parameters are functions of $\mathbf{r}$. Each voxel may consist of *Q* different well-mixed spaces with distribution volumes $v_q(\mathbf{r})$ and concentrations $c_q(\mathbf{r},t)$ so that $C(\mathbf{r},t) = v_1(\mathbf{r})c_1(\mathbf{r},t) + \ldots + v_Q(\mathbf{r})c_Q(\mathbf{r},t)$. A field equation for each $c_q(\mathbf{r},t)$ can be derived by expressing the conservation of tracer mass. Here, three different models are presented to illustrate these principles.

RESULTS (1): If the contrast agent is intravascular and the injection rate or the temporal sampling is sufficiently slow, then each voxel contains one well-mixed plasma space *p*. We assume that indicator is transported by convection through a directed plasma flow $\mathbf{f}_p(\mathbf{r})$ (ml/min/cm^2), which must satisfy $\nabla\cdot\mathbf{f}_p(\mathbf{r}) = 0$ because plasma is incompressible. Conservation of indicator mass leads to:

$$v_p(\mathbf{r})\partial_t c_p(\mathbf{r},t) = -\nabla\cdot\mathbf{f}_p(\mathbf{r})c_p(\mathbf{r},t) \qquad (1)$$

This one-compartment field model has 3 free parameters per voxel (4 fields – 1 constraint), which is one more than the standard tracer-kinetic model of a single intravascular compartment.

RESULTS (2): If indicator leaks into an extravascular-extracellular space, and the leakage is sufficiently slow, then intra- and extravascular concentrations are not well-mixed and the system must be described by two compartments *p* and *e*. The permeability-surface area product is a new field $PS(\mathbf{r})$ (ml/min/ml) which determines the net indicator flux between *p* and *e*:

$$\begin{aligned} v_p(\mathbf{r})\partial_t c_p(\mathbf{r},t) &= PS(\mathbf{r})\Big(c_e(\mathbf{r},t) - c_p(\mathbf{r},t)\Big) \quad -\nabla\cdot\mathbf{f}_p(\mathbf{r})c_p(\mathbf{r},t) \\ v_e(\mathbf{r})\partial_t c_e(\mathbf{r},t) &= PS(\mathbf{r})\Big(c_p(\mathbf{r},t) - c_e(\mathbf{r},t)\Big) \end{aligned} \qquad (2)$$

This two-compartment field model has 5 free parameters per voxel (=6-1), one more than the standard two-compartment exchange model [1]. Interstitial indicator diffusion can be incorporated by adding a diffusion term $\nabla\cdot D_e(\mathbf{r})\nabla c_e(\mathbf{r},t)$ to the equation for *e* [6].

RESULTS (3): An alternative generalization of Eq (1) arises when there is no leakage (PS=0) but bolus injection and temporal sampling are sufficiently rapid to generate strong arterio-venous concentration differences. The plasma space then separates into two compartments *a* (arterial) and *v* (venous) with convective flows $\mathbf{f}_a(\mathbf{r})$ and $\mathbf{f}_v(\mathbf{r})$ (ml/min/cm^2). The plasma flow from *a* to *v* within a voxel is a scalar field $F_p(\mathbf{r}) \geq 0$ with the units of microvascular flow (ml plasma/min/ml tissue). The incompressibility of plasma in *a* and *v* produces two constraints: $F_p(\mathbf{r}) = +\nabla\cdot\mathbf{f}_v(\mathbf{r}) = -\nabla\cdot\mathbf{f}_a(\mathbf{r})$. Conservation of indicator mass leads to two equations:

$$\begin{aligned} v_a(\mathbf{r})\partial_t c_a(\mathbf{r},t) &= -F_p(\mathbf{r})c_a(\mathbf{r},t) - \nabla\cdot\mathbf{f}_a(\mathbf{r})c_a(\mathbf{r},t) \\ v_v(\mathbf{r})\partial_t c_v(\mathbf{r},t) &= +F_p(\mathbf{r})c_a(\mathbf{r},t) - \nabla\cdot\mathbf{f}_v(\mathbf{r})c_v(\mathbf{r},t) \end{aligned} \qquad (3)$$

This two-compartment field model enables a separation of macro- and microvascular plasma flow, thus resolving the classic problem of large-vessel contamination in blood flow values [2]. There is no equivalent model in standard tracer-kinetic theory.

CONCLUSION Tracer-kinetic field theory provides an explicit link between local physiological parameters and the spatio-temporal concentration gradients. It eliminates errors due to dispersion of a global AIF [3] and large-vessel contamination [2], and enables measurement of additional parameters such as the direction of flow [4,5,7] or interstitial diffusion/convection [6,8]. In a separate abstract, a numerical approach is derived for reconstructing the fields from the measured concentrations, and initial simulations are performed to verify robustness with respect to noise and temporal undersampling .

REFERENCES [1] Sourbron and Buckley PMB 2012; 57: R1-R33 **[2]** Le Bihan and Turner MRM 1992; 27:171-178 **[3]** Calamante MRM 2000; 44:466-73 **[4]** Frank et al MRM 2008; 60:1284-91 **[5]** Thacker et al. JMRI 2003; 17: 241-255 **[6]** Pellerin et al MRM 2007; 58: 1124-34 **[7]** Christensen JMRI 2008; 27:1371-81 **[8]** Koh et al MRM 2013; 69: 269-76.