Estimation of the True Arterial Input Function using a Physiological Model in Dynamic Contrast Enhanced MRI

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Target audience:

Researchers who use arterial input function (AIF) in the analysis of DCE or DSC MRI data.

Purpose:

Tracer kinetics analysis of DCE MRI data requires an arterial input function (AIF) [1], which is the contrast concentration time curve ($C(t)$) in incoming blood at a tissue region. However, direct measurement is not viable with current technologies [2,3]. A common practice assumes $C(t)$ at a nearby artery ($C_{art}(t)$) has negligible differences from the true AIF ($C_{AIF}(t)$) other than the bolus arrival time [4]. Alternative approaches such as reference tissue technique [2] and simultaneously determination of both AIF and tracer kinetics parameters [3] are more complex. We attempt to estimate $C_{AIF}(t)$ using a physiological model for AIF that was proposed recently [5].

Theory:

This AIF model accounts for three sets of physiological factors on the AIF: the delay and dispersion of the injected tracer between the injection and measurement points, widening boluses of tracer passing through repeatedly, and the reducing tracer amount due to influx and efflux. This model suggests $C(t)$ in different blood vessels ($C_{ves}(t)$) in a scan can be modeled with different values for parameters ($\boldsymbol{p_1}$) describing the first set of physiological factors, but the same set of values for the remaining parameters ($\boldsymbol{p_2}$, $\boldsymbol{p_3}$) that describe the other two sets of physiological factors. Thus, we could simultaneously fit different $C_{ves}(t)$ using different $\boldsymbol{p_1}$'s and the same $\boldsymbol{p_2}$ and $\boldsymbol{p_3}$. There are three parameters in $\boldsymbol{p_1}$: a scalar related to the area of the first pass (k), the time lag between contrast injection time and bolus arrival time (t_{lag} s), and a relative dispersion of the contrast bolus during the passage from injection point to the measurement point (RD_1). The two parameters in $\boldsymbol{p_2}$ are the minimum time interval between subsequent circulations (t_{recirc} s) and their relative dispersion (RD_2). Lastly, $\boldsymbol{p_3}$ consists of three rate constants K_{12}, K_{21} and K_{31} between vascular space, tissue space and renal excretion, respectively. We hypothesize that with appropriate estimation of these three parameters at the tissue of interest, this model can estimate the true AIF at the tissue of interest.

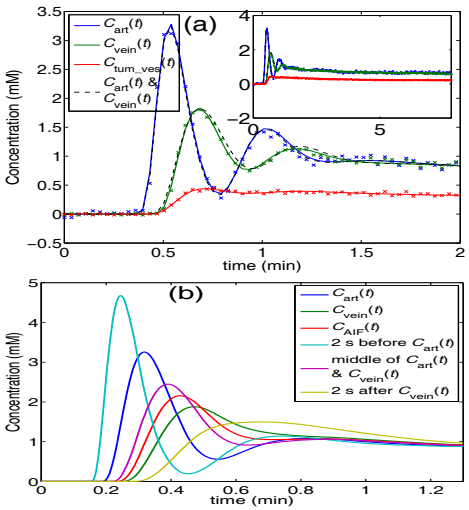

Fig. 1. Concentration time curves measured (crosses) in a representative case and fitting (solid lines) at different vessels, high vasculature tumor region, and simultaneous fitting of curves at artery and vein (black dashed line) (a). Simulated true AIFs at various t_{lag} (b).

Method:

Five DCE MRI data sets of two Nasopharyngeal carcinoma patients from an IRB approved study were examined. MRI scans were performed on a 3T MR scanner (Magnetom Skyra; Siemens, Germany) with a head and neck coil. Axial 3D SPGR FLASH, T1 maps (TR=20ms, FA=5°,13°,20°, FOV 250 mm, 256×256, 16 4mm thickness slices) and subsequent dynamic acquisition (TR=4.5ms, FA=15°, 2.16s per frame for 220 frames). On the seventh dynamic time-point, 0.1mmol/kg of body weight dosage of 0.5M Gadolinium-based contrast agent (Dotarem, Guerbet, France) was administered through a power injector at 3ml/s.

From each patient, we obtained $C(t)$ from three locations: artery ($C_{art}(t)$), vein ($C_{vein}(t)$), and tumor region ($C_{tum\_ves}(t)$) that has a steep fast rise, possibly from blood vessel within. We fitted these three curves individually, and both $C_{art}(t)$ and $C_{vein}(t)$ simultaneously as described above. We simulated $C_{AIF}(t)$ with different t_{lag} by assuming RD_1 changes linearly between $C_{art}(t)$ and $C_{vein}(t)$, and average contrast concentration during the last minute in $C_{AIF}(t)$ and $C_{vein}(t)$ are the same. We performed voxel level tracer kinetics analysis of the tumor using $C_{art}(t)$ and $C_{AIF}(t)$, where t_{lag} is set as based on $C_{tum\_ves}(t)$, as the AIF, using a distributed parameter (DP) model [4] and the extended generalized kinetic (eGK) model [4].

Results:

The AIF model successfully fitted all $C(t)$ curves individually and both $C_{art}(t)$ and $C_{vein}(t)$ simultaneously (Fig 1(a)). Parameters in $\boldsymbol{p_2}$ and $\boldsymbol{p_3}$ from fitting $C_{art}(t)$ and $C_{vein}(t)$ separately and simultaneously were similar (Table 1), but not from the $C_{tum\_ves}(t)$. $C_{AIF}(t)$ with different t_{lag} were simulated (Fig 1(c)). Using $C_{AIF}(t)$ instead of $C_{art}(t)$ achieved slightly lower fitting error, and affected both DP and eGK model parameters in a similar way except v_p, with larger changes in those parameters related to vascular space than K^{trans} and v_e that related more to the tail of AIF (Table 2). Bolus arrival time difference between $C_{art}(t)$ and $C_{AIF}(t)$, Δt_{lag}=2.45s, was reflected in the DP fitting results (Δt_0=2.66s) but not in eGK.

Discussions:

We have demonstrated a feasible way to estimate the true AIF at the tissue of interest when at least one $C_{art}(t)$ and $C_{vein}(t)$ can be obtained. This method does not need knowledge about reference tissue and is independent on the tracer kinetics model used. Similar $\boldsymbol{p_2}$ and $\boldsymbol{p_3}$ parameter values from fitting $C_{art}(t)$, $C_{vein}(t)$ and both simultaneously support the physiological prediction of the AIF model. Simulated $C_{AIF}(t)$ suggests that AIF changes quite significantly corresponding to arrival times. The different magnitude and direction of changes in parameters t_0 and v_p, when $C_{AIF}(t)$ was used, respectively, between the DP and eGK models might be reflecting the limitations of eGK in its assumption that the vascular concentration in tissue vascular space is a scaled down version of the AIF by v_p.

Conclusion:

This method offers a way to estimate the true AIF at the tissue of interest.

Table 1. Model parameters of the representative case.

C(t)	$\boldsymbol{p_1}$			$\boldsymbol{p_2}$			$\boldsymbol{p_3}$	
	k	t_{lag}	RD_1	t_{recirc}	RD_2	K_{12}	K_{21}	K_{31}
$C_{art}(t)$	0.018	9.65	0.249	14.8	0.243	20.5	18.0	1.22
$C_{vein}(t)$	0.015	14.3	0.251	11.8	0.280	27.2	13.7	2.41
$C_{tum\_ves}(t)$	0.005	12.1	0.300	5.00	0.386	7.63	8.86	0.00
$C_{art}(t)$ &	0.0178	9.79	0.244					
$C_{vein}(t)$	0.0168	13.3	0.273	14.8	0.242	24.9	16.6	2.11
$C_{AIF}(t)$	0.016	12.1	0.265					

Table 2. Tracer kinetics analysis results of the tumor in the representative case.

Model	*AIF*	t_0	F	*EF or* K^{trans}	t_1	v_p	v_e	*Fitting error*
DP	$C_{art}(t)$	7.53±5.26	171±145	35.1±43.0	7.42±7.81	10.9±12.1	36.6±20.2	0.569±0.200
	$C_{AIF}(t)$	4.87±5.73	256±231	29.5±38.0	5.71±4.68	12.9±10.6	38.2±20.7	0.541±0.178
eGK	$C_{art}(t)$	9.11±4.89	NA	59.2±60.9	NA	18.1±21.7	62.2±28.9	0.649±0.301
	$C_{AIF}(t)$	8.01±4.96	NA	58.8±63.3	NA	15.8±19.1	59.6±28.3	0.629±0.275

Abbreviation: difference between bolus arrival times of AIF and $C(t)$ (t_0 s), perfusion (F mL/100g/min), first pass extraction ratio (E), mean vascular transit time (t_1 s), fractional vascular volume (v_p %), fractional extravascular extracellular volume (v_e %).

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