# Highly Accelerated Brain DCE MRI with Direct Estimation of Pharmacokinetic Parameter Maps

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**INTRODUCTION:** In T1-weighted dynamic contrast enhanced (DCE) MRI, pharmacokinetic (PK) parameter maps (e.g. $K^{trans}$, abbreviated $K_t$, and $v_p$) are derived from the dynamic image series and used for diagnostic purpose. In accelerated DCE MRI, anatomic image series are typically reconstructed from under-sampled (k,t)-space first, then fit into a PK model to derive the parameter maps [1]. We call this the "indirect" method. As the PK parameter maps have much lower dimensionality than the original multi-coil (k,t)-space, we hypothesize that direct estimation of PK parameter maps will allow higher acceleration and save computational resources required to estimate intermediate steps. Recently, Dikaios *et al* [2] proposed a Bayesian inference framework to directly estimate PK maps from under-sampled (k,t)-space and achieved 8x acceleration in phantom and in-vivo prostate cancer data. In this study, we propose a novel and efficient optimization approach to directly reconstruct the PK parameters from highly under-sampled (k,t)-space, and compare results against a state-of-the-art indirect method [1].

**METHODS:** Fig 1 demonstrates the forward model beginning with PK parameter maps (assuming a Patlak model [3]). The PK parameters ($K_t$, $v_p$) are related to the acquired under-sampled (k,t)-space data ($k_u(t)$) by the steps indicated in Table 1. The proposed model-based reconstruction is to solve ($K_t$, $v_p$) from $k_u(t)$ expressed as a least-squares optimization problem [2]: $(K_t, v_p) = \arg\min_{(k_t, v_p)} \| k_u(t) - F_u S \varphi(P(K_t, v_p)) \cdot \Re 1 + R_0) \|_2^2 + \| \psi K_t \|_1 + \| \psi v_p \|_1$ (Eqn 1), where sparsity is enforced by $l_1$ norm constraints in the wavelet transform ($\Psi$) domain of the PK parameter maps as indicated Eqn 1. This nonlinear optimization problem is solved by a quasi-Newton limited-memory Broyden-Fletcher-Goldfarb-Shanno (L-BFGS) method, where $K_t$ and $v_p$ were solved alternatingly. The $l_1$ norm was relaxed as in [4] to calculate the gradient, which was required for this L-BFGS method. The algorithm was implemented in MATLAB using the minFunc toolbox from [5]. The wavelet penalties were chosen empirically. A fully-sampled DCE data set from a glioblastoma patient was acquired in a 3T GE scanner (FOV: 22×22cm, spatial resolution: 0.9×1.3×7.0mm$^3$, temporal resolution: 5s, fast spoiled gradient echo sequence). The data set was retrospectively under-sampled in the $k_x$-$k_y$ plane, simulating the $k_y$-$k_z$ plane as in a 3D case, using a randomized golden-angle sampling pattern [6]. Then the proposed model-based direct reconstruction was used to calculate the PK maps directly from the under-sampled (k,t)-space. The PK maps were also estimated using images from fully-sampled (k,t)-space, and from indirect reconstruction of under-sampled (k,t)-space using spatial-temporal wavelet and total variation constraints [1].

**RESULTS:** Fig 2 shows the results from the glioblastoma patient at three acceleration rates, compared with the fully-sampled reference and indirect reconstruction. The image quality of the PK maps at the acceleration rate of 20 was comparable to the reference images. For higher acceleration rates, $v_p$ maps degraded in regions containing small vessels, but $K^{trans}$ maps remained accurate in the tumor. This suggests that the most critical diagnostic information is not compromised. Both the indirect and direct approaches used 100 iterations, taking 265s and 296s respectively for reconstruction. The overall image quality at 100x for the direct approach was superior to the indirect approach in terms of small vessel restoration and accurate $K^{trans}$ values in tumor. This retrospective study suggests that an acceleration rate of even 100x may be feasible with this approach.

**CONCLUSION:** We have proposed a novel method to directly estimate PK parameter maps from highly under-sampled (k,t)-space data, and have demonstrated that it can accurately restore PK maps from 100x under-sampled brain DCE-MRI data. Higher spatio-temporal resolution and improved coverage may be achieved when applied to prospectively under-sampled 3D DCE MRI.

**REFERENCES:** [1] RM Lebel, et al. MRM 71(2): 635–644, 2014. [2] N Dikaios, et al. Med Imag Ana 18:989-1001, 2014. [3] PS Tofts, et al. JMR 10: 223-232, 1999. [4] M Lustig, et al. MRM *58*(6): 1182-1195, 2007. [5] M Schmidt: http://www.cs.ubc.ca/~schmidtm/Software/minFunc.html [6] Y Zhu, et al. ISMRM 2014, p. 4365. [7] G Parker, et al. MRM 56:993–1000, 2006

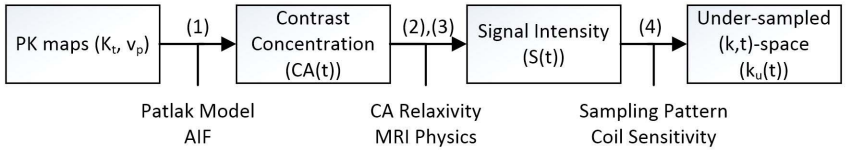


**Figure 1** The forward model of PK maps to under-sampled raw data

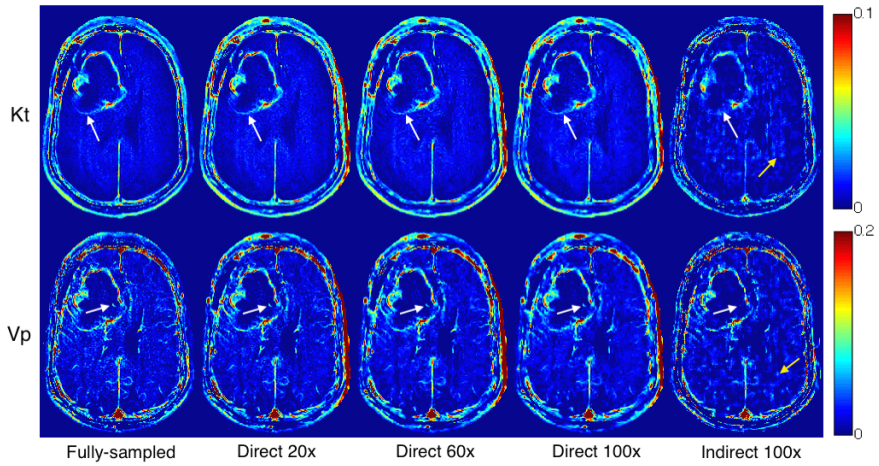


**Figure 2** DCE-MRI results from 20x, 60x and 100x under-sampled (k,t)-space. Direct reconstruction restored accurate PK values and tumor boundaries (white arrows) at all the acceleration rates, with only slight degradation of $v_p$ maps at 100x. The indirect method failed to restore accurate tumor boundary at 100x, and created artifacts (yellow arrows).

**Table 1** Explanation of each step in the forward model.

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| (1) Contrast agent concentration over time (CA(t)) is assumed to follow the Patlak model [3], where $C_p(t)$ is the population-based AIF from [7]: $$CA(t) = P(K_t, v_p) = K_t \int_0^t C_p(\tau) d\tau + v_p C_p(t)$$ |
| (2) R1 relaxation rate over time (R1(t)) is linearly related to CA(t), where $\Re 1$ is the CA relxaxivity, $R_0$ is the pre-contrast R1 calculated from a T1 mapping sequence before DCE is performed: $$R1(t) = CA(t) \cdot \Re 1 + R_0$$ |
| (3) Signal intensity over time (S(t)) is related to R1(t) by the following equation, where TR is the repetition time, α is the flip angle, $M_0$ is the equilibrium longitudinal magnetization that is estimated from the T1 mapping sequence: $$S(t) = \varphi(R1(t)) = \frac{M_0 \sin\alpha (1 - e^{-TR \cdot R1(t)})}{1 - \cos\alpha e^{-TR \cdot R1(t)}}$$ |
| (4) The under-sampled raw (k,t)-space data ($k_u(t)$) is related to S(t) by the coil sensitivities (S), and under-sampled Fourier transform ($F_u$): $$k_u(t) = F_u S(S(t))$$ |