# Patlak Model Selection Using Dynamic Contrast Enhanced T1-weighted MR Measurement of Vascular Permeability

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**Purpose:** To find the best Patlak model, among three of them, that appropriately represents vascular permeability of the human brain tumor using measurement of dynamic contrast-enhanced T1-weighted magnetic resonance perfusion (DCET1MRP).

**Introduction:** The Patlak model [1] has been applied to MRI data obtained with contrast agent to estimate the vascular permeability. Three Patlak models were developed [2]. Model 1 estimates only vascular plasma volume ($V_P$). Model 2 estimates $V_P$ and the influx transfer constant ($K_i$). Model 3 estimates $V_P$, $K_i$, and the reverse transfer constant ($K_b$). Using Gadomer and a T-One by Multiple Read-Out Pulses (TOMROP) sequence MRI measures of T1, Ewing et al. [2] showed that the Model 3 is the best model for the permeability analysis in 15 Fischer rats with day-16 9L cerebral gliomas. Although DCET1MRP is being increasingly used in various clinical trials involving brain tumors, there is no study in the literature to investigate Patlak model selection for tumor patients using DCET1MRP. In this study, we used DCET1MRP dynamic datasets gathered from 31 tumor patients and propose a method for the selection of Patlak model.
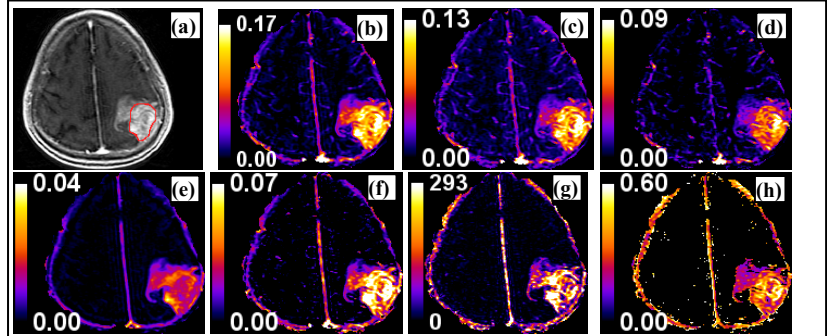


Fig. 1. Voxel-by-voxel pseudocolor parameter maps of a representative patient. (a) Post-contrast T1-weighted image. (b)-(d) Estimated $V_P$ based on Model 1, Model 2, and Model 3. (e)-(f) Estimated $K_i$ based on Model 2 and Model 3. (g) Estimated $K_b$ based on Model 3. (h) F-test for Model 2 versus Model 3.

**Materials and Methods:** DCET1MRP was performed on a 3 Tesla clinical MR system. Pre and post contrast T1-weighted and three dimensional spoiled gradient echo (3D SPGR) images of the tumor bearing brain were acquired before and sequentially for 6 minutes after injection of a gadolinium based contrast agent. We used the following Patlak model [2].

$$C_t(t) = K_i \int_0^t C_p(\tau) e^{K_b(t-\tau)} d\tau + V_p C_p(t) \quad (1)$$

where $C_t(t)$ and $C_p(t)$ are the tissue and the plasma concentrations over time, and $K_i$, $K_b$, and $V_P$ are parameters of the model. After estimating $T_1$ using the multi flip angles SPGR images, $C_t(t)$ and $C_p(t)$ were calculated using the dynamic images [3]. Using the least-square method, Model 1 (with parameter $V_P$), Model 2 (with parameters $K_i$ and $V_P$), and Model 3 (with parameters $K_i$, $K_b$, and $V_P$) were fitted to the measured dynamic data. The F-statistic was used for model comparison [2]. The F-statistic was calculated and mapped on a voxel-by-voxel basis and also computed for the entire tumor ROI as well as normal white matter ROI. Two maps of the F-statistic were calculated for "Model 1 versus Model 2" and "Model 2 versus Model 3."
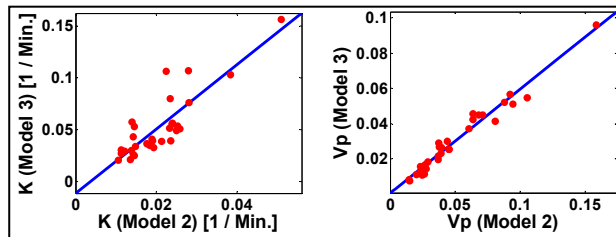


Fig. 3. Scatter plots of the estimated $K_i$ and $V_P$ (in tumor ROIs for 31 patients) using Model 2 and Model 3.
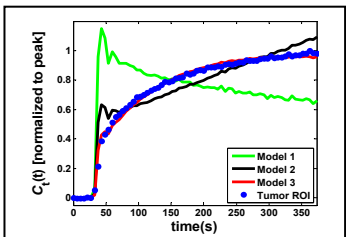
Fig. 2. Illustration of the estimation results using three models to fit the average time course of the tumor ROI, shown in Fig. 1-(a).

Table 1. Mean and STD of parameters (over 31 patients) in tumor and normal white matter (NWM) ROIs.

|  |  | Ki (Model 3) | Vp (Model 3) | Kb (Model 3) | Ki (Model 2) | Vp (Model 2) | Vp (Model 1) | F-test (M1 ver. M2) | F-test (M2 ver. M3) |
|---|---|---|---|---|---|---|---|---|---|
| Tumor | Mean | 0.0524 | 0.0304 | 0.3656 | 0.0204 | 0.0503 | 0.1016 | 943.6 | 381.9 |
| | STD | 0.0307 | 0.0194 | 0.1321 | 0.0085 | 0.0323 | 0.0520 | 521.3 | 197.5 |
| NWM | Mean | 0.0009 | 0.0058 | 0.5344 | 0.0002 | 0.0061 | 0.0067 | 39.1 | 7.9 |
| | STD | 0.0024 | 0.0032 | 0.3685 | 0.0006 | 0.0034 | 0.0039 | 46.8 | 9.3 |

**Results:** 31 patients with brain tumors were included in this study. Fig. 1 shows the estimation results for a representative patient where estimates of $V_P$ and $K_i$ using Model 3, Model 2, and/or Model 1 look similar but values of these parameters are different. High values of the F-statistic in the tumor region (shown in Fig. 1) reject Model 2 in favor of Model 3. For the tumor ROI, the F-tests yielded 777 for the comparison of Model 1 versus Model 2 and 231 for Model 2 versus Model 3 (P < 10$^{-15}$ for both tests), thus rejecting Model 1 in favor of Model 2 and Model 2 in favor of Model 3. Fig. 2 compares fitting of three models to the average time course of the tumor ROI and shows that Model 3 clearly outperforms Model 1 and Model 2. Fig. 3 shows that the estimated $K_i$ and $V_P$ (in tumor ROIs for 31 patients) using Model 2 and Model 3 are correlated. In fact, correlations of ($K_i^{Model\ 2}$, $K_i^{Model\ 3}$) and ($V_P^{Model\ 2}$, $V_P^{Model\ 3}$) are 0.86 (P<10$^{-9}$) and 0.98 (P<10$^{-21}$), respectively. Using the linear least-square fit, we have "$K_i^{Model\ 3}$ = 3.10$K_i^{Model\ 2}$ + 0.11" and "$V_P^{Model\ 3}$ = 3.10 $V_P^{Model\ 2}$ + 0.11." For all of 31 patients, we considered two ROIs, one for tumor and another for normal white matter (NWM), and then calculated mean and standard deviation (STD) of the estimated parameters as well as the F-statistic for model comparison. Referring to the values of the F-statistic given in Table 1, Model 3 is the best model for the tumor ROI. For NWM ROI, however, F-test for rejecting Model 1 in favor of Model 2 and Model 2 in favor of Model 3 is failed and thus we should consider Model 1 for NWM.

**Conclusions:** Using DCET1MRP dynamic images, we have compared three variations of Patlak model and showed that the F-statistic can be used to choose appropriate model for tumor and non-tumor regions. Using the proposed research in this study, the DCET1MRP will be used as a routine neuro-oncologic imaging practice which has not been used so far.

**References:**
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