

## Optimal Period of Linearity using Patlak Analysis in Brain Tumors

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**Introduction:** With the availability of Patlak analysis(1) as a plug-in to ImageJ(2,3), this method of estimating the forward vascular transfer constant,  $K^{trans}$ , is becoming widely used in MRI assessments of cerebrovascular permeability. The linearity of a Patlak plot depends on the assumption that, once contrast agent (CA) has entered the interstitial space, it does not return to the vasculature (4). The correctness of this assumption depends on the rate of leakage, the size of the CA, and the rate and length of data acquisition(4); when the assumption fails, and measurable reflux of CA to the vasculature takes place, a systematic underestimation of  $K^{trans}$ , and an overestimation of vascular fractional volume (fV) occurs.

The purpose of this study was to determine whether, in patients with brain tumors, standard Patlak analysis using different fitting time points (stack size) yielded stable estimates of  $K^{trans}$  and fV, *i.e.*, to determine the fitting time points limit for the assumptions of the linear Patlak model.

**Materials and Methods:**

Five patients with brain tumors (WHO grade II=1, grade III=1, grade IV=2, metastasis=1) underwent MRI studies using a 3 Tesla clinical MR system (Excite HD, GE Medical Systems, Milwaukee, WI). MRI imaging parameters in this gradient-echo sequence were: TR/TE = 5.6/0.75 ms, FOV 240 mm, acquired matrix 256X128, study matrix 256x256, 16 slices of thickness 5 mm, no gap. Baseline  $T_1$  maps were constructed using a variable tip-angle procedure (5). For the dynamic series, gadolinium based contrast agent (0.1 mmol/kg) was injected via a power injector (3cc/sec), followed by flush of 20 cc of normal saline at the same rate. Multiphase acquisition with each phase acquired in 4 to 5.5 sec with CA injection after 6 baseline phases (total imaging time 6.5 min, 70 phases). The TOPPCAT plug-in to ImageJ, which uses Patlak analysis, calculated  $K^{trans}$  and f. Parametric maps of fV and  $K^{trans}$  were generated using fitting time points containing all 70 phases of acquisition, 5.5 min ( $T_{100}$ ), and then reducing the data set by 50% ( $T_{50}$ ) and 25% ( $T_{25}$ ) (*i.e.* for 35 phases and 18 phases of acquisition).

In each patient, four different regions of the brain (normal appearing white matter WM, gray matter GM, enhancing CEL and non-enhancing NEL part of the tumor) were identified using the co-registered post-contrast  $T_1$ -weighted images and these ROIs were used to obtain fV and  $K^{trans}$  values from the various parametric maps with different periods of acquisition.

**Results:** Mean  $K^{trans}$  obtained in the region of CEL using all 70 phases of acquisition ( $T_{100}$ ) was  $0.00566 \text{ min}^{-1}$  (SE 0.00331) as compared to  $0.01333 \text{ min}^{-1}$  (SE 0.01077) for  $T_{50}$  and  $0.01305 \text{ min}^{-1}$  (SE 0.01090) for  $T_{25}$ . Mean fV obtained in the region of CEL using all 70 phases of acquisition ( $T_{100}$ ) was  $0.0396 \text{ ml/g}$  (SE 0.0202) as compared to  $0.0277 \text{ ml/g}$  (SE 0.0239) for  $T_{50}$  and  $0.0336 \text{ ml/g}$  (SE 0.0173) for  $T_{25}$ . Mean fV obtained in the NEL was  $0.0266 \text{ ml/g}$  ( $T_{100}$ ),  $0.0153 \text{ ml/g}$  ( $T_{50}$ ) and  $0.0252 \text{ ml/g}$  ( $T_{25}$ ). Similar results were obtained for mean fV in WM ( $T_{100}$   $0.0071 \text{ ml/g}$ ,  $T_{50}$   $0.0032 \text{ ml/g}$  and  $T_{25}$   $0.0059 \text{ ml/g}$ ) and GM ( $T_{100}$   $0.0321 \text{ ml/g}$ ,  $T_{50}$   $0.0106 \text{ ml/g}$  and  $T_{25}$   $0.0263 \text{ ml/g}$ ). Notably, the estimates of  $K^{trans}$  at the 50% and 25% fit-times are nearly equal; demonstrating that the Patlak plot has entered its linear phase by the 50% point.

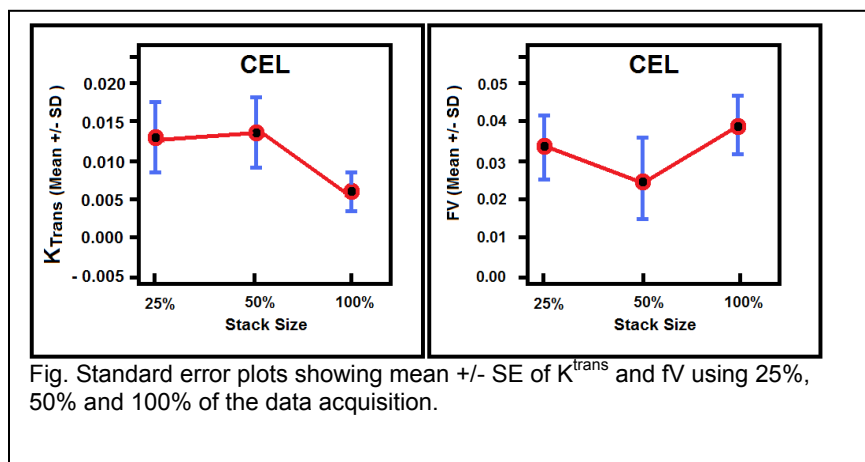


Fig. Standard error plots showing mean +/- SE of  $K^{trans}$  and fV using 25%, 50% and 100% of the data acquisition.

**Conclusions:** DCE  $T_1$ -weighted MR perfusion using Patlak analysis can overestimate fV and underestimate  $K^{trans}$  in the leaky parts of the tumor if the entire data set *i.e.* 5.5 min of data acquisition is used, since this may put the analysis into the non-linear part of the Patlak plot. However, by the 50% point, more accurate (but perhaps less precise) estimates of both  $K^{trans}$  and fV are available.

**References:**

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