

# Improving the Consistency in permeability measurement with DCE-MRI for Longitudinal Follow-up of Brain Metastatic Tumors

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## Introduction

In dynamic contrast-enhanced MRI (DCE-MRI), ideally arterial input function (AIF) should be measured in a feeding vessel as close as to the tissue to be analyzed. But in real cases, the AIF could only be measured from larger vessels, such as middle cerebral artery (MCA) or internal carotid artery (ICA). That usually resulted in some major errors for quantification of permeability in DCE-MRI, because of the partial volume and flowing blood effects from the tortuous feeding vessels. Venous output function (VOF) from the larger and straighter superior sagittal sinus (SSS), with similar shape of the concentration time curves as AIF from MCA or ICA, has been often used in permeability measurement for the reasons of less sensitivity to the partial volume, entering and pulsatile flow effects, and also ease in contouring VOF voxels [1, 2, 3]. Although the scaled AIF by peak of VOF has been proposed to provide an applicable way for permeability measurement, there are still some sources of errors from VOF that may influence the quantification of tissue permeability, particularly the factors occurred in the different scans. The aim of this study is to investigate the clinical applicability of permeability measurement with DCE-MRI, by using a combination of the scaled AIF with VOF and the normalization to the plasma volume (vp) of the adjacent white matter, to estimate  $K^{trans}$  of brain metastatic lesions in the longitudinal patient follow-up.

## Methods

Twelve cases with metastatic brain tumors were included with in this study. DCE-MRI was performed on a 1.5T Siemens symphony Tim MR system with a 3D-T1-GRE sequence. The imaging parameters were TR/TE=3/1.07ms, flip angle=15°, FOV=260\*179 mm, matrix size=128\*88 and time resolution 4.6 s. A bolus of 0.1 mmol/kg Gd (Gadovist 1.0 M) was injected at a speed of 3 ml/s antecubital vein followed by a 20 ml saline flush. T<sub>1</sub> map was also acquired with various flip angles from 5 to 25ms to calculate tissue concentration time curves voxel by voxel in the pharmacokinetic modeling of the tumor.

MR images were analyzed by software of MISTar (Apollo Medical Imaging Technology) to compute  $K^{trans}$ , based on Tofts's model [4]. Initially, we manually picked various numbers of vessel voxels in MCA randomly from 1-2 slices to measure AIF. The vessel voxels in the SSS were also selected randomly from 4-6 slices to measure VOF in each case. Then we scaled the value of each AIF to VOF peak to be new AIF, called sAIF. The procedures were repeatedly performed 4 times by one operator with an interval of one week to comparing the measurement variability. Finally, two sets of 4  $K^{trans}$  maps were collected with the AIF from MCA and the sAIF in each case. Regions of interest (ROIs) were applied to tumors in  $K^{trans}$  maps of twelve cases to get values of mean and standard deviation. Then we calculated the coefficient of variation (CoV) from the  $K^{trans}$  and " $K^{trans}/vp$  of white matter" values by using the AIF and sAIF methods to determine the measurement consistency.

## Results

In this study, the results showed that the measurement variability of  $K^{trans}$  in DCE-MRI was much improved by using scaled AIF. The mean values of  $K^{trans}$  were larger of using AIF from MCA than those using scaled AIF, in the ranges of 68.62 to 486.97 (1 min/1000) and 22.47 to 139.7 (1 min/1000). The CoVs of the mean  $K^{trans}$  by using the sAIF (Table 1) and those after normalization with vp (Table 2) were significantly lower than the mean  $K^{trans}$  by using the AIF (pair t-test, p<0.05). Figure 1 and Table 3 showed a longitudinal follow-up of the brain metastatic tumor in one patient three times. The " $K^{trans}/vp$ " with sAIF presented a better correlation with the disease status on the post-contrast images and clinical manifestations than other two methods.

Case	$K^{trans}$ with AIF			$K^{trans}$ with sAIF		
	Mean (*10 <sup>-3</sup> min <sup>-1</sup> )	SD	CoV(%)	Mean (*10 <sup>-3</sup> min <sup>-1</sup> )	SD	CoV(%)
1	199.54	18.09	9.07	52.49	3.43	6.54
2	239.72	12.58	5.25	48.17	1.55	3.21
3	104.61	10.48	10.02	21.06	0.35	1.66
4	218.28	18.29	8.38	78.82	2.25	2.86
5	178.19	20.10	11.28	33.07	0.76	2.30
6	68.62	3.52	5.13	22.47	0.37	1.64
7	342.05	25.37	7.42	41.36	1.32	3.20
8	274.20	18.40	6.71	41.18	1.15	2.79
9	237.30	11.88	5.01	30.22	0.53	1.76
10	132.86	16.67	12.55	53.73	1.23	2.30
11	294.44	20.69	7.03	93.44	3.55	4.80
12	486.97	25.56	5.25	139.70	2.80	2.01
Mean±SD	7.76±2.54			2.92±1.45		

Table 1. The means and coefficients of variation of  $K^{trans}$  values from 4 different measurements in twelve brain metastatic cases, by using the AIF and sAIF.

## Conclusion

The measurement of lesion permeability would be a useful imaging biomarker for determining the disease activity and guiding the treatment strategies in patients of metastatic brain tumor with relatively high permeability. According to our preliminary results, the inconsistency in permeability measurements would be effectively improved by using sAIF from the larger and straighter SSS to estimate the  $K^{trans}$  in DCE-MRI with the commercial-available automatic software. In addition, the reproducibility in permeability measurements would be much increased by applying the  $K^{trans}/vp$  with the sAIF, which shows the potentially clinical applicability in longitudinal follow-up of brain metastatic tumors.

## References

1. Hamied et al. JMRI 2004; 19:527-536
2. Lavini et al. MRI 2010; 28: 1420-1430
3. Sourbron et al. MRM 2009; 62: 205-217
4. Tofts et al. JMRI 1999; 10: 223-232

Case	$K^{trans}/vp$ with AIF			$K^{trans}/vp$ with sAIF		
	Mean (*10 <sup>-3</sup> min <sup>-1</sup> )	SD	CoV(%)	Mean (*10 <sup>-3</sup> min <sup>-1</sup> )	SD	CoV(%)
1	5.24	0.16	3.11	5.25	0.13	2.56
2	9.84	0.35	3.53	9.76	0.33	3.34
3	4.59	0.21	4.65	4.53	0.10	2.16
4	8.83	0.33	3.70	8.85	0.33	3.69
5	7.47	0.20	2.62	7.44	0.14	1.82
6	3.52	0.03	0.93	3.50	0.02	0.48
7	6.86	0.15	2.20	6.85	0.15	2.21
8	3.95	0.04	1.06	3.95	0.05	1.20
9	4.71	0.05	1.14	4.77	0.01	0.18
10	4.39	0.26	5.98	4.60	0.11	2.45
11	10.06	0.22	2.22	10.05	0.21	2.06
12	19.56	0.35	1.78	19.70	0.45	2.30
Mean±SD	2.74±1.54			2.04±1.03		

Table 2. The means and coefficients of variation of " $K^{trans}/vp$  of white matter values" from 4 different measurements in twelve metastatic cases, by using the AIF and sAIF.

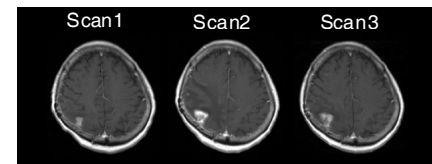


Figure 1. The three follow-up images of brain metastatic tumor in one patient. Scan2 showed mild disease progression and scan3 showed disease regression after radiotherapy.

Scan	$K^{trans}$ with AIF	$K^{trans}$ with sAIF	$K^{trans}/vp$ with AIF
1	101.407	40.176	4.511
2	89.446	24.961	5.617
3	53.147	20.395	3.177

Table 3. The  $K^{trans}$  values using AIF and sAIF and  $K^{trans}/vp$  in 3 different scans.