

## Variability of relative cerebral blood volume normalization in patients with gliomas: Interobserver and intraobserver reproducibility study

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**Purpose:** Due to limited spatial resolution in T2\* dynamic susceptibility contrast-enhanced MR imaging (DSC-MRI) arterial measurements are difficult. Therefore absolute quantification of Cerebral Blood Volume (CBV) is difficult and relative CBV (rCBV) values are reported. In order to reduce intraindividual differences in CBV values determined by DSC-MRI, CBV is normalized to normal appearing white matter (NAWM) or normal appearing gray matter (NAGM). We determined the variability of such rCBV values depending on the choice of the region of interest (ROI) in NAWM or NAGM.

**Materials and Methods:** We retrospectively analyzed 17 patients with pathologically proven gliomas for whom DSC-MRI was available. DSC-MRI used a T2\* weighted sequence with 5mm thickness and 2s temporal resolution. Measurements were performed by two observers. First, observer 1 generated rCBV maps on which a tumor ROI was defined that contained the region with highest tumor perfusion. This ROI was kept constant for the subsequent normalization step using NAWM or NAGM. ROIs were drawn on 1) contralateral NAWM by choice, 2) the same axial section as tumor ROI in the contralateral NAWM, 3) contralateral NAGM by choice, 4) NAWM near corpus callosum, 5) contralateral putamen, 6) contralateral thalamus and 7) a large ROI in contralateral centrum semiovale by both observers. These ROIs were used as internal reference standard to calculate rCBV. After a first evaluation (T1), a second evaluation (T2) was performed using the same method as described above after 2 months. Wilcoxon signed-rank test was used to determine significant difference between rCBV<sub>tumor</sub> measurements of T1 and T2 (intraobserver) and between both observers (interobserver) (significance level  $p < .05$ ). Inter- and intraobserver reproducibility were also both quantified with intraclass correlation coefficient (R) and the coefficient of variation (CV).

**Results:** Intraobserver results are listed in Table 1 and interobserver results are listed in table 2. Wilcoxon signed-rank test did not show significant difference between rCBV<sub>tumor</sub> measurements of the first evaluation and second evaluation for all ROIs and for both observers ( $p > .05$ ). Intraobserver CV ranged between 7% - 19% for observer 1 and 12% - 23% for observer 2. Intraclass correlation coefficient (R) showed excellent intraobserver reproducibility for contralateral putamen, thalamus and centrum semiovale for observer 1 ( $R > .74$ ) and good intraobserver reproducibility for contralateral putamen ( $R = .69$ ) and centrum semiovale ( $R = 0.74$ ) for observer 2.

Wilcoxon signed-rank test did not show significant difference between rCBV<sub>tumor</sub> measurements of observer 1 and 2 for contralateral NAWM by choice, corpus callosum and putamen. Interobserver CV ranged from 12% to 17% (except for NAWM where CV was 42%). Intraclass correlation coefficient (R) showed excellent interobserver reproducibility for contralateral putamen ( $R = .76$ ) and centrum semiovale ( $R = .77$ ).

Table 1

Intraobserver		rCBV <sub>tumor</sub> calculated by normalization in contralateral NAWM by choice						
		NAWM	NAGM by choice	Corpus Callosum	Putamen	Thalamus	Centrum semiovale	
Obs 1	Mean <sub>T1</sub> ±SD <sub>T1</sub>	7.65±2.38	6.15±2.32	2.22±0.75	6.17±2.85	3.84±1.57	4.85±1.62	8.35±2.88
	Mean <sub>T2</sub> ±SD <sub>T2</sub>	9.01±3.55	7.07±2.06	2.15±0.57	5.53±2.18	3.89±1.47	4.71±1.48	8.20±2.75
	p	.15	.063	.758	.309	.795	.605	.532
	CV <sub>T1-T2</sub> (%)	13	19	16	15	12	7	9
	R	.63	.51	.56	.71	.85	.91	.87
Obs 2	Mean <sub>T1</sub> ±SD <sub>T1</sub>	8.53±2.10	8.29±3.24	3.84±1.03	6.19±1.69	4.08±1.48	4.17±1.59	9.35±2.83
	Mean <sub>T2</sub> ±SD <sub>T2</sub>	9.30±2.98	8.02±2.87	4.30±1.44	6.60±2.50	3.78±1.32	4.60±1.76	8.54±3.94
	p	.19	.26	.12	.76	.49	.83	.98
	CV <sub>T1-T2</sub> (%)	17	14	15	23	12	14	17
	R	.56	.60	.49	.39	.69	.57	.74

R<0.4 was considered poor, R of 0.40-0.59 was considered fair, R of 0.60-0.74 was considered good, R>0.74 was considered excellent.

Table 2

Interobserver		rCBV <sub>tumor</sub> calculated by normalization in contralateral NAWM by choice						
		NAWM	NAGM by choice	Corpus Callosum	Putamen	Thalamus	Centrum semiovale	
Mean <sub>obs1</sub> ±SD <sub>obs1</sub>		8.33±3.05	6.61±2.21	2.19±0.66	5.85±2.52	3.86±1.50	4.78±1.53	8.27±2.77
Mean <sub>obs2</sub> ±SD <sub>obs2</sub>		8.92±2.57	8.16±3.02	4.07±1.25	6.39±2.10	3.93±1.39	4.38±1.67	8.93±3.42
p		.149	.005	.000	.309	.850	.523	.09
CV <sub>obs1-obs2</sub> (%)		16	14	42	17	13	14	12
R		.46	.52	.23	.54	.76	.56	.78

R < 0.4 was considered poor, R of 0.40-0.59 was considered fair, R of 0.60-0.74 was considered good, R > 0.74 was considered excellent.

**Conclusion:** Our findings show good intra- and interobserver CV of rCBV measurements. Contralateral putamen chosen as internal reference standard for rCBV shows least interobserver variability and a low intraobserver variability.