

Signal variance-based collateral index in DSC perfusion: A novel method to assess leptomeningeal collateralization in acute ischaemic stroke

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Background and Purpose:

As a determinant of the progression rate of the ischaemic process in acute large-vessel stroke, the degree of collateralization is a strong predictor of the clinical outcome after reperfusion therapy. Thus, besides a precise estimation of the infarct core at admission, knowledge about the leptomeningeal collateralization is essential and may impact on clinical decision-making [1-6]. Although different techniques have been proposed and are applied in the clinical setting for the assessment of collaterals, displaying these reliably remains one of the major challenges in stroke imaging, especially because many of the currently employed techniques for collateral imaging do not allow for quantitative assessment of collateral supply and depend on visual rating scales, thus are highly observer-dependent [7,8]. The purpose of this study was to develop and evaluate a quantitative and observer-independent method for assessing leptomeningeal collateralization in acute large-vessel stroke based on signal

variance characteristics in T2*-weighted dynamic susceptibility contrast (DSC) perfusion-weighted MR imaging (PWI).

Material and Methods:

55 patients (31 female, mean age 67.5 ± 15.7 years) with acute unilateral occlusion of the internal carotid artery and/or middle cerebral artery (MCA), who had received a standardized magnetic resonance imaging (MRI) protocol including diffusion-weighted imaging (DWI) and PWI, were retrospectively included in the study. All patients had received i.v. thrombolysis and/or endovascular thrombectomy. Voxels representing leptomeningeal collateral vessels were extracted according to the magnitude of signal variance in the PWI raw data (*Fig. 1*) from both brain hemispheres and an intraindividual collateral index (CVI_{PWI}) was calculated by dividing the number of voxels representing leptomeningeal collateral vessels on the affected by the number of collateral vessel voxels on the unaffected side. The CVI_{PWI} was tested for its association with imaging-based and clinical outcome measures.

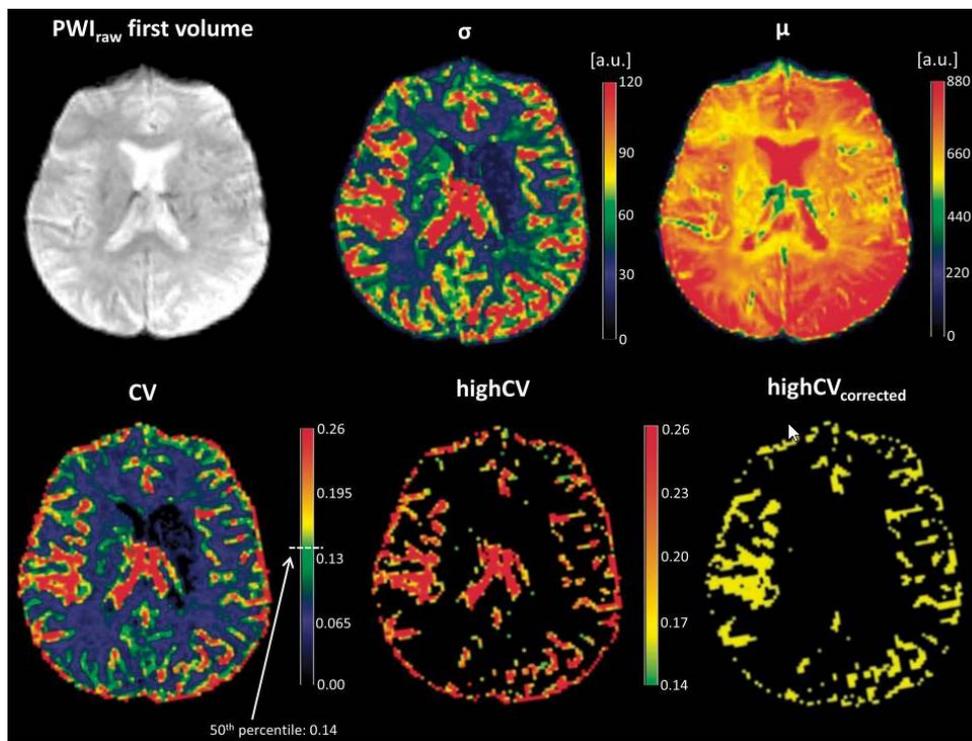


Fig. 1 Illustration of calculation of signal variance in PWI. The top left image exemplarily shows the first volume of the PWI time series. Coefficient of variation (CV) maps were calculated by dividing the standard deviation of every voxel by its mean across time. Feeding vessels of the pial compartment are characterized by a large standard deviation and a relatively low mean signal intensity across time. CV maps (lower left image) were thresholded below the upper 50% of the robust range (lower middle image) and corrected for voxels representing the ventricles and outer CSF spaces. Colour bars represent robust intensity ranges. Standard deviations and mean values of signal intensity across time for the PWI raw data are given in arbitrary units, CV for each voxel is given as dimensionless number. Note the increased image contrast between larger vascular structures and brain parenchyma on the CV map (lower left image) compared to the standard deviation map (upper middle image). The corrected CV map is shown as a binary mask (lower right image). PWI: perfusion-weighted imaging; σ : standard deviation; μ : mean value; a.u.: arbitrary units; CV: coefficient of variance.

Results:

There was a significant negative correlation between CVI_{PWI} and ischaemic core volume at admission ($\rho = -0.459$, $p = 0.0001$). Significant positive correlations were found between CVI_{PWI} and the entire PWI/DWI mismatch ratio ($\rho = 0.494$, $p = 0.0001$) and the PWI tissue at risk/DWI mismatch ratio ($\rho = 0.400$, $p = 0.002$), indicating a higher amount of salvageable tissue in patients with better collaterals. In a pooled analysis of all patients included there was a strong negative correlation between both CVI_{PWI} and final infarct volume ($\rho = -0.430$, $p = 0.002$) and CVI_{PWI} and absolute infarct growth ($\rho = -0.308$, $p = 0.031$). Furthermore, CVI_{PWI} correlated negatively with the neurological deficit as graded on the National Institute of Health Stroke Scale (NIHSS) ($\rho = -0.341$, $p = 0.015$) and modified Rankin Scale (mRS) at discharge ($\rho = -0.305$, $p = 0.023$). In multivariate stepwise backward logistic regression analysis for good clinical outcome (mRS 0–2), the CVI_{PWI} ($\beta = 2.8$, OR = 16.39, 95% CI 1.42–188.7, $p = 0.025$) and the NIHSS at admission ($\beta = -0.69$, OR = 0.501, 95% CI 0.31–0.81, $p = 0.005$) remained the only significant independent predictors for a favourable clinical outcome - even when successful reperfusion and final infarct volume were taken into account.

Conclusions:

CVI_{PWI} derived from signal variance provides useful rater-independent information on the leptomeningeal collateral supply in acute stroke. Further research is required to confirm the validity of this method and to judge its applicability in the clinical setting and for clinical stroke trials.

References:

1. Copen WA, Rezai Gharai L, Barak ER, et al. Existence of the diffusion-perfusion mismatch within 24 hours after onset of acute stroke: dependence on proximal arterial occlusion. *Radiology* 2009; 250: 878–886.
2. Jovin TG, Liebeskind DS, Gupta R, et al. Imaging-based endovascular therapy for acute ischemic stroke due to proximal intracranial anterior circulation occlusion treated beyond 8 hours from time last seen well: retrospective multicenter analysis of 237 consecutive patients. *Stroke* 2011; 42: 2206–2211.
3. Singer OC, Berkefeld J, Nolte CH, et al. Collateral vessels in proximal middle cerebral artery occlusion: the ENDOSTROKE study. *Radiology* 2015; 274: 851–858.
4. Kucinski T, Koch C, Eckert B, et al. Collateral circulation is an independent radiological predictor of outcome after thrombolysis in acute ischaemic stroke. *Neuroradiology* 2003; 45: 11–18.
5. Bang OY, Saver JL, Buck BH, et al. Impact of collateral flow on tissue fate in acute ischaemic stroke. *J Neurol Neurosurg Psychiatry* 2008; 79: 625–629.
6. Bang OY, Saver JL, Kim SJ, et al. Collateral flow averts hemorrhagic transformation after endovascular therapy for acute ischemic stroke. *Stroke* 2011; 42: 2235–2239.
7. Alfke K, Jensen U, Pool C, et al. Contrast-enhanced magnetic resonance angiography in stroke diagnostics: additional information compared with time-of-flight magnetic resonance angiography?. *Clin Neuroradiol* 2011; 21: 5–10.
8. Ernst M, Forkert ND, Brehmer L, et al. Prediction of infarction and reperfusion in stroke by flow- and volume-weighted collateral signal in MR angiography. *AJNR Am J Neuroradiol* 2015; 36: 275–282.