



Imaging leptomeningeal collaterals based on signal variance in perfusion MRI in acute large vessel occlusion: an independent predictor of clinical outcome

Alexander Seiler<sup>1</sup>, Arne Lauer<sup>2</sup>, Ralf Deichmann<sup>3</sup>, Ulrike Nöth<sup>3</sup>, Joachim Berkefeld<sup>2</sup>, Eva Herrmann<sup>4</sup>, Oliver C. Singer<sup>1</sup>, Waltraud Pfeilschifter<sup>1</sup>, Johannes C. Klein<sup>5</sup>, Marlies Wagner<sup>2</sup> (Contact: alexander.seiler@kgu.de)

<sup>1</sup>Department of Neurology, Goethe University Frankfurt/Germany, <sup>2</sup>Institute of Neuroradiology, Goethe University Frankfurt/Germany, <sup>3</sup>Brain Imaging Center, Goethe University Frankfurt/Germany, <sup>4</sup>Institute of Biostatistics and Mathematical Modelling, Goethe University Frankfurt/Germany, <sup>5</sup>Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford/UK

## Background and Purpose:

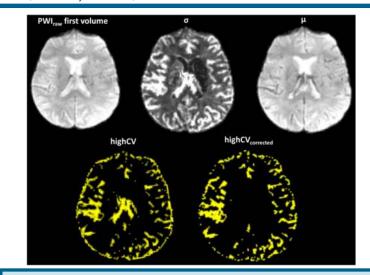
The assessment of leptomeningeal collateralization is of major importance in acute large vessel stroke as it is a determinant of both the amount of salvageable tissue and the progression rate of the ischemic process as well as a predictor of the clinical outcome after reperfusion therapy. However, so far, the evidence of collateral scores obtained from clinical imaging data is limited. This is mainly due to the rater dependence of established scoring systems. In addition, magnetic resonance imaging (MRI) techniques usually applied for collateral imaging have technical limitations and do not allow for direct visualization and quantitative assessment of pial collateral vessels. We therefore introduce a quantitative and observer-independent collateral index (CVI<sub>PWI</sub>) based on perfusion-weighted imaging (PWI) raw data.

## Methods:

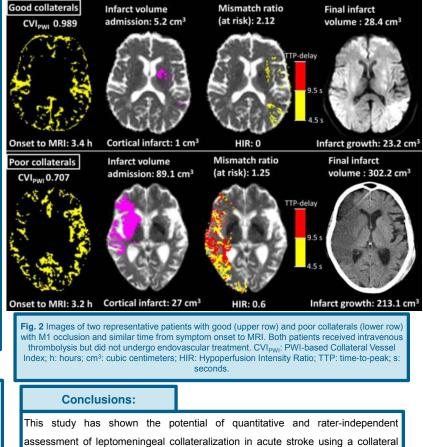
55 patients (31 female, mean age 67.5 ± 15.7 years) with acute internal carotid and/or middle cerebral artery occlusion were included. Median NIHSS at admission was 12 (IQR 8-16). Median time from symptom onset to MRI was 4.05 h (IQR 3-5.35). Besides diffusion-weighted imaging (DWI) to confirm acute cerebral ischemia and PWI to estimate the amount of tissue at risk of infarction, the institutional stroke protocol included a conventional T2-weighted and FLAIR sequence plus sequences to detect intracerebral hemorrhage and assess thrombus length (T2\*-weighted, susceptibility-weighted imaging). Furthermore, a three-dimensional Time-of-flight MR angiography was included for the detection of proximal large vessel occlusion. Coefficient of signal variance (CV) maps were calculated from the PWI raw data time series (Fig.1). An intra-individual collateral vessel index (CVI<sub>PWI</sub>) was calculated based on the volumetric abundance of pial collaterals on each side (affected/unaffected). The initial ischemic core volume was determined on DWI, applying an upper threshold of 600 x 10<sup>-6</sup> mm<sup>2</sup>/s to apparent diffusion coefficient maps. Time-to-peak (TTP) maps were used to delineate areas of hypoperfusion and determine the PWI/DWI mismatch (penumbral threshold TTP-delay ≥4.5s) as well as areas of severe hypoperfusion (TTP-delay ≥9.5 s). The Hypoperfusion Intensity Ratio (HIR) was calculated as the proportion of tissue at risk with a TTP-delay ≥9.5 s.

**Results:** 

 $CVI_{PWI}$  correlated significantly with the initial ischemic core volume (r = -0.459, p = 0.0001) and the PWI/DWI mismatch ratio (r = 0.494, p = 0.0001) as an indicator of the amount of salvageable tissue (Fig. 2).  $CVI_{PWI}$  was significantly negatively correlated with NIHSS and mRS at discharge (r = -0.341, p = 0.015 and r = -0.305, p = 0.023). In multivariate logistic regression,  $CVI_{PWI}$  was an independent predictor of favourable functional outcome (mRS 0-2) (OR = 16.39, 95% CI 1.42-188.7, p = 0.025).



**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. CV maps were thresholded below the upper 50 % of the robust range and corrected for voxels representing the ventricles and outer CSF spaces. PWI: perfusion-weighted imaging; σ: standard deviation; μ: mean value; CV: coefficient of variance



vessel index derived from signal variance in PWI source data ( $CVI_{PWI}$ ). 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.