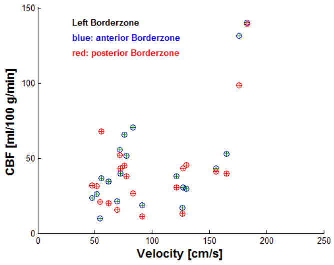
Selective ASL delineates borderzone territories in patients with stenosis of the middle cerebral artery

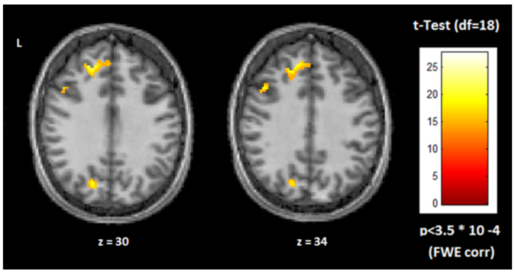
Andrea Federspiel[1], Mirjam Rachel Heldner[2], Urs Fischer[2], Jan Gralla[3], and Roland Wiest[3]
[1]*Psychiatric Neurophysiology, University Hospital of Psychiatry, University of Bern, Bern, Bern, Switzerland,* [2]*Department of Neurology and Stroke Center, University of Bern, Bern, Bern, Switzerland,* [3]*Institute of Diagnostic and Interventional Neuroradiology, University of Bern, Bern, Bern, Switzerland*

Introduction: Non-invasive imaging of vascular territories supplied by major feeding arteries in the human brain is of utmost importance to assess the risk of hemodynamic failure. This can be performed by a non-invasive magnetic resonance imaging (MRI) method: the selective arterial spin labeling (sASL). This technique can be applied in clinical settings and provides detailed information about cerebral blood flow (CBF) and collateral supply. However, the method is limited by several factors such as reduced signal to noise ratio (SNR) and poor temporal resolution. The measure of CBF velocity can provide high temporal resolution in basal cerebral arteries only and may be accomplished by tanscranial color-coded doppler sonography (TCCD). Here, we aimed to investigate how the degree of proximal stenosis affects the linearity of regional cerebral blood flow (rCBF) along the watershed territories of the human brain and whether voxel-wise information about rCBF can be used to delineate watershed areas.

Methods: All patients are participants of the ongoing Swiss Intracranial Stenosis Study (SAISS) that investigates clinical and hemodynamic evolution during best medical treatment of patients with intracranial stenosis. A total of 20 patients with proven intracranial stenosis were included in the study (mean age: 37.4 years ± 8.5; 12 male and 12 female). All patients underwent TCCD and mean flow velocities in the M1 segment of the middle cerebral artery (MCA) were voxel-wise contrasted against the mean rCBF obtained from sASL. We assume a non-linear relationship between CBF and blood velocity measure in the presence of moderate to severe intracranial stenoses [1]. We thus postulated that linearity of the measures would be violated along territories supplied by stenotic vessels and that linearity is preserved along watershed areas that receive blood supply via collateral flow from unaffected vascular territories. MRI was performed with a 3T Siemens TRIO TIM scanner, including a ***anatomical T1w sequence*** (MDEFT) [2] followed by ***selective ASL scan*** using vessel-selective pseudocontinuous ASL (pCASL) sequence [3, 4] with an 12-channel head coil FOV=220 mm, matrix=64 x 64, axial slices=16, slice thickness=7 mm, gap=1.5 mm, TE/TR[ms]=17/4000, slice-selective gradient = 6 mT/m, tagging duration τ = 700 ms and postlabeling delay (w) = 1000 ms. In total, 156 volumes were collected during ASL scan. Matlab/SPM8 was used for preprocessing of imaging data and calculation of absolute CBF maps [5, 6]. ASL images were motion corrected and CBF was quantified using a single-compartment model (T1blood 1650ms, labeling efficiency 0.85, blood-tissue partition coefficient 0.9 [ml/g]). ***TCCD*** of the intracranial arteries was performed with a Toshiba Aplio 500 Ultrasound System 2 MHz phased array probe. All images were flipped according to the presence of stenosis at the left hemisphere.

Results: Linear regression analysis between the M1 territory and sASL (labeling the left part of basal cerebral arteries) revealed preserved linearity between blood flow and velocity along the anterior and posterior watershed areas of the MCA (Fig. 1 and 2). The correlation between rCBF and CBF velocity is preserved in the range of moderate stenosis (<160 cm/s). In two patients with high grade intracranial stenoses, we observed increase CBF along the anterior watershed territory, indicating collaterals flow either via pial arteries fed by the anterior circulation (Patient 1 , mean velocity 150 cm/s) or directly via the communicating anterior artery (Patient 2, mean velocity 115 cm/s). Variability of CBF velocity measures were substantial (Fig. 3). No significant relationship was observed between the velocity measure and the selective ASL images labeling the right, the whole anterior- and the posterior circulation.





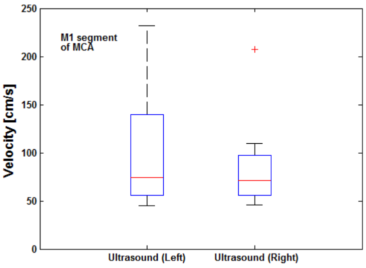
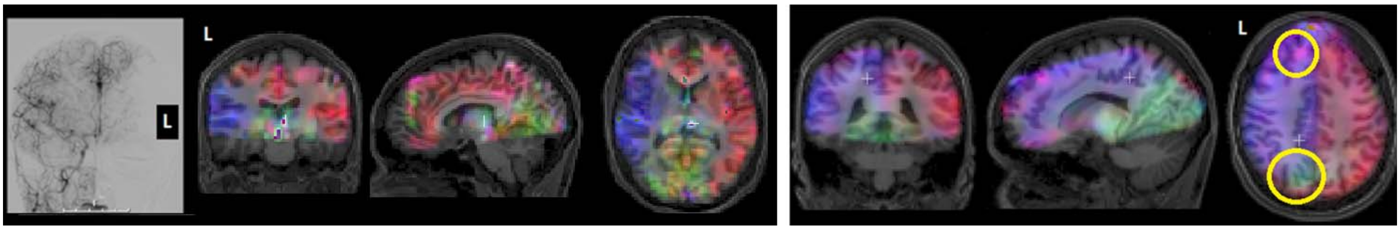


Figure 1: Scatterplot of mean values of CBF as extracted from the two significant clusters of figure 2 (blue color: anterior borderzone; red color: posterior borderzone) and of mean velocity measure of M1 territory. **Figure 2:** SPM maps showing the two clusters of significant linear relationship between the selective ASL images labeled from the left and the corresponding values of ultrasound measure of blood velocity from the M1 territory. The statistics is family-wise corrected (FEW: p<0.05). **Figure 3:** Average values of ultrasound measure of CBF velocity obtained from the M1 territory. No significant differences were observed between the left- and right side ultrasound values.

Figure 4 (left): A Digital Subtraction angiography (DSA) of a representative subject (K.R.) showing collateral flow from the right into the upper left territory. The corresponding selective ASL image showing the equivalent hyperperfusion (blue) from the right side into the left territory. **(right):** selective ASL image showing the average of all 20 patients with equivalent hyperperfusion (red [anterior] and green [posterior]) from the right side/posterior side into the left territory. Yellow rings highlight the two regions of collateral flow.



Conclusions: This study demonstrates that linear relation between rCBF and CBF velocity is preserved in the anterior and posterior watershed territories of the MCA in the presence of moderate to severe intracranial stenoses. The findings are supported by DSA images for each patient (Fig. 4 left). In the present study only linear models were tested and it remains an open question of whether non-linear relationship may additionally be valid. Moreover, it remains an open question whether non-linear models better describe the rCBF-CBF velocity relationship; such models may dominate over linearity especially when possible reductions in vessel diameter due to occlusion become relevant. Our findings indicate that rCBF measures along watershed territories as measured by ASL are reliable markers of sufficient collateral supply.

References: [1] Valdueza J.M. (eds.) Neurosonology and Neuroimaging of Stroke, 2008. Georg Thieme Verlag. [2] Deichmann, R., et al., Neuroimage, 2004. **21**(2): p. 757-67. [3] Dai, W., et al., Magn Reson Med, 2008. **60**(6): p. 1488-97. [4] Wu, W.C., et al., Magn Reson Med, 2007. **58**(5): p. 1020-7. [5] Orosz, A., et al., Neuroimage, 2012. **61**(3): p. 599-605. [6] Wong E.C. Magn Reson Med, 2007. **58**(6): p. 1086-91.