Collateral supply patterns in patients with internal carotid stenosis and occlusion investigated with territorial and reactivity arterial spin labeling

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Introduction: Classically, catheter angiography is used to assess the collateral flow routes towards the brain tissue. Nowadays, several non-invasive MRI methods have been developed for the same purpose. The circle of Willis is considered to be the primary collateral flow route. With a decrease in perfusion pressure with a carotid occlusion or severe stenosis collateral flow from the contralateral ICA or posterior circulation can be distributed to the affected hemisphere via respectively the anterior communicating artery and the posterior communicating artery. Other collateral pathways such as collateral flow via the ophthalmic artery or leptomeningeal collaterals are considered to be secondary collateral flow routes meaning that these collaterals are only recruited when the primary collaterals fail. From the secondary collateral flow routes the presence of leptomeningeal collateral flow is correlated with a higher recurrent stroke risk (1). In the present study we show (i) the presence of primary and secondary collateral flow routes by combining MRA flow patterns via the circle of Willis with territorial arterial spin labeling (TASL) MRI assessment of collateral perfusion territories in patients with internal carotid artery occlusion or severe stenosis. Furthermore (ii), we compare the ASL (diamox) reactivity measurements between patients with primary and secondary collateral flow patterns. Finally (iii), we show patient examples of borderzone infarcts between the borders of the (collateral) perfusion territories.

Methods: Twenty eight patients of whom 17 patients (12 men; mean age±standard deviation (SD), 69±7 years) with a recently symptomatic internal carotid artery (ICA) stenosis and 12 patients (8 men; 59±6 years) with a symptomatic ICA occlusion were investigated on a 3 Tesla MRI scanner (Philips Healthcare). All patients had a non-disabling ischemic stroke ipsilateral to the ICA stenosis or occlusion. The MR protocol consisted of MR angiography, two consecutive 2D phase-contrast (2D-PC) MRA measurements for detecting the presence of primary collateral flow in the circle of Willis, planning-free territorial perfusion imaging ASL sequence for determination of the flow territories of the ICAs and the basilar artery (2), and non-selective perfusion ASL sequences (4) before and 15 minutes after intra venous administration of 14mg/kg acetazolamide to determine hemispheric cerebral blood flow (CBF) and reactivity. The pseudo-continuous ASL parameters were as follows: FOV 240x240 mm2; 17 slices; SENSE 2.5; background suppression; label duration 1650 ms, TR 4000 ms; TE 14 ms. Selective labeling for regional perfusion imaging was as outlined in a previous reports (2,3). An inversion recovery (IR) sequence was acquired for M0-determination and gray matter segmentation purposes. Post-processing was performed in Matlab (Mathworks, Natick, MA). The flow territories of the left ICA, right ICA and basilar artery were identified by means of k-means clustering (3). Hemispheric CBF was calculated using a GM mask to avoid partial voluming and reactivity was calculated from the CBF before and after acetazolamide. The presence of anterior primary collaterals (ie. blood flow via the anterior communicating artery [Acom] or pre-communicating segment [A1] of the anterior cerebral artery [ACA]) and the presence of posterior primary collateral blood flow (ie. blood flow via the posterior communicating artery [Pcom]) was scored using the 2D-PC MRA and TASL maps. Blood flow to a complete perfusion territory (either ACA or MCA territory) visible on the TASL map was considered primary collateral perfusion and partial blood flow to a perfusion territory was considered secondary collateral blood flow via leptomeningeal vessels. Asymmetry of hemispheric reactivity was compared between patients with and without secondary collateral blood flow by calculating the ratio of reactivity between the symptomatic and asymptomatic hemisphere.

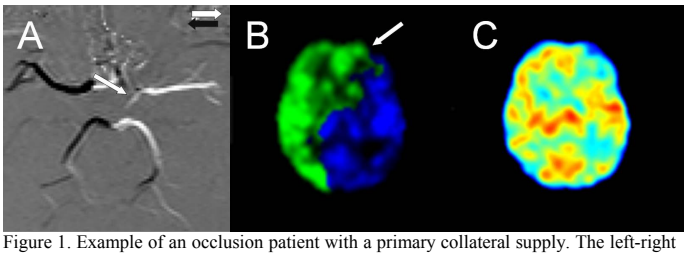

Figure 1. Example of an occlusion patient with a primary collateral supply. The left-right phase-contrast MR angiogram (A) shows posterior collateral flow via the Pcom (besides arrow) from the basilar artery to the MCA territory. This is also shown on the TASL map (B), which also depicts primary anterior collateral flow (besides the arrow) via the Acom from the contralateral ICA. The reactivity map (C) shows a uniform low reactivity throughout the brain.

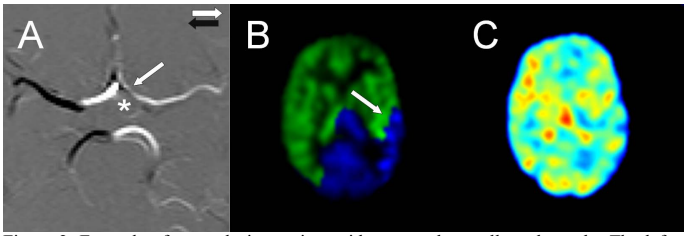

Figure 2. Example of an occlusion patient with a secondary collateral supply. The left-right phase-contrast MR angiogram (A) shows a missing left Pcom (besides star) which rules out primary collateral flow via this route. The MR angiogram also shows primary collateral flow via the A1 segment (besides arrow). The TASL map (B) shows partial contribution to the MCA territory from the basilar artery, illustrating secondary collateral blood flow. The reactivity map (C) shows an asymmetry in reactivity against the left hemisphere.

Patients	Collateral blood flow	Anterior circulation	Posterior circulation
Stenosis	Primary, *n* (confirmed)	10 (4)	
	Secondary, *n* (confirmed)	-	1 (0)
Occlusion	Primary, *n* (confirmed)	11 (5)	6 (5)
	Secondary, *n* (confirmed)		6 (5)

Table 1. Prevalence of primary and secondary collateral blood flow from the anterior circulation (via the Acom and A1 segment from the contralateral ICA) or posterior circulation (via the Pcom from the basilar artery) on TASL maps and number of confirmed cases on 2D-PC MR angiogram of the circle of Willis.

	Hemispheric reactivity (%)		
Collateral blood flow	Symptomatic	Asymptomatic	Ratio
Only primary	47.0 ± 12	45.9 ± 11	1.05 ± 0.2
Secondary as well	29.4 ± 11	38.3 ± 8.2	0.76 ± 0.2 *

Table 2. Hemispheric reactivity in patients with only primary collateral blood flow and in patients with additional secondray blood flow. * indicates a significant difference between both patient groups in the ratio between hemispheres ($p < 0.004$, independent *t*-test)

Results: In 10 patients with ICA stenosis the TASL maps showed primary anterior collateral blood flow from the contralateral ICA, which could be confirmed in 4 cases with 2D-PC MRA showing collateral blood flow via the Acom. In 11 patients with ICA occlusion the TASL maps showed primary anterior collateral blood flow, which could be confirmed with 2D-PC MRA in 5 cases. In the remaing 1 patient with ICA occlusion the TASL map showed primary posterior collateral blood flow to the ACA territory, which could be confirmed with the 2D-PC angiogram showing blood flow via the Pcom. In 5 patients with ICA occlusion the TASL maps showed primary posterior collateral blood flow to the MCA territory, which could be confirmed with 2D-PC MRA in 4 cases. In no patient the TASL maps showed secondary anterior collateral blood flow. In 1 patient with ICA stenosis and 6 patients with ICA occlusion the TASL maps showed partial contribution to the MCA territory indicating secondary posterior blood flow, which could be confirmed in 5 occlusion patients with 2D-PC MRA showing collateral blood flow via the Pcom. These 7 patients with partial contribution to the MCA territory from the posterior circulation were considered to have leptomeningeal blood flow. There was a significant difference in asymmetry of hemispheric reactivity between patients with only primary collateral blood flow (n=22, mean ratio 1.05±0.21%) versus patients with secondary collateral blood flow as well (n=7, mean 0.76±0.2%): p<.004 (independant t-test).

Discussion: The combined information from territorial ASL and a vascular challenge revealed significantly worse reactivity in affected hemispheres feed via secondary collaterals. In general a low reactivity is considered a marker for bad outcome and our finding thereby supports earlier findings indicating that steno-occlusive patients with presence of leptomeningeal collaterals have a higher stroke recurrence (1). Neuroimaging modalities such as the territorial and reactivity ASL which can correlate anatomical with functional status of regional cerebral perfusion could greatly enhance our understanding of collateral circulation, and potentially supplement or replace conventional catheter angiography in the clinical assessment of patients with cerebrovascular disease.

References: [1] Persoon et al., J Neurol Neuros. Psyc. 2011:521-6 [2] Wong, MRM 2007:1086 [3] Gevers et al., AJNR. [Epub] 2011 [4] Dai, MRM 2008:1288

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