Regional Perfusion Imaging using Arterial Spin Labeling in the assessment of Collateral Circulation – a Comparison with Digital Subtraction Angiography

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INTRODUCTION: Collateral circulation plays an important role in patients with cerebral artery occlusion. Studies have shown the importance of collateral flow in predicting stroke outcome, correlating the degree of collateral circulation with infarct volume and functional status [1-2]. Diagnostic strategies to evaluate the collateral circulation have traditionally involved digital subtraction angiography (DSA) which directly visualizes the collateral blood vessels. This has so far been the only modality giving temporal as well as spatial regional blood information. There are several disadvantages associated with DSA: it is invasive and entails certain peri-operative risks, uses ionizing radiation as well as iodinated contrast media (with its attendant risks of allergic and other reactions), and is expensive (in terms of unit cost and demands in medical resource and personnel). In the past years, MR angiography has made rapid technological advances in the non-invasive visualization of intracranial blood vessels, and recently, a new class of arterial spin labeling (ASL) methods has been developed, allowing for independent regional perfusion imaging (RPI) without the need for injection of intravenous contrast media [3-6]. In this work, our aim was to assess how RPI compares with DSA in the assessment of collateral circulation in a patient population with cerebral artery steno-occlusive disease.

METHODS: Ten consecutively recruited patients presenting with either extra- or intracranial artery stenosis or occlusion, and with prior DSA studies were included in this study. The experiments were approved by the local ethics committee. All patients underwent DSA for clinical indications. All DSA studies were performed using a biplane angiography unit (Advantx, GE Medical Systems) to assess both the extra- and intracranial circulation. The MR angiography and RPI investigations were performed using a 3T clinical system (Philips Medical Systems, Best, The Netherlands). Scan protocols for global and regional perfusion were: 6-9 slices; thickness = 8 mm; gap = 2 mm; matrix = 64 × 64; FOV = 240 mm; $\alpha = 35°$; T_R / T_E = 4000 / 23 ms; $TI_1/\Delta TI$ = 100 / 300 ms; time points = 18; SENSE = 3; 60 averages; scan time 4 min. A QUASAR sequence was used [7]. The planning of the labeling volume for the left- and right-internal carotid artery (ICA) as well as the posterior circulation was performed according to Hendrikse et al [8] on the basis of the MIPs from a TOF acquisition covering the carotid bifurcation to the circle of Willis. Collateral assessment on both DSA and MRI were evaluated using a grading system similar to Kim et al [9] by assessing the presence of flow through 10 segments of the main intracranial arteries (A1,2; M1-6; P1,2) as well as the perforating ones (insula, basal ganglia and corona radiata), using a scale from 0 to 3 (0=no collaterals visible to ischemic site; 1=collaterals to the periphery of the ischemic site; 2=complete irrigation of the ischemic bed via collateral flow; 3=antegrade flow). In addition, each study was separately graded on the presence or absence of Willisian and pial collaterals. The 2 sets of data from both DSA and RPI were evaluated in consensus in a double-blinded manner by 3 neuroradiologists. Statistical analysis on the diagnostic quality of RPI compared with DSA was performed using various contingency tests. In particular, both contingency coefficient (C) and Cramer's (V) coefficients were calculated from a χ^2 analysis. In addition, a kappa test was also performed as a measure of agreement between both methods.

RESULTS and DISCUSSION: The DSA studies in all 10 patients were of adequate diagnostic quality, while 1 examination of the 10 RPI studies was non–diagnostic due to heavy motion artifacts. This is an intrinsic problem of ASL that suffers from low signal-to-noise ratio necessitating averaging and long scans times, which may be especially problematic in seriously ill patients. In 1 of the DSA studies, the posterior circulation could not be assessed due to difficulty with cannulating the vertebral arteries. In this aspect, RPI combined with MRA is able to avoid this technical problem in patients with tortuous vessels which are often a challenge to cannulate. In general, the diagnostic quality of RPI was good compared with DSA (case example in Fig 1). Statistical analysis was performed on the 9 patients on whom data from both DSA and RPI were available (after exclusion of the posterior circulation in one additional patient due to missing DSA data), resulting in 230 anatomical sites. The presence of collateral perfusion was assessed on 70 sites. A significant contingency was found between DSA and RPI (C=0.66, V=0.51, est. $p < 0.0001$). This contingency remained unchanged after separation between proximal and distal perfusion sites (C=0.66, V=0.51, est. $p < 0.0001$ and C=0.69, V=0.55, est. $p < 0.0001$ respectively), or when considering gray matter territories only, after exclusion of the perforating ones (C=0.66, V=0.51, est. $p < 0.0001$). Furthermore, Cramer's V coefficient was V=0.53 for the presence of collaterals resulting in $p<0.0001$ (using Fisher's exact method). Finally, a weighted kappa=0.70 was found for the presence of flow and kappa=0.62 for the presence of collaterals, both of which can be considered as "substantial agreement" according to [10].

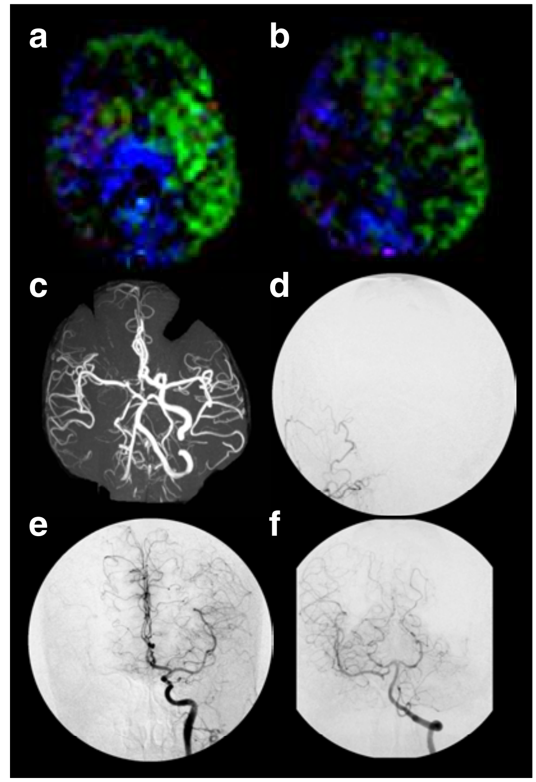

Fig. 1: Patient with right ICA occlusion. a) and b) RPI of the patient with posterior circulation coded in blue, left ICA in green and right ICA in red, showing collateral flow to the right anterior cerebral and right middle cerebral artery territories from the left ICA and posterior circulation, respectively. c) TOF MRA of the same patient which gives corresponding anatomic information on the collateral flow pattern. This correlates with the patient's DSA study in d) right common carotid angiogram which shows occluded right ICA, e) left ICA collateral flow to the right anterior cerebral territory via the anterior communicating artery and f) left vertebral artery collateral flow to the right middle cerebral artery territory via the posterior communicating artery.

Observed Frequencies for DSA, RPI

	0	1	2	3	Totals
0	0	6	0	0	6
1	2	30	7	1	40
2	1	7	14	10	32
3	5	4	8	135	152
Totals	8	47	29	146	230

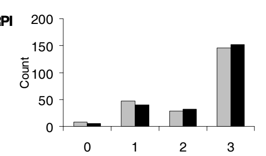

***Fig. 2:** (left) Contingency table of evaluated presence of flow through 13 segments (see text). DSA is horizontal, RPI is vertical. Scale: 0=no collaterals; 1=collaterals to the periphery; 2=complete collateral flow; 3=antegrade flow. (Right) Corresponding histograms for RPI (gray) and DSA (black)*

CONCLUSION: Combined with MR angiography, RPI can provide information comparable to DSA on the extent and nature (whether by primary channels such as the anterior and posterior communicating arteries or secondary pial arteries) of collateral supply to ischemic brain tissue. RPI does not involve ionising radiation or exogenous contrast media injection, and may be combined with diffusion-weighted MR imaging and high-resolution conventional MR imaging in the same examination. Neuroimaging modalities such as RPI that can correlate anatomical with functional status of regional cerebral perfusion could greatly enhance our understanding of collateral circulation, and potentially supplement or replace DSA in the clinical assessment of patients with cerebrovascular disease.

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