

Serial perfusion imaging using arterial spin labeling in acute ischemic stroke

George William John Harston¹, Thomas Okell², Fintan Sheerin³, Martino Cellerini³, Stephen Payne⁴, Peter Jezard², Michael Chappell⁴, and James Kennedy¹
¹Radcliffe Department of Medicine, University of Oxford, Oxford, Oxfordshire, United Kingdom, ²Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, Oxfordshire, United Kingdom, ³Oxford University Hospitals NHS Trust, Oxford, Oxfordshire, United Kingdom, ⁴Department of Engineering Science, University of Oxford, Oxford, Oxfordshire, United Kingdom

Target audience: Stroke physicians and research scientists with an interest in stroke or arterial spin labeling techniques

Purpose

In the context of acute ischemic stroke, arterial spin labeling (ASL) perfusion imaging permits the serial absolute quantification of cerebral blood flow (CBF) without need for repeated contrast administration. Acute, single time point, contrast agent-based perfusion imaging has not been shown to add value to selecting patients for intervention in acute stroke and as a result a recent consensus statement has prioritized serial imaging studies within stroke research to better understand the pathophysiology of this disease.¹

Methods

Patients with ischemic stroke (<6hours from symptom onset) were recruited into an observational cohort study following informed consent or agreement from a representative, according to a protocol agreed by the UK National Research Ethics Service committee (ref:12/SC/0292). Serial MRI scans were performed (at presentation, 2 hours, 1 day, 1 week and 1 month). A 3.0T Siemens Verio scanner was used with a scanning protocol that included quantitative perfusion imaging using multi-post labeling delay vessel-encoded pseudocontinuous ASL (3.4x3.4x4.5mm, TR=4080ms, TE=14ms),² 3-direction diffusion-weighted imaging with automated apparent diffusion coefficient (ADC) calculation, T1-weighted imaging and FLAIR imaging (at 1 month). Analysis was restricted to patients with lesions greater than 5mm axial diameter in whom more than one cerebral perfusion scans were acquired. Final infarct extent was defined manually using the FLAIR image. The presenting ADC lesion and perfusion deficit were objectively defined using pre-validated thresholds (620mm²/s and 20ml/100g/min respectively).^{3,4} Co-registered composite regions of interest (ROIs) were created in each image space to define core infarct (acute ADC lesion within final FLAIR infarct), non-core infarct (final FLAIR lesion not within acute ADC lesion), and non-infarct (hypoperfused tissue outside final FLAIR lesion). Analysis was restricted to grey matter (GM) voxels, performed using FMRIB Software Library.⁵⁻⁷

Results

36 perfusion datasets of adequate quality were acquired from 8 stroke patients with a median symptom to first research MRI time of 3hrs 14mins. Serial CBF values within the co-registered ROIs were extracted for each patient (Figure 1). In a patient-wise analysis, absolute CBF did not differ significantly between core infarct and non-core infarct, nor between non-core infarct and non-infarct ($p=0.13$ and 0.21). A voxel-wise analysis, within individual patient data for whom the relevant ROIs could be determined, showed a significantly different CBF in the core infarct vs. the non-core infarct ($p<0.05$) for only 4 of 7 patients at the presenting scan, and for non-core infarct vs. non-infarct in only 3 of 5 patients. Similarly patterns of subsequent perfusion did not vary consistently between ROIs including between those regions that infarcted and those that did not (Figure 1). The exception to this is that hyperemia was observed in 2 patients within core and non-core infarct on reperfusion that was not seen in the non-infarct GM. In analyzing the contralateral CBF values, there was a marked heterogeneity at presentation between patients within the mirrored hypoperfusion mask ($p<0.001$ using one-way ANOVA). To explore the possibility of diaschisis a correlation analysis was performed, but the variability did not appear to correlate with the degree of hypoperfusion of the ipsilateral hemisphere ($r^2=0.25$, $p=0.32$).

Discussion

Despite widespread use of perfusion imaging to identify tissue amenable to intervention in acute stroke, these data suggest that perfusion imaging alone does not reliably distinguish tissue at risk from that which is destined to infarct at presentation. For a proportion of patients CBF is lower within core infarct than in non-core infarct, which in turn has a lower CBF than non-infarct GM. However, this is neither consistent nor generalizable across patients. Furthermore, the subsequent perfusion characteristics of GM that survives does not appear to differ from tissue that infarcts (other than hyperemia in some patients, which is likely to be a reflection of tissue state rather than causal of infarction). CBF within contralateral tissue varies significantly across all patients suggesting caution should be used if using relative measures of CBF.

Conclusion

Although hypoperfusion is necessary for tissue injury in acute ischemic stroke, these results suggest that knowledge of CBF alone is not sufficient to predict tissue outcome. Other factors such as cellular metabolism, or different susceptibilities of regions and individuals to ischemia will determine the fate of hypoperfused tissue. This observation may explain the difficulty of using perfusion thresholds to select patients for treatment and highlights the need for use of other imaging modalities to complement perfusion data. Finally the widespread practice of using relative perfusion measures in stroke patients should be challenged in light of the variability seen within the contralateral hemisphere between patients at presentation.

References

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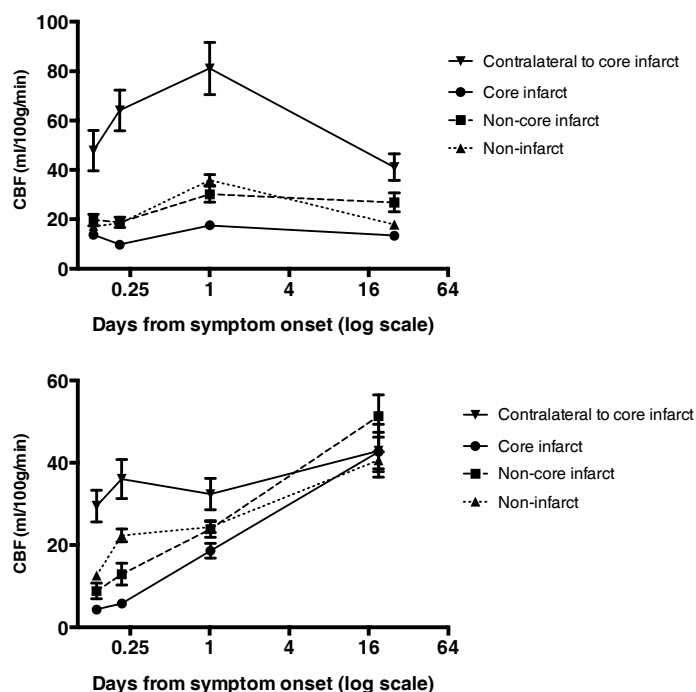


Figure 1: Serial CBF measures within defined ROIs in 2 patients with ischemic stroke without (top) and with (bottom) reperfusion. A contralateral ROI generated by reflection of the core infarct is shown for reference.