Non-invasive MRI measurement of CBF: validating an arterial spin labelling sequence with 99mTc-HMPAO CBF autoradiography in a rat stroke model

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Introduction

Arterial spin labelling (ASL) is becoming increasingly available for stroke research. and offers the opportunity for non-invasive, quantitative cerebral blood flow (CBF) measurement. In this study, a modification of a published ASL technique[1] has been set up and validated in a rodent stroke model using the SPECT ligand , ^{99m}TC-D, Lhexamethylpropyleneamine (^{99m}Tc-HMPAO), for CBF autoradiography.

Methodology

Male Sprague Dawley rats (300-350g) were initially anaesthetised (2% isoflurane), surgically tracheotomised, artificially ventilated (2-3% isoflurane, 30%:70% mixture of O_2 and N_2O) and the middle cerebral artery permanently occluded (MCAO) by the intraluminal filament technique[2]. Rats were immediately transferred to a Bruker Biospec (7T/30cm) MRI scanner equipped with a 72mm birdcage resonator and a 2cm surface coil placed on the head of the rat. Blood pressure was continuously monitored and blood gas analyses performed. Non-invasive quantitative CBF was carried out on 4 coronal slices throughout the MCA territory using a form of pseudo-continuous ASL based on a train of adiabatic inversion pulses[1]. The sequence employs a spin-echo EPI imaging module (Te 20ms, Tr 7000ms, matrix 96 x 96, FOV 25 x 25mm, slice thickness 1.5mm, 16 averages, 4 shots) preceded by 50 hyperbolic secant inversion pulses in a 3s train. Diffusion weighted imaging (DWI) was performed prior to each ASL scan to track evolution of the ischaemic lesion. ^{99m}Tc-HMPAO was injected (i.v. , 6.05 mCi (225 MBq) in 0.8ml isotonic saline) halfway through the ASL scanning protocol. Thirty minutes after radiotracer injection, the rat was killed, the brain removed, frozen in isopentane and coronal sections (30µm) cut on a cryostat. Sections within MCA territory were exposed, alongside calibrated standards, to Kodak Biomax MR film for 1.5 hrs before autoradiographic analysis. ASL CBF maps were co-aligned with the corresponding autoradiographic image. On each ASL slice and corresponding composite autoradiogram (generated from 5 consecutive coronal cryostat sections), three regions of interest (ROIs) were selected on the ipsilateral hemisphere (n=8). Perfusion weighted image (ASL) /DWI mismatch images were produced to aid in identifying ROIs in the ischaemic core and presumed penumbra. For each ROI using ASL (ml/100g/min) and ^{99m}Tc-HMPAO autoradiography (nCi/g), CBF measurements were expressed as a percentage of the mean contralateral CBF.

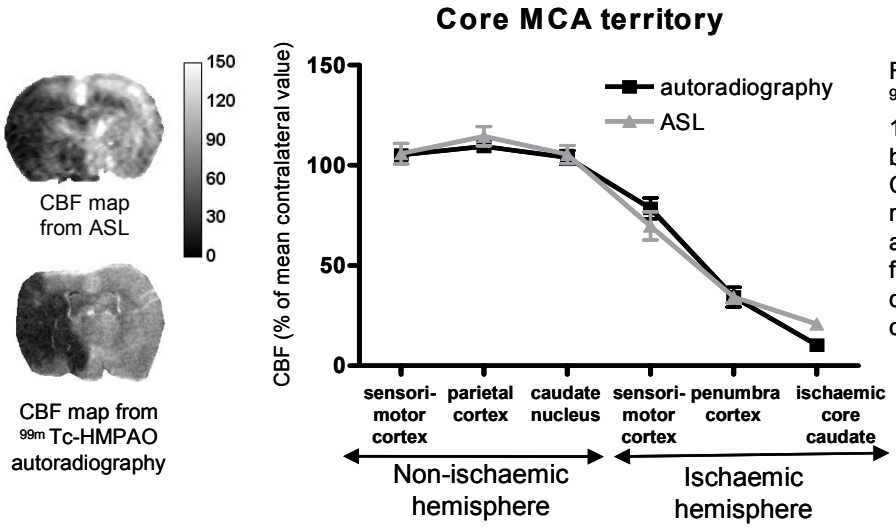

Figure 1: Left, representative ASL (top) and ^{99m}Tc-HMPAO (bottom) CBF maps (approx 1.92mm posterior to bregma). Calibration bar is % of mean contralateral flow. Right, CBF data (n=8, mean ± SD) from homotopic regions of interest (ROI) in the ipsilateral and contralateral hemispheres generated from ASL maps & autoradiography. All ROI data are expressed as a % of mean contralateral CBF.

Results

In general there was good agreement between blood flow values generated by ASL and ^{99m}Tc-HMPAO autoradiography (see Figure 1) with similar relative CBF values across non-ischaemic and ischaemic tissue. The ASL technique was able to accurately detect the reductions in CBF caused by occlusion of the middle cerebral artery and these CBF estimates closely matched those generated by the established autoradiographic technique.

Conclusions

ASL and ^{99m}Tc-HMPAO autoradiography appear highly correlated over a range of CBF values and suggest that our modified ASL sequence is a valid MRI technique which should also be capable of providing fully quantitative CBF values in ROIs across non-ischaemic and ischaemic brain tissue.

References

[1]*Moffat et al, 2005*
[2]*Koizumi et al, 1986*

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