Volumetric Perfusion Mapping with Continuous Arterial Spin Labelling in Rat Brain

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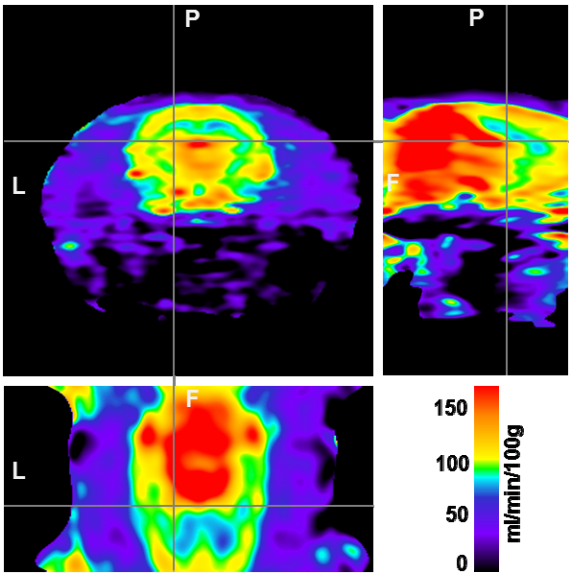
Background – Arterial spin labelling (ASL) has proven a valuable tool for non-invasively quantifying cerebral perfusion, which is deemed a proxy for neural activity in functional MRI in preclinical and clinical settings. In rodents, ASL with continuous inversion (CASL) for perfusion tagging has been successfully implemented and extensively used for pharmacological fMRI [(1)]. CASL theoretically provides superior sensitivity compared to other labelling schemes [(2)], but it lacks true multi-slice or even 3D capabilities due primarily to magnetisation transfer effects. More recently, new variants of CASL, i.e. pseudo CASL (pCASL) and sine wave-modulated CASL (smCASL), have been described that should remedy this shortcoming [(3,4)]. Whereas in humans the usage of pCASL is quite advanced, implementation of equivalent methods in the preclinical arena has lagged behind. Only very few studies have demonstrated multi-slice acquisition and current implementations of pCASL in preclinical settings required that the labelling plane be at the magnet's centre [(5,6)]. Here, we report on the successful implementation and first application of pCASL and smCASL in rat brain at 4.7 and 9.4 T with 3D volumetric perfusion acquisition and arbitrary off-centre placement of the labelling plane.

Methods – pCASL and smCASL were implemented on Bruker BioSpec 4.7T/40cm and BioSpec 9.4T/20cm instruments, each equipped with a BGA12 gradient set, a 7cm transmit resonator and a receive-only rat head coil. Perfusion images were acquired using a centred-RARE readout with TR/TE = 3500ms/5.5ms, RARE factor = 32, FOV = 4cm x 4cm x 2cm, 128 x 64 x 20 matrix, 1 average, 2.8s labelling, 0.4s post labelling delay and -25mm labelling offset. The unbalanced variant of pCASL (ubpCASL) was employed with 0.4ms Hanning-shaped labelling pulses and an interpulse delay of 1.1ms, 4uT labelling strength ($B_{1(average)}$), 2.5mT/m labelling gradient ($G_{L(average)}$), and a 6-fold raising of peak labelling gradient and pulse strength over average strengths. smCASL was performed with G_L = 10mT/m, B_1 = 6.8uT, and a sine modulation f_{AM} resulting in an 1.5mm separation of the double-inversion planes. In vivo studies were carried out in male Sprague-Dawley rats maintained under isoflurane anaesthesia (2-2.5% in 1:5 oxygen/air). Breathing rate, composition of inhaled and exhaled gases and body temperature were monitored. Rectal temperature was maintained with a feedback loop-controlled electric heating blanket.



Results and Discussion – ubpCASL and smCASL were realised as PVM methods in ParaVision (Bruker) according to the theoretical considerations detailed in the literature [(1-6)]. In particular, pulse phase compensation for off-centre labelling in ubpCASL and adjustable separation of the double-inversion planes in smCASL were implemented. Figure 1 shows representative coronal, sagittal and transversal cuts through a 3D perfusion map acquired in 4.5 minutes with smCASL in rat brain at 4.7T. The centred-RARE module used for data readout provided high signal efficiency combined with virtually distortion-free depiction of the geometry throughout the brain. The high quality of the perfusion maps readily allowed numerous functionally different entities of the brain to be identified. For optimisation of the labelling parameters we could draw on literature values and extensive experience with CASL [(1-6)]. Labelling in smCASL is essentially identical to that in single-slice CASL and thus needed no further tuning. Also for ubpCASL, high labelling efficacy could be established with similar parameters even for off-centre labelling, thus suggesting that field inhomogeneity in the labelling plane was of no major concern. However in our hands, tuning of $G_{L(average)}$ and f_{AM} for the control scans was particularly crucial. Small deviations from optimal settings lead to partial labelling of inflowing blood which rapidly degraded the overall labelling efficacy and thus the quality of the perfusion maps. Finally, 3D versus single-slice perfusion acquisition yielded a gain in signal-to-noise of close to 100% and approximately 80% of the theoretical value based on the number of acquired transients for smCASL and ubpCASL, respectively.

Conclusions – We have demonstrated experimentally that pCASL and smCASL with 3D acquisition and off-centre labelling combined with RARE-based data readout both provide high-quality volumetric perfusion maps of rat brain. High signal efficiency together with a nearly distortion-free image geometry thus render these modalities compelling for quantitative functional MRI in preclinical research.

References –
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