

Neonatal perfusion imaging with pulsed continuous arterial spin labelling (pCASL)

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Purpose: Arterial spin labelling (ASL) is a fully non-invasive magnetic resonance perfusion imaging method which can be used to detect alterations in cerebral haemodynamics associated with a variety of disease processes in adults and children.¹⁻⁵ However, although cerebral perfusion abnormalities appear to be integral to a number of pathologies seen in the developing brain,^{3,4} to date the use of ASL perfusion imaging in neonates has been extremely rare.⁵ Various technical issues, combined with rapid developmental changes in vascular flow,⁶ hematocrit (and hence T_1),⁷ myelination and perfusion^{3,5,8-9} during the neonatal period can confound the absolute quantification of perfusion and the direct comparison of perfusion values derived at different developmental stages. The purpose of this study was to address some of the potential sources of error in the quantitative assessment of ASL perfusion during the neonatal period, and to develop an acquisition and analysis protocol suitable for longitudinal perfusion assessment and the absolute quantification of perfusion in neonates.

Outline of Content: This study systematically addresses several potential sources of error and variability in the quantification of perfusion in neonates and young children using pCASL, including the vascular anatomy and the position of the labelling plane, vascular flow, transit time effects, and differences in blood T_1 . These effects are investigated *in vivo* in a group of seven unsedated preterm neonates (scanned at term-equivalent age) and their impact on the accuracy of perfusion values is discussed. A pCASL acquisition and quantification protocol suitable for use in neonates is presented.

Summary: The default labelling plane location seems to be suitable even for young neonates, but an increased transit time necessitates the use of a longer post-labelling delay (~2 seconds) than that typically required for studies in adults and older children. Incorrect choice of the post-labelling delay can lead to a significant underestimate of the quantitative perfusion values, approaching 50% in some cortical regions. An incorrect post-labelling delay can also negatively impact the qualitative, visual interpretation of the perfusion maps, as variations in transit times between the right and left hemispheres may lead to an apparent asymmetry in perfusion arising from differences in transit time rather than genuine hemispheric differences in perfusion. *In vivo* T_1 mapping using a variable flip angle spoiled gradient echo (SPGR) method demonstrates that the blood T_1 is also significantly longer in neonates than in older children and adults (2100 ms vs 1600 ms), which may lead to an overestimate of perfusion values if the perfusion is quantified assuming an adult blood T_1 value. However, differences in the blood-brain barrier partition coefficient between neonates and older children or adults may partially compensate for any errors in perfusion arising from an incorrect assumption of the blood T_1 , since the partition coefficient is thought to be larger in neonatal subjects. An *in vivo* investigation of the blood brain barrier partition coefficient in neonates as well as older children and adults is the subject of ongoing work.

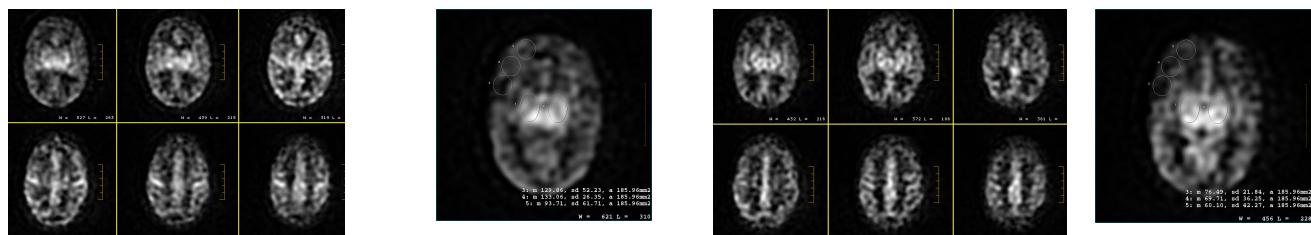


Figure 1. Axial pCASL perfusion images acquired from a neonatal subject with a post-labelling delay of 2 seconds (left) and 1.5 seconds (right). Increased perfusion is seen in the basal ganglia and regions undergoing myelination, as described previously.^{5,7-9} With a post-labelling delay of 1.5 seconds the average perfusion values in the basal ganglia are underestimated by 15-18% and the average perfusion values in the cortex are underestimated by 36%-48%, relative to the values derived with a post-labelling delay of 2 seconds.

This study demonstrates that cerebral perfusion maps can be acquired successfully from unsedated neonates using pCASL. If the sources of error addressed in this study are taken into account in the acquisition and analysis protocol, this method can provide reliable perfusion measurements suitable for longitudinal assessment and the evaluation of perfusion changes with both typical and atypical brain development during the neonatal period.

References: ¹Wang JJ and Licht DJ. Neuroimag Clin N Am 16 (2006) 149-167, ²Deibler AR, et al. Am J Neuroradiol (2008) 29:1235-1241,1428-1435. ³Huisman T and Sorensen AG. Eur Radiol (2004) 14:59-72, ⁴Wintermark P, et al. JMRI(2008) 27:1229-1234, ⁵Miranda MJ, et al. Pediatric Research 60:359-363, ⁶Ilves P, et al. J Ultrasound Med (2008) 27:199-207, ⁷Jopling J, et al. Pediatrics (2009)123:e333-e337, ⁸Takahashi T, et al. (1999) Am J Neuroradiol 20:917-922, ⁹Kennedy C, et al. (1970) Neurology 20:613-618