THE EFFECT OF HAEMATOCRIT LEVELS AND ARRIVAL TIMES ON ASL MEASURES IN NEONATES.

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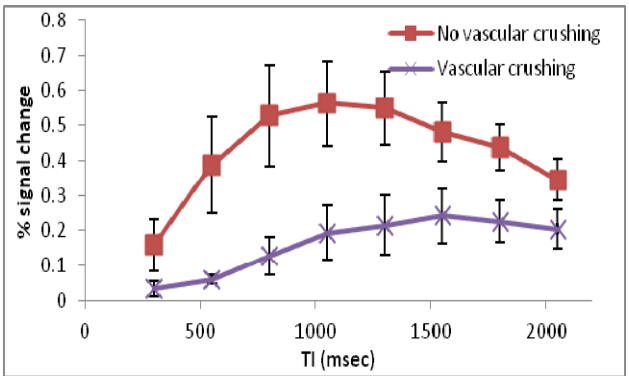
Target Audience: Clinicians and MR researchers involved in ASL measures in neonates.

Purpose: Arterial spin labelling (ASL) is a non-invasive means of measuring cerebral blood flow (CBF) by manipulating the spins from inflowing blood water to act as an endogenous tracer. The current alternative is to use gadolinium-based contrast agents which carry the risk of gadolinium toxicity, particularly nephrogenic systemic fibrosis [1], and are generally not licensed for use in infants under the age of 2. Hence, there is a clear need to consider the use of ASL in neonatal imaging. However, there are potential sources of error that can affect CBF quantification in the neonatal brain using ASL, namely haematocrit variability [2] and prolonged arrival time [3]. Haematocrit can alter the T1 of arterial blood, leading to an error in CBF estimation if not corrected [4]. The first aim of this study is to assess the affect on CBF of using an assumed adult T1 value compared to the true value from individual haematocrit measurement. It is currently standard practice to acquire ASL data at a single timepoint in order to measure of CBF. For accurate quantification it is often assumed that all of the labelled blood has entered the tissue voxel at this time. However, there is evidence that arrival time may be prolonged in the neonatal brain [3], leading to inaccuracies in this assumption. The Look-Locker ASL (LL-ASL) sequence [5] allows for a multi-timepoint measure of the dynamics of the ASL signal change, allowing estimation of both arrival time and CBF. The second aim of this study is to determine the mean arrival time in the neonatal brain through use of a LL-ASL sequence.

Method: Seven neonates (mean age 26.3±25.7 days) were scanned at Alder Hey Children's Hospital, Liverpool with the Look-locker ASL scans as part of an existing study approved by the North West Research Ethics Committee. Haematocrit levels were obtained from the babies at Royal Womens' Hospital in Liverpool and were measured a few days prior to the scans. All scans were carried out on a 3T Philips Achieva scanner. Look-Locker EPI readout data was acquired with STAR labelling and 8 readout times from 300 to 2050 ms with a step size of 250msec with the following parameters (TR:4000 ms; 3x3x6.6mm voxels; 9 slices; FA:40 deg; TE:12 ms (without vascular crusher)/ TE:20 ms (with vascular crusher)). ASL data was analysed using in-house MATLAB routines using a single blood compartment model [6] adapted for LL readout [7]. 3 analysis procedures were compared: i) 2 parameter fits producing maps of CBF and arrival time with fixed T1 of blood 1600 ms, ii) 2 parameter fits producing maps of CBF and arrival time with individual values of T1 of blood calculated from haematocrit values [2] (reference Varela paper) and iii) a single parameter fit producing a map of CBF with arrival time fixed at 1000ms and individual values for T1 of blood. Whole brain values for CBF and arrival time were extracted.

Results:

Subject	Age (days)	Model: Individual T_1	Model: T_1 assumed at 1.6s		Model: Arrival time fixed at 1s	
		CBF (ml/min/100ml)	CBF (ml/min/100ml)	% error	CBF (ml/min/100ml)	% error
S1	20	139	151	8	70	50
S2	6	84	77	9	61	27
S3	11	77	88	15	80	4
S4	63	118	147	25	109	7
S5	63	107	132	23	90	16
S6	4	131	155	19	90	31
S7	17	58	64	10	54	7
Mean ± SD	26 ± 26	102 ± 30	116 ± 39	16 ± 7	78 ± 20	20 ± 17



Mean Hct was 0.44, varying from 0.3 to 0.58. This produced mean T1 of 1.72 s, varying from 1.55 s to 1.93 s. If fixed T1 of 1.6s is assumed, this lead to a mean error in CBF of 16% **(Table 1).** Mean arrival time was 917 ± 157 ms; and this was largely insensitive to the haematocrit correction. If fixed arrival time of 1 s is assumed this leads to a mean error in CBF of 20% (Table 1).

Figure 1: Plot of the mean subtraction signal with and without vascular crushing. SE bars are shown. This figure shows the dynamics of the whole brain ASL signal. The signal is reduced and peaks later with the addition of vascular crushing, as expected given the loss of signal from large vessels which will show an early signal change. It is clear that, for single time point ASL measures, the inversion time needs to be greater than at least 1.5s for the CBF estimation to be independent of arrival time (i.e. past the peak, indicating that the complete labeled bolus has entered the tissue).

Discussion: This study has shown that arrival time for neonates appear to be longer than seen in the adult brain (mean value of 917 ms compared to 754 ms in adults [8]. Recently, O'Gorman et al [3] suggested use of a post labelling delay time of 2 seconds to prevent underestimation of perfusion in neonates when using a single time-point measurement. Our results are in broad agreement, suggesting perhaps a shorter time may be adequate. This will depend strongly on the age of the baby, and we noted peaks as late as 1.8s in our youngest babies. We find errors in perfusion of approximately 16% in neonates if an assumed T1 value of 1.6 s is used rather than individual T1 values corrected for Haematocrit. This is in agreement with work by Varela et al [2].

Conclusion: We show that in clinical applications of CBF measures using ASL in neonates it is important to consider the effects of varying HCT levels and choice of delay time.

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