Can Arterial Spin Labeling be used to identify perfusion distribution differences using group analysis?

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Introduction Assessment of changes in perfusion patterns has been shown to be a valuable tool in improving our understanding of pathological processes in brain diseases, like Alzheimer's disease, migraine, epilepsy and CNS-neoplasms. Arterial spin labeling (ASL) provides a completely non-invasive tool for quantitative measurement of cerebral blood flow (CBF), and can therefore easily be added to clinical research protocols. Most frequently a voxel-based morphometry-like analysis method is employed to identify differences in the perfusion distribution between a patient group and control subjects. However, it is uncertain how well such a method performs in identifying local perfusion differences and what the optimal post-processing method would be, especially regarding registration and normalization aspects. The goal of this study is to investigate the accuracy and precision of arterial spin labeling MRI in identifying local differences in blood flow distribution between groups and its optimal processing within that context. This is investigated by locally increasing the perfusion in one group of volunteers by means of neuronal activation and by comparing these CBF maps to CBF maps of another group of volunteers who are scanned at rest. Since each volunteer is both scanned at rest and during activation, a ground truth of the CBF change due to activation is obtained and this setup enables therefore a comparison of the outcome of the group analysis with a true ground truth.

Methods 27 subjects (aged 19 to 35, mean age 23, 13 males) were scanned using a 3-Tesla MRI scanner (Philips, Best, Netherlands) equipped with locally developed software enabling pseudo-continuous ASL imaging (labeling duration 1.65 s, postlabeling delay 1.525 s with background suppression, 17 slices, voxel-size 3x3x7 mm, 4.5 minutes). Three activation scans (8 Hz alternating checkerboard, watching a cartoon and bilateral fingertapping), together with one scan in resting conditions were performed. The ground truth for each activation task was obtained by subtracting the mean perfusion map during the rest condition from the ones during activation; this ground truth reflects the change in CBF in ml/100ml/min (named ground truth ΔCBF). As a second ground truth, a voxelwise paired t-test was performed between rest and activated CBF-maps (ground truth t-test). The volunteers were subsequently split into two groups A and B. To simulate a perfusion study that compares a patient group with a control group, we only considered the resting CBF maps of group A and the activation CBF maps of group B. Images were put into a common atlas orientation by using SPM99/SPM5. Two approaches were studied: normalization of the perfusion maps towards the PET template and normalization via the anatomical 3D T1 scan of each volunteer towards the T1-template. Subsequently, a t-test was performed between the scans of group A and B to identify CBF distribution differences; this was both done for the CBF maps as well as for the CBF maps divided by the averaged whole brain perfusion of that individual, a frequent procedure in PET to reduce the influence of baseline CBF-values ("proportional scaling"). The resulting t-maps were compared to both ground truths by means of correlation. Additionally, the mean t-value and maximal CBF increase was determined in respectively the visual and motor-cortex.

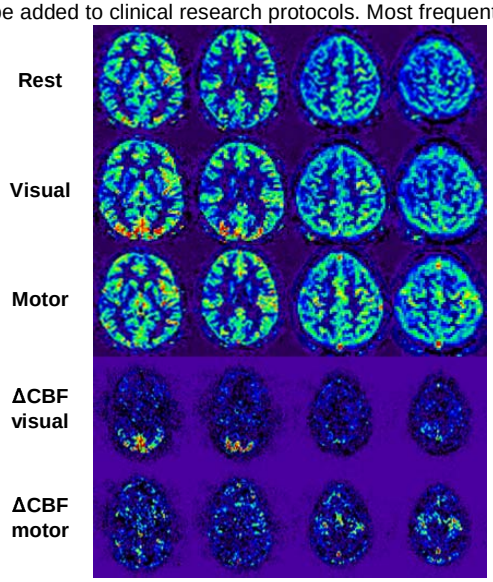

Fig.1: Examples of CBF and ΔCBF-maps of a single subject.

Results *Figure 1* shows an example of CBF and ΔCBF scans from a single volunteer. *Figure 2* shows both the ΔCBF-ground truth and the t-test-ground truth in the three tasks performed. Furthermore, this figure shows the outcome of the group analysis when using normalization towards the PET or T1 template and with or without dividing by the averaged whole brain perfusion. Finally, *Table 1* shows the maximum difference in CBF and mean t-values as measured in the visual/motor cortex, and the correlation with the ΔCBF and t-test-ground truth.

Discussion and Conclusions: As can be observed in Figure 2, group analysis of ASL data can be used to identify changes in perfusion distribution between groups, although the identified regions from the group analysis were smaller than the underlying perfusion changes as evidenced by the ground truth. Registration of the CBF-map to the PET template or registration via the T1 template resulted in comparable results, as can be observed in table 1. Apparently two effects cancel each other out: it is expected that using the CBF-maps with its large gray/white matter contrast for registration, will guarantee maximal overlap of the gyri thereby improving the statistical power, although, some perfusion differences might disappear in the registration process, since the deviating CBF-maps are registered to a PET atlas reflecting normal perfusion. Proportional scaling led only to marginal improvements.

In summary, it can be concluded that ASL can be used for identifying changes in CBF patterns via group analysis, even in relatively small groups of 13 patients versus 13 control subjects. However, it should be noted that the current study employed strong stimuli (leading to 20-40 ml/100ml/min increases in CBF), whereas changes are frequently more subtle in patients.

References: 1. Wolf RL Neurotherapeutics (2007) 2. Ashburner J Neuroimage 11: 2000. 3. Chalela JA Stroke 31: 2000.4. Golay X et al. MRM (2005).

Table 1: Maximum difference in CBF during task, maximum T-value in a ROI comprising the visual cortex or the motor cortex and correlation of the activation-map with both ground truths.

	Checkerboard				Motor				Cartoon			
	max ΔCBF (ml/100ml/100g)	mean t-value	R (ΔCBF)	R (tmap)	max ΔCBF (ml/100ml/100g)	mean t-value	R (ΔCBF)	R (ttest)	max ΔCBF (ml/100ml/100g)	mean t-value	R (ΔCBF)	R (ttest)
Normalised to PET-template	39.4	1.57	0.51	0.51	27.5	2.16	0.4	0.41	26.4	1.25	0.41	0.4
normalised to PET-template / mean CBF	-	1.98	0.47	0.44	-	2.61	0.47	0.46	-	1.58	0.46	0.44
Normalised to T1	38.5	3.14	0.4	0.36	27.8	1.27	0.43	0.42	26.5	1.39	0.47	0.45
Normalised to T1 / mean CBF	-	3.04	0.43	0.4	-	1.68	0.47	0.46	-	2.02	0.51	0.49

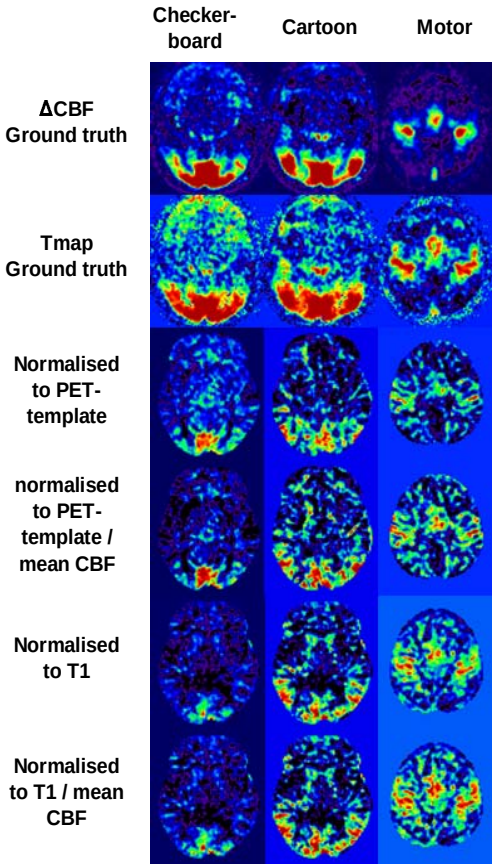

Fig.2: First two rows: ΔCBF-ground truth and t-map-ground truth. Lower 4 rows; results of group analysis showing comparable patterns, although more confined.