Improving the Quantification of Cerebral Blood Flow for the Assessment of Alzheimer's Risks

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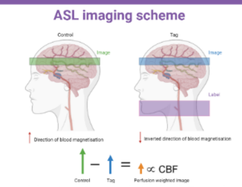
Abstract

Motivation: There is an urgent clinical need to improve patient outcomes for those suffering from terminal neurodegenerative diseases such as Alzheimer's disease. Better understanding is needed of the cerebral pathophysiology underpinning such conditions so that earlier diagnosis and appropriate interventions are possible, and one such avenue is through the study of cerebral blood flow (CBF) changes with the onset of these diseases [1]. Arterial Spin Labelling (ASL) is a promising measurement technique that has not been adopted clinically due to limited understanding on how certain imaging parameters affect CBF quantification between subjects. One such limitation may be the inversion efficiency of ASL, which is theorised to be greatly affected by the blood flow velocity in the internal carotid artery (ICA) for a subject [2]. The inversion efficiency quantifies the percentage of blood that has been 'labelled' by the ASL scheme and imaged as it enters the brain. Methods for assessing vascular health through CBF involve imposing a stimulus, such as increased carbon dioxide inhalation, to then measure a CBF ratio between the absolute CBF in the resting state and the stimulus state.

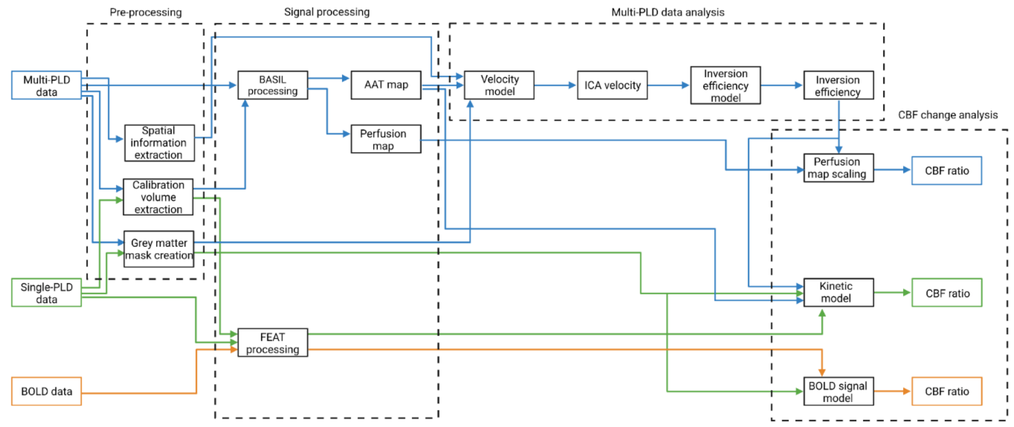
Objective: This work aims to improve the quantification of cerebral blood flow with the pseudo-continuous Arterial Spin Labelling (ASL) imaging technique, through data analysis carried out on a subject set. The primary aim is to develop a procedure to estimate the ICA velocity to act as an input into a model relating the ICA velocity to the inversion efficiency. This could then be incorporated into CBF analysis to calculate a corrected CBF ratio.

Data Acquisition



- The subject set consisted of 5 males, 5 females with age 20 ± 1 years.
- ASL imaging was carried out on this subject set for two conditions: in a resting state when breathing air, and in a hypercapnic state through breathing air with an elevated carbon dioxide concentration.
- Two ASL data types known as multi-PLD and single-PLD data were acquired. Another imaging technique called BOLD was also carried out (to be used for verification processes for the CBF measurements).

Overall process



Process flow diagram outlining the three data sets used and the analysis carried out to produce CBF measurements.

Multi-PLD data

This was used to develop a modelling tool that is able to improve the CBF quantification from both single-PLD and multi-PLD data.

Single-PLD data

This was used to verify the CBF improvement after incorporating the inversion efficiency derived in multi-PLD data analysis into CBF estimation.

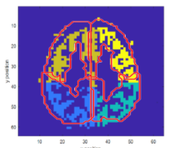
BOLD data

This data set does not have a CBF quantification based on inversion efficiency so can be used as an external verification to determine whether the CBF outputs align well.

Model development and preliminary results

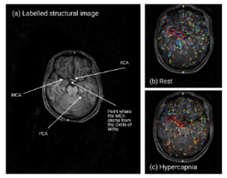
Vascular region segmentation

It was theorised that the route of the blood flow may be most accurately described by segmenting the brain into regions fed by the same artery and taking the average path to each of these segments using 3D geometry. This was confirmed by implementing an algorithm that clustered the arterial arrival time (AAT) maps by similarity, which coincided almost exactly with the red vascular region boundaries shown in the diagram.



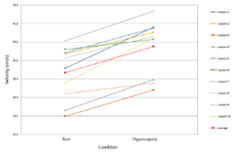
Macro-vascular AAT maps

It was possible to obtain an AAT map for larger vessels that exist in the brain, which include the larger arteries that were desirable to use for modelling purposes. The most promising region was shown to consistently be the right hand side middle carotid artery (MCA), as this structure was able to be identified through voxels in the macro-vascular AAT map for all subjects. As such, the AAT information in the highlighted voxels were used in subsequent analysis.



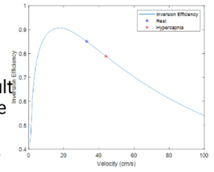
Exponential model and velocity fit

In order to derive the ICA velocity, an exponential model was fitted between an origin and a chosen region of interest and the gradient gave an indication of the velocity at the origin. The two points were the MCA as the origin and the MCA-fed region as the region of interest. Index values were then used to relate the MCA velocity to the ICA velocity. The velocity results shown indicated a consistent increase for the hypercapnic condition, which was expected due to vasodilation effects.



From velocity to inversion efficiency

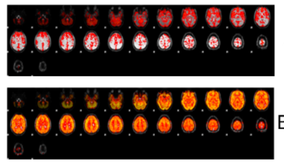
A pre-existing model was used which was developed from a pulse sequence to infer the inversion efficiency as a function of ICA velocity. This gave inversion efficiencies that were consistently lower for the hypercapnic condition as the velocities all fell within the monotonically decreasing part of the curve. This result is shown for one subject but is reflective of the trend shown by all subjects in the data set. Lower inversion efficiencies for the hypercapnic state means that the increase in CBF would have been underestimated compared to the resting state.



Results

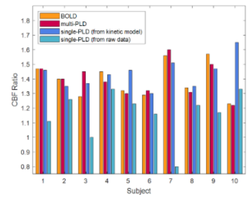
Signal processing

Signal processing was carried out for the single-PLD ASL and BOLD data through a software called FEAT. The following maps were the contrast outputs showing the activated voxels from the stimulus. The quantification of the voxel-wise contrasts could then be used in subsequent analysis to extract the CBF ratios.



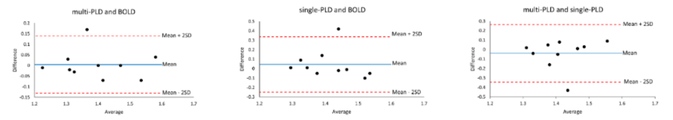
CBF quantification

The CBF ratios calculated by CBF(air)/CBF(hypercapnia) were then able to be extracted from each data set. With the exception of one subject, the values seemed to be similar, but further statistical analysis was required to quantify their alignment.



Bland Altman analysis

The Bland-Altman test assesses the strength of agreement between two techniques in their measurement of the same variable, rather than their correlation, using a graphical based method [3]. Given that 90% of the data points fell within the lines of agreement for this test carried out on each pair of techniques, this indicated that they all align well with little to no bias existing between them. Hence, this suggested that the CBF quantification had been improved for the ASL techniques through the determination of the inversion efficiency.



Conclusion

Key Findings

This work aimed and succeeded in the development of a tool that improved the quantification of CBF in ASL imaging through identifying a revised inversion efficiency to be used in CBF analysis. It has been shown that it is possible to derive bespoke patient-specific and condition-specific inversion efficiencies for such a purpose. An additional result that was notable, although beyond the scope of the aims of this report, was the apparent ability to segment the brain into vascular regions via a clustering algorithm applied to the AAT maps. This could provide a simple, patient-specific segmentation method for cerebral vascular regions to aid the understanding of neurodegenerative disease.

Clinical impact

These insights give scope for the ASL imaging technique to be translated into a clinical setting to determine the presence and severity of conditions such as Alzheimer's in a vulnerable patient set through CBF quantification. Furthermore, this work has also presented a means to identify different inversion efficiencies for vascular regions and hence enabled a more accurate CBF assessment of different cerebral territories. This is critical for diseases such as Alzheimer's where understanding the localisation of the degeneration may significantly improve patient outcomes.

Future work

The main limitation of this work was the unknown robustness of the velocity derivation and the suitability of the assumed physiological parameters within the modelling due to lack of experimental data. Further work would need to collect experimental data on a more varied demographic of subjects. This would be able to indicate the suitability of the velocity derivation model for this application and provide sufficient measurements to facilitate a more complex model to be developed if required. This would also ensure physiological parameters used were translatable to a wider population of subjects.

Acknowledgements

I am incredibly grateful to my supervisor Professor Daniel Bulte and Joana Pinto for their incredible support throughout this project. The results derived from this project would also not have been possible without building upon the great work undertaken by Thomas Okell in his doctoral thesis.

References

[1] Michael Malek-ahmadi et al. "Cerebral blood flow in Alzheimer's disease"
[2] Sina Aslan et al. "Estimation of labeling efficiency in pCASL"
[3] Jllakovac Vesna. "Understanding Bland Altman Analysis"

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