ASAP: Automatic Software for ASL Processing

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Target audience: Physicians, psychologists, radiologists and MR researchers.

Purpose: The availability of ASL as a routine method for assessment of basal CBF data has provided the possibility to examine brain physiology and generate a marker to probe functional differences between groups. Currently, there are no commercial packages for processing ASL data, so ASL methodologies have evolved independently[1]. Therefore, apart from a handful of packages[2,3] for academic use, there is no recognised standard for normalising ASL data to a common frame of reference. This lack of a harmonised processing pipeline contributes to the potential discrepancies in studies of brain perfusion across different laboratories[4]. In this work, we describe an Automatic Software for ASL Processing (ASAP) that can automatically process several ASL datasets, from their raw image format to a spatially normalised, smoothed (if desired) version, with minimal user intervention and resulting in data ready for second level statistical analysis. The data can be written in a variety of formats to facilitate its inclusion in several software packages for group analysis.

Methods: ASAP has been developed in MATLAB with the goal of simplifying the process of quantifying and pre-processing ASL studies. Processing functions from both SPM-8[5] library and FSL[6] software have been incorporated, which are two of the most widely available image processing platforms for MRI. These are invoked by the toolbox and are transparent to the user. Different processing strategies have been made available depending on user requirements:

1. **CBF quantification** for pCASL sequences according to the formula found in the recent ASL white paper[7].
2. **Reorient** structural and ASL images. This is recommendable for better performance of the following steps.
3. **Rough skull-stripping** of the ASL maps using a conservative threshold. This step is useful for noisy ASL maps for better co-registration with the structural scan.
4. **Estimation of the brain mask** from the structural volume. The brain mask is needed for excluding out-of-brain voxels that are often founded in ASL image.
5. **Co-registration** between ASL and structural images, T1-weighted (T1w) or T2-weighted (T2w), so they can be later normalized to the MNI space, or any other standard space, for group analysis. When direct co-registration of ASL and structural images is not possible, the proton density image can be used as reference for co-registration.
6. **Partial Volume Effect (PVE) Correction** of the ASL maps using the two methods available[8,9].
7. **Skull-stripping** of the ASL data using the brain mask previously calculated for excluding extra-cranial voxels.
8. **Spatial normalization** of the structural scan and co-registered and skull-stripped CBF maps to the MNI space.
9. **Smoothing** of the final CBF maps. The SPM8 Gaussian smoothing kernel is applied to the final ASL maps.
10. **Get perfusion measures** (mean and standard deviation) from the cortical and subcortical brain structures obtained using the software FreeSurfer[10] (when they are available).

Results: ASAP is an open-source package developed for fully automated processing of ASL data. It provides a user friendly Graphical User Interface (GUI) (Figure 1) where users can perform several interactions with the embedded functions. In addition, the advanced mode includes: (1) a "Load batch files" where a large number of ASL data can be loaded for subsequent processing to avoid having to select the input data individually through the GUI and (2) the "ROI Statistics" GUI that offers the option to extract CBF values from anatomically or functionally defined Regions of Interest (ROI). This facility can simultaneously extract mean, median and maximum values from several ROIs in several CBF maps. Examples of ASAP processing results are: Figure 2 shows the axial, coronal and sagittal planes of a PVE corrected CBF map in grey matter using the linear regression method proposed by Asllani[6] with a regression-kernel of size 5x5x1voxels, Figure 3 shows the sagittal, coronal and axial planes of a normalised and skull-stripped CBF map (first and third row). The CBF in the first row was calculated using a T1w scan (second row) as reference and SPM-8 routines, while CBF in the third row was obtained using a T2w scan (fourth row) as reference and FSL software functions. Equivalent CBF maps were obtained with both pipelines. Finally, Table 1 shows the perfusion measures in the subcortical brain structures obtained using the FreeSurfer software for both, left and right hippocampus.

Conclusions: The key advantage of ASAP is that it automates all the processing steps of ASL datasets for any number of subjects. Working with reduced user input minimises the possibility of random and systematic errors. ASAP can produce perfusion data that is ready for statistical group analysis. Besides, it has a very friendly and easy to use GUI, allowing users to select the preferred options for each case. Depending on the datasets, users may change the options of some processing steps to optimize the processing quality. Whilst some existing processing toolboxes require a degree of customised scripting; ASAP is graphically driven and requires no prior programming skills. In summary, ASAP provides a simple, flexible and reliable solution for ASL-related studies with an extendable design to include processing steps of the best practice at the moment. The ASAP manual and software can be obtained at **sites.google.com/site/asltoolbox/**. We welcome user feedback and hope for rich participation from the ASL community.

Figure 1. ASAP GUI

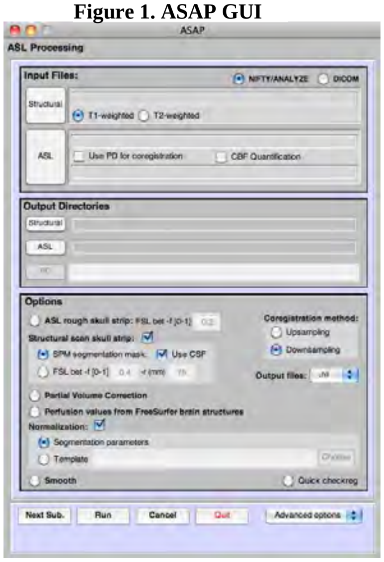

Figure 2. PVE corrected CBF map

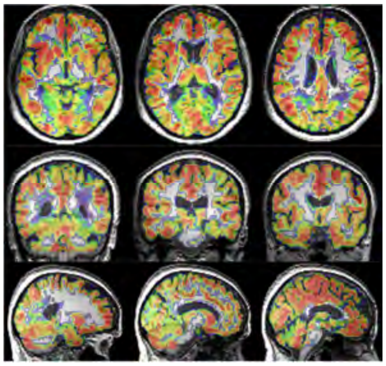

Figure 3. Normalised CBF map using the T1w and the T2w images as reference

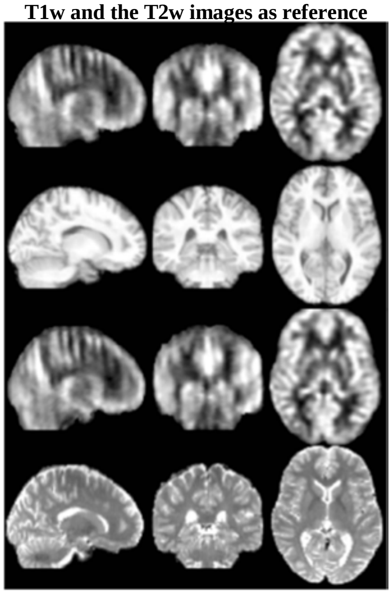

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Table 1.Perfusion values in subcortical areas

	Perfusion [ml/100g/min]	
	Left Hemisphere	Right Hemisphere
	Mean ± SD	Mean ± SD
Thalamus	46.28 ± 8.5	43.36 ± 10.0
Caudate	32.68 ± 6.8	31.18 ± 6.3
Putamen	38.05 ± 4.9	34.80 ± 5.5
Pallidum	38.98 ± 15.2	36.52 ± 8.7
Hippocampus	42.08 ± 7.7	35.50 ± 5.2
Amygdala	36.44 ± 6.3	32.24 ± 7.2
choroid-plexus	48.06 ± 12.8	44.90 ± 12.7

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