MRI-derived Arterial Input Functions for PET Kinetic Modelling in Rats

Eleanor Evans[a], Stephen J. Sawiak[a,b], T. Adrian Carpenter[a]
[a]Wolfson Brain Imaging Centre, Addenbrooke's Hospital, University of Cambridge, Cambridge, UK
[b]Behavioural and Clinical Neuroscience Institute, University of Cambridge, Cambridge, UK

1. Introduction

The development of combined Positron Emission Tomography and Magnetic Resonance Imaging (PET/MR) has been driven by the need for high temporal and spatial resolution MRI imaging to enhance the quantitative and specific molecular imaging data given by PET. In combined PET/MR, the concentration-time curve of a gadolinium-based MR contrast agent can be measured and converted into a PET tracer activity-time curve or arterial input function (AIF), as confirmed by Poulin et al. [1]. The Poulin et al. AIFs were fitted to the Wedeking bi-exponential model and were found to diverge in the long decay phase. The AIFs could, however, be interchanged if the correct conversion factors were determined empirically for the patient group [1]. The gold standard method for AIF determination is blood sampling, though this is highly invasive and prohibitive in small animal studies. Although it is difficult to obtain accurate AIFs by image-based methods in PET due to its restricted spatial and temporal resolution [2], Echo Planar Imaging (EPI) sequences can be used to determine the first pass bolus AIFs of contrast agents in Dynamic Susceptibility Contrast (DSC)-MRI. Within the first pass bolus regime (typically 30s, depending on injection rate) there is less variation between modalities than at longer time points and therefore the conversion between MRI AIFs into PET tracer AIFs should be more accurate.

Detecting blood vessels is difficult on high temporal resolution EPI due to low SNR, and therefore manually selecting arterial voxels to determine the AIF is vulnerable to human error and low reproducibility. Automatic AIF determination algorithms have been developed to solve this problem [3] and an application of one such algorithm is presented here.

2. Materials and Methods

Arterial Voxel Detection Data were collected to assess whether voxels covering major vessels could be automatically detected. DSC-MRI datasets of five spontaneously hypertensive (SHR) rats were acquired using a 4.7T Bruker Biospin 47/40 Scanner. Rapid EPI (TR/TE 250/9ms, spatial resolution 320×390μm^2, 5 slices, thickness 1.5mm, 150 images per slice at 250ms intervals) was performed during bolus injection through the femoral vein of 0.5mmol/kg Gadovist (Gd-BT-D03A) 5s after the start of the scans. ΔR2* measurements (proportional to the concentration of contrast agent) were taken from the EPI images to determine the first pass bolus AIF. Broad ROIs encompassing the Middle Cerebral Artery (MCA) and Superior Sagittal Sinus (SSS) were manually selected as good candidate voxels after consultation with the literature [3-4]. Voxels were selected by a progressive inclusion scheme adapted from work by Singh et al. and Bleeker et al. [5-6]. Criteria describing known AIF characteristics were ranked and applied to a selection of data around the artery of interest using empirically determined thresholds. These criteria were: short rise time (maximum value of signal within 5s time window centred on observed bolus arrival: <3s from steady state to maximum value), high peak height (top 10% survive), low first moment (lowest 50% survive) and low bolus peak FWHM (lowest 50% survive). The manual ROI selection was a delineation of a chosen blood vessel, illustrated in Figure 1.

INSERT FIGURE 1

Quantification To provide a quantitative measure of contrast agent, T1 values in an aqueous phantom of known Gd concentrations (0, 0.14, 0.28, 0.42, 0.56, 0.7, 0.84mM) were measured. A set of 3D FLASH images were acquired at 4.7T and 20°C (TR/TE 10/4.51ms, matrix 128×128×128, spatial resolution 600×600×600μm^3, 15 flip angles [2, 4, 5, 6, 7, 8, 10, 12, 15, 18, 20 , 25, 30, 40, 60]°, total acquisition time 20 minutes 16s) and an IR-RARE technique (TR/TE 20000/10ms, matrix 256×256, spatial resolution 300×300μm^3, TI [16 values 100-3000ms], RARE factor 4) was performed under the same conditions to assess the accuracy of the T1 measurement. Relaxivity (r1) values were determined by a linear regression of the change in relaxation rate against Gd concentration.

3. Results

Arterial voxel detection The automatic voxel selection method provided AIFs with more consistent peak heights and curve shapes, in addition to uniform bolus arrival times. The resulting population (mean) AIF for the rat cohort had a larger peak height in the case of automatic selection as a result. The comparison between AIFs generated by the different selection methods for the MCA is shown in Figure 2, with matched peak positions used for comparison across subjects. Bolus Arrival Times (BATs) were 3.50-3.75s for automatic selection, whereas manual BATs were spread between 3.00-4.75s. Gamma variate fits were successfully performed on the individual AIFs, proving the viability of the technique for determining perfusion parameters [6]. Only rat 4 had a superior manual AIF, giving the largest peak height and a clearly defined recirculation peak. This indicates that the algorithm excluded viable voxels in this case, and improvements are required. Angiography data obtained using Time Of Flight (TOF) MRI sequences which are bright in areas of high blood flow will be used in future work to guide the automatic selection algorithm in manually selected ROIs.

INSERT FIGURE 2

Quantification r1 was determined as 4.6 ± 0.2 mMs^{-1} from the phantom T1 map using the FLASH images and 4.6 ± 0.1 mMs^{-1} using the IR-RARE images. These values are in good agreement with the literature [7-8] and suggest that Gd concentrations can be obtained in FLASH images with an accuracy of ~1.5%. We plan to develop this by repeating the experiment with intravenous co-injection of ^{18}F-FDG and Gd-DTPA, determining the concentration of Gd-DTPA via T1 mapping at high temporal resolution.

4. Conclusions

AIFs determined from our automatic algorithm are consistent between animals and compare well with manual methods without any need for *a priori* voxel selection. The VFA FLASH sequence was confirmed to provide accurate measurement of aqueous Gd concentration in a phantom study with an acceptable acquisition time of 1 minute 22s per flip angle. Both the DSC-MRI and T1 mapping protocols tested will be compared to AIFs obtained by blood sampling for an estimation of overall accuracy

5. References

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Figure Captions

Figure 1: Dynamic EPI image during peak concentration of first pass bolus, showing manual segmentation of ROI in blue with automatically selected voxels in orange.

Figure 2: Image derived AIFs in 5 rats, from top: manual selection, automatic selection and population (mean AIFs).