DSC-MRI: How accurate does the arterial input function need to be in practice?

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Introduction

Dynamic susceptibility contrast (DSC) MRI is the most commonly used MR technique to assess perfusion in clinical studies. Cerebral blood flow (CBF) quantification requires measurement of the arterial input function (AIF), and its deconvolution from the concentration time curve [1]. Several approaches to measuring the AIF (either manually or automatically) have been proposed (e.g. [2,3]), and the effect of errors in the AIF (e.g. due to partial volume effect [4] or bolus dispersion [5]) has been assessed. In this study we aim to investigate (a) the accuracy with which, *in practice*, the AIF needs to be measured; and (b) which aspects of the shape of the AIF have the greatest influence on the accuracy of perfusion quantification. In this context, it is important to note that, even for a perfect AIF, the deconvolution analysis itself will introduce errors to CBF quantification (due to its regularization nature); how accurate does the AIF need to be therefore, in order that the concomitant error in CBF remains similar to that resulting from regularization alone? The study was performed using numerical simulations, where the exact solution is known.

Methods

Perfusion data (corresponding to TR=1s) were simulated using standard methods [1,5]: the AIF was modeled as a gamma-variate function, and the residue function R(t) as an exponential function. The concentration time curves C(t) were then calculated for a range of tissue types. Gaussian noise was added to the converted signal intensity data to generate typical *in vivo* SNR levels (defined as the ratio of the baseline to its standard deviation): SNR_{tissue}=50 and SNR_{AIF}=200 (Note: SNR_{AIF} is higher since the AIF is usually calculated by averaging a number of voxels). To determine the required accuracy of AIF estimation, 10 *distorted* AIF (AIF_{dist}) were generated (see Fig.1), each of them created by modifying certain aspects of the true AIF shape (e.g. keeping the same width but with an earlier peak, or with a faster initial rise and a slower decreasing tail, etc); the degree of distortion was chosen to produce approximately the same absolute area of the difference between each curve and the true AIF. The AIF_{dist} and true AIF curves were normalized to the same area. Each of these AIF_{dist} curves was used to deconvolve the simulated C(t) curves, and their corresponding CBF values were estimated from the maximum of the deconvolved impulse response function [1]. Deconvolution was performed using the iterative ML-EM algorithm [6], with the number of iterations chosen to minimize the area between the calculated impulse response and the true simulated impulse response function. The analysis was repeated for 100 different noise repeats, and the median CBF (and 25/75 percentiles) calculated for each set (Note: the median was used since deconvolution can lead to outliers). For each tissue type simulated, an AIF_{dist} curve was considered acceptable when it led to a median CBF error ≤ the maximum absolute error of the 25/75 percentile of the CBF measured using the true AIF. To assess the effect when only *relative CBF* (CBF_{rel}) measures are sought, the calculated CBF for each tissue type was quantified as a ratio to the calculated value for the normal grey matter case (CBF=60ml/100g/min, MTT=4sec [5]); this was performed separately for each AIF. For this case, an AIF_{dist} curve was deemed acceptable when, for all tissue types simulated, it led to a median CBF_{rel} error ≤ the maximum absolute error of the 25/75 percentile error of the CBF_{rel} measured using the true AIF.

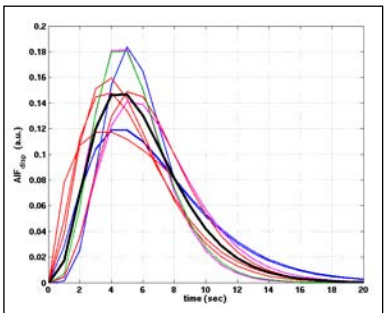

Fig. 1: True AIF (thick line) and 10 simulated distorted AIF, AIF_{dist} (thin lines). Blue: acceptable for absolute CBF quantification; magenta: acceptable for relative CBF; green: acceptable for both absolute and relative CBF; red: unacceptable for CBF quantification.

Results

The table shows the results (for CBV=4ml/100g and variable CBF) of using the various AIF_{dist} as approximations to the true AIF. The grey cells indicate the cases where CBF quantification was acceptable. From the 10 curves simulated, only 4 were acceptable for all the tissue types considered (see blue and green curves in Fig.1). By assessing the relative effects of the various distortions that were simulated, the initial slope of the AIF_{dist} was found to be the major contribution (when compared to the peak height, the width, and the tail of the curves) to errors in CBF quantification (data not shown).

When quantification of *relative* CBF is sought, only 3 of the AIF_{dist} curves were acceptable (numbers 3, 5 and 8; magenta and green curves in Fig.1). Figure 2 shows the relative CBF errors (compared with the true values) for one of the acceptable AIF_{dist} (No.5, blue line) and for an inadequate AIF_{dist} (No.6, red line); for comparison, the corresponding values for the true AIF case are also plotted (black dashed line).

	True CBF (ml/100g/min)							
AIF_{dist}	10	20	30	40	50	60	70	80
1								
2		✓		✓	✓	✓	✓	✓
3		✓	✓	✓	✓	✓	✓	✓
4	✓	✓	✓	✓	✓	✓	✓	✓
5								
6								
7	✓	✓	✓	✓	✓	✓	✓	✓
8	✓	✓	✓	✓	✓	✓	✓	✓
9	✓	✓	✓	✓	✓	✓	✓	✓
10								

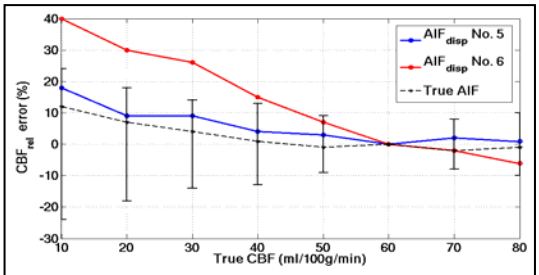

Fig. 2: Error in relative CBF. As shown by the blue line, the AIF_{dist} No. 5 is an acceptable AIF: it introduces an error < the maximum absolute errors (Note that error bars are symmetric around 0% error) of the CBF_{rel} measured using the true AIF (black dashed line). Normal grey matter corresponds to CBF=60ml/100g/min.

Discussion

The results from this study showed that, in practical situations, some specific inaccuracies in the AIF can be tolerated when quantifying CBF. It was found that even relatively large distortions to the AIF shape (e.g. blue lines in Fig. 1) do not always lead to CBF errors larger than those seen with the true AIF. However, it is important to note that this is the case for certain type of distortions. For example, to avoid introducing larger errors, the slope of the distorted AIF must not have a steeper slope than the true AIF: a steeper slope (e.g. for AIF_{dist} Nos. 1 and 10) would lead to CBF underestimation, which combined with the regularization effect of the deconvolution process would further underestimate CBF, leading to very large errors. Interestingly, the AIF_{dist} curves acceptable for *absolute* quantification were not, in general, suitable for *relative* CBF measurements; in fact, even a distorted curve that was completely unacceptable for absolute quantification (AIF_{dist} No. 5, which introduced severe underestimation for all tissue types), led to adequate errors for CBF_{rel} (see blue line in Fig. 2).

An interesting outcome of these findings is that they could be used in designing criteria for algorithms to define an AIF automatically (e.g. by setting more emphasis on the slope than on the width and height when identifying peaks) [2,3].

References: [1] Østergaard L et al, MRM 1996;36:715. [2] Mouridsen K et al, MRM 2006;55:524. [3] Duhamel G et al, MRM 2006;55:514. [4] van Osch MJP et al JMRI 2005;22:704. [5] Calamante F et al MRM 2000;44:466. [6] Vonken EPA et al. MRM 1999;41:343.