A comparison of patient-specific carotid arterial input functions in head and neck DCE examinations

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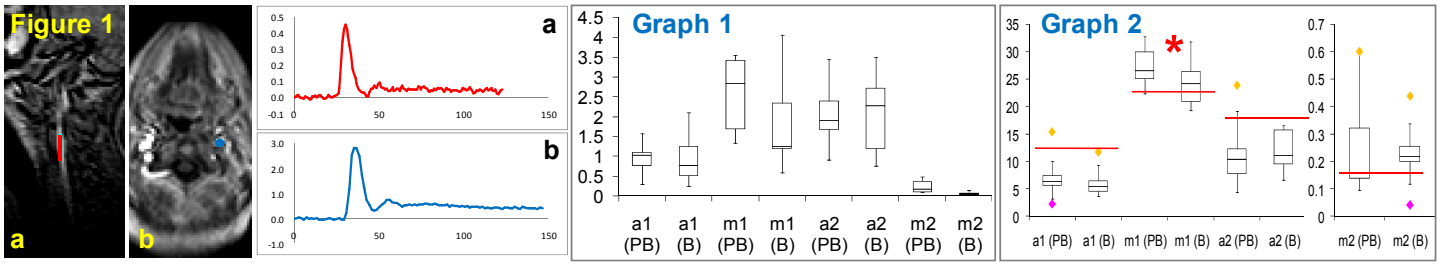
Introduction

Dynamic Contrast-Enhanced (DCE) MRI has proved to be useful in the diagnosis and staging of head and neck carcinoma [1,2]. Reliability of functional parameters depends on the accuracy of DCE modelling approaches, and the Arterial Input Function (AIF) is an important component of the perfusion model. While the use of a population AIF from published data is a common choice to reduce variability, patient-specific AIFs could improve the accuracy of functional parameter estimates[3]. In this work we compare two different approaches to measuring patient-specific AIF: (i) using a pre-bolus (10% of the dose) prior to DCE acquisition and (ii) using a local enhancing vessel present in the DCE examination. Both approaches are compared in a cohort of patients with histologically proven head and neck carcinoma undergoing radical chemoradiotherapy and enrolled in a longitudinal study. Reproducibility of the AIF is assessed in longitudinal measurements and variability of patient-specific AIFs is investigated with reference to a published population-based AIF[4].

Materials and Methods

Clinical Examinations: Nine subjects were scanned after written consent - as approved by the Local Ethics Committee - at the following time points: baseline, following two cycles of induction chemotherapy (Cisplatin and 5-fluorouracil), after 40 Gy of chemoradiation, three and six months post-treatment. Dynamic data were acquired on a 1.5 Tesla Philips Intera scanner following gadolinium injection (0.2 mg/kg), with a transaxial 3D FFE using the following parameters: TR 4.0ms, TE 1.0ms, flip-angle (FA) 20°, 2x2x5mm voxel, 1.5s temporal resolution, 100 timepoints. To enable T1 estimation 20 pre-contrast images were acquired with FA 4°. The pre-bolus measurement used 1/10th of the full dose followed by 20 ml of saline and a sagittal acquisition with similar sequence and parameters: TR 4.0ms, TE 1.8ms, FA 10°, 2.3x2.3x4mm voxel, 0.8s temporal resolution, flow compensation, 150 timepoints, 40 pre-contrast images with FA 2°.

Data Analysis: Data were analysed using the in-house software tool MRIW[5]. Data fitting made use of a cosine modeled function based on 4 parameters[4]: a1 and a2 (first pass [mM min] and washout [mM] amplitude constants respectively), m1 and m2 (first pass and washout rate constants respectively, [min^{-1}]). For pre-bolus data a sagittal slice with a straight portion of carotid was identified on the most-enhanced frame and a ROI of a few pixels (6 to 8) was drawn at the centre of the vessel in order to avoid partial-volume effects. Regions were placed as superior in position as possible to reduce in-flow effects. T1 calculation was adjusted using measurements of T1 of fat in the slice as a reference. To obtain a full-dose AIF the averaged pre-bolus curve was convolved with a rectangular function accounting for the duration of the pre-bolus injection in relation to the full injection. Additionally, to convert from whole-blood to blood plasma concentration, the curve was scaled by 1/(1-Hct), where Hct is the haematocrit fraction, taken as 0.42[5]. To evaluate the AIF on bolus DCE data avoiding partial-volume effects, the brightest pixel of a visible carotid section was extracted in the central slice of the transaxial volume, centered on the primary lesion. T1 calculation was adjusted using fat as reference. The full-dose AIF was directly computed employing the same cosine model and scaled to account for the haematocrit fraction. For both pre-bolus and full dose data, the median of the repeated measurements for each subject was taken to construct patient-specific AIFs. As an index of longitudinal variability, the standard error (SE) was evaluated for each patient-specific AIF and compared in the two groups.



Figures. *Figure 1:* Example of AIF extracted from (a) pre-bolus (b) DCE data in the same patient. *Graph 1,2:* Box plot showing distributions of (Graph 1) standard error and (Graph 2) values of measured AIF parameters, paired by method; (PB) indicates pre-bolus, (B) bolus data; in (Graph 2) red lines indicates the population values from [4] and asterisks indicates statistically significant difference between the two methods.

Results

Using pre-bolus data, it was not always possible to find a region of interest free of pulsatile flow artifacts to measure pre-contrast image intensity accurately. The average over the limited number of pixels could not compensate for the lower signal-to-noise ratio (SNR) due to the reduced contrast agent dose and the decreased FA, and the curves were in general noisy. From the evaluation of the chi-square of residuals from the fit, the quality of the pre-contrast baseline and the presence of pulsatile flow, 16 of 41 curves extracted were considered to have a poor profile. AIFs extracted from DCE data benefit from higher SNR and in most cases it was possible to obtain a clear profile, with a more stable baseline. T1 measurements of fat showed a consistent overestimation of the nominal FA in both acquisitions. In Graph 1 the box plot visualizes the distributions of standard error from repeated measurements across AIF parameters, showing that the ranges are similar for the two methods (in pairs in the graph), with the exception of m2 (washout rate constant), where a clear reduction was observed for full dose data. Graph 2 shows the distributions of measured AIF parameters. Only for m1 (first pass rate constant) the difference between the mean values was statistically significant (paired t-test, $p<0.01$). m1 has also good correlation ($r^2=0.880$) between the two measurements - in general poor ($r^2<0.290$) for the other parameters - but values are consistently lower for DCE data. In Graph 2 red lines represent for each parameter the population values from [4].

Discussion and Conclusions

Pre-bolus data seems less reliable, as more datasets were of poor quality, and may not confer any direct advantage over direct AIF measurement from DCE data. The possibility of extracting the AIF from DCE data is justified by the high temporal resolution of our examination, and the higher SNR is expected to yield more reliable values of a2 and m2. Nevertheless, the significantly higher values found for m1 with pre-bolus data can be attributed to the higher temporal sampling. The intra-patient variability is unlikely to be related to disease progression, and, with the exception of m2, is similar with both methods. However, the correlation between the two measurements is poor. The two methods investigated to estimate AIF are expected to be differently affected by blood velocity, as the flow is through plane in the DCE examination (axial) and in plane in the pre-bolus examination (sagittal); in this sense the agreement of a1 and a2 between the two methods is unexpected. Further work is required to increase the SNR of the pre-bolus examination and to quantify flow effects, for a better understanding of non-steady-state contributions.

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