Preliminary analysis of arterial input function derived from dynamic contrast enhanced MRI in children with cancer

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Introduction: Although dynamic contrast enhanced (DCE) MRI is now widely implemented in adult clinical trials of novel anti-cancer therapeutics, there is little experience within the paediatric cohort. There is a need to assess the feasibility and potential of DCE-MRI in paediatric patients as there is increasing evidence for the value of the technique in providing early therapeutic response assessments. When performing quantitative DCE-MRI data analysis, published population arterial input functions (AIFs) are conventionally used in the analysis. However, due to physiological differences, these population AIFs measured in adults, may not necessarily be appropriate in children. The aim of this study is to investigate the feasibility and challenges of obtaining AIFs from DCE-MRI studies performed in children. We report the initial findings comparing AIFs obtained using a power-injector versus manual injection.

Materials and methods: The study was approved by the local research and ethics committee and patient informed consent was obtained. DCE-MRI was performed twice in seven paediatric patients with extra-cranial tumours (mean age = 11.3 years, range = 6 – 15 years) on a 1.5 T Siemens Avanto scanner with a phased array body coil. Repeat scans were performed within 48 hrs. Coronal 3D-VIBE sequences with the following parameters were employed: TR/TE = 3.0/1.0 ms, 14 partitions, 5 mm thick, matrix size = 256x256 (interpolated), flip angle/NSA = 3°/8 (static) and 16°/1 (dynamic). 80 dynamic images were acquired over 4 mins (temporal resolution = 3 s). A single dose contrast (0.1 mmol/kg) was injected followed by 10 ml of saline either by a power injector through a cannula inserted in the ante-cubital vein (flow rate varied between 1-3 ml/s depending on the size of the cannula) or manually by hand into a Hickman line via a three-way connector tap. Regions-of-interest (ROIs) were drawn along the descending aorta on the central partition. Dynamic signal intensities averaged over the ROI were converted to contrast agent concentrations by calculating dynamic T1 values using the method described previously [1]. An input function model which accounts for re-circulation was fitted to the data [2]. A population-averaged paediatric AIF was constructed by taking the median of the individual AIF parameters. Variations in haematocrit were accounted for in the individual AIFs.

Results and Discussion: In six out of seven patients, it was possible to place the imaging volume so that the central partitions include both the tumour as well as the descending aorta. It was not possible to obtain an AIF from one patient as the tumour was located posterior to the descending aorta and there was no other suitable vessel to use. In three patients, it was necessary to hand inject through the implanted Hickman line to avoid additional invasice procedure, given that peripheral cannulation can be particularly distressing in children. Six power-injected input functions and six hand-injected input functions are shown in figures 1a and b respectively (black = individual concentration curves, red = median curve). To facilitate AIF curve shape comparisons, the AIFs have been normalized by the respective area under the entire AIF curve and onsets have been shifted to match. For display purposes, only the first 2.0 mins of the curves are shown. When a power-injector was employed, consistent vascular enhancements were obtained and significant re-circulation peaks were observed. Large variations in AIFs were observed when hand injection was employed. The inconsistencies are clearly seen in AIFs obtained from a single patient on two separate days (figure 2), where the AIF obtained on day 1 is typical following a bolus whilst that obtained on day 2 is not. AIFs obtained from another patient following manual injection demonstrated a "double-peak" effect on both days, an example is shown in figure 3. This effect is likely to have resulted from the combination of the relatively large volume of contrast injected (10.7 ml) and delay between injecting the contrast agent and saline. On the basis of the above observations, three out of six hand-injected AIFs were not used when constructing the paediatric population AIF. All power-injected AIFs were used. To compare the input function curve shapes between paediatrics and adults, the paediatric population AIF obtained in this study and the adult population AIF published in the literature [3] were normalised as above and displayed in figure 4. The paediatric input function is found to have a sharper first-pass peak and more clearly defined re-circulation peak compared with the adult input function. This is consistent with the relatively high rate of circulation seen in children. The amplitude of the first-pass peak is a highly variable feature and more data is needed to evaluate this further.

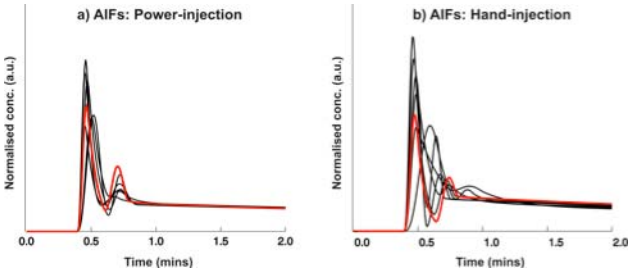

Figure 1: Normalised vascular concentration curves: (a) six obtained using a power-injector and (b) six by manual injection. Black = model-fitted individual curves, red = median curve. Large variations in concentration curves were observed when contrast agent was injected manually rather than via a power-injector.

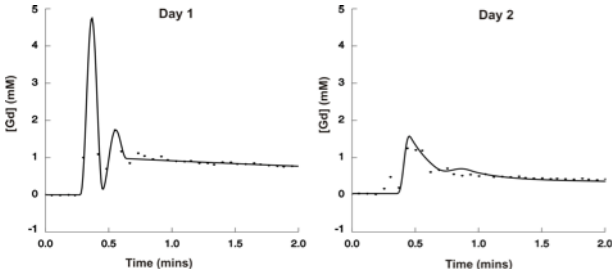

Figure 2: AIFs obtained from one patient on two separate days where contrast agent was injected manually through a Hickman line. Although the AIF obtained on day 1 is typical following a bolus, that obtained on day 2 is not. This example further highlights the inconsistencies of manual contrast injection.

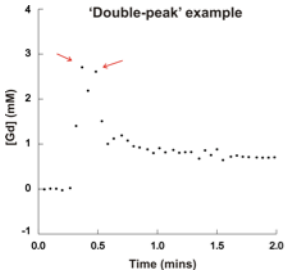

Figure 3: "Double-peak" effect seen in a hand-injected AIF (red arrows) arising from the delay between injecting the contrast agent and the saline.

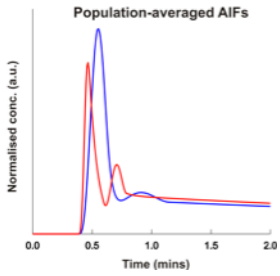

Figure 4: Normalised population vascular concentration curves from paediatrics (red) and adults (blue).

Conclusions: Preliminary analysis of AIFs obtained from paediatric DCE-MRI data havs shown that it is possible to obtain consistent AIFs using a power injector. Inconsistencies in hand-injected AIFs found in this study have highlighted the need to optimize modes of contrast agent delivery through central lines. We are currently investigating the feasibility of implementing power-injector compatible central lines in the clinic. In this continuing study further data will continue to be acquired to build a more representative paediatric population AIF. This input function will be used to perform quantitative DCE-MRI data analyses in early phase paediatric clinical trials of antiangiogenic and other targeted agents for childhood cancers, such as the BEACON-Neuroblastoma trial.

References: [1] Miyazaki K. et al. InProc.ISMRM 2010. 1092, [2] Orton MR. et al. InProcISMRM 2010, 1726, [3] Parker G. et al, MRM. 2006. 56:993-1000.

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