Average Arterial Input Function and Quantitative Dynamic Contrast Enhanced (DCE)-MRI of Nodal Metastases in the Neck

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Introduction: Quantitative analysis of the DCE-MRI data requires knowledge of the time-dependent contrast agent concentration in the arterial blood feeding the tissue of interest (Arterial Input Function [AIF]). The absolute accuracy of the pharmacokinetic parameters K^{trans} (transfer rate constant) and v_e (interstitial fluid space volume fraction) depend on the AIF accuracy. These parameters are clinically relevant and have been used in oncological imaging for tumor detection and to evaluate response to treatment. DCE-MRI has become a useful tool also in evaluating head and neck cancers, differentiating tumor from non-tumor in the cervical lymph nodes, lymphoma vs squamous cell carcinoma, and prediction of response (1-5). The need for reliable measurements of pharmacokinetic parameters has been the impetus for measurement of AIFs in the carotid artery in head and neck cancer patients (1-2). In a recent study in cancer (6) has indicated that the use of a high-temporal-resolution population-based AIF allowed assessment of detailed physiological information with a good degree of precision even when individual AIF (Ind-AIF) measurement was not possible. In the present study, we determined the feasibility of using an average AIF (Avg-AIF) for pharmacokinetic modeling of DCE-MRI data from patients with nodal metastases in the neck. Potentially, such Avg-AIF can be used in clinical trials to examine the effects of drugs on K^{trans} and v_e or in situations where Ind-AIF cannot be obtained.

Materials and Methods: Tumor perfusion was assessed in 9 patients with nodal metastases in the neck using DCE-MRI prior to chemo-radiation therapy. Perfusion data were acquired on a 1.5 Tesla G.E. MRI scanner (GE, Milwaukee, WI). The study consisted of MR imaging using a neuro vascular phased array coil. Antecubital vein catheters delivered a bolus of 0.1mmol/kg gadodiamide (Omniscan) at 2 ml/sec, followed by saline flush. Dynamic perfusion studies were acquired on the nodes using a 2D-fast multi-phase spoiled gradient echo (FMSPGR) sequence with acquisition parameters: TR=9ms, TE=2ms, flip angle=30°, FOV=18-20, Time course data points=40-80 that provided a temporal resolution between 3.75-7.5 sec/image which was sufficient to observe the initial uptake of contrast agent into the region. In order to calculate the longitudinal relaxation rate constant, R_1, for each DCE-MRI data point, proton density images were acquired prior to DCE-MRI using the same pulse sequence and similar parameters as DCE-MRI except TR=350ms. Data were exported to a Windows PC and the pharmacokinetic analysis was done using in-house software written to display and analyze data using IDL windows version 6.0 (Research Systems, Boulder, CO, USA) based on the Toft's model (7). For the tumor tissue time course data, a ROI (region of interest) was manually drawn by an experienced neuro-radiologist outlining the contrast enhanced tumor for signal intensity measurements. All the slices containing the tumor were outlined and analyzed. In all patients studied, the carotid artery was visible in most of the image slices but to minimize partial volume effects the appropriate image slice was chosen that contained the central portion of the artery. A region of interest (ROI) was placed within the carotid artery (Figure 1a) and this allowed the direct measurement of the AIF by monitoring the signal intensity time course which was then converted into contrast agent plasma concentration time course (Figure 1b). The wash out phase of the AIF was fitted with a biexponential decay function. Avg-AIF was obtained by simple averaging of the Ind-AIFs, aligning the peak height of each Ind-AIF. Quantitative DCE-MRI analyses of the tumor tissue time course data was done in all the patients for the ROI, as well as each pixel within the ROI using histogram analyses. The latter analyses calculated the pixel K^{trans} and v_e and the median values of these parameters. Additionally to evaluate the hypothesis that an AIF from the feeding artery is more accurate than using another artery in the body for the analysis, ROI K^{trans} from the patients with nodal disease were calculated using Avg-AIF from carotid artery as well as using Avg-AIF from the femoral artery of the lower extremity sarcoma patients. Student paired t test was used to evaluate differences in pharmacokinetic parameters resulted from the use of Ind-AIFs and Avg-AIFs.

AIF	Ind-AIF*	Avg-AIF*	p value
ROI K^{trans} min^{-1}	0.68±0.72	0.44±0.20	0.36
Histogram Median K^{trans} min^{-1}	0.68±0.68	0.44±0.20	0.35
ROI v_e	0.46±0.25	0.42±0.18	0.69
Histogram Median v_e	0.40±0.19	0.38±0.15	0.78

Table 1. DCE-MRI parameters K^{trans} And v_e calculated from Ind-AIF and Avg-AIF. * Mean ±SD

Results and Discussion: Scatter plots show the tumor K^{trans} calculated with both Ind-AIFs and the Avg-AIFs for the 9 patient's using both ROI (Figure 2a) and histogram median methods (Figure 2b). The straight lines connect the data points from the same patient. There were no statistically significant differences between K^{trans} values derived with Ind-AIFs and those derived with the Avg-AIF ($p = 0.36$ for ROI K^{trans} and 0.35 for histogram median K^{trans}; paired t test) [Table 1]. There were also no statistically significant differences between v_e values derived with Ind-AIFs and those derived with the Avg-AIF ($p = 0.69$ for ROI v_e and 0.78 for histogram median v_e; paired t test) [Table 1]. The use of limited-population-based Avg-AIF for nodal metastasis in the neck seems reasonable to use on a larger population, as it will allow acquisition of higher-spatial-resolution, and thus lower temporal resolution images without requiring evaluation of AIF in individual patient. Additionally, it was observed that the K^{trans} values increased substantially ($P<0.001$) when Avg-AIF from the femoral artery was used instead of the carotid artery (Figure 3). This implicates that Avg-AIF from the adjacent feeding artery should be preferred over AIF obtained from an artery far away from the tumor. Our preliminary results suggest that Avg-AIF obtained in this study may be used in calculating the pharmacokinetic parameters in a larger patient population with nodal metastasis in the neck, e.g. in clinical trials that evaluate the effects of drugs by measuring K^{trans} and v_e.

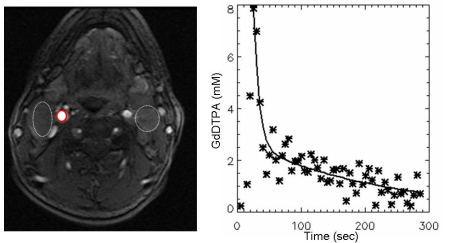

Figure 1a Post contrast MR image from a patient showing bilateral nodal metastasis (dashed white lines) and carotid artery (solid red line), 1b) An AIF plot showing (plasma contrast agent concentration time course). The AIF data points were obtained from the region of interest (ROI) placed within the right carotid artery.

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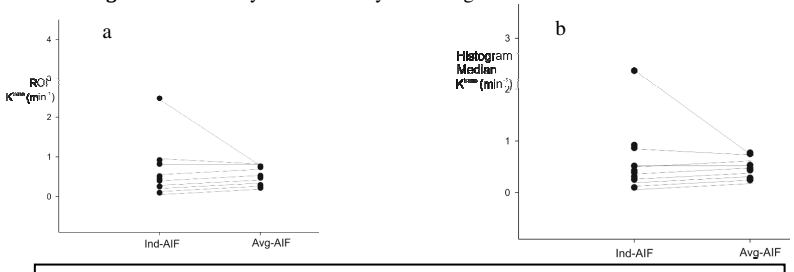

Figure 2. Scatter plots of K^{trans} obtained from DCE-MRI data. Kinetic analysis using Ind-AIF and Avg-AIF: (a) tumor tissue ROI (b) histogram median methods.

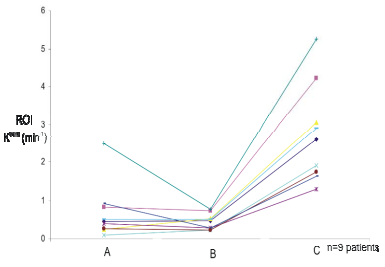

Figure 3. Scatter plots of K^{trans} from tumor tissue ROI from nine patients with nodal metastases; (A) using Ind-AIF from carotid artery (B) using Avg-AIF from carotid artery (C) using Avg-AIF from femoral artery of sarcoma patients.