Reducing Inter-Reader Variability in MRI Perfusion Assessment Through Automated AIF Detection

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Introduction: Dynamic contrast enhanced MRI (dceMRI) has demonstrated considerable utility in both diagnosing and evaluating the progression and response to treatment of malignant tumors. By making use of a two-compartment model, with one compartment representing blood and the other abnormal extra-vascular extra-cellular space (EES), the observed uptake curves in tissue and blood can be used to estimate various physiological parameters [1]. The parameter of primary interest in this work is the volume transfer constant between blood and EES, commonly referred to as K^{trans} [1]. This parameter is related to both blood flow and endothelial permeability-surface area, and is therefore a good endpoint for estimating the blood supply available to a target malignancy. One of the challenges in estimating vascular parameters is identifying an accurate blood uptake curve. The MR signal in arteries is frequently corrupted by flow artifacts, with the result that regions of interest at different points in the same artery or in other nearby vessels can provide grossly different uptake curves (see Fig. 1).

We have developed a method for the identification of an optimized blood signal, described below, which is intended to eliminate this source of measurement variability and thereby increase the sensitivity to change of vascular parameter measurements. The uptake curve generated by this method is shown in red in Fig. 1, along with curves taken from the interior of two large arteries. Note that this curve shows a greater enhancement peak than that of either vessel, a smoother plateau, and a shape more characteristic of a bolus i.v. injection. The primary purpose of this study was to assess the utility of this automated blood identification technique with respect to that of the generally used method of manual blood identification.

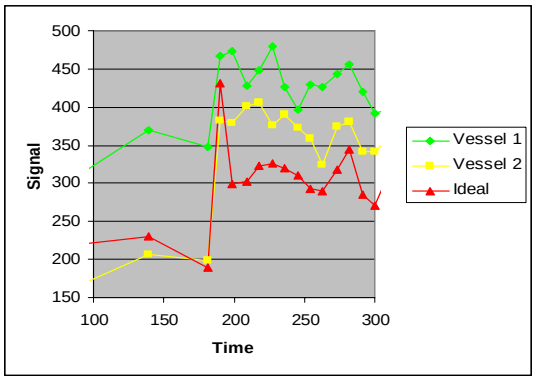

Figure 1: Uptake curves taken from the interior of two large arteries (yellow and green) along with the calculated optimal arterial uptake curve (red) for this data set.

Methods: Tumor margins were identified in this study using Geometrically Constrained Region Growth (GEORG) [2]. Blood region identification was done using manual tracing with a computer mouse. The identified blood region was used for parameter calculation, as described below. In addition, the identified blood region was used to initialize an automated search algorithm whose intent was to identify an optimized blood signal for the data set under consideration. Each voxel in the data set was assigned a score based on time point of maximum uptake, slope at maximum uptake, peak value, and conformance to a gamma-variate curve. The highest scoring twenty-five voxels in the data set were then assigned to the ideal blood region of interest. The intent of this algorithm is similar to that presented by Rijpkema *et al.* in [3]. Our method differs in that it is fully automated. Also, because the Rijpkema method selects most or all arterial voxels, it is vulnerable to the arterial flow artifacts our method is designed to eliminate.

After blood had been identified by either manual or automated means, uptake curves were generated for both tumor and blood. These were designated $Ct(t)$ and $Cp(t)$, respectively. In the interests of noise reduction, both blood and tumor data were fit to gamma-variate curves.

The vascular bed was modeled as a linear system, such that $Ct(t)=Cp(t)*h(t)$, with impulse response $h(t)$ given by $h(t)= K^{trans}\ exp(-k_{ep}\ t)$ where k_{ep} is the rate constant between the EES and blood. Given $Ct(t)$ and $Cp(t)$, K^{trans} and k_{ep} were estimated using a gradient-descent energy minimization scheme. Local minima were avoided through the use of multiple instantiations with different initial parameter settings.

Experimental data were derived from three dogs with naturally occurring mammary tumors. Each animal was imaged three times over a period of 12 weeks. Images for this study were acquired using a GE 1.5T LX/CV scanner. Three slices through each tumor were acquired using a cardiac coil. Perfusion images used a GRE pulse sequence with a repetition time of 20ms, echo time of 1ms, and a flip angle of 40 degrees. Imaging time for each image set was seven seconds, with a two second scanner delay. The reconstruction matrix was 256x192, FOV was 140mm, and slice thickness was 4mm.

Experimental Procedure and Results: The experiments involved in this study were intended to assess the inter-reader reproducibility of perfusion measurements using manual and automated blood identification, and to determine the percentage of measurement variability due to differences in tumor margin and blood region of interest, respectively. Four analysts were trained in the use of the analysis software. Each analyst was asked to identify and delineate both tumor and blood in each of the nine data sets. Once all regions of interest were delineated, K^{trans} values were calculated first using the regions of interest as identified by the analyst, and then using the analyst's tumor identification with the automatically identified blood uptake curve. By comparing the variance seen between analysts using manually identified blood with that seen between analysts using the automatically identified blood, which was identical across analysts, it was possible to isolate variability related to blood signal from that related to differences in tumor margin identification.

Coefficients of variability in measurement of K^{trans} among the four analysts, defined as measurement standard deviation divided by measurement mean, were calculated separately for manual and automatic blood identification, and for each of the nine cases examined. For the nine manual blood identifications, coefficients of variability ranged from 3.1% to 39.2%, with a mean of 20.1% and a median value of 21.5%. For the nine automated blood identifications, coefficients of variability ranged from 3.1% to 11.8%, with a mean of 6.7% and a median value of 6.2%. From this we conclude that roughly 67% of observed measurement variability is due to differences in blood identification, with the remainder resulting from differences in tumor margin identification

Manual blood identification for perfusion parameter calculation is currently standard practice for both clinical and experimental purposes. The results of this study indicate that increased accuracy and sensitivity to change could be achieved by making use of an automated method for blood identification such as the one described here. It should be noted that the difficulty of identifying a suitable blood signal is typically greater in smaller animals such as the dogs used in this study than in humans. This is due to small animals' higher blood velocity, which exaggerates flow artifacts in the arteries, as well as to the lower signal to noise ratio that is achievable when imaging smaller anatomy on a clinical scanner. The values given in this work for parameter variability due to differences in blood identification should be considered an upper limit when estimating likely variability in human studies.

References:

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