ABCDEFGHI: Anatomic Basis Construction for Dynamic Enhancement Following Gadolinium cHelate Injection

D. K. Ragan[1], and J. A. Bankson[1]

[1]Imaging Physics, M. D. Anderson Cancer Center, Houston, TX, United States

Introduction Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) techniques permit the assessment of vascular permeability and blood flow by modeling the uptake of low-molecular weight contrast agent into tissue. Quantification of these parameters depends on measurement of the contrast agent concentrations in both tissue and blood; the latter is known as the arterial input function (AIF). Contrast agent concentrations are calculated indirectly using measurements of signal changes in T_1-weighted gradient echo images and knowledge of the relaxation rate changes introduced by the contrast agent. The time course of the contrast agent concentration in tissue depends not only on the AIF but also on the local perfusion and microvascular permeability. Analysis of the concentration time courses using pharmacokinetic models results in parameters describing the vascular state of the tumor. Precise and reproducible measurement of these parameters is a prerequisite for using DCE-MRI to evaluate the response of the tumor vasculature to therapy[1].

The quality of the AIF measurement has a large effect on the quality of the final pharmacokinetic parameters. Measuring the AIF is generally challenging because it requires both high temporal resolution to image rapid changes in the blood signal and high resolution to avoid partial volume effects in blood vessels. The measurement becomes particularly challenging in small animal models of cancer, because their small blood volumes and rapid heartbeats cause extremely fast kinetics in their arterial input functions. In humans a temporal resolution of one second for the AIF is desired[2]; even faster sampling is required for mice.

In addition, measurement of the AIF must be insensitive to partial volume effects, both in-plane and through plane. Scanning blood vessels at sufficient spatial resolution to avoid these effects unacceptably compromises the temporal resolution of the AIF sampling. However, if measurement of the AIF were to be performed in a large structure, such as the heart, partial volume effects could be avoided. However, this requires the ability to sample quickly enough to avoid errors from cardiac motion. Spending multiple cardiac cycles to fully encode an image of the heart at a single cardiac phase, as in retrospective gating techniques, unacceptably compromises the temporal resolution of the AIF. Sampling of the AIF every heartbeat is the ideal goal, but cannot be achieved with presently existing imaging techniques because only a few phase encode lines can be acquired during the time span of a single murine cardiac phase if tumor imaging is to be interleaved with AIF acquisition.

Even with the recent activity in the development of undersampled image reconstruction techniques, reconstruction of a complete image from a single phase encode line is not possible. However, for measurement of the AIF, fine structural details are not important; the ultimate goal is the signal drawn within a region of interest (ROI) in normal tissue. Tailoring the reconstruction to include the definition of the ROI permits a dramatic reduction in the amount of data required for AIF measurement at each time point.

A novel analysis technique is presented which, in conjunction with a reference image and the identification of ROIs, allows for extremely undersampled measurement of the AIF. This will simultaneously achieve both high temporal resolution sampling of the AIF and enable motion-artifact free imaging of the heart, which will minimize partial volume effects on AIF measurement. This improvement in AIF measurement will directly produce more reliable and reproducible measurement of pharmacokinetic parameters.

Theory Physically, the approximation is made that each tissue in the imaging plane will enhance homogenously. Under this approximation, each tissue can be represented by a pre-contrast reference image and a single scalar contrast scaling factor. The reference image is denoted by I_0 and it partitioned into N separate ROIs. For the ith ROI, define the indicator function χ_i to be 1 inside of the ROI and 0 outside, and also define the contrast scaling factor $k_i(t)$ to be $I(x, y, t)/ I_0(x, y)$, when x,y corresponds to a point within the region of interest. Considering the Radon transform (**R**) of an image at angle θ, it follows that:

$$\begin{aligned} R\left[I(x,y;t)\right] &= R\left[\sum_i \chi_i(x,y) I(x,y;t)\right] \\ &\approx R\left[\sum_i k_i(t)\chi_i(x,y) I_0(x,y)\right] \\ &= \sum_i k_i(t) R\left[\chi_i(x,y) I_0(x,y)\right] \end{aligned}$$

This provides a system of equations relating a projection of the dynamic image to the unknown scaling factors and the segmented reference image. The equations will generally be overdetermined even when only a single acquired projection is used and the contrast scaling factors may be found in the least-squares sense.

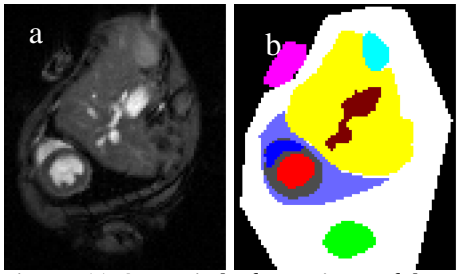

Figure 1 (a) Anatomical reference image of the heart. (b) Segmentation used in the reconstruction

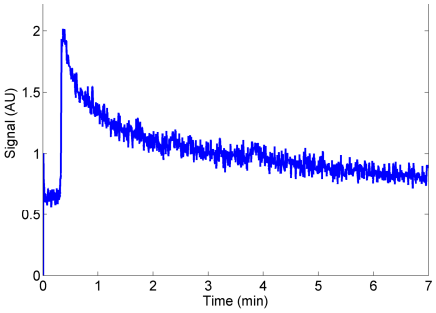

Figure 2 AIF measured in the left ventricle

Methods In vivo data was acquired on a Bruker Biospec 7.0T small animal scanner. For anatomical reference, a retrospectively gated short-axis image of the heart was acquired with TE = 3 ms, TR = 6 ms, matrix size = 128x96, 250 repetitions. The k-space lines were retrospectively sorted using the center of k-space according to cardiac phase and reconstructed into anatomical images of the heart at 18 cardiac phases. The images were manually segmented by tissue type, as shown in Figure 1.

To test the analysis technique for the measurement of the AIF, dynamic images were acquired of a single projection through the heart with no phase encoding and matrix size = 128x1, TE = 1.8, TR = 25, flip angle = 25°, slice thickness = 1 mm, acquisition time = 7 minutes. Three fully encoded (128x96) slices through the brain were acquired interleaved with the AIF measurement. Contrast agent was injected approximately 45 seconds after the start of the scan using a power injector. Flow enhancement from incoming spins was suppressed by using a spoiled-sideband RF pulse[3]. The mean signal in each ROI identified from the gated image was calculated using the system of equations. Retrospective respiratory gating was performed based on the phase of the liver signal. A 1 s sliding window median filter was applied to the signal from the left ventricle to generate an arterial input function.

Results A high temporal resolution AIF was measured and is shown in Figure 2. The initial rise of the blood signal curve is sharp and clearly defined. Respiratory motion artifacts were successfully removed from the signal, and the fluctuations at adjacent time points due to noise and cardiac motion are relatively small.

Discussion In quantitative contrast enhanced MRI of small animal cancer models, measurement of the AIF is challenging due to the conflicting requirements of achieving the temporal resolution needed to capture the early dynamics of the AIF, while also achieving the spatial resolution necessary to accurately image blood vessels. Variations in AIF measurement due to these effects are associated with poor reproducibility of pharmacokinetic parameters and substantially reduce the power of DCE-MRI techniques. We have developed a novel reconstruction technique which permits extraordinary undersampling of regions with known anatomy. This will permit imaging of the rapidly beating heart, allowing high temporal resolution AIF measurement which is free from partial volume contamination. As a result, the reproducibility and reliability of small animal-DCE-MRI will be greatly improved.

References

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