A demonstration of the feasibility of DSC in evaluating breast tumor blood volume

M. L. Wagner Schuman[1], D. Bedekar[1], E. S. Paulson[1], Q. Kern[1], D. E. Prah[1], and K. M. Schmainda[1,2]

[1]Biophysics, Medical College of Wisconsin, Milwaukee, Wisconsin, United States, [2]Department of Radiology, Medical College of Wisconsin, Milwaukee, Wisconsin, United States

Introduction

Dynamic susceptibility contrast (DSC) MRI has been the most frequently used perfusion technique to determine brain and tumor cerebral blood volume (CBV). This approach assumes that the contrast agent remains intravascular, setting up a gradient of susceptibility between the vessel and tissue, thereby resulting in a transient signal decrease. It is well known that if contrast agent leaks out of the vessels the CBV can be underestimated. Compensation for these leakage effects using a contrast-agent preload together with a post-processing correction algorithm have demonstrated more statistically significant results.[1] The purpose of the present study is to determine the feasibility of using leakage-corrected DSC to obtain reliable estimates of blood volume in breast tissue and tumor, where gadolinium contrast agent readily extravasates during the first pass of Gd contrast agent. DSC measurements will be compared to DCE (dynamic contrast enhancement) perfusion measurements, which are more commonly obtained for the evaluation of breast cancers. Our hypothesis is that DSC parameters of blood volume and flow will be more specific indicators of breast cancer malignancy than the DCE - derived parameter K^{trans}, which is dependent on both flow and permeability effects.

Methods

Thirteen female Fisher rats, weighing approximately 300g (Sprague Dawley, Harlan Indianapolis), were anesthetized with 80mg/kg sodium pentobarbital IP and inoculated with the Mat B III cell line (ATCC #CRL-1666), a rapidly growing, well vascularized, rat mammary adenocarcinoma.

For a voxel-wise estimate of T1, three sets of pre-contrast images were acquired with a fast-spoiled gradient recalled echo (SPGR) sequence with flip angles of α=2°, 10°, and 35°. T1-weighted dynamic contrast enhanced (DCE) data was collected using a SPGR sequence (TE=4 msec, TR=34 ms, α=35°). Images were obtained every 10 seconds before, during and after a bolus injection of 0.1mmole/kg of gadolinium contrast agent (Omniscan, Nycomed Amersham, Princeton NJ). This data was used to calculate the DCE parameters. The bolus of Omniscan served as the leakage-diminishing preload for the DSC study.[2] Next, the DSC study was performed using a GE sequence (TE = 26.8 ms, TR = 1150 msec, FOV = 6 cm, MAT=64^2, ST=2 mm). These images were collected for 30 seconds before and 60 seconds after the bolus administration of a 2nd dose (0.2mmole/kg) of Gd contrast agent.

Data analysis was performed offline using AFNI and additional programs developed at our institution. The Patlak model[3] was used to compute K^{trans} on a pixel-by-pixel basis from the DCE data. The DSC-MR signal intensity time courses were converted into delta R2* concentration-time curves. Relative blood volume (rBV) estimates were obtained by finding the area under the leakage corrected concentration-time curves and corrected for contrast leakage effects[1]. Voxel-wise estimates of rBV were normalized to their average skeletal muscle rBV. DSC-MR time courses were used to determine the arterial input function (AIF) from large vessels in uninvolved skeletal muscle. Using singular value decomposition, the intravoxel tissue residue function was derived by deconvolving the tissue concentration time curves with the AIF. Blood Flow (BF) estimates were determined as the maximum point of the residue function. Mean transit time (MTT) was estimated as MTT=BV/BF. Regions of Interests were chosen for tumor and uninvolved skeletal muscle and used to determine the mean rBV, BF, MTT, and K^{trans} values.

Statistical analysis was performed using GraphPad Prism version 4.0a for Mac OS X (GraphPad Software, San Diego, CA). Parametric statistical test was performed to compare the CBV, CBF, MTT, and K^{trans} measures of skeletal muscle to breast cancer. A *P*-value less than or equal to 0.05 was considered statistically significant.

Results and Discussion

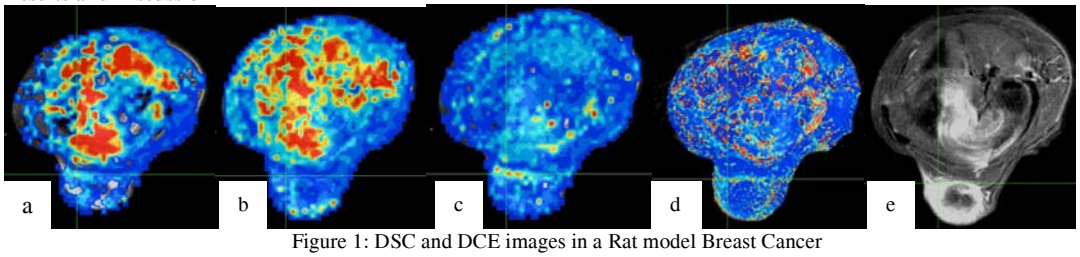

Figure 1: DSC and DCE images in a Rat model Breast Cancer

Figures 1a through 1c display DSC parameters BV, BF, and MTT, respectively, figure 1d displays DCE parameter K^{trans}, and figure 1e is the corresponding anatomical image, demonstrating a large breast tumor. The images of figure 1 exhibit the potential of using DSC-MRI in the evaluation of breast cancer. The green cross hair demonstrates a contrast-enhanced area of the tumor that has increased blood volume, blood flow, mean transit time, and K^{trans}. Figure 2 is a comparison of the DSC parameters to the DCE parameter, K^{trans}. Figures 2a through 2c display the average tumor blood volume, blood flow, and mean transit time compared to uninvolved skeletal muscle, respectively. Figure 2d displays average tumor K^{trans} compared to average uninvolved skeletal muscle K^{trans}. All DSC and DCE parameters were shown to be significantly different from uninvolved skeletal muscle; however, the three DSC parameters had a greater significant difference (i.e. lower *p* values) than the DCE parameter K^{trans}. This suggests that DSC MRI is more sensitive to indicators of breast cancer malignancy than DCE. Independent validation of these imaging markers, with tissue markers of vascular function and morphology are planned to confirm which parameter(s) provide more accurate information about the tumor breast biology.

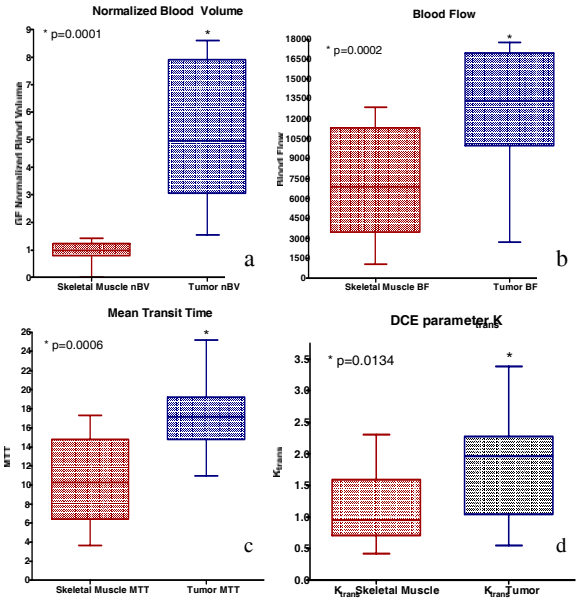

Figure 2: Comparison of DCE parameter (Ktrans) to DSC parameters (BV, BF, MTT)

References

1. Boxerman JL, et al. AJNR. 2006 Apr; 27(4):859-67.
2. Schmainda KM et al. AJNR. 2004 Oct; 25(9):1524-32.
3. Patlak CS et al. J Cerebral Blood Flow Metab 1985;5: 584-590.

Acknowledgements

This work was supported by NIH/NCI CA082500.