Perfusion correction of brain tumor functional diffusion maps

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Target Audience
Brain cancer imaging researchers, radiologists and clinicians.

Purpose Advanced imaging techniques have been developed to assess brain tumor progression. These include diffusion weighted MRI (DWI) derived apparent diffusion coefficient (ADC), dynamic susceptibility contrast MRI (DSC) derived relative cerebral blood volume (rCBV), and functional diffusion maps (FDMs) generated by subtracting and thresholding ADC maps from serial imaging sessions. Each ADC map is calculated using two b-values, typically, b=0 and1000 s/mm^2. Low b-values (i.e. b=0), however, include blood flow contributions, while higher b-values (>200 s/mm^2) are insensitive, as the signal from fast moving blood is suppressed[1,2]. The goal of this study was to evaluate the effect of perfusion changes on longitudinal diffusion differences by comparing FDMs calculated with both low and high b-values. We hypothesize that voxels with perfusion driven diffusion changes can influence FDM results suggesting that greater b-values for ADC should be used for the creation of more accurate functional diffusion maps.

Methods Data from thirty brain tumor patients were retrospectively analyzed, with diagnoses of Grade 4 GBM (n=8), Grade 3 (n=12), and low-grade (n=10) lesions. Functional diffusion maps (FDMs) were generated using previously published methods[3]. FDM voxels were categorized as having significantly increased ADC (iADC), decreased ADC (dADC), and no change in ADC (ncADC). Two sets of FDMs were calculated. Traditional FDMs (tFDMs) were generated with ADC maps calculated using b=0,1000 s/mm^2. Flow compensated FDMs (fcFDMs) were generated with ADC maps calculated using b=500,1000 s/mm^2. Voxelwise images of rCBV were created from the DSC data using methods previously published with leakage correction followed by intensity standardization[4,5]. Perfusion change (ΔrCBV) was then evaluated in voxels where ADC changed on the tFDM, but not on the fcFDM. These voxels are those voxels theoretically classified as changing ADC on the tFDM solely due to perfusion changes.

Results Figure 1 shows scatter plots of ADC from TP2 (time point 2) versus ADC from TP1 (time point 1) in one representative patient. The *colors* of the dots are dictated by the direction of change of the rCBV with red colors indicating positive ΔrCBV and blue colors indicating negative ΔrCBV. The *location* of the dots on the plots is dictated by the direction change of ADC. Specifically, dots in the upper left region of the plot, above the upper diagonal line, were classified as iADC, while dots in the lower right region of the plot, below the lower diagonal line, were classified as dADC. These results are quantified for all patients in Figure 2 and Table 1. Mean ΔrCBV in voxels that changed from iADC on the tFDM to ncADC on the fcFDM was significantly greater than zero (1.26 (0.37) a.u. p = 0.002). Mean ΔrCBV in voxels that changed from dADC on the tFDM to ncADC on the fcFDM was significantly less than zero (-0.97 (0.37) a.u. p = 0.01). Mean ΔrCBV in tFDM voxels that did not change categories on the fcFDM was not significantly different from zero (-0.9 (2.5) a.u. p = 0.7).

Table 1. Mean ΔrCBV values on tFDMs and fcFDMs

	iADC	dADC	ncADC	
ΔrCBV in Classification Changing voxels (tFDM→fcFDM)	1.26 (0.37) p = 0.0023	-0.97 (0.35) p = 0.010	-0.086 (0.25) N.S.	iADC>dADC** iADC>ncADC* dADC<ncADC*

Values are given in means (standard errors); *p<0.05, **p<0.01; N.S. = Not Significant; tFDM = Traditional Functional Diffusion Map; fcFDM = Flow Compensated Functional Diffusion Map.

Discussion Perfusion can confound functional diffusion maps, as diffusion MRI can be made sensitive to blood flow[1]. As new vessels are created or recede in tumor as a result of successful treatment, ADC in that area increases or decreases respectively. In general, iADC voxels tended to have positive Δ rCBV, and dADC voxels tended to have negative Δ rCBV. Those voxels that changed categories from the tFDM to the fcFDM were those that were also associated with large ΔrCBV. This indicates voxels classified as iADC or dADC on the tFDM solely due to perfusion effects are now classified as ncADC on the fcFDM, and thus the fcFDM compensates for these effects.

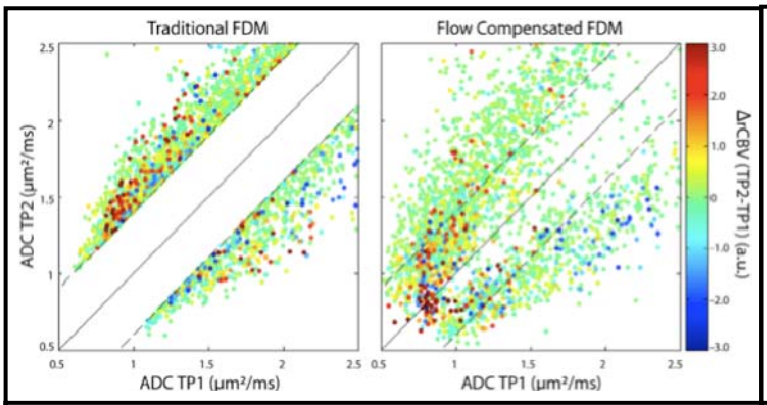

Figure 1. FDM scatter plots from one representative patient. Each point represents one voxel. The horizontal axis is the ADC from TP1, and the vertical axis is the ADC from TP2. The color of each point represents Δ rCBV from TP1 to TP2. Red and blue colors indicate an increase and decrease in rCBV respectively. Column 1 shows iADC and dADC voxels on the tFDM, and column 2 shows those *same* voxels on the fcFDM.

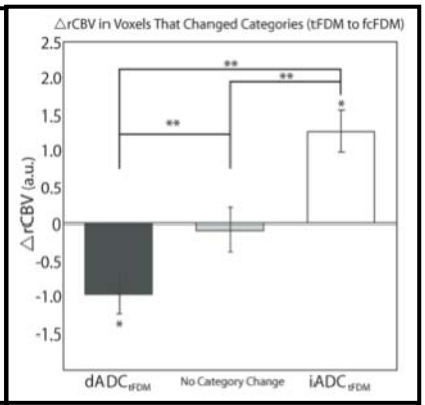

Figure 2. Mean ΔrCBV in voxels that changed from dADC$_{tFDM}$ and iADC$_{tFDM}$ to ncADC$_{fcFDM}$ and mean ΔrCBV in voxels that did not change from the tFDM to the fcFDM. * = significant difference via one-sample t-test, p < 0.05; ** = significant difference via two-sample t-test, p< 0.025

Conclusion This study used b = 500 s/mm^2 in place of b = 0 s/mm^2 to calculate ADC changes over time, resulting in flow compensated FDMs. These maps were less sensitive to perfusion effects.

References
1. Le Bihan et al. Radiology 168: 497-505, 1988. **2.** Padhani A et al. Neoplasia 11: 102-125, 2009. **3.** Ellingson BM et al. J Magn Reson Imaging 31: 538-548, 2010. **4.** Bedekar D et al. Magn Reson Med 64: 907-913, 2010. **5.** Boxerman JL et al. AJNR Am J Neuroradiol 27: 859-867, 2006