# Utility of Multiple b-value DWI derived metrics in differentiation of high grade from low grade glioma

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**Introduction:** The accurate grading of glioma is required to select the appropriate treatment planning. There have been constant efforts to develop non-invasive imaging means to correctly classify glioma in order to overcome the limitations and to some extent obviate the surgical intervention in case the lesion is placed at surgically challenging positions. Currently MR perfusion imaging using dynamic susceptibility contrast (DSC) and dynamic contrast enhanced (DCE) methods have been successfully used in glioma grading and characterization[1,2] but these methods require administration of exogenous contrast agents which limits its use in patients with renal dysfunctions. Diffusion weighted imaging is a powerful technique which is routinely used in assessment of a brain tumors[3]. It has been proposed that at low b-values (<200s/mm$^2$) movement of blood in microvasculature can be modeled as a pseudodiffusion process and it can be distinguished from diffusion by using a biexponential curve fit on a multiple b-value DWI data[4]. In addition, DWI at higher b-value has been reported to discriminate high grade from low grade glioma[5]. In this study we prospectively compared DCE- MRI metrics and DWI derived apparent diffusion coefficient (ADC), perfusion fraction ($f_p$), slow ($D_{slow}$) and fast component ($D_{fast}$) using multi b-value in glioma grading with histology as gold standard.

**Materials and methods:** *Subjects*-Sixteen (11 male and 5 female; mean age=41 yrs) untreated consecutive patients (11 high grades & 5 low grades on histopathology) with definitive diagnosis of glioma were included in this study.

***Data acquisition*:** All patients underwent conventional, DCE and DW MRI on a 3.0T scanner (Signa HDxt, General Electric, Milwaukee, USA) using a 8 channel head coil. DWI was acquired using TR/TE/NEX/slice thickness/FOV/matrix size= 14s/94ms/1/3mm/240×240mm/80×128mm; 12 b values (0, 50, 100, 150, 200, 300, 400, 600, 800, 1000, 1500 and 2000 s/mm$^2$). DCE-MRI was performed using a three dimensional spoiled gradient recalled echo (3D-SPGR) sequence [TR/TE/flip angle/ number of excitation(NEX)/slice thickness/ field of view (FOV)/matrix size=5.0ms/2.1ms/10$^o$/0.7/6mm/240×240mm/128×128mm, number of phases=32]. At the fourth acquisition, Gd-DTPA-BMA (Omniscan, GE Healthcare, USA) was administered intravenously through a power injector at 5ml/sec, followed by 30ml saline flush. A series of 384 images in 32 time points for 12 slices were acquired (Temporal resolution: 6.03sec). Prior to 3D SPGR, two inversion recovery FSE (TR/TE/NEX/slice thickness/FOV/matrix size= 940ms/8ms/0.75/6mm/240×240mm/128×128mm) with inversion time 800 and 1600ms were performed for the same slice position to quantify voxel wise tissue $T_{10}$.

***MRI data processing and quantitative analysis*:** The DWI derived $f_p$, $D_{slow}$ and $D_{fast}$ were calculated by fitting the biexponential model $S(b)=S_0(f_p\ exp(-b\ D_{fast})+(1-f_p)exp(-b\ D_{slow}))$ with signal intensity of all the 12 b values DWI data[6]. Initial guess was made by assuming the model behaving monoexponential for higher b values (b≥250) and fit the data. The decay rate of this fit was taken as $D_{slow}$ and the low-b intercept was taken as $f_p$. ADC was calculated by fitting the monoexponential model $S(b)=S_0(exp(-b\ ADC))$ for all the 12 b values. Voxel wise tissue $T_{10}$ was calculated from two inversion recovery sequences. Quantitative analysis of concentration time curve was performed for calculation of cerebral blood volume (CBV) and cerebral blood flow (CBF). Pharmacokinetic model was implemented for permeability ($k^{trans}$ & $k_{ep}$) and leakage ($v_e$) calculation. Corrected CBV map was generated by removing the leakage effect of the disrupted BBB[1]. The ROIs were drawn on the lesion for quantification of perfusion and DWI metrics. Relative CBV (rCBV) and CBF (rCBF) were quantified by placing ROI on normal contra-lateral portion of the brain for DCE MRI (Fig 1&2).

***Statistical analysis*:** Student's independent t-test was used to look for the parameters with significantly different values in low and high grade tumors. A p-value ≤0.05 was considered as significant.

**Results:** None of the DWI derived ADC, $f_p$, $D_{slow}$ and $D_{fast}$ showed any significant differences between high and low grade glioma whereas all the DCE derived metrics except $v_e$ (p=0.15) were found to be significantly higher in high grade as compared to low grade glioma (p<0.005) (Fig 3, Table 1).

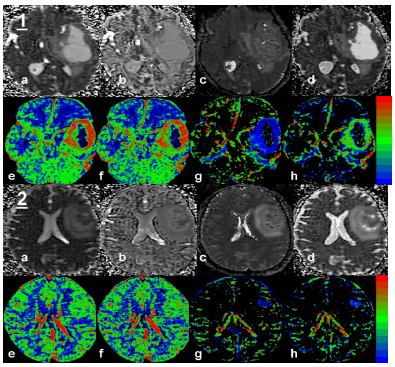

*Fig:1)(a-d) Showing a glioblastoma with central necrosis and peripheral hypointense rim representing cellularfraction of tumor on ADC, appeared isointense on fast component ($D_{fast}$), demonstrating hetrogenous signal intensity on slow component ($D_{slow}$) and similar signal intensity pattern as that of ADC on perfusion fraction ($f_p$) maps respectively, 2)(a-d), a low grade glioma with surrounding edema on ADC, appeared iso to hypointense on fast component ($D_{fast}$), showing hyper intensity on slow component ($D_{slow}$) and similar signal intensity pattern as that of ADC on perfusion fraction ($f_p$) maps respectivel.y*

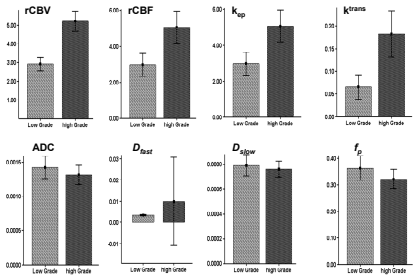


*Fig 3: Bar diagrams showing differences in values of DCE and DWI metrices in low and high grade glioma. Error bar represent mean±0.5sd*
*rCBV=relative cerebral blood volume; rCBF=relative cerebral blood flow; $k_{ep}$=rate transfer constant; $k^{trans}$=volume transfer coefficient; ADC=apparent diffusion coefficient; $D_{fast}$=fast component, $D_{slow}$=slow component; $f_p$=perfusion fraction*

| Parameter | Mean ± SD | | p-value |
|---|---|---|---|
| | Low Grade | High Grade | |
| ADC (mm$^2$/s) | 0.001±0.0003 | 0.001±0.0003 | 0.22 |
| $f_p$(%) | 0.36±0.09 | 0.32±0.07 | 0.11 |
| $D_{slow}$(mm$^2$/s) | 0.001±0.0002 | 0.001±0.0001 | 0.51 |
| $D_{fast}$ (mm$^2$/s) | 0.003±0.0005 | 0.009±0.041 | 0.34 |
| rCBF | 2.97±1.27 | 5.07±1.78 | <0.001 |
| rCBV | 2.92±0.73 | 5.21±1.08 | <0.001 |
| $k^{trans}$ (Min$^{-1}$) | 0.06±0.05 | 0.18±0.10 | <0.001 |
| $k_{ep}$ (Min$^{-1}$) | 0.49±0.50 | 0.97±0.52 | 0.002 |
| $v_e$ | 0.12±0.18 | 0.19±0.10 | 0.15 |

***Table.1:** Mean and standard deviation values of DWI and DCE derived perfusion metrics*

**Discussion:** On higher field strengths, attempts are been made to develop non-contrast methods to assess cerebral perfusion as well as characterization of various lesions. DWI is one such non-contrast technique which has wide implication. The $f_p$ has been shown to correlate with the increased vascularity in renal neoplasm[6]. However, in this study none of the DWI derived metrices ($f_p$, $D_{fast}$, $D_{slow}$ and ADC) showed significant difference in low grade as compared to high grade glioma. These findings are in disagreement with previous studies which report these imaging parameters as important in differentiating and characterizing tumors. In this study, DCE-MRI proved to be superior in differentiating high grade from low grade glioma as compared to multi b-value DWI imaging. DCE-MRI provides pharmacokinetic ($k^{trans}$ and $k_{ep}$) as well as hemodynamic parameters (CBV and CBF), which helps to characterize tumor physiology in a more comprehensive manner by providing information about the degree of blood brain barrier disruption as well as neoangiogenesis. We conclude that multi b-value DWI is not a reliable technique to differentiate between high and low grade glioma and DCE perfusion MRI is still the best available technique to differentiate as well as characterize the glial neoplasm.

**References**: 1) Singh et al. *J Magn Reson Imaging* 2007;26 :871-80. 2)Lacerda et al. *Neuroimaging clin N Am* 2009; 19:527–57. 3)Gerstner et al. *Semin Radiat Oncol.* 2011;21:141-6. 4)Le Bihan et al. *Radiology* 1988;168:497-05. 5)Seo et al. *AJNR* 2008;29 :458-63. 6)Chandarana et al. *Investigative Radiology*; 46:285-91.