Fusion of Dynamic Contrast Enhanced (DCE) Perfusion Metrics with DTI Metrics Results in Better Assessment of Corticospinal Tract Infiltration in Malignant Gliomas

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Introduction: Malignant gliomas spread in a way to destruct white matter (WM) tracts [1,2]. It has been reported that edema surrounding the tumors is a morphological sign of tumor infiltration in the adjacent white matter[1,2]. Diffusion tensor imaging has been used to differentiate the infiltrative white matter tract from the normal white matter tract[1,2]. The most commonly used DTI indices are fractional anisotropy (FA) and mean diffusivity (MD). Besides FA and MD, other DTI indices i.e., linear case (CL), planar case (CP) and spherical case (CS) may provide additional information with respect to tissue micro-structural integrity[3]. Earlier it has been reported that the increased MD and low FA in the peritumoral edematous region is an indicator of peritumoral tract invasion[2]. The Malignant gliomas have shown high value of cerebral blood volume (CBV), cerebral blood flow (CBF), permeability (k^{trans}) and leakage (v_e)[4]. In the current study, we fused DTI indices maps with perfusion maps with a hypothesis that the perfusion maps when combined with DTI maps should able to separate the edematous region from infiltrating fibers which may not be possible alone on DTI.

Materials and Methods: In this prospective study, we have included 18 patients (mean age±SD=43.9±4.7) with malignant brain tumors as initially identified on conventional MRI and confirmed on histology. All these patients had infiltrative tumor in the corticospinal (CST) tract of the ipsi-lateral hemisphere while there was no tumor infiltration in CST of the contra-lateral hemisphere. With the informed consent all patients underwent for both dynamic contrast enhanced (DCE) perfusion imaging and DTI on a 1.5 T GE scanner using quadrature birdcage head coil in the same sitting. DCE MR imaging was performed using a three dimensional spoiled gradient recalled echo (3D-SPGR) sequence [TR/TE/flip angle/ NEX/slice thickness/ field of view (FOV)/matrix size=5.0ms/1.4ms/15°/0.5/6mm/360×270mm /128×128mm, number of phases=32]. At the fourth acquisition, Gd-DTPA-BMA (Omniscan, GE Healthcare, USA) was administered intravenously with the help of a power injector at a rate of 5ml/sec, followed by a bolus injection of 30ml saline flush. A series of 384 images in 32 time points for 12 slices were acquired with a temporal resolution approximately of 5.25sec. Prior to 3D SPGR, fast spin echo (FSE) T_1-weighted (TR/TE/NEX/slice thickness/FOV/matrix size=375ms/9.4ms/ 1/6mm/360×270mm/256×256mm) and fast double spin echo PD and T_2 weighted (TR/TE1/TE2/NEX/slice thickness /FOV/matrix size= 3500ms/25ms/85ms/1/6/ 360×270mm/256×256mm) imaging were performed for the same slice position to quantify voxel wise pre-contrast tissue T_{10}[5]. DTI (TR/TE/NEX/ slice thickness/FOV /image matrix =8sec/100ms/8/3mm/240mm/256×256 (following zero-filling), diffusion weighting b-factor=1000 smm^{-2}) was performed for the same slice position as was done in DCE study. DTI data were acquired using a single-shot echo-planar dual spin-echo sequence with ramp sampling.

DCE and DTI data registration: All the DTI directional data b1 to b_{10} were registered on b0. All the 3D-SPGR , 32 time point data set, FSE T2 and FSE PD were registered on FSE T1.After that registered FSE T2 data was co-registered on b0 , then the same parameters were applied on all 3D SPGR time series data as well as on FSE PD. For registration we have used affine transformation model, mutual information as similarity measure. An iterative based maximization algorithm was used for maximization of mutual information[6].

Data processing and analysis: The DTI and perfusion data were processed as described in details elsewhere[5,7]. The CBV is also corrected for the leakage (v_e)[5].The perfusion indices (CBV, CBF, k^{trans} and v_e) and DTI indices (FA, MD, CL, CP and CS) were calculated by placing the region of interests (ROIs) on the CST of the lesion side (at tumor infiltration site, adjacent to the lesion and away from the lesion) and edematous region. For comparative analysis the contralateral ROIs with respect to the above mentioned ROIs were also placed in the opposite normal brain hemisphere.

***Statistical Analysis*:** Independent student t-test was performed to compare the quantitative values calculated for each ROIs from both side of cerebral hemisphere.

Results: The perfusion and DTI indices in different region of CST and edematous region are reported in table 1. The infiltrative CST region showed significant increased MD, CS, CBV, CBF, k^{trans} and v_e while the FA and CL were significantly decreased compared to their contralateral values. The CST WM adjacent to the lesion showed significant decreased FA and CL while MD, CP, CBV, CBF, k^{trans} and v_e were significantly increased compared to contra-lateral values. In case of CST WM away from the lesion, we did not find any significant change in perfusion as well as DTI indices values compared to the contralateral values. The edematous region showed significant increase in MD and CS along with significant decreased FA, CL, CP, CBV and CBF compared to contralateral ROIs values. No quantifiable permeability and leakage were observed in edematous region.

Discussion: The tumor infiltration is usually characterized by the low FA and high MD while increased CBV, CBF, k^{trans} have been the hall mark of the malignant gliomas[1,2,4]. In this study, we have observed low FA along with increased MD and all perfusion indices characteristic of the malignant gliomas in CST where the tumor was visibly infiltrated on the FA maps and where it was significantly abnormal in the adjoining normal appearing CST. In one of the recent study no significant difference was found for the FA values between the normal appearing white matter adjacent to the lesion and contralateral white matter[2]. They further suggested, that the fiber tract destruction which is not visible on T_2 weighted image in the vicinity of tumor without peripheral edema cannot be postulated from the DTI data. In current study quantitative FA and MD values in the CST WM adjacent to the lesion were abnormal and were supported by the high value of perfusion indices suggesting infiltration of CST by the tumor even in absence of visible abnormality on T_2 weighted image. In current study, the decreased FA and MD in edematous region may indicate infiltrative nature of tumor that is not supported by the decreased CBV and CBF values with no quantifiable k^{trans} and v_e. Low values of CBV in the edematous part of malignant gliomas are well reported[8]. It appears that vasogenic edema around the tumor is responsible for the separation of the white matter tracts bundles resulting in low FA with increased MD. We conclude that fusion of DTI maps with perfusion maps provides an opportunity to precisely localize tumor infiltration along white matter tracts and thus may help in efficient surgical as well as radiotherapy planning in future.

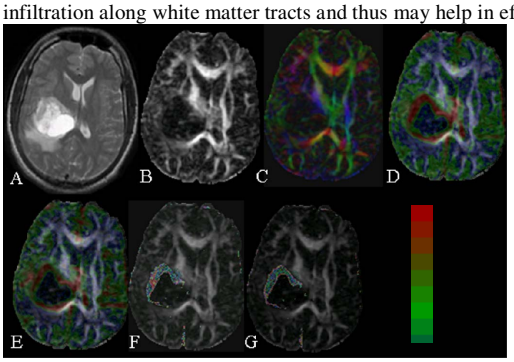

Figure: Glioblastoma multiforme in the right parietal region of 46 year old male patients as visible on T2 weighted (A) image. The FA, RGB-FA and the FA map fused with the CBV, CBF, k^{trans} and v_e showing the infiltrative nature of tumor

Parameters	Corticospinal tract-1		Corticospinal tract-2		Corticospinal tract-3		Tumor edema	Contra-lateral
	Infiltrative lesion	Contra-lateral	Adjacent to lesion	Contra-lateral	Away from lesion	Contra-lateral		
FA	0.14±0.06	0.47±0.03	0.40±0.07	0.48±0.03	0.45±0.05	0.44±0.04	0.12±0.04	0.32±0.05
MD	1.14±0.30	0.69±0.05	0.72±0.08	0.65±0.04	0.69±0.04	0.68±0.03	1.11±0.12	0.67±0.04
CL	0.05±0.03	0.28±0.03	0.19±0.05	0.28±0.03	0.24±0.05	0.24±0.04	0.05±0.02	0.18±0.05
CP	0.08±0.03	0.09±0.03	0.16±0.06	0.08±0.03	0.11±0.05	0.10±0.05	0.06±0.03	0.16±0.05
CS	0.83±0.06	0.59±0.06	0.60±0.07	0.58±0.03	0.60±0.04	0.61±0.04	0.85±0.04	0.62±0.05
CBV	61.2±14.9	4.51±0.60	11.4±5.2	4.27±0.79	4.56±0.83	4.42±0.76	1.73±0.56	3.81±0.88
CBF	189.7±42	40.8±6.03	64.5±16.8	39.3±10.3	39.2±7.5	42.5±8.9	17.2±8.04	42.8±10.7
k^{trans}	0.58±0.32	0.0±0.0	0.014±0.02	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
v_e	0.21±0.10	0.0±0.0	0.003±0.006	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0

Table 1: showing the values of DTI as well as perfusion indices for the various regions of interests. Unit of MD is (10^{-3} mm^2s^{-1}) and k^{trans} is (min^{-1}).

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