Changes in DTI Metrics in Normal Appearing White Matter and Gray Matter after Radiotherapy in Patients with Low Grade Glioma

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Introduction:

Diffusion tensor imaging (DTI) has been widely used for the detection of white matter abnormality in various clinical conditions[1]. The two commonly used DTI metrics are fractional anisotropy (FA) and mean diffusivity (MD), which depends upon the integrity of white matter tracts and hindrance to water mobility by structural and sub-structural components[1]. The role of DTI in the grading of gliomas and in surgical interpretation has also been described[2]. In this study, we have evaluated the dose dependent effects of radiation on these metrics in normal appearing white matter (NAWM) of patients with low grade gliomas (LGGs), and tried to ascertain if a threshold dose level exists below which no apparent changes in NAWM occur.

Materials and Methods:

Ten patients (mean age=37.2±5.65 years) of histologically proven low grade gliomas were included in this study following maximal safe resection. All patients underwent a post-op, MRI - Radiotherapy Treatment Planning (RTP) scan following immobilization in a thermoplastic face mask with fiducial markers. Data acquisition consisted of conventional (T_2-W, T_1-W, post-contrast T_1-W and FLAIR images) and DTI imaging. The T_2 or FLAIR images were transferred using DICOM protocol to a RTP system in which the gross tumor, as visualized by the high signal intensity, was contoured in axial slices. The Planning Target Volume (PTV) was expanded from the T_2-W / FLAIR gross tumor volume in 3-D by 1 - 1.5 cm with appropriate editing for anatomical barriers to tumor spread. Radiotherapy (RT) to a dose of 54 Gy in 30 fractions over 6 weeks was delivered conformally with 2-3 beams to the PTV with 6MV photons from a linear accelerator. The 95% isodose line covered the PTV in all cases and dose heterogeneity within the PTV was restricted to -5% to +7% of the prescribed dose. All patients underwent the same sequences in a follow up MR scan three months following completion of RT.

Image Acquisition and Data Processing: Conventional MRI and DTI images of the head were acquired on a 1.5 Tesla MRI scanner using standard quadrature birdcage head coil. DTI data were acquired using a single-shot echo planar dual spin echo sequence with ramp sampling. The acquisition parameters were: TR=8sec/TE=100ms/number of slices=36-40/slice thickness=3mm/ interslice gap=0/FOV=240mm/image matrix=256×256 (following zero-filling)/NEX=8/diffusion weighting b-factor=1000 s mm^{-2}. The DTI data was processed and evaluated using a JAVA based in-house developed program[3]. Before region of interest (ROI) analysis, dose bins were identified on axial slices of interest by generating isodoses at intervals of 5Gy. Elliptical ROIs varying from 2×2 to 6×6 pixels were placed in the NAWM in the corresponding areas of both pre RT and post RT follow up image acquisitions. The FA and MD values in corresponding ROIs selected inside the dose bins in NAWM were evaluated using anatomical landmark-based matching to ascertain changes post treatment. Evaluation was done for the dose bins from 20 Gy to >55 Gy, with class intervals of 5 Gy. Statistical analysis was performed using the t-test on the SPSS v.12 statistical software.

Results:

The pre- and post-RT FA and MD values in corresponding NAWM ROIs for different dose bins are reported in Table 1. The FA values decreased significantly in the >55 Gy, 50-55 and 45-50 Gy volumes while the MD values increased significantly in the >55 and 50-55 Gy bins, with NAWM in lower dose bins showing non significant differences.

Dose Bins (Gy)	Pre-RT FA (mean±SD)	Post-RT FA (mean±SD)	Mean difference	p-value	Pre-RT MD (mean±SD)× 10^{-3} mm^2/sec	Post-RT MD (mean±SD)×10^{-3} mm^2/sec	Mean difference ×10^{-3}	p-value
>55	0.375±0.049	0.309±0.021	0.066	0.000	0.673±0.065	0.773±0.205	-.100	0.000
50-55	0.378±0.050	0.327±0.018	0.051	0.000	0.672±0.071	0.745±0.094	-.070	0.000
45-50	0.376±0.042	0.356±0.022	0.019	0.020	0.676±0.075	0.686±0.072	-.010	0.565
40-45	0.374±0.041	0.375±0.039	-0.002	0.915	0.650±0.058	0.657±0.050	-.007	0.767
35-40	No ROI could be placed due to sharp gradient between isodose lines.							
30-35	0.381±0.054	0.372±0.018	0.009	0.727	0.729±0.106	0.656±0.023	0.073	0.173
25-30	0.360±0.038	0.359±0.024	0.001	0.948	0.684±0.056	0.677±0.130	0.006	0.889
20-25	0.360±0.041	0.371±0.033	-0.011	0.232	0.687±0.076	0.705±0.046	-0.018	0.223

Table 1: Comparison of pre- and post-RT FA and MD values within dose bins.

Discussion:

DTI is a unique tool for assessing white matter structural integrity (WMSI)[1]. The FA values have a direct correlation with WMSI[1]. A decrease in the FA suggests distortion of the WM structure here. We wished to ascertain (1) if radiotherapy had any effect on WMSI; and (2) the distortion, if any, could be related with the RT dose. To lessen the confounding effect of direct tumour infiltration, we chose LGGs rather than high grade gliomas, and studied the changes in NAWM rather than intralesional or boundary region areas. We found that a threshold dose did exist for FA and MD value changes. At doses >45 Gy FA values decreased significantly, while MD values increased significantly only at doses >50 Gy. These data suggest that RT does affect NAWM structure; that there does appear to be a threshold dose required to cause an appreciable distortion; and that FA values might be a more sensitive indicator for assessing post-RT WMSI distortion. This study may form the basis for designing protocols for evaluating a quantitative effect of RT dose v/s WMSI distortion; and also might serve as a baseline for measuring time trends in the WMSI distortion or recovery, if any, post-radiotherapy.

References:

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