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Spatial Variation of Apparent Diffusion Coefficient and Fractional Anisotropy within the Nonenhancing Component of Glioblastomas as a Function of Distance from Enhancing Tumor - Application to Predicting Clinical Outcome

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Abstract:

Purpose

Explore the variation of apparent diffusion coefficient (ADC) and fractional anisotropy (FA) within the nonenhancing component of glioblastomas as a function of distance from enhancing tumor. MR diffusion parameters of glioblastomas have been previously described in the literature; however, the goal of the current work is to more completely characterize the spatial variation of these parameters to improve the classification of glioblastomas and to predict clinical outcome.

Materials & Methods

As part of The Cancer Genome Atlas (TCGA) MRI characterization project of the National Cancer Institute, the multiinstitutional TCGA Glioma Phenotype Research Group has been investigating MRI, including diffusion and diffusion tensor imaging, as a means of predicting clinical outcomes for glioblastoma patients. For the current work, a previously described interactive machine learning method for segmenting MRI of glioblastomas into various components, including nonenhancing and enhancing tumor, was applied. A Euclidian distance transform was performed to compute the distance from enhancing tumor. Volumes of interest (VOIs) containing nonenhancing tumor were generated at increasing distances from enhancing tumor: 0 to 2 mm, 2 to 4 mm, 4 to 6 mm, and 6 to 8 mm from enhancing tumor. FA and ADC were computed for the VOIs. 35 of the tumors have been processed thus far. Clinical outcomes including days of survival were obtained from the publicly available TCGA data. Analysis of variance and Kaplan-Meier survival analysis was performed. For initial analysis, tumors were divided into two groups based on the medians of the parameters (e.g. high ADC versus low ADC).

Results

A suggestion of a minimal increase in ADC was noted with greater distance from enhancing tumor, but was only statistically significant ($p<0.05$) between the volumes of tumor 0 to 2 mm compared to 4 to 6 mm and between 2 to 4 mm compared to 4 to 6 mm. In the subset of tumors currently evaluated, no significant difference in survival was identified between tumor with high FA versus low FA. However, tumors with high ADC in enhancing tumor demonstrated significantly longer survival ($p = 0.004$, 543 days versus 187 days). High ADC in nonenhancing tumor adjacent to enhancing tumor (within 0 to 2 mm) was also associated with longer survival ($p = 0.03$, 654 versus 357 days). In the next layer of nonenhancing tumor (2 to 4 mm from enhancing tumor), there was only a suggestion of improved survival with higher ADC ($p=0.052$).

Conclusion

Low ADC within enhancing tumor and the immediately adjacent nonenhancing tumor may help predict survival. The threshold value preliminarily identified is approximately 1.2×10^{-3} mm^2 s^{-1}. These findings suggest a more sophisticated method of characterizing the spatial variations of MR diffusion parameters may be helpful in predicting clinical outcomes.

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