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Connecting MRI Physics to Glioma Microenvironment: Comparing Simulated T2-Weighted MRI Models of Fixed and Expanding Extracellular Space

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Abstract : Glioblastoma Multiforme (GBM), the most common primary brain tumor, often presents with hyperintensity on T2-weighted or T2-weighted fluid attenuated inversion recovery (T2/FLAIR) magnetic resonance imaging (MRI). This hyperintensity corresponds with vasogenic edema, however there are likely many infiltrating tumor cells within the hyperintensity as well. While MRIs do not directly indicate tumor cells, MRIs do reflect the microenvironmental water abnormalities caused by the presence of tumor cells and edema. The inherent heterogeneity and resulting MRI features of GBMs complicate assessing disease response. To understand how hyperintensity on T2/FLAIR MRI may correlate with edema in the extracellular space (ECS), a multi-compartmental MRI signal equation which takes into account tissue compartments and their associated volumes with input coming from a mathematical model of glioma growth that incorporates edema formation was explored. The reasonableness of two possible extracellular space schema was evaluated by varying the T2 of the edema compartment and calculating the possible resulting T2s in tumor and peripheral edema. In the mathematical model, gliomas were comprised of vasculature and three tumor cellular phenotypes: normoxic, hypoxic, and necrotic. Edema was characterized as fluid leaking from abnormal tumor vessels. Spatial maps of tumor cell density and edema for virtual tumors were simulated with different rates of proliferation and invasion and various ECS expansion schemes. These spatial maps were then passed into a multi-compartmental MRI signal model for generating simulated T2/FLAIR MR images. Individual compartments' T2 values in the signal equation were either from literature or estimated and the T2 for edema specifically was varied over a wide range (200 ms – 9200 ms). T2 maps were calculated from simulated images. T2 values based on simulated images were evaluated for regions of interest (ROIs) in normal appearing white matter, tumor, and peripheral edema. The ROI T2 values were compared to T2 values reported in literature. The expanding scheme of extracellular space is had T2 values similar to the literature calculated values. The static scheme of extracellular space had a much lower T2 values and no matter what T2 was associated with edema, the intensities did not come close to literature values. Expanding the extracellular space is necessary to achieve simulated edema intensities commiserate with acquired MRIs.

Keywords : extracellular space, glioblastoma multiforme, magnetic resonance imaging, mathematical modeling
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