

Purpose: We investigate treatment planning for intensity-modulated radiotherapy (IMRT) for glioma based on a computational tumor growth model. Currently, the target consists of the tumor mass visible on MRI plus a 1-2 centimeter isotropic expansion to account for tumor cell infiltration into adjacent brain tissue. Observations suggest that glioma primarily grow along white matter fiber tracts. Accounting for the anisotropic infiltration pattern may potentially improve the efficacy of radiotherapy and prolong survival.

Methods: We assume that tumor growth is characterized by local proliferation of tumor cells and diffusion into neighboring tissue. Mathematically, this can be described via a partial differential equation of reaction-diffusion type (Fisher-Kolmogoroff-Equation). Diffusion-Tensor-Imaging provides the spatial distribution of the diffusion tensor. Solution of the model equations yields a spatial distribution of the tumor cell density. Radiation-induced cell kill is described via the linear-quadratic cell survival model. Modification of current treatment planning procedures can be approached in three steps: 1) the target contour is adapted to match an isoline of the tumor cell density while keeping the total volume constant; 2) dose within the target can be redistributed to maximize overall cell kill while keeping the integral dose constant; 3) unavoidable dose outside the target can be redistributed to affect brain tissue more likely to be infiltrated by tumor cells.

Results: Treatment planning studies suggest that overall cell survival can be reduced by 1-3 orders of magnitude compared to the isotropic margin approach – depending on model parameters. Accounting for uncertainties in model parameters reduces the expected benefit, but a sensitivity analysis over a range of realistic parameters suggests that substantial improvements can be expected.

Conclusions: Since current planning procedures based on isotropic margins do not reflect known growth characteristics of glioma, computational tumor growth models have the potential to improve radiotherapy efficacy despite uncertainties in model parameters.

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