ABSTRACT

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# Improving control of high-grade glioma by ultra-hyper-fractionated radiotherapy.

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Ionizing radiation is a mainstay of high-grade glioma therapy. The current standard radiotherapeutic schedule involves a total 60 Gy split in 2.0 Gy fractions delivered on weekdays for six weeks. Thereafter, almost invariably the tumor relapses and progresses. In vitro studies have demonstrated that the therapeutic effectiveness of ionizing radiation towards high-grade glioma cells is greatly increased by splitting the total dose in fractions ten times smaller [0.1-0.5 Gy instead of standard 2.0 Gy-ultra-hyper-fractionated radiotherapy (ultra-hyper-FRT)]. Recently, it became possible to consistently translate this therapeutic effect to the animal setting, by using glioma-initiating cell-driven faithful animal modeling. A re-analysis of the literature reporting radiotherapeutic clinical trials also suggests that the lower the average fraction size, the higher is the achievable overall survival of patients. However, average fraction sizes ≤ 0.5 Gy have never been thoroughly investigated in the clinics. We propose to study in the clinical setting the therapeutic effect of an ultra-hyper-FRT schedule promptly extending the conventional radiation component of the current guidelines ("Stupp") therapeutic protocol.



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