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Abstract

Analysis of Potential Interactions in the Concurrent Use of Electromagnetic Anti-Mitotic Therapy with Radiation Therapy

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Objectives: After proven survival benefit in recurrent Glioblastoma, an overall survival benefit has been found with the use of tumor-treating fields (TTFields) in a randomized phase 3 trial of 695 patients with glioblastoma following definitive chemoradiation (Stupp et al. JAMA 2017;318(23):2306-2316). The next evolution is to study the use of upfront concurrent TTFields and radiation. But in the field of radiation oncology there is concern of treating through dense objects, so patients currently need to wait until the completion of radiation therapy to begin TTFields therapy. Clinical trials of TTFields for other histologies such as pancreas cancer (PANOVA), lung cancer (LUNAR), and brain metastases from lung (METIS EF-25) are ongoing. This presentation investigates the effects of the TTFields array on the radiation dose distribution when used concurrently, or when interleaved between alternating-day fractions of shorter courses of radiation therapy, to achieve potential synergistic effects with the timing of vascular damage and normal tissue repair kinetics.

Methods: To investigate whether the presence of TTFields affects radiation dose distribution, a series of phantom measurements were performed to assess the effects on the radiation field that would occur if the TTFields array was in place on the patient's head during radiation therapy treatments. Plans from 10 consecutive glioblastoma patients were recalculated onto a head phantom without the TTFields array, as well as with the TTFields array in three different positions, to simulate the effects of periodically replacing the array. Dose volume histogram (DVH) analysis of the plans were compared in terms of Dx/Vx dose/volume values for planning target volume (PTV) coverage and skin dose.

Results: The presence of TTFields arrays decreased PTV V97% and D97% by as much as 1.7% and 2.7%, respectively, for a single array position, but this decrease was mitigated due to feathering by array repositioning. On averaging the three array positions, there was no statistically significant difference in any dosimetric parameter of PTV coverage (V95%-V97%, D95%-D97%) across all cases as compared to no array. Mean increase in skin D1cc and D20cc were both 3.1% averaged over the cohort, and skin surface dose with TTFields electrodes was less than that with 5 mm superflab bolus.

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Conclusions: The change in the radiation dose distribution from the TTFields array was small and surface dose was not increased to clinically meaningful levels. Given the significant survival benefit demonstrated by the TTFields array in the adjuvant setting for glioblastoma, it is therefore important to conduct prospective clinical trials to systematically investigate potential synergistic effects of the anti-mitotic electromagnetic therapy concurrent with radiation therapy. Our study shows that this may be feasible without adverse interaction. The use of hypofractionated alternate day treatments lends itself for array changes without interrupting therapy, and may lead to its usefulness in H&N (Yazici et al. Radiat Oncol 2013;8:242) and prostate SBRT (King et al. IJROBP 2012;82(2):877-882) also exploiting delayed tumor cell kill after high dose per fraction radiation (Song et al. IJROBP HyTEC issue, In Press).