Title

RTHP-02. CHARACTERIZATION AND EVOLUTION OF RADIOTHERAPY-INDUCED VASCULAR INJURY AND CORRESPONDING CHANGES IN WHITE MATTER STRUCTURE: AN INVESTIGATIVE STUDY IN 125 PATIENTS WITH GLIOMAS

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maintenance treatment with TMZ. In the past 3 years, several publications demonstrated that besides exerting anti-mitotic effects, TTFields can also inhibit DNA Damage Repair (DDR), thus leading to enhanced efficacy. Taken together with the fact that in most cancer types an earlier treatment start is favorable, applying TTFields in concomitant with radiotherapy (RT) shortly after diagnosis, has the potential to improve treatment outcome. The goal of the present work was to explore efficacy and safety aspects of TTFields application together with RT. The efficacy of TTFields application after RT was tested in glioma cells based on their survival rates. Effect on DDR was tested using the alkaline comet assay or by analyzing γH2AX or Rad51 foci formation and resolution. RT energy absorption by the transducer arrays was measured by applying RT doses of 2 Gy through the transducers placed on a solid-state phantom. Skin toxicities were tested in rats irradiated with 2 Gy, 5 times a week for 2 weeks through arrays placed on the dorsal skin. Applying TTFields shortly after irradiation, synergistically enhanced the effect of RT in glioma cells. Application of TTFields to irradiated cells impaired DDR, possibly by blocking homologous recombination. The presence of the transducer caused a minor reduction (<4%) in irradiation intensity at 20 mm and 60 mm below the arrays but led to a significant increase (344%) in irradiation dosage at the phantom surface. Transducer arrays on the rat skin during irradiation exposure did not lead to adverse skin reactions. Results support the application of TTFields therapy before and immediately after RT as a viable treatment regimen to enhance the outcome of RT.

RADIATION THERAPY

RTHP-01. SPECTROSCOPIC MRI PREDICTS RECURRENCE PATTERNS IN GLIOBLASTOMA

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Radiation therapy (RT) targeted by conventional MRI may not fully identify the tumor profile of (GBM), which may in part account for high recurrence rates. Identifying the extent of GBM margins remains a challenging task due to the infiltrative nature of these tumors and limitations in current standard imaging methods. Multiple studies have demonstrated that MR spectroscopic imaging, or spectroscopic MRI (sMRI), can detect areas of infiltrating tumor with a high degree of sensitivity, and could be an essential tool in targeting tumor margins. sMRI enables the identification of non-enhancing, infiltrating cells that are marked by increased Choline/N-Acetylaspartate ratio (Cho/NAA), including regions undetected by standard MRI and therefore left untreated. sMRI shows considerable promise for improving the efficacy of RT and may delay recurrence. In this study, we correlated pre-treatment sMRI metabolite maps with recurrence patterns to validate that sMRI could provide coverage for untreated regions that later recurred, and provide support for its adjunctive use in tumor contouring for RT planning. In an ongoing NCI-funded trial (U01CA172027), metabolite and their ratio maps were obtained pre-chemoradiation and normalized to the patient's normal-appearing contralateral white matter (NAWM) and then compared to contrast-enhancing recurrence patterns with at least 6 months follow-up. A Cho/NAA ratio of twice the NAWM mean was used to identify regions of potential infiltration in our patients, and the resulting planning target volumes were compared with actual treated target volumes based on conventional MRI. For 9 out of 11 cases, the addition of sMRI data expanded RT volumes to better encompass regions of tumor recurrence, which were not completely covered by the CTV60. Thus, RT planning for GBMs augmented by sMRI could reduce recurrence rates. A multi-institutional clinical trial has been initiated to prospectively assess potential for sMRI to guide RT and assess treatment response (R01CA214557).

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INTRODUCTION: While radiation therapy (RT) remains a standard practice in the upfront treatment of high-grade gliomas and low-grade gliomas at the time of recurrence, it is often associated with long-term effects including vascular injury and cognitive decline. The former typically manifests as size-varying hemosiderin deposits in the brain called cerebral microbleeds (CMBs), and can be accompanied by changes in the surrounding white-matter (WM) microstructure. As the median survival of lower grade gliomas can be 10 years or longer with current treatment strategies, minimizing the deficits incurred through treatment becomes especially important. Prior studies have shown increases in CMB formation over time that were dependent on RT dose and were not observed in patients treated only with chemotherapy. The goal of this study was to characterize the evolution of CMBs in a much larger cohort with serial scans and relate their changes over time to alterations in WM structure. **METHODS:** 125 patients (age:46 ± 12) were scanned on a 7-Tesla GE scanner either once or serially for 2-8 scans. The cohort included patients treated with RT for a glioma 2 months to 27 years prior, and a subset of nonirradiated control patients. Susceptibility-weighted vascular imaging and multi-directional, multi-shell diffusion-tensor imaging were acquired. Characteristics of RT-induced CMBs were evaluated within- and across patients, correlated with clinical and treatment parameters, and related to global and local WM changes. **RESULTS:** Total CMB burden increased over time and was more severe for larger irradiated volumes and frontal lobe tumors. WM fractional anisotropy and diffusivity changes initially decreased as a function of CMB burden before improving approximately 6 years post-treatment. **CONCLUSIONS:** Although there was initially a direct relationship between RT-induced vasculature injury and degradation of WM microstructure, changes in WM structure appeared to be reversible over time, whereas CMBs, potential markers of vascular injury, persisted.

RTHP-03. PROGNOSTIC IMPACT OF TIMING BETWEEN SURGERY AND RADIOTHERAPY (RT) IN PATIENTS WITH GLIOBLASTOMA (GBM)

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OBJECTIVE: This retrospective study evaluates whether the time interval between surgical resection and start of radiotherapy impacts outcomes in patients with newly diagnosed GBM. **METHODS:** Adult patients with GBM who were followed with serial imaging after concurrent RT and temozolomide between January 2007 and December 2013 at a single tertiary cancer center were included. Prognostic factors including age, Karnofsky performance status (KPS), extent of surgery, and interval between surgery and start of RT were collected. Extent of surgery was categorized as either gross total resection (GTR) or other. Outcomes included overall survival (OS) and progression free survival (PFS). Univariate (UVA) and multivariable (MVA) analyses were conducted using cox proportional hazard models. **RESULTS:** A total of 150 patients with median age of 55 (range 21-73) were analyzed. Median time interval was 26 days [interquartile range (IQR) 21-33, range 8-62] and median survival was 26 months [IQR 12-49, range 0-98]. On UVA, age (HR 1.03, p< 0.0001; CI 1.02-1.05), KPS (HR 0.97, p= 0.001; CI 0.95-0.99), and GTR (HR 0.65, p= 0.03; CI 0.44-0.95) were prognostic for OS, whereas shorter time interval (HR 1.3, p= 0.17; CI 0.89-1.90) was not prognostic for OS. Shorter time interval (HR 1.39, p= 0.06; CI 0.99-1.96) was also not prognostic for PFS. On MVA, age (HR 1.03, p= 0.0002; CI 1.02-1.05), KPS (HR 0.98, p= 0.02; CI 0.96-0.99), and GTR (HR= 0.65, p= 0.03; CI 0.44-0.96) were independent predictors for OS. **CONCLUSION:** Within this cohort of patients who largely started RT between 3 to 5 weeks of surgery, the particular time interval between surgery and RT was not prognostic for OS or PFS. Studies that include patients with longer time intervals between surgery and RT may identify a threshold time interval beyond which time interval becomes negatively prognostic for OS.

RTHP-04. DOSIMETRIC IMPACTS FROM A TUMOR TREATING FIELDS (TTFIELDS) DEVICE FOR GLIOBLASTOMA MULTIFORME (GBM) PATIENTS UNDERGOING SIMULTANEOUS RADIATION THERAPY

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PURPOSE: Recently an approach to treat Glioblastoma has been the introduced using tumor treating fields (TTFields), in which alternating electric fields are applied via transducer arrays to a patient's scalp. This