Title

NIMG-23. DEVELOPMENT OF PRACTICE ALGORITHMS TO GUIDE TREATMENT PLANNING WITH TTFIELDS FOR THE MANAGEMENT OF GLIOBLASTOMA

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volumes, apparent diffusion coefficient (ADC; reflecting tumor cellularity), K^{trans} (reflecting vascular permeability), and relative cerebral blood volume (rCBV) and flow (rCBF; reflecting perfusion) on spin echo (SE) and gradient echo (GE) sequences ($rCBV_{SE}$, $rCBF_{SE}$, $rCBV_{GE}$, $rCBF_{GE}$, respectively). RESULTS: Fourteen patients were included. Percent changes during treatment were compared to pre-treatment values. Within the CE region of interest (ROI), the respective median percent changes during CRT, post-CRT, and pre-cycle 2 were: CE volume -0.75%, 19.98%, 5.93%; ADC 10.15%, 18.03%, 27.21%; K^{trans} 32.05%, 22.48%, 7.06%; $rCBV_{SE}$ -18.82%, -33.21%, -32.86%; $rCBF_{SE}$ -11.42%, -28.80%, -26.99%; $rCBV_{GE}$ -17.05%, -23.92%, -30.39%; and $rCBF_{GE}$ -21.98%, -24.29%, -32.12%. Within the peri-tumoral FLAIR ROI, the respective median percent changes during CRT, post-CRT, and pre-cycle 2 were: FLAIR volume 20.36%, 80.29%, 69.36%; ADC -3.63%, 6.59%, 11.51%; K^{trans} 5.88%, -7.40%, -31.45%; $rCBV_{SE}$ -11.62%, -34.60%, -20.18%; $rCBF_{SE}$ -0.31%, -22.42%, -25.23%; $rCBV_{GE}$ -0.80%, -13.05%, -22.32%; and $rCBF_{GE}$ 6.30%, -6.25%, -19.57%. CONCLUSIONS: Chemoradiation in nGBM results in increased edema and permeability early during treatment, likely related to tumoral and peri-tumoral inflammation; decreased tumor cellularity, reflected by increased ADC; and decreased perfusion. ADC, K^{trans}, and perfusion parameters are thus helpful in better characterizing tumor microenvironment during treatment.

NIMG-23. DEVELOPMENT OF PRACTICE ALGORITHMS TO GUIDE TREATMENT PLANNING WITH TTFIELDS FOR THE MANAGEMENT OF GLIOBLASTOMA

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TTFields are becoming a key modality in the management of glioblastoma, and are delivered to patients in 2 paired orthogonal planes via direct application of transducer arrays to the shaved scalp. Array placement is planned through the NovoTAL software using MRI morphometric head size and tumor location measurements. As TTFields non-uniformly distribute through the brain parenchyma, treatment planning aims to optimize field intensity delivered to the tumor volume. Tumors can be radiographically heterogeneous, presenting with enhancing and/or nonenhancing areas on imaging. Newly diagnosed patients may receive TTFields following a gross total resection with no post-op MRI enhancement and interpreting imaging in recurrent disease may be complicated due to the effects of prior therapies and patterns of recurrence. Therefore clinical guidance is needed for physicians to appropriately plan TTFields across a spectrum of clinical scenarios, and to ensure standardization of practices across specialties and institutions. Neuro-oncologists with significant collective TTFields planning experience (mean 31, range 15-68 cases in 2015) collaboratively developed TTFields treatment planning algorithms, which have been prospectively incorporated into draft practice guidelines developed for the multi-disciplinary team caring for glioblastoma patients. Algorithms were developed for enhancing and non-enhancing tumors in the newly diagnosed and recurrent disease settings, for multi-focal and gross totally resected tumors, and for assessing response to therapy in these diverse clinical settings. Guidance has also been developed for re-planning therapy based on sequential imaging changes. CONCLUSIONS: TTFields in combination with TMZ have improved overall survival in newly diagnosed glioblastoma. As TTFields become increasingly incorporated into standard glioblastoma management, clinical practice guidelines are acutely needed in order to optimize efficacy and outcomes via standardization of treatment across patients and institutions. The development of these algorithms represents the first-ever clinical practice guidelines for the use of TTFields in glioblastoma.

NIMG-24. CLINICAL CORRELATES OF PATHOLOGY-CONFIRMED PSEUDOPROGRESSION IN GLIOBLASTOMA MULTIFORME - EXPERIENCE OVER FIVE YEARS.

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INTRODUCTION: Glioblastoma multiforme (GBM) patients are typically followed closely with serial magnetic resonance imaging (MRI) but discerning true disease progression from treatment-related changes or "pseudoprogression" is challenging. Metrics to distinguish these processes such as RANO criteria are helpful, but can often be imprecise. Here we report a series of glioblastoma patients at first imaging recurrence who underwent repeat biopsy or surgical resection, and examined their clinical course as it relates to their ultimate pathology. METHODS: Surgical operative reports over five years at a single institution were reviewed for cases of surgery for first recurrence of glioblastoma. Pathology results were reviewed to determine true progression versus pseudoprogression (necrosis, gliosis, and/or inflammation without viable tumor). Patient demographics, time from completion of radiation and chemotherapy, corticosteroid use, symptoms, and suggestion of pseudoprogression in the preoperative MRI report were recorded. RESULTS: 83 patients were identified. Of these, 15 (18%) demonstrated pseudoprogression. Repeat resection within three or six months after completing radiation was associated with an increased rate of pseudoprogression (odds ratio 8.25 [1.24-54.72], p=0.03 and 7.49 [2.18-25.72] p=0.001, respectively). Corticosteroid treatment at presumed recurrence and the presence of clinical symptoms were not significantly associated with treatment effect versus true disease progression (odds ratios 2.63 [0.68-10.21] p=0.18, 1.45 [0.47-4.44] p=1.0, respectively). Five of 15 patients with pseudoprogression met all RANO criteria for disease progression. Seven of 15 patients met radiographic criteria but were asymptomatic. CONCLUSION: Identifying treatment-related changes versus true disease progression in patients with "recurrent" GBM presents a significant challenge. Current clinical and imaging metrics are insufficient to clearly delineate the two entities. Identifying a larger patient cohort with histologically-proven pseudoprogression may be helpful in delineating MRI correlates of this phenomenon.

NIMG-25. RADIOMIC PROFILING MAPS AREAS OF PATHOLOGICALLY CONFIRMED TUMOR AND PREDICTS OVERALL SURVIVAL IN PRE-TREATMENT GLIOBLASTOMA

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INTRODUCTION: Quantifying tumor heterogeneity in glioblastoma (GBM) plays a critical role in diagnosis as well as therapy design. Magnetic resonance imaging (MRI) can be used to identify and differentiate heterogeneous GBM characteristics such as hypercellularity, necrosis, and treatment effects. This study involves encoding four different types of MRI contrasts to produce a single radiomic image and quantify both inter and intra tumor heterogeneity. We hypothesized that patient prognosis can be predicted by the volume and location of specific radiomic profiles (RP) prior to therapy. METHODS: Initial imaging data from 82 patients pre-treatment was retrospectively analyzed for this experiment. This included T1 (pre and post Gd contrast), apparent diffusion coefficient (ADC), and fluid attenuation inversion recovery (FLAIR) images. The volume of each RP was assessed on a patient by patient basis within the T1 enhancement and FLAIR hyperintensity. These values were normalized by tumor size to correct for known relationships between tumor size and prognosis. We first performed an exploratory analysis correlating RP volume to patient survival. A log-rank test with an iterative threshold was performed to determine what RP volume cutoff best predicted prognosis. The final pre-mortem imaging was analyzed similarly in three additional autopsied patients. Tissue samples were obtained from RPs that correlated with survival in the larger group. RESULTS: After correction for multiple comparisons, six RPs were significantly correlated with overall survival: three within contrast enhancement and three within FLAIR hyperintensity. Regions of pseudopalisading necrosis and hypercellular tumor were found in the areas indicated by these RPs. CONCLUSION: We present a pathologically-validated method for generating MRI-based radiomic profiles correlated with overall survival in patients with glioblastoma. These predictive profiles were generated prior to treatment, indicating potential as a precision medicine tool.

NIMG-26. PERIODIC TRANSDUCER ARRAY SHIFTING PRESERVES BOTH TTFIELDS INTENSITY IN THE GROSS TUMOR VOLUME (GTV) AND PROMOTES SCALP HEALTH DURING THE COURSE OF GLIOBLASTOMA THERAPY

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OBJECTIVES: TTFields are delivered locally to the brain in glioblastoma patients through the continuous application of insulated ceramic transducer arrays placed on the scalp. Skin irritation under the arrays is the most common adverse event associated with treatment and can generally be prevented with periodic array shifting back and forth (in a prescribed direction) at each array change. Maintaining scalp health is critical given the continuous mode of delivery and minimum duration of compliant treatment required to observe antitumor effects. Given the non-focal nature of TTFields delivery, this study examines the impact of periodic array shifting on the EF intensity delivered