Title

RTHP-11. REIRRADIATION OF RECURRENT HIGH GRADE GLIOMAS: OUTCOMES AND PROGNOSTIC FACTORS

Journal

Neuro-oncology, 20(Suppl 6)

ISSN

1522-8517

Authors

Chapman, Christopher
Hara, Jared
Clarke, Jennifer
et al.

Publication Date

2018-11-01

Peer reviewed

/ Boston Childrens Hospital, Boston, MA, USA, 5Massachusetts General Hospital, Boston, MA, USA

BACKGROUND: Standard treatment for medulloblastoma in children over age 3 includes resection and radiotherapy, followed by chemotherapy. Some studies have found disease control decrements if chemotherapy was delivered before radiotherapy. However, these studies recommended radiation interruptions for hematologic toxicity, which were more severe in children receiving chemotherapy prior to craniospinal radiotherapy. We report outcomes of pediatric medulloblastoma patients treated postoperatively with radiotherapy-first (RT1) or chemotherapy-first CT1). POPULATION/METHODS: 206 patients age 2–23 years with medulloblastoma were treated with proton radiotherapy from May 2000 to December 2016. We analyzed the effect of sequencing radiotherapy first (n=164) or chemotherapy first (n=42) after surgery on event-free (EFS) and overall survival (OS) controlling for known risk factors. RESULTS: Median follow-up was 5.8 years. Children who received CT1 sequencing were younger (p<0.0001), more likely to receive high-dose chemotherapy (p<0.001), have high/intermediate risk disease (p<0.0001), M1-M3 stage (p<0.001), and large-cell/anaplastic histology (p=0.04). M1-M3 stage (p=0.01), high/intermediate risk disease (p=0.03), and anaplastic/large-cell histology (p=0.04) were all predictive of worse EFS. Despite higher proportions of risk factors in the CT1 cohort, 5-year EFS and OS in the RT1 versus CT1 groups were no different at 89% versus 84% (p=0.39) and 90% versus 84% (p=0.33), and remained equivalent when controlling for M1-M3 stage and unfavorable histology (p=0.86). Radiation treatment duration was equivalent at a median of 43 days (RT1) and 42 days (CT1) (p=0.4). Children with anaplastic/large-cell histology had lower EFS only in the RT1 cohort (64% vs. 87%, p=0.01) and equivalent EFS in the CT1 cohort (73% vs. 78%, p=0.88), suggesting a possible benefit to high-dose chemotherapy before RT in children with unfavorable histology. CONCLUSIONS: Disease control and overall survival were equivalent in the radiotherapy-first and chemotherapy-first cohorts when radiation treatment times were minimized.

RTHP-09. DYSREGULATION OF Wnt SIGNALING PATHWAY CORRELATES WITH TREATMENT OUTCOME IN GLIOBLASTOMA MULTIFORME

Eric Weterings[1], Christopher Morrison[1], Nicholas Gravbrot[2], Michael Hammer[3], Daruka Mahadevan[1] and Baldassarre Stea[4]; [1]University of Arizona, Tucson, AZ, USA, [2]Department of Radiation Oncology, University of Arizona College of Medicine, Tucson, AZ, USA, [3]University of Arizona Cancer Center, Tucson, AZ, USA, [4]University of Arizona Medical Center-University Campus, Tucson, AZ, USA

Glioblastoma multiforme (GBM) is the most common and most aggressive primary brain cancer with a median life expectancy of 13–15 months after surgery and chemo-radiation treatment. GBM is hallmarked by a poor response to radiation therapy (RT), which is generally attributed to upregulation of several DNA repair pathways. To identify pathways which predict poor chemo-radiation treatment outcome, we conducted a retrospective clinical-genetic study in which we evaluated the mRNA expression profiles of 24 GBM tumor samples, stratified on the basis of patient survival post chemo-radiation treatment. All patients were treated at our institution by surgical resection and intensity-modulated RT with concurrent and adjuvant temozolomide. Expression profiles were obtained utilizing a commercially available PanCancer Pathways Panel (NanoString Technologies, Inc.). Our data analysis shows a distinctly significant correlation between 5 members of the Wnt pathway and overall patient survival. A 2- to 9-fold higher expression of negative regulators of the Wnt pathway and a 2- to 3-fold lower expression of positive Wnt regulators was observed in tumor material of patients with a longer than median survival. We conclude that upregulation of the Wnt pathway correlates with poor chemo-radiation treatment outcome in GBM. *In vitro* experimentation by other groups has recently demonstrated a role for Wnt signaling in activation of Non-Homologous End-Joining mediated DNA double-strand break repair and the subsequent onset of radio-resistance. These preliminary findings support the hypothesis that the Wnt pathway may be used as a predictive marker for RT outcome in GBM and suggest new strategies to increase the radiation sensitivity of GBM.

RTHP-10. LESS IS MORE OR BIGGER IS BETTER? RADIATION TREATMENT VOLUME FOR GLIOBLASTOMA PATIENTS DOES NOT IMPACT SURVIVAL

Andrew Song[1], Sonia Gowda[2], Maria Werner-Wasik[1], Voichita Bar-Ad[1], Lyndon Kim[1], Jon Glass[1], Kevin Judy[1], Christopher Farrell[1], David Andrews[1] and Wenyin Shi[1]; [1]Thomas Jefferson University, Philadelphia, PA, USA, [2]Drexel University, Philadelphia, PA, USA

PURPOSE: To investigate if the extent of the planning target volume (PTV) for glioblastoma (GBM) patients receiving adjuvant radiation treatment (XRT) has correlation with survival. METHODS: We retrospectively examined patients with newly diagnosed GBM received adjuvant radiation at our institution from 2011 to 2016. Our institution follows the RTOG guidelines for GBM volumes. We included 87 patients with sufficient follow up. We examined the treatment plan documents to determine the PTV treated to 46 Gy (PTV46) and 60 Gy (PTV60). We measured overall survival (OS) as well as progression-free survival (PFS). We performed summary statistics on baseline patient characteristics, Kaplan-Meier analysis for outcomes with log-rank tests to compare PTV subgroups as well as Cox regression analysis for treatment volume. RESULTS: Of the 87 patients for analysis, 42 were female and 45 were male. Median age was 61 y/o, with median follow-up of 16.6 months (range 2.6 to 61.1 months). For PTV46 analysis, 1 patient was excluded due to receiving whole brain radiation to 40 Gy before receiving cone down to total 60 Gy. Median PTV60 was 297.9 cc (120.04 to 907.6 cc) while median PTV46 was 452 cc (120.04 to 907.6 cc). OS at 1 year was 67.8% and at 2 years was 32.2%, with median OS of 16.6 months. PFS at 6 months was 58.6% and at 1 year was 27.6%, with median time to progression of 6.8 months. On Cox regression analyses, neither PTV46 nor PTV 60 were statistically significant correlated with OS (p=0.11 and 0.68) and PFS (p=0.54 and 0.64). On log rank test, neither PTV46 nor PTV60 subgroups have any statistically significant survival differences, for PFS or OS. CONCLUSION: Extent of PTV does not appear to have an impact on recurrence or survival for GBM. Further validation with an independent dataset is warranted.

RTHP-11. REIRRADIATION OF RECURRENT HIGH GRADE GLIOMAS: OUTCOMES AND PROGNOSTIC FACTORS

Christopher Chapman, Jared Hara, Jennifer Clarke, Nicholas Butowski, Susan Chang, Shannon Fogh, Penny Sneed, Jean Nakamura, David Raleigh and Steve Braunstein; University of California San Francisco, San Francisco, CA, USA

PURPOSE/OBJECTIVE(S): Identify prognostic factors for progression-free survival (PFS) and overall survival (OS) after reirradiation (re-RT) for recurrent high grade glioma (HGG). MATERIALS/ METHODS: Patients with HGG received re-RT from 2010 to present. PFS and OS prognostic variables were examined using Cox models. Receiver operative curve (ROC) analysis identified predictive thresholds for continuous variables. RESULTS: 58 patients received surgery and adjuvant radiation for HGG (51 grade IV, 7 grade III). The median time to first progression after initial radiation was 11 months. 36% received single fraction stereotactic re-RT (SRS) (median 18 Gy) and 64% received fractionated re-RT (median 35 Gy in 10 fractions). The median planning target volume (PTV) was 16.8 mL. The median biologically effective dose (BED10) of re-RT was 47 Gy (range 15–72). 50% received chemotherapy and 36% received bevacizumab concurrent to re-RT. Toxicity ≥ grade 3 was 7%. The median PFS after re-RT was 4.7 months and the median OS was 11 months. Lower PFS was significantly associated with shorter time to first progression, lower KPS, and lower re-RT dose. Lower OS was associated with shorter time to first progression, lower KPS, and larger PTV. Other factors were not significantly associated with PFS or OS. ROC analysis of time to first progression and re-RT dose showed best predictive thresholds at time > 12 months and BED10 > 42 Gy. CONCLUSIONS: Reirradiation was tolerated with infrequent high grade toxicity. PFS and OS after re-RT were both predicted by time to progression after initial radiation. Published prognostic scores have used total time from first to second radiation courses; however in our series the period from initial progression to re-RT did not add prognostic information. There was evidence for a dose threshold irrespective of radiotherapy technique. Use of chemotherapy and bevacizumab with re-RT were not associated with improved outcomes.

RTHP-12. COMPARATIVE ANALYSIS OF TUMOR TREATING FIELDS USING CONVENTIONAL VERSUS ALTERNATIVE ARRAY PLACEMENT FOR POSTERIOR FOSSA GLIOBLASTOMA

Edwin Lok, Pyay San, Victoria White and Eric Wong; Beth Israel Deaconess Medical Center, Boston, MA, USA

BACKGROUND: There is an alternative transducer array placement configuration to treat infratentorial tumors using TTFields but coverage for posterior fossa glioblastoma is unknown. METHODS: Patient anatomy-based models were created by segmenting MRI images into tissue "masks". The physical properties and boundary conditions for physics modeling were set up within COMSOL Multiphysics. Electric field maps were compared for models using conventional array placement for supratentorial tumors versus alternative array placement for infratentorial tumors. Electric field–volume histograms (EVHs) and specific absorption rate–volume histograms (SARVHs) were constructed to evaluate volumetric differences between models. RESULTS: The alternative configuration consists of array placement at the vertex, the bi-occipital regions and the upper neck. Highest E_{AUC} was found at the epidural space surrounding the spinal cord and scalp for both types of configurations, whereas the lowest was located at the