potentially influence the prognosis. Furthermore, advanced diagnostic and therapeutic developments may provide novel prognostic factors. As a pretreatment variable, diffusion-weighted (DW) magnetic resonance imaging (MRI) with quantitative apparent diffusion coefficient (ADC) can be a clinical biomarker. Many neurosurgeons advocate tumor resection as extensive as possible and early postoperative MRI within 72 hr after surgery is thought to reliably detect residual tumors. The purpose of this study was to determine which factors can predict survival more convincingly in patients with GBM.

Materials/Methods: Between January 2000 and September 2009, 138 patients with GBM underwent postoperative RT and longitudinal MRI preoperatively, in the early postoperative period, and at 1-month intervals thereafter until recurrence. On early postoperative MRI, the surgical status was classified into biopsy, partial resection (PR), and gross total resection (GTR). Patient age, Karnofsky performance scale (KPS) score, minimum ADC, and surgical status were assessed by factor analysis of overall survival (OS). Radiation therapy oncology group-recursive partitioning analysis (RTOG-RPA) criteria were used to validate prognostic values of the MRI-derived factors, i.e., minimum ADC and surgical status. Kaplan-Meier survival curves, the log-rank test, and the multivariate Cox proportional hazards model were used to evaluate the prognostic factors.

Results: Median OS associated with low ($< 0.93\times10^{-3}$ mm^2/sec) and high ($\geq 0.93\times10^{-3}$ mm^2/sec) minimum ADC was 11.2 and 18.0 months, respectively ($p < 0.001$). According to surgical status, median OS associated with biopsy or PR and GTR was 11.7 and 18.9 months, respectively ($p < 0.001$). Substantial independent prognostic factors were KPS score (hazard ratio = 1.812; 95% confidence interval (CI), 1.185-2.771), minimum ADC (2.365; 95% CI, 1.482-3.776), and surgical status (1.777; 95% CI, 1.073-2.943). The MRI-derived factors assigned patients to different prognostic groups in RTOG-RPA classes and stratified into high risk of low minimum ADCs with residual tumors, low risk of high minimum ADCs without residual tumors, and intermediate risk of the others. Median OS among low, intermediate, and high risk group was 28.2, 14.7, and 10.8 months, respectively ($p < 0.001$).

Conclusions: The minimum ADC on pretreatment DW-MRI and surgical status on early postoperative MRI can predict survival in patients with GBM.

Author Disclosure: R. Murakami: None. H. Nakamura: None. T. Hirai: None. M. Kitajima: None. Y. Nakaguchi: None. S. Nishimura: None. H. Uetani: None. J. Kuratsu: None. Y. Yamashita: None.

2133 Results of Early Reoperation for Suspected Pseudoprogression in Patients with Glioblastoma Multiforme

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Purpose/Objective(s): Many patients with glioblastoma multiforme (GBM) develop apparent radiologic progression after standard chemotherapy and radiation. A subset of these patients has no evidence of active tumor at the time of re-operation. We performed a retrospective analysis of patients undergoing reoperation for suspected tumor progression at a single high-volume academic institution.

Materials/Methods: Patients were included in this review if the following criteria were fulfilled: 1) diagnosis of GBM; 2) completion of concurrent temozolomide and radiation therapy with or without maintenance temozolomide; 3) surgical re-exploration within one year of completing adjuvant chemoradiation therapy. Patient data were collected by chart review and the protocol was approved by the institutional IRB.

Results: From 2005 to 2009, 38 patients with an initial surgical diagnosis of GBM met the above eligibility criteria. At initiation of therapy, median age was 56 years (range, 33 - 80), 55% were male, and 66% had Karnofsky performance status of >90. Median overall survival for the entire cohort of patients was 16.2 months from the time of initial surgery. All reoperations were debulking surgeries rather than needle biopsies and pathology demonstrated that 32% of patients had quiescent tumor or necrosis (95% CI 18 - 49%) and 68% of patients had active GBM. Patients younger than 55 were more likely to have active tumor at the time of re-operation compared with older patients (87% vs 55%, $p = 0.03$). There was no significant difference in the median time elapsed before second surgery in patients with necrosis/quiescent tumor (8.5 months, 95% CI 6.5 - 10.5 months) compared to those with active GBM (9.2 months, 95% CI 8.1 - 10.3 months). Patients with active tumor at the time of second surgery had a twofold increase in hazard of death (HR 1.95, 95% CI 0.8 - 4.6) using a Cox proportional hazard model adjusted for age, performance status, and extent of resection. Median survival following second surgery was 5 months for patients with active tumor vs. 10 months for patients with quiescent tumor/necrosis.

Conclusions: During the first year after diagnosis of GBM over 30% of our patients undergoing a second debulking surgery for radiologic progression had no evidence of active tumor. Time elapsed before reoperation was not a significant factor in determining whether a patient will be found to have pseudoprogression versus recurrent disease. However, pathology at the time of reoperation is an important prognostic factor. It should be noted that 1) patients selected for repeat debulking surgery may not be representative of all GBM patients and 2) pathologic interpretation may vary from institution to institution which could limit the generalizability of this data.

Author Disclosure: S.G. Yovino: None. X. Ye: None. S. Grossman: None.

2134 Does the Timing of Radiotherapy Impact Survival of Glioblastoma Multiforme Patients?

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Purpose/Objective(s): The current standard treatment of glioblastoma multiforme (GBM) is maximal safe surgical resection followed by radiotherapy (RT) with concurrent and adjuvant temozolomide (TMZ) chemotherapy; however the

optimal time of RT after surgery and the effect of timing on prognosis are controversial. GBM patients from 15 centers were retrospectively reviewed in order to investigate the effect of time interval between surgery and initiation of RT on prognosis.

Materials/ Methods: In this study, 1288 patients with newly diagnosed, pathologically confirmed GBM treated between 1997 and 2008 were evaluated. Median age was 55 years (range 18-86 years), median KPS score was 80 (range 30-100). Type of surgery was gross total resection in 54%, subtotal resection in 36% and stereotactic biopsy in 10%. All patients received median dose of 60 Gy (range 4-72 Gy) RT, 45 % received concurrent TMZ and 38 % received adjuvant TMZ.

Results: The median time between surgery and RT was 28 days (range 1-220 days). Median progression free survival and overall survival (OS) were found to be 7 months and 12 months, respectively, for the all cohort. The median OS for patients with waiting times of less than or equal to 28 days and >28 days, were 12 months and 13 months, respectively ($p = 0.001$). The median OS differed significantly between patients whose KPS scores were less than or equal to 70 and >70 (10 vs. 14 months, $p<0.0001$). Younger age (<55 years) also correlated with better OS (14 vs. 11 months, $p<0.0001$). The median OS was also significantly different between patients who received RT with concurrent TMZ and RT only (15 vs. 10 months, p28 days were 13 months and 16 months respectively ($p = 0.021$).

Conclusions: In this study longer time intervals between surgery and RT did not show any negative effect on survival in GBM patients. In fact, waiting times of >28 days were correlated with better survival with a higher effect on patients receiving concurrent TMZ. This is a subject that needs further clinical and radiobiological research.

Author Disclosure: E.K. Tezcanli: None. A. Ucuncu: None. S. Sarihan: None. A. Aksu: None. C. Eroglu: None. G. Alco: None. S. Kamer: None. M. Ekenel: None. S. Aytac Arslan: None. U. Abacioglu: None.

2135 Stereotactic Radiation Treatment in Recurrent High-grade Glioma

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Purpose/Objective(s): High-grade gliomas (HGG) are aggressive malignant tumors characterized by resistance to available therapies. Salvage options for recurrent HGG are limited but stereotactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (FSRT) is often used. We sought to determine the efficacy of stereotactic treatment in recurrent HGG.

Materials/Methods: Between 1998 and 2008, 47 patients with recurrent HGG (29 WHO grade IV, 18 WHO grade III) were treated with salvage SRS (n = 32) or SRT (n = 15). All patients received initial postoperative fractionated RT to a median dose of 60 Gy; 32 patients (68%) received concurrent temozolomide. Thirty-six patients (77%) also received salvage chemotherapy. Log-rank tests and Cox regression models were used to analyze survival outcomes.

Results: Median follow-up interval from diagnosis was 26 months (range, 6-216). Median PFS was 18 months (95%CI: 13-34) for grade III patients versus 5 months (95%CI: 4-9) for grade IV patients ($p < 0.001$). Median OS was 52 months (95% CI: 36-125) for grade III versus 21 months (95%CI: 15-27) for grade IV patients ($p < 0.001$). Median OS from re-irradiation was 33 months (95%CI: 4 - 57) for grade III patients versus 13 months (95%CI: 10 - 16) for grade IV patients ($p = 0.07$). Median OS from re-irradiation for patients who received ≥37.5 (median BED) was 16 months (95% CI: 11-20) versus 10 months (95% CI: 2-23) for patients who received <37.5 ($p < 0.05$). A similar improvement was associated with patients who received salvage chemotherapy where median OS from re-irradiation was 16 months (95% CI: 11-29) versus 6 months (95% CI: 2-13, $p < 0.05$).

Conclusions: SRS or hypofractionated FSRT is an effective salvage option in carefully selected patients with small and localized recurrences of HGG. Grade III disease, use of salvage chemotherapy, and BED ≥37.5 were associated with improved survival.

Author Disclosure: M. Abazeed: None. A. Niemierko: None. A. Abazeed: None. J.S. Loefller: None. K. Oh: None.

2136 A Pilot Study of Low-dose Fractionated Radiotherapy and Chemotherapy as Second-line Treatment for Recurrent or Progressive Glioblastoma Multiforme: A Final Report

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Purpose/Objective(s): Standardized salvage treatment in recurrent or progressive glioblastoma multiforme (GBM) patients, who previously received radiotherapy plus concomitant and adjuvant temozolomide (TMZ), has not yet been defined. Hyperradiosensitivity of human malignant glioma cell lines to low doses fractionated radiotherapy (LD-FRT) and a synergism between LD-FRT and chemotherapy have been demonstrated by several *in vitro* and preclinical studies. To evaluate the feasibility and efficacy of this approach, we performed a prospective pilot study in which LD-FRT and concurrent chemotherapy was used in patients with recurrent or progressive GBM.

Materials/Methods: We enrolled patients with radiological diagnosis of recurrent or progressive GBM, previously treated by surgical resection followed by 3D-CRT (total dose 59,4 Gy) plus concomitant and adjuvant TMZ. If recurrent or progressive disease was observed during TMZ, patients received 30 cGy twice a day on days 1-2,8-9,15-16, q42, concurrently with cisplatin (30 mg/m^2 on days 1, 8, 15) and fotemustine (40 mg/m^2 on days 2, 9, 16), whereas if it was observed during the follow-up we used 40 cGy twice a day, over consecutive 5 days, q 28, concurrently with TMZ (150/200 mg/m^2). Primary endpoints were safety and toxicity (RTOG criteria); Clinical response (RECIST criteria), Progression Free Survival (PFS) and Overall Survival (OS) were also evaluated.

Results: From February 2008 to January 2011, 20 patients were enrolled. The median total dose of LD-FRT delivered was 760 cGy (range, 240-1200). Thirteen patients received LD-FRT and TMZ, 7 patients received LD-FRT with cisplatin and fotemustine.