tumor volume reduction than meningiomas that were 2 (8.94% vs. 7.59% per year). These results suggest that a notable tumor volume reduction is predicted within 3 to 4 years after irradiation, and thereafter, the tumor volume decreases at a slower rate for more than 10 years.

Conclusions: The quantitative volumetric analysis of the pattern of tumor volume reduction in response to irradiation gives an insight into the radiobiological nature of intracranial meningiomas after conventionally fractionated radiation therapy.

PO-0797
Hyperfractionated concomitant boost proton radiotherapy for supratentorial glioblastoma multiforme
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Purpose/Objective: To evaluate the safety and efficacy of postoperative hyperfractionated concomitant boost proton radiotherapy for supratentorial glioblastoma multiforme (GBM).

Materials and Methods: Forty-six patients with supratentorial GBM were treated by high dose (96.6 GyE) photon and proton radiotherapy. There were 24 males and 22 females, and the median age was 58 years old (range: 24 - 76). The KPS were 50, 60, 70, 80, 90, and 100 % in 1, 4, 10, 12, 11, and 8 patients, respectively. The median MIB-1 index was 30.8 (range: 5-70). The gross total resection, subtotal resection, and partial resection were performed for 2, 29, and 15 patients, respectively. Photon beam were delivered to the T2-weighted high area on magnetic resonance imaging (MRI) in the morning (50.4 Gy in 28 fractions). More than 6 hours later, proton beams were delivered to the enhanced area plus a 10-mm margin in the first half of the protocol (23.1 GyE in 14 fractions) and to the enhanced volume in the latter half (23.1 GyE in 14 fraction). Concurrent chemotherapy with nimustine hydrochloride (80 mg/m2) during first and fourth weeks or daily temozolomide (75mg/m2) was administrated in 23 and 23 patients, respectively.

Results: The overall survival rates after 1 and 2 years were 80.4% and 44.6%, respectively. The median survival period was 21.1 months (95% CI: 13.0-29.1). The 1- and 2-year progression-free survival rates were 34.8% and 8.7%, respectively. There was no significant survival difference between nimustine hydrochloride and temozolomide groups respectively. Late radiation necrosis and leukoencephalopathy were seen in 11 and 2 patients, respectively, but all patients with radiation necrosis were controllable. There was no significant survival difference between nimustine hydrochloride and temozolomide groups respectively. The 1- and 2-year progression-free survival rates were 34.8% and 8.7%, respectively. The median survival period was 21.1 months (95% CI: 13.0-29.1). The 1- and 2-year progression-free survival rates were 34.8% and 8.7%, respectively. There was no significant survival difference between nimustine hydrochloride and temozolomide groups respectively. The overall survival rates after 1 and 2 years were 80.4% and 44.6%, respectively. The median survival period was 21.1 months (95% CI: 13.0-29.1). The 1- and 2-year progression-free survival rates were 34.8% and 8.7%, respectively. There was no significant survival difference between nimustine hydrochloride and temozolomide groups respectively. The overall survival rates after 1 and 2 years were 80.4% and 44.6%, respectively. The median survival period was 21.1 months (95% CI: 13.0-29.1). The 1- and 2-year progression-free survival rates were 34.8% and 8.7%, respectively. There was no significant survival difference between nimustine hydrochloride and temozolomide groups respectively. The overall survival rates after 1 and 2 years were 80.4% and 44.6%, respectively. The median survival period was 21.1 months (95% CI: 13.0-29.1). The 1- and 2-year progression-free survival rates were 34.8% and 8.7%, respectively. There was no significant survival difference between nimustine hydrochloride and temozolomide groups respectively.

Conclusions: Hyperfractionated concomitant boost proton radiotherapy (96.6 GyE in 56 fractions) with nimustine hydrochloride or temozolomide for GBM was tolerable and beneficial for patients with supratentorial GBM.

PO-0798
Bevacizumab treatment in recurrent malignant glioma patients - mono-institutional experience in 125 patients
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Purpose/Objective: Bevacizumab has been extensively studied in recurrent high-grade glioma patients as first and second-line therapy. To date, there is a limited number of reports on its epidemiological use in an unselected patient cohort. Therefore, we report on our experience on a large number of patients treated at our institution.

Materials and Methods: After receiving standard radiotherapy (with or without TMZ) patients with recurrent malignant glioma were treated with bevacizumab (10mg/kg intravenously, q2w), either as mono/combination therapy (27.2%), upfront (12%) or in combination to re-irradiation, with (22.4%) or without maintenance therapy (38.4%). Median prescribed radiation dose during re-treatment was 36Gy, conventionally fractionated.

Results: 125 patients were included in this retrospective analysis with proven high-grade glioma. Median age was 50 years and median KPS at re-treatment 80. Median number of bevacizumab cycles preceding progression was three, with median four cumulative cycles. Median follow-up after initiation of bevacizumab treatment was 37 months and median overall survival since first diagnosis 29 months (WHO grades III + IV). Median post-recurrence survival was 9 months, median post-recurrence PFS 5 months (PFS-6 36.5%). Univariate testing revealed that sex, WHO grade, time interval from initial diagnosis, MGMT methylation, IDH mutation, combination with irinotecan and age had no significant influence on neither PRS nor PR-PFS. Significant factors according to PRS/PR-PFS were a KPS < 70 (PR-PFS 5 months (PFS-6 36.5%)) and a larger number of bevacizumab cycles and the respective treatment group (most favorable: re-RT + bevacizumab + maintenance therapy).

Conclusions: Bevacizumab appears to be a valuable agent in recurrent malignant glioma therapy. Activity of monotherapy was seen, especially in combination with reirradiation. KPS was the most important predictor for both PRS and PR-PFS.

PO-0799
Normal brain, neural stem cells and glioblastoma responses to FLASH radiotherapy
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Purpose/Objective: Glioblastoma (GBM) is a very aggressive and radioresistant tumor associated with bad prognosis. Current trends in GBM treatments are based on a
Materials and Methods: Two LINACs prototypes are used: a 4.5 MeV (Institut Curie) and a 6 MeV (CHUV) to investigate the normal brain response and the antitumor effect of FLASH irradiation on GBM models in a preclinical study with an ultimate aim to apply this treatment to GBM bearing patients. For the studies on normal brain, C57Bl6/J mice were irradiated at the whole brain level at single doses ranging from 10 to 80 Gy FLASH (>50Gy/s), at 10 Gy CONV (0.04Gy/s) and sham irradiated (6 mice in each group). Two months post-irradiation, cognitive tests were performed on mice to evaluate the mid-term memory with a novel object recognition test (Acharya et al. 2009) and brains were sampled. Two hours before the sampling, mice were injected with BrdU, brains were collected and immunohistochemistry and NSCs quantification were performed on brain sections. To evaluate the FLASH antitumor effect, human GBM were engrafted to nude mice. The tumors were locally irradiated at 10 Gy CONV, from 10 to 30 Gy FLASH and sham irradiated. Tumor growth delay was measured.

Results: Our preliminary results show that 50Gy FLASH irradiation on the whole brain does not induce any macroscopic toxicity nor mice’s health alteration whereas a pan-encephalic irradiation of 10Gy CONV is the maximum tolerated dose for long term follow-up. The cognitive tests’ results show a drop in cognitive skills after 10Gy CONV irradiation whereas mid-term visual memorization is not significantly affected at 50Gy FLASH. In correlation, two months after irradiation, the quantification of NSCs shows their preservation in the SGZ at doses up to 20Gy FLASH whereas 10Gy CONV eradicates all the hippocampal NSCs at the same timepoint. Astrocytic toxicity has also been investigated and shows that 10Gy CONV irradiation induces a high level of gliosis and astrocytes’ remodeling whereas few gliosis and astrocytes’ modifications are observed after 50Gy FLASH. At the tumor level and at similar doses, the FLASH and CONV irradiations induce a similar growth retardation. Nevertheless, the FLASH irradiation’s innocuousness on normal tissue does allow a dose escalation and thus an enhancement of the tumor growth delay. We are currently escalating the dose to achieve the tumor control.

Conclusions: Altogether these results suggest that the FLASH radiotherapy allows the delivery of very high doses to the whole brain, sparing normal tissues and NSCs and eradicating tumor cells. In the follow up of these preliminary experiments we are developing orthotopic and spontaneous GBM models in mice (in collaboration with K. Schhors and D. Hanahan, EPFL) to define the molecular basis of the FLASH differential effect.