hippocampus dose was Dmax less than 17Gy without compromising the coverage of planning target volume (PTV) and other organs at risk were prioritized over hippocampal constraint. The mini-mental state examination (MMSE) and Seoul verbal learning test for total recall, delayed recall and recognition (SVLT-TR, DR, R) were performed at baseline and at 7 and 13 or 16 months after radiotherapy.

Results: A total of 41 patients were accrued. Median age was 48 years (range 26-76) and 51.2 % of the patients were male. Eighteen patients (43.9%) had WHO grade I or II tumor whereas 23 patients (56.1%) had grade III or IV tumor. Median volume of PTV was 192.8 cc (range 33.4-522.6) and median prescribed dose was 60Gy (range 46-66). Concurrent chemotherapy was given to 18 patients (43.9%). Median D100% and Dmax to the contralateral hippocampus were 7.7Gy (range 0.6-24.8) and 16.6 Gy (range 3.56-60.4) respectively. Mean dose to contralateral hippocampus could be spared to less than 21 Gy in 39 patients with median value of 11.6 Gy (range 0.3-37.3) which was lower compared to previous documentation. Median value of maximal dose to lenses and eyeballs were 4.3 Gy (0.4-8.1) and 13.7 Gy (0.5-46.6) respectively. At median follow up of 7.8 months (range 0-14.8), median progression-free survival and overall survival were not reached. Cognitive function tests at 7 months were analyzable in 12 patients. For these patients, MMSE, SVLT-TR, SVLT-DR and SVLT-R at 7 months showed improved results compared to the baseline with 2.0% (95% CI, -0.8% to 4.7%), 11.0% (95% CI, 3.3% to 18.8%), 20.1% (-5.5% to 45.8%) and -0.6% (95% CI, -6.6% to 8.2%) increase respectively. No grade 4 or 5 toxicity was reported.

Conclusion: Hippocampus could be spared effectively in radiotherapy to primary brain tumors using VMAT. Despite limited follow up data, cognitive function tests of the patients showed promising results. Further follow up data would clarify the effect of hippocampal sparing on the cognitive function of the patients treated with radiotherapy for primary brain tumor.

PO-0645

18F-FET PET and MRI for treatment planning in glioblastoma

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Purpose or Objective: To analyze pre-treatment MRI- and 18F-fluoroethylthyrosine-PET- (FET-PET) based target volumes and patterns of failure following radiotherapy (RT) with concurrent temozolomide (TMZ) for primary glioblastoma multiforme (GBM).

Material and Methods: Thirty-four patients with primary GBM were treated using MRI based treatment volumes (GTVrm). Before treatment patients underwent FET PET/CT scans and biological tumor volume (GTVpet) were contoured but not used for target definition. Progression were defined according to RANO criteria. Tumor progression and pre-treatment MRI and PET scans were co-registered to the radiation dose map. Failures were classified based on location of primary GTVs and dose delivered at the site of failure. We investigated volumetric size and uniformity of MRI- vs. FET-PET/CT-derived GTVs and progression patterns assessed by means of FET PET/CT and MRI.

Results: FET-PET based GTVs measured 10 minutes after radionuclide injection (a.r.i.) (median 37.3 cm3) were larger than GTVs measured 60 minutes a.r.i. (median 27,7 cm3). GTVpet were significantly larger than corresponding MRI based GTVs (median 19,3 cm3). The congruence of MRI and FET signals for the identification of glioblastoma GTVs is poor with mean uniformity index of 0.4 (p=0,0). 74% of failures were located inside primary GTVpet. 68% of failures occured within the 95% isodose line, and 9% within 60 Gy isodose.

Conclusion: The size and geometrical location of GTVs differed in a majority of patients. The volume of GTVpet depends on time a.r.i. Tumor progression were mostly inside FET-PET volumes. FET PET better defined failure site then MRI. Finally dose inhomogenity inside GTVpet and GTVrm and favourable tumor control within 60Gy isodose advocates further studies with PET-MR based high-dose radiation therapy of GBM.

PO-0646

Temozolomide during radiotherapy of glioblastoma multiforme: daily administration improves survival

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Purpose or Objective: Temozolomide (TMZ) based chemoradiotherapy defines the current gold standard for the treatment of newly diagnosed glioblastoma. Data regarding the influence of TMZ dose density during chemoradiotherapy are currently not available. We retrospectively compared outcomes in patients receiving no TMZ, patients receiving TMZ during radiotherapy on radiotherapy days only (5/7) and patients receiving TMZ constantly 7 days a week (7//7).

Material and Methods:
From 2002 to 2012 a total of 432 patients with newly diagnosed glioblastoma received radiotherapy in our department. 118 patients had radiotherapy alone, 210 had chemoradiotherapy with temozolomide (75 mg/m²) daily (7/7 days a week) and 104 chemoradiotherapy with temozolomide only on radiotherapy days (5/7 days a week, Monday till Friday). Radiotherapy was applied in 30 fractions to a total dose of 60 Gy.

Results: Median survival after radiotherapy alone was 9.1 months, compared to 12.6 months with temozolomide 5/7 and to 15.7 months with temozolomide 7/7. The 1 year survival was 33% in the radiotherapy only group, 52% in the 5/7 group and 64% in the 7/7 group. Kaplan Meier analysis showed a significant improvement of temozolomide 7/7 vs. 5/7 (p=0.01 by the log-rank test), while temozolomide 5/7 was still superior to no temozolomide at all (p=0.02).

Conclusion: Our results confirm the findings of the EORTC/NCIC-trial by Stupp et al., establishing the daily temozolomide chemoradiotherapy as standard therapy for glioblastoma. Also a reduced temozolomide scheme can at first prolong the survival of glioblastoma patients, but not as much as the daily application.

PO-0647

Subventricular zones: new key targets for glioblastoma treatment

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Purpose or Objective: We aimed to identify subventricular zone (SVZ)-related prognostic factors of survival and patterns of relapse among patients with glioblastoma.

Material and Methods: Forty-three patients with primary diagnosed glioblastoma treated in our Cancer Center between 2006 and 2010 were identified. All patients received surgical resection, followed by temozolomide-based

chemoradiation (60 Gy, 2 Gy per fraction). Ipsilateral (iSVZ), contralateral (cSVZ), and bilateral (bSVZ) SVZs were retrospectively segmented following two delineation methods: with (TH+) and without (TH-) temporal horns. Dose-volume histograms were retrospectively generated on the original plans. Progression was defined according to the RANO criteria. Multivariate analysis using the Cox proportional hazards model including significant covariates in univariate analysis was assessed to examine the relationship between prognostic factors and time to progression (TTP).

Results: Median age was 59 years (range: 25-85). Median follow-up, OS and TTP were 52.8 months (95% CI 43.4-61.1), 26.2 months (95% CI 20.3-34.2) and 6.4 months (95% CI 4.4-9.3), respectively. On univariate analysis, initial contact to SVZ was a poor prognostic factor for OS (20.5 vs 56.4 months, p = 0.011) and TTP (4.6 vs 12.9 months, p = 0.002). With TH-method, patients receiving mean dose to bSVZ greater than 40 Gy had a significantly improved TTP, as well as patients whose V20 Gy to bSVZ was greater than 84% (17.7 months vs 5.2 months, p = 0.017). On multivariate analysis, initial contact to SVZ and V20 Gy to bSVZ lesser than 84% remained poor prognostic factors for TTP (HR = 3.07, p = 0.012 and HR 2.67, p = 0.047, respectively).

Conclusion: Our results suggest that contact to SVZ, as well as insufficient bSVZ coverage such as a V20 Gy lower than 84%, are independent poor prognostic factors for TTP. Therefore, targeting SVZ is of crucial interest for optimizing glioblastoma treatment.

PO-0648

Pilot study in the assessment of contouring variability in stereotactic radiosurgery

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Purpose or Objective: The accuracy in contouring the target is one of the key factors for the success of stereotactic radiosurgery (SRS). This is particularly important when delivering one large fraction of radiation with small or no margins, since the consequence of not defining the correct clinical target volume can be that intended treatment results are not achieved. Furthermore, accurate contouring of the relevant Organs-at-Risk (OARs) is essential to minimize any normal tissue toxicity. The aim of this study was to analyze and quantify the variability of target and OAR contouring for two lesions in the brain.

Material and Methods: A multicenter analysis of the variability in contouring the target and the OARs for two typical cases of brain disorders, a cavernous sinus meningioma and a vestibular schwannoma was performed. Twelve Gamma Knife centers from around the world have participated in the study by contouring the targets and the OARs. The resulting treatment plans were analyzed with respect to the agreement in target and OARs contouring.
The 50 %-agreement volume, AV50, and the common volume, AV100, together with the encompassing volume, AV100/N, were determined based on a binary analysis method. A novel metric for the variability in delineation defined as the Agreement-Volume-Index was introduced and additionally calculated. The variability of the contoured structures was also analyzed with respect to the position of their centers of mass (COMs).

Results: Substantial disagreement in target delineation was observed with an Agreement-Volume-Index of 0.22 for the meningioma case and 0.50 for the vestibular schwannoma case, respectively. Very high disagreement was also observed for the delineation as OARs of the optic apparatus and cochlea with an Agreement-Volume-Index ranging from 0 to 0.13. The disagreement was observed with respect to the shape, size and position of the contoured volumes. The resulting disagreement in target volumes was highest for the meningioma (range 5.29-7.80 cm3) while a lower disparity was observed for the schwannoma (range 3.56-4.48 cm3). The majority of structures analyzed displayed the highest disagreement of the COM in longitudinal direction. An illustration of the displacement of the COMs together with the common volume and encompassing volume is shown in Figure 1 for the cavernous sinus meningioma case.

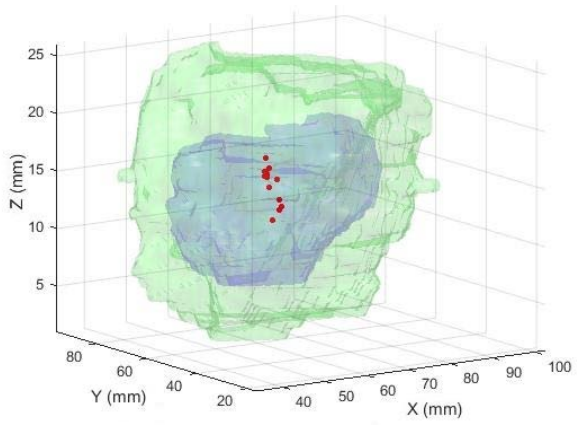

Figure 1. Illustration of the displacement of the COMs (red dots) together with the common volume (blue) and encompassing volume (green) for the cavernous sinus meningioma case.

Conclusion: Differences in target and OARs contouring expressed using different parameters, including a novel metric, emphasize the importance of further investigating and standardizing the contouring in SRS. Therefore, clinically significant differences in target and OARs delineation might lead to the need of better contouring tools, education and standardized protocols in SRS.

PO-0649

Evaluation of distant brain failure among patients undergoing SRS for lung cancer brain metastases

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Purpose or Objective: The latency, overall extent, and rate, of distant brain failure for non-small cell lung cancer patients undergoing SRS for brain metastases is not well characterized. We evaluated the impact of multiple pre-treatment parameters including age, KPS, extracranial disease status (ECD), initial number of metastases, initial aggregate tumor volume, and histological/molecular subtypes, on distant brain failure. We also evaluated the impact of WBRT performed before, combined with, or after SRS.

Material and Methods: The retrospective study population included 118 NSCLC patients with brain metastases treated with SRS between 11/2008 and 01/2014. The distant brain metastasis-free survival (DBMFS) was defined as latency in months from initial SRS to first subsequent radiographic evidence of new brain metastasis. The extent of overall distant brain failure (ODBF) was defined as the total number of new metastases that developed following initial SRS treatment. The distant brain failure rate (DBFR) was defined as the ODBF/RFI where RFI was defined as the maximum radiographic follow-up interval in months. Kaplan Meir analysis was used to evaluate DBMFS and Log Rank test was used to determine the significance (p-value <0.05 was considered significant). For ODBF and DBFR, Independent