Aim of this prospective study is to evaluate the expression of HIF-1 after RT and correlate it with the development of rectal mucosal angiectasias and bleeding.

Material and Methods: Patients with histological proof of prostate cancer without distant metastases, undergoing a standard course of external beam radiation therapy (3D-RT), were considered eligible. Each patient underwent a rectosigmoidoscopy with bioptic sampling prior to and one month and one year after RT. The development of rectal mucosal angiectasias was graded according to the Vienna Rectoscopy Score (VRS). HIF-1 was evaluated by immunohistochemistry and western blot analysis; the mean number of blood vessels per field was also assessed. Radiation-induced side effects (e.g. rectal bleeding) were recorded during follow-up visits.

Results: Thirty-one patients were enrolled (median age 72 years, IQR 67-75). After the end of a median follow-up of 19.8 months (IQR 18.4-20.9), 10 patients (32.3%) developed rectal bleeding needing intervention. All these patients presented a grade II or III VRS (p=0.03). The difference in the mean number of blood vessels between bleeders and not bleeders was not significantly different (p=0.47). The expression of HIF1 in bleeding patients was down regulated in 2 cases, unchanged in 3 and up regulated in 4 cases (p>0.99); in one case it was not feasible to determine the expression. There was no correlation between the expression of HIF1 and the VRS.

Conclusion: The expression of HIF1 does not correlate with the development of rectal mucosal angiectasias and bleeding in patients irradiated for prostate cancer.

Poster: Radiobiology track: Biomarkers and biological imaging

PO-0993

Genetic profiles of glioblastoma in proximity to the subventricular zone receiving chemoradiation

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Purpose or Objective: Subventricular zone-infiltrating (SVZ-infiltrating) glioblastomas (GBMs) with subependymal spreads along ventricle walls are associated with decreased patient survival. The heterogeneity in patient survival and recurrence patterns of GBM with SVZ infiltration might be related to neuronal therapy resistant stem cells, located in the SVZ. It has not been systematically investigated if specific molecular genetic patterns of SVZ-infiltrating GBMs exist, and therefore are responsible for the unfavorable course after chemoradiation.

Material and Methods: The current study assessed the molecularbiologic profile of 55 primary GBM cases that underwent chemoradiation. GBMs with SVZ infiltration and subependymal tumor spread (n = 24; 43.6 %) and peripherally located GBMs (n = 31; 56.4 %) were included. Genome methylation patterns were determined and copy number profiling was performed using an Illumina Infinium HumanMethylation450K (450K) Array, and the prognostic influence on progression and survival was evaluated.

Results: The majority of patients showed the characteristics of a "classic" GBM subtype, independent of the tumor localization in regard of the SVZ, demonstrating a chromosome 7 gain and chromosome 10 loss, as well as deletion of Cyclin-Dependent Kinase Inhibitor 2A (CDKN2A) and amplification of Epidermal Growth Factor Receptor (EGFR). Second, RTK I subtype, showing Platelet-Derived Growth Factor Receptor Alpha (PDGFRA) amplifications, could be detected equally in both groups. However, SVZ-infiltrating GBMs with subependymal spreading showed a decreased overall survival (OS) compared to their peripheral counterparts.

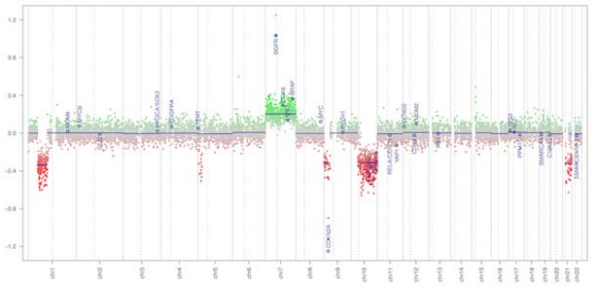

Figure: Genome wide copy number profiling of a classic primary gliolblastoma with chromosome 7 gain and chromosome 10 loss

Conclusion: Genome methylation patterns were distributed independently of tumor localization in regard of the SVZ, suggesting that the biological entities in both GBM groups are identical. However, survival rates of GBMs with proximity to the SVZ were inferior and therefore the central localization seems to be responsible for the poor clinical courses.

PO-0994

Assessment of [11C]-metformin PET for identification of patients suitable for metformin treatment

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Purpose or Objective: Evidence to support a role for the antidiabetic drug metformin in the prevention and treatment of cancer has emerged over the last decade. In particular, recent studies demonstrate that metformin enhances tumor response to radiation in experimental models. Metformin may therefore be of utility for nondiabetic cancer patients treated with radiation therapy. Despite being in clinical use for almost 60 years, the underlying mechanisms for metformins action remain elusive. We have therefore applied a novel PET-tracer, [11C]-metformin, to determine the uptake mechanism and elimination of the drug *in vitro* and in *vivo*.

Material and Methods: To verify transporter-mediated uptake of metformin in tumor cells, a selection of cell lines were incubated with [11C]-metformin in the absence or presence of blocking unlabelled metformin. Two tumor models A549 (lung) and SiHa (cervix) was chosen for *in vivo* experiments. Mice bearing subcutaneous tumors in the lower back were administered ~10 MBq [11C]-metformin and dynamically PET scanned for 90 minutes. As a "proof of principle" experiments using PET/CT with [11C]-metformin organ specific uptake of [11C]-metformin was determined in healthy humans. Dynamic whole-body PET was performed on four healthy volunteers (2 male). Two minutes before scan start, a bolus injection of ~200 MBq [11C]-metformin was injected and five consecutive whole-body scans with increasing frame durations were obtained: 1, 1.5, 2, 2.5 and 3 minutes per bed position. Time intervals for the PET scans were 2-8, 9-18, 19-32, 33-48 and 49-67 minutes (see figure 1). Source organs for the dosimetry calculations were the liver, kidneys, salivary glands and the bladder.
Results: *In vitro* metformin uptake varied widely but a high and inhibitable uptake was observed in A549 and SiHa cells.