CONCLUSION: MRI paramagnetic/diamagnetic signal aberrations, consistent with CM and/or microcalcifications, are common findings which evolve over time and may impose late effects of radiotherapy in adult brain tumor patients surviving >2 years after treatment. These lesions are benign and do not require intervention.

P07.14 CORRELATION OF MOLECULAR AND IMAGING BIOMARKERS IN PRIMARY BRAIN TUMOURS
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PURPOSE: Positron emission tomography with carbon-11 labelled mehionine (11C-METH PET) is a well-established imaging modality allowing to characterise tumour lesions on a metabolic and molecular level. The aim of the current study was to evaluate the relationship between 11C-METH PET semi-quantitative metrics and molecular biomarkers in patients affected by brain glioma candidate to surgery, and determine their prognostic role with respect to disease outcome.

MATERIALS AND METHODS: A consecutive series of 145 patients affected by pathologically proven gliomas, who were referred to our Institution for tumour resection from March 2012 to January 2015 and submitted to pre-operative evaluation with 11C-METH PET, was retrospectively analysed. The demographics, clinical-radiological features and follow up data were available for 109 patients (M:F=64:45; median age 43 years). In all cases, semi-quantitative metrics were obtained on 11C-METH PET, i.e. SUVmax, SUVratio and metabolic tumour volume (MTV). These data were correlated to disease outcome, in terms of progression-free survival (PFS), and compared to other clinical-biological information, i.e. IDH mutation, 1p/19q co-deletion and MGMT promoter methylation. The entire cohort was monitored for a median period of 16.7 months (median 13).

RESULTS: According to WHO classification, we investigated 40 low grade gliomas (LGG; 36.7%) and 69 high grade gliomas (HGG; 63.3%). In all patients, tumours were identified on 11C-METH PET median SUVmax 3.3, median SUVratio 2.3, and median MTV 9.6 cm3. We observed a statistically significant difference for SUVmax, SUVratio and MTV values based on tumour grade (p<0.001) and glioblastoma tumours (p=0.001, p=0.005 and p=0.045, respectively). According to molecular analyses, IDH1 resulted mutated in 49 patients, 1p/19q co-deleted in 58 patients and MGMT promoter methylated in 24 patients. We observed a statistically significant correlation between SUVmax and SUVratio and IDH1 mutation (p=0.0001).

During follow up, relapse or progression was documented in 48 cases (median PFS 8.7 months). We observed a statistically significant correlation to PFS on univariate analysis for SUVmax and SUVratio, tumour grade (p<0.001), and in particular to IDH1 mutation, 1p/19q co-deletion and MGMT promoter methylation. In all patients, tumours were identified on 11C-METH PET median SUVmax 3.3, median SUVratio 2.3, and median MTV 9.6 cm3. We observed a statistically significant difference for SUVmax, SUVratio and MTV values based on tumour grade (p<0.001) and glioblastoma tumours (p=0.001, p=0.005 and p=0.045, respectively). According to molecular analyses, IDH1 resulted mutated in 49 patients, 1p/19q co-deleted in 58 patients and MGMT promoter methylated in 24 patients. We observed a statistically significant correlation between SUVmax and SUVratio and IDH1 mutation (p=0.0001).

CONCLUSIONS: Metabolic characteristics on 11C-METH PET significantly correlate with histological grading and IDH1 mutation status in primary brain tumors. With respect to disease outcome, grading, molecular biomarkers, SUVmax and SUVratio resulted prognostic factors to PFS in this cohort of patients candidate to surgery.

P07.15 DIAGNOSTIC VALUE OF 2-HYDOXYGLUTARATE DETECTION BY 1H MR SPECTROSCOPY IN PATIENTS WITH GLIOMA AND CORRELATIONS WITH TUMOR PHENOTYPE AND TISSUE DOSAGE

INTRODUCTION: The overproduction of the oncometabolite 2-hydroxylglutarate (2HG) in IDH1 mutated gliomas can be detected non-invasively by magnetic resonance spectroscopy (MRS). In this study, we used two approaches for 2HG detection, e.g., difference spectroscopy (MEGA-PRESS) and conventional spectroscopy optimized for 2HG detection (PRESS). We assessed specificity and sensitivity and we related the results to patients’ natural history, 2HG tissue dosage and tumor molecular status.

METHODS: Thirty patients were included: six subjects before surgery, five with suspected brain glioma, and ten pre-operative cohort of patients affected by an IDH1 mutated glioma (post-operative cohort). IDH status was assessed for all patients combining detection of expression of IDH1-R132H mutant by immunohistochemistry (IHC) and Sanger sequencing for IDH1 and IDH2 gene mutations. Acquisitions were performed using a 3 T whole-body MRS. MRI sequences were optimized for 2HG detection: 1) a single-voxel MEGA-PRESS sequence (TR=2s, TE=68ms, 128 averages, scan time = 9 min), measuring the 2HG signal at 4.05 ppm; 2) a single-voxel PRESS sequence (TR=2.5s, TE=97ms, TE1=128mseg, TE2=65ms, 128 averages, scan time = 2.25 ppm. VOI size was 2x2x2 cm3, adapted to tumor size in order to minimize partial volume effects (minimum size 6 cm3). Sensitivity of the measurement was performed by gas chromatography-tandem mass spectrometry (GC-MS/MS).

RESULTS: In the pre-operative cohort, 2HG was detected in five out of the six patients using MEGA-PRESS and only in two patients by PRESS. Histopathological analysis proved that all the five patients with 2HG signature on MRS also were affected by an IDH mutated glioma (two grade II and three grade III gliomas). The patient with no 2HG signature on MRS resulted to be affected by an IDH wild-type ganglioglioma [MEGA-PRESS sensitivity 100% (0.4 to 1.0, 95% CI); specificity 100% (0.02 to 1.0, 95% CI)]. In the post-operative cohort of patients affected by an IDH1 mutated glioma (post-operative cohort), 2HG dosages performed in tissue significantly correlated to the 2 HG quantitative measures by MRS for the five IDH mutated glioma patients scanned before surgery (r=0.8, P<0.02).

CONCLUSIONS: These preliminary results suggest that MEGA-PRESS can provide high sensitivity/specificity for prediction of IDH mutation status before surgery, in contrast to PRESS. The MRS values significantly correlate with 2HG tissue dosage by GC-MS/MS. In the post-operative cohort sensitivity is lower. Factors which may affect the sensitivity of the measurement and correlation with the molecular pattern will be further analyzed in a larger cohort.

P07.16 PROGNOSTIC VALUE OF CONTRAST ENHANCEMENT AND HISTOPATHOLOGICAL GRADING IN DIFFUSE GLIOMAS DEPENDS ON IDH1/2 MUTATION
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BACKGROUND: Contrast enhancement (CE) and anaesthesia have been reported to indicate poor outcome in diffuse gliomas. Recently, mutational status of the IDH1/2 gene and loss of heterozygosity on chromosome 1p/19q (LOH1p/19q) have gained relevance for the evaluation of clinical outcome. Currently, a three-way classification based on IDH1/2 mutation and LOH1p/19q has gained further importance and will eventually supersede the current WHO grading system in terms of risk stratification and treatment planning. Thus, we aimed in the present study to re-evaluate CE and histopathological WHO grading as risk factors for survival within the framework of these molecular markers.

METHODS: 332 patients with diffuse glioma WHO grade II (n=189) or grade III (n=143) were stratified into 3 groups: IDH1/2 wild type (n=118), IDH1/2 mutated with (n=123) and without (n=91) LOH1p/19q. Preoperative magnetic resonance (MR) imaging was reviewed for presence of contrast uptake and multivariate analyses were conducted taking into account CE, WHO grading, molecular as well as age, Karnofsky performance status, surgical procedure and adjuvant therapy.

RESULTS: In univariate analysis, CE was not associated with OS in IDH1/2 wild type tumors whereas histopathological WHO grading had a strong independent prognostic value on OS in (p<0.001). In gliomas with IDH1/2 mutation, CE independently predicts shorter survival (p<0.04) and this effect seems to be especially pronounced in the IDH1/2 mutated group without LOH1p/19q.

CONCLUSIONS: In patients with diffuse gliomas WHO grade II/III and IDH1/2 wildtype, CE is not associated with survival in contrast to WHO grading. In patients with an IDH1/2 mutation, presence of CE on initial MRI is linked to inferior survival while grading is not.

Abstracts