P07.03Clinical parameters outweigh diffusion- and perfusion-derived MRI parameters in predicting survival in newly-diagnosed glioblastoma

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1/23, tuberculosis 1/23, and a histiocytosis was found in 1/23. MRI findings revealed 15 patients with diffuse lesions vs 8 focal lesions respectively and 21 patients with enhancing lesions vs 2 patients with nonenhancing brainstem lesions.

CONCLUSION: Despite its retrospective nature, our study underlines the risk of misdiagnosis and therapeutic mistakes in the evaluation of infiltrating mass suggesting brainstem glioma. It illustrates the need to promote a more systematic "check-list" based approach of brainstem lesions, including biopsies when needed, as recently shown in the pediatric population.

P07.03 CLINICAL PARAMETERS OUTWEIGH DIFFUSION- AND PERFUSION-DERIVED MRI PARAMETERS IN PREDICTING SURVIVAL IN NEWLY-DIAGNOSED GliOBLASTOMA

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BACKGROUND: To determine the relevance of clinical data, apparent diffusion coefficient (ADC), relative cerebral blood volume (rCBV) from DSC-perfusion and volume transfer constant (kt) from DCE-perfusion for predicting overall survival (OS) and progression free survival (PFS) in newly diagnosed treatment-naïve glioblastoma patients.

METHOD: We performed preoperative MR scans including standardized contrast enhanced T1 (cT1), T2 FLAIR, ADC, DSC and DCE of 125 patients with later histopathologically confirmed (IDH-wildtype) primary glioblastoma were performed on a 3 Tesla MRI scanner. ADC, DSC and DCE parameters were analyzed on semiautomatically segmented tumor volumes on contrast enhanced cT1 (CE) and hyperintense signal changes on T2 FLAIR (ED). Univariate and multivariable Cox proportional hazard analyses including age, sex and Karnofsky Performance Score (KPS) were performed to assess the influence of each parameter on OS and PFS.

RESULTS: In the univariate Cox-regression analysis, age (p=0.007) and KPS (p=0.007) were significant for shorter PFS. Age, KPS, low ADC and high rCBV values were associated with shorter OS. In the multivariable Cox-regression analysis (p=0.06, HR=1.70) and KPS (p=0.04, HR=0.87) were significant. For OS, age (p=0.01, HR=1.05) and KPS (p=0.01, HR=0.83) reached statistical significance, while rCBV tended towards a significance (p=0.06).

CONCLUSIONS: The presented volume of interest-based histogram analysis of 125 patients with IDH-wildtype glioblastoma showed that MRI parameters help to predict OS in a univariate cox regression analysis. However, the findings suggest that their relevance is outperformed by clinical parameters when included in a multivariable cox regression analysis which limits their prognostic value for survival prediction at the time of initial diagnosis.

P07.04 PSEUDOPROGRESSION - A STUDY OF INCIDENCE AND ASSOCIATIONS

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INTRODUCTION: Glioblastoma (WHO grade IV glioma; GBM) is the most common malignant primary tumour in adults. Assessing response to treatment is complicated by pseudoprogression (PsP), which is defined as a scan appearing to show disease progression after treatment, but then improving while staying on the same or no treatment. Estimates of the incidence of PsP are very variable, ranging from 11 - 64%. There have also been associated gene mutations to PsP, namely methylation of MGMT (mMGMT) and IDH-1 mutations.

We investigated the incidence and genetic associations of PsP in patients undergoing concurrent chemo-radiotherapy GBM at Charing Cross Hospital.

METHOD: We identified 50 patients with grade IV glioblastomas who underwent maximal feasible surgical resection and post-operative CRT + adjuvant chemotherapy with temozolomide for 6 - 12 months. Patients included underwent contrast enhanced MRI assessment prior to CRT, followed by sequential MRI scans to determine treatment response/disease progression. The first post-treatment scan was completed after 4 weeks of CRT, and subsequent scans were performed every 3 months.

Pseudoprogression defined as patients who showed signs of progression on the first scan post CRT and identified as having reductions in contrast enhancement in subsequent scans within 3 months whilst on planned adjuvant chemotherapy.

Gene mutations were determined from histopathology reports of the cohort.

RESULTS: Of the 50 patients, 30 were male and 20 female with 32 patients over 55 years old. The median overall survival was 15.6 months and median progression free survival of 5.8 months. 21 patients (42%) appeared to have disease progression within 3 months of completing CRT. 25 of all patients had mMGMT and 5 had IDH-1 mutation. Of those that appeared to have pseudoprogression (PsP), 10 were identified as having a reduction in PsP. Among those with PsP, 3 had mMGMT and 1 had an IDH-1 mutation. 12 of 17 who developed true progression had mMGMT.

CONCLUSION: The incidence of pseudoprogression is lower than many previous estimates in the literature. MGMT methylation does not seem to strongly predict PsP rather than true progression.

P07.05 INTRACELLULAR PH MEASURED BY 31P MR-SPECTROSCOPY PREDICTS SITE OF PROGRESSION IN RECURRENT GliOBLASTOMA UNDER ANTAGiOniGENIC THERAPY WITH BEVACiZUMAB

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PURPOSE: In solid tumors, major changes in the expression and/or activity of plasma membrane ion pumps and transporters facilitate proton efflux from tumor cells to maintain a higher intracellular pH (pHi), while the microenvironment [pHi] is commonly more acidic compared to normal differentiated adult cells. An alkaline pHi supports various mechanisms involved in cellular proliferation and limits apoptosis, therefore promoting cell survival. We proposed that early changes in pHi take place before a MR-detectable recurrence occurs. To prove our hypothesis, we employed in-vivo 31P MR spectroscopic imaging (MRSI) in patients with recurrent glioblastoma (rGBM) before and under antiangiogenic therapy (bevacizumab, BEV) until tumor progression.

MATERIALS AND METHODS: At our institution we prospectively enrolled 83 patients with recurrent glioblastoma or gliosarcoma that were treated with BEV. All patients received a full baseline and 8-weeks-follow up MRI and 1H/31P MRSI until further progression. According to the pre-defined criteria by Pope et al. for distant or diffuse tumor progression, 14 patients of this group were selected based on their tumor progression patterns at time of on-study progression (subsequent tumor). An area of interest for voxel selection on baseline MRSI data was defined retrospectively at the site of the subsequent tumor. The area of interest showed no detectable lesions before BEV on standard MRI sequences.

RESULTS: The pH in the area of interest (subsequent tumor) showed a significantly higher pHi (7.065, SD = 0.031, p < 0.001) compared to contralateral normal appearing tissue (control) and a similar pH compared to the existing tumor. The pHi decreased at time of best response (8 weeks-follow up, p=0.33), followed by an increase upon further progression (SD=0.035, p=0.66), which has been previously described for the initial tumor. Only at the time point of subsequent progression the histologically invisible tumor was detectable on standard diagnostic MRI sequences (T1 with contrast agent and T2).

CONCLUSION: Elevated pH in radiographically normal appearing tissue at baseline might be useful to predict the site of subsequent progression in patients with recurrent glioblastoma treated with BEV. As hypothesized above, the observed pHi changes precede T1 or T2 detectable lesions. 31P-MRSI therefore might facilitate the early detection of recurrent tumor, which is a key element of follow-up care and therapy surveillance.

P07.06 DOES IDH R132H MUTATION ALTER PHOSPHOLIPID METABOLISM IN GliOma? A 31P-MRSI IN VIVO STUDY

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PURPOSE: IDH1 mutations have been identified in approximately 70-80% of cases of diffuse glioma (grades II-III) and secondary glioblastoma multiforme (grade IV). The mutation in IDH1 confers a gain of function neomorphic activity to the enzyme, which results in NADPH-dependent conversion of α-Ketoglutarate (α-KG) to (R)-2-hydroxyglutarate (2-HG). The mutated IDH enzyme consumes both α-KG and NADPH and lacks reductive carboxylation capacity. α-KG and NADPH are important components for lipogenesis. It has been demonstrated by Esmaeili et al. (Cancer Research, 2014) in preclinical data and surgical specimen (n=11, grade III, IV), that patients carrying an IDH1 mutation display a phospholipid profile, which significantly differs from that in patients with wild-type IDH1.

MATERIALS AND METHODS: At our institution we prospectively enrolled 25 patients with grade II-IV glioma. The enrollment of 40-50 patients is planned. 15 patients were IDH1mut, 10 patients were IDH1wt as determined by immunostaining and Infinium HumanMethylation450