tion (p<0.05). There was no effect of hemispheric tumor localization. At T2, compound repetition and odd-picture-out also became impaired (p<0.05) and there was a decline compared to T1 on all repetition tasks (p<0.05). At T3, only sentence completion remained impaired (p<0.01) with a deterioration compared to T1 (p<0.01). *Standard tests:* At T1, patients were impaired on BNT, Category- and Letter Fluency (p<0.01). HGG patients performed worse than LGG patients on BNT and TT (p<0.01). Patients with left-hemispheric tumors performed worse on BNT and Letter Fluency compared to right-hemispheric tumors (p<0.05). At T2, TT also became impaired (p<0.05) and patients declined compared to T1 on Verbal Fluency tests (p<0.01). At T3, only BNT and Category Fluency remained impaired (p<0.05), with no significant declines compared to T1. CONCLUSION: The DIMA is the first test-battery to detect peri-operative impairments at different linguistic levels (phonology, semantics, syntax) in patients with left- or right-hemispheric gliomas. It even appeared more sensitive to detect surgical effects than standard tests: all phonological DIMA subtests captured short-term decline (T1-T2), in line with earlier evidence for the value of (non-)word repetition. DIMA sentence completion detected long-term decline (T1-T3), reflecting earlier spontaneous speech analyses. As expected, Verbal Fluency was also sensitive to short-term postoperative decline. Left-hemispheric tumor localization only affected standard test performance. HGG patients had more severe impairments than LGG on DIMA repetition and standard tests (BNT and TT). We advise adding the DIMA to standard language evaluation of glioma patients, as it allows for more detailed counseling about language outcome.

OS08 MULTILAYER DIAGNOSTICS

OS08.4.A RETROSPECTIVE ANALYSIS OF *IN VIVO* ^{1}H-MAGNETIC RESONANCE SPECTROSCOPY BASED ON A MACHINE LEARNING APPROACH ENABLES RELIABLE PREDICTION OF *IDH* MUTATION IN PATIENTS WITH GLIOMA

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BACKGROUND: Mutation of *isocitrate dehydrogenase (IDH)* is not only an important landmark in the development of low-grade gliomas, but also has prognostic significance and is a potential therapeutic target. There is a high need to determinate *IDH* mutation status at diagnosis and during the course of therapy in a non-invasive and reliable manner. We established a machine learning approach based on a support vector machine to detect *IDH* mutation status in *in vivo* standard ^{1}H-magnetic resonance spectroscopy (^{1}H-MRS) at 3T with an accuracy of 88.2%, a sensitivity of 95.5% (95% CI, 77.2–99.9%), and a specificity of 75% (95% CI, 42.85–94.5%) in a prospective monocentric clinical trial. Here, the same method is applied in a retrospective cohort at 1.5T and tested for transferability. MATERIAL AND METHODS: *Validation cohort.* The validation cohort comprised 100 patients with glioma for which standard *in vivo* ^{1}H-MRS spectra had been acquired between 2002 and 2007. Standard single voxel spectroscopy had been measured at 1.5T using a PRESS sequence with a TR of 1500ms and a TE of 30ms. One sample had to be excluded due to non-malignant histology and for 15 samples the *IDH* mutation status was not available. Therefore, the validation cohort comprised 84 samples, of which 35 were bearing an *IDH* mutation in immunohistochemistry (sequencing for confirmation is outstanding). *Machine learning.* To transfer our method to an independent validation cohort our previously established machine learning approach was first trained on all samples of the 3T group. The trained algorithm was then applied to the data of the validation cohort. Here, among other factors the different field strengths, with which the spectra were acquired (3T vs. 1.5T) had to be considered. RESULTS: 27 samples of the validation cohort had to be excluded due to poor spectra quality. Our approach correctly detected *IDH* mutation status in 47 of 62 patients (75.8%), although the technical conditions were significantly different from our published prospective cohort. 17 of 30 patients bearing an *IDH* mutation were correctly identified, while 30 of 32 wild type patients were determined successfully. CONCLUSION: Our approach to detect *IDH* mutation status has promising application in an unselected retrospective cohort, demonstrating transferability across different technical conditions. Further investigations to improve our technique and an advanced neuropathological processing of the samples are planned.

OS08.5.A PROTEOMIC ANALYSIS OF MENINGIOMA

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BACKGROUND: Meningioma is the most common primary intracranial tumor. Although ~80% are benign some WHO grade I are clinically aggressive. Chemotherapies are ineffective and biomarkers for clinical management are lacking. Approximately 60% sporadic meningiomas harbor mutations in the *NF2* gene andutations in *TRAF7*, *KLF4*, *AKT1*, *SMO* and *PIK3CA* have been identified in the majority *NF2*-positive tumors esp lower grade. However, the molecular mechanisms behind meningioma tumourigenesis is still unclear. We aim to identify novel biomarkers and therapeutic targets of meningioma by characterizing the proteomic landscape. MATERIAL AND METHODS: We analysed grade I, II and III frozen meningioma specimens and three different mutational groups: *AKT1/TRAF7*, *KLF4/TRAF7* and *NF2-/-* using LC-MS/MS to analyse global proteins, enriched phosphoproteins and phosphopeptides. Differential expression and functional annotation of proteins was completed using Perseus, IPA® and DAVID. For mutational subtypes quantitative phosphoproteomics was performed using TMT 10plex labeling approach followed by motif analysis using motif-X algorithm. We validated differential expression of proteins and phosphoproteins by Western blot and immunohistochemistry. RESULTS: We quantified 3888 proteins and 3074 phosphoproteins across all meningioma grades. Bioinformatics analysis revealed commonly upregulated (phospho)proteins to be enriched in Gene Ontology terms associated with RNA metabolism. Validation confirmed significant overexpression of proteins such as EGFR, CKAP4, the nuclear proto-oncogene SET, the splicing factor SF2/ASF as well as total and activated phosphorylated form of the NIMA-related kinase, NEK9, involved in mitotic progression. Hexokinase 2 was overexpressed in higher grades. For the mutation subtypes we have quantified 4162 proteins across all mutational meningioma subgroups. Analysis showed distinct proteomic profiles of mutational subgroups. Comparative analysis showed 10 proteins were commonly significantly upregulated among all mutational subtypes *vs*. normal meninges. 257 proteins were commonly significantly downregulated and enriched with molecular functions including aldehyde dehydrogenase and oxido-reductase. Mutational subtype-specific analysis identified 162 proteins significantly upregulated in *AKT1/TRAF7 vs*. remaining sample groups to be enriched in the oxidative phosphorylation pathway. 14 and 7 proteins were commonly significantly upregulated in *KLF4/TRAF7* and *NF2$^{-/-}$* mutant meningioma subtypes respectively. Several of these up-regulated proteins including ANNEXIN-3, CRABP2, CLIC3 and Endoglin were verified via WB. Lastly, analyses of 6600 phosphosites predicted regulatory kinases CONCLUSION: We show extensive proteomic and phospophoproteomics analysis of meningioma and suggest new therapeutic and biomarker candidates.

OS08.6.A GLIOBLASTOMA TREATMENT RESPONSE MACHINE LEARNING MONITORING BIOMARKERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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BACKGROUND: The aim of the systematic review was to assess recently published studies on diagnostic test accuracy of glioblastoma treatment response monitoring biomarkers in adults, developed through machine learning (ML). MATERIAL AND METHODS: PRISMA methodology was followed. Articles published 09/2018-01/2021 (since previous reviews) were searched for using MEDLINE, EMBASE, and the Cochrane Register by two reviewers independently. Included study participants were adult patients with high grade glioma who had undergone standard treatment (maximal resection, radiotherapy with concomitant and adjuvant temozolomide) and subsequently underwent follow-up imaging to determine treatment response status (specifically, distinguishing progression/recurrence from progression/recurrence mimics - the target condition). Risk of bias and applicability was assessed with QUADAS 2. A third reviewer arbitrated any discrepancy. Contingency tables were created for hold-out test sets and recall, specificity, precision, F1-score, balanced accuracy calculated. A meta-analysis was performed using a bivariate model for recall, false positive rate and area-under the receiver operator characteristic curve (AUC). RESULTS: Eighteen studies were included with 1335 patients in training sets and 384 in test sets. To determine whether there was progression or a mimic, the reference standard combination of follow-up imaging and histopathology at