BACKGROUND: Clinical and laboratory markers have been exploited to model risk in patients with primary CNS lymphoma (PCNSL), but the derived risk models do not fully exploit existing data. Here we present an extended framework of phenotype-epigenotype correlations that reveal novel prognostic constellations and enable prioritizing epigenetic therapy. MATERIAL AND METHODS: In this retrospective diagnostic and validation study, we leverage radiomic feature analysis of medical images and supervised binominal integration of DNA methylation profiles. We integrate both data modalities synergistically using machine learning-based prediction and cross-domain alignment. Ultimately, we validate the most relevant biological associations in tumor tissues and cell lines. RESULTS: We leverage a cohort of 191 patients across 9 sites in Austria, and an external validation site in South Korea, and use T1-weighted contrast-enhanced magnetic resonance imaging to derive a radiomic score that consists of 20 mostly tissue-based features. We determine the risk score as strong and independent predictive factor (multivariate HR=6.56), and confirm its prognostic value in an external validation cohort. Radiomic features align with DNA methylation sites in distinct, biologically meaningful ways, and radiomic risk is predictable from selected DNA methylation sites (AUC=0.78). Ultimately, gene-regulatory differences between radiometrically-defined risk groups converge on ctc6 binding activity, which is posed as testable treatment strategy in a subset of patients. CONCLUSION: The radiomic risk score is a robust and complementary predictor of survival and is reflected at the level of DNA methylation in PCNSL. Assessing risk and selecting epigenetic treatment based on imaging phenotypes represents a huge step forward, and the ability to define radiomic risk groups provides a concept on which to advance prognostic modeling and precision therapy for this aggressive brain cancer.

PL01.5.A. TOWARDS MODERNIZING INTRAOPERATIVE HISTOPATHOLOGICAL ASSESSMENT IN BRAIN AND SPINAL TUMORS: COMPARISON OF THE NOVEL STIMULATED RAMAN HISTOLOGY WITH CONVENTIONAL H&E STAINING

In a time period of 4 months, patients with different brain or spinal tumors were included in this study. Tumor tissue samples were collected intraoperatively whenever safely possible for analysis with SRH. Subsequently, unprocessed tissue samples were then sent for routine neuropathological workup. In an overall analysis, SRH images and H&E staining of all patients were analyzed separately by two board certified neuropathologists. Information on age, localization and suspected diagnosis was provided in each case in order to simulate the situation of intraoperative fresh frozen section. In a next step the technical feasibility and diagnostic accuracy of SRH was calculated. RESULTS: In this study, tissue samples of 95 patients who underwent neurosurgical resection or open/stereotactic biopsy at the Dept. of Neurosurgery, Medical University Vienna were included in this study. Tumor tissue samples were collected intraoperatively whenever safely possible for analysis with SRH. Subsequently, unprocessed tissue samples were then sent for routine neuropathological workup. In an overall analysis, SRH images and H&E staining of all patients were analyzed separately by two board certified neuropathologists. Information on age, localization and suspected diagnosis was provided in each case in order to simulate the situation of intraoperative fresh frozen section. In a next step the technical feasibility and diagnostic accuracy of SRH was calculated.

CONCLUSION: By intraoperative analysis of fresh frozen sections, neuropathologists provide important information of different brain and spinal tumors to the neurosurgeon during surgery. This facilitates characterization of these tumors intraoperatively to optimize the surgical strategy and patient management. However, weaning away from using conventional techniques of intraoperative fresh frozen section. Stimulated Raman Histology (SRH) was introduced as novel technique providing high-resolution digital images of unprocessed tissue samples directly in the operating room comparable to conventional histopathological images. Additionally, SRH images are fast and easily accessible by neuropathologists. Recently, first data showed promising results on the accuracy and feasibility of SRH in comparison to conventional H&E staining. MATERIAL AND METHODS: In a time period of 4 months, patients with different brain or spinal tumors who underwent neurosurgical resection or open/stereotactic biopsy at the Dept. of Neurosurgery, Medical University Vienna were included in this study. Tumor tissue samples were collected intraoperatively whenever safely possible for analysis with SRH. Subsequently, unprocessed tissue samples were then sent for routine neuropathological workup. In an overall analysis, SRH images and H&E staining of all patients were analyzed separately by two board certified neuropathologists. Information on age, localization and suspected diagnosis was provided in each case in order to simulate the situation of intraoperative fresh frozen section. In a next step the technical feasibility and diagnostic accuracy of SRH was calculated. RESULTS: In this study, tissue samples of 95 patients who underwent neurosurgical resection or open/stereotactic biopsy of different brain and spinal tumors were collected intraoperatively and analyzed by SRH. In total, 31 gliomas, 30 meningiomas, 19 metastases, 7 neurinomas and 8 rare tumors were analyzed. In the present study, the use of SRH was technically feasible in all cases and could be easily integrated in the neurosurgical workflow to provide rapid digital histopathological images for the analyzing neuropathologists. According to our data, SRH provided high diagnostic accuracy (>95%) in the investigated different brain and spinal tumors. CONCLUSION: Based on our preliminary data the technical use of SRH is feasible and showed a high rate of diagnostic accuracy in a large series of different brain and spinal tumors. By using this promising technique, we intend to modernize intraoperative histopathological assessment by providing rapid digital images of brain and spinal tumors to optimize the management of these patients.