long-term sequelae in their later lives. We searched for clinical and histopathological features to predict the prognosis and affect treatment response, with a future goal of treatment stratification. METHODS: A total of 154 GCT cases were included in the analysis. Total of 114 germinoma cases underwent measurement of tumor cell content on H-E specimen, and 82 GCT cases underwent 450K methylation analysis. 12p gain was determined on methylation-based copy number computation and FISH. Association with progression-free and overall survival (PFS/OS) was investigated. RESULTS: The tumor cell content was widely distributed from < 5% to 90% in the specimens, with a median value of 50%. Patients with a higher tumor cell content (≥50%) showed shorter PFS than those with a lower tumor cell content (< 50 %) (p=0.03). In multivariate analysis with tumor location, tumor cell content was the sole statistically significant prognostic factor (p=0.04). 12p gain was found in 25-out-of-82 cases (30%) and was more frequent in NGGCTs, particularly in cases with malignant components. The presence of 12p gain correlated with shorter PFS and OS, even with histology and tumor markers incorporated in the multivariate analysis. Among NGGCTs, 12p gain still had prognostic significance for PFS and OS. The 12p copy number status was shared among histological components in mixed GCTs. Whole-genome amplification was suggested by FISH. CONCLUSIONS: We found that tumor cell content significantly affected the prognosis of germinomas. 12p gain predicts the presence of malignant components of NGGCTs, and poor prognosis of the patients. Furthermore, 12p is likely to be an early event in the tumorigenesis of GCT. These potentially open the possibility of leveraging these pathological and molecular factors in future clinical trials when stratifying the treatment intensity.

PATH-43. RAMAN SPECTROSCOPY AS A TOOL IN NEUROSURGERY

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BACKGROUND: Raman Spectra have been shown to be sufficiently characteristic to their samples of origin that they can be used in a wide range of applications including distinction of intracranial tumors. While not replacing pathological analysis, the advantage of non-destructive sample analysis and extremely fast feedback make this technique an interesting tool for surgical use. METHODS: We sampled intractanial tumors from more than 300 patients at the Centre Hospitalier Luxembourg over a period of three years and compared the spectra of different tumor entities, different tumor subregions and healthy surrounding tissue. We created machine-learning based classifiers that include tissue identification as well as diagnostics. RESULTS: To this end, we solved several classes in the intracranial tumor classification, and developed classifiers to distinguish primary central nervous system lymphoma from glioblastoma, which is an important differential diagnosis, as well as meningioma from the surrounding healthy dura mater for identification of tumor tissue. Within glioblastoma, we resolve necrotic, vital tumor tissue and peritumoral infiltration zone.We are currently developing a multi-class classifier incorporating all tissue types measured. CONCLUSIONS: Raman Spectroscopy has the potential to aid the surgeon in the surgery theater by providing a quick assessment of the tissue analyzed with regards to both tumor identity and tumor margin identification. Once a reliable classifier based on sufficient patient samples is developed, this may even be integrated into a surgical microscope or a neuronavigation system.

PATH-44. RAMAN SPECTROSCOPY AS A DIAGNOSTIC TOOL IN NEUROPATHOLOGY

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BACKGROUND: Although microscopic assessment is still the diagnostic gold standard in pathology, non-light microscopic methods such as new imaging methods and molecular pathology have considerably contributed to more precise diagnostics. As an upcoming method, Raman spectroscopy (RS) offers a "molecular fingerprint" which could be used to differentiate tissue heterogeneity or diagnostic entities. RS has so far been successfully applied on fresh and frozen tissue, however more aggressively, chemically treated tissue such as formalin-fixed, paraffin-embedded (FFPE) samples are challenging for RS. METHODS: To address this issue, we examined FFPE samples of a broad range of intracranial tumors (e.g. glioblastoma and primary CNS lymphoma) and also different areas of morphologically highly heterogeneous glioblastoma tumor tissue. The latter in order to classify not only the tumor entity but also histologically defined GBM areas according to their spectral properties. We applied linear and nonlinear machine learning algorithms (Logistic Regression, Random Forest, Support Vector Machine) on our spectroscopic data and compared statistical performance of resulting classifiers. RESULTS: We found that Random Forest classification distinguished between glioblastoma and primary CNS lymphoma with a balanced accuracy of 94%, only using Raman measurements on FFPE tissue. Furthermore, our established support vector machine-based classifier identified distinct histological areas in glioblastoma such as tumor core and necroses with an overall accuracy of 70.5% and showed a clear separation between the areas of necrosis and peritumoral zone. CONCLUSIONS: This relatively cheap and easy-to-apply tool may serve useful to complement histopathological and molecular diagnostics. It provides an unbiased approach to tumor diagnostics with very little requirements (e.g. histopathological feature completeness of the tumor entity) to the sample. As a conclusion, we propose RS as a potential future additional method in the (neuro)-pathological toolbox for tumor diagnostics.

PATH-45. APOLLO: RAMAN-BASED PATHOLOGY OF MALIGNANT GLIOMA

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BACKGROUND: DNA methylation is an essential component for integrative diagnosis in glioma. Methylation subtype prediction of gliomas is currently done via sample extraction of high-quality of reasonable amount of DNA (~1ug), methylome profiling, followed by probe identification, curation and subsequent analysis via different random forest classifiers. However, the DNA methylation classification is not always available for all the samples. METHODS: Raman Spectroscopy performed of the regions of interest using 1mm^2 FFPE tissue spots from 45 patient samples with LGm1 to LGm6 methylation subtypes. Spectral information was then used to train a convolutional neural network (CNN) and develop a prediction algorithm. 70 % of dataset - model training while the remaining 30% for validation. Supervised wrapper methods and random forests were used to identify the top 109 most discriminatory Raman frequencies out of 1738. RESULTS: We identified the most discriminatory features from these analyses and demonstrated that these frequencies show differential spectral intensities for these frequencies depending upon the glioma subtypes across the larger areas of the tissue. We compared the results of the Ward linkage clustering with the separation induced by the “frequency criterion”, an empirical observation that Raman spectra of tumor spots are characterized by intensities higher than 5000 on some of the frequencies from 1463 to 1473. For each of the 45 samples we ran Ward linkage clustering with a variable number of clusters (from 2 to 7), with the majority cluster corresponding to tumor spots and the others corresponding to (various types of) non-tumor spots. We found that the majority cluster matches very well the tumor spots characterized by the frequency criterion, The average accuracy over all samples was 90:3%, the average precision was 99:6% and the average recall was 90:2%. For most samples, two clusters were sufficient to distinguish between tumor and non-tumor spots with accuracy.

PATH-46. DIAGNOSTIC IMPACT OF THE CNS TUMOR METHYLATION PROFILING IN A NEUROPATHOLOGY CONSULT PRACTICE

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