PATH-06. PRE-OPERATIVE TUMOUR CLASSIFICATION USING NANOPORE SEQUENCING OF CEREBROSPINAL FLUID

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BACKGROUND: The introduction of tumour classification by analysis of DNA methylation has changed the landscape of paediatric neuro-oncology. With the launch of Oxford Nanopore sequencing, generation of sequencing data is possible in real-time, including information on base-modifications. Diverse classification tools for tumour tissue have been developed recently. While this is an important step towards optimization of surgical treatment, pre-operative knowledge on tumour entity would further facilitate surgical planning. Therefore, we investigated the possibility of liquid biopsy for rapid pre-operative tumour classification. METHODS: CSF samples from patients with pre-operative extra-ventricular drain (EVD) (n = 5) as well as samples obtained via Ommaya reservoirs in cases of suspected recurrence (n = 3) were analysed. Additionally, samples from non-tumour patients (epilepsy, inflammation) who had lumbar puncture were available as controls. Samples were sequenced on MinIon devices (Oxford Nanopore) and subsequently classified with previously published tumour classification pipelines (NanoDx, crossNN, Sturgeon). RESULTS: Even though CSF derived from EVD has been stored on room temperature for up to 72 hours before processing, cfDNA isolation was possible with the advantage of higher CSF input amounts. DNA fragments showed a distribution characteristic for cell-free DNA, with a maximum peak at 170bp. The amount of total input DNA ranged from 0.35ng to 12ng, with higher input amounts generating more sequencing data but not resulting in better classification. Classification by sturgeon and crossNN/nanoDx using CSF derived cfDNA was possible in exemplary cases, such as a medulloblastoma patient with a new inoperable lesion, where CSF analysis resulted in medulloblastoma Group 4 within the first hour of sequencing. In total, 38% of samples were correctly classified. CONCLUSION: Liquid biopsy as a method to pre-operatively classify tumours and thereby enable risk-adjusted surgery is feasible. Ongoing efforts focus on optimisation of cfDNA based tumour classification by extension of the cohort.