THE FEASIBILITY OF USING LIQUID BIOPSIES AS A COMPLEMENTARY ASSAY FOR COPY NUMBER ABERRATION PROFILING IN PEDIATRIC CANCER PATIENTS

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Pediatric tumors are often characterised by the presence of DNA copy number alterations (CNAs). These DNA copy number profiles, obtained from a tissue biopsy, can aid in the correct prognostic classification and therapeutic stratification for several pediatric cancer entities (e.g. MYCN amplification in neuroblastoma). Liquid biopsies (LQB) offer a potentially safer alternative for invasive tumor tissue biopsies and can provide deeper insight into tumor heterogeneity. We performed retrospective CNA profiling using shallow whole genome sequencing (sWGS) on paired plasma cfDNA and tissue DNA samples from pediatric patients (n = 140) representing different tumor entities including osteosarcoma, Ewing sarcoma, rhabdomyosarcoma, Wilms tumor, brain tumors and neuroblastoma. The main cause of CNA discordance between tissue DNA and cfDNA was found to be the cfDNA sample quality (i.e. the percentage of cfDNA out of total DNA, which decreases due to e.g. white blood cell lysis). Furthermore, for several samples (n = 11), copy number aberrations were found to be only present or higher abundant in the cfDNA, potentially caused by tumor heterogeneity and/or sampling bias. In conclusion, in future prospective studies liquid biopsies can serve as a complementary assay, as either cfDNA or tissue DNA can contain CNAs that are not present in the other material. Whether the plasma cfDNA captures more aggressive subclones, and treatment based on these aberrations results in a better survival for the patients or only adds additional toxicity, remains yet to be investigated.