A liquid biopsy approach to detect copy number variations by low coverage whole genome sequencing in Hodgkin Lymphoma and post-transplant lymphoproliferative disorder

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ABSTRACT

Introduction: Liquid biopsy is a minimally-invasive approach that could be used for early detection of cancer, monitoring disease progression or response to personalised therapy. Genomic aberrations such as single nucleotide variant, translocations/fusions and copy number variations (CNVs) can be detected in liquid biopsies. In this study, low coverage-whole genome sequencing (lcWGS) was used to investigate the feasibility of detecting CNVs in liquid biopsies collected retrospectively. **Methods:** Cell-free DNA (cfDNA) was isolated from pre-treatment plasma of 44 classical Hodgkin lymphoma (cHL) patients, 16 monomorphic post-transplant lymphoproliferative disorder (PTLD) patients and ten controls. Six tissue samples from PTLD patients were also included for comparison. All samples were subjected to lcWGS at an average coverage of 0.2X. CNV analysis was performed with R packages CNAclinic and ichorCNA. **Results:** CNVs were detected in cfDNA of 59.1% cHL and 68.8% PTLD patients but not detected in any of the controls. Full concordance (100%) was observed for CNVs detected in paired cfDNA and tissue in PTLD patients. Estimated tumour fraction based on CNVs were 0-21.8%, 0-90.7% and 0-4.7% in cHL, PTLD and controls, respectively. **Conclusion:** CNVs detected by liquid biopsy reflect that of the tissue, indicating that cfDNAs are derived from tumour. Low estimated tumour fraction in few controls were likely due to clonal haematopoiesis of indeterminate potential. The sensitivity to detect CNV in liquid biopsies was good despite minimal amount of cfDNA from retrospective samples were used, and sequencing was performed at low coverage. In conclusion, this approach is minimally-invasive, low cost and could be applied in the clinical setting for informed decisions.