Multi-Omics Approaches For Early Cancer Detection In Serial Liquid Biopsy Samples Of Cancer Predisposition Patients

Abstract Submitter: Benedikt Kirchner, Germany*

Co-Authors: Stefanie Volz, Nike Simon, Sema Hamurcu, Christina Dutzmann, Birte Sänger, Kristian W. Pajtler, Christian Kratz, Kendra Maaß

*German Cancer Research Center (DKFZ), Division of Pediatric Neurooncology, Hopp-Children's Cancer Center Heidelberg (KiTZ), 69120 Heidelberg, Germany

Abstract

Background

Liquid biopsies have revolutionized cancer surveillance by enabling non-invasive detection of circulating tumor DNA (ctDNA) and other biomarkers, offering insights into early tumorigenesis and disease progression. Especially for patients with a genetic predisposition to cancer, serial sampling collected at standard-of-care screening appointments presents an opportunity to enhance early detection, personalize risk assessment, and improve clinical decision-making.

Objective

This study aims to evaluate the clinical utility of serial liquid biopsies in monitoring cancer development and progression in individuals with hereditary cancer predisposition syndromes. By integrating low-coverage whole-genome sequencing (lcWGS) and methylation analysis, we seek to detect early genomic and epigenomic alterations indicative of malignant transformation. Our objective is to assess the sensitivity, specificity, and predictive value of these techniques in longitudinal surveillance, ultimately refining risk-adapted strategies for early cancer detection in high-risk populations.

Methods

This study included a cohort of over 1000 plasma samples derived from individuals diagnosed with hereditary cancer predisposition syndromes who underwent serial liquid biopsy sampling at routine clinical surveillance visits. lcWGS and methylation analysis were performed to assess genomic and epigenomic alterations. Fragment sizes were analyzed together with end motifs to increase specificity and calculate ctDNA estimation scores (CES) prior to integration with copy number variation (CNV) profiling and methylation signatures to identify tumor-associated patterns. An integrated risk score was developed and validated against clinical tumor history to assess its predictive performance.

Results

Our analysis demonstrated an increased sensitivity in detecting tumor-positive cases using serial liquid biopsies. The integration of multi-omics data improved early detection rates substantially compared to single-modality approaches. Analysis of serial samples helped in establishing patient individual base lines, reducing risks of false-positive findings and highlighting the need of cross-validation with clinical tumor history and further refinement of classification algorithms

Conclusion

Serial liquid biopsies offer a promising non-invasive approach for cancer surveillance in predisposed individuals. As analytical methods continue to improve, complementing conventional surveillance strategies such as MRT with liquid biopsies may provide a more comprehensive and personalized approach to cancer monitoring, ultimately improving patient outcomes and secondary prevention in high-risk populations.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.