

Optimized whole-genome sequencing workflow for tumor diagnostics in routine pathology practice

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Abstract

Two decades after the genomics revolution, oncology is rapidly transforming into a genome-driven discipline, yet routine cancer diagnostics is still mainly microscopy based, except for tumor type-specific predictive molecular tests. Pathology laboratories struggle to quickly validate and adopt biomarkers identified by genomics studies of new targeted therapies. Consequently, clinical implementation of newly approved biomarkers suffers substantial delays, leading to unequal patient access to these therapies. Whole-genome sequencing (WGS) can successfully address these challenges by providing a stable molecular diagnostic platform that allows detection of a multitude of genomic alterations in a single cost-efficient assay and facilitating rapid implementation, as well as by the development of new genomic biomarkers. Recently, the Whole-genome sequencing Implementation in standard Diagnostics for Every cancer patient (WIDE) study demonstrated that WGS is a feasible and clinically valid technique in routine clinical practice with a turnaround time of 11 workdays. As a result, WGS was successfully implemented at the Netherlands Cancer Institute as part of routine diagnostics in January 2021. The success of implementing WGS has relied on adhering to a comprehensive protocol including recording patient information, sample collection, shipment and storage logistics, sequencing data interpretation and reporting, integration into clinical decision-making and data usage. This protocol describes the use of fresh-frozen samples that are necessary for WGS but can be challenging to implement in pathology laboratories accustomed to using formalin-fixed paraffin-embedded samples. In addition, the protocol outlines key considerations to guide uptake of WGS in routine clinical care in hospitals worldwide.