

Topics: [CTCs / CECs \(circulating tumor cells/ circulating epithelial cells\)](#)

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Abstract

Title

CTCs 2020: How far we are from routine use in clinical?

The recent advances in molecular biology and pharmacology offer to the oncologist the opportunity to design the therapeutic strategy on the tumor biology of individual patient. This encouraging perspective requires considering factors that may influence treatment effectiveness, including tumor heterogeneity and selective pressure determined by the treatment itself. Indeed, even in case of targeted drugs, often appear genomic alterations able to sustain resistance to ongoing therapy or rare tumor clones emerge that might benefit from treatment not yet exploited.

Since liquid biopsy is a minimally invasive procedure, through serial sampling it allows investigating the evolution of malignancies.

Nowadays, liquid biopsy comprises a class of biomarkers, including circulating tumor cells (CTCs), cell free-circulating tumor DNA (ctDNA) and tumor-derived extracellular vesicles (tdEV). Among these, CTCs are the most suitable to identify malignancies more prone to give metastasis, only because, until proven otherwise, intact cells, and not their DNA, have the potential to cause metastasis.

Indeed, CTCs have been revealed in almost all disease stages of solid tumors and their levels have been reported both prognostic, and predictive of treatment efficacy. Consistently with clinical validity proved in metastatic breast cancer, the quantitative evaluation of CTCs has been entered in the ASCO and NCCN guidelines (2015) as prognostic biomarker.

However, despite CTC level promises to be an appealing tool for reevaluating disease conditions throughout the continuum of the care, there is some limiting the definitive enter of CTC assay in clinical.

First, the available technologies are able to detect CTCs in no more than 50% of metastatic patients. Since these technologies are mostly EpCAM-dependent, this raises doubt that others cells - e.g. more aggressive? Undifferentiated? EMT cells? - are not yet quantified.

Moreover, beyond enumerating CTCs, their most intriguing use in clinical could be to provide the genetic landscape of all cancerous lesions at any time; since CTCs are rare, these analyses encounter technical issues.

Overall, these limits are discouraging the inclusion of CTCs in prospective studies that conversely are mandatory to prove clinical utility and validity of the test.

Main pitfalls and work in progress will be critically discussed.