Outlook of Clinical Applications of Liquid Biopsy

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In 1869, for the first time, Australian physician Thomas Ashworth recognized that small numbers of cells circulating in the bloodstream were morphologically identical to primary tumor cells of the same patient. Today, over 150 years after this monumental observation, the scientific community has progressed beyond the collection and enumeration of CTCs to gauge extent of disease to the serial molecular characterization of these cells to aid in treatment selection based on the biologic profile of an individual patient's tumor. The use of minimally invasive liquid biopsies including CTCs, circulating cell free DNA (ccfDNA), and circulating nucleic acids such as microRNA, and the co-development of targeted therapies, has the potential to revolutionize patient care by limiting clinical trial enrollment to the patients most likely to respond, shortening drug development times, and reducing patient exposure to unnecessary toxicity from ineffective treatments. However, analogous to a drug's indication, the clinical use of liquid biopsy assays requires the rigorous generation of evidence through analytical validation, the demonstration of clinical validity and utility, and clinical qualification. Analytical validation interrogates an assay's performance characteristics and determines whether the result generated is reproducible. Clinical validation involves demonstrating the performance of the rest for specific contexts of use including the predication of drug sensitivity and or efficacy and clinical utility, showing that use of the test result to inform management improves patient outcomes relative to the non-use of the result. The promise and practice of precision medicine is real, but to do so requires understanding on how best to deploy and utilize "liquid biopsies" to better enable drug development and improve medical decision making.