

Tumor Profiling: The Good, The Bad and the Future

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Dr. Hamilton described tumor profiling, with emphasis on the emerging area of liquid biopsies.

Based on a definition from the Mayo Clinic, tumor profiling is a method of testing that evaluates each person's tumor to determine genomic and other molecular characteristics. The results are used as biomarkers that are targets for, or influences on, therapy in order to improve response to and outcome after directed treatment. Tumor profiling has both good and bad points. Among the good are its wide availability, the availability of companion diagnostic tests for many therapies, and dramatic examples of improved outcomes for selected patients. Among the bad points are the low frequency of actionable alterations in many tumor types, the slow adoption of panel testing, the slow uptake of combination therapies, the variable reliability of tests, the high cost and low reimbursement, and the variable decision support.

Liquid biopsies are the future of tumor profiling. These tests use bodily fluids instead of solid tissue for analysis. The fluid used is often blood, but may also be urine, saliva, tears, cerebral spinal fluid, effusion (ie, discharge), aqueous humor of eye, mucus, gastrointestinal secretions, or semen. In cancer, the collected liquid is analyzed for intact tumor cells or their parts, such as cell-free DNA, RNAs, and proteins, including those packaged in circulating membrane-bound sacs (exosomes and vesicles).

Liquid biopsies have a number of advantages over tumor biopsies, including less invasive or even noninvasive collection procedures, more extensive sampling of tumor mutations due to perfusion throughout body, the possibility of real time sampling over the course of the tumor due to the short life of analytes in the body, the ability to assess sequential specimens, and lower overall costs. Disadvantages include the emerging nature of the methods, questions about reliability, the low analyte concentrations, high volume of specimen needed, and the sometimes "secret" proprietary algorithms used to determine yes/no decisions.

Even though tumor biopsies are not a gold standard for (they are more of a bronze standard), they do have some advantages. These include the standard acquisition techniques, the ability to view tumor histopathology (which allows tumor classification), the larger quantity of specimen, and the well established analytic methods. Disadvantages include the invasive nature of the procedures, inaccessibility of some tumor sites, variable operator skill, costs, limitation to a fixed point in time, and the limitation to a single part of the tumor (ie, unable to detect intra- and intertumor heterogeneity).

Tumor profiling has become standard of care in medicine, but challenges in methodological standardization remain. Many different methods are currently available and the clinical questions to be

answered drive the choice of tests. Tumor specific characteristics are not yet certain; some tumors shed more cells and DNA into the blood than others.

Audience Questions and Answers

- *Can you comment on the potential for false positives in liquid assays?* One issue seems to be that the analyte levels can vary week to week. Alterations that seem to be present one week may be gone the next.