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In recent years, liquid biopsy has emerged as a potential alternative/adjunct to standard tissue biopsy in the diagnosis of malignancies. Current use of this technique, which tracks distinctive molecules released from neoplastic cells including circulating tumor cells (CTCs), exosomes, circulating tumor DNA (ctDNA), cell-free DNA (cfDNA) and miRNA, has generally been limited to determining therapies in lung cancer based on detectable mutations (EFGR, EML4-ALK). However, recent studies have demonstrated the possibility for using these molecules as more efficient prognostic and diagnostic biomarkers in breast, colon, rectum, lung, liver, and pancreatic cancer. Due to the need for standardization in sampled material (serum, plasma, urine), the types of molecules being investigated, and the techniques used to evaluate these molecules (ARMS/Scorpion assay, PNA probing, BEAM analysis, digital PCR, etc.), the idea of using liquid biopsy as a stand-alone method of diagnosis and prognosis requires further examination and collaboration among practitioners. Yet, its low invasiveness compared to standard methods of diagnosis as well as its capability of lending practitioners a more enhanced ability to track the development of a malignancy over time, particularly in patients who cannot tolerate repeated tissue biopsies, and to identify mutational heterogeneity in malignancies merits continued interest in its potential.