the treatment intensity is prematurely reduced based solely on this negative result, it may affect the long-term treatment outcome (Faulkner et al., 2022; Hoang et al., 2025).

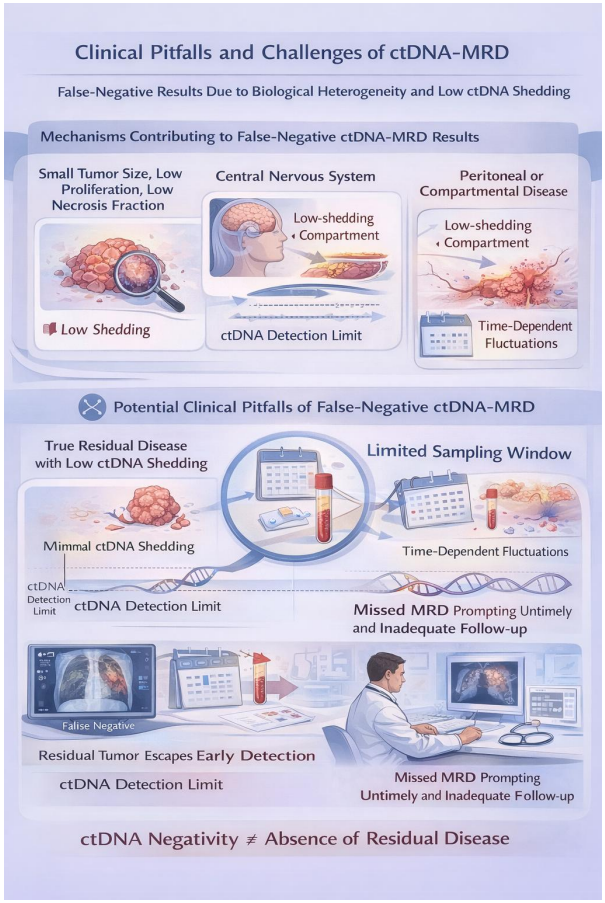

Figure 2 Biological and Technical Determinants of ctDNA-MRD Accuracy

Conversely, relying solely on positive ctDNA results and blindly intensifying high-cost and high-risk treatments will also expose patients to unnecessary risks, especially when there is no reliable evidence from randomized controlled studies to support it (Zhu et al., 2023). Over-interpreting ctDNA results can also lead to excessive imaging examinations, invasive surgeries, or prolonged systemic treatment times, which not only increase the economic burden on patients but also bring additional clinical risks (Semenkovich et al., 2023). Therefore, ctDNA-MRD can only serve as an auxiliary tool for clinical decision-making and cannot be used as the sole basis for decision-making. It must be combined with the patient's pathological characteristics, imaging results, treatment history, and other biomarkers, and also requires confirmation through prospective trials to determine whether MRD-guided intervention measures can truly improve the survival benefits of patients (Chen et al., 2025).

5 The Integrated Application of ctDNA-MRD and Imaging Technology

5.1 Complementarity in time and information

ctDNA-MRD and imaging do not look at the tumor from the same angle. ctDNA focuses on molecular signals circulating in the whole body and often raises an alarm before structural changes become visible. Imaging, on the other hand, shows where the lesion is, how large it is, and how it should be staged—information that remains essential for treatment planning (Pantel and Alix-Panabières, 2024). In non-small cell lung cancer and colorectal cancer, ctDNA conversion from negative to positive frequently precedes radiographic relapse by several months, a period described as the “molecular recurrence window” (Zheng et al., 2024; Azzi et al., 2025). Imaging abnormalities usually appear only after the tumor reaches a detectable size or metabolic threshold.

From a practical perspective, ctDNA reflects residual tumor burden, clonal shifts, and emerging resistance, while imaging answers a more direct clinical question: where is the disease and can it be treated locally? (Semenkovich