sampling time, and failing to meet the required detection sensitivity can all lead to the actual residual being "missed". Therefore, a more accurate understanding of ctDNA negativity should be "no signal detected at present", rather than complete clearance. On the other hand, CHIP, technical noise, and threshold differences between different platforms may also lead to false positives. If there is a lack of strict preprocessing procedures and variant filtering strategies, the interpretation of results can easily be disturbed, and even unnecessary examinations or treatment intensification may be triggered.

ctDNA-MRD does not work well as a standalone decision tool. In practice, its results need to be interpreted alongside imaging findings, pathological features, and the broader clinical context. ctDNA may signal molecular relapse earlier than structural changes appear, but it cannot indicate where the lesion is or how extensive it is—questions that imaging still answers more directly. Looking at both together usually provides a clearer and more dependable picture of residual disease. With further integration of multi-omics data, functional imaging, and artificial intelligence models, ctDNA-MRD may gradually move beyond simple risk estimation toward a more practical role in clinical decision-making. However, until stronger prospective evidence is available, a cautious approach remains advisable—combining multiple modalities, discussing cases within multidisciplinary teams, and, whenever possible, enrolling patients in clinical trials to ensure that potential benefits do not come at the expense of safety.

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Conflict of Interest Disclosure

The author affirms that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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