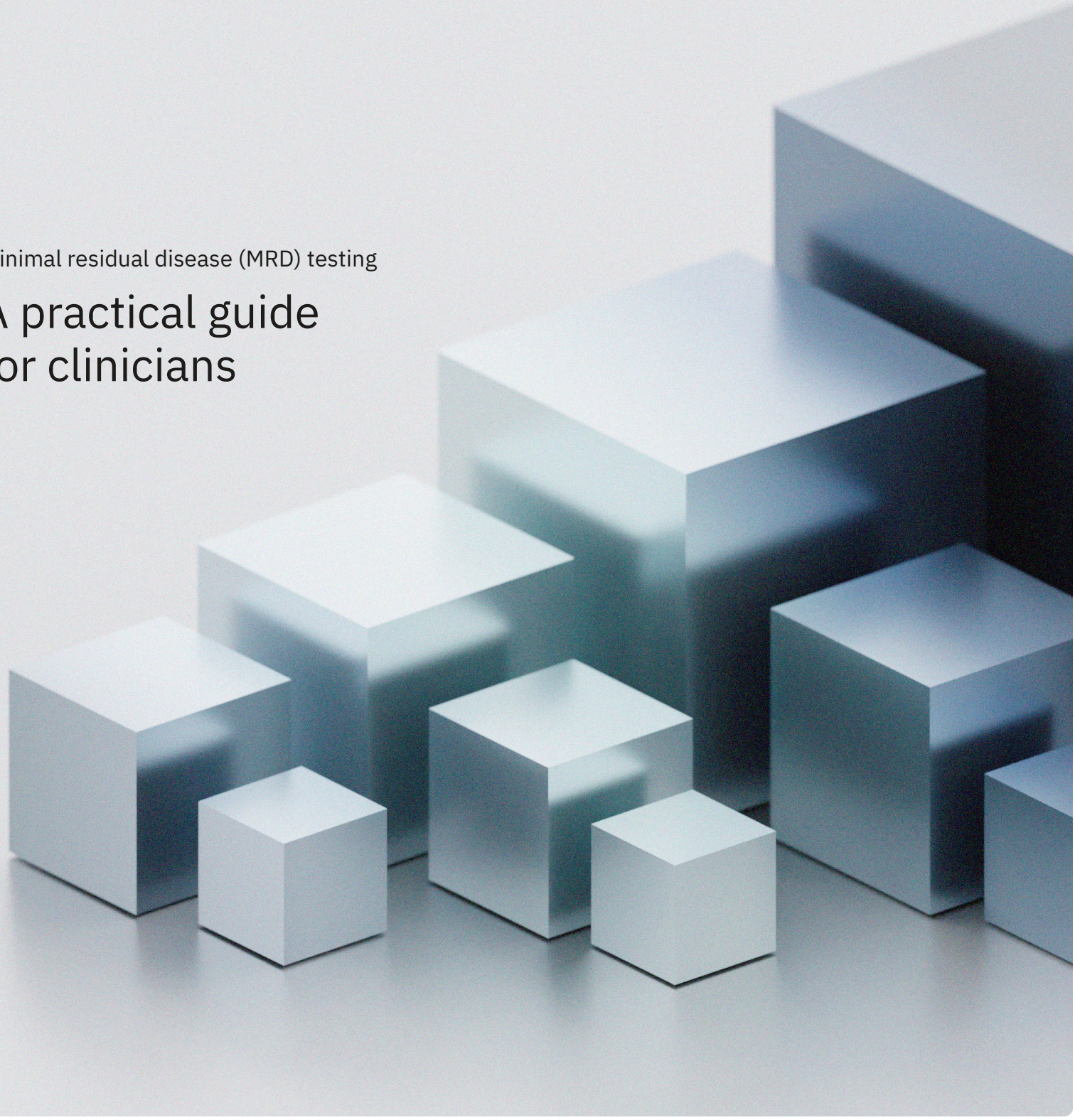
TEMPUS | ONCOLOGY

Minimal residual disease (MRD) testing

A practical guide for clinicians



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Introduction: Why MRD matters in day-to-day oncology

Minimal residual disease (MRD) testing can transform how clinicians approach cancer surveillance and manage recurrence risk. MRD testing post-resection offers clinicians a minimally invasive and highly sensitive approach to detect molecular recurrence, often preceding detection by standard radiographic imaging or other conventional monitoring methods. By incorporating MRD as an additional data point, this technology helps support clinical decision-making for patient management and surveillance strategies.

Tempus provides both tumor-naïve and tumor-informed MRD testing by xM and xM (NeXT Personal® Dx), respectively. This dual-modality approach enables clinicians to use MRD across various clinical contexts and considerations based on tumor tissue availability or turnaround time constraints.

What MRD testing does

MRD testing is used to identify the presence of circulating tumor DNA (ctDNA) in a patient's blood after initial cancer treatment, which may be detected weeks or even months before disease progression is visible through radiographic imaging or standard biomarker detection. MRD testing may be a valuable tool for clinicians evaluating post-treatment management by identifying whether residual disease remains after curative-intent therapy. As an additional data point, MRD results can help clinicians:

- Predict risk of relapse
- Guide the intensity of surveillance
- Treatment monitoring

These insights can support decisions that may influence a patient's clinical trajectory and provide clinicians with added confidence when managing cancer follow-up.

Choosing the right MRD test for the right clinical moment

Tumor-informed MRD testing

A tumor-informed MRD test requires a sample of the patient's tumor, which is sequenced to identify unique somatic variants. The test is then personalized to track these specific variants in the blood over time. This method offers high specificity and is best suited for long-term surveillance where maximizing sensitivity is the primary goal. However, the personalization process requires additional time, with results typically available in 3 to 6 weeks at the landmark timepoint.

Tumor-naïve MRD testing

A tumor-naïve MRD test does not require a tissue sample. Instead, it uses a predefined panel of common cancer-related mutations and epigenomic features to quantify ctDNA from a blood sample. This approach provides a faster turnaround time (typically 7 to 14 days) and is ideal when tissue is unavailable or a timely decision is needed, such as guiding post-operative care.

Selecting the appropriate assay may involve considering more than just traditional metrics like analytical sensitivity. The most effective test is the one that best answers the clinical question at hand. For a post-operative decision on adjuvant therapy, the speed of a tumor-naïve test may be more clinically valuable than the higher sensitivity of a tumor-informed test that takes several weeks. Conversely, maximizing sensitivity with a tumor-informed approach may be preferable for long-term surveillance where timing is more flexible.

Tempus provides both platforms for select cancers, allowing clinicians to select the right tool for the right clinical context.

Choosing the right MRD test for the right clinical moment

Navigating the challenges of integrating mrd into clinical practice

Despite its potential, adopting MRD testing into routine clinical care faces several hurdles. Understanding these challenges can help clinicians effectively integrate this technology into clinical practice.

- Lack of standardized guidelines. Universal guidelines delineating the optimal timing, testing frequency, and actionable clinical responses to MRD assessment have yet to be established for many cancer types. This requires clinicians to rely on emerging data and clinical judgment to determine the best testing strategy for each patient.
- The trade-off between sensitivity and turnaround time. In clinical scenarios where timely decision-making is flexible, a highly sensitive, tumor-informed assay may be the preferred approach to enhance risk stratification and guide subsequent management. However, in time-sensitive situations, such as making post-operative adjuvant therapy decisions, the faster turnaround of a tumor-naïve test may provide more immediate clinical value.
- Clinical performance varies across tumor types. Understanding the performance of an MRD assay across different tumor types and clinical scenarios is essential for clinical adoption. Evidence generated in one cancer type, colorectal cancer, for instance, cannot be assumed to apply to others, including lung or breast cancer, without disease-specific evidence. Tumor-specific factors, including differences in ctDNA shedding rates and anatomical barriers, partly drive variability in clinical performance. For example, the blood-brain barrier in central nervous system tumors can limit the release of ctDNA into the bloodstream.
- Evolving prospective data. Prospective evidence for MRD testing in solid tumors is still being explored, with the most mature data to date reported in colorectal cancer (CRC), particularly in the context of postoperative risk stratification and recurrence monitoring.
- Low clinical awareness. As a relatively new technology in many solid tumors, awareness and understanding of MRD testing, including its appropriate clinical applications, remain limited among healthcare providers and patients. Targeted education is essential to increasing familiarity and building confidence in its clinical utility.
- Reimbursement. Reimbursement for MRD testing is evolving and will be based on a specific plan's criteria.

How to implement MRD testing in clinical practice

Tempus designed its MRD testing workflows to integrate seamlessly into clinical practices. Ordering is straightforward through the Tempus Hub (online ordering portal) and does not require specialized laboratory handling. We provide sample collection kits, and clinicians can perform MRD testing using a standard blood draw. Once processed, results are returned through the Tempus Hub and can be integrated with common EMR systems.

For tumor-naïve testing, clinicians typically receive results within 7 to 14 days. The report provides a binary ctDNA detected or ctDNA not detected result, in addition to a quantitative score to support clinical decision-making. This provides clinicians with the opportunity to consider intervention following molecular recurrence. Potential clinical use case examples include:

- Early detection of molecular relapse
- Surveillance following curative-intent treatment
- Post-adjuvant therapy risk stratification and monitoring
- Surrogate endpoint for clinical trials

Integrating MRD assessment into standard care pathways provides clinicians with more comprehensive insights to support individualized follow-up.

Clinical utility of MRD testing in select solid tumors

Prognostic value of MRD testing available through Tempus

The prognostic significance of minimal residual disease (MRD) testing has been consistently demonstrated across multiple solid tumor types. In colorectal cancer (CRC), MRD positivity following surgical resection has been associated with an approximately 10-fold or greater increased risk of clinical recurrence.[1,2] In breast cancer, MRD testing offers a sensitive method for detecting residual disease post-treatment. ctDNA positivity is a strong early predictor of relapse, often preceding clinical or radiographic progression by several months.[3] In lung cancer, particularly early-stage adenocarcinoma, ctDNA positivity after curative-intent therapy was correlated with significantly worse recurrence-free survival (RFS).[4] Additionally, in patients treated with immune checkpoint inhibitors (ICIs), ctDNA clearance has emerged as a meaningful marker for treatment response.[5]

Beyond its prognostic value, MRD testing is increasingly being studied to improve clinical outcomes when incorporated as an additional data point in treatment decision-making.

MRD testing in colorectal cancer

In colorectal cancer, findings from the GALAXY study, part of the larger CIRCULATE-Japan platform, underscored the clinical impact of MRD status. As stated previously, patients with stage II or III CRC who were ctDNA-positive post-operatively experienced higher rates of clinical recurrence compared to their ctDNA-negative counterparts.[1] These findings align with preliminary results from the VICTORI study, which demonstrated similar prognostic utility of ctDNA testing in a prospective clinical setting.[2]

Beyond risk stratification, MRD testing may be increasingly used as an additional data point to inform adjuvant treatment decision-making, particularly for patients with ambiguous indications for chemotherapy or where treatment de-escalation is being considered.

MRD testing in breast cancer

In breast cancer, MRD testing offers a powerful window into subclinical disease persistence. Garcia-Murillas et al. used whole-genome sequencing-powered ctDNA assays to track residual disease post-treatment, demonstrating that ctDNA-positive patients often relapsed earlier and more frequently than ctDNA-negative patients.[3] Notably, MRD positivity often preceded clinical relapse by several months, offering an opportunity for earlier therapeutic intervention. The ability to detect relapse before standard radiographic progression highlights the role of MRD testing in refining surveillance strategies and potentially guiding the timing of therapies.

MRD testing in lung cancer

In early-stage lung adenocarcinoma, MRD testing is emerging as a critical biomarker for post-surgical risk assessment. In a 2025 study, Black et al. found that ctDNA-positive patients had significantly shorter recurrence-free survival, despite curative-intent resection.[4]

This suggests MRD testing may help identify high-risk patients who may benefit from adjuvant therapy or intensified surveillance, even within early-stage disease cohorts typically managed conservatively.

Monitoring immunotherapy response with MRD

MRD testing is proving useful in monitoring response to immunotherapy. In a pan-tumor analysis of patients treated with immune checkpoint inhibitors, ctDNA clearance was correlated with improved progression-free and overall survival.[5] This reinforces the potential for MRD to serve not only as a prognostic biomarker but also as an early indicator of therapeutic efficacy, particularly in the context of personalized oncology.

Summary of clinical utility in select solid tumors

Collectively, these studies affirm that MRD testing via ctDNA is a clinically meaningful tool across solid tumors mentioned above, in addition to several others, enabling earlier detection of recurrence, refined patient stratification, and an additional data point in informing treatment decisions. As MRD-guided management strategies continue to evolve, their integration into routine care has the potential to improve patient outcomes.

Conclusion: High-value care in clinician's hands

MRD testing brings precision to everyday oncology. With accessible workflows, rapid turnaround times, and optionality of MRD modalities provided by Tempus, clinicians are well-positioned to implement MRD testing as part of routine cancer care. The ability to personalize decisions, minimize overtreatment, and monitor patients non-invasively helps drive better outcomes and higher patient satisfaction. In addition, Tempus provides support services, including prior authorization assistance, to simplify reimbursement workflows for clinical practice.

Tempus distinguishes itself as the premier choice for MRD testing by offering a comprehensive suite of services within a single, integrated system. As a leader in AI-enabled technologies, we offer comprehensive genomic profiling (CGP) testing for treatment selection, germline testing for hereditary risk assessment, and now quantitative ctDNA testing for recurrence monitoring, surveillance, and treatment response. Tempus allows providers to access all essential tests and unified reporting through one platform, streamlining the entire patient care process.

The information contained in this guide does not constitute medical advice. Any decisions related to patient care and treatment choices should be based on the independent judgment of the treating physician and should take into account all information related to the patient, including, without limitation, the patient and family history, direct physical examination, and test results. Collectively, these studies affirm that MRD testing via ctDNA is a clinically meaningful tool across solid tumors mentioned above, in addition to several others, enabling earlier detection of recurrence, refined patient stratification, and an additional data point in informing treatment decisions. As MRD-guided management strategies continue to evolve, their integration into routine care has the potential to improve patient outcomes.

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xM is a finely tuned MRD assay that delivers rapid results from one blood draw to help detect residual disease or recurrence in stage II-IV resectable colorectal cancer (CRC).

xM (NeXT Personal® Dx)* is an ultra-sensitive, whole-genome assay that enables detection of ctDNA at very low levels to monitor residual disease and recurrence, and IO treatment response monitoring.

Test by Personalis.

References

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4 Black JRM, Bartha G, Abbott CW, et al. Ultrasensitive ctDNA detection for preoperative disease stratification in early-stage lung adenocarcinoma. *Nat Med*. 2025;31(1):70-76.

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