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No scalpel required: The rise of liquid biopsy in UK cancer diagnostic pathways

The NHS is the first health system worldwide to prioritise commissioned blood-based testing over traditional tissue biopsies within specific diagnostic pathways.

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Minimally invasive, quick and cost-effective, liquid biopsy is proving to have numerous benefits over traditional tissue biopsies following trials in England and Wales. Sian Morgan reports on the integration of liquid biopsy into NHS cancer diagnostics.

Cancer remains one of the leading causes of mortality worldwide, with early and accurate diagnosis being critical to improving patient outcomes. Traditional diagnostic methods, such as tissue biopsies, have long been the cornerstone of cancer diagnostic testing pathways. However, tissue biopsies are invasive, time-consuming and sometimes impractical for certain types of cancer sites. In response to these challenges, the NHS in the UK has begun integrating liquid biopsy – a minimally invasive technique that analyses circulating tumour DNA (ctDNA) from blood samples – into its cancer diagnostic pathways.

Liquid biopsy refers to the analysis of biomarkers, primarily ctDNA, which is usually found in blood, although they may also be found in urine or saliva. Unlike traditional biopsies that require surgical extraction of tumour tissue, liquid biopsies offer a non-invasive alternative that can provide real-time insights into tumour genetics. This technology enables clinicians to detect genetic variants, monitor treatment response and identify resistance mechanisms, without subjecting patients to repeated invasive tissue biopsy procedures.

The European Society for Medical Oncology has developed comprehensive guidelines to support the use of precision medicine following ctDNA testing, particularly in the context of liquid biopsy. These recommendations aim to standardise clinical implementation and ensure high-quality, evidence-based decision-making in oncology.

Incorporating liquid biopsy into NHS practice

Speed and accessibility

Liquid biopsies can deliver results faster than tissue biopsies, thereby improving cancer diagnostic pathway delivery to meet defined quality standards.

Precision medicine

The ability to identify actionable genetic variants allows for tailored/personalised therapies that improve efficacy and reduce unnecessary side effects. Integration of genomic data at the point of multidisciplinary team (MDT) discussion will improve overall efficiency and decision-making.

Patient comfort

Minimally invasive testing reduces physical and psychological burden, especially for patients with hard-to-reach tumours, those who would otherwise require repeated tissue biopsies, or those unfit for surgery. Avoiding surgical biopsies minimises risks such as infection, bleeding and anaesthesia-related complications.

Cost efficiency

Early data suggests that liquid biopsy may reduce overall healthcare costs by avoiding unnecessary treatments and hospital stays. The use of ctDNA testing will reduce the need for repeat tissue biopsies, which are resource-intensive and often delay treatment.

Workforce

Securing and enhancing the genomic diagnostic workforce of the future is another key factor. By streamlining the diagnostic workflow, ctDNA can help alleviate workforce pressures across pathology and oncology services.

A pioneering step

In May 2025, NHS England (NHSE) took a pioneering step by commissioning liquid biopsy testing through the NHSE Genomic Test Directory, making it routinely accessible to eligible patients with lung cancer and advanced breast cancer. This initiative established the NHS as the first health system worldwide to prioritise commissioned blood-based testing over traditional tissue biopsies within specific diagnostic pathways.

Lung cancer diagnostic pathway

The World Cancer Research Fund documents lung cancer as the 4th most common type of cancer in the UK across men and women, with 48,904 new cases in 2021 (totalling 12.4% of all new cancer cases in men and women combined), noting it as the UK's biggest cancer killer. Most patients are diagnosed with the disease at an advanced stage. However, personalised treatment options for lung cancer have expanded significantly, particularly for non-small cell lung cancer over the last few years.

Targeted therapies are available for several genetic variants, including *EGFR, KRAS, BRAF, ALK, ROS1, BRAF, MET, RET NTRK1, NTRK1* and *NTRK3* genes. Additionally, immune checkpoint inhibitors targeting PD-L1 are used for tumours expressing high levels of this protein. Genomic analyses are requested from tissue biopsy at the lung cancer MDT meeting, where histological diagnosis is reviewed and future treatment is decided.

The National Optimal Lung Cancer Pathway currently recommends that morphology results should be available within 3 days of the biopsy and the genetic results should be available within 10 days of the biopsy, in time for the MDT meeting before referral to oncology. Many challenges remain in ensuring all patients have timely access to molecular genomic testing, which is crucial for identifying suitable targeted therapies. Patients with advanced lung cancer can deteriorate rapidly and die if treatment is not received in time.

Pilot studies in England and Wales

In 2022, NHS England commissioned a pilot study to evaluate how large gene panel ctDNA testing could be integrated into the standard NHS lung cancer pathway and the impact it would have on patients. The lung cancer pilot programme involved over 10,000 patients with suspected stage 3 or 4 lung cancer across 176 hospitals. Results demonstrated that liquid biopsy could identify genetic variants up to 16 days faster than conventional tissue-based testing. This acceleration enabled earlier initiation of targeted therapies, improving patient outcomes and quality of life.

The implementation has been supported by other national programmes, such as the QuicDNA programme in NHS Wales. Wales uses an in-house, NHS-validated, fully interpreted large gene panel ctDNA test. This programme has demonstrated the delivery of the ctDNA results to the clinical team for the first MDT meeting. It includes people who would not have received effective, life-prolonging personalised treatment in the absence of the QuicDNA test. These initiatives have provided valuable insights into operational logistics, stakeholder engagement and clinical cancer pathway integration.

In NHS England, an independent evaluation estimated that the NHS could save up to £11 million annually in lung cancer care alone by adopting liquid biopsy. These savings stem from reduced hospital admissions, fewer unnecessary treatments, and more efficient resource allocation.

Breast cancer diagnostic pathway

The National Institute for Health and Care Excellence (NICE) approved elacestrant on 5 February 2025 for treating oestrogen receptor-positive, HER2-negative advanced breast cancer with an *ESR1* gene variant detected specifically in ctDNA. Following this, the diagnostic test was made routinely commissioned in NHS England and Wales after its publication on the NHSE Genomic Test Directory in May 2025.

This marked the first targeted treatment on the NHS for this specific subtype of advanced breast cancer, which develops from the *ESR1* gene variant that causes resistance to standard hormone therapies. Since the launch of the commissioned ctDNA service in NHS Wales in May, actionable *ESR1* gene variants were detected in 50% of patients tested. Detections were most frequent in hotspot codons 537 and 538, with interpretive reports issued within an average of 12.5 days from sample receipt in the laboratory.

Limitations to liquid biopsy

Despite its promise, the implementation of liquid biopsy faces several challenges.

Sensitivity and specificity

ctDNA may not detect all variants due to low tumour DNA shedding or technical constraints. Negative ctDNA results should be followed up with tissue biopsy when clinically indicated.

Standardisation

Variability in testing platforms and protocols can affect result consistency and clinical interpretation.

Infrastructure and training

Scaling up liquid biopsy requires investment in genomic laboratories and equipment across the UK.

Workforce development

Clinicians require training in interpreting the genetic report and integrating it into rapid treatment decisions.

Informed consent

Patients must understand the implications of genetic testing, including incidental findings and familial risk.

Expanding liquid biopsy provision

The NHS is now exploring the expansion of liquid biopsy to other cancer types, including cancer of unknown primary, colorectal, prostate and pancreatic cancers. Additionally, multi-cancer early detection tests based on liquid biopsy are being evaluated for population-wide screening programmes.

The integration of liquid biopsy aligns with UK NHS strategies (e.g. NHS 10-Year Health Plan in England, Scottish Genomics Strategy and Wales Genomics Delivery Plan), broader cancer research organisations (e.g. Cancer Research UK) and patient focus groups (e.g. EGFR Positive UK). Continued government support and strategic investment will be crucial to sustain and expand liquid biopsy implementation to additional cancer sites. Further collaboration with industry partners, academic institutions and patients will accelerate the innovation and evidence generation required for timely implementation.

The integration of liquid biopsy into the NHS cancer diagnostic pathways represents a transformative shift toward precision medicine. By offering faster, less invasive and more personalised diagnostics, liquid biopsy has the potential to improve patient outcomes, reduce healthcare costs and democratise access to cutting-edge cancer care. While challenges remain, the NHS's pioneering efforts provide a blueprint for other health systems worldwide. As technology advances and evidence accumulates, liquid biopsy is poised to become a cornerstone of modern oncology.

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