Bronchoscopic Liquid Samples for Molecular Testing

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Educational background

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Professional experience

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Next-generation sequencing (NGS) has become the standard of care for molecular profiling in non-small cell lung cancer (NSCLC), but tissue samples remain limited by invasiveness, low yield, and infeasibility of repeated biopsies. Plasma circulating tumor DNA (ctDNA) offers a minimally invasive alternative, yet its sensitivity is reduced in patients with low tumor burden or early-stage disease, resulting in false negatives in up to one-third of advanced NSCLC cases.

To address these limitations, a novel bronchoscopic approach—targeted washing fluid (TWF) collection—was developed using a 3 mm ultrathin bronchoscope. By instilling small aliquots of saline directly at the tumor site, TWF enables the collection of ctDNA concentrated around the primary lesion. This method is less invasive than forceps biopsy, while overcoming spatial heterogeneity and sampling challenges.

In a prospective trial at Pusan National University Hospital (NCT05517083), EGFR T790M mutations were detected in 29% of TWF samples, compared with 22% in tissue and 10% in plasma. Importantly, four patients had T790M mutations identified exclusively by TWF, which were later confirmed upon repeated biopsies. A subsequent pilot feasibility study (NCT06141005) demonstrated the potential of TWF for NGS testing. Among enrolled NSCLC patients, the detection rate of actionable mutations was 65% with TWF, compared with 47% in plasma and 48% in tissue. Notably, 18% of druggable mutations were detected solely by TWF, while no patient had mutations detected exclusively by tissue. Concordance analysis further confirmed high reliability of TWF with both plasma and tissue.

These findings indicate that TWF provides a higher detection rate for actionable mutations than conventional plasma or tissue testing. By combining minimal invasiveness with enhanced sensitivity, targeted washing offers a promising platform for molecular profiling, particularly in patients with low ctDNA shedding or insufficient tissue. Integration of this technique into routine practice could significantly improve the accuracy of precision oncology in NSCLC.

References

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