



Poster #:
EP2.185

Juwhan Choi¹, Mi Ran Kang ², Hyun Jin Yun², Jun Ho Ko² , **Sung Yong Lee¹**
¹*Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Republic of Korea.*
²*Gencurix, Inc., Seoul, Republic of Korea.*
Correspondence: syl0801@korea.ac.kr



IASLC 2026 World
Conference on Lung Cancer
SEPTEMBER 12 – 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

Molecular profiling is essential for guiding targeted therapies in non-small cell lung cancer (NSCLC), with FFPE tissue serving as the current standard. However, limited tissue availability frequently restricts comprehensive genomic testing in real-world clinical settings. Next-generation sequencing (NGS) enables broad genomic profiling but is often constrained in clinical practice by long turnaround times, higher sample input requirements, and dependence on specialized infrastructure. In contrast, digital PCR (dPCR) allows rapid and highly sensitive detection of target mutations from minimal input material, offering a pragmatic solution for timely clinical decision-making, particularly in limited-sample settings. While plasma-based liquid biopsy provides a minimally invasive alternative, its clinical utility is frequently limited by low tumor DNA fraction, resulting in suboptimal sensitivity and frequent false-negative findings. Bronchial fluid samples, including bronchoalveolar lavage fluid (BALF) and bronchial washing fluid (BWF), directly reflect the tumor microenvironment and may provide enhanced detection sensitivity. However, their clinical utility in multiplex digital PCR-based mutation profiling remains insufficiently characterized. This study aimed to evaluate the clinical value of bronchial fluid-based liquid biopsy by comparing mutation detection concordance across multiple sample types.

METHODS

Study Population and Specimens

Patients with newly diagnosed NSCLC or undergoing repeat biopsy for treatment modification were enrolled. Matched tumor tissue, plasma, bronchoscopic washing fluid, and BAL fluid were collected for detection of EGFR, KRAS, BRAF, ERBB2, MET, ALK, ROS1, RET, and NTRK1/2/3 mutations. Bronchoscopic specimens were collected when clinically indicated; patients without bronchoscopic sampling were evaluated using tissue and plasma. All specimens were analyzed using a dPCR-based assay at Gencurix, Inc. (registered genetic testing laboratory No. 265, Republic of Korea).

Multiplex Digital PCR Testing

Molecular testing was performed using the DigiPlex Lung Cancer Panel (Gencurix, Korea), a multiplex digital PCR-based NSCLC assay targeting >250 clinically relevant DNA mutations and RNA fusion alterations in EGFR, KRAS, BRAF, ERBB2, ALK, ROS1, MET, RET, and NTRK1/2/3.

FFPET was used as the reference specimen, and molecular results from matched plasma, BWF, and BALF specimens were compared for concordance.

DISCUSSION AND CONCLUSION

DISCUSSION

This study demonstrates the potential of **bronchial fluid specimens as complementary liquid biopsy sources** for multiplex digital PCR-based molecular profiling in non-small cell lung cancer (NSCLC). BALF and BWF showed higher overall DNA concordance with FFPE tissue than plasma (**84.8% and 82.2% vs. 70.2%, respectively**). These findings suggest that bronchial fluid specimens may provide a useful source of tumor-derived nucleic acids compared with peripheral blood. Notably, **positive agreement between FFPE tissue and BALF/BWF showed an apparent stage-dependent pattern**. Positive agreement was relatively low in Stage I disease, whereas **100% of evaluable FFPE-positive alterations in Stage II and Stage III were detected in both BALF and BWF**. This stage-dependent difference may be associated with tumor size and extent, lesion characteristics, the degree of tumor-derived nucleic acid shedding, or the proximity of bronchoscopic sampling to the tumor. However, because the number of alteration-positive cases in the more advanced stages was limited, particularly in **Stage II (n=3) and Stage III (n=1)**, these findings should be considered exploratory and require validation in a larger clinical cohort.

In addition, several clinically relevant alterations that were not detected in plasma were identified in BALF or BWF. This finding further supports the potential complementary role of bronchial fluid specimens when plasma ctDNA levels are insufficient for molecular detection. Because BALF and BWF are collected directly from the tumor-bearing airway or adjacent regions, they may serve as **local sources of tumor-derived DNA and RNA**. Therefore, when tissue specimens are limited or plasma-based testing provides insufficient molecular information, bronchial fluid testing may offer a complementary strategy to tissue- and plasma-based molecular profiling. BALF and BWF may also have practical clinical value because they can be obtained from patients undergoing bronchoscopy as part of the diagnostic workup for lung cancer. Applying the same multiplex digital PCR approach to FFPE tissue, plasma, and bronchial fluid specimens enables molecular findings from different specimen types to be compared and complemented, supporting the potential development of a **multi-specimen molecular profiling strategy** that is not solely dependent on the availability of tissue specimens. This study has several limitations. The overall cohort size was relatively small, and fully matched FFPE tissue, plasma, BALF, and BWF specimens were available only for a subset of patients. In addition, factors related to bronchoscopic sampling—including the distance between the tumor and sampling site, recovered sample volume, tumor cell content, and nucleic acid concentration—may influence molecular alteration detection but were not systematically evaluated in this study. Future prospective studies with larger numbers of matched FFPE tissue, plasma, BALF, and BWF specimens are needed to validate the observed stage-dependent pattern of positive agreement and to further evaluate the clinical and specimen-related factors affecting molecular detection in bronchial fluids.

CONCLUSION

In this study, **BALF and BWF demonstrated higher overall DNA concordance with FFPE tissue than plasma**, while positive agreement for FFPE-positive alterations showed a trend toward lower agreement in Stage I and higher agreement in Stage II–III disease. These findings support the potential utility of **BALF and BWF as complementary liquid biopsy specimens** for multiplex digital PCR-based molecular profiling in NSCLC, particularly as a complement to tissue- and plasma-based testing. Larger prospective studies are warranted to validate the observed stage-dependent pattern and to further establish the **clinical utility of bronchial fluid-based liquid biopsy in NSCLC**.

REFERENCES & ACKNOWLEDGEMENTS

Reference

- Rolfo C, et al.** *J Thorac Oncol.* 2021;16(10):1647–1662.
- Ryu WK, et al.** *Lung Cancer.* 2023;186:107390.
- Kim MH, et al.** *JCO Precis Oncol.* 2025;9:e2500299.
- Kim IA, et al.** *Cancers (Basel).* 2022;14(11):2744.
- Jiang J, et al.** *J Mol Diagn.* 2020;22(2):228–235.
- Sugimoto A, et al.** *Clin Cancer Res.* 2023;29(8):

RESULTS

1. Study Population Characteristics

A total of **53 patients with NSCLC** were included in the study. The mean age was **67.3 ± 8.5 years**, and the majority of patients were male (**83.0%**) and smokers (**84.9%**). Adenocarcinoma (**49.1%**) and squamous cell carcinoma (**45.3%**) were the predominant histologic subtypes.

Table 1. Baseline Characteristics of the Study Population

Characteristics	N (%)
Sex	
Male	44 (83.0%)
Female	9 (17.0%)
Total	53 (100.0%)
Ages	
(N) Mean ± SD	53, 67.3 ± 8.5 years
Smoking Status	
Smoker	45 (84.9%)
Non-smoker	8 (15.1%)
Total	53 (100.0%)
History of non-small cell lung cancer (NSCLC)	
Present	53 (100.0%)*
No history	0 (0.0%)*
Total	53 (100.0%)
Histological Classification	
Adenocarcinoma	26 (49.1%)
Squamous cell carcinoma	24 (45.3%)
Others	3 (5.7%)
Total	53 (100.0%)
Stage (AJCC 8th)	
Stage I	20 (40.8%)
Stage II	6 (12.2%)
Stage III	14 (28.6%)
Stage IV	9 (18.4%)
Total	49 (100.0%)

Cancer stage was classified according to the AJCC 8th edition. Stage information was available for 49 of 53 subjects. Stage could not be determined for one subject with incomplete TNM information (pTbN0), and stage information was unavailable for three subjects.

2. Molecular Alterations Detected in FFPET

Patients represented both early- and advanced-stage NSCLC, enabling exploratory evaluation of molecular detection according to disease stage.

Table 2. Comparison of hospital prior molecular results and DigiPlex LC Panel results in FFPE tissue according to AJCC 8th disease stage

Gene / alteration	Total H/D	IA H/D	IB H/D	IIA H/D	IIB H/D	IIIA H/D	IVA H/D	IVB H/D	Unknown H/D
KRAS Total	9/9	4/4	2/2	1/1	1/1	0/0	0/0	1/1	0/0
G12V	3/3	1/1	2/2	0/0	0/0	0/0	0/0	0/0	0/0
G12C	2/2	1/1	0/0	1/1	0/0	0/0	0/0	0/0	0/0
G12D	1/1	0/0	0/0	0/0	1/1	0/0	0/0	0/0	0/0
G12A*	2/—	2/—	0/—	0/—	0/—	0/—	0/—	0/—	0/—
G13D*	1/—	0/—	0/—	0/—	0/—	0/—	0/—	1/—	0/—
G12/13X*	—/3	—/2	—/0	—/0	—/0	—/0	—/0	—/1	—/0
EGFR Total	8/6	3/3	1/1	1/1	0/0	1/1	0/0	0/0	2/0
L858R	5/4	3/3	0/0	1/1	0/0	0/0	0/0	0/0	1/0
E19Del	2/1	0/0	0/0	0/0	0/0	1/1	0/0	0/0	1/0
L861Q	1/1	0/0	1/1	0/0	0/0	0/0	0/0	0/0	0/0
ALK fusion	0/2	0/0	0/0	0/1	0/0	0/0	0/1	0/0	0/0
RET fusion	1/1	0/0	0/0	0/0	0/0	0/0	1/1	0/0	0/0
Overall alteration count	18 / 18	7/7	3/3	2 / 3†	1/1	1/1	1 / 2†	1/1	2 / 0

H, hospital prior result; D, DigiPlex LC Panel FFPE result. *In the prior hospital results, KRAS subtypes were specifically reported as G12A or G13D, whereas DigiPlex reported some of these cases as G12/13X. Therefore, differences across these rows should be interpreted as differences in reporting resolution between the assays, rather than as simple subtype discordance. † DigiPlex identified additional alterations in some cases; therefore, the total alteration count may exceed the number of alteration-positive patients. In particular, Patient No. 20 had concurrent KRAS G12C and ALK alterations detected by DigiPlex.

Comparison	Hospital	DigiPlex FFPE	Interpretation
Total alterations	18	18	Overall alteration counts comparable
KRAS	9	9	Same gene-level detection count
EGFR	8	6	Two hospital-positive cases had no evaluable DigiPlex FFPE result
ALK	0	2	Additional alterations detected by DigiPlex
RET	1	1	Concordant
Stage IA alterations	7	7	Comparable
Stage IB alterations	3	3	Comparable
Stage IIA alterations	2	3	Additional ALK in a KRAS G12C-positive case
Stage IIIA alterations	1	1	Comparable
Stage IVA alterations	1	2	Additional ALK detected by DigiPlex
Stage IVB alterations	1	1	Comparable

Comparison of molecular alterations according to disease stage demonstrated generally comparable gene-level results between prior hospital testing and DigiPlex LC Panel testing of FFPE tissue. KRAS alterations were identified in nine cases by both methods, while six EGFR alterations were detected by DigiPlex compared with eight in the prior hospital results; the two additional hospital EGFR-positive cases had no available DigiPlex FFPE results and therefore did not represent discordant results. DigiPlex additionally identified ALK alterations in two cases, including one concurrent KRAS G12C/ALK-positive case. Importantly, tissue alteration detection remained substantial in early-stage disease, with seven alterations identified in stage IA and three in stage IB by DigiPlex, providing a tissue-positive reference population for subsequent evaluation of liquid biopsy detection according to disease stage.

3. Concordance According to Specimen Type

Among patients with matched specimens, concordance between FFPET and liquid biopsy specimens was evaluated for DNA mutations and RNA fusion alterations.

For DNA mutation detection, BWF (82.2%) and BALF (84.8%) showed higher overall concordance with FFPET than plasma (70.2%). For RNA fusion detection, concordance was comparable across specimen types, ranging from 85.1% to 91.3%.

Table 3. Comparison of molecular alterations detected by DigiPlex LC Panel across FFPET, plasma, BWF, and BALF specimens

Gene / alteration	FFPET	Plasma	BWF	BALF
KRAS Total	9	0	4	4
└ G12V	3	0	1	1
└ G12C	2	0	1	1
└ G12/13X	3	0	1	1
└ G12D	1	0	1	1
EGFR Total	6	0	2	3
└ L858R	4	0	1	1
└ E19Del	1	0	1	1
└ L861Q	1	0	0	1
ALK fusion	2	0	0	0
RET fusion	1	0	0	0
cMET	0*	0	1*	0
Total alteration count	18	0	7	7
Alteration-positive subjects	17	0	7	7
NMD	31	49	39	40
Invalid	0	0	1	1
Valid/evaluable results	48	49	46	47
Alteration-positive rate	35.40%	0.00%	15.20%	14.90%

Specimen	DNA concordance with FFPET	RNA concordance with FFPET
Plasma	70.2%	85.1%
BWF	82.2%	89.1%
BALF	84.8%	91.3%

4. Stage-Dependent Detection of Tissue-Positive Alterations in Bronchial Fluid

Patients represented both early- and advanced-stage NSCLC, enabling exploratory evaluation of molecular detection according to disease stage. Using FFPET, the DigiPlex LC Panel detected a broad spectrum of clinically relevant alterations, including KRAS and EGFR mutations as well as ALK and RET fusions. KRAS alterations included G12V, G12C, G12D, and G12/13X, while EGFR alterations included L858R, exon 19 deletion, and L861Q

Because release of tumor-derived nucleic acids may vary according to tumor burden and disease extent, the positive agreement of BALF and BWF with FFPET was further explored according to disease stage.

Among patients with evaluable stage information, FFPET alterations were detected in:

The ability of bronchial fluid specimens to reproduce these FFPET-positive results differed substantially according to stage.

Table 4. Stage-specific detection of FFPET-positive alterations in bronchial fluid

Stage group	FFPET alteration detection	BWF detection among FFPE-positive	BALF detection among FFPE-positive
Stage I	10	2/10 (20.0%)	3/10 (30.0%)
Stage II	3	3/3 (100.0%)	3/3 (100.0%)
Stage III	1	1/1 (100.0%)	1/1 (100.0%)
Stage IV	3	NA	NA

In Stage I disease, positive agreement with FFPET was relatively low:

In contrast, all evaluable FFPET-positive alterations in Stage II and Stage III diseasewere also detected in both BWF and BALF.

These findings suggest a stage-dependent trend in bronchial fluid molecular detectability, with lower detection in Stage I disease and substantially higher agreement in patients with Stage II or higher disease.

Because the number of alteration-positive patients in individual stage groups was limited, these findings should be interpreted as an exploratory trend rather than definitive evidence of a quantitative association between disease stage and analytical sensitivity.