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Clinical Study to Validate a Universal Panel for Liquid Biopsy

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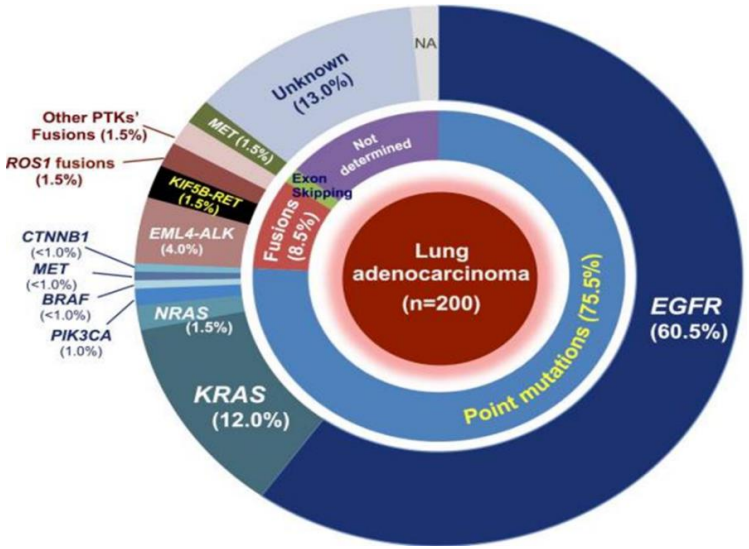
Background

Lung cancer has a high mortality and incidence worldwide. In Korea, the incidence rate of lung cancer ranks second, and the incidence rate is increasing every year. In particular, more than 80% of lung cancers are NSCLS. Early detection is most important for the patient survival. Recently, low-dose CT is a representative diagnostic method, but there is high false-positive rate. Therefore, many people are focusing on the development of molecular diagnostics and more accurate early diagnosis methods. More recently, liquid biopsy has been used to overcome the limitations of tissue biopsy. Liquid biopsy has been used to diagnose various diseases including cancer. Various fluids contain many substances, such as cells, proteins, and nucleic acids from normal tissues, but very few substances from the disease area. The investigation and analysis of these substances in the liquid play a pivotal role in diagnosis of various disease. Therefore, it is important to accurately isolation and analysis of the required substances, and many techniques are used for this.



우리나라 폐선암 환자에서 확인된 유전자변이의 빈도
(*Seo, et al., Genome Res. 2012;22:2109-2119*)

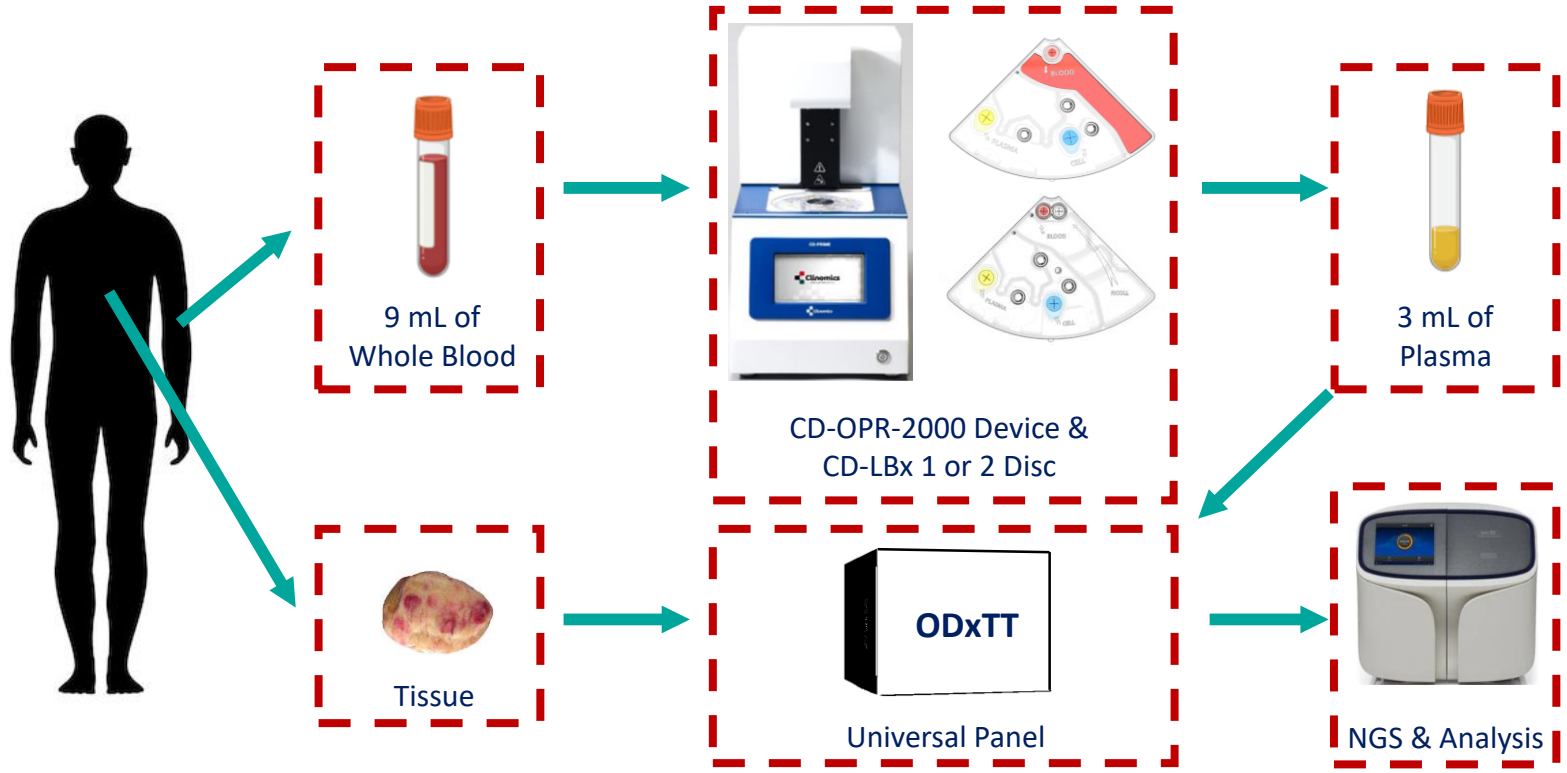
Materials and Methods

Clinical Information in Study

Pathological Information	N=100
Histology	
Squamous cell carcinoma	13(13%)
Adenocarcinoma	81(81%)
NSCLC_NOS	4(4%)
Other	2(2%)
Site of biopsy	
Lung	65(65%)
Lymph node	34(34%)
Pleural	1(1%)
Clinical stage	3(3%)
IA	0(0%)
IB	1(1%)
IIA	6(3%)
IIB	9(6%)
IIIA	3(3%)
IIIB	4(4%)
IIIC	21(21%)
IVA	53(53%)
IVB	10(10%)
Recurrence	3(3%)

Many cancer-related molecular markers are already known. Recently, NGS panels that can analyze a large number of markers at once have been widely used. However, most of the panels still mainly use tissues. The need for a panel that accurately detects a small amount of material, such as liquid biopsied substances, has emerged. In this study, we confirmed the performance of ODxTT panel that can be universally used in cfDNA and tissues. For this study, tissues and blood were collected individually from 100 lung cancer patients.

Experiment Schematic



Concordance of Results

Summary of Detection

Mutation Status Information	N=100
EGFR Mutation status	
Negative	72(72%)
Positive	24(24%)
Not done	4(4%)
EGFR Mutation type	
Exon 19 deletion	12(50%)
Exon 20 insertion. 3 dup	1(4%)
S768I	1(4%)
L858R	9(38%)
L861Q	1(4%)
ALK Fusion status	
Negative	92(92%)
Positive	2(2%)
Not done	6(6%)
ROS1 Fusion status	
Negative	82(82%)
Positive	4(4%)
Equivocal	2(2%)
Not done	12(12%)
BRAF Mutation status	
Negative	11(11%)
Positive	0(0%)
Not done	89(89%)

In our results, the concordance rate was 58.06% (54/93) between tissue and plasma. In particular, the EGFR mutation detection result shows a sensitivity of about 85.71% (18/21) in tissue and 28.57% (6/21) in plasma compared to qRT-PCR. In addition, the specificities are approximately 89.86% (62/69) and 98.55% (68/69), respectively. PPV was 72% in tissue and 85.71% in plasma, and NPV were 95.38% and 81.61%, respectively. Comparisons with more panels, such as liquid biopsy panels, are needed, but we found the possibility that ODxTT could also be used for liquid biopsy.

Concordance between Tissue and Plasma

Platform	ODxTT			ODxTT
Specimen	Tissue	Plasma		Tissue and Plasma
Positive	45	14	Concordance	58.06% (54/93)
Negative	48	83		
ND	3(*4)	2(*1)		

* QC failed

Sensitivity and Specificity of EGFR, ROS1, ALK and BRAF

EGFR

Specimen	Tissue		Tissue	Plasma
Platform	qPCR		ODxTT	ODxTT
Positive	24	Sensitivity	85.71% (18/21)	28.57% (6/21)
Negative	72	Specificity	89.86% (62/69)	98.55% (68/69)
ND	4	PPV	72.00% (18/25)	85.71% (6/7)
		NPV	95.38% (62/65)	81.61% (71/87)
19del	12	Sensitivity	75.00% (9/12)	33.33% (4/12)
20ins	1		0.00% (0/1)	0.00% (0/1)
L858R	9		100.00% (8/8)	25.00% (2/8)
L861Q	1		-	-
S768I, G719C	1		100.00% (1/1)	0.00% (0/1)

KRAS

Case	ODxTT		Case	ODxTT	
	Tissue	Plasma		Tissue	Plasma
1	P	P	9	P	N
2	P	N	10	N	N
3	P	N	11	P	P
4	P	N	12	P	N
5	P	N	13	N	N
6	N	N	14	P	N
7	-	N	15	N	N
8	P	N	16	N	P

P : Positive, N : Negative

ROS1

Specimen	Tissue		Tissue	Plasma
Platform	qPCR		ODxTT	
Positive	3	Sensitivity	0.00% (0/3)	0.00% (0/3)
Negative	82(*3)	Specificity	91.46% (75/82)	0.00% (0/82)
ND	13(*1)			

* QC failed

ALK

Specimen	Tissue		Tissue	Plasma
Platform	IHC		ODxTT	
Positive	1	Sensitivity	0.00% (0/1)	0.00% (0/1)
Negative	89(*4)	Specificity	96.63% (86/89)	0.00% (0/89)
ND	6			

* QC failed

BRAF

Specimen	Tissue		Tissue	Plasma
Platform	??		ODxTT	
Positive	0	Sensitivity	-	-
Negative	10(*1)	Specificity	100.00% (10/10)	100.00% (10/10)
ND	86(*3)			

* QC failed