

Comparison of the analytical performance of the Oncomine Dx Target Test focusing on bronchoscopic biopsy forceps size in non-small-cell lung cancer.

T. Sakaguchi*^a, Y. Nishii^a, S. Esumi^a, M. Esumi^a, Y. Nakamura^a, Y. Suzuki^a, K. Ito^a, K. Fujiwara^a
H. Yasui^a, O. Taguchi^a, O. Hataji^a

^a Matsusaka Municipal Hospital, Matsusaka, JAPAN

INTRODUCTION & OBJECTIVE

- Next-generation sequencing (NGS) has been implemented in clinical oncology to analyze multiple genes and to guide targeted therapy.
- The Oncomine Dx Target Test (ODxTT) is one of the NGS panels, and was approved by the Ministry of Health, Labor and Welfare of Japan in February 2019, as a companion diagnostic for targeted therapies on four driver mutations: EGFR, ALK, ROS1, and BRAF(p.V600E).
- Although the pathological diagnosis and biomarker tests for patients with advanced lung cancer have mostly been obtained with small biopsy samples, especially with bronchoscopic approaches, the performance for NGS with respect to the different sizes of biopsy forceps remains little known.
- Therefore, in this study we retrospectively evaluated the analytical performance of the ODxTT on endobronchial biopsy/transbronchial biopsy (EBB/TBB) samples focusing on the biopsy forceps size in clinical settings.

METHODS

Patient selection

- Consecutive patients who were diagnosed with NSCLC and whose formalin-fixed and paraffin-embedded (FFPE) samples obtained by EBB/TBB had been submitted for the ODxTT from August 2019 to July 2020.
- Samples collected in other hospitals, and archived samples, were excluded.

Sample processing

- FFPE samples were prepared according to The Japanese Society of Pathology Practical Guidelines on the handling of pathological tissue samples for cancer genomic medicine.¹⁾
- Multiple samples with suitable tumor content were selected with marking and macro-dissection, collectively placed on a slide, and submitted for the ODxTT.

Outcomes

- Success rate for the ODxTT
- Tissue size measured in area

We evaluated the outcomes, dividing cases into three groups as shown in the figure on the right.

Group A: the group with EBB/TBB performed using only standard forceps, circled in green

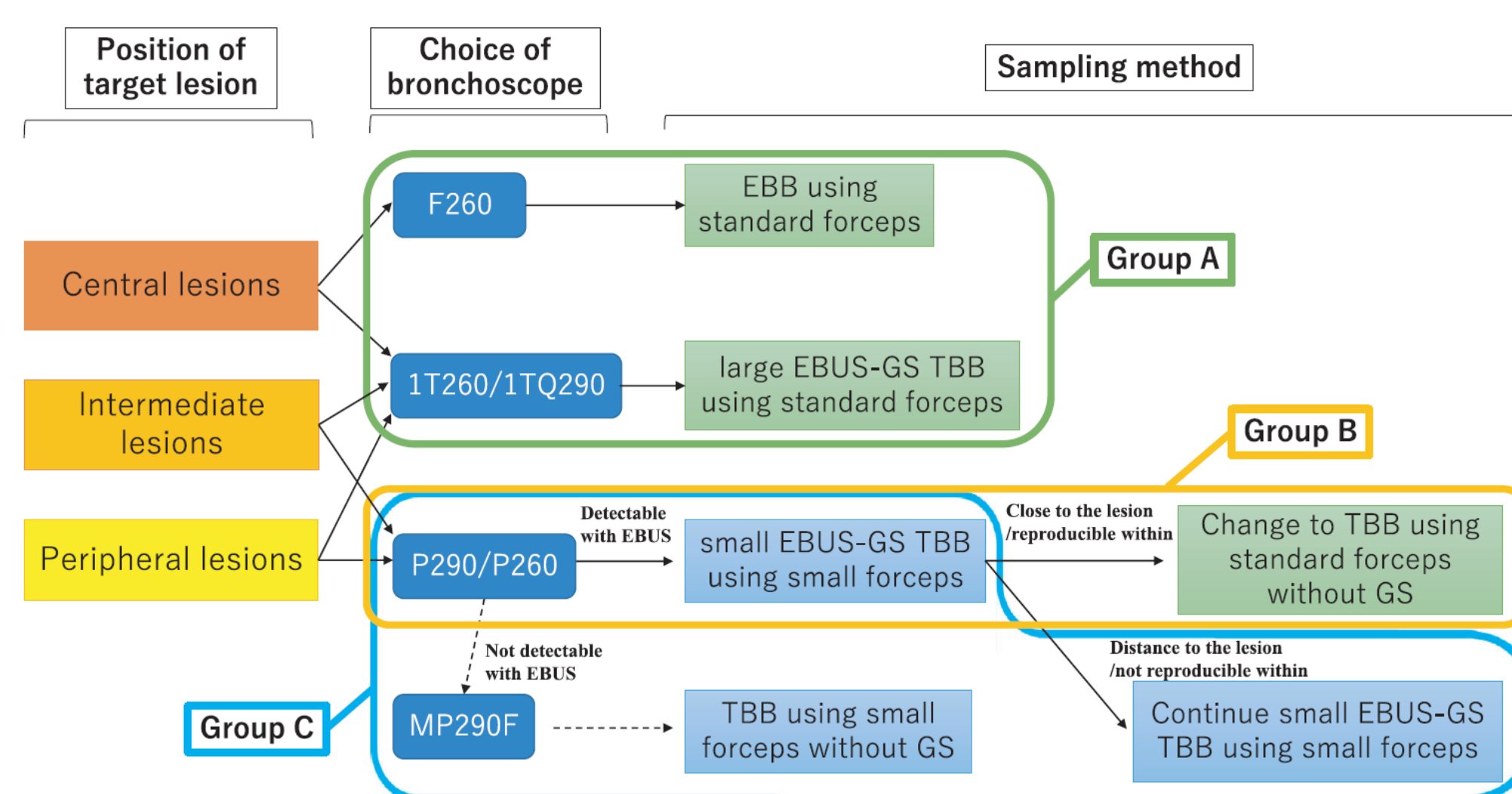
Group B: the group with TBB performed using standard forceps and small forceps, circled in orange

Group C: the group with TBB performed using only small forceps, circled in blue.

Main analysis: combined Groups A and B vs. Group C

Subanalysis: Group B vs. Group C

Sampling strategy and methods



Abbreviations: EBB, endobronchial biopsy; EBUS, endobronchial ultrasonography; GS, guide sheath; TBB, transbronchial biopsy.

RESULTS

Sample characteristics

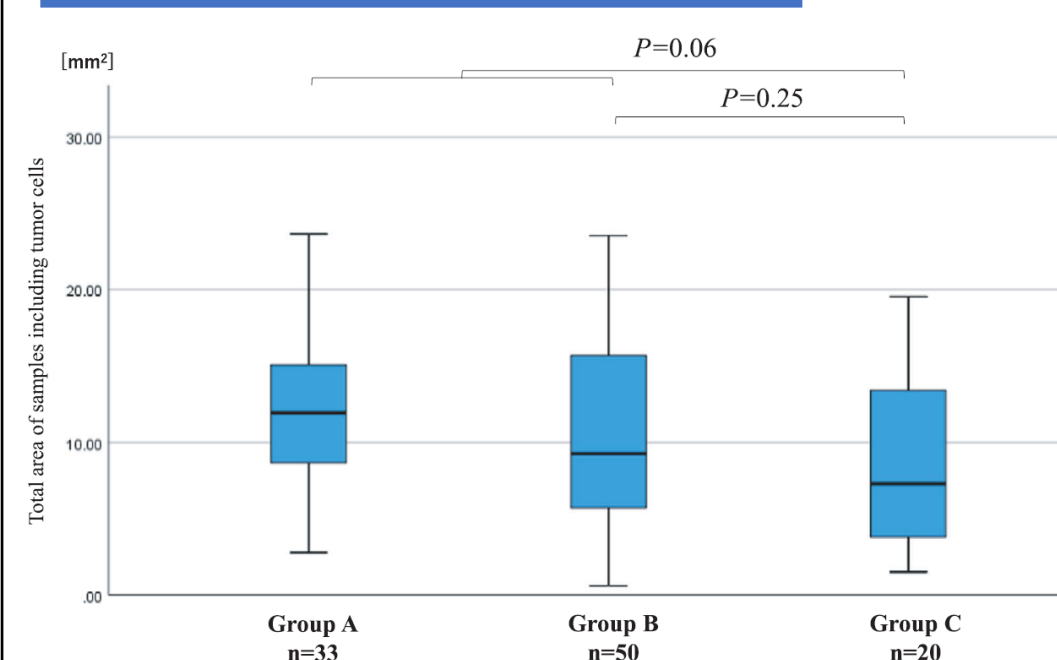
	Group A		Group B		Group C	
	n=33	(%)	n=50	(%)	n=20	(%)
Median age	76		74		75	
Range	55-93		55-90		39-94	
Sex						
Female	9	27%	18	36%	4	20%
Histology						
Non-sq	20	61%	33	66%	15	75%
Sq	13	39%	17	34%	5	25%
Radiological location						
Central	25	76%	8	16%	2	10%
Intermediate	6	18%	21	42%	9	45%
Peripheral	2	6%	21	42%	9	45%
Median lesion size (mm)	41		27		25	
Range	11-110		7-67		9-52	
Nodule classification						
Pure GGN	1	3%	0	0%	2	10%
Part solid nodule	1	3%	6	12%	4	20%
Solid nodule	31	94%	44	88%	14	70%
CT bronchus sign						
positive	32	97%	50	100%	19	95%

Abbreviations: GGN, ground glass nodule.

Analysis results of ODxTT

	Group A		Group B		Group C	
	n=33	(%)	n=50	(%)	n=20	(%)
Results of ODxTT						
Success of analysis	28	85%	41	82%	14	70%
Not passing the nucleic acid concentration threshold	1	3%	2	4%	3	15%
Invalid results for DNA only (EGFR, BRAF)	3	9%	4	8%	2	10%
Invalid results for RNA only (ALK, ROS1)	1	3%	3	6%	1	5%
Invalid results for DNA and RNA	0	0%	0	0%	0	0%

The comparison of tissue size



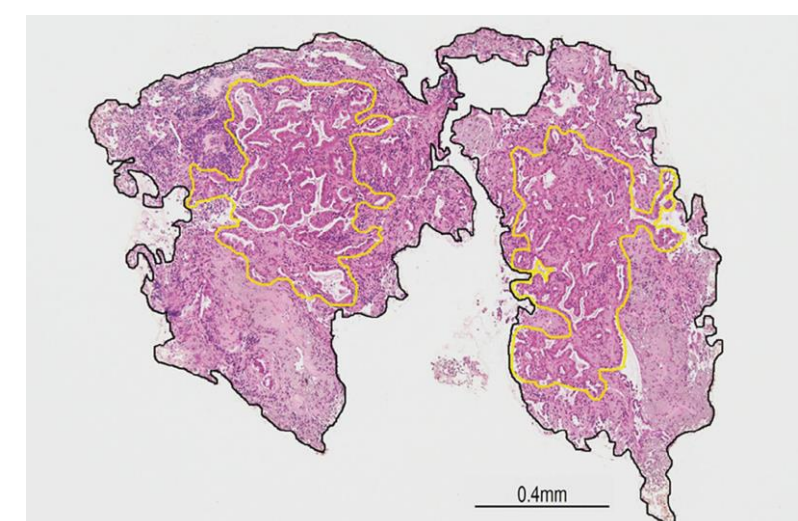
Student's t-test

Tissue size (4mm² cutoff)

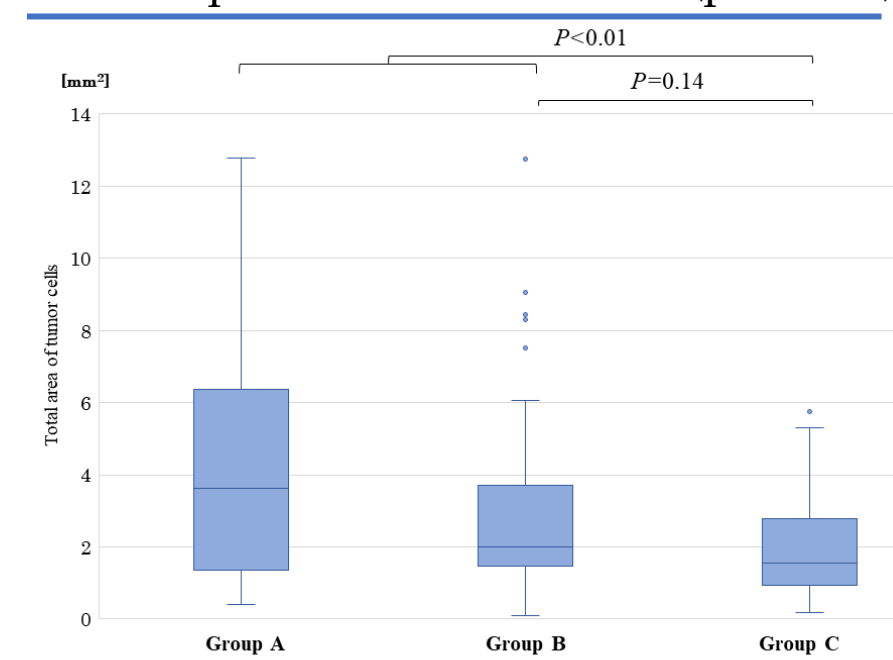
	Group A		Group B		Group C	
	n=33	(%)	n=50	(%)	n=20	(%)
Total area of samples including tumor cells						
≥4mm ²	32	97%	45	90%	14	70%
<4mm ²	1	3%	5	10%	6	30%

Fisher's exact test

Evaluation of the tissue and tumor size.
Areas surrounded by black are tissue size.
Areas surrounded by yellow are tumor size.

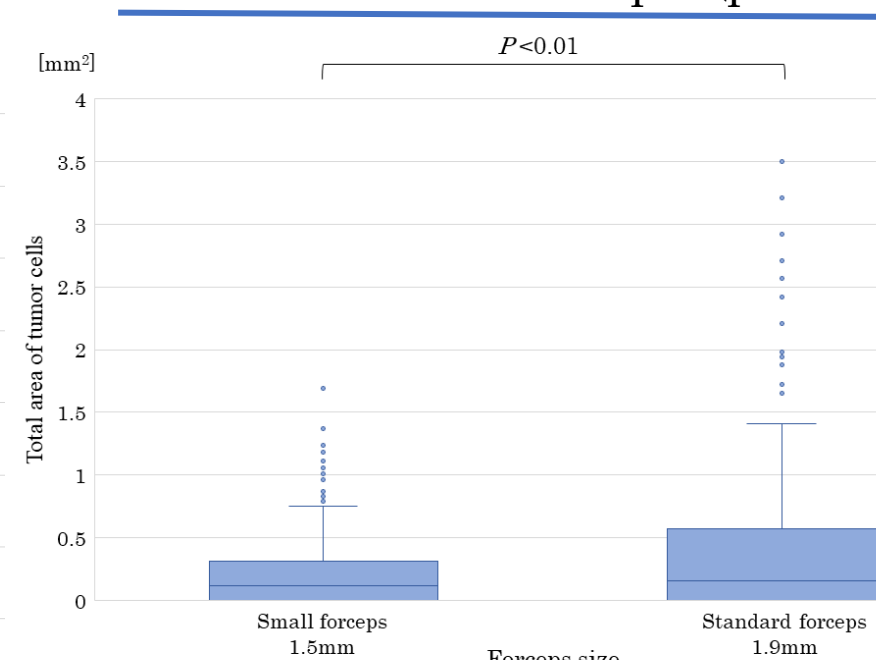


The comparison of tumor size (post hoc)



Student's t-test

Tumor sizes in one sample (post hoc)



Student's t-test

SUMMARY and CONCLUSION

- Our results showed that the TBB cases performed using only small forceps were prone to unsuccessful analysis.
- The main reason for the lower success rate of ODxTT in Group C, compared with Group A and B, was due to an insufficient amount of nucleic acid, and not due to a low quality of nucleic acids.
- A retrospective study reported a favorable success rate for the ODxTT when tumor specimens with a tissue size of 4 mm² or larger were used.²⁾
- The proportion with tissue sizes 4 mm² or larger was significantly lower in Group C compared with combined Groups A and B.

In conclusion, the analysis of ODxTT for TBB specimens using only small forceps is prone to be unsuccessful due to an insufficient amount of nucleic acid.

REFERENCES

- Hatanaka Y, et al. The Japanese Society of Pathology Practical Guidelines on the handling of pathological tissue samples for cancer genomic medicine. *Pathol Int.* 2021;71(11):725-740. doi: 10.1111/pin.13170.
- Takeyasu Y, et al. Feasibility of next-generation sequencing (Oncomine™ DX Target Test) for the screening of oncogenic mutations in advanced non-small-cell lung cancer patients. *Jpn J Clin Oncol.* 2021 ;51(7):1114-1122. doi: 10.1093/jco/hyab059.

Disclosure of funding source(s):

Matsusaka Municipal Hospital received research grant funding from Novartis, GlaxoSmithKline, AstraZeneca, Daiichi Sankyo, Bayer, and Boehringer Ingelheim. K. Ito has received speaker fees as honoraria from Eli Lilly Japan, Chugai, AstraZeneca, MSD, Boehringer Ingelheim Japan, Ono, and Pfizer Japan. O. Taguchi received speaker fees as honoraria from AstraZeneca. O. Hataji received speaker fees as honoraria from Novartis Pharma, AstraZeneca, and Boehringer Ingelheim Japan. The remaining authors declare no conflict of interest.