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Findings of virtual bronchoscopic navigation can predict the diagnostic rate of primary lung cancer by bronchoscopy in patients with peripheral lung lesions

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Abstract

Background and objective: Despite being highly invasive, bronchoscopy does not always obtain pathological specimens. Therefore, we investigated whether virtual bronchoscopic navigation (VBN) findings were associated with the diagnostic rate of primary lung cancer by bronchoscopy in patients with peripheral lung lesions.

Methods: This study included patients with suspected malignant peripheral lung lesions who underwent bronchoscopy at our hospital from October 2013 to March 2020. Patients diagnosed with primary lung cancer were grouped according to whether their pathology could be diagnosed by bronchoscopy, and their clinical factors were compared. In addition, the distance between the edge of the lesion and the nearest branch (distance by VBN) was calculated. The distance by VBN and various clinical factors were compared with the diagnostic rates of primary lung cancer.

Results: The study included 523 patients with 578 lesions. After excluding 55 patients who underwent multiple bronchoscopies, 381 patients were diagnosed with primary lung cancer. The diagnostic rate by bronchoscopy was 71.1% (271/381). Multivariate analysis revealed that the lesion diameter (odds ratio [OR] = 1.107), distance by VBN (OR = 0.94) and lesion structure (solid lesion or ground-glass nodule, OR = 2.988) influenced the risk of a lung cancer diagnosis. The area under the receiver operating characteristic curve for diagnosis based on the lesions diameter and distance by VBN was 0.810.

Conclusion: The distance by VBN and lesion diameter were predictive of the diagnostic rates of primary lung cancer by bronchoscopy in patients with peripheral lung lesions.

Background

The use of virtual bronchoscopic navigation (VBN) and endobronchial ultrasound-guide sheath (EBUS-GS) for diagnosing peripheral lung lesions by bronchoscopy has become common in recent years. However, bronchoscopy is a highly invasive procedure, and it is not always possible to obtain pathological specimens. The sensitivity of bronchoscopy for primary lung cancer depends on the lesion size, and it has been reported that the sensitivity of bronchoscopy can be as low as 34% in patients with lesions smaller than 2 cm (1). In addition, computed tomography (CT) is usually performed before bronchoscopy to identify the bronchus involved in the lesion and assess the presence of the “CT bronchus sign”. The presence of the CT bronchus sign is used to determine whether the lesion can be reached by bronchoscopy and clarify the indication for bronchoscopy (2). However, this method is subject to inter-observer variability (3).

Conversely, if the diagnosis can be predicted before bronchoscopy more objectively based on data obtained by VBN and other methods, the decision regarding the indication for bronchoscopy will be more objective. If the diagnostic rate is expected to be low, procedures other than bronchoscopy, such as CT-guided needle biopsy or surgical lung biopsy, can be recommended.

SYNAPSE VINCENT® versions 5.5 (Fujifilm Medical Systems, Tokyo, Japan) has various applications including surgical assistance, and one of its functions is virtual bronchoscopy. When the target lesion is marked, the software automatically identifies the nearest bronchus and calculates the shortest path to the lesion. The distance between the edge of the lesion and the nearest bronchus (distance by VBN) is also automatically calculated (4, 5).

Therefore, we investigated whether the distance by VBN and clinical factors obtained before bronchoscopy are associated with the diagnostic rate of primary lung cancer by bronchoscopy.

Methods

Study subjects

This was a retrospective cohort study conducted at a single centre. This study included patients with suspected malignant peripheral lung lesions who underwent bronchoscopy at our hospital from October 2013 to March 2020.

Patients who had undergone multiple bronchoscopies were excluded from the study. In addition, patients who received diagnoses other than primary lung cancer were excluded.

Bronchoscopy and sedation

At our hospital, CT was performed at a thickness of 1.0 or 1.25 mm, and a VBN image was created on the basis of the CT data using LungPoint (Broncus Medical Inc., Mountain View, CA, USA) (6). All bronchoscopy procedures were performed using VBN by LungPoint and EBUS-GS. In all patients, we performed radial EBUS using an endoscopic ultrasound system (EU-ME1; Olympus, Tokyo, Japan) equipped with 20-MHz mechanical radial-type probes that were 1.4 (UM-S20-17S; Olympus) or 1.7 mm (UMS20-20R; Olympus) in diameter. A thin bronchoscope (channel diameter, 2.0 mm; BF-P290 or BF-P260; Olympus) and GS (external diameter, 1.95 mm; K-201; Olympus) were used for the 1.4-mm probe, whereas a thicker bronchoscope (channel diameter, 2.9 mm BF-1T290 or BF-1T260; Olympus) and GS (external diameter, 2.55 mm; K-203; Olympus) were used for the 1.7-mm probe. The appropriate probes and bronchoscopes were selected by the operator (a respiratory specialist).

After brushing cytology and transbronchial aspiration cytology (TBAC) of the lesion, one cytological specimen was evaluated by rapid onsite cytology. After cytology specimen collection, biopsies were taken with forceps under fluoroscopic guidance for histopathological examination. Biopsies were repeated until specimens of adequate number and size were collected. The procedures followed those of Kitamura et al. (7).

All procedures were performed under local anaesthesia and sedation with intravenous midazolam and pethidine.

Study design

At a different time than the actual bronchoscopy procedures, we compared the associations of the distance by VBN using VINCENT with the diagnosis rate of primary lung cancer and clinical factors. In addition, one observer (A.K., respiratory specialist) read the CT image and assessed the presence of the CT bronchus sign based on the location of the nearest branch and the lesion (2). Clinical factors included age, gender, lesion diameter, lesion structure, presence of the CT bronchus sign, EBUS-GS image (within, adjacent to, invisible) and pathological diagnosis. The lesion structure was classified as ground-glass nodule (GGN) or solid lesion, and solid lesions included cavities, consolidation and nodules.

Follow-up and statistical analysis

For lesions that could not be diagnosed by bronchoscopy, pathological specimens were obtained (to the extent possible) using other diagnostic methods such as surgery, EBUS-guided transbronchial needle aspiration or endoscopic ultrasound-fine needle aspiration. Cases for which pathological specimens could not be obtained were diagnosed after at least 1.5 years of follow-up by both a radiologist and respiratory specialist.

The chi-squared test was used for univariate analysis, and logistic regression analysis was used for multivariate analysis. $P < 0.05$ was regarded as statistically significant. All statistical analyses were conducted using R version 3.6.2, which was also used to draw the prediction graph. The prediction graph was created by randomly selecting 80% of the total patients for analysis. The area under the receiver operating characteristic curve (AUC) of the prediction graph was generated and evaluated in the remaining 20% of patients.

This study was approved by the Ethics Committee of St. Luke's International Hospital (18-R177) on February 27, 2019.

Results

In this study, 523 patients (n = 578 lesions) underwent bronchoscopy. Meanwhile, 55 patients who had undergone multiple bronchoscopies were excluded from the study. In addition, 142 patients who received diagnoses other than primary lung cancer were excluded, and 381 patients were finally diagnosed with primary lung cancer. The pathological diagnosis was made by bronchoscopy in 271 of those patients; thus, the diagnostic rate of primary lung cancer by bronchoscopy was 71.1%. Of the lesions that could not be diagnosed by bronchoscopy, 19.9% (76/381) were diagnosed by surgery, and 8.9% (34/381) were diagnosed by other methods (Figure 1).

The patients' characteristics are presented in Table 1. Next, clinical factors were compared between patients according to whether the malignancy was diagnosed by bronchoscopy. Multivariate analysis illustrated that the lesion location, age and gender were not associated with an increased risk of a lung cancer diagnosis, whereas the lesion diameter, the distance by VBN and lesion characteristics were associated with an increased odds of a lung cancer diagnosis (Tables 1–2). The overall median distance by VBN was 5.19 mm. The median for the group diagnosed by bronchoscopy was 0.73 mm, versus 3.78

mm for the group that was not diagnosed by bronchoscopy mm (Table 1, Figure 2A). The overall median lesion diameter was 21 mm. The median lesion diameter in the group diagnosed by bronchoscopy was 24 mm, compared with 14.5 mm in the group that was not diagnosed by bronchoscopy (Table 1, Figure 2B).

Next, a graph was created to predict the diagnostic rate based on the lesion diameter and distance by VBN. In patients with GGNs, the diagnostic rate of primary lung cancer by bronchoscopy was approximately 40% if the lesion diameter was 10 mm and the distance by VBN was 0 mm. By contrast, the diagnostic rate of primary lung cancer by bronchoscopy approached 80% when the lesion diameter was 30 mm and the distance by VBN was 0 mm (Figure 3A). In patients with solid lesions, the diagnostic rate of primary lung cancer by bronchoscopy was 60% if the lesion diameter was 10 mm and the distance by VBN was 0 mm. Conversely, the diagnostic rate of primary lung cancer by bronchoscopy exceeded 90% when the lesion diameter was 30 mm and the distance by VBN was 0 mm (Figure 3B). The AUC for diagnosis was 0.810.

There were no serious complications associated with bronchoscopy in this study.

Discussion

***** The distance by VBN and the lesion diameter were significantly associated with a higher diagnostic rate of primary lung cancer (Table 2, Figure 3A, B). The AUC of the diagnostic prediction graph was 0.810, and the predictive accuracy appeared to be extremely high. The data from this study are extremely useful because they may allow us to make data-based decisions regarding patients and bronchoscopic indications, such as recommending surgery after a bronchoscopic diagnosis for lesions that are expected to have a high primary lung cancer diagnosis rate based on these diagnostic prediction graphs, whereas surgery could be recommended without a bronchoscopic diagnosis for lesions that are expected to have a low diagnostic rate.

GGN-type lesions are often less malignant and more difficult to identify than solid lesions even under fluoroscopy, and thus, it is often difficult to make a pathological diagnosis using a small bronchoscopic specimen (8). This study illustrated that solid lesions were more predictive of a diagnosis of primary lung cancer in multivariate analysis than GGNs (Table 2). Therefore, the predictive graphs for diagnosis were created separately for GGNs and solid lesions.

Solid lesions of 20 mm in diameter with a distance by VBN of 20 mm had a diagnostic yield of 60–70% (Figure 3B). The existence of actual branches that could not be read by VBN is possible, and such lesions could be reached by innovative procedures such as curettage and TBAC. It remains important to use fluoroscopic techniques during actual bronchoscopy.

To reduce the influence of the VBN software, LungPoint was used instead of VINCENT during the actual bronchoscopy. In that cohort, the diagnostic prediction was analyzed using VINCENT.

The CT bronchus sign is a finding that predicts a high diagnostic yield before bronchoscopy (2). In this study, the diagnostic rate was 78.6% in patients with the CT bronchus sign (Table 1). However, judgement of the CT bronchus sign varies among readers, making it less objective (3). This study suggests that the distance by VBN and lesion size, as more objective markers, can replace the CT bronchus sign for predicting the diagnosis.

Conclusions

The distance by VBN and the lesion diameter can predict the diagnostic rates of primary lung cancer by bronchoscopy in patients with peripheral lung lesions.

Abbreviations

virtual bronchoscopic navigation (VBN)

odds ratio [OR]

endobronchial ultrasound-guide sheath (EBUS-GS)

computed tomography (CT)

ground-glass nodule (GGN)

ransbronchial aspiration cytology (TBAC)

area under the receiver operating characteristic curve (AUC)

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of St. Luke's International Hospital (18-R177) on February 27, 2019.

We confirm that all methods were carried out in accordance with relevant guidelines and regulations.

The text confirming informed consent was waived in this study and was waived by the IRB called the Ethics Committee of St. Luke's International Hospital (18-R177) on February 27, 2019.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Not applicable

Authors' contributions

A.K, Y.T., R.I., N.N., K.O., S.R., T.J.and T.T, analyzed and interpreted the patient data. A.K and Y,T.was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Not applicable

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Tables

Table1 Characteristics of the lesions

		Total (n=381)	Diagnosed (n=271)	Undiagnosed (n=110)
Age[years]		71 [38-93]	71 [38-92]	71 [39-93]
Gender	Male	223	163(60.1)	60(54.5)
Lesion size [mm]		21 [6-111]	24 [7-111]	14.5 [6-55]
	20≧ mm	203	174(64.2)	29(26.4)
Lesion location	Rt.upper lobe	127	89(32.8)	38(34.5)
	Rt.middle lobe	18	10(3.7)	8(7.3)
	Rt.lower lobe	80	59(21.8)	21(19.1)
	Lt.upper lobe	103	75(27.7)	28(25.5)
	Lt.lower lobe	53	38(14.0)	15(13.6)
Structure	GGN	117	64(23.6)	53(48.2)
	Solid	264	207(76.4)	57(51.8)
CT bronchus sigh	Positive	245	213(78.6)	32(29.1)
	Negative	136	58(21.4)	78(70.9)
EBUS-GS image	Within	180	169(62.4)	11(10)
	Adjacent to	82	62(22.9)	20(18.2)
	Invisibile	119	40(14.8)	79(71.8)
Diagnosis	Adeno	275	210(77.5)	65(59.1)
	Squamous cell	48	35(12.9)	13(11.8)
	Small cell	19	15(5.5)	4(3.6)
	Atypical carcinoid	4	3(1.1)	1(0.9)
	Adenosquamous	3	3(1.1)	0
	Non Small cell	2	1(0.4)	1(0.9)
	Large cell	1	0	1(0.9)
	Mucoepidermoid	1	1(0.4)	0
	Neuroendocrine	2	2(0.7)	2(1.8)
	Pleomorphic	1	1(0.4)	0

Unknown	25	0	25(22.7)
The ditance byVBN [mm]	5.19(0-44.66)	0.73 [0-33.69]	3.78 [0.01-44.66]

GGN:Ground-glass nodules

EBUS-GS:Endobronchial ultrasound-guide sheath

The distance by VBN: The distance between the edge of the lesion and the nearest bronchus automatically calculated by virtual bronchoscopic navigation (VBN)

n(%) or median [range]

Table2 Logistic Regression Analysis of Factor Affecting Disgnosis by Bronchoscopy

Variables		Univariate		p value	Multivariate		p value
		OR	(95% CI)		OR	(95% CI)	
Lesion location	Rt.upper lobe	1.048	(0.470-2.267)	0.537	-		
	Rt.middle lobe	0.696	(0.205-2.456)	0.677	-		
	Rt.lower lobe	1.202	(0.501-2.849)	0.563	-		
	Lt.upper lobe	1.292	(0.564-2.891)	0.906	-		
	Lt.lower lobe	reference					
Structure	Solid	2.675	(1.595-4.499)	<0.01	2.988	(1.671-5.427)	<0.01
	GGN	reference					
Lesion size		1.112	(1.075-1.155)	<0.01	1.107	(1.067-1.154)	<0.01
The distance by VBN		0.93	(0.899-0.960)	<0.01	0.94	(0.906-0.974)	<0.01

OR: odds ratio

CI: confidence interval

The distance by VBN: The distance between the edge of the lesion and the nearest bronchus automatically calculated by virtual bronchoscopic navigation (VBN)

GGN:Ground-glass nodules

Figures

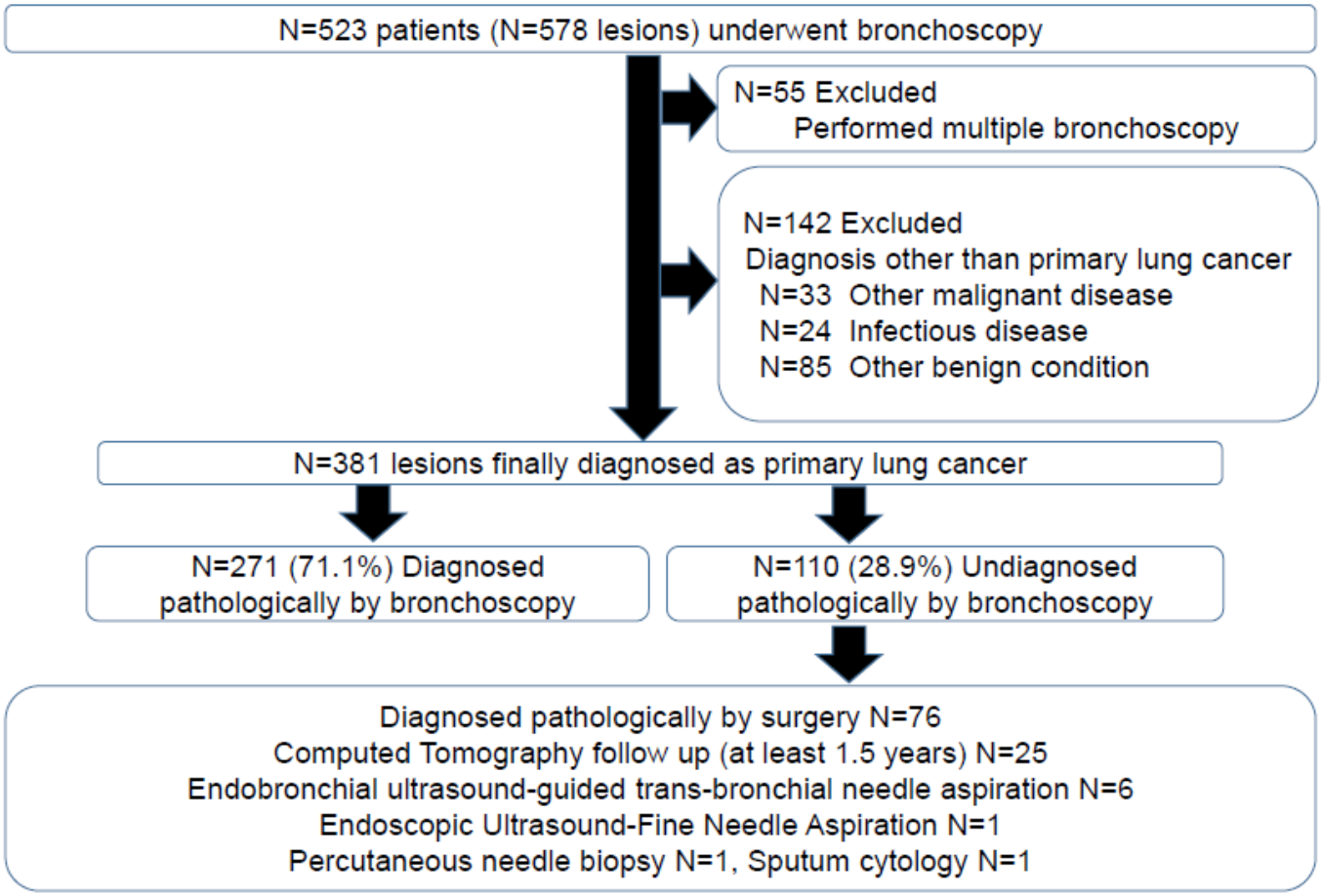

Figure 1

CONSORT flow diagram.

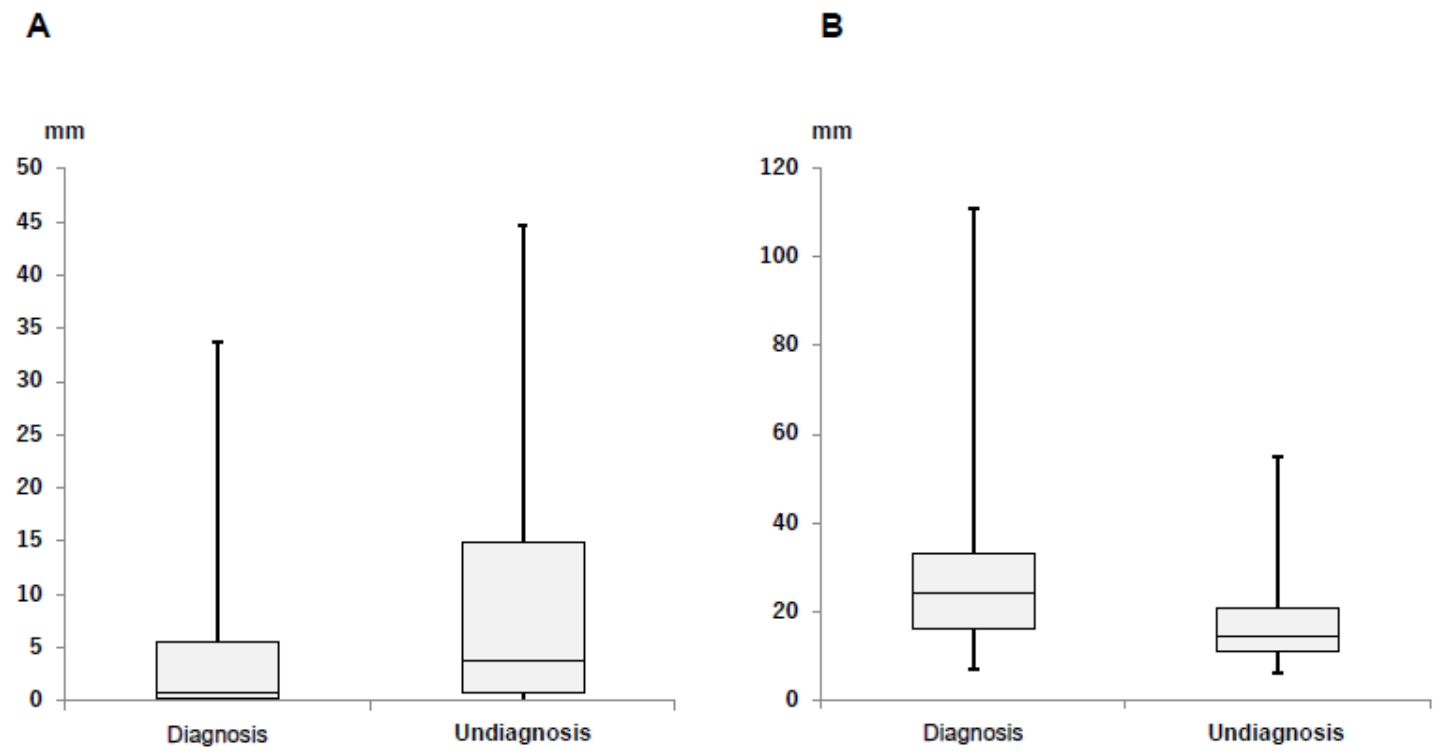

Figure 2

A. Box plot. The distance by virtual bronchoscopic navigation (VBN) in patients who were and who were not diagnosed by bronchoscopy.

B. Box plot. The lesion diameter in patients who were and who were not diagnosed by bronchoscopy.

The distance by VBN: the distance between the edge of the lesion and the nearest bronchus automatically calculated by VBN in VINCENT.

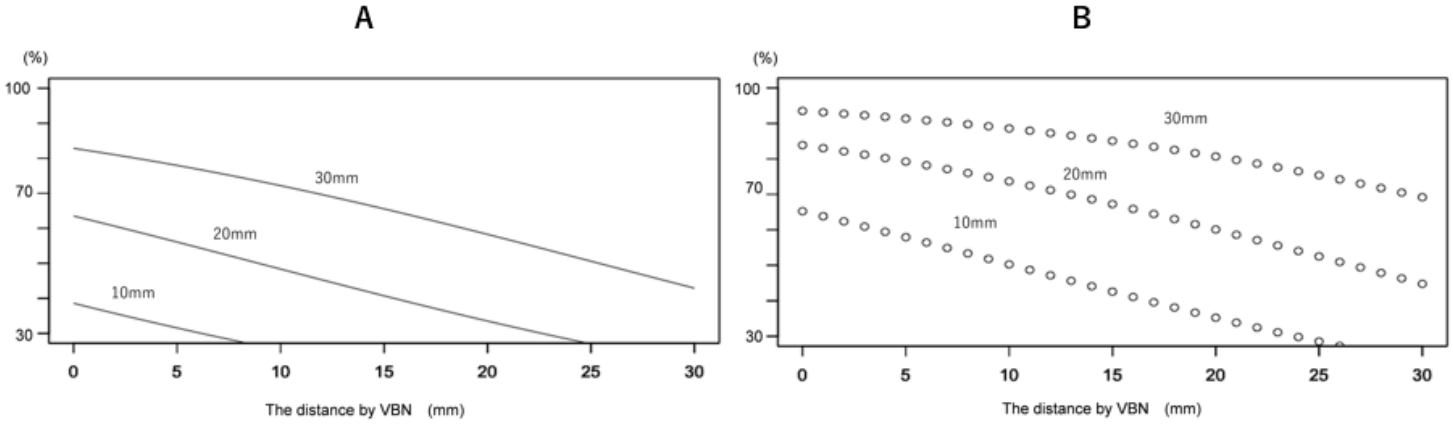

Figure 3

A. Graph of the predicted diagnostic rate of primary lung cancer based on the lesion diameter and the distance by virtual bronchoscopic navigation (VBN) in patients with ground-glass nodules.

B. Graph of the predicted diagnostic rate of primary lung cancer based on the lesion diameter and the distance by VBN in patients with solid lesions.

The distance by VBN: the distance between the edge of the lesion and the nearest bronchus automatically calculated by VBN in VINCENT.