The utility of virtual bronchoscopy using computed tomography workstation for conducting conventional bronchoscopy: A retrospective analysis of clinical practice

Short title: VB in conventional bronchoscopic settings

Shion Miyoshi[1, 2], Kazutoshi Isobe[1], Hiroshige Shimizu[1], Motoko Sunakawa[1], Aika Suzuki[1], Keishi Sugino[1], Nobuyuki Shiraga[3], Susumu Sakamoto[1], Yujiro Takai[1], Akira Iyoda[4], Sakae Homma[1]

[1]Department of Respiratory Medicine, Toho University Omori Medical Center, Ota-Ku, Tokyo, Japan

[2]Department of Respiratory Medicine, Toho University Graduate School of Medicine, Ota-Ku, Tokyo, Japan

[3]Department of Radiology, Toho University Omori Medical Center, Ota-Ku, Tokyo, Japan

[4]Division of Chest Surgery, Toho University School of Medicine, Ota-Ku, Tokyo, Japan

Corresponding Author:

Shion Miyoshi, MD

Department of Respiratory Medicine, Toho University Omori Medical Center, 6-11-1, Omori-Nishi, Ota-Ku, Tokyo, 143-8541, Japan

E-mail: shion.miyoshi@med.toho-u.ac.jp

Phone: +81-3-3762-4151

Fax: +81-3-3768-3620

Key Words: Virtual bronchoscopy, computed tomography workstation, conventional bronchoscopy, clinical practice, SYNAPSE VINCENT, peripheral pulmonary lesion, cost

Abstract

Background: Recent clinical trials demonstrated the benefits of several guided-bronchoscopy technologies for the diagnosis of peripheral pulmonary lesion (PPL). However, introduction of these technologies is expensive. Therefore, in clinical practice, these are unavailable in many hospitals. In contrast, virtual bronchoscopy (VB) using the computed tomography (CT) workstation can be made available immediately without additional cost as many hospitals already have the CT scan facility. However, the effectiveness of VB alone remains to be shown.

Objectives: The aim of this study was to investigate the effect of VB using CT workstation in hospitals performing conventional bronchoscopy.

Methods: Results from consecutive patients who underwent bronchoscopy for small PPLs (major diameter ≦30 mm) were retrospectively reviewed. Sixty-nine patients who underwent bronchoscopy without VB from April 2014 to March 2015 and 56 patients who underwent bronchoscopy with VB from April 2015 to December 2015 were assigned to non-VB and VB group, respectively. We compared the two groups and analyzed the factors affecting the diagnostic yield.

Results: The VB group had significantly higher diagnostic yield than the non-VB group (57.1% vs. 33.3%; $P = 0.008$). In the multivariate analysis, VB was identified as a significant factor affecting the diagnostic yield (odds ratio: 3.30, $P = 0.011$).

Conclusions: In the conventional bronchoscopy settings, VB using the CT workstation is efficient for the diagnosis of PPLs when other guided-bronchoscopy techniques are unavailable.

Introduction

The low-dose computed tomography (CT) screening technique has increased the detection rate of peripheral pulmonary lesions (PPLs) [1]. A recent guideline suggested CT surveillance, non-surgical biopsy or surgical resection for diagnosing PPLs on the basis of the patient's surgical risk and clinical probability of cancer [2]. In patients with an indeterminate or high risk of cancer, surgical resection was often recommended, but unnecessary surgery should be avoided for benign cases. In such cases, non-surgical biopsy is often used to investigate the malignancy using CT scan-guided transthoracic needle aspiration (TTNA) or bronchoscopy. TTNA has a high diagnostic yield of 90%, but it also resulted in a high rate of pneumothorax at 12%–45%, with a 2%–15% probability of requiring chest tube drainage [2, 3]. Furthermore, an earlier study reported that pleural dissemination rate might be more frequent in TTNA than in bronchoscopy or surgery [4]. On the other hand, flexible bronchoscopy was considered a relatively safe procedure compared with TTNA although it has a low diagnostic yield ranging from 15% to 63% in conventional settings [5]. Until recently, bronchoscopy has played a limited role in PPL management.

Presently, several guided-bronchoscopy procedures, such as radial endobronchial ultrasound (EBUS) [6, 7], ultrathin bronchoscope (UB) [8, 9], electromagnetic navigation (EMN) [10, 11], and virtual bronchoscopy (VB) using equipment specifically designed for bronchoscopy [12-14] have been developed to improve the diagnostic yield for pulmonary nodules. These guided-bronchoscopy techniques have been able to contribute to obtaining a higher diagnostic yield than those of traditional bronchoscopy techniques [15]. It was likely that the combination of more than one of these modalities had a better diagnostic yield, compared with the employment of a single method [11, 15]. The diagnostic yield of the combined procedure (88%) was greater than those of EBUS (69%) or EMN alone (59%; $p = 0.02$) [11].

According to previous studies, these guided-bronchoscopy techniques are certainly considered to be useful. However, in clinical practice, these techniques cannot be made available in many hospitals because the advanced equipments, such as EBUS, UB, EMN, and VB

specifically designed for bronchoscopy extremely expensive. Bronchoscopy in clinical practice is not well represented by related clinical studies. Thus, we pay particular attention to the CT workstation, which can be made immediately available as many hospitals already have the CT scan equipment and can create VB without incurring additional expenses. To the best of our knowledge, the utility of VB was often reported for its use in combination with other guided-bronchoscopy techniques [13, 14, 16]. There have been no studies that investigated the utility of VB alone. Therefore, whether VB by itself is an effective diagnostic method remains to be ascertained. It is important to demonstrate the utility of VB alone using CT workstation because this technique can be performed in many hospitals which have CT scan equipment, regardless of the availability of other guided-bronchoscopy equipments. The aim of this study was to investigate the effectiveness of VB using CT workstation in hospitals conducting conventional bronchoscopy for the diagnosis of PPLs.

Materials and Methods

Patients

This was a single-center retrospective study conducted to evaluate the diagnostic utility and impact of employing VB using the CT workstation in the conventional bronchoscopic procedure. Prior approval was obtained from the Institutional Review Board of Toho University Omori Medical Center for conducting this study (No. M16182). Written informed consent was obtained from all patients involved before conducting the study. Consecutive patients who underwent bronchoscopy for small PPLs (major diameter ≦30 mm on axial CT images) at the Toho University Omori Medical Center, Japan between April 2014 and December 2015 were enrolled in this study. Peripheral lesions were identified on the basis of the study by Baaklini et al.[17]. Sixty-nine patients who underwent bronchoscopy without VB from April 2014 to March 2015 and 56 patients who underwent bronchoscopy with VB from April 2015 to December 2015 were assigned to non-VB group and VB group, respectively (Figure 1).

In the present study, “achievement of biopsy” was defined as successful tissue sampling

by forceps at least one time. Malignant lesions were diagnosed on the basis of histological findings or class IV/V cytological findings with Papanicolaou stain. Benign lesions were diagnosed on the basis of histological findings or the presence of bacteria by culture, in addition to the clinical course compatible with the benign disease, which shows a reduction or stability in the lesion size during the follow-up period for at least 12 months. In patients with malignant lesions that were failed to be detected by bronchoscopy, further intervention by TTNA or surgery confirmed the diagnosis of the malignancy. Patients who could not obtain a definitive diagnosis of having benign or malignant lesions despite the above mentioned interventions or follow-up were recorded as indeterminant and diagnosis by bronchoscopy was considered to have failed.

Virtual bronchoscopy

VB was created by 1 pulmonologist (S.M., H.S., or A.S.). All the patients underwent multi-detector CT scanning of the chest before VB and thin-section CT slices (slice width, 0.5–2 mm) were reconstructed. VB was performed using a 3D image analysis system, SYNAPSE VINCENT® (Fujifilm Medical Co., Tokyo, Japan), already available in our hospital. We used "3D viewer" application, which is one of the generic applications on SYNAPSE VINCENT®. VB was created by 1 pulmonologist (S.M., H.S., or A.S.).

The method of constructing VB with CT workstation was as follows (Figure 2). First, we identified the most suitable bronchus for reaching the target PPL by bronchoscopy. Second, we made a pathway to the target PPL by drawing a linear trajectory connecting the dots plotted from the peripheral bronchus to the trachea on the thin-section multiplanar CT images. Third, the CT images were converted to VB images on the above-made pathway and their orientation was adjusted on the basis of the actual bronchoscopy. Finally, a 3D video of the VB images was created automatically, and the construction of VB was completed by transferring the 3D-movie to the server connected to a computerized medical records system. Thus, the completed VB could be viewed anywhere through the computerized medical records system. The bronchoscopist was able to check VB before and during the bronchoscopic procedure.

Bronchoscopic procedure

All the patients were given a premedication of 2% lidocaine gargling, followed by an intravenous sedation with 35 mg of pethidine. Topical anesthesia was administrated by trans-tracheal spray and splashing of 2% lidocaine. Arterial oxygen saturation and heart rate were monitored during the examination.

We used a standard flexible fiber-optic bronchoscope (BF-1T260; outer diameter, 5.9 mm; Olympus, Tokyo, Japan) in all the patients. There was a VB, actual bronchoscopy and X-ray fluoroscopic monitor across from the bronchoscopist. An assistant controlled the VB according to actual bronchoscopic images and navigated bronchoscopist by showing correct direction in real time (Figure 3a). A guide sheath (GS) (K-203; Olympus, Tokyo, Japan) was combined as per the operators' decision. In cases without a GS, after airway examination with the fiber-optic bronchoscope, brush or forceps was introduced to target PPL under fluoroscopic guidance with or without VB. After reaching the target PPL, brushing and biopsies were performed through the working channel of the bronchoscope (Figure 3b). In cases with a GS, after the airway examination, a curette (CC-6DR-1; Olympus, Tokyo, Japan) with a GS was introduced through the working channel to target PPL under fluoroscopic guidance with or without VB. After reaching the target PPL, the curette was withdrawn leaving the GS in place. Brushing and biopsies were then performed through the GS. We tried to obtain at least 3 adequate biopsy specimens whenever possible. Brushes were washed in a test tube containing saline for cytological examination, and the biopsy specimens were immediately fixed in formalin for histological examination. The cytology and pathology results were reported by 2 pathologists, independently.

Analysis

Data were presented as median (range), frequencies, and percentages. The Pearson chi-square test or the Fisher Exact Test was used to compare categorical variables. Continuous

variables were compared using the Mann–Whitney U test. All *P* values were two-sided. A *P* value < 0.05 was considered statistically significant. Logistic regression models were constructed to estimate the factors related to diagnostic yield. The inclusion of variables in the models was on the basis of *P* values (<0.05) in the univariate analysis. Statistical analyses were performed using IBM SPSS Statistics (version 22, IBM SPSS Inc., Chicago, IL).

Results

The demographics of the study population are shown in Table 1. There were no significant differences between the two groups in terms of age, sex, lesion size, lesion location, tumor feature, X-ray fluoroscopic findings or proportion of diagnosis. The rate of positive bronchus sign was significantly lower in the VB group than in the non-VB group [71.4% (40/56) vs. 89.9% (62/69); *P* = 0.008]. Conversely, the use of GS was significantly more frequent in the VB group than in the non-VB group [76.8% (43/56) vs. 36.2% (25/69); *P* < 0.001].

Bronchoscopic examination results are shown in Table 2. The diagnostic yield was significantly higher in the VB group than in the non-VB group [57.1% (32/56) vs. 33.3% (23/69); *P* = 0.008]. And the achievement rate of biopsy was also significantly higher in the VB group than in the non-VB group [75.0% (42/56) vs. 52.2% (36/69); *P* = 0.009]. There were no differences between the two groups in terms of the procedure time [median (range): 27 (11–60) vs 25 (7–69) min; *P* = 0.707].

We further investigated the diagnostic yields according to each parameter (Table 3). Thus, the VB group exhibited significantly high diagnostic yields within the subgroups of lesion of size < 20 mm [54.5% (18/31) vs. 17.1% (6/33); *P* = 0.001], lesions located in the right upper lobe or left upper segment [61.1% (22/36) vs. 33.3% (14/42); *P* = 0.014], bronchus sign positive [67.5% (27/40) vs. 37.1% (23/62); *P* = 0.003], patients using GS [67.4% (29/43) vs. 40.0% (10/25); *P* = 0.027], and patients with malignant disease [64.1% (25/39) vs. 36.8% (21/57); *P* = 0.009].

We compared the diagnostic group and non-diagnostic group to evaluate factors affecting diagnostic yields (Table 4). In the univariate analysis, the diagnostic yield was significant higher

in lesion of size ≥ 20 mm than those <20 mm in size [54.4% (31/57) vs. 35.3% (24/68); P = 0.032], visible lesion by X-ray fluoroscopy than invisible lesions [46.9% (53/113) vs. 16.7% (2/10); P = 0.045], bronchus sign positive patients than negative patients [49.0% (50/102) vs. 21.7% (5/18); P = 0.017], combination with GS than without GS [57.4% (39/68) vs. 28.1% (16/41); P = 0.001] and combination with VB than without VB [57.1% (32/56) vs. 33.3% (23/69); P = 0.008]. In the multivariate analysis using logistic regression model, VB was identified as a significant factor affecting the diagnostic yield (odds ratio: 3.30, P = 0.011) in addition to bronchus sign (odds ratio: 5.00, P = 0.011) and the use of GS (odds ratio: 2.90, P = 0.016).

Discussion

The purpose of the present study was to investigate the diagnostic effectiveness of VB using CT workstation in hospital conducting conventional bronchoscopy. We demonstrated that the diagnostic yield was significantly higher in the VB group than in the non-VB group, and furthermore, in multivariate analysis, VB was identified as a significant factor affecting the diagnostic yield. This suggested two important clinical issues. First, VB alone would be useful for the diagnosis of PPLs even if other guided-bronchoscopy techniques are unavailable. Second, the utility of VB using CT workstation is considered to be independent of the type of CT workstation, which suggests that several hospitals with an existing CT scan facility can improve the diagnostic yield using VB.

First, VB would be useful for the diagnosis of PPLs if other guided-bronchoscopy techniques are unavailable. Some randomized trials indicated that EMN or VB using equipment specifically designed for bronchoscopy was valuable for diagnosing PPLs in combination with EBUS [11, 12, 14] or UB [13]. However, to the best of our knowledge, there have been no studies that compared the diagnostic utility between conventional bronchoscopy with and without VB, and therefore the utility of VB alone remained unclear. In the present study, we investigated the utility of VB alone in conventional bronchoscopy setting. We found that the VB

group had a significantly higher diagnostic yield than the non-VB group. Conventional bronchoscopic situation similar to that in our hospital, will likely be applied in many other hospitals, and therefore bronchoscopic settings in general clinical practice are represented in the present study.

Success or failure of obtaining biopsy specimens is an important determining factor for the diagnosis of lung cancer [18]. The achievement rate of biopsy was significantly higher in the VB group than in the non-VB group in the present study. Because operator generally avoided forceps biopsy if the forceps was outside the target lesion, as confirmed by fluoroscopy, correct guidance to the target lesion was needed to yield forceps biopsies. It was thought that accurate selection of bronchus to target lesions identified by VB contributed to the achievement of biopsies. Moreover, obtaining biopsy specimens itself would simply improve diagnostic yield. These two factors of achievement of biopsy and correct guiding to the target lesion by VB are considered to additionally increase the diagnostic yields of PPLs.

In the present study, there were no difference between the VB group and the non-VB group in terms of the procedure time. However, it is a general belief that the use of VB for guiding the bronchoscope can decrease the amount of procedure time [12, 13]. In the present study, the higher achievement rate of biopsy was thought to explain the unchanged time of procedure in the VB group compared with that in the non-VB group. Forceps biopsies need several minutes depending on the number of biopsies. A possible explanation is that the decreased time for guidance achieved by VB is cancelled-out by the time taken for biopsies. On the other hand, we were not able to evaluate the procedure time from the start of bronchoscopy to the start of sampling in the present study. This was a limitation of retrospective study.

Second, this technique can be immediately executed in many hospitals, which already have the CT scan facility. However, EMN, EBUS, UB, or VB using equipment specifically designed for bronchoscopy cannot be available in many hospitals. In the present study, we used a CT workstation SYNAPSE VINCENT®, already available in our hospital, for creating VB. The SYNAPSE VINCENT® is a 3D-image analysis system with highly practical analysis functions at

the workstation[19, 20] and is a convenient tool for reconstructing virtual endoscopy using previously captured CT or MRI images. Some previous reports showed the utility of VB using CT workstation [16, 21-23]. These reports included different kinds of CT workstations, indicating that the utility of VB using CT workstation is independent of the type of the CT workstation. Importantly, in clinical practice, many hospitals cannot use the advanced equipment including VB using specifically designed equipment for bronchoscopy, EMN, EBUS, and UB because of the high additional expenses necessary to introduce them. In contrast, VB using the CT workstation can be immediately available without additional cost as many hospitals already have the CT scan, and this can contribute to an increased diagnostic yield for PPLs.

There are several differences between VB using CT workstation and using equipment specifically designed for bronchoscopy. We considered the major difference to be that VB using CT workstation was created by manual selection of suitable bronchus and connecting the pathway, while VB using specifically designed equipment for bronchoscopy was created automatically by VB software. VB using CT workstation requires a skill for creating VB, which is not difficult but needs some practice. In the present study, the median VB generation time using CT workstation by an expert is 6.8 min (range 5.5–8.4 min), whereas, a non-expert will need more creation time with VB. Acquiring the skill of manual creation may take more time and effort than automatic creation. However, we can manually create the correct route of suitable bronchus, whereas automatic creation sometimes shows the incorrect route. Thus, there are merits and demerits for manual and automatic operations.

It is important to know who created the VB. The creator of VB can obtain useful information from VB, such as bronchoscopic visual image and rotation around the proper bronchi before a procedure. Moreover, manually conducting and checking the VB can serve as a rehearsal of the actual bronchoscopy. In the present study, VB was created by one of three pulmonologists (S.M., H.S., or A.S.). When the bronchoscopist was the one of the three pulmonologists, the bronchoscopist created VB (VB creator group). When the bronchoscopist was another pulmonologist, one of the three pulmonologists (S.M., H.S., or A.S.) created the VB

instead of the bronchoscopist (non-VB creator group). For reference, the VB creator group generated 32.1% (18/56) of the VBs. The VB creator group had a higher diagnostic yield compared to the non-VB creator group [72.2% (13/18) vs. 50% (19/38); P = 0.153], although there was no significant difference in the present study (Supplementary Table 1). Manual creation itself may provide valuable information to the VB creator; however, larger sample size study would be needed to validate this finding.

Although the present study indicated the possibility that VB alone is valuable for the diagnosis of PPLs, it does not implicate the use of VB alone as sufficient for diagnosis. If other guided-bronchoscopy techniques are available, employing a combination method is thought to be better for diagnosis. In case those techniques are not available, we should effectively utilize VB using CT workstation. Furthermore, it should be kept in mind that the diagnostic rate is not sufficient in the present study, although VB is available. Depending on the patient's situation, other diagnostic methods such as TTNA should also be taken into consideration.

There were several limitations in our study. First, the study was performed in a single center, leading to a possible bias in patient selection. Second, this was a retrospective observational design of a small sample size population. A prospective, randomized, multi-center trial is needed to validate the value of VB using CT workstation in conventional bronchoscopy settings.

In conclusion, conventional bronchoscopy with VB using CT workstation exhibited better diagnostic yield than that without VB for diagnosing PPLs. This result emphasizes the value of VB using CT workstation in conventional bronchoscopy setting if other guided-bronchoscopy techniques are unavailable.

Acknowledgments

The authors thank to Dr. Yasuyuki Mizumori and radiological technologists for their technical assistant in constructing the VB using CT workstation.

Financial Disclosure and Conflicts of Interest

The authors have no conflicts of interest to disclose.

References

1 Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, Gareen IF, Gatsonis C, Marcus PM, Sicks JD: Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 2011;365:395-409.

2 Gould MK, Donington J, Lynch WR, Mazzone PJ, Midthun DE, Naidich DP, Wiener RS: Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143:e93S-120S.

3 Gupta S, Wallace MJ, Cardella JF, Kundu S, Miller DL, Rose SC: Quality improvement guidelines for percutaneous needle biopsy. Journal of vascular and interventional radiology : JVIR 2010;21:969-975.

4 Matsuguma H, Nakahara R, Kondo T, Kamiyama Y, Mori K, Yokoi K: Risk of pleural recurrence after needle biopsy in patients with resected early stage lung cancer. The Annals of thoracic surgery 2005;80:2026-2031.

5 Rivera MP, Mehta AC: Initial diagnosis of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). Chest 2007;132:131s-148s.

6 Paone G, Nicastri E, Lucantoni G, Dello Iacono R, Battistoni P, D'Angeli AL, Galluccio G: Endobronchial ultrasound-driven biopsy in the diagnosis of peripheral lung lesions. Chest 2005;128:3551-3557.

7 Kikuchi E, Yamazaki K, Sukoh N, Kikuchi J, Asahina H, Imura M, Onodera Y, Kurimoto N, Kinoshita I, Nishimura M: Endobronchial ultrasonography with guide-sheath for peripheral pulmonary lesions. Eur Respir J 2004;24:533-537.

8 Oki M, Saka H, Kitagawa C, Tanaka S, Shimokata T, Mori K, Kajikawa S: Novel thin bronchoscope with a 1.7-mm working channel for peripheral pulmonary lesions. Eur Respir J 2008;32:465-471.

9 Oki M, Saka H, Ando M, Asano F, Kurimoto N, Morita K, Kitagawa C,

Kogure Y, Miyazawa T: Ultrathin Bronchoscopy with Multimodal Devices for Peripheral Pulmonary Lesions. A Randomized Trial. Am J Respir Crit Care Med 2015;192:468-476.

10 Gildea TR, Mazzone PJ, Karnak D, Meziane M, Mehta AC: Electromagnetic navigation diagnostic bronchoscopy: a prospective study. Am J Respir Crit Care Med 2006;174:982-989.

11 Eberhardt R, Anantham D, Ernst A, Feller-Kopman D, Herth F: Multimodality bronchoscopic diagnosis of peripheral lung lesions: a randomized controlled trial. Am J Respir Crit Care Med 2007;176:36-41.

12 Ishida T, Asano F, Yamazaki K, Shinagawa N, Oizumi S, Moriya H, Munakata M, Nishimura M: Virtual bronchoscopic navigation combined with endobronchial ultrasound to diagnose small peripheral pulmonary lesions: a randomised trial. Thorax 2011;66:1072-1077.

13 Asano F, Shinagawa N, Ishida T, Shindoh J, Anzai M, Tsuzuku A, Oizumi S, Morita S: Virtual bronchoscopic navigation combined with ultrathin bronchoscopy. A randomized clinical trial. Am J Respir Crit Care Med 2013;188:327-333.

14 Tamiya M, Okamoto N, Sasada S, Shiroyama T, Morishita N, Suzuki H, Yoshida E, Hirashima T, Kawahara K, Kawase I: Diagnostic yield of combined bronchoscopy and endobronchial ultrasonography, under LungPoint guidance for small peripheral pulmonary lesions. Respirology 2013;18:834-839.

15 Wang Memoli JS, Nietert PJ, Silvestri GA: Meta-analysis of guided bronchoscopy for the evaluation of the pulmonary nodule. Chest 2012;142:385-393.

16 Matsumoto Y, Izumo T, Sasada S, Tsuchida T, Ohe Y: Diagnostic utility of endobronchial ultrasound with a guide sheath under the computed tomography workstation (ziostation) for small peripheral pulmonary lesions. Clin Respir J 2017;11:185-192.

17 Baaklini WA, Reinoso MA, Gorin AB, Sharafkaneh A, Manian P: Diagnostic

yield of fiberoptic bronchoscopy in evaluating solitary pulmonary nodules. Chest 2000;117:1049-1054.

18 Schreiber G, McCrory DC: Performance characteristics of different modalities for diagnosis of suspected lung cancer: summary of published evidence. Chest 2003;123:115s-128s.

19 Ogawa C, Minami Y, Morioka Y, Noda A, Arasawa S, Izuta M, Kubo A, Matsunaka T, Tamaki N, Shibatouge M, Kudo M: Virtual sonography for novice sonographers: usefulness of SYNAPSE VINCENT(R) with pre-check imaging of tumor location. Oncology 2014;87 Suppl 1:50-54.

20 Takenaka T, Yamazaki K, Miura N, Mori R, Takeo S: The Prognostic Impact of Tumor Volume in Patients with Clinical Stage IA Non-Small Cell Lung Cancer. Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer 2016;11:1074-1080.

21 Sano A, Tsuchiya T: Virtual Bronchoscopy Using OsiriX. J Bronchology Interv Pulmonol 2014;21:113-116.

22 Iwano S, Imaizumi K, Okada T, Hasegawa Y, Naganawa S: Virtual bronchoscopy-guided transbronchial biopsy for aiding the diagnosis of peripheral lung cancer. Eur J Radiol 2011;79:155-159.

23 Fiorelli A, Raucci A, Cascone R, Reginelli A, Di Natale D, Santoriello C, Capuozzo A, Grassi R, Serra N, Polverino M, Santini M: Three-dimensional virtual bronchoscopy using a tablet computer to guide real-time transbronchial needle aspiration. Interactive cardiovascular and thoracic surgery 2017;24:567-575.

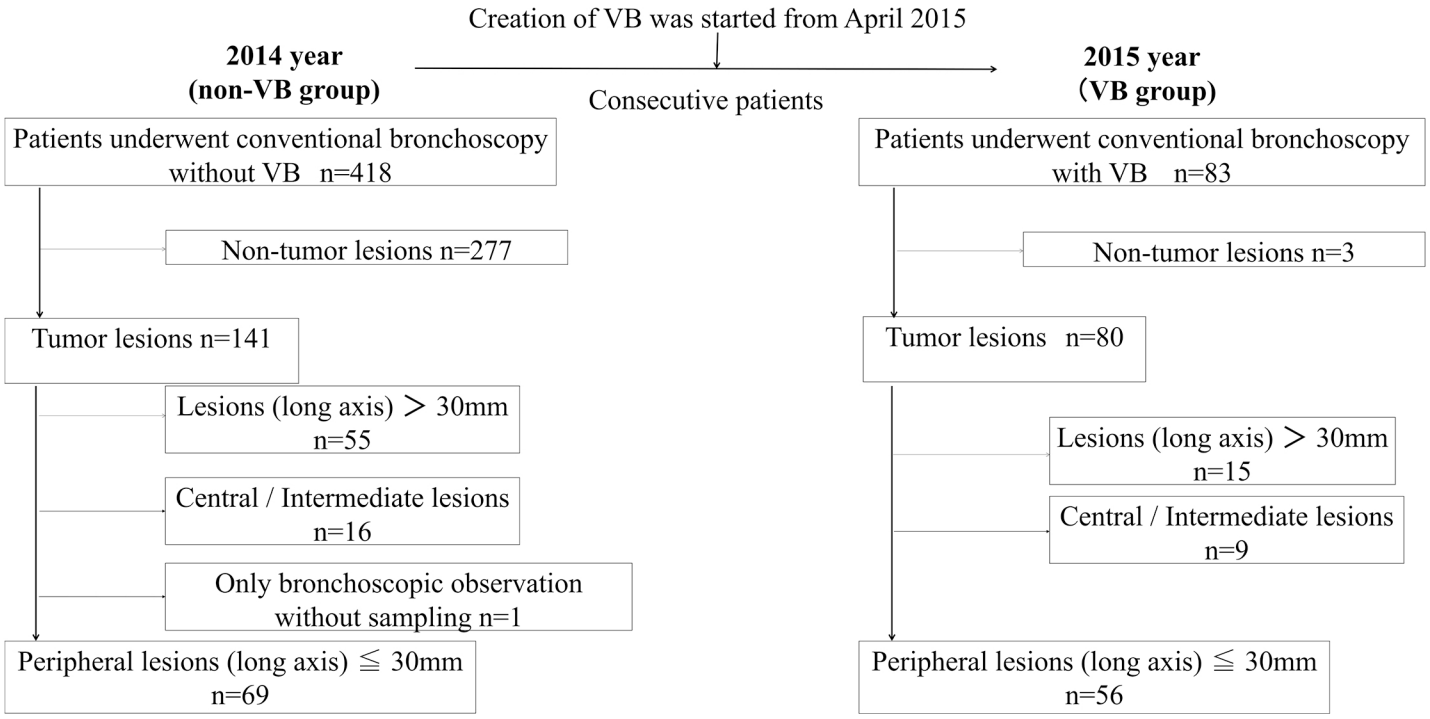
Creation of VB was started from April 2015
2014 year
(non-VB group)
Consecutive patients
2015 year
(VB group)
Patients underwent conventional bronchoscopy without VB n=418
Non-tumor lesions n=277
Tumor lesions n=141
Lesions (long axis) > 30mm n=55
Central / Intermediate lesions n=16
Only bronchoscopic observation without sampling n=1
Peripheral lesions (long axis) ≦ 30mm n=69
Patients underwent conventional bronchoscopy with VB n=83
Non-tumor lesions n=3
Tumor lesions n=80
Lesions (long axis) > 30mm n=15
Central / Intermediate lesions n=9
Peripheral lesions (long axis) ≦ 30mm n=56

Figure 1

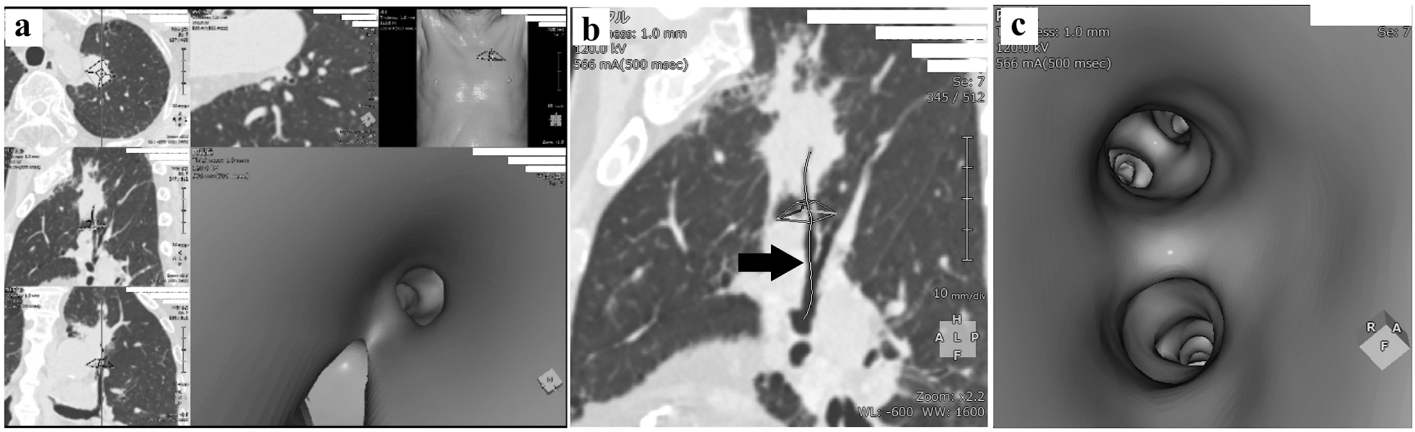
a
b
c
566 mA(500 msec)
Se: 7
345 / 512
10 mm/div
H
A L P
F
Zoom: 2.2
WL: -600 WW: 1600
R A
F

Figure 2

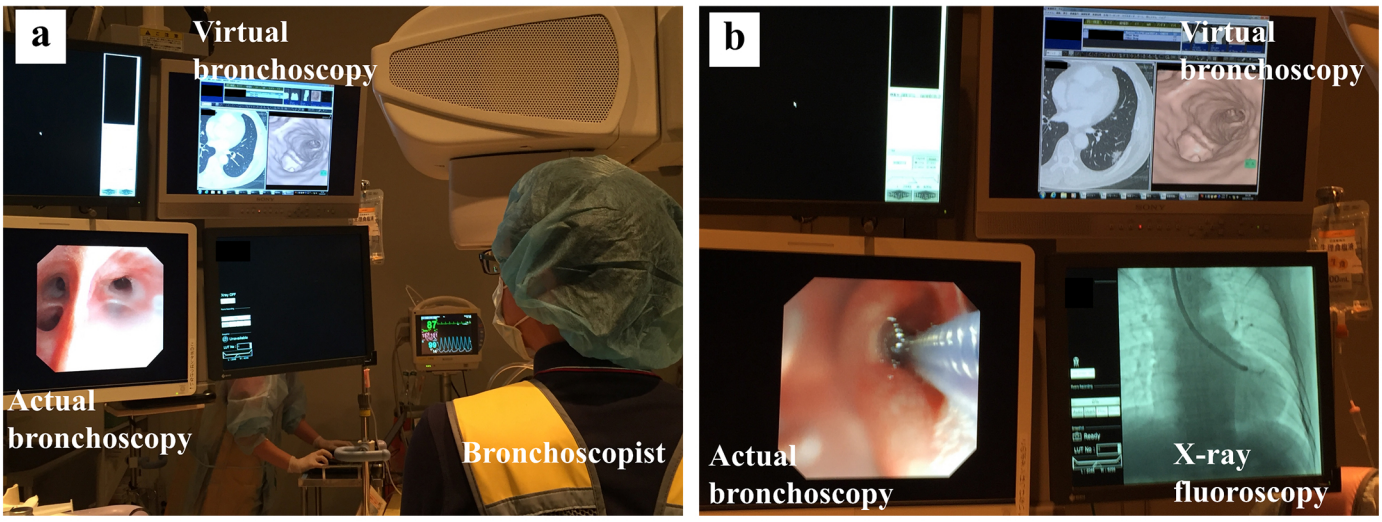
a
Virtual bronchoscopy
Actual bronchoscopy
Bronchoscopist
b
Virtual bronchoscopy
Actual bronchoscopy
X-ray fluoroscopy

Figure 3

Figure legends

Figure 1. Patient disposition

Consecutive patients who underwent bronchoscopy between April 2014 and December 2015 were enrolled in this study. The creation of virtual bronchoscopy (VB) was implemented in April 2015. Sixty-nine patients who underwent bronchoscopy from April 2014 to March 2015 were assigned to non-VB group. Fifty-six patients who underwent bronchoscopy with VB from April 2015 to December 2015 were assigned to VB group.

Figure 2. Creation of virtual bronchoscopy using CT workstation

a) The main window of "3D viewer" application of SYNAPSE VINCENT®. **b)** A pathway to the target lesion was made by drawing a linear trajectory connecting the dots plotted (arrow) from the distal bronchus to the trachea on the thin-section multiplanar CT images. **c)** The CT images were converted to virtual bronchoscopy (VB) images on the above-made pathway, and their orientation was adjusted based on the actual bronchoscopy. Finally, a 3D video of the VB images was automatically created.

Figure 3. Bronchoscopic procedure with virtual bronchoscopy

a) There was a virtual bronchoscopy (VB), actual bronchoscopy, and X-ray fluoroscopy monitor across from the bronchoscopist. An assistant controlled the VB according to actual bronchoscopic images and navigated the bronchoscopist by showing correct direction in real time. **b)** Brush or forceps was introduced to target peripheral pulmonary legion (PPL) under fluoroscopic guidance with or without VB. After reaching the target PPL, brushing and biopsies were performed through the working channel of the bronchoscope.

Table 1. Baseline characteristics of the patients (N = 125)

	VB group n = 56	Non-VB group n = 69	*P* Value
Age (years, median; range)	68 (27–84)	70 (43–85)	0.561
Male, n (%)	43 (76.8)	51 (73.9)	0.712
Lesion size (mm, long axis; range)			0.360
＜ 20mm, n (%)	33 (58.9)	35 (50.7)	
20－30 mm, n (%)	23 (41.1)	34 (49.3)	
Lesion location			0.953
RUL / LUS, n (%)	36 (64.3)	42 (60.9)	
RML / Lingula, n (%)	3 (5.4)	4 (5.8)	
RLL / LLL, n (%)	17 (30.4)	23 (33.3)	
Feature			0.303
Solid, n (%)	51 (91.1)	67 (97.1)	
Mixed GGO, n (%)	4 (7.1)	2 (2.9)	
Pure GGO, n (%)	1 (1.8)	0	
X-ray fluoroscopy			0.371
Visible, n (%)	49 (87.5)	64 (92.8)	
Invisible, n (%)	7 (12.5)	5 (7.2)	
Bronchus sign positive, n (%)	40 (71.4)	62 (89.9)	0.008
Use of GS, n (%)	43 (76.8)	25 (36.2)	<0.001
Creation time of VB, minutes, median (range)	6.8 (5.5–8.4)	NA	NA
Final diagnosis			0.216
malignant disease, n (%)	39 (69.6)	57 (82.6)	
non-malignant disease, n (%)	13 (23.2)	10 (14.5)	
indeterminant, n (%)	4 (7.1)	2 (2.9)	

VB, virtual bronchoscopy; RUL, right upper lobe; LUS, left upper segment; RML, right middle lobe; RLL, right lower lobe; LLL, left lower lobe; GGO, ground glass opacity; GS, guide sheath.

Table 2. Results of the bronchoscopic examination of VB and Non-VB groups

	VB group n = 56	Non-VB group n = 69	*P* Value
Diagnostic yields, n (%)	32 (57.1)	23 (33.3)	0.008
Achievement rate of Biopsy, n (%)	42 (75.0)	36 (52.2)	0.009
Procedure time (minutes, median; range)	27 (11–60)	25 (7–69)	0.488

VB, virtual bronchoscopy.

Table 3. Diagnostic yield of bronchoscopy according to each parameter

	VB group n = 56	Non-VB group n = 69	*P* Value
Lesion size			
＜ 20mm	18/33 (54.5)	6/35 (17.1)	0.001
20－30 mm	14/23 (60.9)	17/ 34 (50.0)	0.419
Lesion location			
RUL / LUS	22/36 (61.1)	14/42 (33.3)	0.014
RML /Lingula	3/3 (100)	2/4 (50.0)	0.429
RLL / LLL	7/17(41.2)	7/23 (30.4)	0.481
Feature			
Solid	30/51 (58.8)	22/67 (32.8)	0.008
Mixed GGO	2/4 (50.0)	1/2 (50.0)	1.000
Pure GGO	0/1	0	
X-ray fluoroscopy			
Visible	30/49 (61.2)	23/64 (35.9)	0.008
Invisible	2/7 (28.6)	0/5 (0)	0.470
Bronchus sign			
Positive	27/40 (67.5)	23/62 (37.1)	0.003
Negative	5/16 (31.3)	0/7 (0)	0.130
Use of GS			
Yes	29/43 (67.4)	10/25 (40.0)	0.027
No	3/13 (23.1)	13/44 (29.5)	0.740
Final diagnosis			
malignant disease	25/39 (64.1)	21/57 (36.8)	0.009
non-malignant disease	7/13 (53.8)	2/10 (20.0)	0.197
indeterminant	0/4	0/2	

VB, virtual bronchoscopy; RUL, right upper lobe; LUS, left upper segment; RML, right middle lobe; RLL, right lower lobe; LLL, left lower lobe; GGO, ground glass opacity; GS, guide sheath.

Table 4. Factors related to diagnostic yield

	Diagnostic group (n = 55)	Non-diagnostic group (n = 70)	Univariate	Multivariate		
			P Value	*P* Value	Odds ratio	95% confidence interval
Lesion size						
< 20mm, n (%)	24 (35.3)	44 (64.7)	0.032	0.052	2.27	0.99–5.20
20－30 mm, n (%)	31 (54.4)	26 (45.6)				
Lesion location						
RUL / LUS, n (%)	36 (46.2)	42 (53.8)	0.158			
RML /Lingula, n (%)	5 (71.4)	2 (28.6)				
RLL / LLL, n (%)	14 (35.0)	26 (65.0)				
Feature						
Solid, n (%)	52 (44.1)	66 (55.9)	1.000			
Mixed GGO, n (%)	3 (50.0)	3 (50.0)				
Pure GGO, n (%)	0	1 (100)				
X-ray fluoroscopy						
Visible, n (%)	53 (46.9)	60 (53.1)	0.045	0.112	4.23	0.71-25.13
Invisible, n (%)	2 (16.7)	10 (83.3)				
Bronchus sign						
Positive, n (%)	50 (49.0)	52 (51.0)	0.017	0.011	5.00	1.45–17.20
Negative, n (%)	5 (21.7)	18 (78.3)				
Use of GS						
Yes, n (%)	39 (57.4)	29 (42.6)	0.001	0.016	2.90	1.22–6.88
No, n (%)	16 (28.1)	41 (71.9)				
VB						
Yes, n (%)	32 (57.1)	24 (42.9)	0.008	0.011	3.30	1.31–8.30
No, n(%)	23 (33.3)	46 (66.7)				

RUL, right upper lobe; LUS, left upper segment; RML, right middle lobe; RLL, right lower lobe; LLL, left lower lobe; GGO, ground glass opacity; GS, guide sheath; VB, virtual bronchoscopy.