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Comparison of bronchoscopic diagnosis for peripheral pulmonary nodule under fluoroscopic guidance with CT guidance

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Summary
Background: A new diagnostic procedure has been established for the selection of appropriate therapy for small lung lesions. We compared the sensitivity of real-time multi-slice computed tomography (MSCT) and X-ray television (TV) fluoroscopic guidance for performing bronchoscopy.
Methods: The first author performed and interpreted all bronchoscopies described in this study. The diagnosis of malignancy or benign was based on the results of histopathological examination, as well as clinical and imaging follow-up MSCT. We also compared the diagnostic yields of lesion size between MSCT and X-ray TV fluoroscopic guidance.
Results: Real-time MSCT and X-ray TV fluoroscopic guidance was conducted in 82 and 78 patients, respectively. The lesion size detected by real-time MSCT and X-ray TV fluoroscopic guidance was <10 mm ($n=21$, 14), 11–15 mm ($n=24$, 12), 16–20 mm ($n=19$,14), 21–25 mm ($n=9$, 12) and >26 mm ($n=9$, 26). The sensitivity of real-time MSCT- and X-ray TV fluoroscopic guidance was 62.2% and 52.6%, respectively. The sensitivity of real-time MSCT fluoroscopic guidance for histopathologic diagnosis of lesions less than 15 mm was higher than that of X-ray TV fluoroscopic guidance. While it was difficult to histopathologically diagnose small lung lesions less than 10 mm in diameter, real-time MSCT fluoroscopic guidance offers a better chance of such diagnosis, irrespective of the size of the lesion, compared with X-ray TV fluoroscopic guidance.

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Conclusion: Real-time MSCT fluoroscopic guidance allows the bronchoscopist to accurately determine the location of the instruments in relation to the lesion in real time, thus helping to reduce the number of negative cases.
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Introduction

Lung cancer is the primary cause of cancer death. The cure rates have remained low because of the difficulty in detecting early stage disease. Mountain[1] reported that stage IA cancer represented 13% of the total population and that the 5-year survival rate of patients with such tumors was 61%. Surgical treatment is expected to be associated with a fairly high 5-year survival rate for small lung lesions <20 mm without nodal involvement, or even a higher rate for those measuring <15 mm that are often free of nodal involvement.[2,3] Accordingly, a diagnostic technique that can detect cancers at an early stage is needed to reduce the cancer-related mortality.

Bronchoscopy is a minimally invasive alternative to surgical procedures for the diagnosis of peripheral lung nodules. Previous studies on solitary pulmonary nodules have consistently shown that lesion size influences the diagnostic accuracy of bronchoscopy.[4–6] In particular, the yield of bronchoscopy is low in lesions measuring <20 mm located in the outer third of the lung.[7] Thus, other diagnostic procedures or alternative protocols for the diagnosis of small nodules including lung cancers may be preferable in this situation. Of these, CT-guided transthoracic needle biopsy could be considered as a first diagnostic step, especially in very small, peripheral, and easily accessible lesions. However, the techniques carry a high risk of complications, e.g., pneumothorax, and may also be difficult to conduct depending on the exact location of the lesion. Since bronchoscopy is a safe procedure with a low complication rate and allows the examination of the central airways before operation, it is the first diagnostic step in our hospital. In this regard, television (TV) fluoroscopy is limited by the two-dimensional display format that produces the overlap of structures, potentially hindering biopsy of the lung peripheral nodules. On the other hand, the CT scan has been proposed as a useful guidance method to provide a cross-sectional view of the relevant anatomy during the bronchoscopy procedure.[8] Real-time multi-slice CT (rMSCT) fluoroscopy permits real time and precise localization of the bronchoscope tip and needle.[9]

In the present study, we report our experience using rMSCT-guided bronchoscopy, which provides images in real time, and the usefulness and diagnostic accuracy of this procedure for peripheral nodules. We also compared the diagnostic yields of rMSCT fluoroscopic guidance and X-ray TV fluoroscopic guidance for performing bronchoscopy. Specifically, our study was designed to evaluate whether this bronchoscopic procedure offers a possible approach in selected patients.

Materials and methods

Bronchoscopist and pathologist

The first author (K.T.) is a pulmonologist with an extensive 10-year experience in bronchoscopy. In this study, K.T. performed and interpreted all bronchoscopies described in this study, including those on patients of Iiyama Red Cross Hospital. On the other hand, the histopathological diagnosis was conducted by the same pathologist (T.H.) at Iiyama Red Cross Hospital and Azumi General Hospital.

Subjects

Chest CT was performed as a part of a CT screening program. Subjects were all patients with well-defined pulmonary nodules identified by chest CT at the Azumi General Hospital, who required final diagnosis by bronchoscopy to select treatments: surgery and administration of antibiotics, which were performed between November 2001 and January 2003. Informed consent was obtained from each patient prior to the bronchoscopy procedure. To compare the diagnostic yields of rMSCT and X-ray TV fluoroscopic guidance for performing bronchoscopy, we also included patients with peripheral pulmonary nodules, as identified by chest CT at the Iiyama Red Cross Hospital, who underwent bronchoscopy to select treatments between September 1999 and September 2001.

Evaluation prior to bronchoscopy

All patients underwent chest radiography and thin-section high-resolution CT images before rMSCT and X-ray TV fluoroscopic guidance for performing bronchoscopy. The CT images were obtained with

a CT fluoroscope (Toshiba Asteion; Tokyo, Japan) with a scan rotation time of 0.75 s, using continuous 1-mm collimation slices. The location of the nodule was determined on the chest CT. The size and presence of bronchus signs of the lesion were determined from the findings of chest CT. The largest dimensions of the lesion parallel and perpendicular to the bronchus were measured. The largest perpendicular dimension was used to define the size of the nodule when calculating the effect of size on the diagnostic yield.

Construction of virtual bronchoscopy

Three-dimensional endoluminal tracheobronchial simulations can be constructed from thin-section high-resolution CT scans, which reproduce the appearances of major endobronchial abnormalities, as confirmed during bronchoscopy. Virtual bronchoscopy was constructed using in software (Navigator; GE Medical Systems, surface rendering method) based on MSCT images. After the construction of virtual bronchoscopy for each patient, we imaged the actual endobronchial findings using virtual bronchoscopy. We selected the nearest bronchus to the peripheral nodules before performing bronchoscopy.

rMSCT fluoroscopy

The rMSCT fluoroscopy (10 mA, 120 kV, 2-mm section thickness, 0.75 s of rotation) was performed with real-time visualization to help confirm the location of the transbronchial brush, needle aspiration and biopsy forceps. For all patients, the use of a 10 mA technique was sufficient to achieve good image quality and to perform bronchoscopy. The patient was placed head first into the scanner, with the bronchoscopist to the head of the MSCT table. The bronchoscope monitor was placed on the same side of the lung lesion. The radiologist operating the MSCT fluoroscopy in the same room stood on the opposite side of the rMSCT fluoroscope monitor. The rMSCT fluoroscope monitor was positioned on the same side as the bronchoscope monitor, such that it was visible to both the bronchoscopist and radiologist. A button on the control panel permitted the release of the MSCT table, so that the position of the table could be adjusted by the radiologists hand in a sliding mode. All physicians who remained in the room during rMSCT fluoroscopic imaging wore lead aprons. The bronchoscopist wore an irradiation monitor on the front of the chest to measure the radiation exposure. Another radiologist operating the rMSCT outside of the rMSCT room could replay the image sequence. An rMSCT fluoroscopic image was obtained to correlate the location of the tip within the target lesions. The brush, aspiration needle or biopsy forceps were inserted through the bronchoscope and implanted in the bronchial wall. The site of implantation was imaged with rMSCT fluoroscopy to ascertain whether the tip was directed properly toward the site of the peripheral lesions. Adjustments were made using rMSCT fluoroscopic images to insure an accurate direction, and the instrument was advanced into the lesion. The biopsy forceps, aspiration needle or brush were directed into the lung segment. Further selection of the appropriate subsegmental region was facilitated with rMSCT fluoroscopic sequences. The location of each instrument, the number of instruments pass and the length of time from the start to end of rMSCT scanning and the amount of overall radiation exposure against patients and bronchoscopist were documented. A final rMSCT fluoroscopic image was obtained to document any complications.

X-ray TV fluoroscopic guidance was performed by bronchoscopy using the above methods under X-ray fluoroscopy, and decided the exact position of the biopsy instrument by changing the patient's body position under X-ray fluoroscopy.

Bronchoscopy procedure

After administration of 1 mg atropine sulfate, 100 μg pethidine hydrochloride and airway anesthesia with 4% lidocaine hydrochloride applied orally, patients lay on the table of the MSCT scanner. Arterial oxygen saturation (SpO_2) and heart rate were continuously measured during bronchoscopy by pulse oximetry. Oxygen was administered via a nasal cannula and the flow was adjusted upward from 1 L/min to maintain SpO_2 above 90%.

A variety of flexible fiberoptic bronchoscopes (Olympus, Tokyo); model BF 3C40 (outer diameter; 3.3 mm, forceps channel; 1.2 mm), and BF P10 (outer diameter; 5.0 mm, forceps channel; 2.0 mm) along with their accessories [brushes (BC-201-c-1006, Olympus), aspiration needles (needle; MAJ-65, sheath; NA-1c-1, Olympus) and biopsy forceps (FB-560-1, Olympus)] were used at Azumi general Hospital and Iiyama Red Cross Hospital. All procedures were performed via the transnasal or transoral route under local anesthesia. After visualization of the vocal cords, additional topical anesthetics were applied as needed. All segments of the bronchial tree were visualized. The presence or absence of endobronchial abnormalities was recorded. The bronchoscope was then advanced

to the lobe and segment known to be the location of the lesion. At first, biopsy forceps using BF 3C40 were advanced into the bronchus under bronchoscope guidance to accurately determine the location of the lesion and performed to obtain at least 2 tissue samples. Next, biopsy using BF P10 was performed to obtain larger 2 tissue samples. After the biopsy forceps, the aspiration needle and brushing were advanced into the lesion, the brushing and aspiration needles were then withdrawn. Specimens obtained by biopsy were placed on glass slides and fixed with 10% formalin. If bacterial or fungal infection was suspected, the brush material was smeared on slides, airdried and processed for Giemsa, acid-fast and PAS staining and was cultured.

Histopathological analysis

Certified cytological technologists blinded to the bronchoscopic findings first confirmed that an adequate sample was collected and then conducted cytological analysis. The diagnosis of malignant disease was based on the results of histopathological analysis of specimens by pathologists also blinded to the bronchoscopic findings. A diagnosis of benign disease was based on results of histopathologic examination, as well as clinical and imaging follow-up MSCTs. Surgical pathological diagnosis was compared with the bronchoscope diagnosis in patients who underwent subsequent resections.

Outcome

We divided the final diagnosis into three groups: Incompletion, Negative and Positive. Incompletion as a final diagnosis was the case in which rMSCT fluoroscopic guidance for performing bronchoscopy could not apparently reach the nodules. Negatives were cases in which the surgical diagnosis differed from the bronchoscopy diagnosis although the biopsy forceps, aspiration needle or brush instruments could apparently reach the nodule(s) under rMSCT. Positives were cases in which the surgical diagnosis was similar to that established using bronchoscopy, or histopathological diagnosis by bronchoscopy that showed granuloma or an inflammatory change, and these findings decreased or disappeared on follow-up CTs.

Statistical analysis

All values described in the text and tables are the group mean $\pm$ standard deviation. One-way analysis of variance, Student's unpaired *t*-test and Fisher's exact probability test for independence were used for comparisons between the groups. A *P*-value less than 0.05 was considered statistically significant.

Results

Eighty-two patients were enrolled in the rMSCT fluoroscopic guidance for performing the bronchoscopy arm of this study (Table 1). The patient population consisted of 43 males and 39 females with a mean age of 65.9 $\pm$ 12.3 years (range, 20–95 years), and 24 were current or ex-smokers. Of the 82 procedures in which rMSCT fluoroscopy was used along with bronchoscopy, 82 were directed toward abnormalities in the peripheral lung fields. Table 2 shows the final diagnosis based on bronchoscopy, operation, clinical follow-up or follow-up MSCTs. The final diagnosis was established using bronchoscope samples in 51 patients (62.2%). Histological diagnosis showed 27 adenocarcinoma, 1 small cell carcinoma, 1 large cell carcinoma, 3 atypical adenomatous hyperplasia, and 1 lymphoangioma. In 31 patients, bronchoscopy could not assist in establishing the diagnosis. Thirty-two positive

Table 1 Lesion characteristics.

Lesion size (mm)	rMSCT fluoroscopic guidance	X-ray TV fluoroscopic guidance
<10	21 (1) [3]	14 (1) [4]
11–15	24 (5) [4]	12 (4) [6]
16–20	19 (8) [12]	14 (6) [11]
21–25	9 (4) [2]	12 (8) [12]
>25	9 (6) [7]	26 (20) [26]
Total	82 (24) [28]	78 (39) [59]

Data in parentheses are nodules with a positive bronchial sign.
Numbers in square brackets represent cases visible under X-ray fluoroscopy.
rMSCT: real-time multi-slice computed tomography; TV: television; BF: bronchoscopy.

Table 2 Final clinical diagnosis of patients under rMSCT fluoroscopic guidance.

	Bronchoscopy	Operation	Follow-up CTs	Therapy
Lung cancer	29	21	2	1
AAH	3	0	0	0
Benign tumor	6	1	0	0
Inflammation	13	0	6	0
Total	51	22	8	1

rMSCT: real-time multislice computed tomography; CT: computed tomography; AAH: adenomatous atypical hyperplasia.

Table 3 Final bronchoscopic results of peripheral lesions under rMSCT fluoroscopic guidance.

Lesion size (mm)	Positive	Incompletion	Negative
<10	9 (1) [2]	10 [1]	2
11–15	13 (5) [3]	6 [1]	5
16–20	12 (4) [8]	5 (2) [2]	2 (2) [2]
21–25	8 (4) [1]	0	1 [1]
>25	9 (6) [7]	0	0
Total	51 (20) [21]	21 (2) [4]	10 (2) [3]

rMSCT: real-time multislice computed tomography; data in parentheses are nodules with a positive bronchial sign. Numbers in square brackets represent cases visible under X-ray fluoroscopy.

cases were diagnosed as malignancy and 19 were diagnosed as benign. In 8 of these 31 patients, diagnosis was established by subsequent CTs. The remaining 22 patients underwent lung lobectomy or video-assisted thoracic surgery. One patient was treated with chemotherapy after diagnosis of a post-operative recurrent lung cancer (Table 2). Nine of 10 negative cases were diagnosed as adenocarcinoma and one was a fibrotic change by surgery. The diagnostic yields that was considered suspicious for malignancy and benign lesions by radiologists based on the chest CT findings were 59.3% (32 of 54) and 64.3% (18 of 28), respectively. The diagnostic yield of bronchoscopy correlated significantly with the lesion size ($P<0.05$).

The mean diameter of 82 peripheral lung lesions was 16.7 mm (range: 5–51 mm). Twenty-eight of 82 (34.1%) lesions could be detected by X-ray TV-fluoroscopy. A bronchus transiting the lesion (bronchus sign) was detected in 24 patients, and 20 of these 24 (83.3%) lesions were diagnosed by bronchoscopy (Table 3). Positive diagnosis was made in 51 patients, negative diagnosis in 10 patients and incompletion diagnosis in 21 patients. Twenty-one of 31 patients who underwent a nondiagnostic rMSCT CT fluoroscopic guidance were confirmed to have lung cancer at surgery, and 1 patient was confirmed to have a benign at surgery. The location of the nodular lesions was 7 in the left upper, 37 in the right upper lobes, 1 in the lingual lobe, 12 in the middle lobe, 9 in the left lower and 16 in the right lower lobe. The morphological data regarding their nodules were 25 solid nodules, 52 ground glass nodules with high density (mixed nodular pattern) and 5 pure ground glass nodules (non-solid nodular pattern) on chest CT scan. In all patients, re-adjustment using rMSCT fluoroscopy was required before biopsy, aspiration or brushing. Table 3 shows the diagnostic yield according to lesion size: <10 mm in diameter, 9 of 21 patients (42.9%); 11–15 mm, 13 of 24 patients (54.2%); 16–20 mm, 12 of 19 patients (57.9%); 21–25 mm; 8 of 9 patients (88.9%) and >25 mm in diameter, 9 of 9 patients (100%). The visualization and localization of the peripheral lesions under rMSCT fluoroscopy were good and each sampling method (brushing, aspiration and biopsy) was performed. In 21 of 82 patients, adequate bronchoscopy could not be performed because we could not accurately localize the correct bronchial subsegment associated with the lesion ($n=14$) with MSCT fluoroscopy, or accurately slide the sampling instrument along the sides of the lesion or through the lesion ($n=5$). In two patients, the ground-glass opacity could be detected under rMSCT. In 8 patients in whom the lesion could not be diagnosed and who had underwent rMSCT fluoroscopic guidance, the lesion resolved spontaneously, as demonstrated on follow-up CTs.[12] In 6 of 8 patients, the nodules or ground glass opacity disappeared on sequential CTs

Table 4 Diagnostic yield of bronchoscopy under rMSCT fluoroscopic guidance.

Lesion size (mm)	Peripheral lung lesions		
	rMSCT (diagnosed number/total number)	X-ray TV (diagnosed number/total number)	Significance
<10	9/21 (42.9%)	1/14 (7.7%)	$P = 0.028$
11–15	13/24 (54.2%)	2 /12 (20%)	$P = 0.039$
16–20	12/19 (63.2%)	9/14 (64.3%)	NS
21–25	8/9 (88.9%)	9/12 (75%)	NS
>25	9/9 (100%)	20/26 (76.9%)	NS
All lesions	51/82 (62.2%)	41/78 (52.6%)	NS

Data are numbers and (percentages) of correctly diagnosed cases.
rMSCT: real-time multi-slice computed tomography; TV: television; NS: not significant.

Table 5 Radiation exposure.

Lesion size (mm)	Patients		Bronchoscopist
	Exposure time (s)		Radiation exposure (μSv)
< 10	330.3±170	925±476	93.5±67
10–15	343.7±203	962±567	65.1±47
16–20	387.3±144	1084±404	94.8±47
21–25	253.5±83.1	710±233	43.9±28
>25	210.4±138	589±386	75.1±45
Conventional CT	12	474	
Conventional with thin-section CT	22	869	

Data are mean±standard deviation.
CT: computed tomography.

after the administration of broad-spectrum antibiotic therapy after rMSCT fluoroscopic guidance.

Comparison of X-ray TV and rMSCT CT fluoroscopic guidance for performing bronchoscopy

Seventy-eight patients were enrolled in the X-ray TV fluoroscopic guidance for performing the bronchoscopy arm of this study. At the Iiyama Red Cross Hospital, the diagnostic yield of X-ray TV fluoroscopic guidance in all lesions was 52.6% (41 of 78 patients). The proportions of cases with accurate final diagnoses by X-ray TV fluoroscopic guidance and rMSCT fluoroscopic guidance for performing bronchoscopy were not significantly different. The diagnostic yields of X-ray TV fluoroscopic guidance and rMSCT fluoroscopic guidance for lung lesions were: for lesions <10 mm in diameter, 7.7% and 43%; 11–15 mm, 20% and 54%; 16–20 mm, 64% and 63%; 21–25 mm, 75% and 89%; >26 mm in diameter, 77% and 100%, respectively. These results indicate that the diagnostic yield of rMSCT fluoroscopic guidance for performing bronchoscopy was significantly superior to that of X-ray TV fluoroscopic guidance for lesions measuring <15 mm ($P < 0.001$) (Table 4).

Radiation exposure

Patients and the bronchoscopist were exposed to a mean radiation dose of 912.2 μSv (range, 138–2313 μSv) and 75.2 μSv (range, 16–208 μSv), respectively. The mean time of the rMSCT fluoroscopic procedure was 325.8 s (range, 49.3–826 s). Table 5 shows the radiation dose and time of bronchoscopy according to lesion size.

Complications

No significant bleeding occurred during the procedures and no dyspnea or ventilatory compromise was noted. None of the procedures resulted in pneumothorax, pneumomediastinum or bacteremia.

Discussion

This study is the first to compare the diagnostic yields of X-ray TV fluoroscopic guidance and rMSCT fluoroscopic guidance for performing bronchoscopy, although it is a historical comparison between the two techniques. However, this study does not serve as a control study unless the nodules are truly matched in terms of their size and location density, although we assessed the diagnostic yield of rMSCT fluoroscopic guidance for peripheral nodules, and compared these results with those of X-ray TV fluoroscopic guidance conducted by a single physician (K.T.). However, the present data can show the use of rMSCT fluoroscopic guidance in patients with peripheral lung lesions. Compared with CT-guided percutaneous thoracic needle biopsy, bronchoscopy has low sensitivity and false negative results. CT-guided percutaneous thoracic needle biopsy may be considered as the first diagnostic step, especially for very small, peripheral and easily accessible lesions. We did not perform CT-guided biopsy for peripheral lesions, although the frequency of pleural dissemination was low. Surgical excision was also performed for the final diagnosis of lung cancer. However, some patients were anxious or refused surgery, or hoped a final diagnosis of the pulmonary lesion could be made before surgery. Moreover, some studies showed that CT-guided bronchoscopy for transbronchial needle aspiration is a safe and efficient tool for providing diagnostic material from mediastinal lymph nodes and peripheral nodules.[8,9,11] Therefore, we performed rMSCT fluoroscopic guidance for the diagnosis of pulmonary lesions and to compare its diagnostic accuracy with that of X-ray TV fluoroscopic guidance. However, the selected approach depends on the location and extent of lesions, as well as other considerations such as referral patterns, expertise and preferences, in addition to the availability of the necessary equipment.

In our study, diagnosis was confirmed by biopsy in 51 of 82 patients. This compares favorably with recent studies in which the overall rate of accurate diagnosis was 50–70% for lesions of various sizes.[7] The sensitivity was markedly better than that of fiberoptic bronchoscopy conducted by Baaklini et al.[7] who reported a positive bronchial wash in 71 of 177 cases (40%). Our conventional diagnostic procedures of bronchoscopy included needle aspiration, brush and transbronchial biopsy. Transbronchial biopsy is the only bronchoscopic method that allows obtaining a biopsy specimen, hence allowing diagnosis of benign lesions. Although transbronchial biopsy is associated with a higher risk of bleeding and pneumothorax than transbronchial needle aspiration,[12] we performed endobronchial biopsy as one of the bronchoscopic procedures when possible. Consequently, it is possible to provide a histological diagnosis by the transbronchial biopsy. Our results showed certain benefits of rMSCT fluoroscopic guidance for performing bronchoscopy. The diagnostic procedure enabled the detection of small lesions, which could not be detected by X-ray TV fluoroscopic guidance. It is important to accurately determine the location of lesions when planning the biopsy and needle aspiration, especially for small peripheral lesions and the lymph nodes adjacent to the major blood vessels. Transbronchial needle aspiration under the rMSCT fluoroscopic guidance can visualize the needle and select an optimal site for needle penetration and can confirm the depth and angle of the needle in real time during the procedure. Although no complications occurred in our study, we performed a CT sequence immediately upon completion of the procedure, which would have permitted immediate detection of and intervention for pneumothorax or hemorrhage.

The most important drawback of rMSCT fluoroscopic guidance for performing bronchoscopy is the radiation exposure of patients, bronchoscopist and assistants (Table 5). The potential concern related to this technique is the use of several minutes of fluoroscopy. Conventional X-ray TV fluoroscopic guidance dose parameters are approximately 90 kV and 4 mA per second. In comparison, these parameters are 120 kV and 150 mA per second in the conventional CT fluoroscopy but only 120 kV and 10 mA per second in our MSCT fluoroscopy. The dose used in MSCT fluoroscopy was at least double that used for conventional X-ray TV-guided fluoroscopy. In conventional CT, exposure of the entire lung requires movement of the sliding table in about 12 s, resulting in a maximum skin dose level of approximately 395 μSv. This time was as much as ~22 s, making the maximum skin dose level of ~869 μSv in conventional CT combined with thin-section CT. As shown in Table 5, this radiation exposure is almost the same as that of rMSCT fluoroscopic bronchoscopy (mean maximum skin dose level; 852 μSv, mean bronchoscope procedure time; 304 s). The bronchoscopist was exposed to a mean maximum radiation dose of 69.5 μSv. Unlike conventional fluoroscopy MSCT fluoroscopy employs a tightly collimated beam (2 mm) that confines to a narrow area. The radiation dose is further dissipated because the sliding table method used in this procedure limits exposure to any particular region. Moreover, we reconstructed the virtual bronchoscopy and selected the precise bronchus with the nodule before performing bronchoscopy.

McAdams et al.[13] reported the use of virtual bronchoscopy for guidance during the transbronchial biopsy procedures. Their results suggested that imaging guidance might improve the diagnostic sensitivity for malignant nodule. Although virtual bronchoscopy provides a ''road map'' that could be viewed by the bronchoscopist before performing bronchoscopy, it does not provide direct guidance during the procedure. The usefulness of virtual bronchoscopy is unfortunately limited because it cannot confirm the correct location of the peripheral bronchus, due to its limited success in reconstructing the peripheral bronchi in detail. However, we believe that virtual bronchoscopy is beneficial as it shortens the procedure of MSCT fluoroscopy since the virtual images could correctly detect fourth-order bronchi under 1-mm collimation high-resolution CT.

rMSCT-fluoroscopic guidance, as well as X-ray TV fluoroscopy are associated with other risk factors. The minute specimens obtained by the BF 3C40 procedure make it difficult to establish a definitive histopathological diagnosis, especially ground-glass opacity with Noguchi type A and type B or adenomatous atypical hyperplasia. Lesions detected by chest CT screening mostly appears as small-diameter lesions. A large proportion of small nodules do not invade the neighboring bronchus. Therefore, even with the brush instrument placed in the center of the lesions, it is difficult to obtain sufficient material from alveolar-lining tumors. Specimens obtained by bronchoscopy are only tiny parts compared with the specimens obtained by operations, and are unsuitable to assess the histological grade of the whole lesion apparent on MSCT. Moreover, it is often difficult to maneuver the biopsy instruments to reach the site of the peripheral lesion, due to the limited flexion inherent in such instruments, compared with brush instruments. In some cases, the peripheral nodules could not be accessed by biopsy forceps but could be reached by the brush instrument. In this study, it was difficult to make a definitive diagnosis for small nodules measuring <10 mm without bronchial signs, using rMSCT fluoroscopic guidance. To obtain samples correctly from nodules <10 mm in diameter, it is necessary to place the bronchoscope at a bronchus adjacent to the nodules, and to perform transbronchial biopsy. In four small nodules measuring <10 mm, diagnosis could not be established using 3C40 bronchoscopy. Instead, we used ultrathin-bronchoscopy (Olympus BF XP 40, outer diameter: 2.8 mm, forceps channel: 1.2 mm) to improve the approach to the small nodules. That bronchoscopy allowed the approach of the deep part of the second-order bronchus better than 3C40 bronchoscopy, although no firm diagnosis could be made in any of these cases. For small nodules <10 mm in diameter, rMSCT fluoroscopic guidance showed clearly superior accuracy compared with X-ray TV fluoroscopic guidance, although the diagnostic accuracy of the former procedure is not yet ideal.

The endoscopic ultrasound-guided bronchoscopy has been adapted for the central mass and peripheral nodules. Kikuchi or Kurimoto et al. reported that even when restricted to peripheral small nodules <20 mm in diameter, the diagnostic sensitivity of endobronchial ultrasonography with guide sheath-guided transbronchial biopsy was 53% or 66%, respectively.[14,15] However, US cannot detect the nodules without solid component less than 15 mm in diameter although the data was not shown on our hospital. Therefore, the bronchoscopy under MSCT is more useful to reach a diagnosis than that under EBUS for the nodules without solid components less than 15 mm in diameter.

The final problem is the cost-utility of this technique. We calculated the cost of rMSCT fluoroscopic guidance for the performance bronchoscopy to be more expensive by $40 compared with X-ray TV fluoroscopic guidance. The screening cost for lung cancer by chest CT per person was $50, based on our 3-year CT screening program (Asakura et al., Japanese publication, 1999). Surgical excision was also performed for a final diagnosis of lung cancer. However, some patients may be anxious or refuse surgery, or hope a final diagnosis of the pulmonary nodule could be made before surgery. We commonly used to follow small nodules by performing serial CTs because its interval growth would be an indication for surgery. However, the cost of more than 2 follow-up CTs was more expensive than that of rMSCT fluoroscopic guidance. To establish a diagnosis at the time of first identification may could be more cost-effective compared with the cost of serial follow-up CTs.

Conclusions

Nodules of different sizes could be assessed using one or more diagnostic procedure. In bronchoscopic procedures for peripheral nodules, small nodules less than 10 mm should be diagnosed based on CT morphologic and density characteristics and the presence or absence of tumor growth tendencies as determined by serial follow-up CTs because of low diagnostic sensitivity of rMSCT fluoroscopic guidance for performing bronchoscopy. For lung

nodules of 10–15 mm in diameter and nodules of 16–20 mm not clearly visible on X-ray TV, rMSCT fluoroscopic guidance is a useful procedure based on the diagnostic sensitivity determined in our study. For nodules more than 20 mm in diameter, rMSCT- or X-ray fluoroscopic guidance for performing bronchoscopy could be selected.

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