Original Article

Thoracoscopic small pulmonary nodule detection using computed tomography-guided cutaneous marking and pleural marking

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Background: In recent years, small lung nodules have been detected by computed tomography (CT). Wedge resection of small pulmonary nodules is widely performed with video-assisted thoracoscopic surgery (VATS). However, it is extremely difficult to identify the position of a small tumor by palpation using a small access port. Therefore, this study aimed to describe a newly devised method of marking the location of the tumor.

Methods: In 51 cases, we marked the skin directly above the tumor under CT guidance before surgery and then placed a pleural marker with dye on the parietal pleura directly below the region marked on the skin using a catheter needle. To evaluate the accuracy of the marking, the distance between the center of the marking and the visceral pleura closest to the tumor was measured.

Results: The mean distance between the center of marking and the visceral pleura closest to the tumor was 12.4 mm. In 47 cases (92%), the tumor was within 30 mm from the marking site. The surgical approach was VATS in 44 cases. In one case, conversion to open surgery was required for palpation of the tumor. All tumors were resected completely. No morbidity was observed during or after surgery.

Conclusions: Our CT-guided cutaneous marking and pleural marking method was able to identify the location of the tumor with high accuracy, making palpation easier during VATS. This new procedure should be implemented in the clinical setting given its ease of application, safety, and accuracy.

Keywords: Tumor; video-assisted thoracoscopic surgery (VATS); pleural marker; resection; palpation

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Introduction

In recent years, small lung nodules have been detected by computed tomography (CT) examination. These nodules are difficult to diagnose by transbronchial biopsy (1). In addition, diagnosis via CT-guided lung biopsy is also difficult owing to breath misalignment. Therefore, the prevalence of surgical resection for pathological diagnosis is increasing (2). Although video-assisted thoracoscopic surgery (VATS) is widely used as a noninvasive surgical approach in wedge resection of small lung tumors (3), it is extremely difficult to identify the position of a small tumor by palpation via a small access port. This is particularly true if the tumor is positioned deep in the lung.

Previously, a CT-guided hook wire has been useful for tumor identification and the localization of small pulmonary nodules. However, if the lung is punctured with the hook wire, this may cause hemoptysis and pneumothorax, and cerebral infarction by air embolism (4,5). In addition, the incidence of pneumothorax is reported to be between 32% and 68%, and the incident of air embolism is 0.62% (6). For that reason, this is considered a dangerous procedure.

The aim of this study was to evaluate our novel method of marking the skin directly above the tumor under CT guidance before surgery with a permanent marker pen, then placing a pleural marker with dye on the parietal pleura (the back side of the skin), followed by performing two-lung ventilation, and marking the visceral pleura just above the tumor by transferring the dye.

Methods

The present study was approved by the Institutional Review Board (IRB) of Kanazawa Medical University Hospital (I265), and the study was registered with UMIN Clinical Trials Registry in Japan (UMIN-CTR ID: UMIN000031848). Individual informed consent was obtained from each patient.

The indications for marking were as follows: a peripheral pulmonary nodule ≤20 mm in diameter, a distance from the nearest pleural surface of ≤20 mm, a planned VATS wedge resection or segmentectomy at Kanazawa Medical University Hospital, and an age of more than 20 years. Patients with no definitive diagnosis before surgery and who needed frozen section diagnosis by VATS wedge resection to perform VATS lobectomy were included. Fifty-four patients were enrolled between February and October 2018.

Technique

(I) Prior to surgery, the patients were placed on the CT table in the same lateral position as they would be in during surgery. Guide markers, in the form of cellophane tape and clips, were attached to the body, directly above the site of the possible lung tumor (*Figure 1A*).

(II) A CT scan was performed at the time of respiratory arrest and marking was carried out on the skin immediately above the tumor with a permanent marker (*Figure 1B*).

(III) After the beginning of thoracoscopic surgery, a catheter needle (23G) was inserted into the thoracic cavity from the skin marking site (*Figure 1C*). After confirming that the tip of the needle was inserted into the parietal pleura (*Figure 1D*), the pleural marker, which was made using sterilized adhesive tape cut into small 1-cm pieces and mixed with dye (Pyoktanin Blue® 1% water solution; Wako Pure Chemical Industries Ltd., Osaka, Japan) and sterilized gel for ultrasonography (Sterlite Aquasonic 100®; Parker Laboratories Inc., Fairfield, NJ, USA) (*Figure 2A*), was attached to the same point (*Figure 2B*).

(IV) After attaching a marker to the parietal pleura, two-lung ventilation was performed at a pressure of 20 cmH_2O for 10 seconds to expand the lungs (*Figure 2C*).

(V) One-lung ventilation was performed again, and we confirmed that the pigment had adhered to the lung surface. Subsequently, the pleural marker was removed (*Figure 2D*).

(VI) In order to accurately measure the distance between the marking point and the pleura closest to the tumor, a 3-0 PDS yarn was pierced and ligated at the center of the portion to which the pigment adhered, and finger palpation was performed.

(VII) Partial resection was performed centering on the palpable tumor.

(VIII) The presence of tumors was confirmed in all resected lungs by intra-operative frozen section diagnosis. To evaluate the accuracy of the marking before creation of the frozen sections, the distance between the center of the marking and the visceral pleura closest to the tumor (DMT) was measured by pathologists (*Figure 3*).

(IX) Indirect marking: if the tumor was localized on the back side of a scapula or on the mediastinum side, and pleural marking directly above was difficult, we marked the skin at two points in the vicinity and measured the distance with eye measurement from the puncture needle in the anteroposterior direction (*Figure 4A,B,C*). We then attached the pleural marker, referring to the distance on the parietal pleura, and marked the visceral pleura directly above the tumor.

In the case of multiple tumors, the evaluation was made only for the largest lesion, and it was a policy to measure only one DMT per case. However, surgeons were allowed to mark multiple tumors, when necessary.

Statistical analysis

We used a *t*-test to analyze the DMT and other quantitative valuables. The primary endpoint was DMT and the secondary endpoint was the cut line margin (Margin). A statistically significant difference was defined as a value of $P<0.05$. The EZR software program (Saitama Medical Center, Jichi Medical University, Saitama, Japan) on a

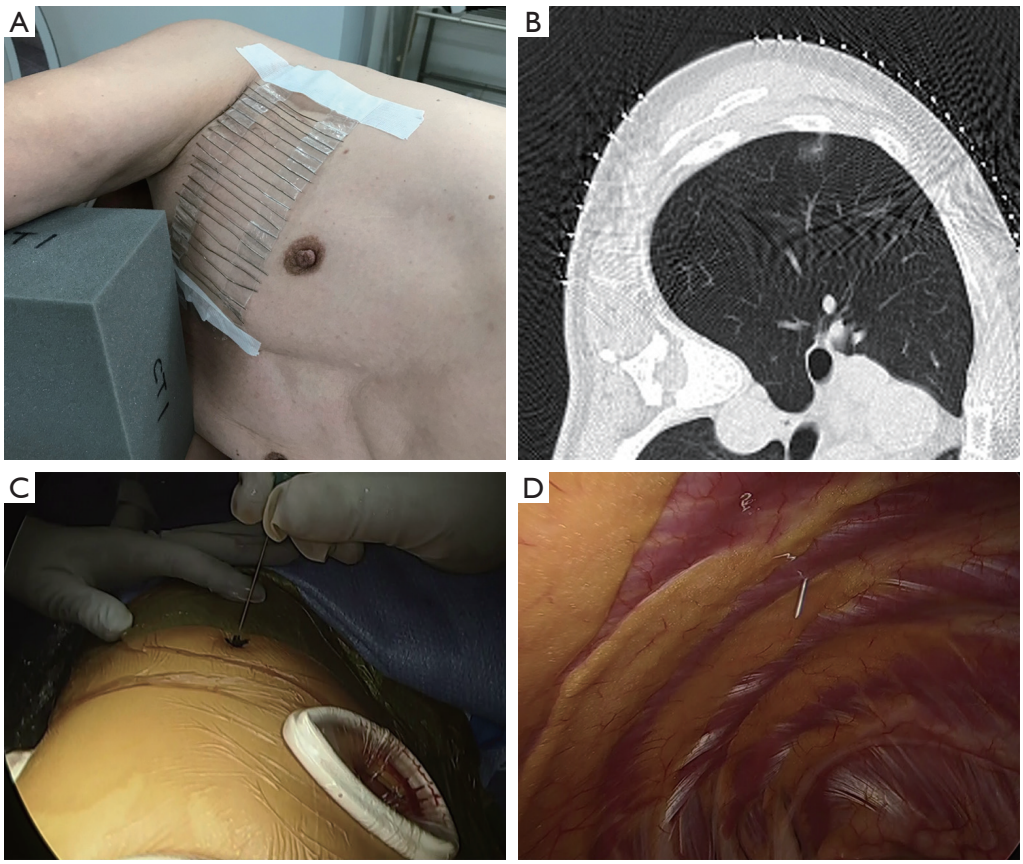

Figure 1 Our novel marking technique 1. (A) The guide markers on the body appear directly above the possible site of the lung tumor; (B) CT is performed 1 or 3 days before surgery. The arrow indicates the marking point above the tumor. The cross mark is marked on this point with a permanent marker; (C) the catheter needle is inserted into the pleural cavity from the marking site; (D) the needle tip indicates the pleural site above the tumor. CT, computed tomography.

personal computer was used for the analysis (7).

In order to verify the changes in surgical outcomes over the period from February to October 2017 with our new marking technique, cases of pulmonary resection with a tumor size less than 20 mm and depth less than 20 mm were extracted (68 cases) as a control group. The control group was compared regarding operation time, the proportion of palpable tumors (palpable rate), and the approach.

Results

In 54 cases enrolled in the present study, three cases were excluded—one due to disappearance of the cutaneous marking, one due to marking near the descending aorta, and one due to avoidance of a partial resection for preoperative diagnosis (*Figure 5*).

The patient characteristics are listed in *Table 1*. There were no significant differences between the two groups, except for age and surgical procedure. In the marking group, the mean tumor size was 12.4 mm (*vs.* 13.1 mm in the control group). Tumor density [consolidation tumor rate (C/T)] was 0.73 (*vs.* 0.75 in the control group).

No morbidity was observed during or after surgery.

The mean DMT was 12.3 mm (0–45 mm) and the mean margin was 13.5 mm (1–45 mm) (*Table 2*). The mean DMT was 14.2 mm (±10.8 mm) in the indirect marking group and 11.5 mm (±8.8 mm) in the direct marking group. These differences were not significantly different.

All tumors were resected completely. In cases where marking defined that the DMT was within 30 mm and the tumor was easily palpable during surgery from the access port, the success rate was 47/51 (92%). In four failure cases,

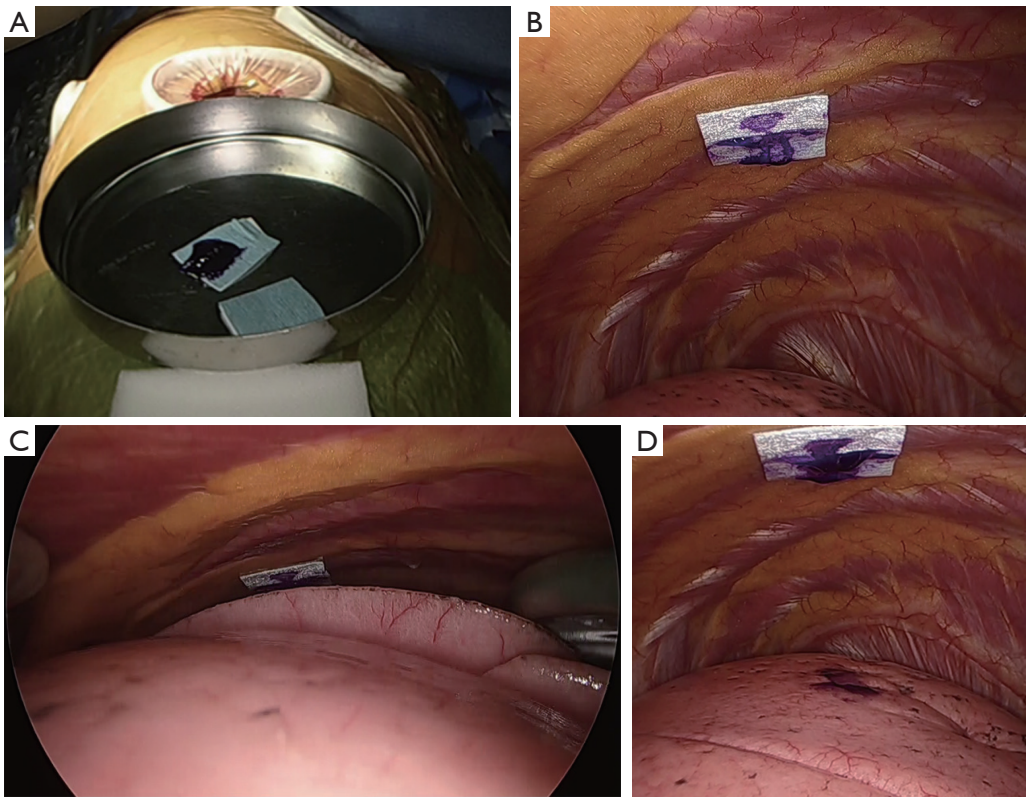

Figure 2 Our novel marking technique 2. (A) The pleural marker made of sterilized tape, dye, and sterilized gel is shown on a sterilized surgical tray; (B) the pleural marker is attached to the pleural site as indicated by the needle tip; (C) by inflating the two lungs for 10 seconds with 20 cmH2O, dye is transferred to the visceral pleura on the tumor; (D) the transferred dye indicates the tumor under the marking site.

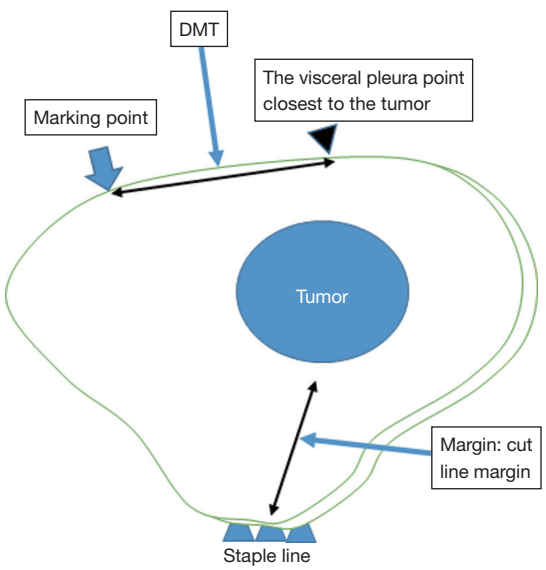

Figure 3 The primary and secondary endpoints. DMT, the distance between the center of marking and the visceral pleura closest to the tumor.

we could not resect the tumors with the marking yarn in two cases, and in the other failure cases, the DMT was not within 30 mm (45 mm in case 4 and 35 mm in case 47).

Surgical procedures in the marking group included 23 wedge resections, 6 segmentectomies, and 22 lobectomies. Two segmentectomies were performed after partial resection, and 20 lobectomies were performed after partial resection. Surgical procedures in the control group included 45 wedge resections, 12 segmentectomies, and 11 lobectomies.

The mean operation time for partial resection was 68.1 minutes in the marking group and 71.7 minutes in the control group. This difference was not significantly different.

The palpable tumor rate was 46/51 in the marking group and 59/68 in the control group (P=0.78). In the marking group, impalpable tumors were resected with wider partial resection in one case, with segmentectomy in one case, and with lobectomy in two cases. There was one case that

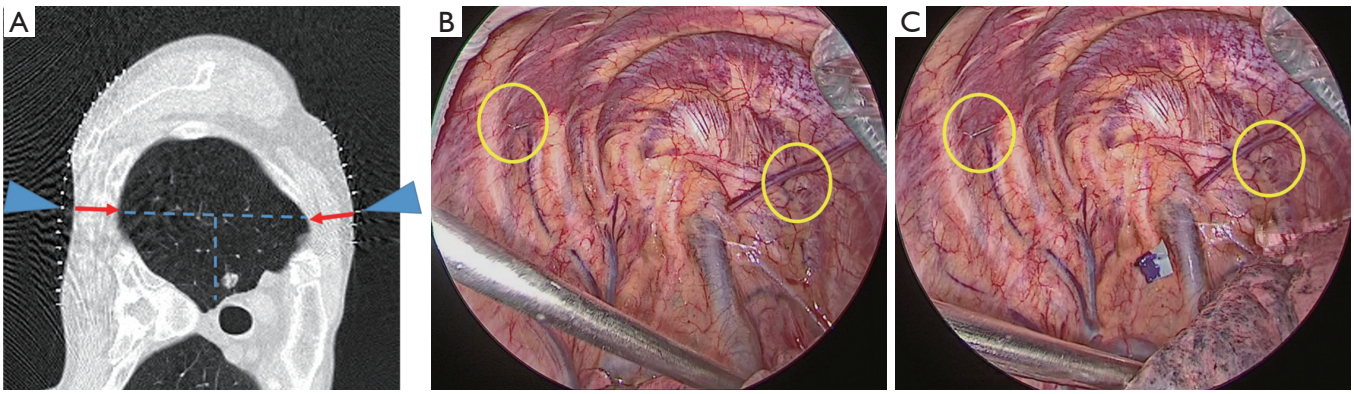

Figure 4 Indirect marking. (A) Preoperative marking under CT. The arrows point to the same level as the tumor and the tumor is present on the perpendicular bisector of these two points. The cutaneous marking is made on these two points. (B) During the surgery, the catheter needle is inserted into the pleural cavity from these two points. Circles indicate the tips of the needle. (C) The pleural marker is applied to the pleura above the trachea on the vertical bisector of these two points.

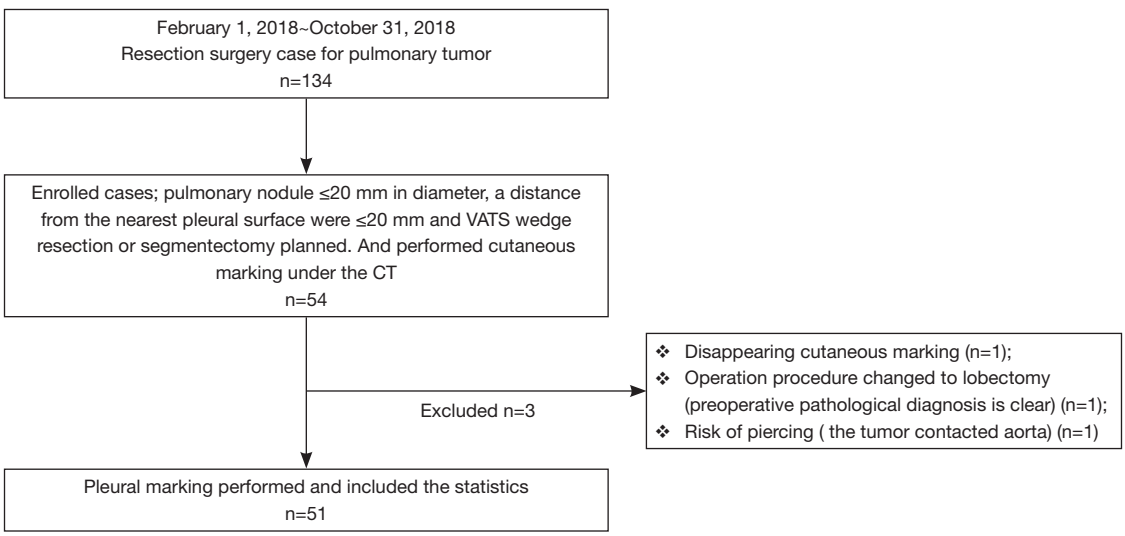

Figure 5 The flow diagram of patient selection. VATS, video-assisted thoracoscopic surgery.

required conversion to open surgery for palpation of the tumor. However, in the control group, conversion to open surgery was required in nine cases (*Table 3*).

The surgical approach was VATS in 44 cases in the marking group and 39 cases in the control group. Hybrid VATS was defined as when the skin incision was less than 8 cm, and it was required in five cases in the marking group and 21 cases in the control group. An open approach was defined as when the skin incision was over 8 cm, and it was required in two cases in the marking group and eight cases in the control group. There was a significant difference in approach between the two groups (P=0.0027).

Discussion

Various methods have already been reported for preoperative marking of peripheral pulmonary nodules in thoracoscopic surgery. A procedure using a hook wire that punctures the lung under CT guidance before surgery and involves pigment injection has severe complications, such

Table 1 Patient characteristics

Characteristics	Marking group (n=51)	Control group (n=68)	P value
Sex			0.46
Male	25	38	
Female	26	30	
Age, median [range] (years)	66 [37–82]	70 [23–83]	0.04[a]
Nodule size, mean (± SD) (mm)	12.4 (±4.76)	13.1 (±3.4)	0.31
Consolidation/tumor, mean (± SD) (mm)	0.73 (±0.37)	0.75 (±0.39)	0.81
Tumor density			0.61
Solid	31	45	
Partially solid	12	11	
Pure GGN	8	12	
Lobe with tumor			0.21
LUL	8	18	
LLL	7	13	
RUL	22	16	
RML	3	6	
RLL	11	15	
Pathology			
Lung cancer	38	52	0.081
Adenocarcinoma	31	40	
Squamous cell carcinoma	3	11	
LCNEC	2	1	
SCLC	2	0	
Meta	4	8	0.482
Others	9	7	
Granuloma	5	2	
Aspergilloma	0	1	
Abscess	0	1	
Hamartoma	1	2	
Lymph node	1	1	
Organizing pneumonia	2	0	

[a], statistically significant. GGN, ground glass nodule; LCNEC, large cell neuroendocrine carcinoma; LUL, left upper lobe; LLL, left lower lobe; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; SCLC, small cell lung cancer; meta, metastatic lung tumor; SD, standard deviation.

Table 2 Primary and secondary endpoints

Endpoints	Mean (± SD)	P value
DMT (mm)		0.35
Total	12.3 (±9.3)	
Direct marking (n=37)	11.5 (±8.8)	
Indirect marking (n=14)	14.2 (±10.4)	
Margin (mm)		0.58
Total	13.5 (±9.5)	
Direct marking (n=37)	14.0 (±10.4)	
Indirect marking (n=14)	12.3 (±6.7)	

Indirect marking is not affected by DMT or margin. DMT, distance between marking and visceral pleura nearest the tumor; margin, cut line margin; SD, standard deviation.

as cerebral infarction caused by air embolism, as well as pneumothorax or hemothorax (4). Hence, marking of the body surface before surgery under CT guidance without lung puncture has also been reported (8-10).

In Nishida *et al.*'s method, a puncture needle is inserted transpercutaneously into the extra pleural space, just above the tumor in the CT room before surgery. During surgery, a guide wire is inserted into the pleural cavity. With this guide wire, a cotton ball filled with dye is fixed to the chest wall. It marks the surface of the lung inflated during two-lung ventilation (8). However, this method is very cumbersome as it is necessary to puncture the chest wall in the CT room prior to surgery and local anesthesia is required.

In Kamiyoshihara *et al.*'s and Mun *et al.*'s method, CT-guided body surface marking is performed on the skin directly above the tumor with an oil pen before surgery (9,10). During surgery, the needle punctures the skin transpercutaneously using the guide wire, and the cotton ball filled with dye is fixed to the chest wall (9,10).

In these methods, marking the skin before surgery is not very complicated; however, it is somewhat cumbersome to fix the cotton ball to the chest wall. Furthermore, if there is a scapula between the tumor and the skin, it is difficult to attach the pigment to the pleura just above the tumor.

With our method, it is possible to attach the pigment to the visceral pleura just above the tumor, even if the tumor is behind the scapula or in the mediastinal side lung. However, in CT-guided preoperative body surface marking, puncture of the lung is not performed, but there may be some misalignment in the positional relationship between the marking site of the lung surface and the tumor

Table 3 Analysis of marking and conventional (without marking) resection of pulmonary nodules

Variables	Marking group (n=51)	Control group (n=68)	P value
Palpable rate, n (%)	46 (90.2)	59 (86.8)	0.78
Op. procedure			0.005[a]
Wedge resection	23	45	
Segmentectomy	6	12	
Lobectomy	22	11	
Op. time (in partial resection), mean (± SD) (min)	68.1 (±20.6)	71.7 (±35.2)	0.64
Approach, n (%)			0.0027[a]
VATS	44 (86.3)	39 (57.4)	
Hybrid VATS	5 (9.8)	21 (30.9)	
Open	2 (3.9)	8 (11.8)	
Conversion rate (in total cases), n (%)	6/51 (11.8)	13/68 (19.1)	0.32
Conversion for palpation (in total cases), n (%)	1/51 (2.0)	9/68 (13.2)	0.042[a]
Conversion rate (in wedge resection), n (%)	1/23 (4.3)	5/45 (11.1)	0.65

A control group is selected and comprises patients seen between February and October 2017 with tumors less than 20 mm in size and depth less than 20 mm who were undergoing partial resection or segmentectomy. For wedge resection, there are no significant differences in operation time in the marking group and the control group. However, there is significant tendency towards conversion to an open approach in the control group compared to the marking group. [a], statistically significant. VATS, video-assisted thoracoscopic surgery; SD, standard deviation; Op., operation.

before surgery, so it is necessary to perform intraoperative palpation.

In the present study, the mean DMT was 12 mm. Mun *et al.* reported a mean distance from the nodule to the marking point of 0.7 cm (range, 0–3 cm). In the present study, there was a case in which the maximum deviation was 4.5 cm, and there were cases where it was impossible to evaluate, such as cases where marking was on the adjacent lung lobe. The cause of discrepancies between the pleural marking site and the location of the tumor was that the marker was dragged and moved by the expanding lungs, and in the case of a puncture in a thick chest wall, the puncture needle was inserted slightly obliquely, as it seemed that position shift would occur. For this reason, in case 3 and beyond, the puncture was performed perpendicularly to the chest wall and the lungs squeezed slightly until just before coming into contact with the chest wall to avoid the pleural marker being shifted.

In cases where the chest wall is thick, the puncture needle is likely to be inserted diagonally, so it is predicted that chest wall thickness affects the DMT. We have examined the distance from the body surface marking portion to the pleura just above the tumor in all cases. Although the correlation between thickness and DMT was examined, no significant association was found. A thick chest wall and obesity were assumed to have little effect on this deviation.

As a localization method for small pulmonary nodules, a method of inserting a dye or a metal marker into the parenchyma around the tumor by a bronchoscope before the operation has been reported (11). The success rate of virtual-assisted lung mapping (VAL-MAP) conducted by Sato *et al.* was reported to be over 90%, and it is a very useful method for surgery where the impalpable pulmonary nodule needs to be resected. However, it is necessary to prepare a virtual bronchoscopic image before bronchoscopy and to inject the pigment faithfully into the parenchyma whilst referring to this image. This requires advanced technology, which is not available at all facilities.

Because the success rate of marking via this method is 92%, wedge resection with marking of impalpable pulmonary nodules is associated with the risk of tumor resection failure. However, this method can reduce the risk of palpation error. In 2017, before the present study in which we used our marking procedure, we experienced nine cases (13.2%) with conversions caused by impalpable nodules. In the present study, we were able to palpate the nodule via a small access port, except for in one case (1.9%). In other studies, the reported conversion rate for tumor localization has been between 13% and 50%, and some tumor markings are considered useful for reducing the conversion rate (3,12).

In this method, the marking is not complicated and is very safe compared to other localization methods. The pleural marker is made of materials just like the pleural markers used in any operating room. Hence, this procedure can be performed in any facility. Furthermore, it does not need any high technology devices. Though we have not

measured the time taken for the marking technique, in partial resection surgery, this method does not show an extension of the operation time compared with that for conventional surgery and it is simple.

We used a sterile echogenic jelly mixed with dye placed on a sterilized surgical tape as a pleural marker, as this prevents the parietal pleura from coming into contact with the echo jelly and dye directly.

A sterilized echo gel is said to be free from tissue degeneration by subcutaneous insertion (13), and is guaranteed to be safe as a material used for marking. In addition to this, with the surgical tape shielding it on the parietal pleura, it is thought to be even safer.

The limitation of this technique is that palpation of the tumor remains indispensable at this stage. Position misalignment between the marking and the tumor is on average about 12 mm; however, this is still quite close to the tumor. In four cases (8%), the site of the actual tumor differed greatly from the marking site. Therefore, our technique cannot guarantee that the marking and the tumor will line up perfectly. If we can reduce the likelihood of the pleural marker being dragged, and if the puncture needle can accurately indicate the pleura just above the tumor, it is expected that the marking accuracy will be further improved. Further research for improvements in this method is thus necessary.

In conclusion, CT-guided cutaneous marking and pleural marking indicated the location of the tumor with high probability, making it easy to palpate the tumor without a high technology device. This new procedure should be implemented in the clinical setting given its ease of application, safety, and accuracy.

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The present study was approved by the Institutional Review Board (IRB) of Kanazawa Medical University Hospital (I265). Individual informed consent was obtained from each patient. The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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