Puncture frequency predicts pneumothorax in preoperative computed tomography-guided lung nodule localization for video-assisted thoracoscopic surgery

Jing-Yang Huang | Stella Chin-Shaw Tsai | Tzu-Chin Wu | Frank Cheau-Feng Lin

Abstract

Background: Iatrogenic pneumothorax is the most frequent complication in preoperative CT-guided localization (POCTGL) of lung nodules. We aimed to determine the predictive factors of iatrogenic pneumothorax.

Methods: We retrospectively analyzed data of consecutive POCTGL procedures in patients who received video-assisted thoracoscopic surgery (VATS) at our hospital between May 2015 and October 2019. All of our patients utilized laser angle guide assembly to aid in the localization procedures.

Results: In 610 consecutive POCTGL procedures, 40 (6.6%) patients developed iatrogenic pneumothorax, and complications occurred in 8.5%. Univariate analyses revealed that puncture frequency, male gender, puncture depth, left decubitus position, and nodule near fissure were factors associated with pneumothorax, while multivariate analysis showed that only male gender (odds ratio 3.58, \( p = 0.012 \)) and puncture frequency (odds ratio 2.39/time, \( p = 0.0004 \)) determined development of pneumothorax. Further collective analysis on puncture frequency revealed that tumor in a difficult zone (1.33/C6 vs. 1.19/C6, \( p = 0.002 \)), especially adjacent to the mediastinum (1.41/C6 vs. 1.21/C6, \( p = 0.002 \)), angle difference of plan-to-practice (\( r = 0.209, p < 0.001 \)), depth to skin (\( r = 0.152, p < 0.001 \)), and depth to pleura (\( r = 0.164, p < 0.001 \)) were factors related to increased puncture frequency in univariate analyses. Only angle difference of plan-to-practice was associated in multivariate analysis (odds ratio: 1.158, \( p = 0.008 \)).

Conclusions: Puncture frequency was the key factor in the development of iatrogenic pneumothorax from POCTGL. Other associated factors, especially angle difference, may have affected the puncture frequency and subsequently have some influence on the incidence of iatrogenic pneumothorax.

KEYWORDS
iatrogenic pneumothorax, preoperative CT guided localization, pulmonary nodule, video-assisted thoracoscopic surgery

INTRODUCTION

Lung cancer is one of the deadliest malignancies in Taiwan and worldwide.\(^1,2\) Low-dose computed tomography (CT) has been the best tool for screening early lung cancer.\(^3\) Consequently, subcentimeter pulmonary nodules are detected efficiently in large numbers, and often require surgical resection for diagnosis and treatment. However, due to the small size of the nodules, preoperative localization methods are warranted and have rapidly emerged.\(^4-9\) Percutaneous CT-guided localization with a dye, hookwire, coils, or radioisotopes is the most popular adopted method.\(^5,9-12\) Other approaches, including the navigator, three-dimensional pulmonary reconstruction, and augmented fluoroscopic bronchoscopy, have also been implemented.\(^8,13\)
Of note, pneumothorax is one of the most common complications of CT-guided invasive lung procedures. Chest pain, dyspnea, desaturation, shock, and death may occur if patients with pneumothorax do not receive adequate treatment. Moreover, if pneumothorax occurs at a missed site, subsequent localization would be rendered even more difficult. However, robust studies on factors responsible for causing pneumothorax during preoperative CT-guided localization (POCTGL) are rare. The incidence of pneumothorax has previously been reported to be in the vast range of 4%–68.4%. In an effort to increase precision of the puncture angle, we invented the laser angle guide assembly (LAGA) to assist POCTGL. Subsequently, pneumothorax incidence at our facility was 6.4%, which was much lower than that reported in other studies. The aims of this study were to evaluate the critical factors for the success of POCTGL, and determine the predictive factors of iatrogenic pneumothorax during POCTGL.

METHODS

Study design

We retrospectively analyzed data of 610 consecutive POCTGL procedures in patients who received video-assisted thoracoscopic surgery (VATS) between May 2015 and October 2019 at a tertiary referral medical center. In all POCTGL procedures, laser angle guide assembly (LAGA) was used to aid in the localization.

Preoperative CT-guided localization assisted by laser angle guide assembly

Procedures

The LAGA system was developed to serve as a visible reference to guide the puncture angle for CT-guided pulmonary procedures. The detailed procedures have been published previously. Briefly, the angle of the LAGA was first established according to the CT scan planned with its tip laser pointed to the needle puncture point (Figure 1a). The portable green laser level was then projected to the front index line of the LAGA, identical to the angle planned on CT. Precise puncturing of the needle was achieved along the intersection of the two laser lines to the lesion (Figure 1b).

The localization was aided with the patent blue vital (PBV) dye (Guerbet, France, 2.5%) or a hookwire (Hawkins II breast localization needles, 20-gauge 7.5 cm). Targets within 20 mm of the pleura were marked by PBV only, and those more than 30 mm from pleura, by a hookwire. The PBV was tattooed with a spinal needle (20-gauge, 90 mm, Meditop) 0.2–0.4 ml at the target, while hookwire was cut 5–10 mm longer than the depth of target-pleura to avoid migration of the hookwire and inadvertent entry of atmospheric air into the pleural space. Two additional PBV tattoos were marked at the nodule and near the pleural surface to ensure double visible indicators for the surgery.

The POCTGL procedures were performed in turn by thoracic surgeons on the team including residents (under direct supervision) and three attending physicians A, B, and C with 1, 8, and 12 years of clinical experience.

Surgery

All 427 surgeries were performed under a double-lumen intubation general anesthesia and with a VATS approach. Intraoperative frozen pathological examination was adopted for most of the cases. A small pleural drain was preferred in most of the surgeries.
Data collection

The patients’ data collected prospectively included sex, age, number of nodules, smoking status, and operating surgeons. Pulmonary nodule data included size, location, pathology, localization angle, depth, time spent, and complications. Operation methods and hospital length of stay data were also included.

The planned puncture angle was measured by the angle between the gravity line (red laser beam) and the line of the skin-puncture point planed-target (green laser beam), whereas the actual puncture angle was measured by the angle between the gravity line (red laser beam) and the needle (Figure 2). Target nodules within 20 mm adjacent to the mediastinum, diaphragm, or fissure of the lung, the location of the nodules would be defined as the mediastinum, diaphragm, and fissure correspondingly. The nodules just beneath the scapula and breast implants were defined as scapula and prosthesis. Meanwhile, a targeted lesion that was localized through a different lobe during POCTGL was defined as cross-lobe. These areas required a high level of technical competency and were summarized as difficult zones. The localization time was defined as the duration between the completion of CT and the last checked CT scan. Successful targeting was simply defined as the PBV/hookwire that contacted the lesion. Incidences of dye spill-out or hookwire dropout were recorded as a failure to target.

### Table 1

| Surgeries | 427 | 100 |
|-----------|-----|-----|
| Gender    |     |     |
| Female    | 301 | 71.2|
| Age       |     |     |
| Mean (range)/SD | 54.7 (24–79) | 10.0 |
| Smoking   | 42  | 6.9 |
| Localization numbers | | |
| 1         | 304 | 71.2|
| 2         | 83  | 19.4|
| 3         | 27  | 6.3 |
| 4         | 8   | 1.9 |
| 5         | 3   | 0.7 |
| 6         | 2   | 0.5 |
| Sum       | 427 | 100 |
| Nodules   | 610 | 100 |
| Lobe      |     |     |
| RUL       | 192 | 31.7|
| RML       | 52  | 8.6 |
| RLL       | 128 | 21.1|
| LUL       | 136 | 22.4|
| LLL       | 98  | 16.2|
| Position  |     |     |
| Supine    | 287 | 47.6|
| Prone     | 222 | 36.8|
| Left decubitus | 61 | 10.1|
| Right decubitus | 33 | 5.5|
| Puncture times | | |
| 1         | 489 | 81.1|
| 2         | 89  | 14.8|
| 3         | 19  | 3.2 |
| 4         | 5   | 0.8 |
| 6         | 1   | 0.2 |
| Mean/SD   | 1.24| 0.575|
| Hookwire  | 124 | 20.9|
| Difficult zone | 152 | 24.9|
| Cross lobe | 21  | 3.4 |
| Mediastinum| 94  | 15.4|
| Diaphragm | 64  | 10.5|
| Scapula   | 32  | 5.2 |
| Fissure   | 46  | 7.5 |
| Breast prosthesis | 2 | 0.3 |

### Table 1 (Continued)

| Median | Range |
|--------|-------|
| Nodule size (mm) | 5 | 2–19 |
| Angle (°) | 19° | 0–91° |
| Δangle (°) | 2.0 | 0–19 |
| Depth to skin (mm) | 55 | 4–120 |

Abbreviations: DLP, dose length produce; Abbreviations: LLL, left lower lobe; LUL, left upper lobe; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe.

a Angle, angle difference between plan and practice.

### Table 2

The performance of preoperative CT-guided localization (POCTGL) by nodule

| n   | %  |
|-----|----|
| Total localizations | 610 | 100 |
| Dye spilled out | 5  | 0.8 |
| Tumor contact | 582 | 95.4 |
| Hookwire too deep | 28  | 4.6 |
| Hookwire drop-out | 0  | 0 |
| Complications | 52  | 8.5 |
| Pneumothorax | 40   | 6.6 |
| Pneumothorax aspirated | 9 | 1.5 |
| Hemothorax | 4  | 0.7 |
| Hemoptysis | 5  | 0.8 |

### Median and Range

- Nodule size (mm): 5, 2–19
- Angle (°): 19°, 0–91°
- Δangle (°): 2.0, 0–19
- Depth to skin (mm): 55, 4–120
The complications of POCTGL were collated. Any air detected in the localization CT scan, even in trace amounts, was recorded as a complication of pneumothorax. Hemoptysis was easier to use as verification sign than was lung parenchymal hemorrhage because the injected dye and hemorrhage appeared similar on the CT scan.

### Statistical analysis

First, univariate analysis was performed. All categorical variables were analyzed using $\chi^2$ tests. Numerical data were analyzed with the Mann–Whitney test. A two-tailed $p$-value <0.05 was considered statistically significant. The variables with $p < 0.2$ were selected for the multivariate analyses with

#### TABLE 3

| Pneumothorax | Without | With | $p$-value |
|--------------|---------|------|-----------|
| Total, $n$ (row %) | 526 (93.26) | 38 (6.74) | |
| Year of surgery, $n$ (%) | |
| 2015 | 16 (88.89) | 2 (11.11) | 0.8853 |
| 2016 | 47 (95.92) | 2 (4.08) | |
| 2017 | 124 (94.66) | 7 (5.34) | |
| 2018 | 197 (91.63) | 18 (8.37) | |
| 2019 | 142 (94.04) | 9 (5.96) | |
| Gender, $n$ (%) | |
| Female | 426 (94.46) | 25 (5.54) | 0.0239* |
| Male | 100 (88.50) | 13 (11.50) | |
| Smoking, $n$ (%) | |
| No | 490 (93.69) | 33 (6.31) | 0.1481 |
| Yes | 36 (87.80) | 5 (12.20) | |
| Age, median (range) | 54 (24–79) | 55.5 (32–75) | 0.9134 |
| Lobe, $n$ (%) | |
| RUL | 165 (93.22) | 12 (6.78) | 0.9467 |
| RML | 110 (93.22) | 8 (6.78) | |
| RLL | 121 (93.80) | 8 (6.20) | |
| LUL | 87 (92.55) | 7 (7.45) | |
| Performers | |
| A | 8 (7.7) | 96 (92.3) | 0.482 |
| B | 4 (10.8) | 33 (89.2) | |
| C | 5 (3.3) | 148 (96.7) | |
| Position, $n$ (%) | |
| Supine | 253 (95.47) | 12 (4.53) | 0.0497* |
| Prone | 195 (92.42) | 17 (7.58) | |
| Left decubitus | 50 (86.21) | 8 (13.79) | |
| Right decubitus | 28 (93.33) | 2 (6.67) | |
| Tumor contact, $n$ (%) | 12 (100.00) | 0 (0.00) | 0.3471 |
| Hookwire, $n$ (%) | 98 (89.91) | 11 (10.09) | 0.1202 |
| Nodule size, median (range), mm | 6 (2–19) | 6 (3–12) | 0.9371 |
| Punctures, median (range), mm | 1 (1–4) | 2 (1–6) | <0.0001* |
| n (%) | |
| 1 | 434 (96.02) | 18 (3.98) | <0.0001* |
| 2 | 73 (82.95) | 15 (17.05) | |
| 3 | 17 (89.47) | 2 (10.53) | |
| 4 | 2 (50.00) | 2 (50.00) | |
| 6 | 0 (0.00) | 1 (100.00) | |
| Angle, median (range), $\circ$ | 19 (0–90) | 17 (0–71) | 0.7466 |
| $\Delta$ angle, median (range), $\circ$ | 2 (0–9) | 1 (0–9) | 0.8626 |
| Depth to skin, median (range), mm | 55 (4–115) | 62.5 (25–90) | 0.0648* |
| Depth to pleura, median (range), mm | 14 (0–60) | 20.5 (1–65.99) | 0.0066* |

#### TABLE 3 (Continued)

| Pneumothorax | Without | With | $p$-value |
|--------------|---------|------|-----------|
| Difficult zone, $n$ (%) | 129 (93.48) | 9 (6.52) | 0.9074 |
| Mediastinum, $n$ (%) | 82 (93.18) | 6 (6.82) | 0.9738 |
| Diaphragm, $n$ (%) | 57 (91.94) | 5 (8.06) | 0.6589 |
| Cross lobe, $n$ (%) | 18 (94.74) | 1 (5.26) | 0.8474 |
| Fissure, $n$ (%) | 36 (85.71) | 6 (14.29) | 0.0427* |
| Scapula, $n$ (%) | 28 (100.00) | 0 (0.00) | 0.1449 |

| Generalized estimating equation (GEE) regression | Odds ratio | 95% CI | $p$-value |
|-----------------------------------------------|------------|--------|-----------|
| Punctures +1 time | 2.39 | 1.48–3.86 | 0.0004* |
| Depth to skin +1 mm | 1.01 | 0.96–1.07 | 0.663 |
| Depth to pleura +1 mm | 1.01 | 0.95–1.08 | 0.692 |
| Age +1 year | 0.98 | 0.93–1.03 | 0.4004 |
| Fissure Yes | 1.89 | 0.56–6.31 | 0.304 |
| Hookwire Yes | 1.2 | 0.16–8.97 | 0.858 |
| Gender Male | 3.58 | 1.32–9.70 | 0.012* |
| Smoking Yes | 1.78 | 0.44–7.19 | 0.417 |
| Position Supine Reference | 2.13 | 0.63–7.27 | 0.226 |
| Prone | 2.38 | 0.21–27.41 | 0.486 |
| Left decubitus | 1.48 | 0.06–38.89 | 0.814 |

Abbreviations: LLL, left lower lobe; LUL, left upper lobe; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe.

* $p < 0.005$. 

The complications of POCTGL were collated. Any air detected in the localization CT scan, even in trace amounts, was recorded as a complication of pneumothorax. Hemoptysis was easier to use as verification sign than was lung parenchymal hemorrhage because the injected dye and hemorrhage appeared similar on the CT scan.22

Statistical analysis

First, univariate analysis was performed. All categorical variables were analyzed using $\chi^2$ tests. Numerical data were analyzed with the Mann–Whitney test. A two-tailed $p$-value <0.05 was considered statistically significant. The variables with $p < 0.2$ were selected for the multivariate analyses with
generalized estimating equation regression. All categorical variables are expressed as raw numbers and percentages.

Identifying factors associated with puncture frequency

For testing the factors associated with puncture frequency, the categorical data were tested with the \( \chi^2 \) test; Fisher’s exact test was used when the number in a cell <5. The associations between continuous variables were made with Pearson’s correlation, \( r \). Multivariate analyses were executed with binary logistic regression.

All statistical analyses were performed using IBM SPSS statistical software version 18 (IBM Corp.).

RESULTS

Demography and performance of the preoperative CT guided localization

Between May 2015 and October 2019, 651 pulmonary nodules underwent POCTGL procedures, followed by 435 VATS surgeries. A total of 41 nodules and eight surgeries had incomplete data. Thus, 610 nodules of 427 surgeries were enrolled (Table 1). Of 427 surgeries, 71.2% were conducted in female patients (mean age, 54.7 years). Smokers constituted 6.9% of surgeries. Either one or two nodules needed POCTGL among 90.6% of operations. The maximum number of nodules that utilized POCTGL was six in two surgeries. Most of the nodules were located at the right upper lobe of the lung, followed by the left upper lobe, and the right lower lobe.

The most frequent position used during POCTGL was supine (47.6%), followed by prone (36.8%). A single puncture was achieved in 81.8% of POCTGL, and 14.8% needed two punctures, with a maximum of six punctures for one nodule. A hookwire was applied for 20.9% of the nodules. Some areas of the lung were deemed difficult zones (24.9%) for POCTGL, which included traditional “danger zones” including the mediastinum (15.4%), diaphragm (10.5%), and structures in the path of the puncture, including scapula (5.2%), breast prosthesis (0.3%), and the structures associated with pleura comprising fissure (7.5%) and cross-lobe (3.4%). The median size of the pulmonary nodules receiving POCTGL was 5 (2–19) mm. The median puncture angle was 19⁰. The puncture skin-lesion depth and pleural-lesion depth were 55 (4–120) mm and 15 (0–66) mm, respectively. The median time spent on one POCTGL was 18 min (range: 4–60) while the radiation exposure (dose-length product) was 427 (range: 135–2471) mGy-cm.

The outcomes of these 610 POCTGL are listed in Table 2. The markers contacted the targets successfully in 95.4% of trials. Dye spilled out in only five (0.8%), and no hookwire dropped out; however, a hookwire was inserted deeper than planned in 28 of the 124 nodules. Complications of POCTGL occurred in 8.5%, the rate of pneumothorax was as low as 40 (6.6%), and nine cases required needle aspiration. No pleural drain was required, hemothorax and hemoptysis were rare, and no air embolism or hookwire dropout took place.

Data analyses of factors associated with pneumothorax

Due to incomplete data on the details of localization and pulmonary nodules, 46 nodules of 39 patients were further excluded, while 564 nodules of 388 patients were entered into the iatrogenic pneumothorax analyses.

### Table 4 The factors affecting puncture times, by nodules

| Factors         | With (Mean, SD) | Without (Mean, SD) | \( p \)-value | Binary logistic regression for puncture times 1 vs. \( \geq 2 \) |
|-----------------|----------------|--------------------|--------------|-------------------------------------------------|
|                 |                |                    |              | Odds ratio | 95% CI | \( p \)-value |
| Difficult zone  | 1.33 (0.71)    | 1.19 (0.45)        | 0.002*       | 0.587      | 0.104 | 3.330 | 0.548 |
| Mediastinum     | 1.41 (0.75)    | 1.21 (0.52)        | 0.002*       | 2.236      | 0.398 | 12.562 | 0.351 |
| Cross lobe      | 1.24 (0.44)    | 1.24 (0.58)        | 0.96         | 3.451      | 0.513 | 23.223 | 0.203 |
| Diaphragm       | 1.36 (0.80)    | 1.23 (0.54)        | 0.096        | 4.458      | 0.672 | 29.568 | 0.112 |
| Fissure         | 1.19 (0.54)    | 1.25 (0.57)        | 0.531        | 0.797      | 0.129 | 4.926 | 0.807 |
| Scapula         | 1.39 (0.84)    | 1.24 (0.56)        | 0.256        | 1.396      | 0.229 | 8.511 | 0.718 |
| Smoker          | 1.21 (0.47)    | 1.25 (0.58)        | 0.734        | 2.325      | 0.736 | 7.340 | 0.150 |
| Hookwire        | 1.26 (0.54)    | 1.25 (0.59)        | 0.813        | 1.389      | 0.541 | 3.562 | 0.494 |
| Correlation R   |               |                    |              |            |      |       |       |
| Angle           | −0.002         | 0.953              |              | 0.996      | 0.976 | 1.016 | 0.669 |
| \( \Delta \)angle\* | 0.209          | 0.000*             |              | 1.158      | 1.010 | 1.289 | 0.008* |
| Depth to skin   | 0.152          | 0.000*             |              | 1.000      | 0.977 | 1.024 | 0.994 |
| Depth to pleura | 0.164          | 0.000*             |              | 1.038      | 0.996 | 1.081 | 0.074 |
| Nodule size     | 0.073          | 0.074              |              | 1.050      | 0.922 | 1.195 | 0.462 |

*\( \Delta \)angle, angle difference between plan and practice.

\( *p < 0.005. \)
The results revealed that puncture frequency, gender, and position of localization, nodule depth, and nodule near fissure were the predictors for POCTGL (Table 3) under univariate analyses. Patients of prone and left decubitus position, males, and nodules adjacent to fissure had more tendency for iatrogenic pneumothorax. The variables above with age and hookwire were selected for multivariate analyses with generalized estimating equation regression, which revealed that male gender (odds ratio 3.58, \( p = 0.012 \)) and puncture frequency (odds ratio 2.39/time, \( p = 0.0004 \)) were factors associated with the iatrogenic pneumothorax.

**Elements contributing to the puncture frequency of POCTGL**

Factors associated with the puncture frequency were further analyzed in the 610 cases of POCTGL (Table 4). Only the target nodules located adjacent to the mediastinum increased the puncture times among all of the difficult puncture zones. The angle differences between the planned and actual puncture, depth of nodule to the skin, and pleura were also related to the puncture frequency, but the nodule size was not. After the multivariate analyses with binary logistic regression for puncture numbers 1/>1, only the angle difference was significant (odds ratio: 1.158, \( p = 0.008 \)).

**DISCUSSION**

In this study, we evaluated the critical factors associated with iatrogenic pneumothorax during POCTGL procedures. Our findings showed that puncture frequency was the key factor in the development of iatrogenic pneumothorax. Other factors may have indirectly impacted the occurrence of iatrogenic pneumothorax.

Pneumothorax is the most frequent complication of POCTGL, which may cause death, vital sign changes, hypoxia, chest pain, chest tightness, and necessitate aspiration or pleural drains.\(^{16}\) Although most cases of iatrogenic pneumothorax POCTGL in this study were subclinical, it might render further POCTGL difficult and even result in failure. Therefore, it is imperative to know the factors associated with pneumothorax to achieve a successful POCTGL.

Our results revealed that only puncture frequency was a determinant of iatrogenic pneumothorax during POCTGL (Table 4). When the needle touched the visceral pleura, pleura dimpling occurred (Figure 3a). Following that, the needle punctured the visceral pleura, releasing the air in the lung. However, this might not always happen as the needle had a stopper effect on the hole. By withdrawing the puncture needle, the visceral pleura was brought toward the parietal pleura. With the visceral and parietal pleura’s elastic fiber contracting to cover the defect, pneumothorax would not happen in most cases (Figure 3b). For repeated punctures adjacent to the same site, the hole might be enlarged. When the visceral pleura was pushed inward and apart from the parietal pleural, the previous hole might not be sealed. Subsequently, air leaked into the pleural space resulting in a pneumothorax (Figure 3c).

Before LAGA was invented, most POCTGL procedures were performed with an “experienced hand” without guidance for the puncture angle. In our study, LAGA assisted 81.1% of our POCTGL in reaching the target lesions at the first attempt and 95.5% within two attempts (Table 1). Iatrogenic pneumothorax incidence was 6.4%, much lower than that of other studies.\(^{17}\) The sole key factor associated with iatrogenic pneumothorax was the puncture frequency. With 105 cases of POCTGL using hookwire and 18.9% resulting in pneumothorax, Yao et al. also concurred that the number of needle insertions was the determining factor of iatrogenic pneumothorax.\(^{19}\)

Various studies have revealed that depth to pleura is an associated factor of iatrogenic pneumothorax. In their study, Loh et al. demonstrated that depth was a factor associated with pneumothorax.\(^{23}\) Ohno et al. reported a study of 162 needle aspirations that both number of punctures and
depth were factors of iatrogenic pneumothorax.\textsuperscript{24} Further, Asai et al. reported a 102-case series of CT-guided lung biopsy. They concluded that the depth to pleura, instead of emphysema status of patients, was the causative factor of pneumothorax.\textsuperscript{25} Interestingly, Saji et al. found that both depth and angle were factors of pneumothorax for a report of 289 CT-guided lung biopsies; the wider the puncture planned angle, the more likely the pneumothorax.\textsuperscript{26} In the univariate analyses of our POCTGL procedures, the angle differences between the planned and actual puncture, depth of nodule to the skin, and depth of nodule to pleura were factors affecting puncture times. Our study is the first investigation focused on the impact of predetermined precise puncture angle on the occurrence of iatrogenic pneumothorax in POCTGL. With the same angle of deviation, the greater the depth, the farther the puncture needle from the target, potentially leading to repeated punctures and increased incidence of pneumothorax. When we used the LAGA system as a reference, the median angle difference of plan-practice (Δ angle) was only 2° (Table 1). In our pooled 610 POCTGL analyses, we showed the Δ angle as the most important factor affecting puncture frequency in both univariate and multivariate analyses (Table 4). With the assistance of the LAGA system, the Δ angle was minimized and had no significant effect in the univariate-paired study (Table 4).

Many reports considered the hookwire as a factor of iatrogenic pneumothorax.\textsuperscript{5,18,27} Gonfiotti et al. conducted a prospective randomized study to compare POCTGL using hookwire versus 22 G needle, and the incidence of pneumothorax was 24% and 4%, respectively.\textsuperscript{7} In three cases, there was hookwire dislodgement, which contributed to pneumothorax.\textsuperscript{7,18,28} Yao et al. further indicated that only puncture frequency mattered for hookwire localization.\textsuperscript{19} In our study, no dislodgement occurred because we employed the safety measure of cutting the hookwire 5–10 mm longer than the depth of lesion to the pleura. Moreover, with and without hookwire, the mean number of punctures was as low as 1.26 and 1.25, respectively (Table 4). The low puncture frequency was not associated with the use of hookwire when analyzed as a factor of pneumothorax.

With the assistance of LAGA, the procedure experience of the physician was no longer an important factor. The youngest and least experienced (Dr. A) was allowed to perform most of the procedures since his participation in this team; he had the least incidence of pneumothorax (without statistical significance, data not shown).

An important fatal complication of POCTGL, air embolism, did not occur in our series. Air embolism may happen when there were connections between the pulmonary vessels and the atmosphere, pneumothorax, or airways.\textsuperscript{18,29} Precautionary maneuvers of cutting hookwire shorter and hiding them in chest walls prevented the outside air from entering the lung vessels. The needle adopted had an inner core needle and outer sheath. During the procedure, the inner core needle was taken out only for seconds during dye injection that further insulated the atmosphere airflow. The low incidence of pneumothorax also helped to minimize the incidence of air embolism. Furthermore, the LAGA system facilitated the hookwire to reach its intended destination without any inadvertent airway and lung vessel exchanges.

This investigation focused on uncovering predictors of pneumothorax associated with POCTGL. The findings were only limited to preoperative localizations, and should not be extrapolated to localizations for other procedures such as biopsy, microwave ablation, or radiofrequency treatment. Further studies are warranted for these other procedures.

In conclusion, our report showed that puncture frequency was the most critical factor associated with iatrogenic pneumothorax for POCTGL. Other associated factors, especially angle difference, may have affected the puncture frequency and the incidence of iatrogenic pneumothorax.

ACKNOWLEDGMENTS

We thank Chuck Lin (College of William & Mary) for technical assistance in writing and editing the manuscript.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

ORCID

Frank Cheau-Feng Lin  https://orcid.org/0000-0001-5301-2345

REFERENCES

1. Ministry of Health and Welfare. 2019 Causes of Death Statistics. https://www.mohw.gov.tw/cp-4964-55572-2.html (9/23/2021, last accessed).
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin. 2017;67:7–30.
3. Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365:395–409.
4. Bolton WD, Cochran T, Ben-Or S, Stephenson JE, Ellis W, Hale AL, et al. Electromagnetic navigational bronchoscopy reduces the time required for localization and resection of lung nodules. Innovations. 2017;12:333–7.
5. Gonfiotti A, Davini F, Vaggelli L, De Francesci A, Caldarella A, Gigli PM, et al. Thoracoscopic localization techniques for patients with solitary pulmonary nodule: hookwire versus radio-guided surgery. Eur J Cardiothorac Surg. 2007;32:843–7.
6. Zhang H, Li Y, Yinin N, He Z, Chen X. CT-guided hook-wire localization of malignant pulmonary nodules for video assisted thoracoscopic surgery. J Cardiothorac Surg. 2020;15:307.
7. Park CH, Han K, Hur J, Lee SM, Lee JW, Hwang SH, et al. Comparative effectiveness and safety of preoperative lung localization for pulmonary nodules: a systematic review and meta-analysis. Chest. 2017;151:316–28.
8. Aways O, Reidy MR, Mehta K, Bianco V, Gooding WE, Schuchert MJ, et al. Electromagnetic navigation bronchoscopy-guided dye marking for thoracoscopic resection of pulmonary nodules. Ann Thorac Surg. 2016;102:223–9.
9. Yang SM, Chen YC, Ko WC, Huang HC, Yu KL, Ko HJ, et al. Augmented fluoroscopic bronchoscopy (AFB) versus percutaneous computed tomography-guided dye localization for thoracoscopic resection of small lung nodules: a propensity-matched study. Surg Endosc. 2020;34:5393–401.
10. Lin MW, Tseng YH, Lee YF, Hsieh MS, Ko WC, Chen JY, et al. Computed tomography-guided patent blue vital dye localization of pulmonary nodules in uniportal thoracoscopic. J Thorac Cardiovasc Surg. 2016;152:535–44.e2.
11. Fu YF, Zhang M, Wu WB, Wang T. Coil localization-guided video-assisted thoracoscopic surgery for lung nodules. J Laparoendosc Adv Surg Tech A. 2018;28:292–7.
12. Wang J, Yao J, Xu L, Shan L, Zhai R, Gao L, et al. Comparison of cyanoacrylate and hookwire for localizing small pulmonary nodules: a propensity-matched cohort study. Int J Surg. 2019;71:49–55.
13. Chen A, Pastis N, Furukawa B, Silvestri GA. The effect of respiratory motion on pulmonary nodule location during electromagnetic navigation bronchoscopy. Chest. 2015;147:1275–81.
14. Bungay HK, Berger J, Traill ZC, Gleeson FV. Pneumothorax post CT-guided lung biopsy: a comparison between detection on chest radiographs and CT. Br J Radiol. 1999;72:1160–3.
15. Chandra S, Agarwal D, Singh V, Mohan A, Galeria R. Pneumothorax: a common complication of CT-guided transthoracic needle lung biopsy. BMJ Case Rep. 2009;2009:bcr0120091496.
16. Yamagami T, Terayama K, Yoshimatsu R, Matsumoto T, Miura H, Nishimura T. Role of manual aspiration in treating pneumothorax after computed tomography-guided lung biopsy. Acta Radiol. 2009;50:1126–33.
17. Tsai SC, Wu TC, Lai YL, Lin FC. Preoperative computed tomography-guided pulmonary nodule localization augmented by laser angle guide assembly. J Thorac Dis. 2019;11:4682–92.
18. Kleeblatt M, Kim DH, Lee FT, Lubner MG, Robbins JB, Ziemlewicz TJ, et al. Preoperative pulmonary nodule localization: a comparison of methylene blue and hookwire techniques. Am J Roentgenol. 2009;50:1126–33.
19. Yao F, Wang J, Yao J, Xu L, Wang J, Gao L. Reevaluation of the efficacy of preoperative computed tomography-guided hook wire localization: a retrospective analysis. Int J Surg. 2018;51:24–30.
20. Chao YK, Pan KT, Wen CT, Fang HY, Hsieh MJ. A comparison of efficacy and safety of preoperative versus intraoperative computed tomography-guided thoracoscopic lung resection. J Thorac Cardiovasc Surg. 2018;156:1974–83.e1.
21. Lin FC, Tsai SC, Tu HT, Lai YL, Wu TC. Computed tomography-guided localization with laser angle guide for thoracic procedures. J Thorac Dis. 2018;10:3824–8.
22. Tomiyama N, Yasuhara Y, Nakajima Y, Adachi S, Arai Y, Kusumoto M, et al. CT-guided needle biopsy of lung lesions: a survey of severe complication based on 9783 biopsies in Japan. Eur J Radiol. 2006;59:60–4.
23. Loh SE, Wu DD, Venkatesh SK, Ong CK, Liu E, Seto KY, et al. CT-guided thoracic biopsy: evaluating diagnostic yield and complications. Ann Acad Med Singapore. 2013;42:285–90.
24. Ohno Y, Hatabu H, Takenaka D, Higashino T, Watanabe H, Ohbayashi C, et al. CT-guided transthoracic needle aspiration biopsy of small (≤20 mm) solitary pulmonary nodules. Am J Roentgenol. 2003;180:1663–9.
25. Asai N, Kawamura Y, Yamazaki I, Sogawa K, Ohkuni Y, O’uchi T, et al. Is emphysema a risk factor for pneumothorax in CT-guided lung biopsy? Springerplus. 2013;2:196.
26. Saji H, Nakamura H, Tsuchida T, Tsuboi M, Kawate N, Konaka C, et al. The incidence and the risk of pneumothorax and chest tube placement after percutaneous CT-guided lung biopsy: the angle of the needle trajectory is a novel predictor. Chest. 2002;121:1521–6.
27. Li W, Wang Y, He X. Combination of CT-guided hookwire localization and video-assisted thoracoscopic surgery for pulmonary nodular lesions: analysis of 103 patients. Oncol Lett. 2012;4:824–8.
28. Iguchi T, Hiraki T, Gobara H, Fujitaka H, Matsui Y, Miyoshi S, et al. CT fluoroscopy-guided preoperative short hook wire placement for small pulmonary lesions: evaluation of safety and identification of risk factors for pneumothorax. Eur Radiol. 2016;26:1114–21.
29. Sakiyama S, Kondo K, Matsuoka H, Yoshiida M, Miyoshi T, Yoshiida S, et al. Fatal air embolism during computed tomography guided pulmonary marking with a hook-type marker. J Thorac Cardiovasc Surg. 2003;126:1207–9.

How to cite this article: Huang J-Y, Tsai SC-S, Wu T-C, Lin FC-F. Puncture frequency predicts pneumothorax in preoperative computed tomography-guided lung nodule localization for video-assisted thoracoscopic surgery. Thorac Cancer. 2022;13(13):1925–32. https://doi.org/10.1111/1759-7714.14457