Transthoracic biopsy of lung masses: Non technical factors affecting complication occurrence

Aykut Recep Aktas¹, Emel Gozlek¹, Rasih Yazkan², Omer Yilmaz¹, Mustafa Kayan¹, Hakan Demirtas¹, Meltem Cetin¹, Nisa Unlu¹, Mustafa Kara¹ & Bumin Degirmenci¹

¹ Radiology Department, Suleyman Demirel University, Isparta, Turkey
² Thoracic Surgery Department, Suleyman Demirel University, Isparta, Turkey

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Abstract
Background: To investigate the transthoracic computed tomography (CT)-guided lung nodule biopsy complications and risk factors associated with the development of these complications.

Methods: We retrospectively evaluated a total of 41 CT-guided transthoracic biopsy complications. Data was analyzed by chi-square and independent sample t-tests.

Results: Twenty-seven patients (28.7%) developed pneumothorax and eight patients (8.5%) developed parenchymal hemorrhage, and four patients (4.3%) hemothorax and two (2.1%) patients developed subcutaneous emphysema. A significant correlation was obtained between the development of pneumothorax and lesion size (P = 0.040), and the distance that traversed the parenchyma (P = 0.001). There was a statistically significant difference between the parenchymal hemorrhage and lesion size and the distance from passed parenchyma (P values were 0.021 and 0.008, respectively). An increased incidence of parenchymal hemorrhage and pneumothorax was observed at small size and deep-seated lesions.

Conclusion: Lesion size and the distance that traversed the parenchyma on the biopsy tract are the most important factors that influence the development of complications in CT-guided transthoracic biopsy.

Introduction
Percutaneous transthoracic biopsies (PTB) guided by computed tomography (CT) are a safe, highly accurate, and effective method used in histopathologic diagnosis of thoracic masses.¹,² The conditions that benefit from CT-guided transthoracic needle biopsy are lesions that cannot be localized with fluoroscopy and ultrasound, such as hilar and mediastinal masses, oblique and angled applications, and common bullous diseases.²

The purpose of this study is to investigate the complications and risk factors that affect complication development in CT-guided transthoracic biopsy of lung masses.

Material and Methods
We evaluated a total of 41 CT-guided biopsy complications retrospectively, with Institutional Review Board approval. Eighty-seven core (tru-cut) and seven fine needle aspiration biopsy (FNAB) procedures were performed under the guidance of a 128-section CT device (Somatom Definition AS Plus 128, Siemens, Forchheim, Germany). As a standard of care, all patients were informed about the purpose and methodology of the biopsy procedure and consent forms for the biopsy were obtained from all patients.

The CT images of all cases were analyzed retrospectively. The lesion location, size, edge features, parenchymal distance passed in the biopsy tract, presence of emphysema around the lesion and in the biopsy tract, presence of the lesion cavity and necrosis, and complications that developed during and after the procedure were recorded.

The cases were divided into three groups according to lesion size: group 1: 0–1.99 cm; group 2: 2–4.99 cm; and group 3 consisted of lesions of 5 cm and above.

Lesions were classified into three groups: the parenchymal distance in group 1 was 0; the parenchymal distance in
group 2 was 0.1–2 cm; and in group 3 it was 2.1 cm and higher.

The chi-square test was used to compare the distribution between nominal and ordinal variables. In the independent samples, a student t-test and a chi-square test was used to compare the relationship between complications and mean values of the patients' age, lesion size, and traversed parenchymal distance. Statistical analyses were performed using the SPSS 15.0 program. A P value < 0.05 was considered sufficient for statistical significance.

Results

The distribution of the groups was based on lesion sizes: seven (7.4%) in group 1; 36 (38.3%) in group 2; and 51 (54.3%) in group 3. The distribution of patients according to the traversed parenchymal distance during biopsy was follows: 63 cases (67%) in group 1, 18 cases (19.2%) in group 2, and 13 cases (13.8%) in group 3. A cavity was detected in nine cases (9.6%) and necrosis was detected in 24 (25.5%) cases. Eighteen of the lesions (19.1%) had smooth edges, while 76 (80.9%) had irregular edges (Fig 1).

Complications developed in 38 patients (44.7%) and two of those patients had more than one complication. The most common complication was pneumothorax (Table 1). Subcutaneous emphysema was detected in 37 (39.4%) patients and seven of them (7.4%) were considered massive.

When the relationship between lesion size and development of pneumothorax was evaluated, there were three (42.9%) pneumothorax observed in group 1, 14 (38.9%) in group 2, and 10 (19.6%) in group 3 (Table 2). When groups formed based on the pneumothorax and lesion size were compared with each other using Pearson chi-square test analysis, there was no statistically significant relationship (P = 0.102). Because groups were formed by ordinal data, statistical analysis using linear by linear association chi-square tests, which show a linear relationship between the variables, was also performed. According to this test, an inverse linear relationship was determined between the groups in terms of the development of pneumothorax (P = 0.043).

Sixty-three of the lesions (67%) were pleural based. Pneumothorax was observed in 11 out of the 63 (17.5%) pleural based patients whose parenchymas were not traversed. In addition, pneumothorax was observed in 16 (51.6%) of 31 (33%) non-pleural based lesions (Table 2).

A statistically significant difference was found between the pleural-based lesions and non-pleural based lesions where parenchyma was traversed in terms of the development of pneumothorax (P = 0.001).

When groups created based on the traversed parenchymal distance were evaluated, 11 cases (17.5%) in group 1, 11 cases (61.1%) in group 2, and five cases (38.5%) in group 3 developed pneumothorax. The statistically significant differences

Table 1 Complication rates after PTB

| Complications            | n  | %   |
|--------------------------|----|-----|
| Pneumothorax             | 27 | 28.7|
| Parenchymal hemorrhage   | 8  | 8.5 |
| Hemothorax               | 4  | 4.3 |
| Subcutaneous emphysema   | 2  | 2.1 |

PTB, percutaneous transthoracic biopsy.
were detected between these groups in terms of development of pneumothorax ($P = 0.001$).

Among the patients that were included in the study group, 76 out of 94 lesions had irregular edges, while 18 had smooth edges. Pneumothorax developed in 22 lesions (28.9%) with irregular edges and in five lesions (27.8%) with smooth edges (Fig 2). There was no significant relationship between the lesions’ edge features and the development of pneumothorax ($P = 0.921$).

In 37 patients, emphysema was detected as a parenchymal finding and seven of them were considered massive. Pneumothorax developed in two patients (28.6%) with massive emphysema, seen on every lobe of the lung, with several bullous cavities. Furthermore, pneumothorax started to develop in 12 patients (40.0%) who had a lighter form of emphysema, with no diffuse or bullous formations present in the parenchyma. In addition, pneumothorax developed in 13 patients (22.8%) without emphysema. There was no statistically significant difference between the development of pneumothorax and the presence of parenchymal emphysema ($P = 0.242$) or presence of cavity in the lesion ($P = 0.219$).

The development of pneumothorax and the presence of necrosis in the lesions had a statistically significant relationship ($P = 0.042$). However, there was no significant relationship between the development of pneumothorax and the patients’ mean age ($P = 0.934$, independent sample t-test) (Table 3).

The average lesion size in patients with pneumothorax was $4.40 \pm 2.18$ cm, versus $5.55 \pm 2.51$ cm in those without pneumothorax. A statistically significant relationship was found between the occurrence of pneumothorax and the average size of the lesion ($P = 0.040$, independent sample t-test).

The mean traversed parenchymal distance in patients with pneumothorax was $1.00 \pm 1.24$ cm, versus $0.46 \pm 0.95$ cm in patients who did not have pneumothorax. This relationship was found to be statistically significant ($P = 0.024$, independent sample t-test).

When the relationship between the development of parenchymal hemorrhage and lesion size was evaluated, parenchymal hemorrhage was observed in two patients (28.6%) from group 1, five patients (13.9%) from group 2, and one patient (2.0%) from group 3. Among the groups formed according to the size of the lesion, statistically significant differences were detected in terms of the development of parenchymal hemorrhage ($P = 0.021$) (Table 4).

In three (4.8%) pleural-based lesions (Fig 3) and five (16.1%) non-pleural-based lesions, post-procedure parenchymal hemorrhage was detected. There was no statistically significant relationship between them ($P = 0.063$).

In groups classified according to the traversed parenchymal distance in the biopsy tract, three cases (4.8%) from group 1, one case (5.6%) from group 2, and four cases (30.8%) from group 3 developed parenchymal hemorrhage and statistically significant differences were detected between those groups in terms of the development of parenchymal hemorrhage ($P = 0.008$).
In addition, there was a significant relationship between parenchymal hemorrhage and age, as well as localization of lesions in the left or right lung ($P = 0.001$ and 0.017, respectively).

Hemothorax was observed in four patients (4.3%) from the study group. No statistically significant relationship was determined between the development of hemothorax and the investigated parameters.

Table 3 Correlations between age, lesion size, traversed parenchymal distance, and pneumothorax

|                         | Px   | n   | Mean | Std. Dev. | Std. mean error | $P$  |
|-------------------------|------|-----|------|-----------|-----------------|------|
| Age                     | No   | 67  | 63.94| 10.45     | 1.28            | 0.934|
|                         | Yes  | 27  | 64.15| 12.15     | 2.34            |      |
| Traversed parenchymal distance (mm) | No   | 67  | 4.6  | 9.5       | 0.12            | 0.024|
|                         | Yes  | 27  | 10   | 12.4      | 0.24            |      |
| Lesion size             | No   | 67  | 55.5 | 25.1      | 0.31            | 0.04 |
|                         | Yes  | 27  | 44   | 21.8      | 0.42            |      |

Std. Dev., standard deviation.

Discussion

The pneumothorax is one of the most common complications of PTB with a reported incidence that ranges between 8–61%.1,3 In our study, and consistent with the literature, pneumothorax was the most common complication.4-7 Pneumothorax developed in 27 out of 94 (28.7%) procedures. In their retrospective study, Yeow et al. reported that...
pneumothorax risk increased seven-fold in lesions with depths up to 2 cm deep compared to lesions adjacent to the pleura, but detected that the rate of pneumothorax decreased with increasing lesion depth. Therefore, they suggested that regardless of the depth of the lesion, passage of the ventilated lung parenchyma is an important factor in the development of pneumothorax. There are further studies in the literature that support this view. Cox et al. reported a pneumothorax rate of about 50% at any traverse ventilated lung parenchymal distance and this rate did not increase with increasing lesion depth. In our study, 17.5% of pleural-based lesions and 51.6% of non-pleural-based lesions developed pneumothorax and this difference was statistically significant ($P = 0.001$). Our results were consistent with the literature. In our study, the pneumothorax occurrence rates were lower in pleural-based lesions, but that rate increased with the traversing of parenchyma. There was no correlation between the type of implemented biopsy and pneumothorax. In our study, a discordant result was found, whereby there was an increased risk of pneumothorax in patients with a “lighter form of emphysema” versus those with “massive emphysema” (40.0% vs. 28.6%; Fig 4). We believe that this is because it is much harder for fibrotic changes to occur in massive emphysema. Fibrotic changes lower the probability to traverse the normal ventilated lung and prevent air leak from emphysematous cavities.

In the literature, there are studies that suggest that pneumothorax rates increase with smaller lesion size. We evaluated the relationship between the lesion size and pneumothorax and determined that pneumothorax was observed in three cases (42.9%) in group 1, 14 (38.9%) in group 2, and 10 (19.6%) in group 3. Because the groups were constituted from ordinal data in our statistical analyses, we showed an inverse linear relationship between the groups in terms of the development of pneumothorax ($P = 0.043$). Moreover, the independent samples $T$ test showed a significant relationship between pneumothorax and mean lesion size ($P = 0.040$). Similar to the literature, we observed that pneumothorax rates increased with decreasing lesion size. As a result of the more technically difficult biopsy procedure in small-sized lesions, a greater number of route corrections and multiple pleural passages may be required to reach the lesions. Therefore, this may result in prolonged procedure time, as well as increased rates of pneumothorax. Cox et al. reported that the presence of emphysema in the lobe where the biopsy was applied increases the rate of pneumothorax. Similarly, Topal and Berkman reported that, in the presence of severe emphysema, the risk of pneumothorax increases to 1.5–2 fold; however, in the presence of blood in the needle, there was a decrease in the rate of pneumothorax in emphysema patients. In our study, pneumothorax developed in 37.8% of patients that had emphysema in the biopsy tract and around the lesion and in 22.8% of patients that did not have emphysema; however, this relationship was not statistically significant ($P = 0.116$). Moreover, pneumothorax developed in 24 out of 70 lesions (34.3%) without necrosis and in three out of

| Statistics of the factors affecting the occurrence of parenchymal hemorrhage |
|-----------------------------|-----------------------------|-----------------------------|
| Parenchymal hemorrhage     | No  | Yes | Total | Hemorrhage (%) | $P$  |
| Lesion size                | Group 1 | 5  | 2   | 7    | 28.6   | 0.021 |
|                            | Group 2 | 31 | 5   | 36   | 13.9   |       |
|                            | Group 3 | 50 | 1   | 51   | 2.0    |       |
| Pleura base lesion         | No  | 26 | 5   | 31   | 16.1   | 0.063 |
|                            | Yes | 60 | 3   | 63   | 4.8    |       |
| Traversed parenchymal distance | 0–1 mm | 60 | 3   | 63   | 4.8    | 0.008 |
|                            | 1–20 mm | 17 | 1   | 18   | 5.6    |       |
|                            | 21 mm | 9  | 4   | 13   | 30.8   |       |
| Biopsy type                | Tru-cut | 80 | 11  | 87   | 8.0    | 0.569 |
|                            | FNAB | 6  | 1   | 7    | 14.3   |       |
| Necrosis                   | No  | 62 | 8   | 70   | 11.4   | 0.083 |
|                            | Yes | 24 | 0   | 24   | 0.0    |       |
| Cavity                     | No  | 77 | 8   | 85   | 9.4    | 0.336 |
|                            | Yes | 9  | 0   | 9    | 0.0    |       |
| Edge property              | Irregular | 69 | 7   | 76   | 9.2    | 0.617 |
|                            | Smooth | 17 | 1   | 18   | 5.6    |       |
| Emphysema                  | No  | 50 | 7   | 57   | 12.3   | 0.256 |
|                            | Yes | 29 | 1   | 30   | 3.3    |       |
|                            | Massive | 7  | 0   | 7    | 0.0    |       |

Lesion sizes; Group 1: 0–19 mm, Group 2: 20–49 mm, Group 3: 50 mm and above. FNAB, fine needle aspiration biopsy.
24 lesions (12.5%) with necrosis. No significant relationship was determined between the presence of necrosis in the lesion and the development of pneumothorax ($P = 0.042$). The average size of non-necrotic lesions was 4.6 ± 2.3 cm, and necrotic lesions was 7.0 ± 1.9 cm. Reduction in the rate of pneumothorax in necrotic lesions was thought to be associated with the large size of lesions that had necrotic components. When other factors affecting the development of pneumothorax were considered, we did not detect any significant relationship between pneumothorax and patient age, lesion edge features, localization of the lesion, or the presence of a cavity.

The second most common complication observed in PTB is parenchymal haemorrhage, with an incidence of 5–10%. In our study, eight patients (8.5%) developed parenchymal hemorrhage, which is consistent with the literature. In all cases observed, hemorrhage was limited to the lesions surrounding and the needle tract, and was resolved without the need for intervention. Khan et al. reported that lesion size, length of the intra pulmonary biopsy tract, and the number of pleural passages were factors affecting hemorrhage. Similarly, Yeow et al. indicated that lesion size, lesion depth, and the absence of pleural effusion in the biopsy-side were risk factors for hemorrhage. In our study, and consistent with the literature, we found that the parenchymal hemorrhage was significantly related to lesion size and traversed parenchymal distance ($P = 0.021$ and 0.008, respectively). We believe that this can be explained as a result of the close localization of the large lesions to the pleural surface and, therefore, less parenchymal distance to traverse, as well as the difficulty in accessing small lesions.

The retrospective nature of our study, the small number of patients, an inability to plan the number of patients, and evaluation parameters were the most important limitations of our study. We believe that prospective studies with larger patient series and planning of evaluation parameters will provide useful information regarding the diagnostic accuracy of PTB in predicting and preventing potential complications.

**Conclusions**

The most important risk factors that affect the development of pneumothorax and parenchymal hemorrhage are the size of the lesion and the parenchyma distance traversed in the
biopsy tract. Decreased lesion size and the passage of the ventilated lung parenchyma in the biopsy tract significantly increased the rate of pneumothorax and parenchymal hemorrhage. Detailed evaluation of risk factors prior to PTB, prediction of potential complications, and precautions to minimize complications in high-risk situations are important steps in the prevention of unnecessary complications.

Disclosure
No authors report any conflict of interest.

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