Feasibility of ultra-low dose CT for bronchoscopy of peripheral lung lesions

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Abstract
Background Thin-section CT is essential for identification of small bronchi during bronchoscopy using radial endobronchial ultrasound. Some patients should receive an additional CT for a thin-section image. We performed a retrospective study with a prospectively collected database to identify the optimal radiation dose for thin-section CT during peripheral bronchoscopy.

Methods In total, 91 patients with peripheral lung lesions underwent thin-section CT (both standard CT as a reference and ultra-low dose CT [LDCT]). The patients were randomly assigned to one of four groups according to the ultra-LDCT parameters: group 1 = 120 kVp, 25 mAs; group 2 = 100 kVp, 15 mAs; group 3 = 120 kVp, 5 mAs; and group 4 = 100 kVp, 5 mAs. Two radiologists and two physicians analyzed both the standard CT and ultra-LDCT.

Results The effective doses (EDs) of ultra-LDCT significantly differed among the four groups (median EDs were 0.88, 0.34, 0.19, and 0.12 mSv for groups 1–4, respectively; P < 0.001). Median differences in peripheral airway wall thickness were higher in group 4 than in other groups (differences in median wall thickness measured by two radiologists were 0.4–0.5 mm and 0.8–0.9 mm for groups 1–3 and group 4, respectively). Bronchus signs on ultra-LDCT in groups 1 and 2 were well correlated with those of the standard dose CT (accuracies of two radiologists and two pulmonary physicians were 95–100%).

Conclusions Our results indicate that ultra-LDCT with ED of > 0.34 mSv (ED of group 2) is feasible for peripheral bronchoscopy.

Background
The frequency of detecting peripheral lung lesions has increased with widespread use of low-dose chest computed tomography (CT) for lung cancer screening [1, 2]. Although the accuracies of non-invasive imaging modalities (e.g., positron emission tomography and high quality CT scans) have improved, a pathological examination remains the main method for a definitive diagnosis of lung cancer [3]. Transthoracic needle aspiration biopsies are generally considered to have good diagnostic performance; however, procedural-related complications, including pneumothorax, hemorrhage, and pleural seeding can occur [4, 5].
The technique of bronchoscopy for peripheral lung lesions, or so-called peripheral bronchoscopy, has substantially improved over the past few decades, such that it has become safer and provides an acceptable diagnostic yield [6–8]. Interpretation of CT scans without any assistance from expensive navigation equipment (e.g., virtual bronchoscopy navigation and electromagnetic navigation bronchoscopy [9, 10]), including identification of the bronchus sign, is considered the most important preparation before bronchoscopy for patients with peripheral lung lesions. Most importantly, a reconstructed thin-section CT scan is necessary to identify small peripheral bronchi; some patients should receive an additional CT scan for a thin-section image. The minimum radiation dose of a thin-section CT scan for bronchoscopy should be evaluated due to concerns regarding radiation exposure.

We performed a retrospective study with a prospectively collected database to determine whether ultra-low dose thin-section CT scans are feasible for peripheral bronchoscopy.

**Methods**

**Study population**

This retrospective study used a prospectively collected database to investigate the feasibility of 3D ultra-low dose CT for bronchoscopy of peripheral lung lesions at Pusan National University Hospital (a university-affiliated, tertiary referral hospital in Busan, South Korea) between May 2017 and March 2018. During the study period, consecutive patients who received a chest CT scan for peripheral bronchoscopy were prospectively registered. Due to the retrospective nature of the study, the Institutional Review Board of Pusan National University Hospital approved the study without the requirement to obtain informed consent from each study subject (approval no. H-2001-005-087).

**CT protocol for bronchoscopy of peripheral lung lesions**

All patients underwent both standard dose and ultra-low dose chest CT. All CT examinations were performed during end-inspiratory breath-holding with patients in the supine position, using a 256-detector row CT (Revolution CT; GE Healthcare, Waukesha, WI, USA). Imaging parameters were held in helical imaging mode: 128 × 0.625 mm detector configuration and a 0.5 s rotation time. The standard dose CT imaging parameters were: 120 kVp, tube current modulation with CTDIvol of ≤ 7 mGy. All patients were randomly assigned to one of four study groups according to different ultra-
low dose CT imaging parameters, as follows: group 1 = 120 kVp, 25 mAs; group 2 = 100 kVp, 15 mAs; group 3 = 120 kVp, 5 mAs; and group 4 = 100 kVp, 5 mAs. Standard dose CT images were reconstructed with filtered back projection, and ultra-low dose CT images were acquired with 50% iterative reconstruction of strength. All reconstructed images were transferred to a dedicated workstation (Advantage Workstation 3.1; GE Healthcare) for analysis by radiologists.

CT results and image analysis
To determine the estimated effective dose, the dose-length product was multiplied by a conversion coefficient of 0.014 mSv/mGy•cm [11]. Two chest radiologists and two pulmonary physicians evaluated the standard and ultra-low dose CT scans for each patient. The ultra-low dose CT scans were reviewed first; the standard CT scans were evaluated independently at least 2 weeks later. Objective image noise, wall thickness, and wall-area ratio of the bronchus leading to peripheral lung lesion were measured by two radiologists; the presence of the bronchus sign was also recorded. Objective image noise was assessed using the standard deviation (SD) of the tracheal lumen attenuation by drawing a region of interest inside the trachea just proximal to the tracheal bifurcation area. Final image noise was calculated by averaging the measurement values obtained by the two radiologists. Wall thickness and the wall-area ratio of the bronchus leading to the peripheral lung lesion were semi-automatically measured using 3D airway analysis software (Advantage Workstation 3.1; GE Healthcare). Peak wall thickness and the peak wall-area ratio were calculated from the reconstructed bronchi when the radiologist delineated a line along the bronchus leading to the peripheral lung lesion. The wall-area ratio was defined as the percentage of wall area to total airway area at the reconstructed plane, orthogonal to the main axis of the bronchus. The bronchus sign was defined as the presence of a peripheral bronchus leading directly to peripheral lung lesions [12, 13]. Two pulmonary physicians independently evaluated the bronchus sign on CT scans.

Statistical analysis
All variables are presented as medians (interquartile range) and numbers (percentage) for continuous and categorical variables, respectively. Categorical variables were compared using Fisher’s exact test. The Kruskal-Wallis test or the Wilcoxon rank-sum test were used for continuous variables, as
appropriate. Differences with P < 0.05 were considered statistically significant. Statistical analyses were performed using SPSS for Windows, version 25.0 (IBM Corp., Armonk, NY, USA).

Results

In total, 91 consecutive patients with peripheral lung lesions were included in the study and assigned to the one of the four groups (25, 20, 24 and 22 patients in groups 1–4, respectively). The median patient age was 70 years (interquartile range, 61–75 years), and 55 patients (60%) were men. The median mean diameter of the lung lesions was 36 mm (interquartile range, 25–50 mm). The median estimated effective dose of the standard CT scan was 3.1 mSv (2.7–3.7) and the effective doses of the ultra-low dose CT scans were significantly different among the four groups (median effective doses were 0.88, 0.34, 0.19, and 0.12 mSv for groups 1–4, respectively; P < 0.001) (Fig. 1).

Objective image noise

Ultra-low dose CT image noise was higher than image noise of standard dose CT and increased significantly from group 1 to group 4 (P < 0.001 for both radiologists 1 and 2) (Table 1).

|                      | Group 1 (n = 25) | Group 2 (n = 20) | Group 3 (n = 24) | Group 4 (n = 22) | P-value |
|----------------------|------------------|------------------|------------------|------------------|---------|
| **Radiologist 1**    |                  |                  |                  |                  |         |
| Image noise on SCT   | 19 (17–20)       | 19 (18–22)       | 19 (17–21)       | 19 (18–22)       | 0.690   |
| Image noise on ultra-LDCT | 25 (24–27)    | 29 (28–32)       | 33 (32–34)       | 38 (36–46)       | < 0.001 |
| Difference of image noise | 6 (4–8)          | 11 (9–13)        | 14 (12–17)       | 18 (17–22)       | < 0.001 |
| **Radiologist 2**    |                  |                  |                  |                  |         |
| Image noise on SCT   | 20 (17–21)       | 20 (17–21)       | 19 (18–21)       | 18 (17–22)       | 0.990   |
| Image noise on ultra-LDCT | 27 (23–29)    | 31 (28–34)       | 34 (32–38)       | 37 (34–41)       | < 0.001 |
| Difference of image noise | 8 (5–10)          | 12 (10–14)       | 16 (13–19)       | 18 (14–21)       | < 0.001 |

Table 1: Image noise of standard dose computed tomography (CT) and ultra-low dose CT

Image noise was assessed using the standard deviation of tracheal lumen attenuation by drawing a region of interest inside the trachea just proximal to the tracheal bifurcation area. SCT = standard dose CT, LDCT = low dose CT. Image noise is presented as median (interquartile range).

Bronchial wall thickness and wall-area ratio

The difference in peripheral airway wall thickness was significantly higher in group 4 than in other groups (P = 0.011) in the analysis of radiologist 2 (Table 2). In the analysis of radiologist 1, the median difference in bronchial wall thickness on ultra-low dose CT tended to be lower in groups 1–3 than in group 4; however, this difference was not statistically significant (0.5, 0.5, 0.5, and 0.9 mm for groups 1–4, respectively; P = 0.103). In the analysis of both radiologists 1 and 2, no significant differences in
wall area ratios were detected among the four ultra-low dose CT protocols (P = 0.058 and 0.375 for radiologists 1 and 2, respectively) (Table 3).

**Table 2**

| Radiologist 1 | Group 1 (n = 25) | Group 2 (n = 20) | Group 3 (n = 24) | Group 4 (n = 22) | P-value |
|---------------|------------------|------------------|------------------|------------------|---------|
| WT on SCT, mm | 1.8 (1.3–2.6)    | 1.6 (1.3–2.0)    | 1.5 (1.2–2.2)    | 1.7 (1.3–2.2)    | 0.649   |
| WT on ultra-LDCT, mm | 1.7 (1.4–2.3) | 1.7 (1.5–2.2) | 2.0 (1.7–2.4) | 2.5 (2.0–3.1) | 0.018   |
| Difference of WT | 0.5 (0.3–0.9) | 0.5 (0.3–0.7) | 0.5 (0.3–0.6) | 0.9 (0.5–1.4) | 0.103   |
| Radiologist 2 |                 |                  |                  |                  |         |
| WT on SCT, mm | 1.9 (1.3–2.6) | 1.7 (1.3–2.0) | 1.5 (1.2–2.1) | 1.6 (1.1–2.1) | 0.322   |
| WT on ultra-LDCT, mm | 1.7 (1.4–2.1) | 1.7 (1.4–1.9) | 1.9 (1.7–2.4) | 2.2 (1.7–3.1) | 0.009   |
| Difference of WT | 0.5 (0.2–1.0) | 0.5 (0.2–0.6) | 0.4 (0.2–0.5) | 0.8 (0.6–1.4) | 0.011   |

**Table 3**

Wall area ratio of the bronchus leading to the peripheral lung lesion

| Radiologist 1 | Group 1 (n = 25) | Group 2 (n = 20) | Group 3 (n = 24) | Group 4 (n = 22) | P-value |
|---------------|------------------|------------------|------------------|------------------|---------|
| WAR on SCT, % | 78 (73–84)       | 77 (76–81)       | 73 (71–79)       | 76 (73–80)       | 0.112   |
| WAR on ultra-LDCT, % | 79 (74–82) | 75 (73–80) | 77 (73–79) | 78 (73–82) | 0.505   |
| Difference of WAR | 5 (4–10) | 3 (1–5) | 4 (2–6) | 7 (3–11) | 0.058   |
| Radiologist 2 |                 |                  |                  |                  |         |
| WAR on SCT, % | 79 (75–84)       | 76 (75–81)       | 75 (71–78)       | 76 (73–81)       | 0.166   |
| WAR on ultra-LDCT, % | 79 (75–81) | 77 (73–80) | 77 (72–79) | 78 (73–81) | 0.553   |
| Difference of WAR | 5 (2–10) | 4 (2–10) | 6 (3–9) | 10 (4–15) | 0.375   |

**Bronchus sign**

In the analysis of radiologist 1, the bronchus sign of ultra-low dose CT in groups 1 and 2 completely corresponded with that of standard CT; however, the accuracies of the bronchus sign of ultra-low dose CT decreased to 83% and 73% in groups 3 and 4, respectively (P = 0.003) (Figs. 2 and 3). In the analysis of radiologist 2, the accuracies of the bronchus sign on ultra-low dose CT in groups 3 and 4 tended to be lower than those of groups 1 and 2; however, these differences were not statistically significant (96%, 100%, 88%, and 82% for groups 1–4, respectively; P = 0.143) (Table 4).
Table 4
Bronchus sign

| Accuracy of bronchus sign on ultra-LDCT | Group 1 (n = 25) | Group 2 (n = 20) | Group 3 (n = 24) | Group 4 (n = 22) | P-value |
|----------------------------------------|------------------|------------------|------------------|------------------|---------|
| Radiologist 1                          | 25/25 (100)      | 20/20 (100)      | 20/24 (83)       | 16/22 (73)       | 0.003   |
| Radiologist 2                          | 24/25 (96)       | 20/20 (100)      | 21/24 (88)       | 18/22 (82)       | 0.143   |
| Pulmonary physician 1                  | 25/25 (100)      | 20/20 (100)      | 23/24 (96)       | 18/22 (82)       | 0.017   |
| Pulmonary physician 2                  | 25/25 (100)      | 19/20 (95)       | 23/24 (96)       | 17/22 (77)       | 0.023   |

LDCT = low-dose computed tomography.

The accuracies of the bronchus sign on ultra-low dose CT in groups 1 and 2 were the same as those of standard dose CT in the analysis of pulmonary physician 1, whereas accuracies decreased to 96% and 82% in groups 3 and 4, respectively (P = 0.017). In the analysis of pulmonary physician 2, a significant difference in the accuracy of bronchus sign was detected on ultra-low dose CT among the four groups (P = 0.023). In particular, the bronchus sign of the ultra-low dose CT was significantly lower in group 4 than in groups 1–3 (100%, 95%, 96%, and 77% for groups 1–4, respectively).

Discussion

Low-dose CT is generally used to screen for lung cancer in high-risk individuals, using minimal ionizing radiation compared with a conventional chest CT scan [14, 15]. Thus far, no study has been performed regarding the feasibility of low-dose CT for peripheral bronchoscopy. This is the first report in which the optimal effective dose CT scan has been evaluated for peripheral bronchoscopy without assistance of novel navigation modalities. In addition, this investigation used ultra-low dose CT protocols with an estimated effective dose of < 1 mSv.

In the present study, the ultra-low dose CT protocols were designed to reduce the effective doses from group 1 to group 4. The results showed that the median estimated effective dose of ultra-low dose CT gradually decreased, from 0.88 mSv in group 1 to 0.12 mSv in group 4. Accordingly, the differences in image noise between standard dose and ultra-low dose CT, as measured by two radiologists, gradually increased from group 1 to group 4 (P < 0.001 for radiologists 1 and 2).

In general, reduction of the radiation dose inevitably increases image noise, which reduces image quality and spatial resolution. Therefore, bronchial walls are more likely to be found spread and their margins are more likely to appear unclear when a lower effective dose is used. Our study showed that
the visibility of the bronchial wall leading to the peripheral lung lesion decreased in group 4, compared with groups 1–3. Median differences in bronchial wall thickness between ultra-low dose and standard dose CT were 0.4–0.5 mm in groups 1–3. In addition, median differences in the wall area ratio of the bronchus leading to the peripheral lung lesions were only 3–6% in groups 1–3.

The presence of a bronchus sign is reportedly a reliable predictor of a successful peripheral bronchoscopy procedure [7, 16]. In the current study, the bronchus sign on ultra-low dose CT in groups 1 and 2 was well correlated with the bronchus sign of a standard dose CT scan. Our results suggested that both radiologists and pulmonary physicians could accurately identify the bronchus sign using reconstructed ultra-low dose CT scans.

This study had several limitations. First, it was designed to focus solely on the interpretation of ultra-low dose CT scans by radiologists and pulmonary physicians. Novel navigation modalities for bronchoscopy (e.g., virtual bronchoscopy navigation and electromagnetic navigation bronchoscopy) have been widely used to diagnose peripheral lung lesions under the guidance of artificial intelligence [17–19]. Therefore, bronchoscopy for peripheral lung lesions that depends solely on the interpretation of a CT scan by a doctor may be regarded as an outdated method. However, newer navigation modalities are not always 100% accurate [10, 20]. In addition, navigation systems (e.g., electromagnetic navigation bronchoscopy) are quite expensive; thus, they are not available at all hospitals. Second, although all study patients were randomly assigned to one of the four groups and the database was updated prospectively, the current study was performed retrospectively with a relatively small study population at a single center. We acknowledge that potential selection bias might have influenced the results of our study. A randomized prospective study with a large number of patients is therefore needed to confirm our findings.

Conclusion
Our results indicate that ultra-low dose CT with an effective dose of > 0.34 mSv (effective dose of group 2) is feasible for peripheral bronchoscopy.

Abbreviations
CT
computed tomography
ED
effective doses
LDCT
low dose computed tomography
SCT
standard dose computed tomography
SD
standard deviation
WAR
wall area ratio
WT
wall thickness

Declarations

Ethics approval and consent to participate
The Institutional Review Board of Pusan National University Hospital approved the study without the requirement to obtain informed consent from each study subject due to the retrospective nature of the study (approval no. H-2001-005-087).

Consent for publication
Not applicable

Availability of data and material
Please contact author for data requests.

Competing interests
The authors declare that they have no competing interests.

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Authors' contributions
JSE and YJJ are the guarantors and take responsibility for the content of this manuscript, including the data and analysis. JSE conceived the initial idea and the study design. GL, IK, HYS, and JR linked the data, contributed to data analysis and interpreted results. GL, JSE, and IK draft the manuscript and all
authors revised manuscript and approved the final manuscript.

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Figures
Comparison of the estimated effective ultra-low dose computed tomography (CT) dose among the four study groups. Significant differences were observed in the median estimated effective dose of ultra-low dose CT scans among the four groups (median estimated effective doses were 0.88, 0.34, 0.19, and 0.12 mSv for groups 1–4, respectively; \( P < 0.001 \)).

Figure 1
Figure 2

Comparison of the accuracy of bronchus sign on ultra-low dose computed tomography (CT) among the four study groups.
Figure 3

Airway analysis of a 63-year-old man with adenocarcinoma. The bronchus sign on an ultra-low dose computed tomography (CT) scan (group 2, 100 kVp, 15 mAs) (a) completely corresponded with the bronchus sign of the standard CT scan (b). The differences in wall thickness and wall-area ratio between the standard and ultra-low dose CT scans were 0.1 and 1.8, respectively.