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Influences of cardiac motion on computed tomography-guided biopsy of lung nodules located near the heart

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Abstract

Computed tomography (CT)-guided lung biopsy of nodules located near the heart may be associated with potential complications. To understand the influences of cardiac motion on lung parenchyma during biopsy, we processed the cardiac phase images of coronary CT angiography (CCTA) and noticed shifts in mediastinum lung margin (MLM) at different zones.

Thirty eight CCTA (27 men and 11 women) were retrospectively evaluated. Image processing was done with Fiji (an open source Java image processing program by Fiji contributors) using 10% to 90% phase images of CCTA; and tissue displacement (MLM shift) was shown on the resulting images.

The participants were 58.29 ± 9.87 years old; their height was 166.32 ± 7.57 cm while their weight was 74.18 ± 13.59 kg. The mean values of MLM shifts in Zones 1 to 9 ranged from 1.98 to 7.76 mm. Large MLM shifts were observed in the free wall of the left ventricle (LV). MLM shift of the upper free wall of the LV was 6.98 ± 1.99 mm and that of the lower free wall of the LV was 7.76 ± 3.26 mm. The largest MLM shift among all patients was 16.05 mm, found in the lower free wall of the LV. The age factor had a weak positive correlation with the wall of the pulmonary artery (r = 0.350, P = .031) and that of the right atrial appendage (r = 0.418, P = .009). In contrast, a weak negative correlation of age factor was observed with the lower free wall of the LV (r = −0.336, P = .039).

In conclusion, we suggest that physicians observe caution when performing lung biopsy if the distance between the lung lesion and the MLM is 1 to 2 cm. CT-guided lung biopsy should be avoided if the distance is <1 cm. Physicians should pay special attention to lung lesions near the LV.

Abbreviations: 2D = 2 dimensional, 3D = 3 dimensional, CCTA = coronary computed tomography angiography, CT = computed tomography, CTF = CT-fluoroscopy, LV = left ventricle, MLM = mediastinum lung margin, RAAPP = right atrial appendage, RV = right ventricle.

Keywords: cardiac injury, cardiac motion, cardiac phase image, complication, computed tomography-guided lung biopsy, coronary computed tomography angiography, hemopericardium

1. Introduction

Computed tomography (CT)-guided lung biopsy or aspiration is a common interventional procedure for histopathological diagnosis of lung lesions. However, it may cause pneumothorax, pulmonary hemorrhage, hemoptysis, hemothorax, and air embolism.[1–5] Cardiac complications, including cardiac tamponade, hemopericardium, pneumopericardium, and right ventricular perforation are rare, but have been reported before.[6–8]

During clinical practice, it is not uncommon to perform a lung biopsy or aspiration of a lung nodule located near the heart. As far as we know, there is no literature that discusses how the cardiac motion influences surrounding lung parenchyma, and the safe distance for performing lung biopsy of nodules located near the heart is unknown.

The main advantage of a CT-guided biopsy is that it can provide cross-sectional images; however, these images are 2 dimensional (2D) and static. It is not known if the heart is in systolic or diastolic phase in each scan during lung biopsy. Therefore, it causes inconvenience to the physicians in performing lung biopsies of nodules located near the heart.

Coronary computed tomography angiography (CCTA) uses an injection of iodine-rich contrast material and CT scanning to examine the coronary arteries with a breath-hold. In addition to the structures of the coronary arteries and heart chambers, CCTA also provides a series of phase images (10–90% of the cardiac cycle) for functional assessment of the heart. These cine-sequences show the motion throughout the whole cardiac cycle. Moreover, the wall motion and the functionality of the heart chambers can be analyzed. The purpose of this retrospective study is to use the CCTA images of the full cardiac cycle to

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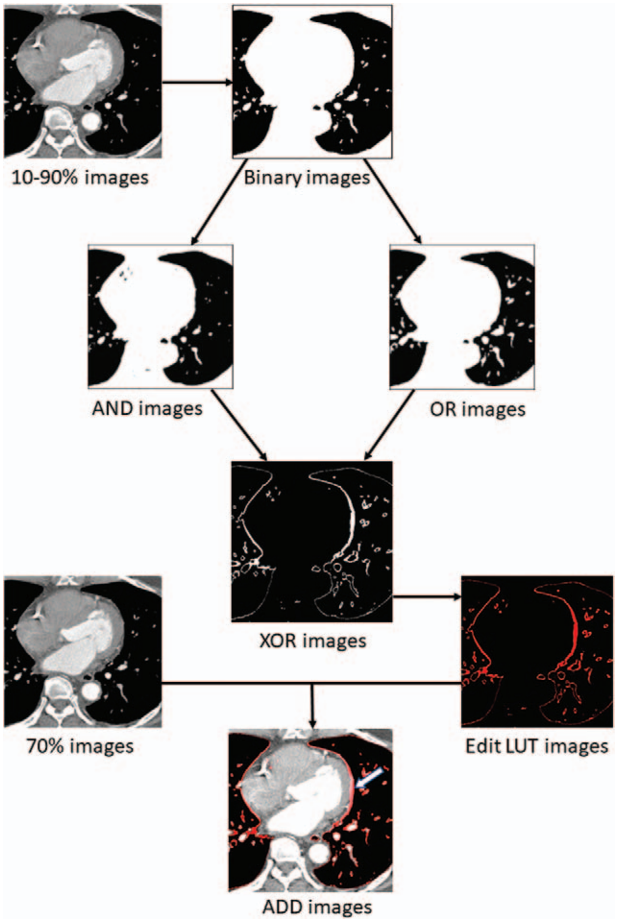

Figure 1. The flow chart of image processing.

evaluate how cardiac motion affects the surrounding lung parenchyma.

2. Methods

2.1. CCTA procedure

The study was approved by the Chang Gung Medical Foundation Institutional Review Boards. We retrospectively reviewed a total of 38 CCTA (27 men and 11 women) from June 2016 to June 2017. These participants underwent CCTA at the time of a coronary artery survey during a health checkup. These examinations were performed with a CT scanner (SOMATOM Sensation 64, Siemens Medical Solutions, Forchheim, Germany) with iodine contrast agent injections. The heart rates were controlled with propranolol, and one tablet of nitroglycerin was given sublingually before each scan. The scan field was from upper mediastinum to upper abdomen. Phase images were reconstructed between 10% and 90% of the RR-interval at 10% distance.

2.2. Image processing

Image processing was done with Fiji[9] (an open source Java image processing program by Fiji contributors) using the 10% to 90% phase images of CCTA. The flow chart of image processing is shown in Figure 1.

First, the 10% to 90% phase images were processed with *Process/Binary/Make Binary* command with the option *Black background* checked to get the clear margin between the mediastinum and lung field.

Second, we used *Process/Image Calculator* command and *AND* operation to process 10% to 90% binary images to get AND images.

In addition, 10% to 90% binary images were processed with *Process/Image Calculator* command and *OR* operation to get OR images.

Then, AND and OR images were combined with *Process/Image Calculator/XOR* operation to get XOR images.

Next, we used *Image/Color/Edit LUT* command to change the Final Entry of XOR images into red color (Red:255 Green:0 Blue:0) to get EDIT LUT images.

Finally, the 70% phase image was fused with EDIT LUT images by *Process/Image Calculator/Add* operation to get ADD images.

2.3. Segmentation

We segmented the MLM shifts into 9 zones (as shown in Fig. 2). The red areas in Figure 2 are the summation of tissue displacement in 10% to 90% phase images. The hila as well as the pulmonary vessels were not included in this study because we usually do not perform a CT-guided biopsy in this area. Nine zones are shown as follows:

Zone 1: the wall of the ascending aorta (AA)
Zone 2: the wall of the superior vena cava (SVC)
Zone 3: the wall of the pulmonary artery (PA)
Zone 4: the wall of left atrial appendage
Zone 5: the wall of the right atrial appendage (RAAPP)
Zone 6: the free wall of the upper left ventricle (LV) (from upper margin of the LV to the coronary sinus)
Zone 7: the free wall of the right ventricle (RV)

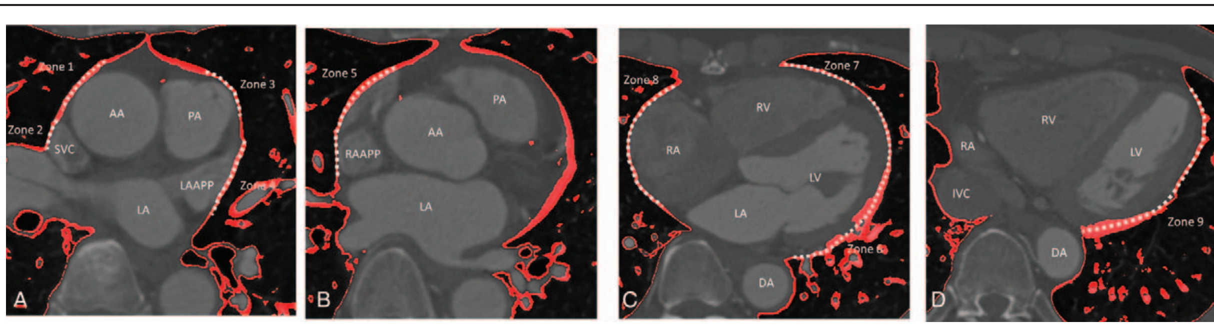

Figure 2. Segmentation of the MLM into (A) Zones 1, 2, 3, and 4; (B) Zone 5; (C) Zones 6, 7, and 8; and (D) Zone 9 (dotted white lines). Red areas indicate tissue displacement in 10% to 90% cardiac phase images.

Table 1

Summary of the characteristics of the participants.

Characteristics	Value
Sex (male)	27 (71%)
Age, y	58.29 ± 9.87*
Height, cm	166.32 ± 7.57*
Weight, kg	74.18 ± 13.59*

* Mean ± SD.

Table 2

Mediastinum lung margin shifts in different zones.

	Mean, mm	SD	95% CI
Zone 1	2.52	0.75	2.27–2.76
Zone 2	1.98	0.80	1.71–2.24
Zone 3	2.83	1.18	2.44–3.22
Zone 4	3.45	1.64	2.91–3.99
Zone 5	2.41	1.15	2.03–2.79
Zone 6	6.98	1.99	6.33–7.64
Zone 7	2.70	1.00	2.37–3.02
Zone 8	2.49	0.89	2.20–2.78
Zone 9	7.76	3.26	6.69–8.83

Zone 8: the wall of the right atrium
Zone 9: the free wall of the lower LV (from coronary sinus to lower margin of LV)

2.4. MLM shift measurement

We measured the largest MLM shifts of the regions closest to the lung in Zones 1 to 9. The measured distances of MLM shifts were perpendicular to the walls of the heart chamber and vessels.

2.5. Statistical analysis

Statistical analyses were performed using MedCalc for Windows, version 17.6 (MedCalc Software, Ostend, Belgium). Different zones of MLM shifts were examined by repeated measures analysis of variance. Sex, age, height, and weight were correlated with MLM shifts by Pearson correlation coefficient, with age, height, and weight having a normal distribution. $P < .05$ was considered statistically significant.

3. Results

The present study included 38 participants (27 men and 11 women) with CCTA. The participant characteristics are shown in

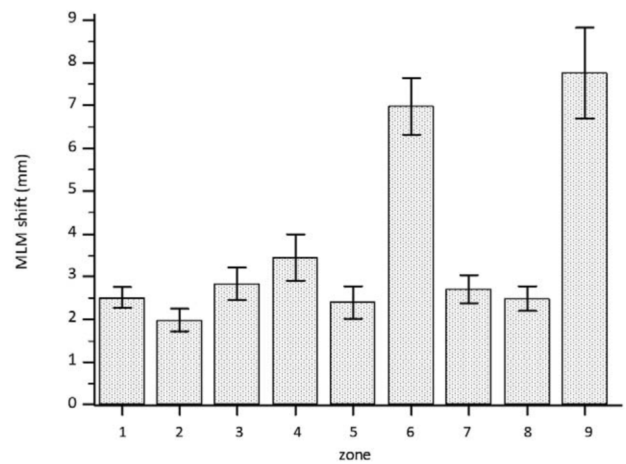

Figure 3. The MLM shifts in different zones.

Table 1. The age of the participants was 58.29 ± 9.87 years; their height was 166.32 ± 7.57 cm, while their weight was 74.18 ± 13.59 kg (Fig. 1).

The MLM shift data of all zones is shown in Table 2, and the plot of MLM shifts are shown in Figure 3. Large MLM shift was observed in the free wall of the LV (Zones 6 and 9). The MLM shift of Zone 6 was found to be 6.98 ± 1.99 mm, while that of Zone 9 was 7.76 ± 3.26 mm.

The pairwise comparison matrix of P values among different zones is shown in Table 3. There were no significant differences between Zones 6 and 9 (P = 1.000). However, there were significant differences in the remaining zones (all $P < .001$). The maximal MLM shift of all patients is 16.05 mm found in Zone 9.

The Pearson correlation coefficients between sex, age, height, weight, and mediastinum lung margin (MLM) shifts is shown in Table 4. The age factor was found to have a weak positive correlation with Zone 3 (r = 0.350, P = .031), Zone 5 (r = 0.418, P = .009), while a weak negative correlation was observed with Zone 9 (r = −0.336, P = .039). Otherwise, there was no significant correlation among MLM shifts and other factors.

4. Discussion

It is not uncommon to perform a lung biopsy of nodules near the heart, and potential complications may make this procedure stressful for physicians. To the best of our knowledge, there is no literature discussing the influences of cardiac motion on lung biopsy.

Table 3

Pairwise comparison matrix of *P* values among different zones.

	Zone 1	Zone 2	Zone 3	Zone 4	Zone 5	Zone 6	Zone 7	Zone 8	Zone 9
Zone 1	—								
Zone 2	.075	—							
Zone 3	1.000	**.007**	—						
Zone 4	**.013**	**<.001**	.940	—					
Zone 5	1.000	1.000	1.000	**.002**	—				
Zone 6	**<.001**	**<.001**	**<.001**	**<.001**	**<.001**	—			
Zone 7	1.000	**.014**	1.000	.290	1.000	**<.001**	—		
Zone 8	1.000	**.042**	1.000	**.005**	1.000	**<.001**	1.000	—	
Zone 9	**<.001**	**<.001**	**<.001**	**<.001**	**<.001**	1.000	**<.001**	**<.001**	—

Bold values are significant after sequential Bonferroni correction.

Table 4

Pearson correlation coefficients between sex, age, height, weight, and mediastinum lung margin shifts.

Zone	1	2	3	4	5	6	7	8	9
Sex	.848	.608	.717	.114	.648	.119	.262	.651	.058
Age	.132	.335	**.031***	.270	**.009**†	.555	.747	.064	**.039**‡
Height	.946	.351	.529	.142	.396	.425	.410	.889	.227
Weight	.190	.798	.398	.054	.941	.296	.444	.839	.296

Correlation coefficient *r*: *0.350, †0.418, ‡−0.336.
Bold *P* values are significant.

We used 10% to 90% phase images in this study because the whole cardiac phase image can cover all motions of the mediastinum. First, we transformed 10% to 90% phase images into Binary images. Different shapes of the mediastinum were summated to form the maximal area of the mediastinum in OR images. In AND images, only the overlapping areas were retained to obtain the minimal area of the mediastinum. Then, we were able to obtain tissue displacement by the *XOR* command.

The mean values of MLM shifts in Zones 1 to 9 ranged from 1.98 to 7.76 mm. Not surprisingly, we found that maximal MLM shifts were in the free wall of the LV. There were only 10 MLM shifts >10 mm in 342 zones of 38 participants, and all of these were in the free wall of the LV (Zones 6 and 9). The maximal shift in this study was 16.05 mm in the lower free wall of the LV (Zone 9), from which we could determine a rough estimation of the safe distance for performing a lung biopsy near the heart. According to these findings, we suggest that physicians should be careful when performing lung biopsy if the distance between the lung lesion and the MLM is 1 to 2 cm. CT-guided lung biopsy should not be performed if the distance is <1 cm.

In fact, MLM shifts can be influenced by both cardiac and respiratory motions. However, we always ask patients to hold their breath when we move the biopsy needle or perform the CT scan during a biopsy. Similarly, patients were asked to hold their breath during CCTA. The only influencing factor in both cases was the cardiac motion; thus, we chose CCTA in this study.

Fiechter et al reported that there is a significant increase in RV ejection fraction with advancing age.[10] Maceira et al showed that right atrial pump function increases with age.[11] These 2 observations may explain why the MLM shifts of the PA (Zone 3) and RAAPP (Zone 5) have a positive correlation with increasing age. However, there is controversy regarding LV ejection functions. According to our data, the MLM shift of the lower free wall of the LV (Zone 9) had a negative correlation with age. We assumed that the pump function or ejection fraction of LV decreases with increasing age.

MLM does not represent the real cardiac motion. It is the difference between expansion and contraction of the mediastinum and heart on axial images. The area of MLM shift is related to the cardiac motion as well as the angle between cardiac motion and the axial plane of a CT scan. If the angle increases, MLM shift magnifies (Fig. 4). However, we do not use the real cardiac motion in 3-dimensional (3D) reformation during lung biopsy. We only perform the biopsy step-by-step with the help of 2D axial images. Therefore, MLM shift is more meaningful than the real cardiac motion during a CT-guided biopsy.

The influences of upper mediastinal fat and epicardial fat pad were not quantified in the present study. However, both can provide protection of the heart and vessels during lung biopsy; examples are shown in Figure 5. The body mass indices (BMI) of 2 cases in our study were 21.86 and 35.20, respectively. The upper mediastinal fat can cover AA, PA, SVC, and RAAPP, and epicardial fat pad can insulate the lower free wall of the LV and

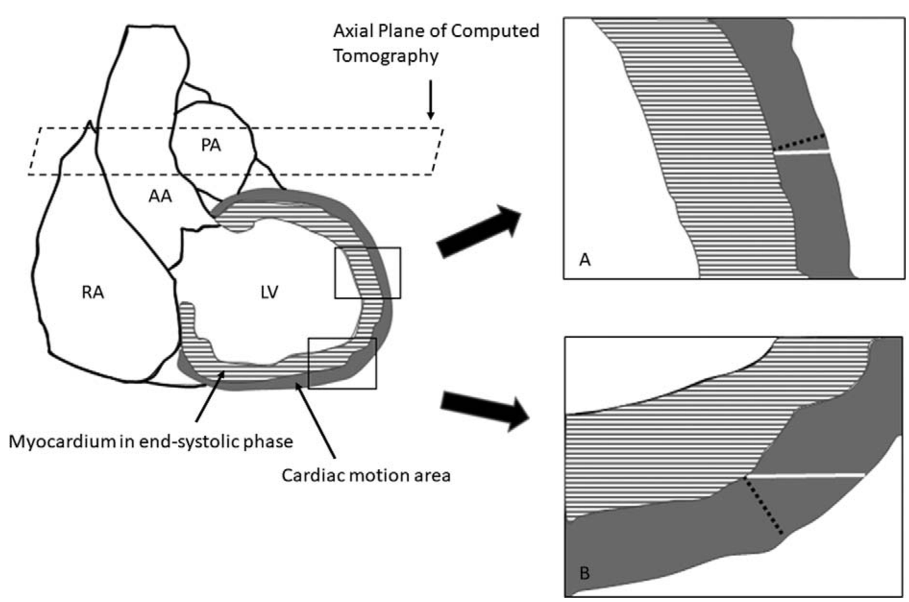

Figure 4. The magnification effect of MLM shifts based on different angles to the axial plane of CT. (A, B) The dotted black lines indicate the real cardiac motion of LV wall and the white lines indicate the MLM shift on CT axial images. While the angle of cardiac motion increases, the MLM shift also increases.

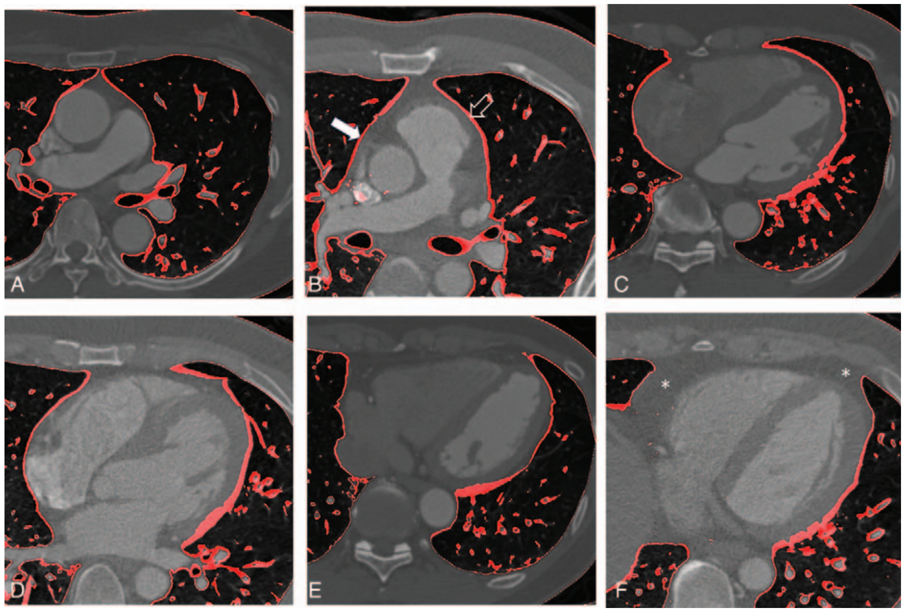

Figure 5. The distribution of upper mediastinal fat and epicardial fat pad in 2 participants. (A, C, E) A case with BMI = 21.86 has less mediastinal and pericardial fat. (B, D, F) Another case with BMI = 35.20. Thicker mediastinal fat covers ascending aorta (white arrow in 5B) and pulmonary artery (open arrow in 5B). Prominent pericardial fat covers left heart apex and right ventricle (* in 5F).

RV from the lung. However, there is little fat to cover the RA, the upper free wall of the LV, as well as the RV, even in a case with high BMI. Prominent upper mediastinal fat, also called mediastinal lipomatosis, is related to obesity, diabetes, steroid use, and Cushing syndrome.[12] The epicardial fat pad is reported to be correlated to insulin resistance, atrial fibrillation, and coronary artery disease.[13]

CT-fluoroscopy (CTF) is another choice for an interventional procedure. The benefits of CTF include real-time images and reduced procedure time and complication rate. However, the increase or decrease in radiation dose of CTF versus the conventional sequential CT-guided procedure is still controversial. CTF inevitably increases radiation exposure to an interventional radiologist and is not available in every hospital.[14–17] Ultrasonography-guided lung biopsy is an alternative procedure that can provide real-time images; however, it is usually applied in the biopsy of lesions near the chest wall or in the pleural space. Most lesions near the heart are difficult to visualize because of the depth, air interference, and lack of a good acoustic window.

However, there exist some limitations in this study. First, due to limited scan field on CCTA, part of the upper lung field could not be covered. However, the upper lung field is less influenced by cardiac motion. Second, there were no cases of associated pathology in our study, including cardiomegaly, pericardial effusion, arrhythmia, and constrictive pericarditis. Third, the lung hila were not included in this study because of structures with complicated anatomy consisting mainly of the major bronchi and the pulmonary veins and arteries; however, the interventional radiologist usually does not perform lung biopsy in this area. Fourth, we only analyzed the 2D axial CT images, not 3D reformation; however, 2D analysis, rather than 3D reformation, meets the requirements of a CT-guided biopsy. Fifth, the upper mediastinal fat and the epicardial fat pad were not quantified or analyzed. Finally, this study is only a concept study, and we did not mention how to angulate or plan the needle path.

In conclusion, we suggest that physicians observe caution when performing lung biopsy if the distance between the lung lesion and the MLM is 1 to 2 cm. CT-guided lung biopsy should be avoided if the distance is <1 cm. Physicians should pay special attention to lung lesions near the LV. Understanding MLM shifts not only helps in lowering the potential risks of cardiac complications but also aids in the planning for a lung biopsy.

References

[1] Chandra S, Agarwal D, Singh V, et al. Pneumothorax: a common complication of CT-guided transthoracic needle lung biopsy. BMJ Case Rep 2009;2009:
[2] Thomas R, Thangakunam B, Cherian RA, et al. Cerebral air embolism complicating CT-guided trans-thoracic needle biopsy of the lung. Clin Respir J 2011;5:e1–3.
[3] Yuan DM, Lü YL, Yao YW, et al. Diagnostic efficiency and complication rate of CT-guided lung biopsy: a single center experience of the procedures conducted over a 10-year period. Chin Med J (Engl) 2011;124:3227–31.
[4] Tai R, Dunne RM, Trotman-Dickenson B, et al. Frequency and severity of pulmonary hemorrhage in patients undergoing percutaneous CT-guided transthoracic lung biopsy: single-institution experience of 1175 cases. Radiology 2016;279:287–96.
[5] Heerink WJ, de Bock GH, de Jonge GJ, et al. Complication rates of CT-guided transthoracic lung biopsy: meta-analysis. Eur Radiol 2017;27:138–48.
[6] Kucharczyk W, Weisbrod GL, Cooper JD, et al. Cardiac tamponade as a complication of thin-needle aspiration lung biopsy. Chest 1982;82:120–1.
[7] Shevland JE. Right ventricular perforation: a rare complication of percutaneous lung biopsy. J Thorac Imaging 1991;6:85–6.
[8] Mitchell MJ, Montgomery M, Reiter CG, et al. Pericardial tamponade following CT-guided lung biopsy. Cardiovasc Intervent Radiol 2008;31 (suppl 2):S227–30.
[9] Schindelin J, Arganda-Carreras I, Frise E, et al. Fiji: an open-source platform for biological-image analysis. Nat Methods 2012;9:676–82.
[10] Fiechter M, Fuchs TA, Gebhard C, et al. Age-related normal structural and functional ventricular values in cardiac function assessed by magnetic resonance. BMC Med Imaging 2013;13:6.
[11] Maceira AM, Cosin-Sales J, Prasad SK, et al. Characterization of left and right atrial function in healthy volunteers by cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2016;18:64.

[12] Singh A. Mediastinal lipomatosis with dyslipidemia: cause of dyspnea. J Assoc Physicians India 2016;64:88–9.
[13] Toth PP. Epicardial steatosis, insulin resistance, and coronary artery disease. Heart Fail Clin 2012;8:671–8.
[14] Carlson SK, Bender CE, Classic KL, et al. Benefits and safety of CT fluoroscopy in interventional radiologic procedures. Radiology 2001; 219:515–20.
[15] Kim GR, Hur J, Lee SM, et al. CT fluoroscopy-guided lung biopsy versus conventional CT-guided lung biopsy: a prospective controlled study to assess radiation doses and diagnostic performance. Eur Radiol 2011; 21:232–9.
[16] Prosch H, Stadler A, Schilling M, et al. CT fluoroscopy-guided vs. multislice CT biopsy mode-guided lung biopsies: accuracy, complications and radiation dose. Eur J Radiol 2012;81:1029–33.
[17] Yamao Y, Yamakado K, Takaki H, et al. CT-fluoroscopy in chest interventional radiology: sliding scale of imaging parameters based on radiation exposure dose and factors increasing radiation exposure dose. Clin Radiol 2013;68:162–6.