Computed tomography-guided cutting needle biopsy for lung nodules

A comparative study between low-dose and standard dose protocols

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Abstract

We aim to compare the diagnostic accuracy, safety, and radiation exposure between low-dose and standard-dose computed tomography (CT)-guided cutting needle biopsy (CNB) for lung nodules.

From January 2016 to August 2017, all consecutive patients admitted with lung nodule underwent low-dose or standard-dose CTguided CNB procedure in our center. Diagnostic accuracy and radiation dose were compared.

A total of 67 and 69 patients who underwent low-dose and standard-dose CT-guided CNB procedure were included in this study. Each patient underwent CT-guided CNB for 1 nodule. The technical success rates were 100% in both groups. The sensitivity, specificity, and overall diagnostic accuracy were 97.7%, 100%, and 98.5% for low-dose group and 91.5%, 100%, and 94.2% for standard-dose group. There was no significant difference in diagnostic accuracy (P=.380) between 2 groups. Pneumothorax was found in 8 and 15 patients in the low-dose and standard-dose groups, respectively (11.9% vs 21.7%, P=.127). Hemoptysis was found in 10 and 10 patients in the low-dose and standard-dose groups, respectively (14.9% vs 14.5%, P=.943). The mean dose-length product was 38.2 ± 17.2 mGy-cm and 375.3 ± 115.7 mGy-cm in the low-dose and standard-dose groups, respectively (P<.001). The mean effective dose was 0.5 ± 0.2 mSv and 5.3 ± 1.6 mSv in the low-dose and standard-dose groups, respectively (P<.001).

Low-dose CT-guided CNB of lung nodules significantly decreased radiation dose compared with standard-dose CT. The lowdose protocol could provide similar diagnostic accuracy and safety as standard-dose CT-guided CNB for lung nodules.

Abbreviations: CNB = cutting needle biopsy, CT = computed tomography, DLP = dose-length product, ED = effective dose. **Keywords:** biopsy, computed tomography, low-dose, lung nodule

1. Introduction

Computed tomography (CT) is a common diagnostic approach that delivers radiation to patients. The increased cumulative radiation dose has the potential to increase cancer risk, especially

Editor: Nesreen E. Morsy.

Program of 2019 Xuzhou clinical technique research (2109GG002).

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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How to cite this article: Zhang HM, Huo XB, Wang HL, Zhang X, Fu YF. Computed tomography-guided cutting needle biopsy for lung nodules: a comparative study between low-dose and standard dose protocols. Medicine 2021;100:3(e24001).

Received: 10 June 2020 / Received in final form: 29 September 2020 / Accepted: 25 November 2020

http://dx.doi.org/10.1097/MD.00000000024001

for the children.^[1–5] In order to reduce the CT-induced radiation, low-dose CT protocol has been developed.

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CT-guided cutting needle biopsy (CNB) is widely used in diagnosis of lung nodules with an overall diagnostic accuracy of 93% to 97%.^[6–8] Compared with the large lung lesions, CT-guided CNB for lung nodules might require more scanning to adjust the position of needle tip. Therefore, it might expose the patients to more radiation.

At present, low-dose protocol is widely used in CT-guided interventions because these procedures usually require repeat scans, which causes more radiation exposure to the patients.^[3–5] However, in most previous studies regarding of low-dose CT-guided lung biopsy, they included both lung masses and lung nodules.^[3,4] The multiple disease types usually caused the potential bias. A study which focuses on unique disease type is required. At present, the study which focused on low-dose CT-guided CNB for lung nodules is still lack.

The purpose of this retrospective study was to compare the diagnostic accuracy, safety, and radiation exposure between low-dose and standard-dose CT-guided CNB for lung nodules.

2. Materials and methods

This retrospective, single-center study was approved by the Institutional Review Board of Binzhou People's Hospital. Requirement for participant written consent was waived owing to the retrospective nature of the study design.

2.1. Patients

From January 2016 to August 2017, consecutive patients with lung nodules underwent CT-guided CNB procedure in our center. From January to December 2016, the standard-dose CT was used for CNB procedure. From January to August 2017, the low-dose CT was used.

The decision to conduct the CNB for these lung nodules was based on chest CT examination results and on the principles of diagnostic multidisciplinary evaluation.^[9]

Patients fulfilling the following criteria were included in the study: (a) a definite lung nodule on CT; (b) lesion size \leq 30 mm and \geq 5 mm; (c) solid nodule (solid component >80% of the total nodule); and (d) no definitive pathological diagnosis. The exclusion criteria were a lesion that had shrunk in size or a lesion with a stable size for 2 years or any lesion without a definite final diagnosis or patients with severe dysfunction of the heart, lungs, kidneys, or coagulation.

2.2. Scanning parameters

The CT instrument was a 16-slice CT device (Philips, Cleveland, Ohio). The same scanning parameters of both low-dose and standard-dose groups included: tube voltage=120kV; thickness = 2 mm; collimation= 16×0.75 mm; pitch=1.063; rotation time = 0.5 s; FOV=350 mm. The tube current in low-dose and standard-dose groups was 15 mA/s and 150 mA/s, respectively.

2.3. CT-guided CNB procedure

All procedures were performed by an experienced radiologist having more than 10 years of experience on CT-guided interventions. Depending on the location of the nodule, patients were placed into either a supine, prone, or decubitus position. Puncture pathways were selected based on the preoperative CT results. The needle was first used to puncture the lung parenchyma, after which an additional CT scan was used to adjust the needle tip location and to move it as appropriate. Once contact was made between the needle tip and nodule, a sample was obtained from the nodule. Samples were placed into 10% formaldehyde until pathological examination.

2.4. Subjective imaging quality evaluation

Two experienced thoracic radiologists evaluated the quality of images independently. The quality was evaluated based on 4 levels: Level A - the nodule and needle tip were readily visible; Level B - the nodule and needle tip were adequately visible; Level C - the nodule and needle tip were only somewhat visible; and Level D - the nodule and needle tip were not visible.^[10] Quality levels of C and D were not suitable for CT-guided CNB.

2.5. Biopsy based diagnoses

Biopsy diagnoses were assigned to one of 4 categories:

- 1. malignant lesions;
- 2. suspected malignant lesions;
- 3. specific benign lesions; or
- 4. non-specific benign lesions.

Specific benign lesions included both benign tumors and infection caused by known microorganisms.^[8] Non-specific benign lesions had benign inflammatory or fibrotic pathology, which could not lead to a definitive diagnosis.^[8]

2.6. Final diagnoses

Final diagnoses were confirmed in one of the following ways^[8] either surgery, or the biopsy based diagnosis demonstrated a malignant or a specific benign lesion it could be considered as the final diagnosis. If a suspected malignant or a non-specific benign lesion was obtained on CT-guided biopsy, follow-up CT could help to make the final diagnosis. If the lesion decreased by $\geq 20\%$ in size or remained stable for 2 years, the final diagnosis would be benign lesion. If a patient underwent anticancer treatment or was lost of follow-up, the lesion was considered as undiagnosed.

2.7. Endpoints and definitions

The primary endpoint was overall diagnostic accuracy. The secondary endpoints included radiation dose and complications.

Procedure time was defined as the time interval from the first localized CT scan to the last CT scan after biopsy.^[11] The actual time of radiation was calculated by multiplying the time of each CT scan by the number of CT scans. The total dose exposure was directly demonstrated by the CT device and it was presented with dose-length product (DLP). When calculating the possible dose exposure for each patient, we used the effective dose (ED). ED was calculated by multiplying the total DLP by the conversion factor (0.014 mSv/mGy-cm).^[11]

2.8. Statistical analysis

The statistical analysis was performed using SPSS 16.0 (SPSS Inc., Chicago, IL). Continuous variables were analyzed with *t*-tests. Categorical data were analyzed with χ^2 tests. The predictors of complication were determined using univariate and multivariate logistic regression analyses. The covariates incorporated into the multivariate analysis included variables with a value of P < .1 in the univariate analysis. Kappa analysis was performed to assess the inter-observer agreement of image quality. A *P* value <.05 was considered statistically significant.

3. Results

3.1. Baseline data

From January 2016 to August 2017, 69 patients underwent lowdose and 70 patients underwent standard-dose CT-guided CNB procedure, respectively. Each patient underwent CT-guided CNB for 1 nodule. The technical success rates of CNB procedure were comparable between low-dose and standard-dose groups, with the value of 100% in both groups. For the final analysis, 2 patients were excluded from the low-dose group and 1 from the standard-dose group because the final diagnosis of the lung nodule could not be made in these patients (Fig. 1, Table 1). The mean duration of procedure (11.8 ± 4.6 minutes vs 12.3 ± 5.5 minutes, P = .612) and actual time of radiation (16.9 ± 6.3 second vs 16.4 ± 4.2 second, P = .649) were both comparable between 2 groups.

3.2. Diagnostic accuracy

In low-dose group (Fig. 2), the CNB-based diagnoses included malignant lesions (n=42), specific benign lesions (n=7), and non-specific benign lesions (n=18). The 7 specific benign lesions included tuberculosis (n=4), hamartoma (n=2), and mycotic infection (n=1). The final diagnoses included malignant (n=43) and benign lesions (n=24). The CNB-based malignant (n=42)



and specific benign (n=7) lesions were directly accepted as the final diagnose. Among the 18 CNB-based non-specific benign lesions, 17 lesions were confirmed as benign lesions according to follow-up (n=16) or surgical (n=1) results, and 1 lesion was confirmed as malignancy by a second time CNB because this patient had distant bone metastasis. Therefore, the sensitivity, specificity, and overall diagnostic accuracy were 97.7%, 100%, and 98.5%, respectively.

In standard-dose group (Fig. 3), the CNB-based diagnoses included malignant lesions (n=42), suspected malignant lesion (n=1), specific benign lesions (n=42), and non-specific benign lesions (n=22). The 4 specific benign lesions were all tuberculosis. The final diagnoses included malignant (n=47) and benign lesions (n=22). The CNB-based malignant (n=42) and specific benign (n=4) lesions were directly accepted as the final diagnose. The 1 CNB-based suspected malignant lesion was confirmed as lung cancer after surgery. Among the 22 CNB-based non-specific benign lesions, 17 lesions were confirmed as benign lesions according to follow-up (n=16) or surgical (n=1) results, while 1

lesion was confirmed as tuberculosis by a repeat CNB, and 4 lesions were confirmed as malignancy by surgery (n=3) or a repeat CNB (n=1). Therefore, the sensitivity, specificity, and overall diagnostic accuracy were 91.5%, 100%, and 94.2%, respectively.

There was no significant difference in diagnostic accuracy between 2 groups (Table 2). This result indicated that low-dose CT did not decrease the diagnostic accuracy of CT-guided CNB for lung nodules. After univariate and multivariate logistic regression analyses, the predictors of diagnostic failure included elder age (P=.049) and occurrence of pneumothorax (P=.027, Table 3).

3.3. Quality of images

In low-dose group, 54 (80.6%) and 13 (19.4%) images can be evaluated as quality level A and B, respectively. In standard-dose group, all images can be evaluated as quality level A. A significant higher rate of quality level A images was achieved in standard-dose group (100% vs 80.6%, P < .001). Neither group had any

Table 1

Baseline data and procedure details of the included patients.

	Low-dose group (n=67)	Standard-dose group (n=69)	Р
Normal data			
Age (y)	63.4 ± 9.8	60.2 ± 12.6	.102
Gender (male/female)	44/23	41/28	.452
Smoking history	28	29	.978
Tumor history	9	7	.552
BMI (kg/m ²)	23.2±3.3	23.0 ± 3.2	.800
Imaging feature			
Diameter (mm) 24.6±6.2 Side (aff/right) 22/25		23.6 ± 6.8	.374
Side (left/right)	32/35	32/37	.872
Lobe (upper/non-upper)	29/38	29/40	.882
Biopsy procedure			
Lesion-pleura distance (mm) 16.4 ± 14.6		20.3 ± 17.3	.167
Needle- pleura angle (degrees) 66.0 ± 18.9		66.6 ± 17.0	.855
Prone/Supine/Decubitus 34/25/8		30/32/7	.564
Number of needle paths 2.1 ± 0.9		2.0 ± 0.8	.412
Number of samples	1.8 ± 0.7	1.6 ± 0.6	.077
Duration of procedure (min)	11.8 ± 4.6	12.3 ± 5.5	.612
Actual time of radiation (s)	16.9 ± 6.3	16.4 ± 4.2	.649
Complications			
Pneumothorax 8		15	.127
Hemoptysis	10	10	.943
Radiation dose			
DLP (mGy-cm)	38.2±17.2	375.3±115.7	<.001
ED (mSv)	0.5 ± 0.2	5.3 ± 1.6	<.001

BMI = body mass index, DLP = dose-length product, ED = effective dose.

level C or D images. The inter-observer agreements were very good in both groups (Kappa value = 0.861 and 1.000, respectively).

3.4. Complications

Pneumothorax was found in 8 and 15 patients in the low-dose and standard-dose groups, respectively. The incident rates of



Figure 2. Low-dose CT-guided CNB for lung nodule.

pneumothorax were comparable between low-dose and standard-dose groups (11.9% vs 21.7%, P=.127). Five patients (low-dose group: 2; standard-dose group: 3) required chest tube insertion. Hemoptysis was found in 10 and 10 patients in the lowdose and standard-dose groups, respectively. The incident rates of hemoptysis were comparable between low-dose and standarddose groups (14.9% vs 14.5%, P=.943).

After univariate and multivariate logistic regression analyses, the predictors of pneumothorax included decubitus position (P=.006), longer lesion-pleura distance (P=.002), and more needle paths (P=.024, Table 4).

3.5. Radiation dose

The mean DLP was significant lower in low-dose group than that in standard-dose group $(38.2 \pm 17.2 \text{ mGy-cm vs } 375.3 \pm 115.7 \text{ mGy-cm}, P < .001)$. The mean ED was significant lower in lowdose group than that in standard-dose group $(0.5 \pm 0.2 \text{ mSv vs} 5.3 \pm 1.6 \text{ mSv}, P < .001)$.

4. Discussion

This study compared the feasibility, diagnostic performance, and radiation exposure between low-dose and standard-dose CT-guided CNB for lung nodules. The technical successful rate was 100% in both groups, although the quality level A images were found significantly more in the standard-dose group. Li et al^[11] performed low-dose CT-guided CNB for 140 lung nodules and the technical successful rate was 97.1%, which is comparable to that in this present study. These findings indicate that low-dose CT does not influence the procedure of CT-guided CNB.

Diagnostic accuracy was the major endpoint of CT-guided CNB for lung nodules. We found similar sensitivity (97.7% vs



Figure 3. Standard-dose CT-guided CNB for lung nodule.

91.5%, P=.413) and overall diagnostic accuracy (98.5% vs 94.2%, P=.380) between low-dose and standard-dose groups. A recent randomized controlled trial also revealed that low-dose CT-guided lung biopsy can yield comparable sensitivity (91.8% vs 89.6%, P=.616) and overall diagnostic accuracy (94.6% vs 92.4%, P=.482) to standard-dose CT guidance.^[12] The sensitivity and overall diagnostic accuracy in this study are comparable to those (93.8% and 95.4%) in a previous study regarding of low-dose CT-guided CNB for lung nodules.^[11]

In addition, we found that the risk factors of diagnostic failure included elder age and occurrence of pneumothorax. The pneumothorax was also proven as a risk factor of diagnostic failure of lung biopsy in the recent randomized controlled trial.^[12] The elder patients might have a poor endurance of the CNB procedure. Therefore, both the elder age and pneumothorax might influence the procedure and reduce the quantity and quality of the samples.

The procedure-related complications, either pneumothorax (11.9% vs 21.7%, P=.127) or hemoptysis (14.9% vs 14.5%, P=.943), were similar between low-dose and standard-dose groups. Previous studies also found that low-dose CT did not decrease the safety of the lung biopsy procedure.^[10–12] The incident rates of pneumothorax and hemoptysis in our low-dose group were comparable to those rates (4.6%–21.4% for pneumothorax and 7.1%–13.6% for hemoptysis, respectively) in previous studies.^[10–12] The risk factors of pneumothorax included decubitus position, longer lesion-pleura distance, and

Table 2

The comparison	of technical	success,	biopsy-based	diagnoses,
final diagnoses, a	and diagnosti	ic perforn	nance between	2 groups.

	Low-dose group	Standard-dose group	P value
Technical success rate	100%	100%	-
Biopsy pathological diagnosis			.534
Malignancy	42	42	
Suspected malignancy	0	1	
Specific benign	7	4	
Non-specific benign	18	22	
Final diagnosis			.628
Malignancy	43	47	
Benign	24	22	
Diagnostic performance			
Sensitivity	42/43 (97.7%)	43/47 (91.5%)	.413
Specificity	24/24 (100%)	22/22 (100%)	-
Overall accuracy	66/67 (98.5%)	65/69 (94.2%)	.380

more needle paths. Similar factors were reported in the previous studies.^[6,8] Kim et al^[12] had performed CT fluoroscopy-guided lung biopsy to reduce the procedure-related complications because it provides real-time monitor. However, it brings radiation exposure to both patients and operators.^[13]

In this study, we got approximately 90% reduction in the patients radiation exposure in the low-dose CT group compared to those in the standard dose group, without negatively affecting the procedure time, diagnostic accuracy and complication rate. The low-dose protocol could also prolong the life of the tube. Some previous studies have reported that the low-dose CT decreased the radiation dose by 53% to 95%.^[10,14] These results might be attributed to the different CT parameters in those and the present studies.

Some researchers performed magnetic resonance (MR)-guided CNB for lung nodules without any radiation;^[15] however, the cost for MR-guided lung biopsy is very high and the duration of MR scanning is quite long and it might lead to a higher incidence of complications.

This study has certain limitations. First, the study was retrospective in nature and future prospective randomized trials are required to confirm the results. Second, the sample size was small. Third, no unified criteria were followed for the number of samples required for recruitment in the study. Instead, the samples were obtained in accordance with our experience. Although the number of samples was not associated with diagnostic accuracy, it might have led to bias in our findings. Fourth, the actual radiation dose to exposure was hard to assess. However, in most previous studies, the authors also compared the DLP and ED when assessing the radiation dose.^[3,10,11] Last, the classification of 3 nodules (low-dose group: 2; standard-dose group: 1) as non-diagnostic lesions might have caused selective bias and influenced the diagnostic performance.

Table 3

Predictors of overall diagnostic accuracy.								
Variables	Univariate analysis			Multivariate analysis				
	Hazard ratio	95% CI	P value	Hazard ratio	95% CI	P value		
Age	1.131	1.005-1.274	0.042	1.145	1.000-1.311	.049		
Pneumothorax	8.325	1.307–53.023	0.025	9.072	1.283–64.157	.027		

CI = confidential interval.

Table 4

Predictors of pneumothorax.

Variables	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% CI	P value	Hazard ratio	95% CI	P value
Body position						
Prone	1			1		
Supine	1.329	0.450-3.930	.607	0.898	0.265-3.046	.863
Decubitus	9.306	2.581-33.559	.001	7.731	1.815-32.933	.006
Lesion-pleura distance	1.060	1.028-1.092	.001	1.057	1.021-1.094	.002
Number of needle paths	1.601	0.970-2.641	.066	1.903	1.088-3.330	.024

CI = confidential interval.

5. Conclusion

In conclusion, this study revealed that low-dose CT-guided CNB of lung nodules significantly decreased radiation dose compared with standard-dose CT. The low-dose protocol could provide similar diagnostic accuracy and safety as standard-dose CT-guided CNB for lung nodules. As such, low-dose CT-guided CNB may be recommended for patients with lung nodules. However, further prospective randomized trials are still required.

Author contributions

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