



Study of the Efficacy of PET/CT in Lung Aspiration Biopsy and Factors Associated with False-Negative Results

폐 흡인 조직검사 시 PET/CT의 임상적 유용성 및 위음성 결과와 관련 있는 인자

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Purpose: We compared the outcomes of percutaneous transthoracic needle aspiration biopsy (PCNA) of lung masses in cases with and without prior positron emission tomography/computed tomography (PET/CT) information, and investigated the factors associated with false-negative pathological results.

Materials and Methods: From a total of 291 patients, 161 underwent PCNA without prior PET/CT imaging, while 130 underwent PET/CT before PCNA. Clinical characteristics, procedural variables, pathological results, and diagnostic success rates were compared between the 2 groups. Among patients with initial negative (non-specific benign) PCNA results, the radiological findings of these groups were compared to evaluate the predictors of false-negative lesions.

Results: No significant difference was found in the clinical characteristics, procedural characteristics, and pathological results of the 2 groups, nor was the diagnostic rate significantly different between them ($p = 0.818$). Among patients with initial negative PCNA results, radiological characteristics were similar in both the groups. In multivariate analysis, the presence of necrosis ($p = 0.005$) and ground-glass opacity (GGO) ($p = 0.011$) were the significant characteristics that indicated an increased probability of initial false-negative results in PCNA.

Conclusion: Routine PET/CT did not have any additional benefit in patients undergoing PCNA of lung masses. The presence of necrosis or GGO could indicate an increased probability of false-negative pathological results.

Index terms

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INTRODUCTION

With the increasing use of chest computed tomography (CT) for lung cancer screening, the frequency of detecting indeterminate peripheral lung nodules has increased, which leads to pathologic confirmation of suspicious lung lesions (1). Several procedure options including bronchoscopy and surgical resection exist, but still, a considerable proportion of patients undergo percutaneous transthoracic needle aspiration biopsy (PCNA).

Meanwhile, positron emission tomography (PET) using fluorine-18 fluorodeoxyglucose (¹⁸F-FDG) is valuable for assessment of suspicious malignant lesions (2). Due to its ability to

detect increased metabolism, PET/CT may reveal malignancy in its very early stages, even before morphological changes are evident on conventional images. Furthermore, PET/CT offers visualization of the viable and biologically aggressive area within a heterogeneous tumor with multiple subregions of cancer cells, necrosis, inflammatory cells, and fibrosis (3). Accordingly, several studies have suggested that PET/CT guidance allows high diagnostic success of percutaneous biopsies for metabolically active lesions (4, 5). Some studies have reported that success rates can be improved and information from a prior PET/CT scan can be used to direct the needle tip to the most metabolically active portion of a heterogeneous mass (6-8). However,

er, the additional clinical value of routine PET/CT in patients undergoing lung PCNA remains to be established. Thus, the purpose of our study was to determine whether the addition of PET/CT augmented the outcomes of PCNA of lung masses and to investigate factors associated with the false-negative pathologic results.

MATERIALS AND METHODS

Our Institutional Review Board approved this study (E-2015 084) and informed consent was waived for reviewing the patients' medical records.

Patient Enrollment

From March 2013 to December 2014, 307 patients who underwent PCNA were enrolled in a lung PCNA database. After enrollment, patient information was retrospectively reviewed from the electronic medical records. As a tertiary referral hospital with a comprehensive cancer center, patients were referred to the radiology department for pathologic confirmation of an abnormal lung lesion under the clinical suspicion made by an internal medicine doctor or thoracic surgeon based on clinical information, laboratory blood tests, and chest CT scans. At the time of referral, a thoracic radiologist decided whether PCNA was feasible after reviewing the contrast-enhanced chest CT scans. Sixteen patients with lesions located adjacent to critical anatomical structures such as central vessels or large bronchi, lesions with minimal solid component with prominent air bronchograms which were considered difficult to avoid by needle pass, and patients with severe respiratory compromise or non-cooperated position which precluded PCNA were excluded. Ultimately, 291 patients were included in this study. Patients underwent the lung mass evaluation process, and according to the individual situation and under the clinical decision made by the referring physician, at the time of PCNA, patients were classified into two subgroups according to the presence of PET/CT scans prior to PCNA: 1) 161 patients did not have PET/CT scans before PCNA and 2) 130 patients underwent PET/CT within 3 weeks prior to PCNA.

Procedure

Needle trajectory planning and positioning was performed

in consideration of chest radiography and contrast-enhanced chest CT images. When the patient had PET/CT scans available before PCNA, the thoracic radiologist performing the procedure reviewed the PET/CT images prior to PCNA. When the mass showed heterogeneous metabolic uptake, the area with highest uptake was chosen as an adequate localization lesion for PCNA.

All procedures were performed by a single thoracic radiologist who had 5 years of PCNA experience under fluoroscopy or CT guidance. Patients were positioned in the supine or prone position, depending on the lesion location. After identification of the target lesion, the puncture area was cleaned with antiseptic solution, followed by subcutaneous injection of local anesthetic. Next, a 20-gauge Westcott biopsy needle (Argon Medical Devices, Athens, TX, USA) was inserted by freehand technique and specimens were placed in 10% neutral buffered formalin solution (BBC biochemical, Mt. Vernon, WA, USA).

Pathologic Analysis and Final Diagnosis

For all patients, the aspiration biopsy needle was placed into the target lesion and cells or lung tissues were present in the specimen. Two lung pathologists reviewed the PCNA specimens in consensus. Apart from definite benign or malignant lesions, negative pathologic results indicated "non-specific benign," which included inflammatory cells or fibrosis, suggesting the presence of benign pathological features, but not enough to make a specific diagnosis, and no evidence of malignancy. For negative (non-specific benign) pathologic results, the final diagnosis was determined by review of pathologic results of a subsequent biopsy/surgery or evaluation of follow-up images. False-negative cases were those in which malignancy was identified by pathologic confirmation from a subsequent repeated biopsy or surgical resection. True-negative cases were those in which the lesion showed complete resolution, stability at serial CT scans for at least 2 years follow-up, or proved to be benign at surgical resection (9, 10).

Radiologic Interpretation and PET

Contrast-enhanced chest CT images which were obtained less than 3 weeks prior to PCNA were reviewed by two independent chest radiologists (with 7 and 16 years of experience in chest CT interpretation, respectively) who were blinded to the

pathologic results and who did not perform any of the PCNA procedures. CT scans were obtained using the following scanners: a 16-detector scanner (Sensation 16, Siemens Healthcare, Erlangen, Germany), a 64-detector scanner (Definition AS plus, Siemens Healthcare, Forchheim, Germany; or Discovery 750, GE Healthcare, Waukesha, WI, USA), or a dual-source CT scanner (Definition, Siemens Healthcare). Images of the whole thorax were acquired using the following CT parameters: 120 kVp, 150–200 mA, section thickness = 5 mm or less; tube rotation = 0.5 s; and detector collimation = 1.25 mm or 0.625 mm.

Radiologic variables were combined atelectasis with the mass, presence of necrosis (including cavitation) within the mass, presence of consolidation (including pneumonia) abutting to the mass, the presence of ground-glass opacity (GGO) in the mass, and the presence of pleural effusion. Atelectasis was defined as increased attenuation with reduced volume adjacent to the mass associated with abnormal displacement of fissures, bronchi, or vessels (11). Low attenuated area within the mass or nodule were defined as necrosis (11). Consolidation appeared as a homogeneous increase in pulmonary parenchymal attenuation that obscures the margins of vessels and airway walls with or without air bronchograms (11). GGO was defined as an area of hazy increased opacity of the lung, with preservation of bronchial and vascular margins (11). In cases of discrepancy, final decisions were made through consensus of the radiologists.

For patients who underwent ^{18}F -FDG PET/CT before PCNA, imaging was performed with a combined PET/CT scanner (Gemini, Philips, Milpitas, CA, USA), consisting of a dedicated germanium oxyorthosilicate, a full-ring PET scanner, and a dual-slice helical CT scanner. Images were obtained at 60 minutes after administering 3.7 MBq/kg ^{18}F -FDG intravenously, from the skull base to the proximal thighs. Low-dose CT (30 mAs, 120 kVp) without any contrast material was performed and PET data were reconstructed iteratively with attenuation correction, and reoriented in axial, sagittal, and coronal slices.

Statistical Analyses

Comparison of the clinical characteristics, procedure related variables, and pathologic results between the two groups with and without PET/CT was performed through chi-square or Fisher's exact test for categorical variables and the independent *t*-test or Mann-Whitney U test for continuous variables. To investi-

gate any features associated with initial negative results, radiological variables were compared between the two groups with and without PET/CT using chi-square or Fisher's exact test.

Next, patients with initial negative results were further grouped into true-negative and false-negative subgroups. Comparison between the true-negative and false-negative lesions was performed through chi-square or Fisher's exact test for categorical variables and the independent *t*-test or Mann-Whitney U test for continuous variables. After univariate analysis, multivariate logistic regression analysis was performed to reveal independent predictors of a false-negative result. Input variables were those with $p < 0.1$ at univariate analysis.

All statistical analyses were performed using SPSS for Windows software (version 18.0; SPSS Inc., Chicago, IL, USA), and $p < 0.05$ indicated statistical significance.

RESULTS

Comparison between Groups with and without PET/CT

Clinical characteristics, procedure characteristics, and pathologic results of patients who underwent PCNA between those with and without PET/CT scans are shown in Table 1. None of the variables were statistically significant between the 2 groups. Diagnostic success rates were not different [$p = 0.818$; 88.5% (115/130) and 87.6% (141/161) for patients with and without PET/CT scans, respectively] between the 2 groups.

Among 130 patients with PET/CT scans, 4 patients had scans performed at outside hospitals, thus the maximum standardized uptake value (SUVmax) could not be measured for these patients. For 126 patients with PET/CT scans, mean SUVmax was 8.95 ± 5.14 (range, 1.2–24.9).

Next, for patients with initial negative PCNA results ($n = 35$), the radiological characteristics were compared between the two groups with and without PET/CT (Table 2). None of the radiological characteristics were statistically significant between the 2 groups.

Comparison between True-Negative and False-Negative Lesions

For patients with initial negative pathologic results, the final diagnosis was confirmed by subsequent surgery or repeated biopsy in 29 lesions, and by follow-up CT in 6 patients.

Among 35 lesions with initial negative pathologic reports, 20 lesions (57.1%) were ultimately diagnosed as malignancy, indicating false-negative results. Among 20 false-negative lesions, adenocarcinoma was the most common pathology result (11 patients; 55%), followed by squamous cell carcinoma (5 patients; 25%), malignant mesothelioma (2 patients; 10%), large cell carcinoma (1 patient; 5%), and thymic carcinoma (1 patient; 5%). Remaining 15 lesions (42.9%) were ultimately diag-

nosed as benign, indicating true-negative results. Among 15 true-negative lesions, 6 patients (40%) demonstrated improvement or stable CT exams during 2-year follow up, 7 patients (46.7%) were diagnosed as tuberculosis, and remaining 2 patients (13.3%) were confirmed as chronic inflammation. Table 3 shows comparison of characteristics between false-negative and true-negative lesions. Regarding the clinical and procedure characteristics, there were no significant differences in age, sex, lesion size, location, types of imaging guidance, and position between the false-negative lesions and true-negative lesions (all $p > 0.05$). Among radiological characteristics, presence of necrosis ($p = 0.011$) was significantly higher in the false-negative group. Furthermore, the presence of PET was higher in the true-negative group and approached statistical significance ($p = 0.076$).

Table 1. Clinical Characteristics, Procedure Characteristics, and Pathologic Results of Patients who Underwent Percutaneous Transthoracic Needle Aspiration Biopsy between Those with and without PET Scans

	No PET (n = 161)	PET (n = 130)	p-Value
Clinical characteristics			
Age (years) ± SD	64.9 ± 11.5	65.7 ± 9.1	0.506
Sex			0.639
Male	108	87	
Female	53	43	
Procedure characteristics			
Lesion size (cm) ± SD	4.7 ± 2.6	4.7 ± 2.5	0.973
Lesion location			0.084
Upper	104	71	
Lower	57	59	
Types of imaging guidance			0.498
CT	89	77	
Fluoroscopy	72	53	
Position			0.400
Supine	66	47	
Prone	95	83	
Pathologic results			
Adequate diagnosis	141	115	0.818
Benign	18	15	
Malignant	123	100	
Negative	20	15	

CT = computed tomography, PET = positron emission tomography, SD = standard deviation

Table 2. Comparison of Radiological Characteristics among Patients with Initial Negative Percutaneous Transthoracic Needle Aspiration Biopsy Results

Radiological Characteristics	No PET (n = 20)	PET (n = 15)	p-Value
Presence of atelectasis	2	2	0.999
Presence of necrosis	11	7	0.625
Presence of consolidation adjacent to lesion	6	4	0.999
Presence of pleural effusion	4	3	0.999
Presence of GGO	6	2	0.419

GGO = ground-glass opacity, PET = positron emission tomography

Table 3. Comparison of Characteristics between False-Negative and True-Negative Lesions

	True Negative (n = 15)	False Negative (n = 20)	p-Value
Clinical characteristics			
Age (years) ± SD	62.9 ± 13.0	63.0 ± 10.6	0.973
Sex			0.680
Male	13	16	
Female	2	4	
Presence of PET			0.076
PET	9	6	
No PET	6	14	
Radiological characteristics			
Presence of atelectasis	1	3	0.443
Presence of necrosis	4	14	0.011*
Presence of consolidation adjacent to lesion	3	7	0.331
Presence of pleural effusion	2	5	0.393
Presence of GGO	1	7	0.101
Procedure characteristics			
Lesion size (cm) ± SD	3.0 ± 1.6	3.9 ± 2.8	0.262
Lesion location			0.324
Upper	10	10	
Lower	5	10	
Types of imaging guidance			0.163
CT	11	10	
Fluoroscopy	4	10	
Position			0.693
Supine	7	8	
Prone	8	12	

*Significant p-value.

CT = computed tomography, GGO = ground-glass opacity, PET = positron emission tomography, SD = standard deviation

Table 4. Results of Univariate and Multivariate Logistic Regression Analysis for Predictors of False-Negative Lesions at Percutaneous Trans-thoracic Needle Aspiration Biopsy

	Univariate			Multivariate		
	OR	95% CI	p-Value	OR	95% CI	p-Value
Age (year)	1.001	0.944–1.062	0.972			
Sex (male)	0.615	0.097–3.908	0.607			
Presence of PET (+)	0.286	0.070–1.168	0.081	0.275	0.040–1.863	0.186
Lesion size (cm)	1.238	0.841–1.821	0.279			
Lesion location (lower)	2.000	0.500–7.997	0.327			
Types of imaging guidance (CT)	0.364	0.086–1.537	0.169			
Position (prone)	1.312	0.339–5.076	0.694			
Presence of atelectasis (+)	2.471	0.231–26.459	0.455			
Presence of necrosis (+)	6.417	1.444–28.511	0.015	34.514	2.958–402.699	0.005*
Presence of consolidation (+)	2.154	0.451–10.287	0.336			
Presence of pleural effusion (+)	2.167	0.358–13.110	0.400			
Presence of GGO (+)	7.538	0.813–69.906	0.075	51.812	2.435–1102.354	0.011*

OR associated with age and lesion size is that the increase in hazard is associated with a 1-year increase in age and 1-cm increase in size, respectively.

*Significant p-value.

CI = confidence interval, CT = computed tomography, GGO = ground-glass opacity, OR = odds ratio, PET = positron emission tomography

Prediction of False-Negative Lesions

Table 4 shows results of univariate and multivariate logistic regression analysis for predictors of false-negative lesions at PCNA. Presence of PET, presence of necrosis, and presence of GGO were included in the multivariate analysis. Results of multivariate analysis demonstrate that the presence of necrosis ($p = 0.005$) and presence of GGO ($p = 0.011$) were significant variables associated with false-negative pathologic results.

DISCUSSION

Our study results can be summarized to two major findings: 1) Routine PET/CT did not have additional diagnostic benefit for patients undergoing PCNA of lung masses and 2) the presence of necrosis or GGO may indicate an increased probability of false-negative pathologic results.

PET/CT has become an essential tool which reflects the metabolic characteristics of tissue and is currently widely used for initial staging, therapy monitoring, and outcome prediction of lung cancer (12-15). Several studies have shown that application of nuclear medicine imaging could improve the image-guided biopsy success rate by directly placing the needle to the hypermetabolic area of a lesion, further obviating subsequent invasive procedures and complication risks (5, 7, 16, 17). However, those studies enrolled only a small number of cases or exhibited selection bias by performing biopsy in patients with lesions

which demonstrated metabolic abnormality on PET without definite CT abnormality (4, 5, 8). In the present study, the diagnostic success rates were similar between the 2 groups with and without PET/CT, thus, routine PET/CT did not have statistically significant benefit for patients undergoing PCNA of lung masses. We believe this is due to the conspicuity of lung lesions as the background lung parenchyma itself serves as an excellent tissue contrast for abnormal lesions, thus the advantage and necessity of additional metabolic information is decreased. Similarly, according to another study, the value of PET/CT was highest in skeletal lesions of which biopsy may be hampered due to low lesion visibility (7). Hence, although PET/CT exhibits excellent per-person performance for detecting malignancies and lung cancer staging, the routine use of PET/CT imaging for all patients undergoing lung biopsies warrants reconsideration.

Despite high diagnostic accuracies for malignancies with PCNA, non-specific benign results from lung biopsies still remain a key clinical problem (18, 19). In this study, two radiological factors of necrosis and GGO were significantly associated with false-negative lesions. First, regarding necrosis, sampling errors due to central necrosis of larger lung masses has also been previously reported (20, 21). Spatial heterogeneity including necrosis within a mass is related to various factors such as outgrowth of tumor blood supply, hypoxia, and regional differences (22-24). In this study, although the radiologist did not obtain specimens from the necrotic areas identified on contrast-

enhanced CT images, the CT resolution may not be enough for identification of minor necrosis. In this aspect, PET/CT may be useful for identifying viable cancer tissue with higher accuracy than CT alone in patients with lung cancer (25, 26). Furthermore, Hua et al. (27) also suggested that nuclear imaging information is especially valuable in patients with large, heterogeneous masses.

Next, the presence of GGO was a significant factor for false-negative pathologic results. In the spectrum of lung adenocarcinomas, GGO frequently reflects the pathologically non-invasive component representing lepidic growth (28-30). In a previous study regarding PCNA of pulmonary GGO lesions, the diagnostic accuracy was significantly influenced by the GGO component, of which pure GGO lesions demonstrated lower accuracy than mixed GGO lesions with a solid portion (31). Other investigators have also reported underestimation of subsolid lesions by biopsy compared to surgical pathology (32, 33). Our study results showed similar aspects as aforementioned studies because GGO lesions are difficult to diagnose via aspiration due to the low cellularity of the lesions (31). According to a study by Suh et al. (34), higher SUVmax, larger lesion size, and subsolid lesions were useful predictors for malignancy in pulmonary lesions with nonspecific benign cytology results at PCNA. Our study results were similar regarding GGO lesions, but the SUVmax value and lesion size were not different between true-negative lesions and false-negative lesions.

Notably, the presence of PET was higher in the true-negative group and approached statistical significance ($p = 0.076$). In a larger study group, we may presume that the presence of PET may be higher in the true-negative group with statistical significance compared to the false-negative group. Therefore, according to this study, although the routine use of PET/CT for all patients undergoing lung biopsies cannot be justified, PET/CT may perhaps be helpful in patients with initial negative results. This issue should be evaluated in future studies with larger study groups.

According to large database lung cancer screening studies, the American College of Radiology has recently introduced a Lung Imaging Reporting and Data System (LungRADS): a nodule discriminating standard based on screening chest CT which divides nodules according to size and content, and guides further management (35). In particular, nodules with the highest probability of malignancy are assigned to Category 4B, includ-

ing large or growing solid and part-solid nodules. However, further management of Category 4B nodules is rather vague, suggesting chest CT with or without contrast, PET/CT, and/or tissue sampling. In other words, there is no established consensus at present as to whether to undergo PET/CT before tissue sampling or tissue sampling without PET/CT. Although CT provides the most important anatomic imaging, CT alone may have limitations, whereas PET provides metabolic imaging. Such two imaging modalities show different biological aspects of the same disease process, offering collaborative insights into the diagnosis of lung lesions. However, in the clinical setting, routine PET/CT may not be necessary for all patients, based on our results. For example, here is a patient with a lung mass demonstrating homogeneous enhancement without any necrosis or GGO, and is considered highly suspicious for lung cancer. Although additional PET/CT might make the possibility of lung cancer even higher, the need to obtain a lung biopsy would obviate additional diagnostic metabolic imaging for this patient in the clinical setting. Furthermore, if the mass demonstrated homogeneous uptake on PET/CT, then in this case, PET/CT would make no difference for this patient (Fig. 1). In our opinion, PET/CT may be of advantage for identifying the most hypermetabolic area of specific lung lesions which have an increased probability for false-negative pathologic results such as involving necrosis or GGO (Fig. 2). In this context, our results add to literature in assisting the selection of candidates who would benefit best from additional metabolic information prior to lung biopsy.

Our study has several limitations. First, although prospectively enrolled, patients were from a single institution, thus, the outcomes may be representative of one tertiary institution. In addition, we only investigated the impact of the presence and absence of PET/CT prior to lung PCNA. Subgroups including whether metabolic information changed the site of biopsy or had high versus low SUVmax could have been a more sophisticated study design offering more valuable information concerning the role of PET/CT prior to lung PCNA. Therefore, regarding the present study only, it may be difficult to make a conclusive statement about routine PET/CT prior to lung PNCA, but hopefully, our results will inspire further investigations. Second, our study is limited by lack of patient randomization with respect to the presence of PET/CT. Instead, the presence of PET/CT was primarily determined by the clinical evaluation flow of the refer-

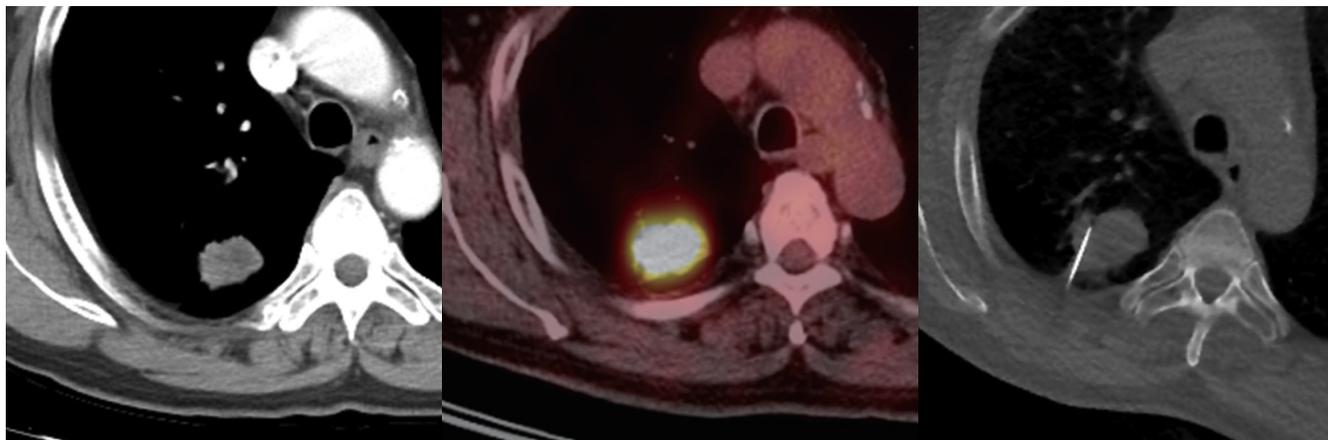


Fig. 1. A 62-year-old male with a mass located at the right upper lobe posterior segment. PET/CT scan shows homogeneous uptake (SUVmax of 14.3), with no definite additional benefit before percutaneous transthoracic needle aspiration biopsy. Pathologic results revealed squamous cell carcinoma.

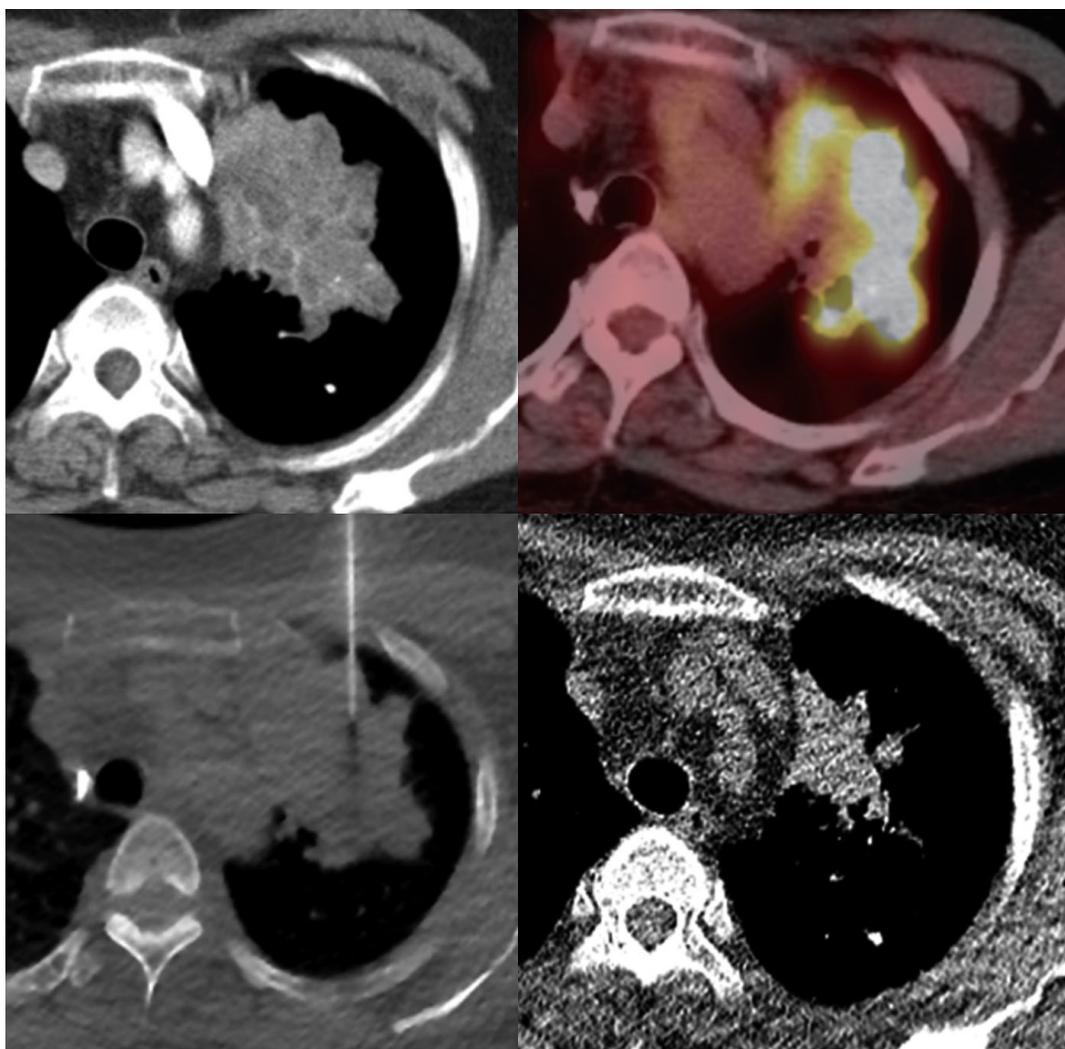


Fig. 2. A 61-year-old female with a heterogeneous, lobulated mass with suspicious necrosis, located at the left upper lobe. PET/CT scan demonstrates high metabolic uptake at the peripheral area of the lesion (SUVmax of 16.7). Thus, the biopsy needle tip is placed at the lesion with highest metabolic uptake. Pathologic results revealed pulmonary tuberculosis. Low-dose chest CT scan (right lower quadrant) after 6 months of anti-tuberculous treatment shows interval decrease of the lesion.

ring physician based on the nature of the lesion, clinical status of the patient including risk of lung cancer, comorbidities, insurance coverage, and economical status. Thus, potential confounding factors and selection bias based on the preference of the referring physician could have existed. However, as mentioned above, this study was performed in the clinical setting and represented everyday imaging algorithms and problems. Finally, the diagnostic accuracy of the present study is somewhat lower than those reported from previous large database studies (10, 21). However, methodology of obtaining lung tissue is different, as those studies used larger cutting needles with coaxial technique or used CT fluoroscopy. Our diagnostic rates are similar to a large database study using CT-guided fine-needle aspiration biopsy of lung lesions (6). In addition, a proportion of patients underwent PCNA using fluoroscopy. Fluoroscopy likely makes it more difficult targeting portions of lesions due to lesser ability to spatially localize as compared with CT.

In conclusion, diagnostic rates are similar regardless of the information from PET/CT scans, thus, a routine PET/CT scan prior to PCNA is not mandatory. Necrosis or GGO were factors significantly associated with false-negative pathologic results, and perhaps, metabolic information from PET/CT may be of some advantage for lesions with these characteristics.

REFERENCES

1. National Lung Screening Trial Research Team, Church TR, Black WC, Aberle DR, Berg CD, Clingan KL, et al. Results of initial low-dose computed tomographic screening for lung cancer. *N Engl J Med* 2013;368:1980-1991
2. Hoffman JM, Gambhir SS. Molecular imaging: the vision and opportunity for radiology in the future. *Radiology* 2007; 244:39-47
3. Bomanji JB, Costa DC, Ell PJ. Clinical role of positron emission tomography in oncology. *Lancet Oncol* 2001;2:157-164
4. Cornelis F, Silk M, Schoder H, Takaki H, Durack JC, Erinjeri JP, et al. Performance of intra-procedural 18-fluorodeoxyglucose PET/CT-guided biopsies for lesions suspected of malignancy but poorly visualized with other modalities. *Eur J Nucl Med Mol Imaging* 2014;41:2265-2272
5. Klaeser B, Mueller MD, Schmid RA, Guevara C, Krause T, Wiskirchen J. PET-CT-guided interventions in the management of FDG-positive lesions in patients suffering from solid malignancies: initial experiences. *Eur Radiol* 2009;19: 1780-1785
6. Guralnik L, Rozenberg R, Frenkel A, Israel O, Keidar Z. Metabolic PET/CT-guided lung lesion biopsies: impact on diagnostic accuracy and rate of sampling error. *J Nucl Med* 2015; 56:518-522
7. Purandare NC, Kulkarni AV, Kulkarni SS, Roy D, Agrawal A, Shah S, et al. 18F-FDG PET/CT-directed biopsy: does it offer incremental benefit? *Nucl Med Commun* 2013;34:203-210
8. Stattaus J, Kuehl H, Ladd S, Schroeder T, Antoch G, Baba HA, et al. CT-guided biopsy of small liver lesions: visibility, artifacts, and corresponding diagnostic accuracy. *Cardiovasc Intervent Radiol* 2007;30:928-935
9. Gelbman BD, Cham MD, Kim W, Libby DM, Smith JP, Port JL, et al. Radiographic and clinical characterization of false negative results from CT-guided needle biopsies of lung nodules. *J Thorac Oncol* 2012;7:815-820
10. Hiraki T, Mimura H, Gobara H, Iguchi T, Fujiwara H, Sakurai J, et al. CT fluoroscopy-guided biopsy of 1,000 pulmonary lesions performed with 20-gauge coaxial cutting needles: diagnostic yield and risk factors for diagnostic failure. *Chest* 2009;136:1612-1617
11. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Müller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. *Radiology* 2008;246:697-722
12. de Geus-Oei LF, van der Heijden HF, Visser EP, Hermsen R, van Hoorn BA, Timmer-Bonte JN, et al. Chemotherapy response evaluation with 18F-FDG PET in patients with non-small cell lung cancer. *J Nucl Med* 2007;48:1592-1598
13. Hicks RJ, Kalff V, MacManus MP, Ware RE, Hogg A, McKenzie AF, et al. (18)F-FDG PET provides high-impact and powerful prognostic stratification in staging newly diagnosed non-small cell lung cancer. *J Nucl Med* 2001;42:1596-1604
14. Takeuchi S, Khiewvan B, Fox PS, Swisher SG, Rohren EM, Bassett RL Jr, et al. Impact of initial PET/CT staging in terms of clinical stage, management plan, and prognosis in 592 patients with non-small-cell lung cancer. *Eur J Nucl Med Mol Imaging* 2014;41:906-914
15. Truong MT, Viswanathan C, Erasmus JJ. Positron emission tomography/computed tomography in lung cancer staging, prognosis, and assessment of therapeutic response. *J*

- Thorac Imaging* 2011;26:132-146
16. Cerci JJ, Pereira Neto CC, Krauzer C, Sakamoto DG, Vitola JV. The impact of coaxial core biopsy guided by FDG PET/CT in oncological patients. *Eur J Nucl Med Mol Imaging* 2013; 40:98-103
 17. Klaeser B, Wiskirchen J, Wartenberg J, Weitzel T, Schmid RA, Mueller MD, et al. PET/CT-guided biopsies of metabolically active bone lesions: applications and clinical impact. *Eur J Nucl Med Mol Imaging* 2010;37:2027-2036
 18. Kim JI, Park CM, Kim H, Lee JH, Goo JM. Non-specific benign pathological results on transthoracic core-needle biopsy: how to differentiate false-negatives? *Eur Radiol* 2017;27: 3888-3895
 19. Minot DM, Gilman EA, Aubry MC, Voss JS, Van Epps SG, Tuve DJ, et al. An investigation into false-negative transthoracic fine needle aspiration and core biopsy specimens. *Diagn Cytopathol* 2014;42:1063-1068
 20. Tsukada H, Satou T, Iwashima A, Souma T. Diagnostic accuracy of CT-guided automated needle biopsy of lung nodules. *AJR Am J Roentgenol* 2000;175:239-243
 21. Yeow KM, Tsay PK, Cheung YC, Lui KW, Pan KT, Chou AS. Factors affecting diagnostic accuracy of CT-guided coaxial cutting needle lung biopsy: retrospective analysis of 631 procedures. *J Vasc Interv Radiol* 2003;14:581-588.
 22. Heppner GH. Tumor heterogeneity. *Cancer Res* 1984;44: 2259-2265
 23. Miles KA, Williams RE. Warburg revisited: imaging tumour blood flow and metabolism. *Cancer Imaging* 2008;8:81-86
 24. Swanton C. Intratumor heterogeneity: evolution through space and time. *Cancer Res* 2012;72:4875-4882
 25. Bar-Shalom R, Yefremov N, Guralnik L, Gaitini D, Frenkel A, Kuten A, et al. Clinical performance of PET/CT in evaluation of cancer: additional value for diagnostic imaging and patient management. *J Nucl Med* 2003;44:1200-1209
 26. Kubota K. From tumor biology to clinical PET: a review of positron emission tomography (PET) in oncology. *Ann Nucl Med* 2001;15:471-486
 27. Hua Q, Zhu X, Zhang L, Zhao Y, Tang P, Ni J. Initial experience with real-time hybrid single-photon emission computed tomography/computed tomography-guided percutaneous transthoracic needle biopsy. *Nucl Med Commun* 2017; 38:556-560
 28. Aoki T, Tomoda Y, Watanabe H, Nakata H, Kasai T, Hashimoto H, et al. Peripheral lung adenocarcinoma: correlation of thin-section CT findings with histologic prognostic factors and survival. *Radiology* 2001;220:803-809
 29. Lee HY, Lee KS. Ground-glass opacity nodules: histopathology, imaging evaluation, and clinical implications. *J Thorac Imaging* 2011;26:106-118
 30. Song YS, Park CM. Pulmonary subsolid nodules: an overview & management guidelines. *J Korean Soc Radiol* 2018;78: 309-320
 31. Hur J, Lee HJ, Nam JE, Kim YJ, Kim TH, Choe KO, et al. Diagnostic accuracy of CT fluoroscopy-guided needle aspiration biopsy of ground-glass opacity pulmonary lesions. *AJR Am J Roentgenol* 2009;192:629-634
 32. Kim TJ, Lee JH, Lee CT, Jheon SH, Sung SW, Chung JH, et al. Diagnostic accuracy of CT-guided core biopsy of ground-glass opacity pulmonary lesions. *AJR Am J Roentgenol* 2008; 190:234-239
 33. Lu CH, Hsiao CH, Chang YC, Lee JM, Shih JY, Wu LA, et al. Percutaneous computed tomography-guided coaxial core biopsy for small pulmonary lesions with ground-glass attenuation. *J Thorac Oncol* 2012;7:143-150
 34. Suh YJ, Lee JH, Hur J, Hong SR, Im DJ, Kim YJ, et al. Predictors of false-negative results from percutaneous transthoracic fine-needle aspiration biopsy: an observational study from a retrospective cohort. *Yonsei Med J* 2016;57:1243-1251
 35. American College of Radiology. Lung-RADS™ version 1.0 assessment categories. Available at: https://www.acr.org/-/media/ACR/Files/RADS/Lung-RADS/LungRADS_AssessmentCategories.pdf?la=en. Published Apr 28, 2014. Accessed Aug 25, 2017

폐 흡인 조직검사 시 PET/CT의 임상적 유용성 및 위음성 결과와 관련 있는 인자

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목적: 우리는 폐종양의 경피적 침흡입생검을 시행했을 때 positron emission tomography/computed tomography (이하 PET/CT) 정보의 유무가 결과에 끼치는 영향을 비교하고, 조직학적 위음성에 영향을 끼치는 인자를 조사하였다.

대상과 방법: 총 291명의 환자중에서 161명은 PET/CT 없이 경피적 침흡입생검을 시행하였고, 130명은 PET/CT를 시행 후 경피적 침흡입생검을 시행하였다. 두 군 사이에서의 임상 특징, 시술 변수, 병리 결과 그리고 진단 성공률을 비교하였다. 병리 결과가 초기 음성(비특이적 양성)이 나온 환자에서 두 군 사이의 영상소견을 비교하고, 위음성의 예측 인자를 평가하였다.

결과: PET/CT의 유무에 따른 임상 특징, 시술 변수, 그리고 병리 결과는 차이가 없었다. 두 군 사이의 진단 성공률도 의미 있는 차이가 없었다($p = 0.818$). 병리 결과가 초기 음성인 환자에서, 두 군 사이의 영상 소견도 차이가 없었다. 다변량 분석에서 괴사의 존재($p = 0.005$)와 간유리음영($p = 0.011$)은 의미 있는 변수였으며, 경피적 침흡입생검시 초기 위음성률을 증가시켰다.

결론: 폐종양의 경피적 침흡입생검을 시행하는 환자에서 관습적인 PET/CT는 추가적 이득이 없었다. 괴사 및 간유리음영의 존재는 병리 결과의 위음성률을 증가시켰다.

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