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Characterization of Pulmonary Lesions with Low F-18 FDG Uptake Using Double Phase F-18 FDG PET/CT: Comparison of Visual and Quantitative Analyses

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Background of the present study was to assess the usefulness of double phase positron emission tomography/computed tomography (PET/CT) to differentiate malignant from benign pulmonary lesions with low fluorine-18 fluorodeoxyglucose (F-18 FDG) uptake.

Of 218 consecutive patients who underwent double phase F-18 FDG PET/CT to evaluate pulmonary lesions found on CT, we retrospectively analyzed 30 who had focal pulmonary lesions with an SUV of <2.5. All patients underwent PET/CT of the thorax at two time points: scan 1 at 60 min and scan 2 at 120 min after the intravenous injection of 2.5 MBq F-18 FDG. The F-18 FDG PET/CT images were analyzed visually and quantitatively.

Of 30 evaluated nodules, 13 (43%) proved to be malignant and 17 (57%) benign. The SUV_{max1} (maximal SUV of early image), SUV_{max2} (maximal SUV of delayed image), $\%\Delta SUV_{max}$ (percent change of maximal SUV), CR_1 (contrast ratio of early image), and CR_2 (contrast ratio of delayed image) of malignant pulmonary lesion were significantly higher than those of benign. However, %ΔCR (percent change of contrast ratio) revealed no statistical differences. Among the quantitative indices, SUV_{max1}, SUV_{max2}, and CR_2 were superior to the visual analysis for differentiation of malignant from benign pulmonary lesions. The SUV_{max1}, SUV_{max2}, and $\%\Delta SUV_{max}$ were superior to %ΔCR for differentiation of malignant from benign pulmonary lesions.

Based on the presented results, the quantitative indices except %ΔCR were higher in malignant nodules than benign pulmonary nodules. However, the diagnostic performances were similar between visual and quantitative analyses. Further studies are needed to confirm these results and improve statistical accuracy.

Key words: F-18 FDG, PET/CT, double phase, SUV

F-18 FDG PET is a noninvasive modality that has been widely used for differentiation of malignant from benign pulmonary lesions [1–4]. Several studies have demonstrated that F-18 FDG PET can reduce the number of patients with pulmonary nodules who undergo unnecessary surgical biopsy [5–7].

A threshold of standardized uptake value (SUV) of 2.5 has been proposed as the optimal criteria for differentiating malignant from benign lung nodules [8, 9]. However, there is considerable overlap between the levels of FDG uptake of malignant and benign lesions. Recent study reported that the sensitivity of SUV cutoff value of 2.5 was lower than that of visual analysis for differentiating malignant lung nodules and this criterion of SUV 2.5 is inappropriate especially in low F-18 FDG uptake lung nodules [10].

Factor such as body habitus, timing of imaging after FDG injection, and plasma glucose level are important factors that

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Abbreviations: AUC: area under curve, CR: contrast ratio, CR1: contrast ratio of early image, CR2: contrast ratio of delayed image, %ΔCR: percent change of CR, DBA: difference between areas, F-18 FDG: fluorine-18 fluorodeoxyglucose, PET/CT: positron emission tomography/computed tomography, ROC: receiver operating characteristic curve, ROI; region of interest, SE: standard error, SUV: standardized uptake value, SUV_{max1}: maximal SUV of early image, SUV_{max2}: maximal SUV of delayed image, $\%\Delta SUV_{max}$: percent change of maximal SUV, FWHM: full width at half maximum

influence the image quality and SUV measurement. For example large, rapidly growing, and metabolic active lesions shows intense F-18 FDG uptake. In contrast, slowly growing, well-differentiated, or small lesions exhibit little or no accumulation [11].

The low FDG uptake of solitary lung lesions face a diagnostic dilemma. Recently, Hashimoto et al. reported that for solid pulmonary lesions with low FDG uptake, semiquantitative approaches did not improve the accuracy of F-18 FDG PET over that obtained with visual analysis [12].

Recently, to better distinguish benign lesion from malignant diseases, some studies have made major findings using dual phase acquisition of F-18 FDG and other radiopharmaceuticals with PET [12–17]. However, very few study adopted the dual phase acquisition of F-18 FDG PET for the evaluation of pulmonary nodules with low F-18 FDG uptake [18].

The aim of the present study was to investigate whether double phase F-18 FDG PET/CT could improve the diagnostic accuracy for the evaluation of low metabolic pulmonary lesions and whether quantitative indices could predict malignant nature of these lesions.

Methods

Patients. From May 2005 to June 2006, a total of 218 patients (154 men and 64 women, age range; 25-83 years, mean; 60 years) with focal pulmonary lesions detected by chest computed tomography (CT), underwent integrated PET/CT. Of the 218 patients, we retrospectively enrolled 73 patients who had focal pulmonary lesions with an SUV of <2.5 on F-18 FDG PET/CT.

Of these 73 patients, 43 were excluded because that follow-up imaging study and cytologic or histologic diagnosis were unavailable. Therefore, the final analysis was conducted in 30 patients (male; 18, female; 12, mean age; 56.2 years old, age range; 26-72 years). These patients underwent trans-thoracic needle biopsy (n=10), video-assisted thoracoscopic surgery (n=1), and lobectomy (n=6). Thirteen patients, in whom CT and clinical findings suggested benignancy but in whom histopathologic diagnosis was not obtained, were regarded to have benign lesion, because lesions showed no change (n = 10) or a reduction (n = 3) in size at CT follow-up. Lesions without size change were followed up at least once or more by CT studies for more than 12 months (mean; 17.4±3.8 months, range; 12~23 months).

Chest computed tomography. Chest CT scans were available in all 30 patients. Chest CT was performed using a four (LightSpeed QX/i scanner; GE Medical Systems, Milwaukee, WI) or 16- (Sensation 16; Siemens, Germany) row multi-detector CT (MDCT). One radiologist with 4-year experience of chest CT reviewed all CT scans and evaluated morphologic features of pulmonary lesions including margin and presence or absence of a satellite lesion. Margins were classified as smooth, lobulated, or spiculated. Long-axis diameters of lesions were also measured.

F-18 FDG PET/CT. An F-18 FDG PET/CT image was done with a dedicated PET/CT scanner (Gemini, Philips, Milpitas, CA, USA), consisting of a dedicated germanium oxyorthosilicate full-ring PET scanner and a dual slice helical CT scanner. Standard patient preparation included at least 8 hours fasting and a serum glucose level of less than 140 mg/dL before F-18 FDG administration. PET/CT imaging was performed 60 and 120 minutes after injection of F-18 FDG (mean dose, 383.7±47.4 MBq; range, 314.5~488.4 MBq). At 60 minutes (early images) after administration of F-18 FDG, low-dose CT (30 mAs, 120kV) covering area from the base of the skull to the proximal thighs was performed for the purpose of attenuation correction and precise anatomical localization. Thereafter, emission scan was conducted in the 3-dimensional mode. Emission scan time per bed position was 3 minutes; 9 bed positions were acquired. Delayed PET emission images of the chest were acquired at 120 min after administration of F-18 FDG, using 2 or 3 bed positions with a 3-min acquisition at each. This acquisition was immediately followed by a transmission scan of the same transverse planes, using a 2-min acquisition at each bed position. PET data were obtained using a high resolution whole body scanner with an axial field of view of 18 cm. The average axial resolution varied between 4.2 mm full width at half maximum (FWHM) in the center and 5.6 mm at 10 cm. The average total PET/CT examination time was 30 minutes. After scatter and decay correction, PET data were reconstructed iteratively with attenuation correction and reoriented in axial, sagittal, and coronal slices. The row action maximum-likelihood algorithm was used for 3-dimensional reconstruction.

F-18 FDG PET/CT image analysis. PET/CT data sets of early and delayed scans were evaluated by two nuclear medicine physicians, respectively blinded to all CT, clinical, and pathological results. Decisions concerning the analysis of F-18 FDG PET/CT data sets were reached by consensus. The intensity of F-18 FDG uptake by pulmonary lesions relative to the background activity in the uninvolved adjacent lung parenchyma and the mediastinum was assessed visually, and the intensity was scored with a 4-point scale (Grade 1; absent, Grade 2; faint, Grade 3; moderate, Grade 4; intense) as reported previously [19]. Also, PET/CT data sets of early and delayed images were analyzed quantitatively by use of the SUV and the contrast ratio (CR) as indices of F-18 FDG uptake. Spherical regions of interest (ROIs) were placed over lesions visible on PET images. The ROIs of lesions that were invisible on PET images were located by use of the corresponding CT images. ROIs were placed in the same area on the selected image for both of early and delayed images. The maximal SUV of early images (SUV_{max1}) and delayed images (SUV_{max2}) were calculated by manually drawing a region of interest (ROI) over the most intense slice of primary lesion visible on early and delayed PET images. The CR was determined by measuring the highest activity in the tumor ROI (T) and in the contralateral normal lung ROI (N) and was calculated as (T-N)/(T+N) for early image (CR_1) and delayed images (CR_2) as previously described [20]. From these quantitative

indices, the % change of SUVmax and % change of CR were calculated as following equations:

% change of SUVmax ($\%\Delta SUV_{max}$)= (SUV_{max2}-SUV_{max1})/ SUV_{max1} X 100

% change of CR ($\%\Delta CR$)=(CR_2-CR_1)/CR_1 X 100

Statistical Analysis. Statistical analyses were performed using commercially available software (MedCalc 9.3, Mariakerke, Belgium). Receiver-operating-characteristic (ROC) curves for each parameter were derived and evaluated by comparing the areas under the curves. The sensitivity and specificity of each parameter were determined at the optimal cutoff values by ROC curve analyses. The Chi-square test, Fisher's exact test, and Mann-Whitney test were used to analyze statistical differences in morphologic features and long-axis diameter of lesions on CT, SUV_{max1}, SUV_{max2}, $\%\Delta SUV_{max}$, CR1, CR2, and $\%\Delta CR$ between malignant and benign pulmonary lesions. Agreement between observer 1 and observer 2 for visual assessment of double phase F-18 FDG PET scan was assessed by means of Cohen kappa statistic and its standard error. The interpretation of the κ is such that κ greater than 0.75 is regarded as excellent agreement, κ greater than 0.40 as good agreement, and κ less than 0.40 as marginal agreement of observer 1 and observer 2. Statistical significance was defined as $p<0.05$.

Results

Lesion Characteristics at Pathology and CT. Of 30 nodules, 13 (43%) proved to be malignant and 17 (57%) benign (Table 1). Of 13 malignant lesions, 11 were histologically confirmed primary lung cancers (8 adenocarcinomas, 2 squamous cell carcinomas, and 1 small cell lung cancer) and two were metastastic lung cancers (1 metastatic adenocarcinoma from colon cancer and 1 metastatic adenoid cystic carcinoma). Four of 17 benign lesions were histologically confirmed (1 tuberculoma, 1 aspergillosis, 1 acute inflammation, and 1 chronic inflammation) (Table 1).

The maximum diameters were not significantly different between malignant (19.0 ± 7.2, range; 8.9~29.4 mm) and benign (21.3 ± 9.9, range; 10.4~42.0 mm) lesions (Table 1, p = 0.722, Mann Whitney test). Marginal characteristics and presence of satellite lesions were not significantly different between malignant and benign lesions. Of 17 benign lesioins, 13 showed lobulated or spiculated margin.

ROC analyses of visual and quantitative assessment of double phase F-18 FDG PET/CT. Table 2 shows the results of ROC analyses of visual and quantitative indices of double phase F-18 FDG PET/CT for differentiation between malignant and benign pulmonary lesions. The optimal visual grade was>grade 2. When> grade 2 was used as cut-off value, the sensitivity and specificity were 46.1% and 82.3%, respectively. The positive and negative predictive values were 66.7% and 66.7%, respectively. The AUC was 0.658 (95% CI, 0.464-0.820) and standard error (SE) was 0.103.

The optimal SUV_{max1} was >2. When SUV_{max1} was >2 was used as cut off point, the sensitivity and specificity were 46.1% and 82.3%, respectively. The positive and negative predictive values were 66.7% and 66.7%, respectively. The AUC was 0.785 (95% CI, 0.597-0.913) and SE was 0.088. The optimal SUV_{max2} was >1.81. When SUV_{max2} was >1.81 was used as cut off point, the sensitivity and specificity were 69.2% and 94.1%, respectively. The positive and negative predictive values were 90% and 80%, respectively. The AUC was 0.848 (95% CI, 0.671-0.952) and SE was 0.076. The optimal $\%\Delta SUV_{max}$ was >-2.3%. When $\%\Delta SUV_{max}$ was >-2.3% was used as cut off point, the sensitivity and specificity were 92.3% and 70.5%, respectively. The positive and negative predictive values were 70.6% and 92.3%, respectively. The AUC was 0.846 (95% CI, 0.668-0.950) and SE was 0.076.

Table 1. Characteristics of pulmonary lesions

		Malignant	Benign	p value
Number		13 (43%)	17 (57%)	0.6954
Histology				
AC		8		
SCC		2		
SCLC		1		
Metastasis		2		
Tuberculoma			1	
Aspergillosis			1	
Inflammation			2	
Size (mm)		19˘Ī7.2	21.3˘Ī9.9	0.722
CT characteristics				
Margin				
	Spiculate	8	11	0.7344
	Lobulate	2	2	0.1745
	Smooth	3	4	0.3745
Satellite lesion		0	2	0.492

AC; adenocarcinoma, SCC; squamous cell carcinoma, SCLC; small cell lung cancer

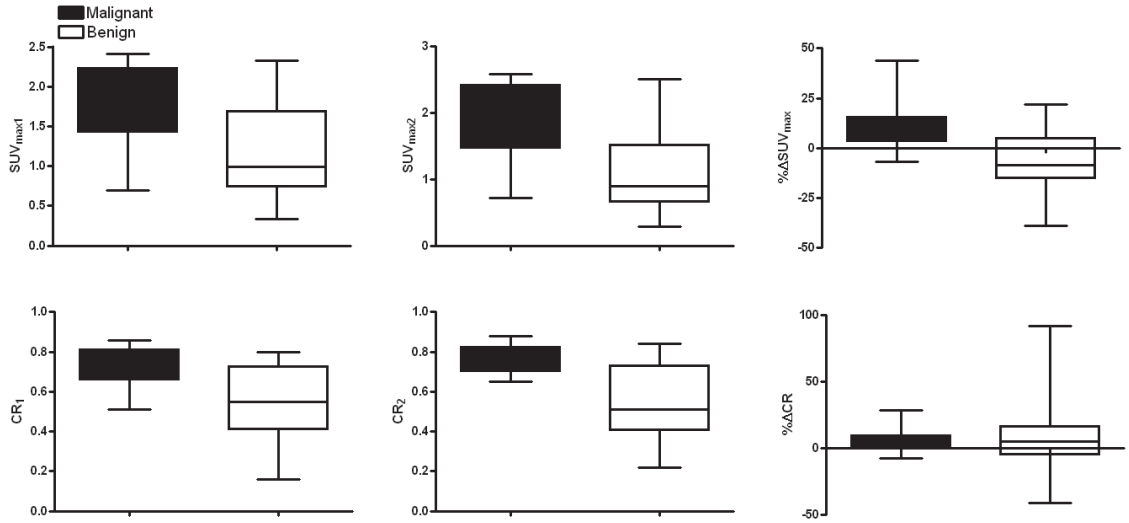

Figure 1. The differences of quantitative indices of double phase F-18 FDG PET/CT of malignant and benign pulmonary lesions.

The optimal CR_1 was >0.68. When CR_1 was >0.68 was used as cut off point, the sensitivity and specificity were 76.9% and 70.5%, respectively. The positive and negative predictive values were 66.7% and 80%, respectively. The AUC was 0.801 (95% CI, 0.615-0.923) and SE was 0.085. The optimal CR_2 was >0.58. When SUV_{max2} was >0.58 was used as cut off point, the sensitivity and specificity were 100% and 70.5%, respectively. The positive and negative predictive values were 72.2% and 100%, respectively. The AUC was 0.842 (95% CI, 0.662-0.948) and SE was 0.077. The optimal %ΔCR was >-1.7%. When %ΔCR was >-1.7% was used as cut off point, the sensitivity and specificity were 92.3% and 41.1%, respectively. The positive and negative predictive values were 54.5% and 87.5%, respectively. The AUC was 0.511 (95% CI, 0.323-0.697) and SE was 0.108.

Comparison of quantitative indices between malignant and benign lesions. Figure 1 reveals the differences of quantitative indices of double phase F-18 FDG PET/CT of malignant and benign pulmonary lesions. The SUV_{max1} of malignant pulmonary lesion was significantly higher than that of benign one (1.82±0.57 vs 1.16±0.58, p=<0.0084). Also, SUV_{max2} of malignant pulmonary lesion was significantly higher than that of benign one (2.01±0.59 vs 1.08±0.58, p=0.0013). The $\%\Delta SUV_{max}$ of malignant pulmonary lesion was significantly higher than that of benign one (11.9±12.9% vs -7.3±15.1, p=0.0014). The CR_1 of malignant pulmonary lesion was significantly higher than that of benign one (0.72±0.09 vs 0.53±0.2, p=0.0054). Also, CR_2 of malignant pulmonary lesion was significantly higher than that of benign one (0.76±0.07 vs 0.53±0.17, p=0.0016). However, %ΔCR revealed no statistical differences (5.9±8.8% vs 8.3±30.9, p=0.9167).

Comparison of ROC curve of quantitative indices and visual analysis. Table 3 showed the results of pairwise comparison of ROC analysis of quantitative indices and vi-

Table 2. Diagnostic accuracy of visual and quantitative analyses of double phase F-18 FDG PET/CT for differentiation malignant from benign pulmonary lesions with <SUV 2.5.

Criterion	Sensitivity	Specificity	PPV	NPV	AUC	SE
Visual						
>2	46.1%	82.3%	66.7%	66.7%	0.658	0.103
SUV						
SUV_{max1}>2	61.5%	94.1%	88.9%	76.2%	0.785	0.088
SUV_{max2} >1.81	69.2%	94.1%	90%	80%	0.848	0.076
$\%\Delta SUV_{max}$>-2.3%	92.3%	70.5%	70.6%	92.3%	0.846	0.076
CR						
CR_1>0.68	76.9%	70.5%	66.7%	80%	0.801	0.085
CR_2>0.58	100%	70.5%	72.2%	100%	0.842	0.077
%ΔCR>-1.7%	92.3%	41.1%	54.5%	87.5%	0.511	0.108

PPV – positive predictive value, NPV – negative predictive value, AUC – area under curve, SE – standard error

Table 3. Pairwise comparison of ROC analysis of visual and quantitative analysis of double phase F-18 FDG PET/CT for differentiation of malignant from benign pulmonary lesions.

		SUV_{max1}	SUV_{max2}	$\%\Delta SUV_{max}$	CR_1	CR_2	$\%\Delta CR$
Visual	DBA	0.127	0.190	0.188	0.143	0.183	0.147
	SE	0.059	0.067	0.126	0.081	0.084	0.113
	p value	**0.031**	**0.005**	0.136	0.079	**0.029**	0.193
SUV_{max1}	DBA		0.063	0.061	0.016	0.057	0.274
	SE		0.043	0.111	0.065	0.068	0.109
	p value		0.137	0.582	0.806	0.408	**0.012**
SUV_{max2}	DBA	0.063		0.002	0.048	0.007	0.337
	SE	0.043		0.097	0.065	0.065	0.104
	p value	0.137		0.981	0.461	0.916	**0.001**
$\%\Delta SUV_{max}$	DBA	0.061	0.002		0.045	0.005	0.335
	SE	0.111	0.097		0.110	0.103	0.130
	p value	0.582	0.981		0.582	0.965	**0.010**
CR1	DBA					0.041	0.290
	SE					0.054	0.084
	p value					0.454	**0.001**
CR2	DBA						0.330
	SE						0.120
	p value						**0.006**

DBA – difference between areas, SE – standard error

sual assessment of double phase F-18 FDG PET/CT for differentiation of malignant and benign pulmonary lesions. Among the quantitative indices, SUV_{max1}, SUV_{max2}, and CR_2 were superior to the visual analysis for differentiation of malignant from benign pulmonary lesions. The SUV_{max1}, SUV_{max2}, and $\%\Delta SUV_{max}$ were superior to $\%\Delta CR$ for differentiation of malignant from benign pulmonary lesions.

Inter-observer agreements of visual analysis of double phase F-18 FDG PET/CT. Table 4 revealed that agreement for visual analysis of double phase F-18 FDG PET/CT was good for differentiation of malignant from benign pulmonary lesions (weighted κ=0.701).

Table 4. Agreement between observer 1 and observer 2 for visual assessment of double phase F-18 FDG PET/CT for differentiation of malignant from benign pulmonary lesion.

	Visual grade of double phase F-18 FDG PET/CT		
	1	2	3
1	10	3	0
2	2	5	1
3	0	2	7

Weighted κ=0.704

Discussion

The major contribution of the present study was that the visual analysis and quantitative analysis of double phase F-18 FDG PET/CT could differentiate malignant from benign pulmonary lesions with low F-18 FDG uptake similarly.

The single-time-point SUV of 2.5~3.8 has been cited as the optimal cut-off value in pulmonary lesions for diagnosing lung cancer [8]. Most inflammatory lesions would fall below this cut-off value, whereas the majority of malignant lesions would have higher SUVs.

Because the uptake of F-18 FDG in malignancies is expected to increase over time, the initial inclination would be to perform a single scan at a time point later than the usual 45–60 min. In theory, this strategy should lead to improved contrast between lesion and background and improved diagnostic accuracy, making dual-time-point scanning unnecessary. However, although this strategy may improve sensitivity, specificity may remain low because of the overall low F-18 FDG uptake of these lesions.

In the current study, delayed quantitative indices (SUV_{max2} and CR_2) showed an increase of sensitivity from 8% to 23% without decline of specificity for differentiation of malignant from benign pulmonary lesions. However, the other quantitative indices such as $\%\Delta SUV_{max}$ and $\%\Delta CR$ showed high sensitivities with low specificities. Therefore, we believe that changes in dual-time-point SUVs would be a more valuable diagnostic tool than imaging at early or delayed single time point alone.

Recently, similar to the present study, Xiu et al. [18] conducted a study to compare the accuracy of dual-time point and single-time FDG PET imaging in the evaluation of lung nodules with minimally increased metabolic activity. In their study, the lowest diagnostic accuracies came from the visual and single SUV analysis on the initial images and the visual and single SUV analyses on the delayed images produced increased accuracy. Moreover, they found that the highest

diagnostic accuracy (84.8%) was obtained when a retention index of more than 10% was used as criterion for malignancy.

Although not performed with double phase acquisition of F-18 FDG PET, Hashimoto et al. [21] compared the visual and quantitative analyses of FDG PET in pulmonary lesions with F-18 FDG uptake below the SUV of 2.5. They concluded that for solid pulmonary lesions with low F-18 FDG uptake, quantitative approaches did not improve the accuracy of F-18 FDG PET over that obtained with visual analysis.

F-18 FDG PET has been widely used for differentiation of malignant from benign pulmonary lesions. Several studies have demonstrated that F-18 FDG PET can reduce the number of patients with pulmonary nodules who undergo unnecessary surgical biopsy [5–7]. However, some benign inflammatory lesions could show F-18 FDG accumulation yielding false positive findings [22–24].

Recently, to better distinguish benign lesion from malignant diseases, some studies have made major findings using dual phase acquisition of F-18 FDG and other radiopharmaceuticals with PET [12–17]. Some studies have demonstrated that malignant disease showed a higher SUV on delayed PET images than on single early point PET images [25, 26].

The degree of F-18 FDG uptake by malignant lesions is influenced by various factors, including biologic nature and lesion size. Among these factors, tissue differentiation of tumors is important [11]. Most malignant pulmonary nodules with SUVs of <2.5 are differentiated adenocarcinomas [10]. Our study showed that 61.5% of the malignant lesions were determined histologically to be differentiated adenocarcinomas.

The present study compared 6 different quantitative indices of double phase F-18 FDG PET/CT for differentiation of malignant from benign pulmonary lesions. One study has indicated that the CR is more sensitive than the SUV in diagnosing faintly positive pulmonary nodules when the classical SUV criterion of 2.5 is applied [10]. However, the comparison of ROC curve of the present study showed that these quantitative indices were similar in terms of overall diagnostic performance except %ΔCR. The %ΔCR revealed the lowest diagnostic accuracy for differentiation malignant from benign pulmonary lesions. Also, among the quantitative indices of double phase F-18 FDG PET/CT, the SUV_{max1}, SUV_{max2}, and CR_2 were superior to visual assessment for differentiation of malignant from benign pulmonary lesions.

Based on the presented results, the quantitative indices except %ΔCR were higher in malignant nodules than benign pulmonary nodules. However, the diagnostic performances were similar between visual and quantitative analyses. Further studies are needed to confirm these results and improve statistical accuracy.

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References

[1] Leef JL, Klein JS. The solitary pulmonary nodule. Radiol Clin Noth Am 2002; 40: 123–143. doi:10.1016/S0033-8389(03)00113-1 PMid:11813815

[2] Lowe VJ, Fletcher JW, Gobar L et al. Prospective investigation of positron emission tomography in lung nodules. J Clin Oncol 1998; 16: 1075–1084.

[3] Prauer HW, Weber WA, Romer W et al. Controlled prospective study of positron emission tomography using glucose analogue F-18 fluorodeoxyglucose in the evaluation of pulmonary nodules. Br J Surg 1998; 85: 1506–1511. doi:10.1046/j.1365-2168.1998.00915.x PMid:9823912

[4] Bury T, Dowlati A, Paulus P et al. Evaluation of the solitary pulmonary nodule by positron emission tomography imaging. Eur Respir J 1996; 9: 410–414. doi:10.1183/09031936.96.09030410 PMid:8729997

[5] Gupta NC, Maloof J, Gunel E. Probability of malignancy in solitary pulmonary nodules using fluorine-18-FDG and PET. J Nucl Med 1996; 37: 943–948.

[6] Gupta NC, Gill H, Graeber G et al. Dynamic positron emission tomography with F-18 fluorodeoxyglucose imaging in differentiation of benign from malignant lung/mediastinal lesions. Chest 1998; 114: 1105–1111. doi:10.1378/chest.114.4.1105 PMid:9792584

[7] Gambhir SS, Shepherd JE, Shah BD et al. Analytical decision model for the cost-effectiveness management of solitary pulmonary nodules. J Clin Oncol 1998; 16: 2113–2125.

[8] Patz EF Jr, Lowe VJ, Hoffman JM et al. Focal pulmonary abnormalities: evaluation with F-18 fluorodeoxyglucose PET scanning. Radiology 1993;188:487-490.

[9] Al-Sugair A, Coleman RE. Applications of PET in lung cancer. Semin Nucl Med 1998; 28: 303–319. doi:10.1016/S0001-2998(98)80035-4 PMid:9800237

[10] Nomori H, Watanabe K, Ohtsuka T et al. Visual and semiquantitative analyses for F-18 fluorodeoxyglucose PET scanning in pulmonary nodules 1 cm to 3 cm in size. Ann Thorac Surg 2005; 79: 984–988. doi:10.1016/j.athoracsur.2004.07.072 PMid:15734419

[11] Higashi K, Ueda Y, Yagishita M et al. FDG PET measurement of the proliferative potential of non-small cell lung cancer. J Nucl Med 2000; 41: 85–92.

[12] Kumar R, Loving VA, Chauhan A et al. Potential of Dual-time-point imaging to improve breast cancer diagnosis with 18F-FDG PET. J Nucl Med 2005; 46: 1819–1824.

[13] Mavi A, Urhan M, Yu JQ et al. Dual time point 18F-FDG PET imaging detects breast cancer with high sensitivity and correlates well with histologic subtypes. J Nucl Med 2006; 47: 1440–1446.

[14] Nishiyama Y, Yamamoto Y, Fukunaga K et al. Dual time point 18F-FDG PET for the evaluation of gallbladder carcinoma. J Nucl Med 2006; 47: 633–638.

[15] Ma SH, See LC, Lai CH et al. Delayed 18F-FDG PET for detection of paraaortic lymph node metastases in cervical cancer patients. J Nucl Med 2003; 44: 1775–1783.

[16] Matthies A, Hickeson M, Cuchiara A, Alavi A. Dual point 18F-FDG PET for the evaluation of pulmonary nodules. J Nucl Med 2002; 43: 871–875.

[17] Kwee SA, Wei H, Sesterhenn I et al. Localization of primary prostate cancer with dual-phase 18F-fluorocholine PET. J Nucl Med 2006; 47: 262–269.

[18] Xiu Y, Bhutani C, Dhurairaj T et al. Dual-time point FDG PET imaging in the evaluation of pulmonary nodules with minimally increased metabolic activity. Clin Nucl Med 2007; 32: 101–105. doi:10.1097/01.rlu.0000252457.54929.b7 PMid:17242561

[19] Vansteenkiste JF, Stroobants SG, Dupont PJ et al. FDG-PET scan in potentially operable non-small cell lung cancer: do anatometabolic PET-CT fusion images improve the localization of regional lymph node metastases? The Leuven Lung Cancer Group. Eur J Nucl Med Mol Imaging 1998; 25: 1495–1501. doi:10.1007/s002590050327

[20] Nomori H, Watanabe K, Ohtsuka T et al. Evaluation of F-18 fluorodeoxyglucose (FDG) PET scanning for pulmonary nodules less than 3 cm in diameter, with special reference to the CT images. Lung Cancer 2004; 45: 19–21. doi:10.1016/j.lungcan.2004.01.009 PMid:15196730

[21] Hashimoto Y, Tsujikawa T, Kondo C et al. Accuracy of PET for diagnosis of solid pulmonary lesions with 18F-FDG uptake below the standardized uptake value of 2.5. J Nucl Med 2006; 47: 426–431.

[22] Goo JM, Im JG, Do KH et al. Pulmonary tuberculoma evaluated by means of FDG PET: Findings in 10 cases. Radiology 2000; 216: 117–121.

[23] Dewan NA, Gupta NC, Redepenning LS et al. Diagnostic efficacy of PET-FDG imaging in solitary pulmonary nodules. Chest 1993; 997–1002. doi:10.1378/chest.104.4.997 PMid:8404239

[24] Nakamoto Y, Higashi T, Kubota R et al. Delayed 18F-fluoro-2-deoxy-D-glucose positron emission tomography scan for differentiation between malignant and benign lesions in the pancreas. Cancer 2000; 89: 2547–2554. doi:10.1002/1097-0142(20001215)89:12<2547::AID-CNCR5>3.0.CO;2-V PMid:11135214

[25] Demura Y, Tsuchida T, Ishizaki T et al. 18F-FDG accumulation with PET for differentiation between benign and malignant lesions in the thorax. J Nucl Med 2003; 44: 540–548.

[26] Hickeson M, Yun M, Matthies A et al. Use of a corrected standardized uptake value based on the lesion size on CT permits accurate characterization of lung nodules on FDG-PET. Eur J Nucl Med Mol Imaging 2002; 29: 1639–1647. doi:10.1007/s00259-002-0924-0 PMid:12458399