Comparison of the diagnostic performance of ^{18}F-fluorothymidine versus ^{18}F-fluorodeoxyglucose positron emission tomography on pulmonary lesions: A meta analysis

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Abstract. A pulmonary lesion is an extremely common and clinically challenging disorder worldwide, and an accurate diagnosis of lung cancer is crucial for early treatment and management. The aim of the present study was to perform a comprehensive meta analysis to compare the diagnostic performance of ^{18}F-fluorothymidine (^{18}F-FLT) positron emission tomography (PET) with ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET in evaluating patients with pulmonary lesions. Relevant studies were identified using the PubMed, EMBASE and Cochrane library databases. The pooled estimated sensitivity, specificity, positive-likelihood ratio, negative-likelihood ratio, and diagnostic odds ratio (DOR) for ^{18}F-FLT PET versus ^{18}F-FDG PET were calculated as the main outcome measures. Summary receiver operating characteristic curves were also constructed by Meta-Disk 1.4 software using a Mose's constant of linear model. The meta analysis showed that ^{18}F-FLT PET had a higher specificity (0.70; 95% CI, 0.61-0.77), but lower sensitivity (0.81; 95% CI, 0.74-0.87) compared to ^{18}F-FDG PET (0.50; 95% CI, 0.41-0.58 for specificity; 0.92; 95% CI 0.86-0.95 for sensitivity). For DOR, ^{18}F-FLT PET (12.58; 95% CI, 6.81-23.24) was higher compared to ^{18}F-FDG PET (10.72; 95% CI, 5.51-20.87). The area under the curve was 0.8592 and 0.9240 for ^{18}F-FLT PET and ^{18}F-FDG PET, respectively (Z=0.976, P>0.05). In conclusion, ^{18}F-FLT PET and ^{18}F-FDG PET had good diagnostic performance for the overall assessment of pulmonary lesions, and ^{18}F-FLT PET had a higher specificity compared to ^{18}F-FDG PET, but was less sensitive than ^{18}F-FDG PET. Therefore, ^{18}F-FLT and ^{18}F-FDG together could add diagnostic confidence for pulmonary lesions.

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Introduction

^{18}F-fluorodeoxyglucose (FDG) with positron emission tomography (PET) or PET/computed tomography (CT) is a well-established functional imaging technique for diagnostic oncologic imaging of a variety of malignancies and has been applied for differentiation between benign and malignant lesions, particularly for patients with pulmonary lesions (1-3). However, FDG is not specific for malignant tumors and can also accumulate non-specifically in certain benign lesions, which potentially results in false-positive findings (4,5). Therefore, several alternative molecular probes have been developed to complement ^{18}F-FDG (6-8). Among them, ^{18}F-fluorothymidine (FLT) is an analog of thymidine and its uptake reflects cellular proliferation (9,10). High sensitivity and specificity of ^{18}F-FLT PET has been reported (11,12) in lung cancer. The comparative diagnostic accuracy of ^{18}F-FLT PET versus ^{18}F-FDG PET for the differentiation of benign from malignant pulmonary lesions has been conducted by numerous studies (8,10,13-16), however, certain discrepancies existed and each study only had a limited sample size (13). Meta analysis is a method of combining data from eligible studies to reduce random error and to define the accuracy of diagnostic tests more precisely. To the best of our knowledge, there has been no meta analysis regarding the effect of ^{18}F-FLT PET versus ^{18}F-FDG PET on pulmonary lesions thus far, even though recent medical studies have shown a considerable growth in published systematic studies and meta-analyses in the field of nuclear medicine, specifically for PET or PET/CT in oncology (17-19). Therefore, the aim of the present study was to perform a comprehensive meta analysis to compare the diagnostic performance of ^{18}F-FLT PET with that of ^{18}F-FDG PET in evaluating patients with pulmonary lesions.

Materials and methods

Study identification. A comprehensive online literature search of studies was conducted by two investigators to identify the relevant studies regarding ^{18}F-FLT versus ^{18}F-FDG in the evaluation of pulmonary lesions in PubMed, EMBASE, Cochrane library using a search algorithm based on the following combination of terms: i) FLT or fluorothymidine or 3'-deoxy-3'-^{18}F-fluorothymidine AND; ii) FDG or fluorodeoxyglucose or 2'-deoxy

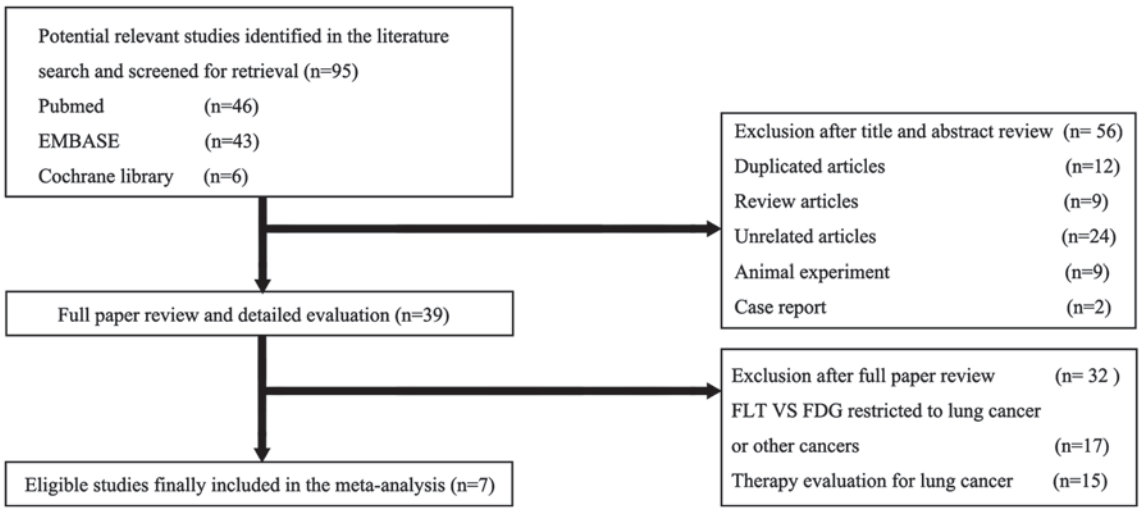


Figure 1. Study flow chart of the search for the eligible studies included in the meta analysis. FLT, fluorothymidine; FDG, fluorodeoxyglucose.

-2'-^{18}F-fluoro-D-glucose AND; iii) PET or positron emission tomography AND; iv) pulmonary or lung or thoracic. There was no limit to the beginning date and the search was updated until February 2014. The final analysis was limited to studies published in English. Conference abstracts and letters to the journal editors were excluded due to the limitations in data presentation. The reference lists of the retrieved studies were also manually reviewed for additional studies.

Study selection. Two investigators independently evaluated the titles, abstracts and complete studies based on the following inclusion criteria: i) Studies with a comparison of ^{18}F-FLT and ^{18}F-FDG in evaluation of patients with pulmonary lesions. ii) The differentiation of malignancy from benign pulmonary lesions was confirmed with histopathological analysis and/or clinical and imaging follow-up. iii) The scan with two imaging tracers (^{18}F-FLT or ^{18}F-FDG) was performed within 2-4 weeks of one another. iv) The studies including >10 patients were selected for inclusion in the meta-analysis. Studies were excluded based on the following criteria: i) Only ^{18}F-FLT or ^{18}F-FDG was performed. ii) Complete data regarding the numbers of the true positive (TP), false positive (FP), true negative (TN) and false negative (FN) were not provided or could not be obtained from calculation. iii) ^{18}F-FLT or ^{18}F-FDG were used to determine the responses to chemotherapy (such as erlotinib) or radiotherapy for non-small cell lung cancer (NSCLC). Any disagreement was resolved by consensus.

Data extraction and quality assessment. Two investigators independently extracted the relevant data from each eligible study, including authors, year of publication, demographic characteristics, sample size, data type, study design, reference standard, PET technique, disease constitution and TP, FP, TN and FN. These data were reported by a form of tabulation. Any difference was resolved by consensus.

The methodological quality of the eligible studies was assessed using the quality assessment for studies of diagnostic accuracy (QUADAS) tool (20). The QUADAS tool includes 14 items and 12 methodological quality items were assessed for each study using the scores 'yes', 'no' or 'unclear'.

Statistical analysis. Forest plots were performed to calculate the pooled sensitivity, specificity, positive-likelihood ratio (PLR), negative-likelihood ratio (NLR) and diagnostic odds ratio (DOR) with the corresponding 95% confidence interval (CI) for ^{18}F-FLT PET versus ^{18}F-FDG PET as the main outcome measures.

Heterogeneity due to the threshold effect was investigated using the Spearman correlation coefficient, and a positive correlation ($P<0.05$) suggested the threshold effect. The degree of heterogeneity due to the non-threshold effect among different studies was reported using the Cochran χ^2 statistic and the inconsistency index (I^2). $P<0.05$ or $I^2>50\%$ indicated heterogeneity. According to the results of the heterogeneity tests, PLR, NLR and DOR were calculated by the Mantel-Haenszel method based on a fixed-effects model (FEM) when there was no heterogeneity observed ($P>0.05$ or $I^2<50\%$), or by the DerSimonian-Laird method based on a random-effects model when heterogeneity was observed ($P<0.05$ or $I^2>50\%$) (21). Each set of data regarding ^{18}F-FLT PET or ^{18}F-FDG PET was fit to a summary receiver operating characteristic (SROC) curve and the area under the curve (AUC) and Q^* index, which represented the point at which the sensitivity and specificity were equal, were also calculated, measuring overall diagnostic accuracy.

Publication bias was assessed by Deek's funnel plots. Statistical analysis was performed using Meta-Disc version 1.4, which is a free statistical software package (21). $P<0.05$ was considered to indicate a statistically significant difference.

Results

Study selection and characteristics analysis. The initial online literature search identified a total of 95 potential studies (Fig. 1). A review of the titles and abstracts excluded 56 studies. These included 12 duplicated studies, nine reviews, two case studies, nine studies based on animal experiments and 24 studies not associated with FLT versus FDG in pulmonary lesions. The criteria excluded a further 32 of the remaining 39 studies: 15 studies focused on FLT and/or FDG PET in the therapy response evaluation for lung cancer, 17 studies were restricted

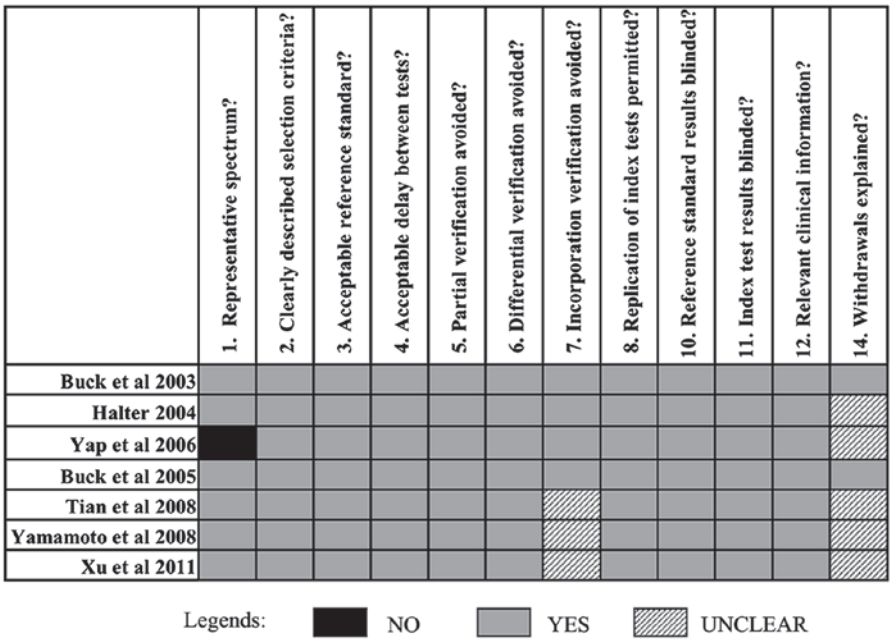


Figure 2. Assessment of the methodological quality of the eligible studies using the quality assessment for studies of diagnostic accuracy (QUADAS) tool.

to comparative diagnostic performance of FLT versus FDG in lung cancer or other cancers but not pulmonary lesions. Finally, seven studies (8,10,13,22-25) met the inclusion criteria and were selected.

Study characteristics. The characteristics of the eligible studies are summarized in Table I. These studies assessed a total of 301 patients with pulmonary lesions (n=166 for malignancy). All the seven studies included were prospective. In two studies, the study population underwent PET and PET/CT (13,25) and PET alone in the remaining studies (8,10,19-21). The dose of FDG or FLT ranged considerably across the studies. The results of the diagnostic performance were patient-based for all the studies except for a study by Yap *et al* (8). The totals of TP, FP, FN and TN for each included study are also presented in Table I.

Quality assessment. The methodological quality of all the eligible studies were assessed according to the 14-item QUADAS assessment tool (20). A total of 12 of the 14 items (without item 9 and 13) could be scored for all the included studies (Fig. 2).

All the studies had well-described selection criteria (item 2) and proper spectrum of patients (item 1), except for Yap *et al* (8). Therefore, histopathological analysis and clinical or imaging follow-up were considered as reference standards in this study (item 3,5-7), so it was not clear whether the FLT and/or FDG PET (index tests) formed part of the imaging follow-up (reference standard) for three studies (13,22,25), and none of the included studies provided sufficient detail of execution of the reference standard (item 9) to permit its replication due to its universality in clinical practice. The reference standard was considered to be blind to the index tests results and vice versa as the index tests (^{18}F-FLT PET and ^{18}F-FDG PET) were performed ahead of the reference standard and they were performed at a different department (item 10,11). The scan with two imaging tracers (^{18}F-FLT or ^{18}F-FDG) was performed within two weeks of one another for all the included studies, except for a study by Yap *et al* (within 1 month) (item 4). All the studies described the ^{18}F-FLT PET and ^{18}F-FDG PET technique in detail (item 8). No study reported whether there were any results that could not be interpreted (item 13). Two studies explained the reasons for patient withdrawal (item 14).

Heterogeneity tests and diagnostic performance. Table II summarizes the results for sensitivity, specificity, PLR, NLR, DOR, P-values for heterogeneity and I^2 values for ^{18}F-FLT PET and ^{18}F-FDG PET, respectively, indicating heterogeneity for specificity and PLR (I^2>50% and P<0.05), but homogeneity for sensitivity, NLR and DOR between studies (I^2<50% and P>0.05). According to the results of the heterogeneity tests, the pooled estimates were calculated by the Mantel-Haenszel method based on an FEM (P>0.05) or by the DerSimonian-Laird method based on a random-effects model (P<0.05).

The overall pooled estimates of sensitivity and specificity for ^{18}F-FLT PET versus ^{18}F-FDG PET in the differentiation between benign and malignant pulmonary lesions were 0.81 (95% CI, 0.74-0.87) and 0.70 (95% CI, 0.60-0.77) versus 0.92 (95% CI, 0.86-0.95) and 0.50 (95% CI, 0.41-0.58), respectively. The DOR is a single indicator of test accuracy that combines the data from sensitivity and specificity into a single number (23), and the estimated DORs based on FEM were 12.58 (95% CI, 6.81-23.24) and 10.72 (95% CI, 5.51-20.87) for ^{18}F-FLT PET and ^{18}F-FDG PET, respectively.

The SROC curves for ^{18}F-FLT PET and ^{18}F-FDG PET are shown in Fig. 3. The SROC plot presents a global summary of test performance and shows the adjustment between sensitivity and specificity. The AUC was 0.8592 and 0.9240 for ^{18}F-FLT PET and ^{18}F-FDG PET, respectively, indicating good diagnostic accuracy and no statistically significant difference (Z=0.976, P>0.05).

Table I. Characteristics of each study included.

Study (ref)	Mean age, years (range)	Gender, F/M[1]	n, M[2]/B	Reference standard	Design	Data type	Tracer	TP, n	FP, n	FN, n	TN, n	PET technique	Malignancy / benign types (n)
Buck *et al* 2003 (10)	62 (37-77)	9/17	26 18/8	Histopathology	Prospective	Per patient	FLT	15	0	3	8	334 MBq, 45 min	NSCLC (13), SCLC (1), metastases (4) / TB (1), IN (1), others (6)
							FDG	17	4	1	4	391 MBq, 45 min	
Halter *et al* 2004 (21)	63 (41-78)	7/21	28 21/7	Histopathology	Prospective	Per patient	FLT	18	0	3	7	265-370 MBq, 45 min	NSCLC (14), SCLC (6), others (1) / TB (1), IN (1), others (5),
							FDG	20	2	1	5	345-550 MBq, 45 min	
Buck *et al* 2005 (20)	62 (36-80)	16/27	43 28/15	Histopathology	Prospective	Per patient	FLT	22	0	6	15	265-370 MBq, 60 min	NSCLC (19), SCLC (1), metastases (8) / TB (1), others (14)
							FDG	27	6	1	9	345-550 MBq, 60 min	
Yap *et al* 2006 (8)	66	11/11	22 19/3	Histopathology	Prospective	Per lesion	FLT	16	1	6	6	185.2 MBq, 60 min	NSCLC (17), metastases (2) / IN (1), fibrosis (1), pneumonia (1)
							FDG	20	3	2	4	0.21mCi/Kg, 60 min	
Tian *et al* 2008 (22)	62 (17-82)	22/33	55 16/39	Histopathology/ follow-up	Multi-center Prospective	Per patient	FLT	11	9	5	30	300-400 MBq, 60 min	Lung cancer (16) / TB (16), IN (7), others (16)
							FDG	14	16	2	23	300-400 MBq, 60 min	
Yamamoto *et al* 2008 (19)	70 (52-88)	17/37	54 36/18	Histopathology/ follow-up	Prospective	Per patient	FLT	31	5	5	13	101-238 MBq, 60 min	NSCLC (34), SCLC (2) / TB (1), IN (11), others (6)
							FDG	32	6	4	12	111-161 MBq, 60 min	
Xu *et al* 2011 (13)	Unclear (17-85)	27/46	73 28/45	Histopathology/ follow-up	Prospective	Per patient	FLT	24	27	4	18	300-400 MBq, 60 min	Lung cancer (28) / TB (18), IN (27)
							FDG	25	33	3	12	300-400 MBq, 60 min	

B, benign; M[1], male; M[2], malignancy; PET, positron emission tomography; F, female; FLT, fluorothymidine; FDG, fluorodeoxyglucose; TP, true positive; FP, false positive; FN, false negative; FP, false positive; MBq, Megabecquerel; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; TB, tuberculosis, IN, inflammation.

Table II. Diagnostic performance of ^{18}F-FLT PET and ^{18}F-FDG PET for the evaluation of pulmonary lesions.

	Sensitivity	Specificity	PLR	NLR	DOR	Threshold effect
^{18}F-FLT PET						
Pooled estimates	0.81	0.7	4.01	0.27	12.58	P=0.383
95% CI	0.74-0.87	0.61-0.77	1.62-9.88	0.20-0.37	6.81-23.24	
Cochran-Q (P-value)	3.85 (0.6973)	40.61 (0.0000)	32.15 (0.0000)	3.74 (0.7114)	8.95 (0.1766)	
I^2 value, %	0.00	85.20	81.30	0.00	32.90	
^{18}F-FDG PET						
Pooled estimates	0.92	0.5	2.01	0.17	10.72	P=0.645
95% CI	0.86-0.95	0.41-0.58	1.38-2.93	0.10-0.29	5.51-20.87	
Cochran-Q (P-value)	2.51 (0.8670)	15.56 (0.0163)	18.92 (0.0043)	4.30 (0.6360)	6.46 (0.3734)	
I^2 value, %	0.00	67.50	68.30	0.00	7.20	

PET, positron emission tomography; FLT, fluorothymidine; FDG, fluorodeoxyglucose; PLR, positive-likelihood ratio; NLR, negative-likelihood ratio; DOR, diagnostic odds ratio.

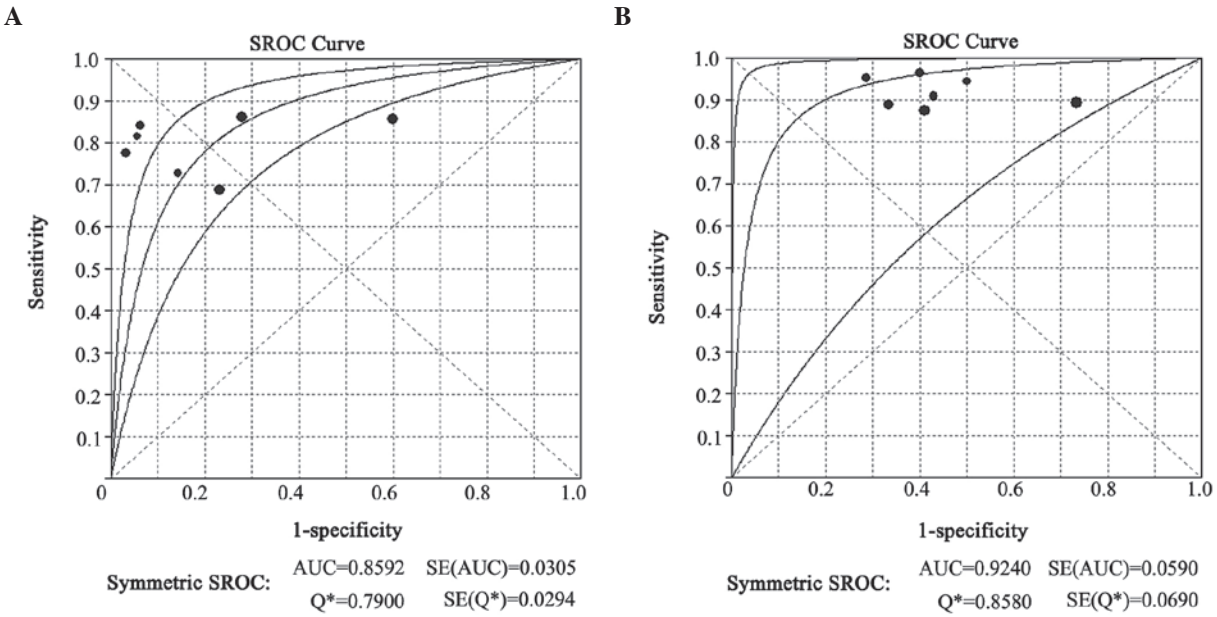


Figure 3. Summary receiver operating characteristic (SROC) curves for (A) ^{18}F-FLT PET and (B) ^{18}F-FDG PET. The middle line was the summary ROC curve and the two beside are 95% confidence intervals. Each black circle represents an individual study included in the meta-analysis, with the size of the circle directly proportional to the sample size of the study. AUC, area under the ROC curve; SE (AUC), standard error of the AUC; Q^*, the maximum joint sensitivity and specificity on a symmetric ROC curve; SE(Q^*): standard error of Q^*; FLT, fluorothymidine; PET, positron emission tomography; FDG, fluorodeoxyglucose.

To explore the possible explanations for the heterogeneity, threshold effect analysis was applied. Spearman correlation coefficient was determined to be 0.393 (P=0.383) and -0.214 (P=0.645) for ^{18}F-FLT PET and ^{18}F-FDG PET, respectively, which indicated an absence of threshold effect in studies included. Meta-regression analysis and subgroup analysis were not conducted in the study owing to the limitations in total sample size and the clinical characteristics information of the included studies.

Assessment of publication bias. The results of Deek's funnel plots (Fig. 4) showed an absence of publication bias for the included studies for ^{18}F-FLT PET (P=0.109) and ^{18}F-FDG PET (P=0.101).

Discussion

A pulmonary lesion is an extremely common and clinically challenging disorder in China, as well as in a number of other countries (27,28), and lung cancer is the first leading cause of tumor-related mortality. The differentiation of lung cancer from benign pulmonary lesions is a well-known diagnostic problem in daily clinical practice. Despite high sensitivity for staging lung cancer with ^{18}F-FDG PET compared to conventional imaging modalities, false-positive findings can occur, particularly in inflammatory lesions (4,5,10). Non-specific uptake by these non-malignant tissues resulted in a positive predictive value of ^{18}F-FDG PET in the pulmonary lesions as low as 44.6% (27). ^{18}F-FLT is an analog of thymidine and its uptake has been found

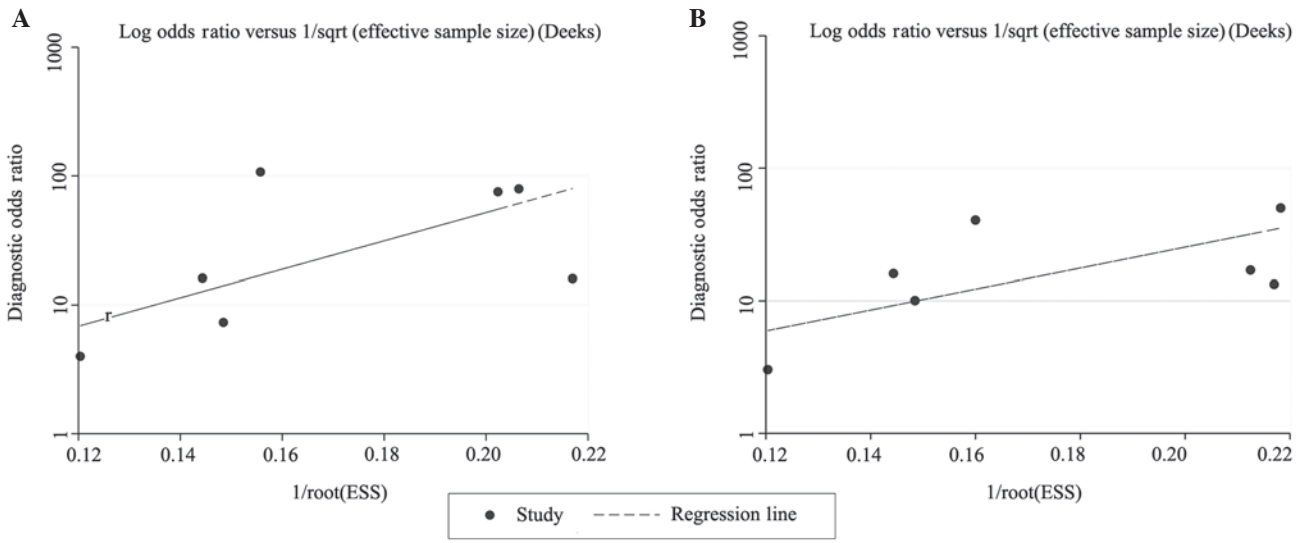


Figure 4. Deek's funnel plots for the evaluation of asymmetry between the included studies regarding the diagnostic performance of (A) ^{18}F-FLT PET and (B) ^{18}F-FDG PET for patients with pulmonary lesions. P>0.05 represents no asymmetry between the DORs of larger and smaller studies. Publication bias was not indicated by the Deek's funnel plots for ^{18}F-FLT PET (P=0.109) and ^{18}F-FDG PET (P=0.101). ESS, effective sample size; FLT, fluorothymidine; PET, positron emission tomography; FDG, fluorodeoxyglucose; DOR, diagnostic odds ratio.

to correlate significantly better with the proliferative activity, as indicated by the Ki-67 index in pulmonary lesions (12). In the majority of cases, ^{18}F-FLT PET showed higher specificity compared to ^{18}F-FDG PET for the characterization of pulmonary lesions as benign or malignant. As reported by Buck *et al* (10,11), the specificity of ^{18}F-FLT PET was ≤100%. However, the specificity in the study by Xu *et al* (13) was significantly lower than that of the other investigations.

As it is known that the result of a single study may be affected by numerous factors, a meta analysis regarding the performance of ^{18}F-FLT PET versus ^{18}F-FDG PET in evaluating patients with pulmonary lesions was performed for the first time to reduce the bias and increase the statistical power of the small sample study. The final analysis indicated that ^{18}F-FLT PET and ^{18}F-FDG PET had good diagnostic performance for the overall assessment of pulmonary lesions, and ^{18}F-FLT PET had a higher specificity compared to ^{18}F-FDG, but was less sensitive compared to ^{18}F-FDG PET.

Even though it was previously widely accepted that ^{18}F-FLT correlates significantly better with the proliferative activity of lung tumors compared to ^{18}F-FDG, ^{18}F-FLT is clearly limited by its low sensitivity with respect to evaluation of pulmonary lesions. This low sensitivity is due to the low ^{18}F-FLT uptake in malignant lesions, which was only half that of ^{18}F-FDG (8,10). Due to its low sensitivity, ^{18}F-FLT PET or PET/CT does not appear to be able to replace ^{18}F-FDG PET or PET/CT for the characterization of pulmonary lesions as benign or malignant. However, the significant correlation between FLT uptake and tumor cell proliferation indicates the importance of ^{18}F-FLT PET or PET/CT for the assessment of therapy response and outcome (12). To a certain extent, this was one of the reasons for the increasing studies regarding the assessment of the responses to erlotinib therapy for NSCLC using ^{18}F-FLT versus ^{18}F-FDG PET and/or PET/CT (25-30).

Several published meta analyses only reported pooled data from statistically heterogeneous studies and possibly provided the misleading information. For example, data from studies using PET and those using PET/CT are often pooled together for the meta analysis on the diagnostic performance of PET or PET/CT in oncology. This could lead to a possible bias on the final results as the overall diagnostic accuracy of PET/CT is usually higher than that of PET alone, as it is known that the CT scanner in PET/CT has allowed the possibility of acquiring metabolic and anatomical imaging data and provides precise anatomical localization. The comparison of the diagnostic performance of ^{18}F-FLT PET was focused on with regards to that of ^{18}F-FDG PET in evaluating pulmonary lesions in the present meta analysis study, but did not utilize the analysis results regarding ^{18}F-FLT PET/CT versus ^{18}F-FDG PET/CT as the relevant studies were only published in Chinese, except for two English studies included in the meta analysis (13,25). The present meta analysis will be updated in the future with the development of relevant studies, particularly for the studies regarding the integration of ^{18}F-FLT PET/CT versus ^{18}F-FDG PET/CT and PET/CT with a combination of ^{18}F-FLT and ^{18}F-FDG in the evaluation of patients with pulmonary lesions.

A notable phenomenon was that the reported specificities in the only two studies included in the present meta analysis that were performed in China were significantly lower compared to the other included studies [particularly for the Xu *et al* (13) study], and the pooled specificity had improved to 0.84 (95% CI, 0.75-0.91) for ^{18}F-FLT PET and 0.61 (95% CI, 0.50-0.71) for ^{18}F-FDG PET, respectively, when the study was excluded. The regional difference (including the different diagnostic criteria and the inclusion of patients with different disease constitution) possibly contributed to the heterogeneity in the specificity value to a certain extent. In general, the final results with regards to the comparison of the overall diagnostic performance of ^{18}F-FLT PET with that of ^{18}F-FDG PET were not markedly influenced with the exclusion of the Xu *et al* (13) study.

Even though ^{18}F-FLT PET and ^{18}F-FDG PET had a good diagnostic performance for the overall assessment of pulmonary lesions, the effectiveness of each tracer alone was limited. Multi-tracer imaging has received attention in recent years (28,29), and a multi-center clinical trial included in the present meta analysis had conducted a dual-tracer (the combination of ^{18}F-FLT and ^{18}F-FDG) study for assessment of pulmonary lesions (25). The ^{18}F-FLT/^{18}F-FDG ratio has been indicated to be more accurate in revealing the nature of the pulmonary lesions and a ratio between 0.4 and 0.90 is the most recommended (25). Cost effectiveness and an increased radiation dose should also be considered as a major difficulty that requires investigating in the future with dual-tracer imaging.

There are numerous potential limitations in the present meta analysis. Firstly, the number of evaluated studies included in the study was relatively small, and therefore, subgroup analyses according to clinical characteristics of patients with pulmonary lesion were not performed. The limited number of available studies and the clinical heterogeneity among them may have affected the generalizability of the results and impaired the strength of the present meta-analysis study. Secondly, for practical reasons only studies written in English were included in the study, which may have incurred a bias as other studies with positive results that are reported in a language other than English may have been published in international journals (30). However, the Deek's funnel plots did not indicate any publication bias, even though the influence of bias in the present analysis was not completely excluded, particularly for the relatively small number of studies. Thirdly, there was no well-accepted reference standard in the meta analysis that ranged from histopathological analysis to clinical or imaging follow-up, and not all the follow-up were performed in the same manner in all the studies. Fourthly, the variability in the quality of the evaluated studies may introduce significant limitations for the interpretation of the meta analysis study. Finally, the present study did not compare ^{18}F-FLT or ^{18}F-FDG PET with other imaging modalities, such as magnetic resonance imaging or diagnostic CT scan, as systematic deviation exists among modalities using different imaging mechanisms. Due to the limitations mentioned above, the results of the meta-analysis should be interpreted with care.

In conclusion, although a large-scale prospective multi-center randomized-controlled trial is required, the evidence in the present study shows that ^{18}F-FLT PET had a higher specificity compared to ^{18}F-FDG PET, but was less sensitive for the evaluation of pulmonary lesions. ^{18}F-FDG and ^{18}F-FLT, which provide information regarding the different aspects of tumor biology, are complementary to each other and may add diagnostic confidence in pulmonary lesions when the combination of ^{18}F-FLT and ^{18}F-FDG is available.

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