

Value of ^{11}C -choline PET/CT for lung cancer diagnosis and the relation between choline metabolism and proliferation of cancer cells

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Abstract. The aim of this study was to investigate the efficacy of ^{11}C -choline PET/CT imaging for lung cancer and the correlation between choline uptake of lung cancer tissue and the expression of choline kinase (ChoK), phosphorylcholine-cytidyl transferase and Ki-67 index. Between March 2008 and June 2010, 53 patients diagnosed or suspected of having lung cancer underwent integrated ^{11}C -choline PET/CT and contrast-enhanced CT scans before surgery. After surgery, specimens from 42 patients diagnosed with lung cancer were used to detect the expression of ChoK, phosphorylcholine-cytidyl transferase and the Ki-67 index. The PET/CT results were analyzed using visual methods and the standardized uptake value (SUV) of lesions was measured using semi-quantitative methods. Finally, the analyzed results were compared to the histopathological results. The accuracy of the ^{11}C -choline PET/CT for diagnosing lung cancer was 81.13% (43/53), compared with 71.70% (38/53) for CT scanning. The difference was not statistically significant ($P=0.61$). The accuracy of ^{11}C -choline PET/CT for diagnosing lymph nodes was 83.76% (227/271), compared with 66.79% (181/271) for CT scanning. This difference was statistically significant ($P=0.04$); the SUVmean value of lesions correlated positively with the Ki-67 index ($r=0.51$, $P=0.002$). Of the 35 patients with positive ^{11}C -choline PET results, 29 (82.86%) overexpressed ChoK, 26 (74.29%) overexpressed phosphorylcholine-cytidyl transferase. The seven patients with negative ^{11}C -choline PET results did not exhibit overexpression of ChoK or phosphorylcholine-cytidyl transferase; the SUVmean value correlated positively with

the expression of both ChoK and phosphorylcholine-cytidyl transferase ($r=0.52$, $P=0.001$; $r=0.37$, $P=0.029$). In conclusion, compared with contrast-enhanced CT, ^{11}C -choline PET offers nodal staging with higher accuracy. The SUV value of PET is correlated with the proliferation of tumor cells and the mechanism of PET imaging is associated with the overexpression of ChoK and phosphorylcholine-cytidyl transferase.

Introduction

^{18}F -fluorodeoxyglucose (^{18}F -FDG) is the most common radio-tracer and it has been primarily recognized valuable for the diagnosis and staging of lung cancer (1-3). Although ^{18}F -FDG PET/CT imaging has shown better sensitivity in the diagnosis of lung cancer, the specificity of this method is not optimal because of the non-specific uptake of ^{18}F -FDG in inflammatory cells and granulation tissues such as tuberculosis, especially for acute inflammatory and active tuberculosis in which the uptake level of ^{18}F -FDG may even exceed the level in cancer (4,5). In addition, the conspicuous ^{18}F -FDG uptake of normal myocardium usually interferes with the observation of mediastinal lymph nodes. In order to improve the specificity of PET/CT for malignancies, finding a new radiotracer has become a focus for additional research. Although literature relating to this topic remains limited, the diagnostic effect of ^{11}C -choline PET/CT for pulmonary disease has attracted attention from scholars. (6,7). Moreover, the mechanism of ^{18}F -FDG uptake by tumor cells is been well known, while the mechanism of CH uptake has not been thoroughly clarified. By comparing ^{11}C -choline PET/CT with contrast-enhanced CT, our research aimed to investigate the efficacy of ^{11}C -choline PET/CT imaging in diagnosing and staging lung cancer, and to discuss the correlation between choline metabolism and proliferation of lung cancer cells.

Materials and methods

Fifty-three patients histologically diagnosed or suspected of having lung cancer were referred for surgery during March 2008-June 2010. They underwent standard preoperative staging procedures. The patients were in stage I, II and selected IIIA. An allergic reaction to iodinated contrast agents was

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Table I. ChoK, PCYT and β -actin PCR primers.

Gene	Primer sequence	Product size (bp)
ChoK	F: 5'-CAGAAACGAGATCGGGAAGC-3' R: 5'-ATGGGACCAAGAGGGTAAAG-3'	354
PCYT	F: 5'-ACTCCTTGTGAGCGACCTGTG-3' R: 5'-TCGGGTGATGATGTCTGATGT-3'	414
β -actin	F: 5'-CTGGGACGACATGGAGAAAA-3' R: 5'-AAGGAAGGCTGGAAGAGTGC-3'	564

F, forward; R, reverse; ChoK, choline kinase; PCYT, phosphorylcholine-cytidyl transferase.

Table II. Sensitivity, specificity and accuracy of PET/CT and CT scans for lung cancer.

Parameter	TP	FN	FP	TN	Accuracy	Sensitivity	Specificity
PET/CT	35	7	3	8	81.13% (43/53)	83.33% (35/42)	72.73% (8/11)
CT	31	11	4	7	71.70% (38/53)	73.81% (31/42)	63.64% (7/11)
P-value					0.61	0.39	1.0

TP, true positive; FN, false-negative; FP, false-positive; TN, true negative.

considered an exclusion criteria. Patients who received chemotherapy or radiotherapy prior to surgery were also excluded. The enrolled patients underwent integrated PET/CT and contrast-enhanced CT scans of the chest followed by surgical resection and nodal staging. The PET/CT, contrast-enhanced CT and surgery were performed within 2 weeks. Patients included 30 men and 23 women with a median age of 61 years (36-76). Pathologic findings in locoregional lymph nodes were performed as gold standard. The patients whose preoperative diagnoses were unclear initially received a partial resection or pulmonary lobectomy and were then further treated with pneumonectomy and lymph node dissection according to the criterion if the rapid pathological diagnosis of lung cancer was confirmed. Part of the lesion tissue was used for RT-PCR and immunohistochemistry, the other was used for pathological analysis. Selected normal tissue >5 cm around each lesions were collected as the controls. Part of the specimen was stored in liquid nitrogen for RT-PCR, another part was fixed by neutral formalin for immunohistochemistry. The study protocol was approved by the Institutional Review Board of the Provincial Hospital Affiliated to Shandong University (Shandong, China). Informed consent was obtained from each patient.

PET/CT scanning. A hybrid PET-CT system (GE Discovery LS; GE Medical Systems, Milwaukee, WI, USA) was employed for four-slice, helical CT acquisition, followed by a full-ring dedicated PET scan of the same axial range. The CT component was operated with an X-ray tube voltage peak of 140 keV, 80 mA, 6:1 pitch and slice thickness of 4.25 mm, with a rotational speed of 0.8 sec per rotation. PET was performed for 5 min/field of view, each covering 14.5 cm, at an axial sampling of 4.25 mm/slice. Both PET and CT were performed

with normal tidal breathing. PET images were reconstructed using the ordered subset expectation maximization (OSEM) software, using CT-derived attenuation correction.

The attenuation-corrected PET images, the CT images and the fused PET/CT images were available for review in axial, coronal and sagittal planes, as was a cine display of maximum intensity projections (MIP) of the PET data, using the manufacturer's review station (eNTegra & Xeleris, GE Medical Systems).

^{11}C -choline (half-life, 20 min) was prepared using a cyclotron and automated synthetic apparatuses that we constructed. PET scanning was performed in the morning after the patients had fasted overnight. After the transmission scan was completed, a bolus of ^{11}C -choline (370 mBP) was injected intravenously (i.v.), followed by an infusion of a large volume of saline solution using the same i.v. line. The emission scan started 5 min after the injection of ^{11}C -choline.

Two experienced nuclear medicine physicians, who were masked to the results of computed tomography, read the PET images. Standardized uptake values (SUVs) were calculated as the ratio of the regional radioactivity concentration divided by the injected amount of radioactivity normalized to the body weight. CT criteria used to define malignant involvement of mediastinal lymph nodes was a short-axis lymph node diameter of ≥ 1 cm on a transverse CT scan.

Expression of choline kinase (ChoK) and phosphorylcholine-cytidyl transferase (PCYT). (RT-PCR) was used to investigate the expression of ChoK and PCYT genes in the lung tumor tissue and the control tissue. Total RNA was extracted from the specimens with TRIzol reagent (Invitrogen, USA) following the manufacturer's instructions and the expression of ChoK and

Table III. Sensitivity, specificity accuracy, PPV and NPV of PET/CT and CT scans for lymph node staging.

Parameter	TP	FN	FP	TN	Accuracy	Sensitivity	Specificity	PPV	NPV
PET/CT	42	7	37	18	83.76%	85.71%	83.33%	53.16%	96.35%
				5	(227/271)	(42/49)	(185/222)	(42/79)	(185/192)
CT	30	19	71	15	66.79%	61.22%	68.02%	29.70%	88.82%
				1	(181/271)	(30/49)	(151/222)	(30/101)	(151/170)
P-value					0.04	0.02	0.000268	0.005	0.001

TP, true positive; FN, false-negative; FP, false-positive; TN, true negative; PPV, positive predictive value; NPV, negative predictive value.

PCYT mRNA was determined by RT-PCR with reverse transcriptase (MBI Fermentas, USA). PCR primers used for ChoK and PCYT are shown in Table I. PCR conditions consisted of a denaturation at 95°C for 5 min, followed by 40 cycles at 94°C for 40 sec, 55°C for 30 sec and 72°C for 40 sec. β -actin mRNA was amplified and used to normalize the amount of the ChoK and PCYT mRNA in RT-PCR. Amplification products of PCR were analyzed using agarose gel electrophoresis. The gel images were acquired using Amersham Imagemaster VDS-CL to perform the comparative analysis with Bandleader 3.0 software. According to the densitometry of bands under the CCD imaging system, we calculated the densitometry ratio of ChoK or PCYT to β -actin to obtain the relative expression intensity. The average relative expression intensity of the control tissue was at a standard level. When the relative expression intensity was >2 times the average relative expression, there was an overexpression; $<1/2$ was considered low expression; and between $1/2$ and 2 times was a normal expression.

Immunohistochemical staining with Ki-67. Staining was performed on 4-mm sections of formalin-fixed paraffin-embedded specimens.

The H&E staining and streptavidin-biotin immunoperoxidase were applied to the specimens respectively after deparaffinization and microwave antigen retrieval. The antibody for Ki-67 (monoclonal mouse antibody MIB-1, 1:100 Dilution) (Zhongshan Golden Bridge Biotechnology Co., China) was used for measurement of the Ki-67 index: the labeling index of Ki-67 was calculated by determining the percentage of cells with positive nuclei in $>1,000$ tumor cells in >4 fields.

Statistical analysis. Statistical analyses were performed using the SPSS statistical software program (version 16.0 for Windows). The results of CT and PET/CT were compared with a reference standard provided by the pathological examination. Sensitivity, specificity and accuracy for detecting the lesion and lymph node were calculated and the statistical significance was determined with the McNemar's test and the Fisher's exact test. Statistical significance of a positive predicted value and a negative predict value for the detection of lymph node was determined with the Chi-square test. Statistical significance of the expression of ChoK and PCYT was determined with the Wilcoxon test. A P-value of <0.05 was considered to indicate a statistically significant difference. Both the correlation

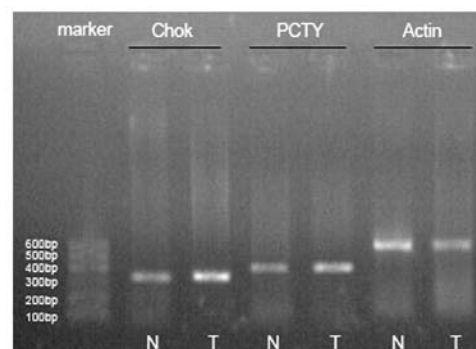


Figure 1. Expression of ChoK and PCYT in a 67-year old male patient with squamous cell lung cancer. The expression of ChoK in cancer tissue was 0.88 and in normal tissue this value was 0.93; the expression of PCYT in the cancer tissue was 0.67 and in normal tissue it was 0.31.

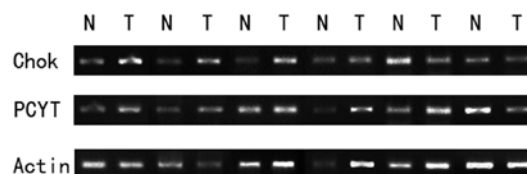


Figure 2. Expression of ChoK and PCYT in part of the lung cancer tissue with positive PET results and normal tissue. T, lung cancer tissue, N, normal tissue.

between the expression of ChoK, PCYT and SUVmean, and the correlation between the Ki-67 index and the SUVmean were determined with the Pearson's correlation analysis. Correlation was assumed for P-value <0.05 ; when r-value <0.3 there was no correlation. Correlation was assumed low with an r-value between 0.3 and 0.5; a medium correlation when r-value was between 0.5 and 0.8 and there was a high correlation at r-value >0.8 .

Results

Pathological findings. Pathological analysis revealed lung cancer in 42 patients (including adenocarcinoma in 15 patients, squamous cell carcinoma in 18, adenosquamous carcinoma in 2, small cell lung cancer in 3, carcinoid in 3 and large-cell neuroendocrine cancer in 1), benign lesion in 11 patients

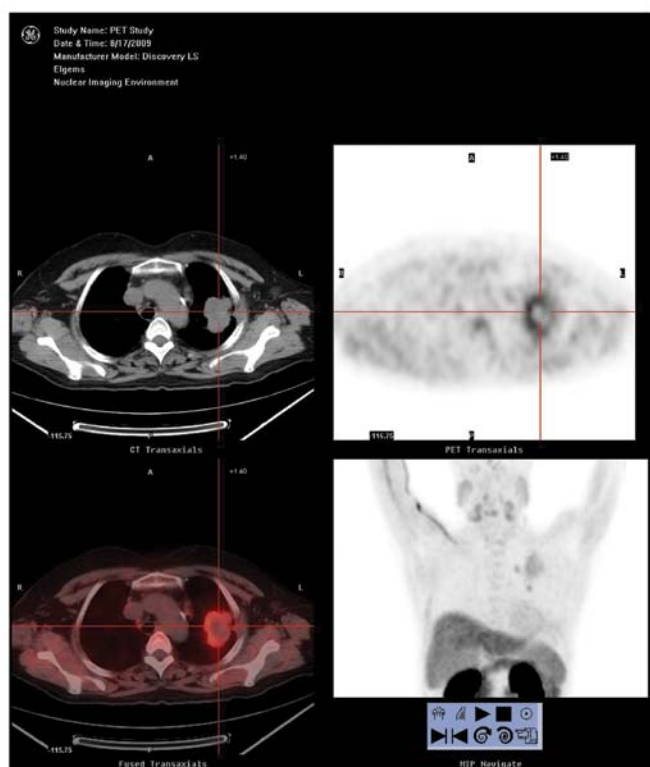


Figure 3. ^{11}C -choline PET image of a 61-year old female patient with squamous cell lung cancer. SUVmax are 6.24, SUVmean are 5.60.

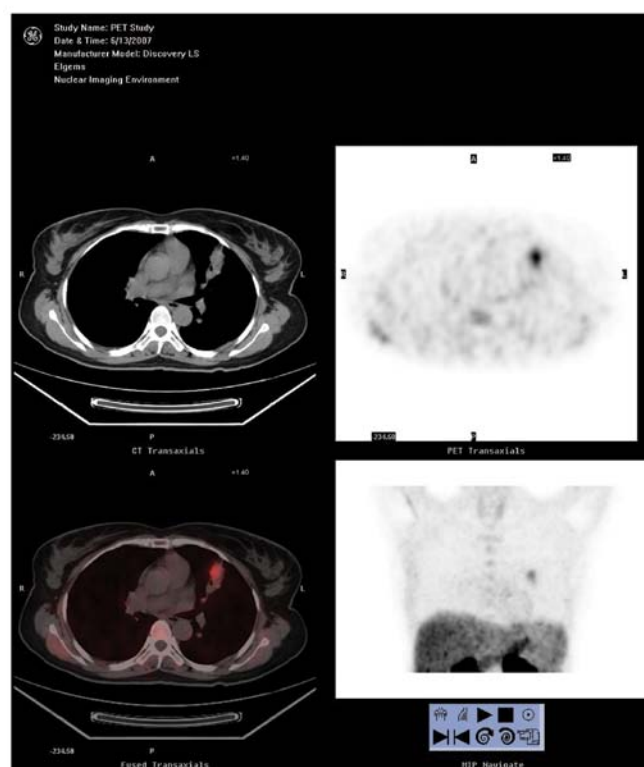


Figure 5. The diagnosis of pathology is tuberculosis with SUVmax is 6.3, SUVmean is 5.3.

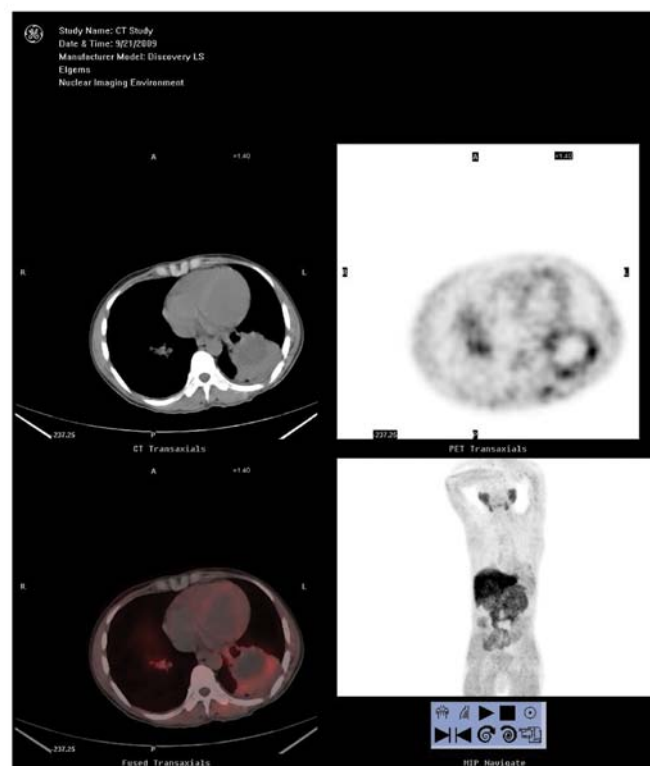


Figure 4. ^{11}C -choline PET image of a patient with lung cancer. SUVmax is 0.90, SUVmean is 0.79.

(including tuberculoma in 4, inflammatory pseudotumor in 4, hamatoma in 2, sclerosing hemangioma in 1). A total of 271

lymph nodal groups were evaluated for pathological analysis. From these 49 nodal groups, 42 patients proved to be positive for malignancy.

CH-PET/CT and CT findings. Thirty-five patients were diagnosed with lung cancer using CH-PET. There were 3 patients with false-positive (FP) results (including tuberculoma in 2, inflammatory pseudotumor in 1), 7 patients with false-negative (FN) results [including adenocarcinoma in 3 (alveolar carcinoma in 2), squamous cell carcinoma in 2, adenosquamous carcinoma in 1, carcinoid in 1].

The overall mean SUV (SUVmean) for lung cancer patients was 3.57 ± 1.88 (0.52-7.84) and the SUVmax of these patients was 4.12 ± 2.05 (0.52-8.46).

Thirty-one patients were diagnosed with lung cancer using CT. There were 4 patients with FP results (including tuberculoma in 2, inflammatory pseudotumor in 2), 11 patients with FN results (including adenocarcinoma in 5, squamous cell carcinoma in 3, carcinoid in 2, adenosquamous carcinoma in 1).

Three patients obtained FN results using both PET/CT and CT; 4/7 FN interpretations on PET/CT were corrected using CT; 8/11 FN interpretations on CT were corrected using PET/CT (Table II).

Preoperative nodal staging was compared with postoperative histopathological staging; 83.33% (35/42) of patients were correctly staged, 9.52% (4/42) of patients were overstaged and 07.14% (3/42) were understaged by PET/CT, with CT values of 52.38% (22/42), 28.57% (12/42) and 19.05% (8/42), respectively (Table III).

Expression of ChoK and PCYT in the lesion and control tissue. According to the result of RT-PCR, in the 35 positive PET patients, the relative expression intensification of ChoK in malignant tissue was 0.69 ± 0.16 (0.31-0.97) and 0.33 ± 0.08 (0.15-0.52) in the control tissue. The difference between them was statistically significant ($Z = -5.16$, $P = 0.000000245$); the relative expression intensification of PCYT in malignant tissue was 0.43 ± 0.15 (0.15-0.67) and 0.23 ± 0.08 (0.12-0.42) in the control tissue. The difference between them was also statistically significant ($Z = -4.92$, $P = 0.000000887$). There were 29 (82.86%) patients with ChoK overexpression and 26 (74.29%) patients with PCYT overexpression (Figs. 1-3).

In the 7 negative PET patients, the relative expression intensification of ChoK in malignant tissue was 0.44 ± 0.08 (0.37-0.60) (Fig. 4) and 0.36 ± 0.12 (0.19-0.52) in the control tissue. The difference between them had no statistical significance ($Z = -1.69$, $P = 0.09$). The relative expression intensification of PCYT in malignant tissue was 0.36 ± 0.15 (0.18-0.52) and 0.34 ± 0.14 (0.15-0.52) in the control tissue. The difference between them also had no statistical significance ($Z = -1.36$, $P = 0.17$). ChoK or PCYT were not overexpressed in these 7 patients.

In the 11 patients with benign disease, the relative expression intensification of ChoK in malignant tissue was 0.38 ± 0.14 (0.18-0.57) (Fig. 5) and 0.31 ± 0.10 (0.17-0.48) in the control tissue. The difference between them was not statistically significant ($Z = -1.43$, $P = 0.15$) the relative expression intensification of PCYT in malignant tissue was 0.33 ± 0.10 (0.19-0.52) and 0.28 ± 0.08 (0.17-0.41) in the control tissue. The difference between them was not statistically significant ($Z = -1.65$, $P = 0.10$). The patients with ChoK overexpression accounted for 27.27% (2 tuberculosis with positive PET result, 1 inflammatory pseudotumor with positive PET result) and the patients with PCYT overexpression accounted for 18.18% (1 tuberculosis with positive PET result, 1 inflammatory pseudotumor with positive PET result).

Correlation between the expression of ChoK, PCYT and SUVmean. According to the Pearson's correlation analysis, in the 35 patients with positive PET results, both the expression levels of ChoK and PCYT were positively correlated with the SUVmean ($r = 0.518$, $P = 0.001$, $r = 0.37$, $P = 0.029$) (Figs. 6 and 7).

Correlation between Ki-67 index and SUVmean. The Ki-67 index of 35 malignant patients with positive PET results are $41.29 \pm 15.59\%$ (16%-83%) (Fig. 8). According to the Pearson's correlation analysis, the Ki-67 index is positively correlated with the SUVmean ($r = 0.505$, $P = 0.002$) (Fig. 9).

Discussion

CH-PET/CT and CT for detection of non-small lung cancer (NSCLC). CT provides precise anatomic details with high spatial resolution, while PET reflects the rate of the tumor cell duplication or activity of cell metabolism. PET/CT, combined together is more useful for diagnosing a disease than either CT or PET alone. ^{11}C -choline PET has several advantages over FDG PET. i) Patients do not have to fast before examination; ii) radiation exposure from ^{11}C -CH is less than that from ^{18}F -FDG because the half life is much shorter (20 vs. 120 min); and ii) less time

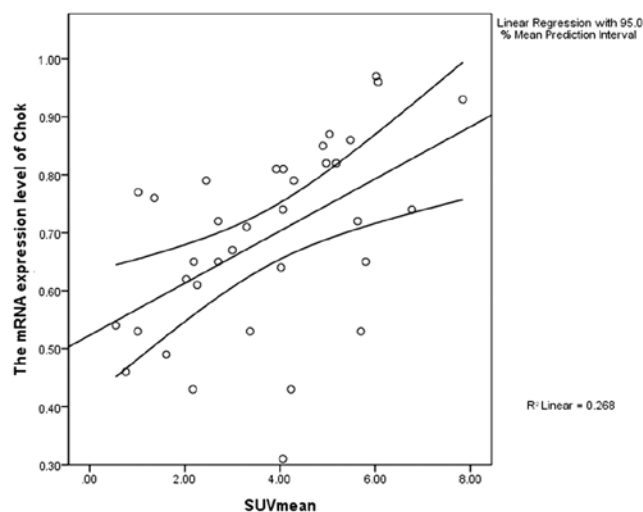


Figure 6. Correlation between SUVmean and expression of ChoK in lung cancer cells.

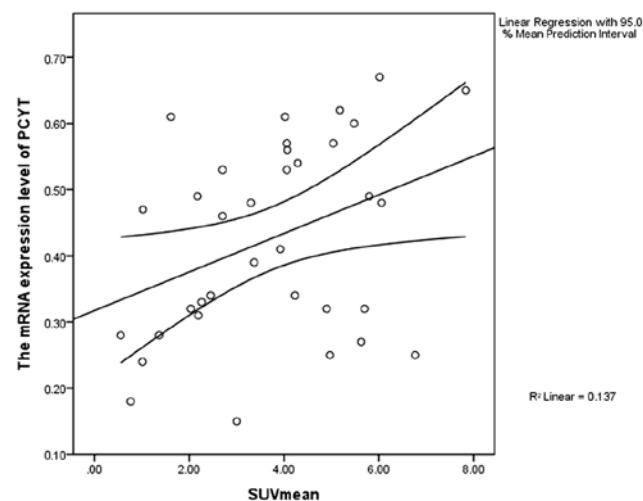


Figure 7. Correlation between the SUVmean and the expression of PCYT in lung cancer cells.

is required for the examination (20 min for CH-PET vs. 90 min for FDG PET). However, Choline is still not a specific tracer for cancer cells. ^{11}C -choline PET also has the defect of FP and FN results (6,7). Granuloma cells undergo active proliferation and therefore need plenty of choline for cell membrane synthesis. In this study, two of the three FP lesions were tuberculoma and one was an inflammatory pseudotumor. The metabolism of choline in tumor cells with high differentiation or low malignant degree is slow. These types of cancers, such as alveolar cancer, usually appear as FN. In this study, 2 of the 3 alveolar cancer appeared as FN. As a result of the high SUV of inflammatory pseudotumors, the low SUV of high differentiated malignancies and the precise anatomic details provided by CT and thin-layer CT, the results of our study revealed that CH-PET is not superior to CT for diagnosing lung cancer.

Diagnosis of metastatic lymph nodes demonstrates the advantage of using PET-CT (3,8). The morphological difference

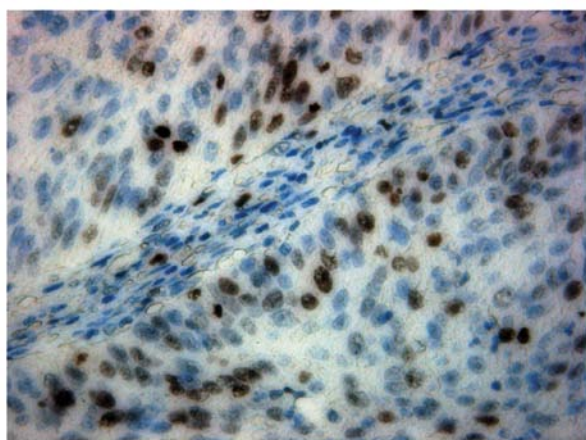


Figure 8. Squamous carcinoma (x400 HP field), Ki-67 index is 41%.

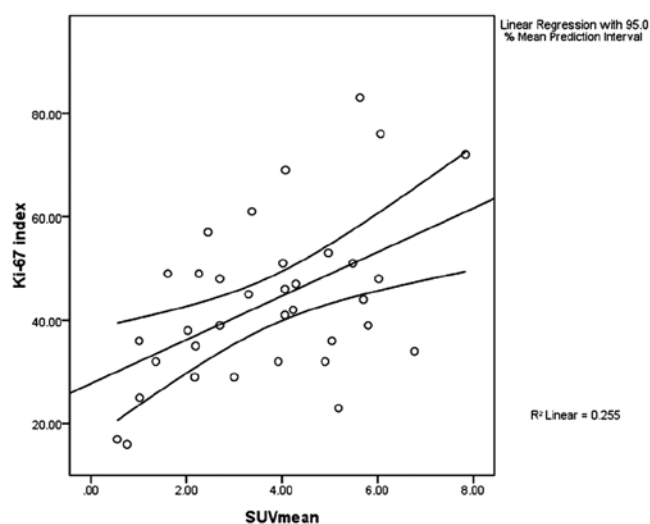


Figure 9. Correlation between the Ki-67 index and the SUVmean.

between benign and malignant lymph nodes is not obvious. Standard diagnostic CT depends on the length of the short diameter of the lymph nodes, that negates a spatial resolution advantage over CT. The benign lymph nodes are commonly caused by chronic inflammation and are seldom caused by granuloma with exuberant metabolism. Thereby PET-CT may distinguish benign and malignant lymph nodes through radiotracer accumulation. According to Hara *et al* (9), CH-PET may be superior to FDG-PET in diagnosing lymph node metastasis; however, choline is not a specific cancer tracer. Especially for granulomatous lymph nodes, owing to the exuberant metabolism of macrophage, uptake of choline is increased and the accumulation of the radiotracer in granulomatous lymph nodes becomes more obvious. This leads to the FP result of choline PET-CT in the diagnosis of lymph node metastasis. In addition, for small lymph nodes, especially <0.5 cm in diameter, uptake of the radiotracer is low, representing a FN result. When comparing a CT diagnosis of a malignant lymph node when the diameter is <1 cm, PET-CT possesses a low FN rate and a high NPV. In this study, when comparing the preoperative N to the pathological

N staging, the accuracy of CH-PET was 83.33% (35/42); 9.52% (4/42) were overstaged and 7.14% (3/42) were understaged. While the accuracy of CT was 52.38% (22/42), 28.57% (12/42) were overstaged and 19.05% (8/42) were understaged.

Correlation between CH uptake and the expression levels of ChoK and PCYT. Choline metabolizes *in vivo* through three pathways (10). The first is phosphorylation. ChoK catalyses the phosphorylation of choline to produce phosphorylcholine, which is transformed into cytidine diphosphate choline in the presence of PCYT and cytidine triphosphate. Finally cytidine diphosphate choline is converted to phosphatidylcholine (lecithin). ChoK and PCYT are two key enzymes of choline phosphorylation. The upregulation of both the activity and expression of these two enzymes promotes lecithin synthesis which is indispensable for tumor proliferation. The second pathway is acetylation. Choline acetyltransferase catalyses the reaction of acetyl coenzyme A with choline to produce acetylcholine. The third pathway is oxidation. Choline is oxidized to form betaine. Continuous cell division undergoes phases G1→S→G2→M in order to complete a proliferation cycle. Lecithin is a necessary component of the cell membrane. Similar to DNA replication, it takes double the amount of time to accumulate in order to meet the needs of the synthesis of cell membrane proliferation (11). The active membrane synthesis of tumor cells leads to a great amount of choline transformed into phosphatidylcholine, thus the activity and expression of ChoK are upregulated correspondingly. The upregulation of ChoK activity results in the increase of its substrate (choline). These two factors cause increases in the utilization rate of choline simultaneously (12). Combined with choline, ^{11}C accumulates more rapidly in tumor cells than in normal cells. Therefore, we may distinguish a malignant from a benign disease through measuring the uptake level of ^{11}C -choline. PCYT is another key enzyme in the biosynthesis of lecithin and its activity also affects cell proliferation (13).

In this study, the expression levels of ChoK in 35 lung cancer tissues with positive PET results were upregulated compared with the normal tissue. This suggests that phosphorylation of choline in lung cancer tissue with positive PET results is enhanced. Phosphorylation of choline may be the foundation of ^{11}C -choline PET imaging. Moreover, the expression of PCYT in lung cancer tissue is also upregulated; thus, illuminating the enhanced choline phosphorylation.

In the 35 lung cancer tissue with positive PET results, the expression of ChoK positively correlated with the SUVmean and PCYT. This suggests that the uptake of choline is correlated with the metabolism of choline. The acceleration of cell membrane biosynthesis results in an exuberant metabolism of choline. Marked with ^{11}C , choline which accumulates in increased amounts in cancer cells, will be displayed in the PET images.

In the three benign tissue with positive PET results (2 tuberculoma and 1 inflammatory pseudotumor), ChoK was overexpressed. Two (1 tuberculoma and 1 inflammatory pseudotumor) also displayed an overexpression of PCYT. This may indicate that choline in the granuloma is at a high metabolic state; thus, resulting in a FP PET result.

In the seven lung cancer tissues with negative PET results, there was no overexpression of ChoK or PCYT. The expres-

sion levels of ChoK and PCYT had no significant differences between 11 benign and the normal tissues. This suggests that the synthesis of the benign tumor cell membrane is slow and the choline metabolism is at a low state. A small accumulation of choline in the cells leads to a FN PET result.

Correlation between CH uptake and Ki-67 expression in lung cancer. Uncontrolled cell proliferation is the primary hallmark of cancer. The rate of cell division is an important prognostic characteristic of malignancies, and a number of important anticancer treatments are aimed specifically at inhibiting tumor cell growth. A number of studies have demonstrated that the proliferative activity as determined by the expression levels of Ki-67 (14,15) are important prognostic factors in NSCLC, and have found significant correlations between the SUV of FDG or FLT and Ki-67 proliferation scores (16-18). It has been reported that FDG uptake is more valuable than Ki-67 expression for predicting the prognosis of patients with resected NSCLC (19). These differences in Ki-67 scores are nearly identical, implying that differences in NSCLC tumor cell proliferation may give rise to commensurate differences in tumor glucose metabolism (20). Therefore, exploring the correlation between the proliferative activity of cancer cells through Ki-67 staining and proliferation imaging using CH-PET may be helpful to further elucidate the mechanism and significance of CH-PET imaging.

Thirty-five malignancies with positive PET results displayed a Ki-67 positive expression. The Ki-67 index was $41.29 \pm 15.59\%$ (16-83%) Pearson's correlation analysis showed a positive correlation between Ki-67 and SUVmax ($r=0.505$, $P=0.002$). Our results showed that the elevated uptake of CH in lung cancers, as assessed by the SUVmean in PET, is correlated with expression of a cell cycle-related molecular biomarker, Ki-67. Measuring SUV is a simple and non-invasive method to determine the cancer cell proliferation potential, which reflects the malignant grade of the tumor, and the determination of the SUVmean in a primary lesion may be useful for selecting patients qualified for organ-sparing limited surgery or radiotherapy for a number of lung cancers.

In conclusion, CH-PET/CT is not superior to CT in diagnosing pulmonary nodules. For lymph node diagnosis, CH-PET/CT is superior to CT, offering more accurate staging and assisting in therapy. There were significant correlations between the SUV of CH and Ki-67 proliferation scores. A correlation exists between the mechanism of CH-PET imaging and the expression of Chok and PCTY in tumor cells.

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