# Feasibility research of combined assay with serum tumor marker and low dose CT on the early diagnosis of lung cancer.

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#### Abstract

Purpose: To explore the feasibility of combined assay with serum tumor marker and low dose CT on the early diagnosis of lung cancer.

Method: 60 newly diagnosed lung cancer patients (lung cancer group), 60 benign lung disease patients (benign group) and 60 healthy subjects (health group) were included. All participants were diagnosed by serum tumor marker and low dose CT.

Result: There are few notable differences in the imaging situation and image quality through CT examination of lung cancer with different volume, P>0.05. Radiation dosage of the ultra-low dose group is obviously lower than that of the other two groups, P<0.05. The level of NSE (Neuron specific enolase), CEA (carcinoembryonic antigen), PTN (Human Pleiotrophin) and Cyfra21-1 among the lung cancer group is significantly higher than that among the benign group and the health group. With the separate detection of NSE, CEA, PTN and Cyfra21-1, the combined measurement of tumor markers and serum tumor marker measurements with low CT dose, positive rate of the lung cancer group detected by the result is considerably higher than that of the benign group, P<0.05.

Conclusion: The combined assay with serum tumor marker and low dose CT proves to be highly feasible on the early diagnosis of lung.

Keywords: The early diagnosis of lung, Low CT dose, Serum tumor marker measurements, Feasibility.

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## Introduction

Lung cancer is one of common clinic neoplasm with higher mortality [1] and it has been a big Challenge in Facing the Lung Cancer Epidemic and Treating Advanced Disease in Latin-America [2]. According to some reports, the mortality of lung cancer is even up to 4.4 and the median follow-up time was 20.5 y [3]. It was mentioned that the continuing struggle against lung cancer epidemic should be focused on early stage diagnosis, minimally invasive treatment strategies and effective prevention [4]. In recent years, the key point calling for the current social attention is to actively control the incidence of lung cancer and reduce the death of patients and Focus must be placed on the increasing improvement of early clinic diagnosis effects of the lung cancer as mentioned before. CT, as one efficient diagnosis method, has been used for many vears. However, the dose of computed tomographic Screening maybe also related to lung cancer. One reported in New Medical Journal has reported that low does computed

tomographic screening can reduce the mortality of lung cancer [5,6]. However, the low dose CT scan will also affect the feasibility of diagnosis. As consequence, this research was aimed to combine the assay with serum tumor marker and low dose CT on the early diagnosis of lung cancer and expect to provide more effective early diagnosis of lung cancer. A retrospective analysis based on the detailed diagnosis process is conducted below.

# **Materials and Methods**

#### General information

Sixty newly diagnosed lung cancer patients were selected from hospital (lung cancer group). 60 benign lung disease patients (benign group) and 60 healthy participants (health group) registered in the hospital in December from the year of 2014 to 2016 as the study objects. Inclusive Criteria: lung cancer and benign lung disease patients are diagnosed by pathological examination; all cases should take a voluntary participation in various examinations during the research. Exclusive Criteria: Patients with severe heart, liver, kidney or spleen and stomach disease; patients with blood or immune system disease; patients with other tumor diseases and patients with conscious disturbance or with the difficulty in cooperating on research [7]. There is a male and female ratio of 33:27 and the age range from 42 to 75 with an average age of 66.1 to 48.7 in the lung cancer group, a male and female ratio of 32:28 and the age range from 42 to 75 with an average age of 66.3to 48.7 in the benign group and a male and female ratio of 31:29 and the age range from 42 to 75 with an average age of 66 to 48.8 in the health group. Make a test of isolated specimens on the general baseline information of individuals from the above three groups and make a comparison in between. It turns out P>0.05 and the comparison is valid. This research was approved by the ethical committee of Zhejiang cancer hospital.

#### Method

All participants engage in combined assay with serum tumor marker and low dose CT (NSE, CEA, PTN, Cyfra21-1) and the lung cancer group are examined by CT with conventional dose, low dose and ultra-low dose. Spiral CT systems of Brilliance, Nano 64 rank and 128 tier and produced by Royal Philips are applied to this conduction of CT examination. The CT examinations with conventional dose, low dose and ultra-low dose are conducted with the scanners tier thickness of 5.0 and pitch of 1.0; voltage and current respectively reach 120 kv and 120 mAs on the condition of conventional dose, 120 ky and 30 mAs on the condition of low dose and 90 kv and 30 mAs on the condition of ultra-low dose. The serum tumor marker measurements are performed under fasting state in the early morning, Collect 5 ml venous blood from the patients with conventional centrifugal separation for 5 min at the rate of 3000 r/min. Take serum to conduct a test and all patients are examined with AU680 Automatic Biochemistry Analyzer and

relevant corresponding kits (Beckman Coulter, USA). Immunoturbidimetry is adopted to the detection. All detecting tasks should be undertaken in comply with operation specification and manual.

## **Observation index**

Do statistical analysis on the imaging situation, image quality and radiation dosage with different doses. The quality of image depends on state of artifact. The excellent result turns out to be no artifact at all, and the good be with artifact but without effects on the observation while the terrible are with artifact making effects on observing.

Does statistical analysis on the testing result and positive conditions of tumor marker from members of the above three groups. Any case with single one positive indicator is diagnosed to be positive. The standard index for the positive is: NSE  $\geq$  18 ng/ml; CEA  $\geq$  3.0 ng/ml; PTN  $\geq$  425 pg/ml; Cyfra21-1  $\geq$  3.3 ng/ml.

## Statistical method

Conduct data processing and analysis through SPSS19.0. Testing results of radiation dosage and tumor marker are demonstrated with standardized mean difference ( $\bar{x} \pm s$ ), and "t" represents "test". Testing results of CT with different doses and the proportion of positive are marked by " $\chi^2$ ", and the difference was statistically significant if P<0.05.

#### Result

There are few notable differences in the imaging situation, image quality and radiation dosage through CT examination of lung cancer with different volume, P>0.05. Radiation dosage of the ultra-low dose group is obviously lower than that of the other two groups, P<0.05, t=40.607, 25.560 and the difference was statistically significant (P<0.05, Table 1).

**Table 1.** Analysis on the imaging situation, image quality and radiation dosage through CT examination of lung cancer with different dose (n (%);  $\bar{x} \pm s$ ; n=60).

Group	Cavity	Calcification	Pleural indentation	Lobular	Spiculation	Image quality	Radiation dosage
Conventional dose	18 (30.0)	9 (15.0)	18 (30.0)	44 (73.3)	13 (21.7)	Excellent	14.1 ± 2.5
Low dose	19 (31.7)	9 (15.0)	19 (31.7)	45 (75.0)	14 (23.3)	Excellent	2.3 ± 0.3
Ultra-low dose	20 (33.3)	10 (16.7)	19 (31.7)	45 (75.0)	15 (25.0)	Excellent	0.9 ± 0.3

## Analysis on tumor marker testing result and positive conditions from members of the three groups

NSE, CEA, PTN and Cyfra21-1 levels of the lung cancer group are comparatively higher than those of the benign group (t=21.688, 12.357, 16.912, 32.176) and the health group (t=36.497, 41.367, 74.942, 45.286), the NSE, CEA, PTN, Cyfra21-1 levels of benign group are significantly higher than those of the health group, t=16.823, 29.464, 52.615, 33.308. The difference was statistically significant (P<0.05, Table 2).

**Table 2.** Analysis on tumor marker testing result and positive conditions from members of the three groups  $(\bar{x} \pm s; n=60)$ .

Group		Nse	Cea	Ptn	Cyfra21-1
Lung group	cancer	41.7 ± 6.3*#	24.8 ± 4.1*#	543.2 ± 48.3 <sup>*#</sup>	17.8 ± 2.6 <sup>*#</sup>

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Benign group	$20.5 \pm 4.2^{*}$	$16.2 \pm 3.5^{*}$	395.6 ± 47.3	6.5 ± 0.8 <sup>*</sup>	
Health group	10.1 ± 2.3	2.8 ± 0.4	70.3 ± 7.5	$2.2 \pm 0.6$	
Note: compare conventional g	ed with the co roup <sup>#</sup> P<0.05.	nventional group	o; *P<0.05 co	ompared with	the

With the separate detection of NSE, CEA, PTN and Cyfra21-1, the combined measurement of tumor markers and serum tumor

marker measurements with low CT dose, positive rate of the lung cancer group detected by the result is considerably higher than that of the benign group, P<0.05. The positive ration of the combined measurement of tumor markers with low CT dose is apparently higher than that of serum tumor marker combination measurements,  $\chi^2$ =9.259, 4.043. The difference was statistically significant (P <0.05, Table 3).

**Table 3.** Analysis on the positive indicator from the two groups under the serum tumor marker measurements and the combined measurement of tumor markers with low CT dose ( $\bar{x} \pm s$ ; n=60).

Group	Nse	Cea	Ptn	Cyfra21-1	STMM	CMTMLC
Benign group	6 (10.0)	17 (28.3)	13 (13.7)	5 (8.3)	23 (38.3)	34 (56.7)
Lung cancer group	40 (66.7)*	44 (73.3) <sup>*</sup>	44 (73.3) <sup>*</sup>	43 (71.7)*	49 (81.7)*	59 (98.3) <sup>*</sup>
X <sup>2</sup>	40.752	24.307	32.114	50.139	23.472	29.869
Р	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Note: Compared with the benign group \*P<0.05; STMM: The Serum Tumor Marker Measurements; CMTMLC: The Combined Measurement of Tumor Markers with Low Ct Dose.

## Discussion

Effected by various facts like poor living environment, bad living habit and infection, the clinical incidence and fatality of the lung cancer are increasingly higher. It causes the highest death rate in malignant tumor complications [8]. Many current study results prove that the important way to lengthen patients' survival time is to conduct early diagnosis and therapy. For patients with early 5 y surgery, it is more than 80% in possibility to survive. Thus, constantly increasing the effects of early clinic diagnosis of the lung cancer remains the key to improve prognosis in patients. Clinical manifestation of the lung cancer at the early stage is not obvious and it bears no specificity, leading to poor diagnosis effects [9-11]. CT scan is a common way to make clinical detection of the lung cancer. The process is simple and convenient with non-inversion. The clear imaging enables to timely realize the pictures of patients' lungs, thus helping to diagnose the pulmonary diseases [12-14]. According to this research, the detection under three kinds of doses bears no significant difference in the testing results of imaging situation and image quality. But it turns out that the radiation dosage of the ultra-slow dose group is lower. This tells that the implement of CT examination with low dose is of higher security [15,16]. Serum tumor marker is a common test index for clinical diagnosis of tumor diseases. It may experience change at early appearance of tumors so that it is helpful for doctors to diagnose early [17-20]. In this research, the tumor maker level of the lung cancer patients is obviously higher than that of the benign group and the health group, and the positive ration of the combined measurement of tumor markers with low CT dose is higher than that of the serum tumor marker. This illustrates that the conduction of combined measurement of tumor markers with low CT dose has significant effectiveness and helps to strengthen effects of diagnosis.

Above all, the combined assay with serum tumor marker and low dose CT proves to be of high feasibility on the early diagnosis of lung. It is able to effectively increase diagnosis effects with high value of application.

#### References

- Zhang Y, Hong Q, Shi W. The application of low-dose spiral ct in lung cancer screening. Chinese Med J 2013; 93: 3011-3014.
- Ohno Y, Koyama H, Dinkel J. Lung cancer. Med Radiol 2016; 179-216.
- 3. Raez LE, Santos ES, Rolfo C. Challenges in facing the lung cancer epidemic and treating advanced disease in Latin America. Clinical Lung Cancer 2016.
- 4. Marcus PM, Bergstralh EJ, Fagerstrom RM. Lung cancer mortality in the Mayo Lung Project: impact of extended follow-up. J Nat Cancer Inst 2000; 92: 1308-1316.
- 5. Pompeo E. The continuing struggle against lung cancer epidemic. Focusing on early stage diagnosis, minimally invasive treatment strategies and effective prevention. Biomed Prev 2016; 20-21.
- National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 2011; 2011: 395-409.
- He Y, Wang WF. The value of chest computed tomography (CT) and serum tumor markers detection for lung cancer screening. Chinese J Health Manag 2013; 7: 325-328.
- 8. Nie XW, He Y. Value of multiple combined PET/CT inspection in the diagnosis of lung cancer. J Clin Pulm Med 2014; 19: 701-703.
- 9. Liu F, Hong Q, Shi H. The validity of 18 fluorodeoxyglucose positron emission tomography (18

FDG-PET) in the early diagnosis of lung cancer. Chinese Med J 2013; 93: 3019-3022.

- Wang Z, Wang H, Liu H. The application of PET/Ct combined detection of tumor markers in diagnosisof lung cancer. J Ningxia Med Coll 2015; 37: 338-340.
- Dang Y, Shang S. Diagnosis of 64 rank CT combined serological examination for non-small cell lung cancer with mediastinal lymph node metastasis. J Kunming Med Univ 2014; 35: 125-128,135.
- Cheng K, Ge L, Fu Z. Relevant research of 18F-FDG PET/CT Suvmax value of the lung cancer and clinnical factors and tumor makers. Chinese J Cancer Prev Treat 2016; 23: 884-887.
- Zhuhui LZ. Application research of PET/CT combined CEA, CA125, CYFRA21-1 detection on differential diagnosis of terminal lung cancer. J Guangxi Med Univ 2016; 33: 495-497.
- Zheng Y, Huang XS. The diagnostic value of PET/CT combined tumor markers for pulmonary cancer. Zhejiang J Traum Surg 2016; 21: 417-419.
- 15. Li F, Zou N, Hu H. The study of combined detection of low dose CT and 4 tumor markers on screening for population with high risk of lung cancer. Jiangxi Med J 2015; 29: 384-387.
- 16. Jiang X. The clinical value of diagnosis of lung cancer of a wide variety of tumor markers associated with CT

examination. Medical Aesthetics Beauty Ten-Day 2015; 33: 290.

- 17. Yang J. The value of 64-MSCT and combined assay with serum tumor marker in the lung cancer diagnosis. Chinese J Coal Indus Med 2014; 17: 361-363.
- 18. Wang M, Zhou F, Gan X. The value of 18F-Naf PET-CT and combined assay with serum tumor marker on the early diagnosis of lung cancer bone metastasis. J Luzhou Med Coll 2015; 38: 375-378.
- Zhen Y, Meng ZJ. Correlative research of peripheral lung cancer ct feature and serum tumor marker. Hebei Med J 2014; 36: 3404-3406.
- Yang Z, Ding XM. Expression Level Analysis of CEA, NSE, SCC-Ag and CYFRA21-1 before and after Chemotherapy. J Sichuan Univ 2014; 51: 177-182.

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