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*Original Article*

# Clinical values of Lung CARE software in qualitative diagnosis of solitary pulmonary nodule

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**Abstract:** Objective: To evaluate the clinical value of Lung CARE software in the diagnosis of benign or malignant solitary pulmonary nodules (SPN). Methods: A total of 96 patients with SPN received treatment from January 2010 to December 2011 were selected. The patients were performed with CT scan and follow-up visits until diagnosis confirmed. According to 96 patients' measurement data, the diagnostic efficiencies of calculating doubling time (DT) by measuring maximum diameters and by Lung CARE software were compared. Sixty-six of them were performed with enhanced scan. They were selected as subjects to compare the diagnostic efficiency of measuring enhancement values by cross-section method and Lung CARE software. Results: The sensitivity (96.0%), specificity (91.3%) and accuracy (93.8%) of DT by Lung CARE software calculating volume were superior to those by maximum diameter method (84.0%, 78.3%, 81.3%) and the *P* values were 0.012, 0.007, 0.008, respectively. The sensitivity (85.7%) and accuracy (84.8%) of measuring enhancement values by Lung CARE software were superior to those by cross-section method (81.0%, 81.8%), the *P* values were 0.033, 0.029 respectively. Conclusion: Using Lung CARE software to measure volume and to calculate DT provides a better efficiency. Also, it is more convenient for measuring enhancement values. Thus, the work efficiency of radiologists can be improved.

**Keywords:** Solitary pulmonary nodules, multi-slice spiral CT, volume enhancement

## Introduction

Solitary pulmonary nodule (SPN) can be seen in lung film with circular or close to circular shadows and the diameter is below 30 mm with high density, and the patients didn't attack by diseases like mediastinal lesions or pulmonary atelectasis [1]. The clinical symptoms of SPN are not obvious. The smaller the nodules are, the less typical manifestation of morphology in image will be. So, at present, identifying the nature of the nodules becomes a tough problem needed to be solved in clinic [2]. Doubling time (DT) is a crucial attribute of nodules. If the DT of nodules, especially small nodules, could be calculated accurately by using software on the basis of imaging detection, that would be very important clinical value for the diagnosis of benign or malignant nodules [3, 4]. Lung Computer-Aided Reliability Estimation (Lung CARE) is a kind of software that can be combined with CT and analyze the shape and the volume of pulmonary nodules, so that relatively accurate DT can be obtained by calculating three-dimensional angle and other data [5-9]. In this study, we evaluated the clinical values of Lung CARE software in the diagnosis of SPN.

## Materials and methods

### *General information*

A total of 96 patients with SPN received by our hospital from January 2010 to December 2011 were selected as subjects. A total of 96 patients were selected as subjects to compare the diagnostic efficiencies of calculating DT by maximum diameter method and Lung CARE software. Sixty-six of them were performed with enhanced scan and were selected as subjects to compare the diagnostic efficiency of measuring enhancement values by cross-section method. Patients with surgical histories and suffered from other diseases were excluded.

**Table 1.** The difference in DT calculated by different methods (malignant tumors, n=24)

| Methods | DT ($\bar{X}$ ± sd, days) | t | P |
|---|---|---|---|
| Maximum diameter | 142.54±39.42 | 9.844 | 0.017 |
| Lung CARE software | 104.32±23.11 | | |

**Table 2.** Comparison of diagnostic efficiencies of measuring maximum diameter method and software method in calculating DT to differentiate malignant and benign SPN

| Methods | Sensitivity (%) | Specificity (%) | Accuracy (%) |
|---|---|---|---|
| Maximum diameter | 84.0 | 78.3 | 81.3 |
| Lung CARE software | 96.0 | 91.3 | 93.8 |
| P | 0.012 | 0.007 | 0.008 |

Patients and their families were informed of this study and participated in this study voluntarily. This study was in line with the requirements of the Ethics Committee of our hospital and was approved by the Ethics Committee.

*Inspection methods*

Ninety-six patients were all performed with conventional CT scan; their chests were scanned with conventional mode, device model: SIEMENS SOMATOM Sensation 16 CT machine. Scanning parameters: 120 kV, preset 120 emAs, 0.5 s/circle, collimation 0.75 mm, collection 16*0.75 mm, pitch 1.15, matrix 512*512, FOV around 350 mm*350 mm.

Enhanced scan: 80 ml iohexol was injected through elbow vein with 3 ml/s. The scan delayed 30 to 40 seconds.

Routine reconstruction: reconstruction thickness was 8 mm, interval was 8 mm and convolution values of lung and mediastinum were B70f (sharp) and B40f (smooth) respectively. Patients with SPN were reconstructed with reconstruction interval of 0.70 mm, reconstruction thickness of 0.75 mm and convolution value of B70f. To reduce the influence of reconstruction algorithm on the measurement and comparison of CT value, in patients performed with enhanced scan, plain scan and enhanced scan were all reconstructed using B70f. After that, Lung CARE software was used for measuring SPN, and the data were recorded. At last, the conventional scanning images, thin layer images (the thin layer images mentioned here and later all referred to images with interval 0.70 mm and thickness 0.75 mm) as well as Lung CARE software measurement data and images were imported into picture archiving and communication system.

*Diagnostic methods*

*Methods of confirming diagnosis:* Methods for confirming diagnosis included that pathology confirmed by surgery or puncture; anti-inflammatory treatment was effective; the size of nodules didn't increase during the follow-up in two years; malignant primary lesions were proved by surgical pathology; SPN found in lung significantly increased to metastatic tumor in the follow-up period. All the included patients were given follow-up visits until confirmed diagnosis.

*The diagnostic method of DT and enhancement values:* The methods included the appearance of lobulated sign, spicule sign, inhomogeneous density, irregular edge of lesions, vacuole sign, pleural indentation sign and vessel convergence sign of bronchus. According to the study conducted by Yankelevitz et al., the pathological nodules, with DT in 30-170 days, were recorded as malignant [10]. The enhancement value of malignant nodules was 20-60 HU.

*Indexes*

The DT was calculated by measuring maximum diameter and Lung CARE software; the sensitivity, specificity and accuracy of measuring enhancement value were performed by cross-section method and by Lung CARE software. The indexes were used to analyze the clinical significance of using Lung CARE for the diagnosis of SPN.

*Statistical methods*

The results were statistically analyzed by SPSS-17.0 software. The measurement data were expressed as mean ± standard deviation ($\bar{X}$ ± sd), and the between-group comparison was performed by t-test. The enumeration data were expressed as percentage, and the between-group comparison was performed by chi-square test; the Youden index was calculated by three-dimensional paired chi-square test for the comparison of diagnostic efficiencies. Statistical results (differences) of $P<0.05$ were statistically significant.

**Table 3.** The three-dimensional paired chi-square test of the 2 methods on calculating DT to diagnose the benign and malignant nodules

| Three-dimensional paired chi-square test | | True positive patients Maximum diameter method | | | True negative patients Maximum diameter method | | |
|---|---|---|---|---|---|---|---|
| | | Positive | Negative | Total | Positive | Negative | Total |
| Lung CARE software method | Positive | 41 | 7 | 48 | 1 | 3 | 4 |
| | Negative | 1 | 1 | 2 | 9 | 33 | 42 |
| | Total | 42* | 8 | 50 | 10# | 36 | 46 |

Note: The Youden index of measuring maximum diameter method was 0.523 and the Youden index of Lung CARE software method was 0.849. The maximum diameter method suggested that in true positive patients, when compare the positives with negatives, *P<0.05; in true negative patients, when compare the positives with negatives, #P<0.05.

**Table 4.** Comparison of the difference in enhancement values between the two methods

| Methods | Enhancement values (HU) |
|---|---|
| Cross-section | 47.59±9.28 |
| Lung CARE software | 58.47±11.43 |
| P | 0.023 |

**Table 5.** Comparison of diagnostic efficiencies of cross-section and Lung CARE software in measuring enhancement values to differentiate malignant and benign SPN

| Methods | Sensitivity (%) | Specificity (%) | Accuracy (%) |
|---|---|---|---|
| Cross-section | 81.0 | 83.3 | 81.8 |
| Lung CARE software | 85.7 | 83.3 | 84.8 |
| P | 0.033 | 0.681 | 0.029 |

## Results

*Basic information*

In the 96 patients selected for the comparison of diagnostic efficiencies of calculating DT value by the maximum diameter and by Lung CARE software, 53 were male and 43 were female, aged 39-64 years, with mean age of 51.29±3.48 years; among them, there were 72 benign cases and 24 malignant cases. In the 66 patients performed with enhanced scan, there were 37 males and 29 females, aged 41-67 years, with mean age of 52.31±4.12 years; among them, there were 49 benign cases and 17 malignant cases.

*Difference of DT calculated by different methods*

The DT obtained by Lung CARE software measuring volume was significantly smaller than that by measuring maximum diameter (t=9.844, P=0.017). See **Table 1**.

*The comparison of diagnostic efficacies of differentiating malignant and benign SPN by measuring maximum diameters and by software calculating volumes to calculate DT*

The sensitivity (96.0%), specificity (91.3%) and accuracy (93.8%) of calculating DT by Lung CARE software were all higher than those by measuring maximum diameters method (84.0%, 78.3%, 81.3%). Thus, the diagnostic efficacy of Lung CARE software was better. The *P* values were 0.012, 0.007, 0.008 respectively, and the differences were statistically significant. See **Table 2**.

Among true positive patients, measuring maximum diameters method suggested that the difference of positive (42 cases) and negative (8 cases) was statistically significant (P<0.05). However, in true negative patients, there were 10 cases of positive, and 36 cases of negative with significant difference (P<0.05). See **Table 3**.

*Comparison of diagnostic efficiencies of differentiating malignant and benign SPN by cross-section method and Lung CARE software to measure enhancement values*

The enhancement values measuring by Lung CARE software were significantly higher than those by cross-section method (P=0.023). The sensitivity (85.7%) and accuracy (84.8%) of measuring enhancement values by Lung CARE were higher than those by cross-section method (81.0%, 81.8%). Thus, the diagnostic efficiency of Lung CARE software was better. The *P* values were 0.033, 0.029 respectively, and the differences were statistically significant. But

**Table 6.** The three-dimensional paired chi-square test of the 2 methods on calculating enhancement values to diagnose the benign and malignant nodules

| Three-dimensional paired chi-square test | | True positive patients Cross-section method | | | True negative patients Cross-section method | | |
|---|---|---|---|---|---|---|---|
| | | Positive | Negative | Total | Positive | Negative | Total |
| Lung CARE software method | Positive | 33 | 3 | 36 | 1 | 3 | 4 |
| | Negative | 1 | 5 | 6 | 3 | 17 | 20 |
| | Total | 34* | 8 | 42 | 4 | 20# | 24 |

Note: The Youden index of the cross-section method was 0.519 and the Youden index of Lung CARE software was 0.658. Cross-section method showed that in true positive patients, when compare the positives with negatives, *P<0.05; in true negative patients, when compare the positives with negatives, #P<0.05.

the difference of the specificity between the two methods was not remarkable; see **Tables 4** and **5**. The difference of cross-section of positive and negative ratio was statistically significant. See **Table 6**.

## Discussion

Radiograph reading of traditional CT diagnosis mainly depends on people. The results were judged by doctors' subjective sense leading to comparatively large deviation. The combination of CT and Lung CARE software can transform that into quantitative measurement data to obtain accurate and objective diagnostic criteria [11]. Study found that the accuracy of the detection can be improved by using computer analysis techniques to calculate the data measured by CT [12]. And the deviation can be narrowed down to sub-cubic millimeter; therefore, the advantages of radiograph reading by Lung CARE were more obvious than by people [13].

The results of this study showed that through Lung CARE calculating volume to calculating DT for the diagnosis of nodules' nature, the sensitivity (96.0%), specificity (91.3%) and accuracy (93.8%) were higher than those data calculated by measuring maximum diameter method (84.0%, 78.3%, 81.3%), with significant differences (all P<0.05). And through Lung CARE calculating enhancement values for the diagnosis of nodules' nature, the sensitivity (85.7%) and accuracy (84.8%) were higher than those data calculated by cross-section method (81.0%, 81.8%), with significant difference (both P< 0.05), but the difference of specificity of the two methods was not obvious. In the aspect of measuring volume, the analysis method Lung CARE was to measure nodules' volume by three-dimensional analysis method and calculate DT values according to the volume calculation formula of DT value, $DT=(\Delta t * \ln 2)/\ln (V_2/V_1)$. Compared with the results of surgical pathological diagnosis, Lung CARE had better accuracy of diagnosis in calculating both DT and enhancement values [14-16].

The traditional method of calculation was to diagnose the pulmonary nodules' shape and volume by simulation. Some scholars held the idea that the structure of pulmonary is complex and it is controversial that whether this method could accurately define the scope of nodules or not [17-21]. The results of this study showed that the accuracy and sensitivity of Lung CARE method were superior to traditional calculation method.

At present, the study of SPN is very important in clinic. The results of this study showed that Lung CARE also had an advantage of accuracy in measuring enhancement values. In theory, the internal blood flow of SPN is not even. Many scholars were only researching blood flow model in a certain level without considering the factor of blood flow in other ways. Hence, big errors were existed. Besides, in the choice of measurement level, there will be some difficulties and divergences in selecting a uniform and accurate level, and it takes a comparatively long time, which is not beneficial to clinical repeated examinations. There were scholars carrying out preliminary researches on nodules' volume enhancement perfusion imaging by using multi-dimension scan and Lung CARE software. Therefore, the volume enhancement study of structures, which have no obvious density unevenness, necrosis, calcification in plain scan, are theoretically feasible and valuable, and Lung CARE pulmonary nodule processing software provides corresponding tool for the study of nodular volume enhancement in this aspect. While the size of samples included in

this study was small, it might impact on the results. So, bigger sample size and deeper research are recommended for future studies.

In summary, Lung CARE software can provide comparatively accurate results of nodules' volume and the DT of nodules, and provide an effective clinical basis for the diagnosis of nodule's nature.

## Disclosure of conflict of interest

None.

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## References

[1] Lin PL, Huang PW, Lee CH and Wu MT. Automatic classification for solitary pulmonary nodule in CT image by fractal analysis based on fractional Brownian motion model. Pattern Recognition 2013; 46: 3279-3287.

[2] Sun T, Wang J, Li X, Lv P, Liu F, Luo Y, Gao Q, Zhu H and Guo X. Comparative evaluation of support vector machines for computer aided diagnosis of lung cancer in CT based on a multi-dimensional data set. Comput Methods Programs Biomed 2013; 111: 519-524.

[3] Zhang R, Wiegmann B, Fischer S, Dickgreber NJ, Hagl C, Kruger M, Haverich A and Zardo P. Simultaneous cardiac and lung surgery for incidental solitary pulmonary nodule: learning from the past. Thorac Cardiovasc Surg 2012; 60: 150-155.

[4] Demir Y, Polack BD, Karaman C, Ozdogan O, Surucu E, Ayhan S, Akkoclu A and Ozdemir N. The diagnostic role of dual-phase (18)F-FDG PET/CT in the characterization of solitary pulmonary nodules. Nucl Med Commun 2014; 35: 260-267.

[5] Sim YT, Goh YG, Dempsey MF, Han S and Poon FW. PET-CT evaluation of solitary pulmonary nodules: correlation with maximum standardized uptake value and pathology. Lung 2013; 191: 625-632.

[6] Shaheen K, Alraies MC and Alraiyes AH. Role of positron emission tomography in the diagnostic workup of solitary pulmonary nodule. South Med J 2012; 105: 676-677.

[7] Kinoshita T, Yoshida J, Ishii G, Hishida T, Wada M, Aokage K and Nagai K. The availability of pre- and intraoperative evaluation of a solitary pulmonary nodule in breast cancer patients. Ann Thorac Cardiovasc Surg 2015; 21: 31-36.

[8] Dale CR, Madtes DK, Fan VS, Gorden JA and Veenstra DL. Navigational bronchoscopy with biopsy versus computed tomography-guided biopsy for the diagnosis of a solitary pulmonary nodule: a cost-consequences analysis. J Bronchology Interv Pulmonol 2012; 19: 294-303.

[9] Soardi GA, Perandini S, Motton M and Montemezzi S. Assessing probability of malignancy in solid solitary pulmonary nodules with a new Bayesian calculator: improving diagnostic accuracy by means of expanded and updated features. Eur Radiol 2015; 25: 155-162.

[10] Yankelevitz DF, Reeves AP, Kostis WJ, Zhao B and Henschke CI. Small pulmonary nodules: volumetrically determined growth rates based on CT evaluation1. Radiology 2000; 217: 251-256.

[11] Zhao L, Tong L, Lin J, Tang K, Zheng S, Li W, Cheng D, Yin W and Zheng X. Characterization of solitary pulmonary nodules with 18F-FDG PET/CT relative activity distribution analysis. Eur Radiol 2015; 25: 1837-1844.

[12] Koyama H, Ohno Y, Seki S, Nishio M, Yoshikawa T, Matsumoto S, Maniwa Y, Itoh T, Nishimura Y and Sugimura K. Value of diffusion-weighted MR imaging using various parameters for assessment and characterization of solitary pulmonary nodules. Eur J Radiol 2015; 84: 509-515.

[13] Farid K, Poullias X, Alifano M, Regnard JF, Servois V, Caillat-Vigneron N and Petras S. Respiratory-gated imaging in metabolic evaluation of small solitary pulmonary nodules: 18F-FDG PET/CT and correlation with histology. Nucl Med Commun 2015; 36: 722-727.

[14] Asano F, Shinagawa N, Ishida T, Tsuzuku A, Tachihara M, Kanazawa K, Yamada N, Oizumi S and Moriya H. Virtual bronchoscopic navigation improves the diagnostic yield of radial-endobronchial ultrasound for peripheral pulmonary lesions with involved bronchi on CT. Intern Med 2015; 54: 1021-1025.

[15] Cohen JG, Reymond E, Lederlin M, Medici M, Lantuejoul S, Laurent F, Arbib F, Jankowski A, Moreau-Gaudry A and Ferretti GR. Differentiating pre- and minimally invasive from invasive adenocarcinoma using CT-features in persistent pulmonary part-solid nodules in caucasian patients. Eur J Radiol 2015; 84: 738-744.

[16] Huang YE, Lu HI, Liu FY, Huang YJ, Lin MC, Chen CF and Wang PW. Solitary pulmonary nodules differentiated by dynamic F-18 FDG PET in a region with high prevalence of granulomatous disease. J Radiat Res 2012; 53: 306-312.

[17] Patel VK, Naik SK, Naidich DP, Travis WD, Weingarten JA, Lazzaro R, Gutterman DD, Wentowski C, Grosu HB and Raoof S. A practical algorithmic approach to the diagnosis and

management of solitary pulmonary nodules: part 1: radiologic characteristics and imaging modalities. Chest 2013; 143: 825-839.

[18] Dabrowska M, Krenke R, Korczynski P, Maskey-Warzechowska M, Zukowska M, Kunikowska J, Orlowski T and Chazan R. Diagnostic accuracy of contrast-enhanced computed tomography and positron emission tomography with 18-FDG in identifying malignant solitary pulmonary nodules. Medicine (Baltimore) 2015; 94: e666.

[19] Cheng CY, Lee KW, Lee CH, Tyan YS, Cheng CY, Wang JJ, Yang CW, Huang WS and Oliver Wong CY. Time sensitivity factor of single pulmonary nodule: a new cancer characteristic metabolic parameter by (18)F-FDG PET. Biomed Res Int 2014; 2014: 830135.

[20] Bertagna F and Giubbini R. F18-FDG-PET/CT standardised uptake value threshold in discriminating benign vs. malignant lesions. Doubts and certainties in the era of evidence-based medicine. Acta Oncol 2012; 51: 122-144; author reply 123-124.

[21] Mizuuchi H, Suda K, Kitahara H, Shimamatsu S, Kohno M, Okamoto T and Maehara Y. Solitary pulmonary metastasis from malignant melanoma of the bulbar conjunctiva presenting as a pulmonary ground glass nodule: Report of a case. Thorac Cancer 2015; 6: 97-100.