

*Full Length Research Paper*

# Clinical analysis of nodular ground- glass opacity appearance of lung cancer on computerized tomography (CT)

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The aim of the study is to investigate the diagnosis and treatment of patients who had appearance of nodular ground- glass opacity (NGGO) on computerized tomographic (CT). We retrospectively analyzed 14 cases who appeared NGGO on thin section CT: Male 5, female 9, aged from 31 to 76 years, average 56.3 years old; NGGO diameter was 1.0 to 3.0 cm, average 2.1 cm. Among all the cases, 12 patients have solid parts in the center, called mixed nodular ground- glass opacity (MNGGO). All the cases accepted operations of lobe resection, and were followed up for 4 to 24 months. The pathologic diagnosis of all the cases were malignant, 3 were adenocarcinoma while 11 were bronchioloalveolar carcinoma. All the cases did not find the metastasis of lymph node or far organ, and were alive in the period of following up. Most of the MNGGO were malignant, and it is better for the patients to receive an operation. For pure nodular ground-glass opacity (PNGGO), we suggested the patients should be followed up for 3 month; if the PNGGO did not absorbed, or even became larger, or started to consolidate, operation should be done as soon as possible.

**Key words:** Lung cancer, nodular ground-glass opacity, operation.

## INTRODUCTION

Lung cancer, whose morbidity and mortality have risen rapidly in recent decades, is the most common malignant primary tumor of lung (Wu et al., 1996). Computerized tomographic (CT) scan is still the first choice in diagnosis for lung cancer. As we all know, most appearance of lung cancer on CT are typical, such as sub lobe, barb, vacuole sign, and pleural indentation sign and so on. However, still some appearance of lung cancer on CT is atypical, nodular ground- glass opacity (NGGO) is the one. The conception and significance of ground- glass opacity (GGO) was proposed by Remy- Jardin and Engeler one by another in 1993 (Engeler et al., 1993; Remy-Jardin et al., 1993). In 1996 (Austin et al., 1996), the American Vocabulary Named Commission defined ground-glass opacity (GGO) as: The vague dense shadow in which bronchus or pulmonary artery can be seen on high-resolution CT. GGO lesion with solid change is called

mixed nodular ground-glass opacity (MNGGO), otherwise known as pure nodular ground-glass opacity (PNGGO). As the extensive use of high-resolution CT and the use of CT for early lung cancer screening, the discovery of covered NGGO gradually increased; problems related to the diagnosis of NGGO cause attention of thoracic surgery and radiologist gradually.

To explore the diagnosis and treatment of NGGO, 14 cases with NGGO appearance on CT were collected from January 2008 to January 2010, and were retrospectively analyzed.

## MATERIALS AND METHODS

14 cases showed NGGO on CT, 5 males, 9 females, aged from 31 to 76 years, an average of 56.3 years. All patients were scanned by GE Hispeed CT scan machine; scan parameter is: Slice thickness 7 mm, scan time 1 s. All cases experienced enhanced thin section scanning (1 mm), after injected a non-ionic contrast agent, with dose 1.5 ml/kg and a rate of 1.5 ml/s. Among them, 13 patients without obvious symptoms, were revealed pulmonary masses by

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physical examination with image; one case with a dry cough as the main clinical manifestations. They all underwent lobectomy opening or thoracoscopically, and were followed up for 4 to 24 months, an average of 12.3 months.

## RESULTS

14 cases underwent enhanced and thin CT scanning, on which showed NGGO appearance (Figure 1), with diameter 1.0 to 3.0 cm, an average of 2.1 cm. 12 cases showed solid lesions in the NGGO lesions on CT, as MNGGO (Figure 2). The patients were undergoing open or thoracoscopic lobectomy, were all pathologically confirmed malignant, of which 3 cases were adenocarcinoma (Figure 3), while 11 cases were bronchioloalveolar carcinoma (Figure 4); the whole group did not found metastasis. Follow-up to January 2010, all 100% survived.

## DISCUSSION

In the diagnosis of NGGO, in order to make the appearance reliable and repeatable, to avoid misdiagnosis or missed diagnosis, tube current of CT usually takes 200 to 400 mA, because low tube current can produce excessive noise, which is hard to display GGO; tube voltage takes 120 to 140 kV, matrix 512 × 512, slice thickness 1.0 to 1.5 mm, if thicker, due to partial volume effects, it can cause false NGGO or NGGO be missed. Scan time should be less than 1 s during observation, the window width should be set in the 1500 to 2000 HU, windows high be in 500 to 700 HU (Collins and Stern, 1997). At the present, the pathological basis of ground glass opacity on CT is believed as follows: (1) Alveolar gas chamber with liquid (such as edema) or bleeding, result in increasing Hounsfield value; (2) Interstitial thickness due to inflammation, edema, fibrosis tumor or other reasons, resulting in "tissue" increased and air reduced relatively in each pixel, so as to cause Hounsfield value also increase; (3) In the terminal of breath, the alveolar air reduced, although the pulmonary interstitial is normal, the number of alveolar wall increases in the pixel, which can also cause ground glass opacity (Collins and Stern, 1997; Park et al., 2007; Xu et al., 2010).

Collins and Stern (1997) reported a total of 19 kinds of diseases can cause NGGO on CT, including benign lesions such as focal interstitial fibrosis, inflammation or bleeding; precancerous lesions, such as atypical adenomatous hyperplasia; lung cancer, such as bronchioloalveolar cell carcinoma, adenocarcinoma (Nakata et al., 2002; Lee et al., 2007; Park et al., 2007). According to Henschke's report (Kakinuma et al., 2004), in the positive expression of CT lesions, NGGO occupied 19%. Most NGGO are well-differentiated adenocarcinoma or bronchioloalveolar carcinoma (BAC),

a small number of atypical adenomatous hyperplasia (AAH), organizing pneumonia, or others. Their CT performances are very similar, but how to determine the type of NGGO is the most concerning for thoracic surgeon.

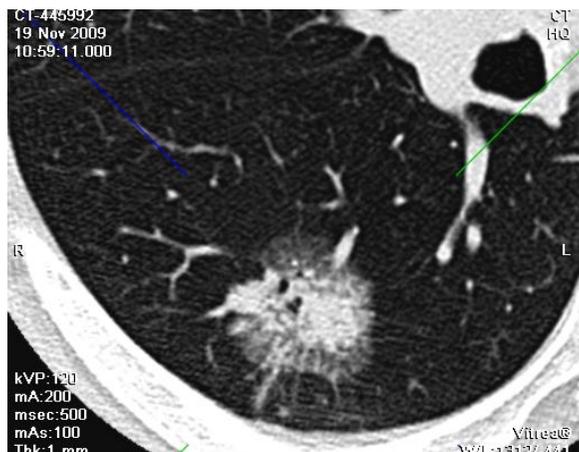
Li et al. (2004) screened 17,892 cases with low-dose CT, and found that 747 cases had lung nodules on CT, of which 222 further underwent thin (1 mm) CT scan. However, they divided nodules into pure nodular ground-glass opacity (PNGGO), mixed nodular ground-glass opacity (MNGGO) and solid opacity. They found malignant tumor is more than benign one in round lesion of PNGGO; in MNGGO, if center is high density area while surrounding is NGGO, malignant is much more possible. In addition, the proportion of solid component in NGGO also can differentiate benign or malignant lesion, 1 level's (solid component ≤ 25%) malignant rate is 83%, 2 to 4 level's (the solid component were ≤ 50%, ≤ 75%, > 75%) malignant rate is 100%. Characteristics of lesion's size and edge are not much helpful in differentiating benign and malignant. Lee et al. (2007) analyzed 96 NGGO in 55 cases, his results showed that, in PNGGO of ≤ 10 mm, malignant rate was 42%, including AAH and BAC; in PNGGO of > 10 mm, malignant rate was 40%, including AAH, BAC and adenocarcinoma; in MNGGO of ≤ 10 mm, malignant rate was 100%; in MNGGO of > 10 mm, malignant rate was 93%.

Most researchers believe that it is important to follow-up for judging NGGO is benign or malignant and generally recommend follow-up period should be 3 months (Li et al., 2004; Lee et al., 2007). Except focal interstitial fibrosis, NGGO of inflammation, focal hemorrhage, and edema can be completely absorbed spontaneously or after using appropriate antibiotics or corticosteroid during the 3 months of follow-up period, while the NGGO caused by tumor or focal interstitial fibrosis will not shrink or be absorbed in follow-up period (Kakinuma et al., 2004; Park et al., 2007). Lee et al. (2007) and Kakinuma et al. (2004) reported that if PNGGO kept stable in follow-up period, it might be focal interstitial fibrosis, AAH, focal alveolar carcinoma or adenocarcinoma histologically. It should be neoplasm if the size or density of PNGGO increased, or lesions reduced but solid part came out in the follow-up period. Note that doubling time of tumor with PNGGO is up to 813 days, which is significantly long, compared with 457 days of MNGGO and 149 days of solid tumor. Most of the lesions showed MNGGO are malignant, of which 17% become bigger in the follow-up period (Li et al., 2004).

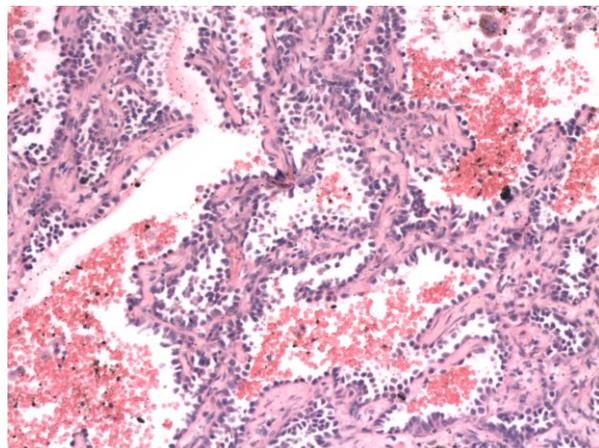
Japanese scholars Ikeda used multi-layer CT scan, and did three-dimensional computerized quantitative analysis for the CT value to judge pathologic type of lesion. The result showed: Three-dimensional computerized quantitative analysis for NGGO could judge the pathological type much more accurately, so as to provide the basis for the following treatment and prognosis. However, in the light of the limitations of computer tech-



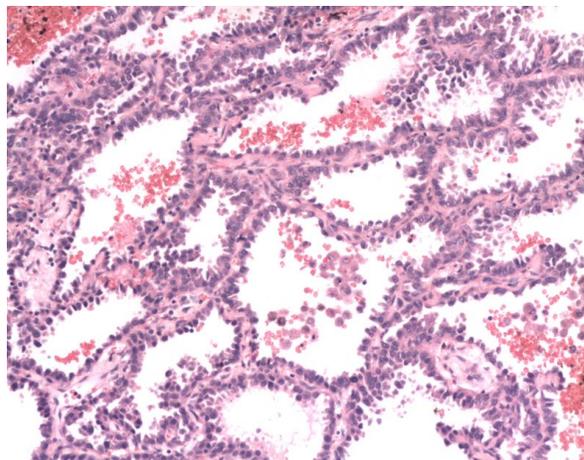
**Figure 1.** Ground- glass opacity (GGO) in right lower lung, bronchial and pulmonary vascular shadow.



**Figure 2.** Solid lesions in GGO. The change on CT is called mixed ground glass nodules (MNGGO).



**Figure 3.** Adenocarcinoma of lung.



**Figure 4.** Bronchioloalveolar cell carcinoma.

nology and computer-aided diagnosis (CAD) system, the reality of CT three-dimensional computerized quantitative analysis is limited at present (Zhen-Jun Zhao, 2009).

With the popularity of CT screening, wider application of the high-resolution CT, number of NGGO detected increases significantly than before; most of the MNGGO is malignant, such as BAC and adenocarcinoma. The data in our group also corroborates this result. Lesions of PNGGO increase the likelihood of benign, and a follow-up for 3 months is proposed to the patient. However, if the lesion is not absorbed, or even increased, or if the solid component did not come out, it is most likely malignant, and surgery is needed as soon as possible. As the lesions are usually small and soft, it is difficult to touch the lesions obviously; as such, lobectomy is mostly needed.

The lung cancer with appearance of PNGGO is usually without metastasis and its 5-year survival rate is up to 100%. In MNGGO, if solid component ratio is less than 50%, lymph node metastasis and vessel invasion are also rare, the prognosis is excellent; if solid component ratio is more than 50%, lymph node metastasis and vascular invasion may have happened (Park et al., 2007).

At last, the patients of our group were followed up for a limited time, no longer than 2 years; although, further follow-up observation was needed.

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