Clinical Research Paper

Radiologic-pathologic study on bronchial changes in peripheral solitary pulmonary lesions

Peng-Fei Sun,1,2 Xiang-Sheng Xiao,1,* Hui-Min Li,1 Hong Yu1 and Shi-Yuan Liu1

1Department of Medical Imaging; Changzheng Hospital; Second Military Medical University; Shanghai, P.R. China; 2Department of Medical Imaging; Second Affiliated Hospital of Lanzhou University; Gansu, Lanzhou P.R. China

Key words: lung neoplasm, solitary pulmonary lesions, bronchus, multi-slice CT (MSCT), pathology, diagnosis

Background and Objective: At present, the diagnosis and differential diagnosis of peripheral solitary pulmonary lesions is a hot-spot in the research of thoracic imageology, and bronchial changes are the morphologic basis of peripheral solitary pulmonary nodules, especially peripheral lung cancer. This study investigates the usefulness of multi-slice CT (MSCT) in evaluating bronchial changes of peripheral solitary pulmonary lesions through a radiologic-pathologic study. Methods: Thirty patients with solitary pulmonary lesions were scanned using MSCT. Image data were reconstructed to display bronchial changes, and then compared with the results of postoperative pathology. Results: The CT bronchial sign was positive in all patients. The bronchus on the pathologic section appeared in 19 (63.3%) patients, but not in 11 (36.7%) patients. Among the 15 patients with bronchial cutoff and bronchial wall thickening, on CT, 11 lung cancer patients had bronchial wall invasion on pathology. Among the seven patients with normal bronchial walls, on CT, five lung cancer patients had no bronchial wall invasion on pathology. Among the five lung cancer patients with air bronchogram, one had bronchial wall invasion, and one showed bronchial epithelial hyperplasia. Among the three patients with bronchus distributed at the periphery of the lesion, one lung cancer patient had bronchial wall invasion on pathology. Conclusion: MSCT can accurately evaluate the bronchial changes of peripheral solitary pulmonary lesions, and may be helpful for diagnosis and differential diagnosis of solitary pulmonary lesions.

Peripheral solitary pulmonary lesions refer to an isolated pulmonary nodule or mass in segment or below commonly seen in primary lung cancer. Prognosis of lung cancer is closely related to clinical staging. According to a reference report, the 5-year survival rate of a patient with stage 0 lung cancer could be as high as 90% or more, while the 5-year postoperative survival rate of a patient with stage IA lung cancer was 60%. However, the overall 5-year survival rates of patients with stage II to IV lung cancer were reduced to 5% from 40%. Therefore, the diagnosis and differential diagnosis of pulmonary solitary lesions are the keys for curing lung cancer and improving its prognosis.

Peripheral pulmonary carcinoma primarily originates from bronchial epithelium, and abnormality of the bronchus usually develops during the progression of the disease. Thus, a multi-slice CT (MSCT) of bronchial changes is helpful in diagnosing and differential diagnosing peripheral lung cancer such as peripheral isolated pulmonary lesions. Currently, multi-slice CT (16 slices or 64 slices) can achieve a volume scan, which is beneficial in assessing the relationship between isolated lesions and the bronchi as well as impalpable changes in the bronchial wall. In this study, MSCT was used to assess bronchial changes in peripheral isolated pulmonary lesions. These changes were checked against postoperative pathological examination in order to provide theoretical evidence for the diagnosis and differential diagnosis of lung cancer.

Patients and Methods

Studied subjects. From March 2006 to December 2006, MSCT examination was performed on 30 cases of peripheral isolated pulmonary lesion with complete clinical data in Shanghai Changzheng Hospital and checked against both postoperative samples and pathological examinations. Twenty-seven cases were peripheral pulmonary carcinoma and three were inflammatory granuloma. The diameters of the lesions ranged from 0.8 to 5.6 cm, with an average of 2.8 cm. Twenty of the subjects were male and ten were female, with the age range of all subjects falling between 35 and 78 years (and with a medium age of 56).

MSCT imaging equipment and technical parameters. The GE LightSpeed VCT 64-slice CT and the TOSHIBA Acquilion
16-slice CT scanner were used. Scanning parameters were: (1) GE LightSpeed VCT 64-CT: collimation 0.625 mm, thickness 5 mm, SFOV 50 cm, pitch 0.516:1; (2) Acquilion 16-slice CT: collimation 1 mm, thickness 7 mm, SFOV 40 cm, pitch 15 (0.98). Parameters for enhanced scan were: 70–90 ml contrast agent was injected at a rate of 3–5 ml/s. The delaying scan time for angiographic period was 20–25 seconds, while that for parenchyma period was 90 seconds. For isolated pulmonary nodules, especially those under 2 cm, a target scan was used.

**Image processing and analysis.** After a routine scan, lesions involved in pulmonary lobe were targetedly reconstructed. Parameters for reconstruction were: (1) GE LightSpeed VCT 64-CT: thickness 0.625 mm, interval 0.3–0.5 mm, DFOV 16–20 cm; (2) Acquilion 16-slice CT: thickness 1 mm, interval 0.8 mm, DFOV 18–20 cm. The reconstructed image was transferred to a Vitrea 1 or AW 02 processing station for the multi-planar reconstruction (MPR) of bronchi along their directions: pulmonary window (WW 1,300–1,500 Hu, WL -350–-500 Hu), arterial period in mediastinal window (WW 340–360 Hu, WL 40–70 Hu), and medium window. The relationship between lesion and bronchi was observed, as well as bronchial lumen and changes in the bronchial wall.

The assessment standard for changes in the bronchial wall followed the standard of relationship between tumor and bronchi set by Gaeta et al. and the standard specifically set for this study:

(1) The bronchus was cut off at the edge of the lesion; the MSCT showed that the bronchus abruptly terminated when reaching the edge of the lesion.

(2) An air bronchogram meant the aerated bronchi entered within the lesion and, thus, could be classified into five types according to presentation:

Type I The aerated bronchus appeared as stenosis in lesion and disappeared.

Type II The aerated bronchus was abruptly interrupted with the stump being flat or dull and round.

Type III The aerated bronchus was twisted and expanded, while its lumen surface was not smooth.

Type IV The aerated bronchus was branched in lesion, but the branched pattern was still natural.

Type V The aerated bronchus was further branched with stiffness in its flowing pattern.

(3) The bronchus traveled along the edge of the lesion site, where the bronchus was pressed and relocated, while displaying different degrees of stenosis.

(4) The bronchus was pulled by the lesion and relocated.

**Pathological examination.** A fresh surgical sample was obtained and the bronchus was filled with a 10% formaldehyde solution to expand it. After two days, along the long axis of the bronchus, the sample was cut open to observe the relationship between the bronchus and the lesion, and to identify its type. After the specimen was fixed, along the traveling direction of bronchus, a pathologic section (4 μm) was made (HE stain). Changes in the bronchus within the lesion were observed, including the bronchus closely bound to the lesion site.

### Results

**Display of bronchi related to peripheral isolated pulmonary lesion.** In the 30 cases of isolated pulmonary lesions examined in this study, the use of CT showed different types of bronchial changes in all cases, while pathologically, it revealed 19 cases of related bronchi (63.3%) and didn't reveal 11 cases (36.7%) (Table 1).

**CT-pathologic contrast on peripheral isolated pulmonary lesion.** In all 30 cases (27 cases of lung cancer and three cases of inflammatory granulomatosis) the use of MSCT showed different types of bronchial changes. After the operation, 19 cases of lung cancer samples and pathological sections showed bronchial changes. Eight cases of lung cancer and three cases of inflammatory granulomatosis (two cases of chronic inflammation and one case of tuberculosis) showed no sign of bronchus.

In 15 cases, CT showed the bronchi being cut off at the edge of the lesion and bronchial wall thickening. Out of these 15 cases, 11 cases of postoperative surgical samples showed abrupt bronchial interruption and pathological examination revealed the infiltration of a tumor in the bronchial wall (Fig. 1). Two cases of lung cancer and two cases of inflammatory granulomatosis showed no related bronchi in samples and pathological examination.

In seven cases of lung cancer, CT showed abrupt bronchial cut-off at the edge of the lesion site accompanied with thickening of the bronchial wall. Five of the cases showed abrupt bronchial interruption in postoperative samples and pathology, but there was no sign of tumor infiltration in the nearby bronchial walls.

Five cases of lung cancer showed air bronchogram on CT, of which one case showed bronchial cut-off within a lesion while pathological examination revealed tumor infiltration in the bronchial wall (Fig. 2). The CT of one case showed dendritic bronchus within a lesion, while pathological examination showed proliferative changes in bronchial epithelium. Three cases showed no sign of related bronchus.

Three cases showed bronchi traveling along the edge of a lesion and the lumen spaces were compressed on CT. One of the cases of lung cancer showed tumor infiltration in the bronchial wall in pathological examination. One case of atypical carcinoid cancer and one case of inflammatory granulomatosis showed no sign of bronchi in samples and pathological examination.

### Table 1 The comparison of bronchial displaying between on CT and on pathology

<table>
<thead>
<tr>
<th>CT bronchial sign</th>
<th>Cases</th>
<th>Pathology (cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Presence</td>
</tr>
<tr>
<td>Marginal cutoff</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>Thickening</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>No thickening</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Air bronchogram</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral distribution</td>
<td>30</td>
<td>19</td>
</tr>
</tbody>
</table>

In seven cases of lung cancer, CT showed abrupt bronchial cut-off at the edge of the lesion site accompanied with thickening of the bronchial wall. Five of the cases showed abrupt bronchial interruption in postoperative samples and pathology, but there was no sign of tumor infiltration in the nearby bronchial walls.

Five cases of lung cancer showed air bronchogram on CT, of which one case showed bronchial cut-off within a lesion while pathological examination revealed tumor infiltration in the bronchial wall (Fig. 2). The CT of one case showed dendritic bronchus within a lesion, while pathological examination showed proliferative changes in bronchial epithelium. Three cases showed no sign of related bronchus.

Three cases showed bronchi traveling along the edge of a lesion and the lumen spaces were compressed on CT. One of the cases of lung cancer showed tumor infiltration in the bronchial wall in pathological examination. One case of atypical carcinoid cancer and one case of inflammatory granulomatosis showed no sign of bronchi in samples and pathological examination.
Radiologic-pathologic study on bronchial changes in peripheral solitary pulmonary lesions

Wall could be seen more clearly as well. However, it was difficult to determine the thickening of the bronchial wall, usually because the accompanying blood vessel overlapped it. MPR at the arterial period distinguished accompanying blood vessels from the bronchi, which aided assessment of the thickening of the bronchial wall. Simultaneous regulation of window width and window center (medial window) also revealed the continuity of the bronchial wall. A mediastinal window during the arterial period, in combination with a medial window, provided a more detailed view of the bronchial interrupted site (mucous or inflammatory, soft tissue mass), which was beneficial in the differential diagnosis between an inflammatory lesion and a malignant one.

Comparison of bronchial changes in MSCT and pathological examination. On MSCTs, 30 cases of peripheral isolated pulmonary lesions all showed bronchial changes (including bronchi being cut off at the edge, thickening in bronchial wall, air bronchogram, and bronchi traveling along the edge). There were 19

Discussion

The value of MSCT in displaying bronchial changes in peripheral isolated pulmonary lesion. This research employed the GE LightSpeed VCT 64-CT and TOSHIBA Acquilion 16-slice CT. The scanning thicknesses of 64 CT and 16-slice CT were 0.625 mm and 1 mm, respectively. Scanned data could undergo any thickness overlapping reconstruction and had high spatial resolution and Z-axis resolution. Through target reconstruction, MPR reconstruction clearly showed sub-segmental bronchi. In this group of data, it showed that the 64-slice CT clearly displayed bronchi of grade 6 or more.

Multiple window widths and window centers improved the display of bronchial changes. Sequential observation in an axial pulmonary window, in combination with MPR, clearly displayed bronchial changes (marginal abrupt interruption, air bronchogram and traveling along the edge) and the continuity of the bronchial wall could be seen more clearly as well. However, it was difficult to determine the thickening of the bronchial wall, usually because the accompanying blood vessel overlapped it. MPR at the arterial period distinguished accompanying blood vessels from the bronchi, which aided assessment of the thickening of the bronchial wall. Simultaneous regulation of window width and window center (medial window) also revealed the continuity of the bronchial wall. A mediastinal window during the arterial period, in combination with a medial window, provided a more detailed view of the bronchial interrupted site (mucous or inflammatory, soft tissue mass), which was beneficial in the differential diagnosis between an inflammatory lesion and a malignant one.

Figure 1. CT and pathologic images of bronchial marginal cutoff in peripheral lung adenocarcinoma. (A) On MPR image of a solitary lesion in the inferior lobe of the right lung, the sub-segmental bronchi of the superior segment are interrupted at the edge of lesion, and the local bronchial wall is incrassate (white arrow). (B) On pathology, the tumor obviously invaded the bronchial wall. White arrows point to bronchial cartilage; black arrows point to bronchial outer membrane and gland (HE x100).

Figure 2. CT and pathologic images of Type II air bronchogram in peripheral lung adenocarcinoma. (A) On sagittal MPR image, the lateral segmental bronchus of the right middle lobe is abruptly interrupted within the nodule (Type II air bronchogram), and the bronchial wall is not incrassate at the juncture of lesion-bronchus (white arrow). (B) On axial MPR image, the bronchus within the nodule is also interrupted (white arrow). (C) On pathology, the bronchial wall is destroyed by tumor tissue (black arrow) (HE x100).
cases which showed bronchial changes (including the bronchial wall) in postoperative surgical samples and pathological slides. The bronchial changes of these cases primarily occurred in bronchi of grade 3 to 4, while the non-displayed eight cases of lung cancer all had related bronchi at grade 4 or above. In patients who CT showed bronchial wall thickening, their pathological sections could see tumor infiltration to the bronchial wall. Air broncho-gram in CT could also see abrupt interruption of bronchi within lesions and the infiltration of tumors to the bronchial wall in pathological examination. The bronchus that traveled along the edge and appeared pressed on CT showed infiltration of a tumor to the bronchus in a pathological examination.

Pathologically, the sign of bronchus was not seen because, (1) pathological sampling of bronchiole (grade 4 or above) was difficult. Sampling from a whole sample and continuous slicing could improve the bronchial display rate and (2) three cases of inflammatory granuloma showed as granulation tissue and necrotic tissue, which made it difficult to display the bronchus.

Pathological basis of bronchial changes in peripheral isolated pulmonary lesions. The growth pattern of peripheral lung cancer is divided into expansive growth and lining growth. Expansive growth involves the growth and accumulation of tumor cells into solid nodules which press and push neighboring bronchi. Also, because the tumor is bronchial in origin, it usually causes the bronchus to be abruptly interrupted at the edge of tumor. The latter instance involves the growth of tumor cells along the alveolar wall and inter-alveolar space and expands through alveolar holes or bronchiole; however, the bronchus is usually still not constricted, which results in different types of bronchial aeration. Lining growth is usually accompanied by localized expansive growth, which causes bronchial stenosis and interruption within lesions (Type I and II bronchial sign). A tumor’s infiltration into the bronchus causes the bronchial wall to thicken and become stiff, while the lumen surface becomes rough. In addition, the contracting and pulling of fibrosis within the tumor results in unobstruction and even to some extent expansion of bronchus (type III and V bronchial sign). The tumor will infiltrate along the surrounding bronchial blood vessel bundle and lobular septation, causing neighboring bronchi to be pulled toward the tumor by intra-tumor fibrosis. When a tumor infiltrates neighboring bronchi or a tumor is located in the submucous membranous layer, it usually will cause the bronchus to travel along the edge of lesion, and show signs of lumen stenosis.

Air bronchogram in the inflammatory nodule is primarily caused by exudation and consolidation of pulmonary space, while the bronchus appears as a natural branch (type IV bronchial sign). The organization of an inflammatory nodule can cause the twisting and expansion of the bronchus (type III of bronchial aeration). In bronchial lumen, there can be a secretion which makes the bronchus appear discontinuous. As inflammatory granuloma tissues fill and block the bronchus, it can cause the appearance of an abrupt interruption of the bronchus within the lesion. In addition, the filling of the bronchus by inflammatory granuloma tissues can also cause abrupt interruption of the bronchus at the edge of the lesion. Inflammatory nodular fibrosis can also pull the nearby bronchus toward the lesion.

Thus, MSCT can accurately reflect morphological changes of the bronchi in relation to lesions (abrupt interruption of the bronchus and infiltration of the bronchial wall) and it is helpful in the diagnosis and the differential diagnosis of an isolated pulmonary lesion site.

Acknowledgements
Grant: Sci-Tech Key Subject Foundation of Shanghai (No. 06DZ19503).

References