Local Recurrence at Bronchial Stump Site in Post Operated NSCLC patients: Comparison between CT findings and Bronchoscopy.

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Abstract

Purpose: The recurrences of lung cancer after treatment are frequent. There may be more common distant recurrence and locoregional recurrence. Among them, recurrences at bronchial stump site are rare. To present CT images comparing with bronchoscopy of local tumor recurrence at bronchial stump site in postoperated non-small cell lung cancer (NSCLC) patients.

Materials & Methods: A retrospective study was conducted to review CT images of 9 recurred lung cancers at bronchial stump site on 576 resected primary non-small cell lung cancers during 9-year period. The CT images of bronchial stump site recurrence were classified as: bronchial wall thickening, nodular or endobronchial polypoid lesion; multiplicity; and enhancement patterns. We classified bronchoscopic findings based on the bronchoscopic findings of the revised classification by the Japan Lung Cancer Society.

Results: The histologic types of 9 recurred cancers, for which the CT images were available, were composed of 7 squamous cell carcinomas, 1 adenocarcinoma, and 1 adenoid cystic carcinoma. The CT findings revealed bronchial wall thickening with nodules (n=6) and endobronchial polypoid nodules (n=3) with heterogeneous enhancement. They were classified as 1 superficial infiltrating type, 5 nodular infiltrating type, and 3 polypoid type on bronchoscopy.

Conclusion: Both bronchoscopy and CT can be used as complementary and cooperative tools evaluating bronchial stump site recurrences.

Keywords : Lung, lung neoplasms, lung neoplasms-diagnosis, lung neoplasms-CT, endoscopy, bronchoscopy
Abbreviations: NSCLC = non-small cell lung cancer, CT = computed tomography

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I. Introduction

The recurrences of non-small cell lung cancer (NSCLC) are frequent episodes after treatment such as curative resection, chemotherapy, radiation therapy and multimodal therapy. In patients with stage I disease confirmed at surgery, 5-year recurrence rates 20 to 39% have been reported [1-3]. Among them, 10 20% cases show locoregional recurrences and 60 70%

cases show distant recurrences [1, 4, 5]. Locoregional recurrence means recurrent disease in the ipsilateral hilar or mediastinal lymph nodes and in the surgical margin including bronchial stump, pleura, and chest wall [6, 7].

In the past days, most cases of the recurred lung cancer were found on advanced stages because they had been diagnosed using chest X-ray and bronchoscopy. Nowadays, technical advances in both chest computed tomography (CT) and bronchoscopy have been helpful in diagnosing the locoregionally recurred lung cancer on earlier stages [7-10]. Previous study suggested a relationship between bronchoscopic findings and chest X-ray findings of bronchial stump recurrence [8]. To our knowledge, however, there has been no study that tried to suggest a relationship between CT findings and bronchoscopic findings of bronchial stump recurrence.

Thus the aim of our study was to present CT images individually with corresponding bronchoscopic findings of local tumor recurrence at bronchial stump site based on recently reported bronchoscopic classification

II. Materials and Methods

No specific approval by our institutional review board is necessary for retrospective study. Informed consents were obtained from all patients before performing follow-up chest CT scans.

From January 1995 to December 2004, 3872 patients had been diagnosed with lung cancer. Of them, 576 patients with NSCLC under stage IIIA underwent radical surgery. The stages of all patients were reported in accordance with the New International Staging System for Lung Cancer. Staging definitions for the T (primary tumor), N (regional lymph nodes), and M (distant metastasis) components were in accordance with the International Staging System for Lung Cancer [11, 12]. In this study, bronchial stump recurrence was defined as recurrent disease only in the surgical margin of bronchus, not in regional lymph nodes, chest wall or pleura. Twelve (2.08%) cases had recurrences at the bronchial stump sites. In all cases, the resection margin was microscopically negative for tumor cells at the time of surgery. Three of them were excluded because their CT images were unavailable on our image data base. Therefore, our study included 9 patients. There were 8 men and 1 woman, with a mean age of 66 years (range: 56 to 74 years). During follow-up periods, patients performed CT or bronchoscopy as scheduled: three month, six month and every one year after surgery. If there were any abnormal findings on chest X-ray or symptoms,

CT or bronchoscopy was performed without hesitation. The recurrences were confirmed histopathologically by bronchoscopic biopsy.

Retrospectively, we acquired individual informations about histopathologic types of lung cancers, operation types, postoperative pathologic staging, time interval between operation and recurrence, and bronchoscopic findings from medical records.

CT scans were obtained using a single-detector helical CT scanner (Tomoscan SR-7000, Philips Medical Systems, Best, Netherland), a 4-slice CT scanner (LightSpeed, GE Medical Systems, Milwaukee, Wis.) or a 16-slice CT scanner (LightSpeed Pro 16, GE Medical Systems, Milwaukee, Wis.). The CT protocol was consisted of a 5.0- (single-detector helical CT scanner), 2.5- (multi-slice CT scanners) mm collimation, pitch of 1.0 (Tomoscan SR-7000, LightSpeed Pro 16), 1.5 (LightSpeed) at 120 kVp, 180-200 mAs, 40 seconds after administration of 100-120 mL (3 mL/sec via intravenous route) of contrast medium (Ultravist, Schering, Seoul, Korea); covering the lung apices to both adrenal glands.

All CT images were reviewed as a consensus interpretation by two radiologists who are specialists in chest imaging. The images were photographed at mediastinal (width, 350 H; level, 50 H) and lung (width, 1600 H; level, -600 H) window settings. The CT scans were assessed for the presence and distribution of the following recognized features of bronchial stump site recurrence: bronchial wall thickening, nodular and endobronchial polypoid lesion; multiplicity; and enhancement patterns.

Bronchial wall thickening signifies the difference between the pathologic site and the normal site which shows smooth tapering. Nodular infiltrating type means the round protrusion from the bronchial stump to the lumen. Polypoid type means the lobular protrusion with a single stalk from the bronchus to the lumen.

Two physicians, pulmonary specialists, reviewed all lesions on bronchoscopy as a consensus interpretation and classified them based on the bronchoscopic findings of the revised classification by the Japan Lung Cancer Society (Fig. 1) [13]: First, bronchoscopic findings were divided into mucosal invasion type and submucosal invasion type. The mucosal invasion type means tumor growth mainly in the mucosal epithelium, and is subclassified as follows: superficial infiltrating type (thickened type); nodular infiltrating type; and polypoid type. Superficial infiltrating types of recurrences were revealed as mucosal changes, such as redness or whitish patch at mucosa, without contour abnormality. Nodular infiltrating type means mucosal change with the round mucosal protrusion from the bronchus to the lumen. Polypoid type means the lobular mucosal protrusion with a single stalk from the bronchus to the lumen. Submucosal types show tumor growth in layers deeper than the lamina propria and are classified into superficial type; infiltrating type; and extramural type.

III. Results

Out of 576 patients, 12 (2.08%) had bronchial stump recurrences. The histologic types of 9 recurred cancers, for which the CT images were available, were composed of 7 squamous cell carcinomas, 1 adenocarcinoma, and 1 adenoid cystic carcinoma. Surgical resections involved lobectomy (n = 2), bilobectomy (n = 1), and pneumonectomy (n = 6). Postoperative pathologic stages of tumors were stage IB (n = 3), IIB (n = 4), and IIIA (n = 2) at the time of surgery. The interval between the time of operation and recurrence ranged from 17 to 72 months (mean 32 ± 9 months). The relationships between age, sex, histopathologic type, operation type, TNM staging, the interval between operation and recurrence, bronchoscopic findings and CT findings for individual patients are the followings (Table 1).

On bronchoscopic findings, all of the lesions were mucosal invasion types and there was no submucosal invasion type in this study. Bronchoscopic findings showed 1 superficial infiltrating type, 5 nodular infiltrating types and 3 polypoid types of recurrences.

CT scans revealed all recurrences as soft tissues occupying the space around stump site. Despite of classifying all recurrences into 3 different bronchoscopic classifications, all of the cases demonstrated heterogeneous enhancing nodular lesions on CT. Six cases of superficial infiltrating and nodular type recurrences demonstrated nodular infiltrations around bronchial

stumps and into the bronchial wall. The remaining 3 cases of polypoid type recurrences demonstrated lobular infiltration to the lumen on the CT scan. There were 3 cases showing multiple sites of recurrences at the time of recurrence was diagnosed, 2 nodular infiltrating types and 1 polypoid type of recurrence.

IV. Discussion

Radical resection is considered as an adequate treatment in providing survival benefits for early NSCLC, especially for the patients without metastasis into the lymph nodes. But, even after radical resection, recurrence of lung cancer is an inevitable. There may be tumor recurrence at the bronchial stump, even when the margin of the resected specimen is negative for cancer and the resected margin is sufficiently distant from the tumor. One of the reason why, visual examination of the stump site after a curative resection does not reveal any tumor, but pathologists report the presence of microscopic, residual tumor tissue at the bronchial resection margin for approximately 4 5% of all lung resections [14]. Especially, squamous cell carcinomas revealed proximal microscopic extension more often as compared to adenocarcinomas after radical excision. And most of the proximal extensions occur from mucosal or submucosal layers. In adenocarcinomas, peribronchial extension was more often [15-17].

In this study, the recurrences at the bronchial stump were seen in 12 (2.08%) of all cases of resected lung cancers, and this result is the same when compared with previous studies that report up to 2.2% [7, 8]. However, the cases included in previous studies were of mostly submucosal type [7], whereas all of the recurrences in this study were of mucosal type on bronchoscopic findings: 1 superficial infiltrating type, 5 nodular infiltrating

types, and 3 polypoid types. These difference may have occurred because we targeted the patients who had recurrences at the bronchial stump sites and excluded those who had recurrence at the lymph nodes. Another possibility for the discrepancy is that we used the revised classification by the Japan Lung Cancer Society for the classification of bronchoscopic findings.

All nodular infiltrative type recurrences were from squamous cell carcinoma in keeping with the results of other studies, which demonstrated heterogeneous enhancing nodules on the CT scan [8]. Three out of 9 cases had endobronchial polypoid nodules. One of them was from squamous cell carcinoma, and the other polypoid type recurrences were from adenocarcinoma and adenoid cystic carcinoma. Previous studies reported bronchial stump recurrences from squamous cell carcinoma only [7]. However, the studies that precede the aforementioned study report recurrences from various types of lung cancer, and after considering how the result of this study matches with the preceding study [8], it is clear that lung cancer recurrences at bronchial stump are not limited to squamous cell carcinoma.

Because bronchoscopy is limited to evaluating mucosal changes and contour changes in bronchial lumen, there is a tendency to underestimate bronchoscopic findings compared to CT findings, especially on superficial infiltrative type recurrence. There was one superficial infiltrating type recurrence on bronchoscopy in this study. But, on CT findings, there was a

heterogeneous enhancing nodular soft tissue lesion at bronchial stump site. On the other hand, bronchoscopy is thought to be more sensitive than chest CT when evaluating early local recurrences that do not show bronchial wall thickening or nodular infiltration. In summary, when bronchoscopy reveals possibility of local infiltration, cross-sectional examination, such as CT, should be performed in order to know how much the cancer has advanced. However, when finding early recurrent cancer that is not easily visible on a chest CT, bronchoscopy is more advantageous. In that sense, the two examinations complement each other.

Five cases of nodular infiltrative type showed nodular lesions originated from post-operated bronchial stump site on CT findings (Fig. 2). Both superficial infiltrative type and nodular infiltrative type of recurrences appeared as heterogeneous enhancing nodules which showed imprint and direct invasion to adjacent bronchus or trachea. On the contrary, 3 polypoid type recurrences were revealed to be endobronchial polypoid nodules. Unlike superficial infiltrative type and nodular infiltrative type, which invades from deeper portion of bronchial wall into the lumen, the recurrences of polypoid type seem to originate from the superficial layer, and some invade into the bronchial lumen (case 7), while others invade into both the bronchial lumen and into the bronchial wall (case 8, 9) (Fig. 3.). Considering this result, the recurrence of polypoid type may originate at the superficial layer of the bronchus, compared to the other types. According to the previous study, residual tumor cells can infiltrate the entire bronchial wall or can be confined

to a specific part of the bronchial wall and the involved part can be classified as mucosal such as carcinoma in situ and invasive carcinoma, and extra-mucosal such as submucosal residual disease and peribronchial residual disease [14]. We expect to be proven that the polypoid type recurrences originate from the mucosal layer, the superficial infiltrative type and nodular infiltrative type recurrences originate from extra-mucosal layer in near future.

There are several limitations to our study: first, sample size was small because of the low incidence of bronchial stump recurrence after primary radical surgery. Accordingly, the ability of our data to represent all the recurrences at bronchial stump site is limited, and we did not perform any statistical analysis to determine any correlations between bronchoscopic findings, CT findings and other factors. Secondly, the study was unable to determine the origin of the recurrent tumors pathologically, because additional operations were not performed in some patients. So, we could not pinpoint the bronchial layer that gave rise to the tumor. Another concern is that we used 3 different CT scanners with different protocols, and therefore, may not have obtained consistent result.

V. Conclusion

In conclusion, variable findings of CT for recurrent lung cancer at bronchial stump are demonstrated, such as bronchial wall thickening, nodule, endobronchial polypoid nodule with or without enhancement. Correlation with bronchoscopic findings and CT findings is possible in verifying the presence of a recurrence at the bronchial stump site. In other words, both bronchoscopy and CT can be used as complementary, cooperative tools in evaluating bronchial stump site recurrences. Also, when referring to chest CT findings for polypoid type and nodular infiltrative type recurrences, the location of the origin of the tumor may lead to different types of recurrence.

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Legend of Figures

Figure 1 Classification of Bronchoscopic Findings (Revised classification by the Japan Lung Cancer Society) [11].

Figure 2

A. 56-year-old man with squamous cell carcinoma, 22 months after left pneumonectomy. There is a heterogeneous enhancing nodular lesion at the bronchial stump site (arrow).

B. At the same site on bronchoscopy, endoluminal mucosal lesion is noted (arrows).

Figure 3

A. 64-year-old man with squamous cell carcinoma, 27 months after left pneumonectomy. CT image shows endobronchial, heterogeneous enhancing mass at the adjacent bronchial stump (arrow).

B. Heterogeneous enhancing mass involves carina (arrow).

C. On bronchoscopy, there is a polypoid mass filling left main bronchus involving carina.

NOTE: Bronchoscopic images were flipped horizontally to show the same point of view on both CT and bronchoscopy.

Table 1. Individual Information of the patients.

No	Age / Sex	Histopathologic type	Operation	Stage	Recur period	Bronchoscopic Finding	CT findings	
							Feature	Enhancement pattern
1	66/M	SqCC	P	IB	48 months	Superficial infiltrating	Nodule	Heterogeneous enhancement
2	69/M	SqCC	P	IIIA	17 months	Nodular infiltrating	Multiple nodules	Heterogeneous enhancement
3	56/M	SqCC	P	IIB	22 months	Nodular infiltrating	Nodule	Heterogeneous enhancement
4	65/M	SqCC	B	IIB	24 months	Nodular infiltrating	Multiple nodules	Heterogeneous enhancement
5	73/M	SqCC	P	IB	24 months	Nodular infiltrating	Nodule	Heterogeneous enhancement
6	63/ F	SqCC	P	IIIA	31 months	Nodular infiltrating	Nodule	Heterogeneous enhancement
7	70/M	AdenoCA	L	IB	26 months	Polypoid	Endobronchial polypoid nodule	Heterogeneous enhancement
8	64/M	SqCC	P	IIB	27 months	Polypoid	Endobronchial polypoid nodule	Heterogeneous enhancement
9	67/M	ACC	L	IIB	72 months	Polypoid	Multiple endobronchial polypoid nodules	Heterogeneous enhancement

SqCC = Squamous cell carcinoma, AdenoCA = Adenocarcinoma, ACC = Adenoid cystic carcinoma
P = Pneumonectomy, L=lobectomy, B=bilobectomy

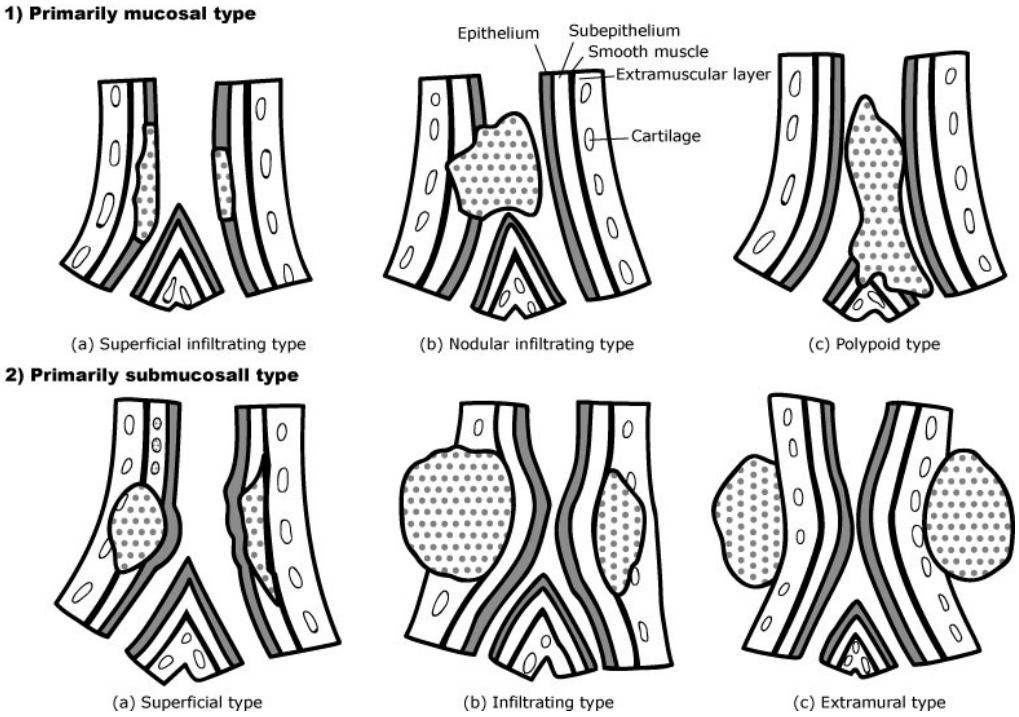

Figure 1. Classification of Bronchoscopic Findings (Revised classification by the Japan Lung Cancer Society).

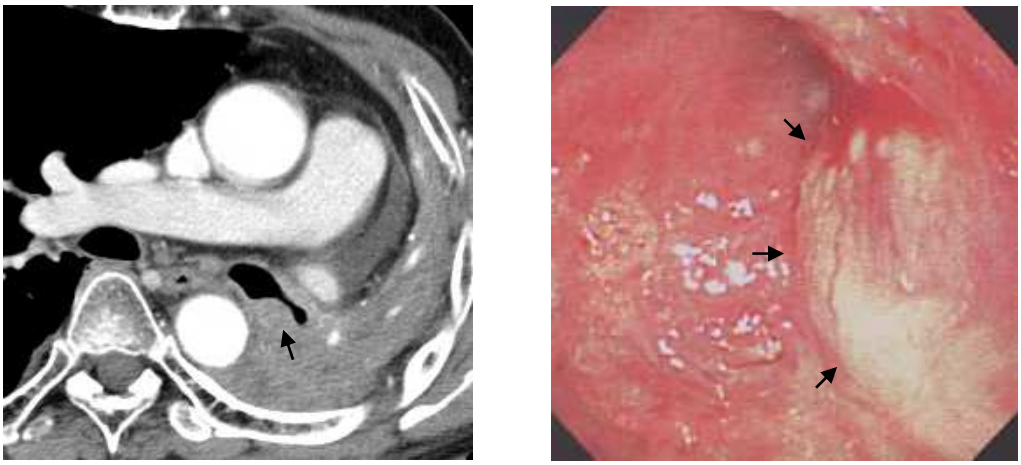

Figure 2. 56-year-old man with squamous cell carcinoma, 22 months after left pneumonectomy.

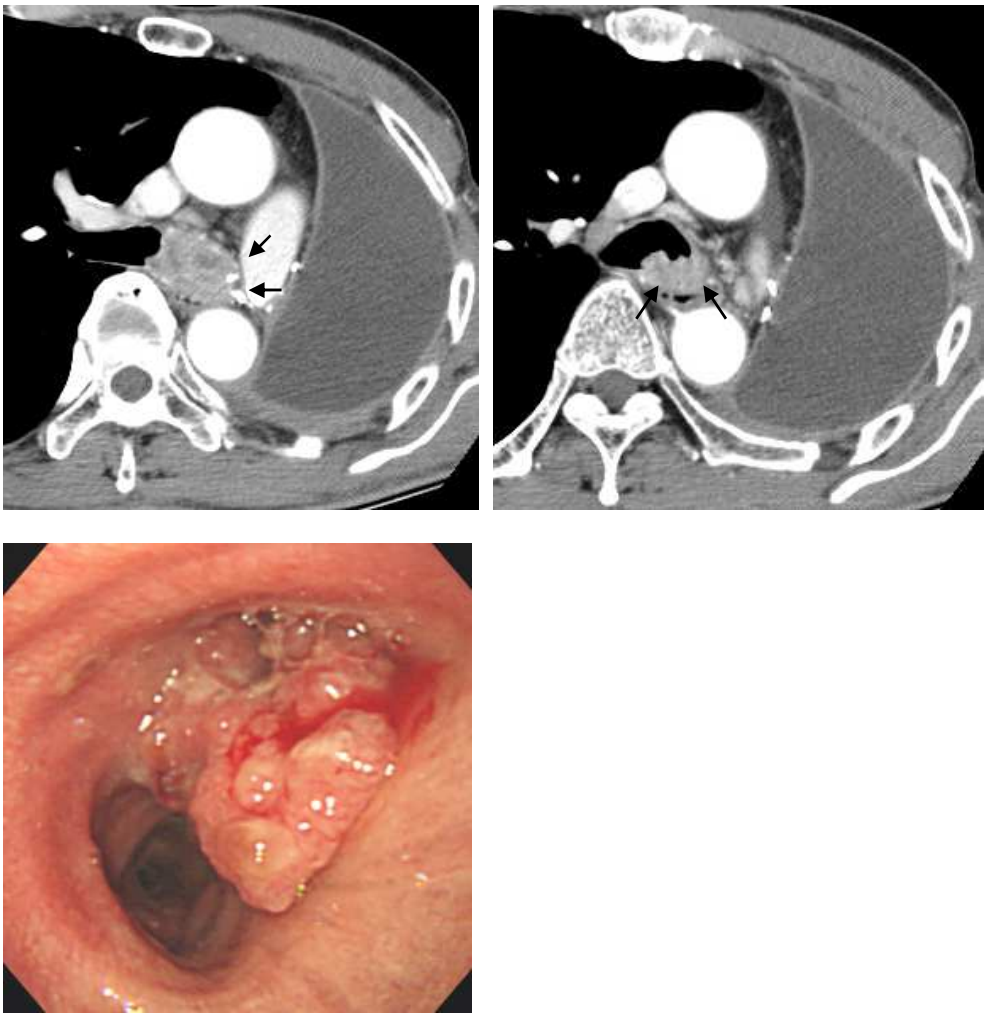

Figure 3. 64-year-old man with squamous cell carcinoma, 27 months after left pneumonectomy.

Abstract in Korean

목적: 수술 후 비소세포 폐암 환자에 있어서, 기관지 잘린 끝에 국소 재발암의 전산화 단층촬영 소견과 기관지 내시경 소견을 비교하고자 하였다.

대상과 방법: 근치적 수술을 받은 총 576 명의 원발성 비소세포 폐암 환자들 중, 기관지 잘린 끝에 재발을 보인 9 명의 환자를 대상으로 후향적 연구를 진행하였다. 9 명의 환자들의 기관지 내시경 소견을 the bronchoscopic findings the revised classification by the Japan Lung Cancer Society 에 입각하여 분류하였으며, 이후 전산화 단층촬영 소견과 비교, 분석하였다.

결과: 환자들의 원발암은 조직학적으로 7 명의 편평세포암종, 1 명의 샘암종, 1 명의 샘낭암종으로 구성되어 있었다. 기관지 내시경 소견에서 각각 1 예의 얕은 침윤형, 5 예의 결절 침윤형, 3 예의 용종형으로 분류하였다. 전산화 단층촬영 소견에서 결절을 보인 예는 6 개, 기관지 내강에 소엽상을 보인 예가 3 개였으며 이들은 모두 불균일한 조영증강을 보였다.

결론: 기관지 잘린 끝의 국소 재발의 진단에 있어서, 기관지 내시경 소견과 흉부 CT 소견은 각각의 결점을 충족시켜주는 상호보완적인 도구로 사용할 수 있다.

주요어:폐/폐신생물/폐신생물-진단/폐신생물-컴퓨터전산화단층촬영/내시경/기관지내시경