USEFULNESS OF COMPUTED TOMOGRAPHIC IMAGING OF THE CHEST IN EVALUATION PATHOLOGIC CELL TYPE OF PRIMARY LUNG CANCER DISEASE

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ABSTRACT

Computed Tomographic (CT) imaging provides precise information about the size, shape, and location of tumors. The aim of this study is to evaluate the CT imaging patterns of lung cancer based on cell type. CT imaging features of 67 cases with pathology were verified and collected between 1995-2000 and were retrospectively analyzed for size, location, margins, internal characteristics and metastasis. The number of squamous cell carcinoma, adenocarcinoma, large cell carcinoma, and small cell carcinoma were 28, 23, 7, and 9 cases, respectively. The accuracy, predictive value and 95% confidence interval (95%CI) were calculated.

There was a significant location of squamous cell carcinoma in central and adenocarcinoma in the periphery ($p<0.05$). High incidence in squamous cell carcinoma (29%) had cavitation. Central lesion with cavitation had possibility of squamous cell carcinoma, at least for the differentiation of characteristics presented in CT imaging, such as size, edge, infiltration, internal characteristics, lymph node enlargement, pleural effusion, and metastasis to other organs. We can not evaluate cell type of lung cancer from CT imaging patterns. The accuracy of CT imaging for evaluated squamous cell carcinoma, adenocarcinoma, large cell carcinoma, and small cell carcinoma were 82% (95%CI 73-91), 65% (95%CI 54-77), 0% and 44% (95%CI 33-56), respectively. Predictive value were 64% (95%CI 52-75), 65% (95%CI 54-77), 0%, and 57% (95%CI 45-69), respectively. In conclusion, we can not evaluate pathological cell type of primary lung cancer from CT imaging, because the accuracy is low. However, CT imaging of the chest has usefulness to provide precise information about the size, location, margin, internal characteristics and metastasis.

KEY WORDS: COMPUTED TOMOGRAPHIC IMAGING / LUNG CANCER / PHATOLOGICAL CELL TYPE / SQUAMOUS CELL CARCINOMA / ADENOCARCINOMA / LARGE CELL CARCINOMA / SMALL CELL CARCINOMA.

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การศึกษาถึงประโยชน์ของภาพถ่ายทางรังสีวิทยาแบบตัดขวางของทรวงอก ในการวินิจฉัยโรคมะเร็งปอดตามลักษณะทางพยาธิวิทยา (USEFULNESS OF COMPUTED TOMOGRAPHIC IMAGING OF THE CHEST IN EVALUATION PATHOLOGICAL CELL TYPE OF PRIMARY LUNG CANCER DISEASE).

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บทคัดย่อ

ปัจจุบันการใช้เครื่องเอกซเรย์คอมพิวเตอร์ (CT) ตรวจวินิจฉัยโรคมะเร็งปอดเป็นที่นิยมมากขึ้น เพราะภาพที่ได้จาก CT แสดงถึงรายละเอียดต่างๆ เช่น ขนาด รูปร่าง ตำแหน่งของมะเร็งปอด วัตถุประสงค์ในการศึกษาครั้งนี้คือเพื่อศึกษาถึงประโยช์ของภาพถ่ายทางรังสีวิทยาแบบตัดขวางของทรวงอกในการวินิจฉัยโรคมะเร็งปอด และศึกษาถึงรายละเอียดลักษณะต่างๆของมะเร็งปอดแต่ละชนิด โดยศึกษาจากภาพ CT ในผู้ป่วยมะเร็งปอดที่รับการตรวจด้วยเครื่อง CT ของโรงพยาบาลศิริราช ในปี พ.ศ. 2538-2543 จำนวน 67 ราย เป็นชนิด squamous cell carcinoma 28 ราย, adenocarcinoma 23 ราย, large cell carcinoma 7 ราย, และ small cell carcinoma 9 ราย

จากผลการศึกษาพบว่า ก้อนมะเร็งที่อยู่ตำแหน่ง central เป็นชนิด squamous cell carcinoma และก้อนมะเร็งที่อยู่ตำแหน่ง peripheral เป็นชนิด adenocarcinoma อย่างมีนัยสำคัญ ($p<0.05$). และพบว่า 29% ของ squamous cell carcinoma เกิดโพรงภายในก้อนมากกว่าชนิดอื่น จึงมีความเป็นไปได้ว่าก้อนมะเร็งที่มีโพรงและอยู่ตำแหน่ง cental เป็นชนิด squamous cell carcinoma. รายละเอียดต่างๆที่เห็นจากภาพ CT มีความถูกต้องในการแยกมะเร็งปอดชนิด squamous cell carcinoma, adenocarcinoma, large cell carcinoma, and small cell carcinoma เท่ากับ 82% (95%CI=73-91), 65% (95%CI=54-77), 0% และ 44% (95%CI=33-56) ตามลำดับ.โดยค่า Predictive value ของ squamous cell carcinoma = 64% (95%CI=52-75), adenocarcinoma = 65% (95%CI=54-77), large cell carcinoma = 0%, และ small cell carcinoma = 57% (95%CI 45-69).

ภาพ CT ของทรวงอก มีประโยชน์ในการตรวจผู้ป่วยมะเร็งปอด คือ สามารถแสดง ขนาด รูปร่าง ตำแหน่ง และการกระจายของมะเร็ง แต่ลักษณะดังกล่าวยังไม่สามารถทำให้แยกได้ว่าเป็นมะเร็งปอดชนิดใด

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CHAPTER 1

INTRODUCTION

1.1 Background and rational

Lung cancer continues to be a major medical problem. From statistical report of Siriraj cancer center in year 2001 show the incidence of lung cancer is 4th in all cancer sequence(1). The incidences are more in male than female, and continue to increase. The prognostic of lung cancer gets worse. The 1-year survival rate (the number of people who live at least 1 year after their cancer is diagnosed) for lung cancer was 42% in 1998, the last year for national data. This had not changed in 10 years. (2) The 5 - year survival rate is 5-15%, and it has largely remained unchanged for decades (3, 4, 5). Most lung cancers begin to grow silently, without any symptoms. Patients with lung cancer often do not develop symptoms until the cancer is in an advanced stage. There are many different in pathological characteristic cell type in lung cancer. Treatment and prognostic of lung cancer depend on cell type and staging. Each type of lung cancer develops in unique ways and requires different treatments. If undiagnosed and untreated, lung cancer may spread to the lymph nodes or other tissues in the chest (including the other lung). The disease also may spread (metastasize) to other organs, such as the bones, brain, or liver (6).

For all types of cancer, an accuracy diagnostic and early detection are essential to successful treatment and recovery. To find the cause of symptoms, a physical examination and medical testing are required. During the exam, the doctor will review to personal medical history, family history, tobacco use, exposure to environmental dangers, and potential symptoms. The patient will also receive one or more of the following medical tests ,such as sputum cytology, needle biopsy, bronchoscopy, chest radiography, Computed Tomography (CT) , Ultrasonography, Magnetic Resonance Imaging (MRI), Positron emission Tomography (PET).

Each procedure has limitations for example: Sputum cytology has high specificity but its low sensitivity for finding lung cancer and can not perform locates and spread of mass (4). Needle biopsy and bronchoscopy are complicated and invasive procedure for the patient. The method a fore-mentioned can not perform to evaluated shape, size, location, and spreading of lung cancer .Chest radiography remains the primary means of radiographic assessment of lung carcinoma. However, 12-30% of lung cancers are missed on chest radiographs (7). A peripheral lung lesion is usually detectable by chest x-ray when its diameter exceeds 1 centimeter (8). The lesion is greater than 1 cubic, that meaningless to cancer is an advanced stage and spread to other organ (4). A nodule smaller than 2-3 mm may not be detected by using chest radiographs, and overlapping soft tissue opacities may hide small endobronchial lesions. Chest radiographs depict indirect signs of endobronchial lesions such as obstructive pneumonia or atelectasis. These signs may well be secondary to benign tumors or mucus plugging or foreign body. In a solitary lung nodule, probability of malignancy is approximately 40% overall; therefore nodule identified on a chest x-ray requires further diagnostic workup to exclude lung cancer (3).

The uses of Nuclear medicine such as PET scanning, PET is expanding rapidly but the major disadvantage of PET imaging is that the anatomic detail seen in a PET scan is inferior to that of a conventional CT scan. This means that although PET can see the general location of an area of abnormal glucose uptake, the exact localization of the abnormality can be difficult using PET images alone and most hospitals do not have access to the equipment.

Ultrasonography has limited to evaluation of the lung cancer disease, because of the large amount of air contained within the thorax. The gas and/or bone obstruct the passage of the sound into the soft tissues and thus there is no opportunity or window for the sound to see through to interact in the soft tissues.

Nowadays, Computed Tomography (CT) has become widely accepted as primary crossectional modality for evaluation of the thorax (8). CT is excellent method for visualizing mediastinal and hilar structures, including central airways (9). CT improved visualization of lung parenchyma, particularly to costophenic angles and adjecent to the mediastinum, as well as improved visualization and differentiation of soft tissue structuers in the hilar region, mediastinum, and chest wall, particularly with the use of intravenous contrast media. CT is well suited for evaluating pulmonary neoplasms. Specific characteristics help determine the etiology, and the exact size and location are established. Adenopathy and associated findings such as effusion or occult lung disease can be detected. Pulmonary neoplasm can be divied into benign, primary malignant, and metastatic category (10).

Other diagnostic method, such as Magnetic Resonance Imaging (MRI), which uses a completely different series of physical principles and interactions but similar computed reconstruction techniques, allowed imaging of the entire body including the thorax in various planes with great contrast sensitivity. Compare with CT whole body MRI, however, is more expensive and somewhat more cumbersome to perform. Also, MRI has the added disadvantage that 5% to 7% of patients are claustrophobic and thus unable to complete the scan (11).

Currently there is a little to choose between CT and MRI in staging the disease al thought CT is more widely available and less expensive. PET imaging offers heightened sensitivity for both detection of the primary malignancy and disease spread although it is not 100% accurate and is only available in a few centers.

Because, The CT scan will provide precise information about the size, shape, and position of a tumor, and can help find enlarged lymph nodes that might contain cancer that has spread from the lung. This test is also used to find masses in the other internal organs that may be affected by the spread of lung cancer. And CT scanners are becoming more sophisticated in design and versatility and seem likely to remain the principal imaging modality for lung cancer disease. A radiologist skilled in CT scanning will review and interpret the CT findings in the chest. Generally, on interpretation to CT imaging, a radiologist will described that CT finding but not specify cell type of lung cancer.

So, we interested in CT imaging characteristics of lung cancer in 4 cell types, as for instance squamous cell carcinoma, adenocarcinoma, large cell carcinoma and small cell lung cancer.The pathological report is Gold standard. We study in chest Computed

Tomographic imaging of the patient who has pathological report to confirm that they have lung cancer. Computed Tomographic imaging from the patient in Siriraj hospital since 1995 – 2000 will be collected.

1.2 The objective in this study

1. For study to evaluate the Computed Tomographic imaging patterns of lung cancer base on pathologic cell type.
2. For study the Computed Tomographic imaging characteristics of lung cancer cell types.

CHAPTER II

LITERATURE REVIEW

2.1 Lung cancer

Lung cancer is the uncontrolled growth of abnormal cells in one or both of the lungs. While normal lung tissue cells reproduce and develop into healthy lung tissue, these abnormal cells reproduce rapidly and never grow into normal lung tissue. Lumps of cancer cells (tumors) then form and disrupt the lung, making it difficult to function properly. Lung cancer usually progresses rapidly. The median survival time after diagnosis is less than four months and about 80% of patient's die within one-year (12).

2.1.1 Type of lung cancer

There are two main types of primary lung cancer: non-small cell and small cell. These behave and respond to treatment quite differently.

2.1.1.1 Small Cell Lung Cancer (SCLC)

Small cell lung cancer, which constitutes approximately 20% and 25% (13, 14). SCLC tends to spread widely through the body. This is important because it means that treatment must include drugs to kill the widespread disease. The cancer cells can multiply quickly, form large tumors, and spread to lymph nodes and other organs such as the bones, brain, adrenal glands, and liver. This type of cancer often starts in the bronchi near the center of the chest. Small cell lung cancer is almost always caused by smoking. It is very rare for someone who has never smoked to have small cell lung cancer. Other names for SCLC are oat cell carcinoma and small cell undifferentiated carcinoma (15).

2.1.1.2 Non-Small Cell Lung Cancer (NSCLC).

The remaining 80% - 85% of lung cancers are non-small cell (NSCLC). There are three sub-types of NSCLC. The cells in these sub-types differ in size, shape, and chemical make-up. Behave as group in a biologically similar fashion and respond similarly to therapeutic intervention.

- **squamous cell carcinoma:** About 25% - 30% of all lung cancers are

squamous cell carcinomas. They are associated with a history of smoking and tend to be found centrally, near a bronchus. It relative incidence appears to be falling probably because the prevalence of smoking is falling (16, 17).

- **adenocarcinoma:** This type accounts for about 40% of lung cancers. It is

usually found in the outer region of lung. People with one type of adenocarcinoma, known as bronchioloalveolar carcinoma (sometimes called bronchoalveolar carcinoma or bronchioalveolar carcinoma) tend to have a better outlook (prognosis) than those with other types of lung cancer. Women have a higher incidence of localized disease at presentation and of adenocarcinoma (18).

- **large-cell undifferentiated carcinoma:** This type of cancer accounts for about

10%-15% of lung cancers. It may appear in any part of the lung, and it tends to grow and spread quickly resulting in a poor prognosis.

2.1.2 Epidemiology

Thailand is divided into four major regions, the North, Northeast, Central and South. The incidence of lung cancer, a highly lethal malignancy, continues to in crease. Results from three cancer registries (Chiang Mai, Khon Kaen, and Songkhla) in different regions of Thailand and from a cancer survey in the population of Bangkok during the years 1988-1991 are presented. Lung cancer is second in frequency, with the highest rates in northern Thailand, where the incidence in women is among the highest in the world (19, 20).

From statistical report of Siriraj cancer center in year 2001 show the incidence of lung cancer is 4th in all cancer sequence and high proportion of adenocarcinoma. For both male and female with high incidence accounting to lung cancer patient age 65+ years (1).

Internationally:

Worldwide, lung cancer is the most frequently occurring cancer and the leading cause of cancer mortality. Approximately 1.04 million new cases of lung cancer were diagnosed in 1990, accounting for 12.8% of the worldwide total cancer incidence. The number of new cases is increasing each year; a 16% increase occurred between 1985 and 1990 (3). Lung cancer occurs predominately in persons aged 50-70 years, and during the last 10 years, the incidence of lung cancer has increased more rapidly in women (18).

2.1.3 Causes of lung cancer

Exposure to carcinogens, such as those present in tobacco smoke, immediately causes cumulative changes to the tissue lining the bronchi of the lungs the and more tissue gets damaged until a tumor develops.

There are 7 major causes of lung cancer (and, actually, cancer in general):

- Carcinogens such as those in cigarette smoke
- Cancer-causing Agents in the Workplace

- Inhaled chemicals or minerals such as Asbestos exposure, arsenic, beryllium, vinyl chloride, nickel chromates, coal products, mustard gas, and chloromethyl ethers.

- Fuels such as gasoline.

- Diesel exhausts.

- Radiation exposure.
- Recurring Inflammation.

- Personal and Family History.
- Diet.
- Air pollution.

2.1.3.1 The role of smoking

Smoking, particularly of cigarettes, is believed to be by far the main cause of lung cancer, which at least in theory makes it one of the easiest diseases to prevent. An estimated 80% of lung cancers result from smoking due to the hundreds of known carcinogens, such as polynuclear aromatic hydrocarbons, present in cigarette smoke. The length of time a person continues to smoke as well as the amount smoked increases the person's chances of contracting lung cancer. If a person stops smoking, these chances steadily decrease as the lung damage is repaired.

Passive smoking, the inhalation of smoke from another's smoking, has recently been identified as a much larger cause of lung cancer in non-smokers than previously believed.

Stephen H.Hecht. (21) reported that smoking is by far the most important risk factor for lung cancer. At the beginning of the 20th century, lung cancer was rare. The introduction of manufactured cigarettes, which made them readily available, changed this. About 87% of lung cancers are thought to result from smoking or passive exposure to tobacco smoke.

2.1.3.2 Asbestos

Asbestos is the group of minerals that used in industries. Asbestos fibers tend to break easily into particles that can float in the air and stick to clothes. When the particles are inhaled, they can lodge in the lung, damaging cells, that cause to lung cancer. Asbestos can cause a variety of lung diseases. It increases the risk of developing lung cancer. There is a synergistic effect between tobacco smoking and asbestos in the formation of lung cancer.

2.1.3.3 Talc and Talcum Powder

In the past, some studies suggested talc miners and millers have a higher risk of lung cancer and other respiratory diseases because of their exposure to industrial grade talc. Recent studies of talc miners have not found an increase in lung cancer rate. Talcum powder is made from talc, a mineral that in its natural form may contain asbestos. By law since 1973, all home-use talcum products (baby, body, and facial powders) have been asbestos-free. The use of cosmetic talcum powder has not been found to increase the risk of lung cancer.

2.1.3.4 Radiation exposure

Radon is a colorless and odorless gas generated by the breakdown of radioactive radium, which in turn is the decayed product of uranium, found in the earth's crust. Radon exposure is the second major cause of lung cancer after smoking. The radiation ionizes genetic material, causing mutations that sometimes turn cancerous. Radon gas levels vary by locality and the composition of the underlying soil and rocks.

Patient who has had radiation therapy to the chest for cancer is at higher risk for lung cancer, particularly if they smoke. The most typical patients are those treated for Hodgkin disease or women who receive radiation to the chest after a mastectomy for breast cancer. Women who receive radiation therapy to the breast after a lumpectomy do not have a higher than expected risk of lung cancer. But if they smoke, their chance of lung cancer goes up markedly.

2.1.3.5 Recurring Inflammation

Tuberculosis and some types of pneumonia often leave scars on the lung. People who have this scarring, it can increase your risk of developing the adenocarcinoma type of lung cancer.

2.1.3.6 Personal and Family History

If people who have had lung cancer, they have a higher risk of developing another lung cancer. Brothers, sisters, and children of those who have had lung cancer may have a slightly higher risk of lung cancer themselves. Recently, a group called the

Genetic Epidemiology of Lung Cancer Consortium studied families with a strong history of lung cancer. They found that the susceptibility to lung cancer might reside on a particular chromosome (chromosome 6). People who have the abnormality on chromosome 6 will more readily develop lung cancer even if they only smoke a little. Other family members who lack the genetic abnormality have to smoke more to develop lung cancer (22).

2.1.3.7 Diet

Some reports have indicated that a diet low in fruits and vegetables may increase the chances of getting cancer if you are exposed to tobacco smoke. Evidence is growing that fruits and vegetables may protect you against lung cancer.

2.1.3.8 Air Pollution

In some cities, air pollution may slightly increase the risk of lung cancer. This risk is far less than that caused by smoking.

2.1.4 Clinical Signs and Symptoms (23).

Most patients with lung cancer present with symptoms related to the respiratory tract. Symptoms caused by local tumor growth depend on the initial tumor size and location and on the involvement of adjacent structures. Symptoms can be related to local tumor growth in an airway, to chest wall invasion, to mediastinal invasion, to metastasic disease, or to a tumor related paraneoplastic syndrome. A careful search for these signs and symptoms provides information about the tumor and directs further evaluation.

2.1.4.1 Local Tumor Growth

Tumors are classified based on their location as either central (endobronchial or mediastinal) or peripheral (distal to the major bronchi). Those arising in large airways or centrally located can produce local symptoms including cough, localized wheezing, hemoptysis, focal atelectasis, dyspnea, or post obstructive pneumonitis. A cavitating tumor or post obstructive pneumonitis mimics a primary infection or abscess and can produce symptoms of fever, chills and productive cough. Tumors arising in small airways or peripherally located are usually asymptomatic but may present with hemoptysis. Consequently, more peripheral than central tumors are found incidentally on a chest x-ray.

2.1.4.2 Local/Regional Invasion

When the tumor grows and invades adjacent structures or spreads to the mediastinal nodes, systemic symptoms are more common. In this setting, systemic symptoms include fatigue, weight loss, anorexia, cachexia, and fever. Mediastinal invasion can cause some specific syndromes related to tumor involvement of adjacent structures. With mediastinal invasion on the left side, the recurrent laryngeal nerve may become entrapped or compressed. These patients will present with hoarseness and ipsilateral vocal cord paralysis. Involvement of the recurrent laryngeal nerve classifies these tumors as stage IIIB. The phrenic nerve can also be involved with mediastinal invasion. Phrenic nerve involvement manifests as diaphragmatic paralysis and positional dyspnea. Rarely the esophagus is involved and may produce dysphagia. With esophageal invasion the patients may also develop a bronchoesophageal fistula with recurrent aspiration and pneumonia.

Right upper lobe tumors or paratracheal adenopathy can compress the superior vena cava (SVC) and cause the SVC syndrome (Figure.2-1 and Figure 2-2). An apical lung tumor, also known as a Pancoast tumor, may invade local neural structures and produce a characteristic syndrome of pain and possible Horner's syndrome. Horner's syndrome may occur with a Pancoast tumor or whenever a tumor impinges on the sympathetic chain.

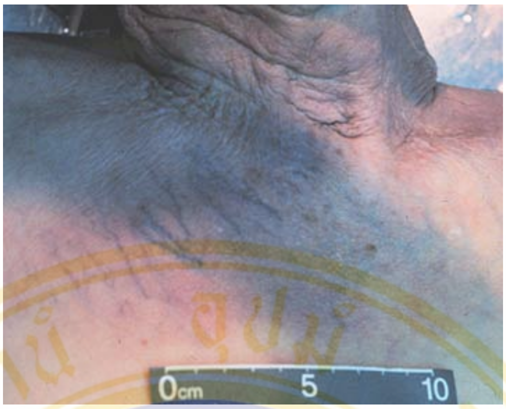
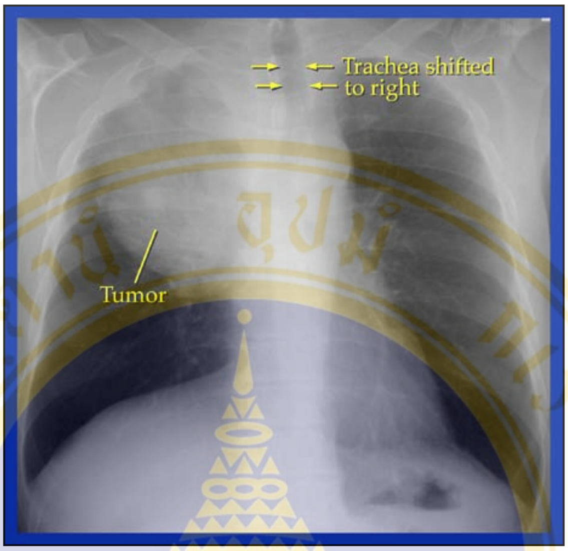


Figure 2-1 A photograph of a patient with superior vena cava syndrome. Note the distended neck veins and purple discoloration. (from http://www.vh.org/adult/provider/radiology/LungTumors/ParaneoplasticProcesses/Text/SVCSyndromePhoto.html



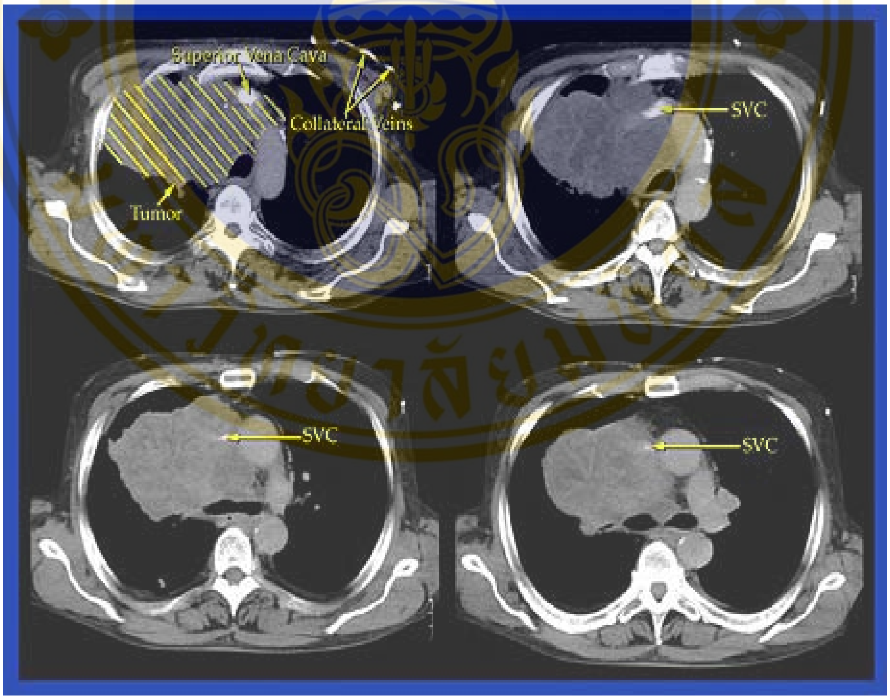


Figure 2-2 Selected radiographic images (x-ray and CT) from a patient with superior vena cava syndrome (from http://www.vh.org/adult/provider/radiology/LungTumors/ParaneoplasticProcesses/Text/SVCRadiology.html)

2.1.4.3 Intrathoracic Metastases

The thoracic manifestations of metastatic lung cancer result from hematogenous, lymphatic or intra-alveolar tumor dissemination. Detecting these nodal and distant metastases is essential in properly staging the patient.

Lung cancers may involve any of the normal chest structures. Large cancers eventually affect the heart in 15-35% of cases. Pericardial involvement is more common than myocardial involvement. Pericardial involvement causes pericardial effusions, tamponade, or dysrhythmias, and is suggested by an enlarging heart silhouette on chest x-ray, by a paradoxical pulse, by a pericardial friction rub or Kussmaul's sign, by new congestive failure or by venous engorgement. The diagnosis is confirmed using echocardiography.

Pleural involvement occurs in 8-15% of lung cancer patients. Common symptoms of pleural involvement are dyspnea, cough and chest pain. Pleural involvement manifests as pleural effusions, pleural masses or rarely pneumothorax. Pleural effusion from lung cancer can arise because of lymphatic obstruction or due to direct pleural invasion by the tumor. This is an important distinction for the clinician because a small percentage of patients with pleural effusion due to lymphatic obstruction are still candidates for surgical resection. Direct pleural invasion by the tumor is diagnosed by thoracentesis, closed pleural biopsy or pleuroscopy. The sensitivity of these procedures in diagnosing pleural involvement increases in that respective order.

Tumor growth into the chest wall, ribs, or vertebral bodies most commonly produces localized pain, pleural effusions, or paresis.

Intra-alveolar spread is most often seen with bronchioloalveolar carcinoma and results in multicentric lung involvement with bronchorrhea in about half the cases. This type of spread gives an alveolar pattern on chest X-ray and CT scan.

2.1.4.4 Extrathoracic Metastases

Distant metastases from lung cancer have been found in every organ. However, the four most common sites for metastases are adrenal (Figure 2-3), bone, brain, and liver (Figure 2-4). The frequency of metastases and specific locations vary with histological tumor type. Brain and bone metastases can produce signs and symptoms detectable through careful history and physical exam, however detecting liver and adrenal metastases usually requires radiographic and/or laboratory evaluation.

Brain metastases carry a poor prognosis and high morbidity. Common symptoms of brain metastases are headaches, focal neurologic dysfunction, or seizures. Symptoms will depend on the area of CNS involved. Metastatic lesions can present as solitary or multiple intracranial masses, as meningeal carcinomatosis, or with spinal cord involvement.

Skeletal system metastases are reported in up to 30% of non small cell lung cancer patients. Patients with bone metastases often present with localized pain, however, some patients may present only with elevated calcium or elevated alkaline phosphatase on laboratory screen.

Liver metastases are found in 10-20% of non small cell lung cancer patients. Patients with metastatic disease present in one of three ways:

(1) symptoms from the lung primary with asymptomatic liver involvement discovered during evaluation;

(2) nonspecific symptoms such as weakness, fever, sweating , or weight loss and liver abnormalities on liver or abdominal CT scan;

(3) clinical features of liver disease including abdominal pain, ascites or hepatomegaly.

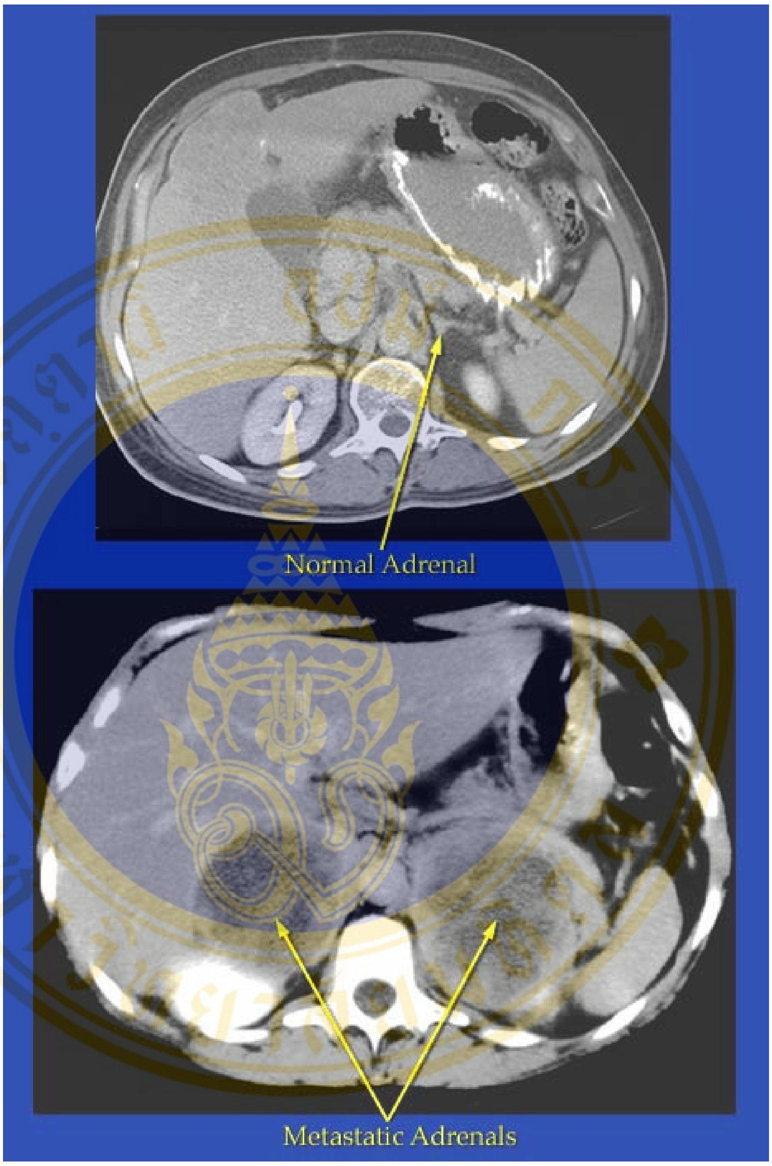


Figure 2-3 Lung cancer frequently metastasizes to the adrenal glands without causing any specific signs or symptoms. Because these lesions are clinically silent, chest CT scans to evaluate for lung cancer should include cuts through the adrenals.

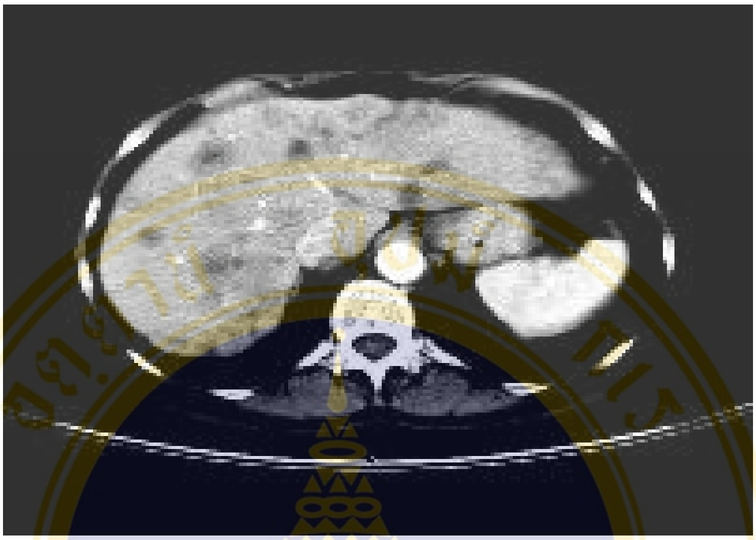


Figure 2-4. Small cell lung cancer, Contrast-enhanced CT scan of the abdomen. Axial section through the liver shows multiple hypoattenuating areas in the liver. Poorly defined margins, attenuation greater than that of water, and scattered distribution in a patient with known lung cancer is most consistent with metastatic disease.

(from http://www.emedicine.com/radio/topic405.htm)

2.1.4.5 Paraneoplastic Syndromes

About 10% of lung cancer patients develop a paraneoplastic syndrome. The pathophysiology of these syndromes is poorly understood but many are related to ectopic hormone production. Although many of these syndromes have been reported, few are clinically important. Ectopic hormone production is most often associated with small cell lung cancer. Especially common are the syndrome of inappropriate antidiuretic hormone (SIADH) and ectopic ACTH production. While ectopic ACTH production is not unusual, Cushing's syndrome is unusual because patients do not often survive long enough to develop the full clinical syndrome. Hypercalcemia due to ectopic PTH-like hormone is most often associated with squamous cell carcinoma.

Digital clubbing and hypertrophic osteoarthropathy (HPO) also occur with lung cancer (Figure 2-5). Neuromuscular disorders occur in lung cancer patients with up to 5% of patients having some neuromyopathy. Probably the best described syndrome is Eaton- Lambert syndrome. This is a myasthenic-like syndrome; however, it differs from myasthenia gravis because motor strength improves with repetitive stimulation while in myasthenia gravis muscle strength decreases with repetitive stimulation.

Figure 2-5 The hands of a patient with severe clubbing. Note the bulging of the distal phalynx and periungual erythema of the nail bed (from http://www.vh.org/adult/provider/radiology/LungTumors/ParaneoplasticProcesses/Text/ClubbingPict.html

2.1.5 Staging for non small cell lung cancer .

The aim of diagnostic and clinical staging of lung cancer is appropriate treatment for patient that especially to be feasible surgical cure. Not only that ,clinial staging to aid prognosis disease.

TNM classification of lung cancer by The international Union Againt Cancer (UICC = Union Internationale Centre Ie Cancer) to beginning in1966, with modification, was revised in 1986 and recently in 1997 by the American Joint

Committee on Cancer (AJCC) (Table 2-1 and Table 2-2). New TNM staging is depending on easily to obtain and needless duplication of examination offering identical or similar information should be avoided (24). Percentage survival at 5 yrs by clinical stage for the more advanced stages remains poor, emphasizing the importance of early detection (Table 2-3).

Table 2-1 Tumor, node, metastasis (TNM) classification (1997).

Tumor	
T1	A tumor 3 cm in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus
T2	A tumor with any of the following features: >3 cm in greatest dimension; involvement of the main bronchus, 2 cm distal to the carina; invasion of the visceral pleura; atelectasis or obstructive pneumonia extending to the hilum but not involving the entire lung
T3	A tumor of any size directly invading any of: chest wall (including superior sulcus tumors), diaphragm, mediastinal pleura or parietal pericardium; or tumor in a main bronchus within 2 cm of the carina but not involving it; or atelectasis of the entire lung
T4	A tumor of any size invading any of: mediastinum, heart, great vessels, trachea, oesophagus, vertebral body or carina; or tumor with a malignant pleural or pericardial effusion or with satellite tumor nodules within the ipsilateral primary-tumor lobe of the lung
Nodes	
N0	No regional lymph node metastases
N1	Metastases to ipsilateral peribronchial and/or hilar nodes and direct tumour extension into intrapulmonary nodes
N2	Metastases to ipsilateral mediastinal and/or subcarinal nodes
N3	Metastases to contralateral mediastinal, contralateral hilar, scalene or supraclavicular nodes
Metastases	
M0	No distant metastases
M1	Distant metastases present

Table 2-2 Staging classification

Stage	TNM classification
IA	T1 N0 M0
IB	T2 N0 M0
IIA	T1 N1 M0
IIB	T2 N1 M0
	T3 N0 M0
IIIA	T3 N1 M0
	T1 N2 M0
	T2 N2 M0
	T3 N2 M0
IIIB	T4 N0 M0
	T4 N1 M0
	T4 N2 M0
	T1 N3 M0
	T2 N3 M0
	T3 N3 M0
	T4 N3 M0
IV	Any T Any N M1

TNM: tumor, node, metastasis

Table 2-3 Cumulative percentage survival at 5-yrs post-treatment by clinical stage

Stage	5-yr survival %
Ia 61	61
Ib 38	38
IIa 34	34
IIb 24	24
IIIa 13	13
IIIb 5	5
IV 1	1

2.1.6 Staging for small cell lung cancer .

Almost all-solid tumors are staged by utilizing the tumor, node, and metastases (TNM) system because it provides important prognostic information and is used to design management plans. However, the TNM system has failed to provide important prognostic information in patients with SCLC and is useful only in a few patients (<5%) who may benefit from a very detailed staging according to the TNM system.

The 2-stage system used for SCLC initially was proposed by the Veterans Administration Lung Group. Patients with disease confined to one hemithorax, with or without mediastinal, contralateral hilar, or ipsilateral supraclavicular or scalene lymph nodes are considered to have limited-stage disease, while those with disease involvement at any other location are considered to have extensive-stage disease. (The involvement of supraclavicular nodes and the presence of cytologically positive pleural effusion subsequently have been placed in different stage groupings in slightly revised staging classifications.) The key variable in this purposely vague staging definition is the ability to encompass the entire disease within one radiation therapy port. A slight modification of this system is used currently and is provided in Table 2-4.

Table 4 Staging of Small Cell Carcinoma of Lung.

Stage	**Discription**
Limited stage	Disease confined to one hemithorax; includes involvement of mediastinal, contralateral hilar, and/or supraclavicular and scalene lymph nodes. Malignant pleural effusion is excluded.
Extensive stage	Disease has spread beyond the definition of limited stage, or malignant pleural effusion is present.

2.2 Diagnosis for lung cancer

2.2.1 Medical History and Physical Exam

The doctor will take a medical history (health-related interview) to check for risk factors and symptoms. Doctors will also examine patient to look for signs of lung cancer and other health problems.

2.2.2 Imaging Tests

Imaging tests use x-rays, magnetic fields, or radioactive substances to create pictures of the inside of the body. Several imaging tests are used to find lung cancer and determine where it may have spread in the body.

2.2.2.1 Chest x-ray: This is the first test, the doctor will order to look for any mass or spot on the lungs. It is a plain x-ray of the chest and can be done in any outpatient setting. If this is normal, the probably don't have lung cancer. If something suspicious is seen, the doctor may order additional tests.

2.2.2.2 Computed tomography (CT): The CT scan is an x-ray procedure that produces detailed cross-sectional images of the body. Instead of taking one picture, as does a conventional x-ray, a CT scanner takes many pictures as it rotates around body. A computer then combines these pictures into an image of a slice of body. CT will take pictures of multiple slices of the part of body that is being studied. Often after the first set of pictures is taken an intravenous that helps better outline structures in the body. A second set of pictures is then taken.

CT scans take longer than regular x-rays and the patient will need to lie still on a table while they are being done. The newest CT scans take only seconds to complete. The CT scan will provide precise information about the size, shape, and position of a tumor, and can help find enlarged lymph nodes that might contain cancer that has spread from the lung. CT scans are more sensitive than a routine chest x-ray in finding early lung cancers. This test is also used to find masses in the adrenal glands, brain, and other internal organs that may be affected by the spread of lung cancer. A chest CT scan is the criterion standard for staging; however, it rarely is indicated emergently.

2.2.2.3 Magnetic resonance imaging (MRI): MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of tissue and by certain diseases. A computer translates the pattern of radio waves given off by the tissues into a very detailed image of parts of the body. Not only does this produce cross sectional slices of the body like a CT scanner, it can also produce slices that are parallel with the length of the body.

A contrast material might be injected just as with CT scans, but is used less often. MRI scans take longer, often up to an hour. Also, the patient has to be placed inside a tube-like piece of equipment, which is confining and can upset people with claustrophobia. The machine makes a thumping noise that the patient may find annoying. MRI images are particularly useful in detecting lung cancer that has spread to the brain or spinal cord.

2.2.2.4 Positron emission tomography(PET): Positron emission tomography (PET) uses glucose (a form of sugar) that contains a radioactive atom. Cancer cells in the body absorb large amounts of the radioactive sugar and a special camera can detect the radioactivity. This can be a very important test if the patient have early stage lung cancer. The doctor will often use this test to see if the cancer has spread to lymph nodes. It is also helpful in telling whether a shadow on the chest x-ray is cancer. PET scans are also useful when the cancer has spread, but doesn't know where. PET scans can be used instead of several different x-rays because they scan your whole body. Newer devices combine a CT scan and a PET scan to even better pinpoint the tumor.

2.2.2.5 Bone scans: In a bone scan, a small amount of radioactive substance (usually technetium diphosphonate) is injected into a vein. The amount of radioactivity used is very low and causes no long-term effects. This substance builds up in areas of bone that may be abnormal because of cancer metastasis. However, other bone diseases can also cause abnormal bone scan results. Bone scans are routinely done in patients with small cell lung cancer. Usually, they are only done in patients with non-small cell lung cancer when other test results or symptoms suggest that the cancer has spread to the bones.

2.2.3 Procedures that Sample Tissues and Cells

One or more of these tests will be used to confirm that a lung mass seen on imaging tests is a lung cancer, rather than a benign condition. These tests are also used to determine the exact type of lung cancer patient may have and to help determine how far it may have spread.

2.2.3.1 Sputum cytology: A sample of phlegm (the best way is to get early morning samples from you 3 days in a row) is examined under a microscope to see if cancer cells are present.

2.2.3.2 Needle biopsy: A needle can be guided into the mass while the lungs are being viewed with fluoroscopy. CT scans can also be used to guide the placement of needles. Unlike fluoroscopy, CT doesn't provide a continuous picture so the needle is inserted in the direction of the mass, a CT image is taken, and the direction of the needle is guided based on the image. This process is repeated a few times until the CT image confirms that the needle is within the mass. A tiny sample of the tumor is sucked into a syringe and examined under the microscope to see if cancer cells are present.

2.2.3.3 Bronchoscopy: The patient will need to be sedated for this exam. A fiberoptic flexible, lighted tube is passed through a mouth into the bronchi. This can help find some tumors or blockages in the lungs. At the same time, it can also be used to take biopsies (samples of tissue) or samples of lung secretions to be examined under a microscope for cancer cells or precancerous cells. Studies are underway to see if annual exams will be beneficial in finding premalignant changes in people at high risk.

2.2.3.4 Mediastinoscopy and mediastinotomy: For both of these procedures, the patient will receive general anesthesia (be put into a deep sleep). With mediastinoscopy a small cut is made in the neck and a hollow lighted tube is inserted behind the sternum. Special instruments, operated through this tube, can be used to take a tissue sample from the mediastinal lymph nodes (along the windpipe and the major bronchial tube areas). Looking at the samples under a microscope can show whether cancer cells are present.

Mediastinotomy also removes samples of mediastinal lymph nodes while the patient is under general anesthesia. Unlike mediastinoscopy, the surgeon opens the chest cavity by making a small incision beside the sternum or the ribs. This allows the surgeon to reach more lymph nodes that are not reached by standard mediastinoscopy.

2.2.3.5 Thoracentesis and thoracoscopy: These procedures are done to

find out whether or not a build-up of fluid around the lungs (pleural effusion) is the result of cancer spreading to the membranes that cover the lungs (pleura). The build-up might also be caused by a condition such as heart failure or an infection. For thoracentesis, the skin is numbed and a needle is placed between the ribs to drain the fluid. The fluid is checked under a microscope to look for cancer cells.

Chemical tests of the fluid are also sometimes useful in distinguishing a malignant pleural effusion from a benign one. Once a malignant pleural fluid has been diagnosed, thoracentesis may be repeated to remove more fluid. Fluid build-up can prevent the lungs from filling with air, so thoracentesis can help the patient breathe better.

Thoracoscopy is a procedure that uses a thin, lighted tube connected to a video camera and monitor to view the space between the lungs and the chest wall. Using this, the doctor can see cancer deposits and remove a small piece of the tissue to be examined under the microscope. Thoracoscopy can also be used to sample lymph nodes and fluid.

2.2.3.6 Bone marrow biopsy: A needle is used to remove a sample of bone about 1/16 inch across and 1 inch long (usually from the back of hip bone) after the area has been numbed with local anesthesia. The sample is checked under the microscope for cancer cells. This procedure is done mostly to help in finding spread of small cell lung cancer.

2.3 Computed tomography

Computed tomography (CT) is one of the most widely used imaging modalities in medicine and other areas. CT's success in medical applications is largely responsible for the surging interest in the development of modern tomographic imaging technique (25). CT image is the display of the anatomy of a thin slice of the body developed from multiple x-ray absorption measurements made around the body's periphery. The absorption of each tissue element is calculated and the result displayed as a grey scale image on a video monitor. The basic principle of CT-scanning is that the internal structure of an object can be reconstructed from multiple projections of that object. The mathematical principle was established by Radon in 1917. Cormack in South Africa became interested in cross sectional imaging in the late 1950's and published his work on image reconstruction in 1963 and 1964. In addition, early research work was conducted in Russia. However, it was not until 1972 that Hounsfield in the UK appreciated the significance of Cormack's work and used computer technology to apply it to diagnostic imaging. The first clinical images were published in 1972 (26).

2.3.1 Technical principle

The technique produces images of a cross-sectional layer or slice of the body. Each slice is divided into many tiny volume elements called voxels (Figure 2-6) for this purpose. When displayed on a video monitor each voxel is represented in two dimensions by a pixel. The task is to assign to each voxel a number proportional to the degree to which that the particular voxel attenuates the X-ray beam.

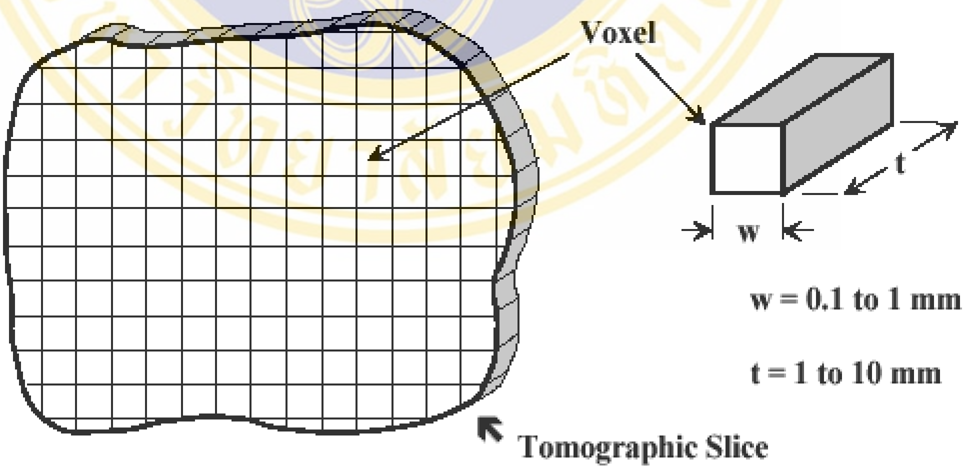


Figure 2-6 Schematic of a tomographic slice represented by a large number of voxels.

(http://www.life.rmit.edu.au/mrs/subject/mr100/xrayct.html)

The composition and thickness of each voxel, along with the quality of the beam, determine the degree of attenuation represented by the linear attenuation coefficient, μ. The image reconstruction technique is based on the x-ray attenuation equation (Lambert -Beer law) (27, 28).

$$I = I_0 e^{-\mu L} \qquad (1)$$

I_0 is the incident intensity of x-ray beam on surface of object of thickness L, and I is the transmitted intensity. The linear attenuation coefficient (μ) is a property that is depends on the atomic number and density of the material and on energy spectrum of the x-ray beam (29).

Table 2-5. Linear attenuation coefficient (μ) of the tissue in human body at energy spectrum of the x-ray beam 60 keV, 84 keV and 122 keV (27).

Tissue	**μ (cm^{-1})**		
	60 keV	**84 keV**	**122 keV**
Bone	0.528	0.464	0.410
Blood	0.208	0.182	0.163
Gray matter	0.212	0.184	0.163
White matter	0.213	0.187	0.166
CSF	0.207	0.181	0.160
Water	0.206	0.180	0.160
Fat	0.185	0.162	0.144
Air	0.0004	0.0003	0.0002

But the human body to be composed of various tissues, so it is non-uniform medium. This is cause to change Lambert-Beer law to

$$I = I_0 e^{-\int \mu dx} \qquad (2)$$

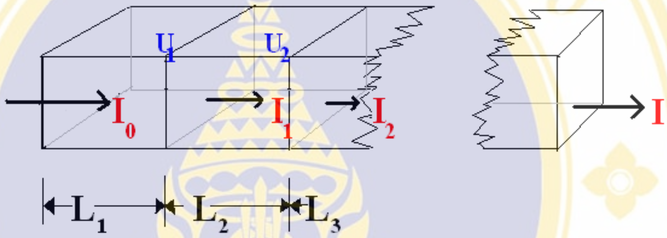


Figure 2-7 Illustration of equation 2

$\int \mu dx$ is term of line integral that x-ray beam through pass the body. This equation to be used to basic calculated for CT imaging. For easy to manipulation, one can then write to natural logarithm.

$$p = -\ln \frac{I}{I_0} = \int \mu dx \qquad (3)$$

p is ray sum or ray projection or line integral that x-ray beam through pass the body (Figure 2-8).

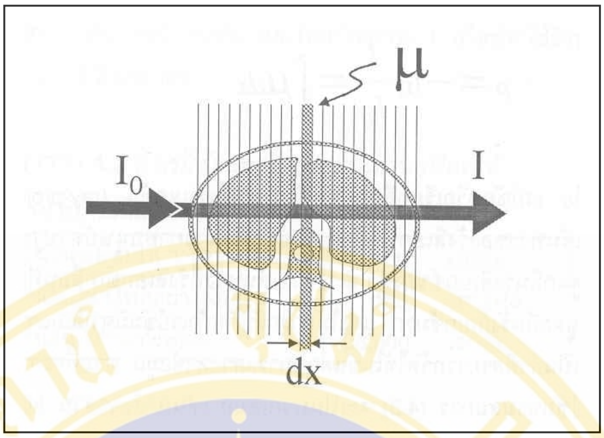


Figure 2-8 Illustration of equation 3

Data Acquisition System

Data Acquisition System (DAS) is very important for CT. The accumulated transmission data is then subjected to a tomographic reconstruction algorithm to generate the image of a slice. The most widely applied algorithm is called Filtered Back Projection (Figure 2-9). The data is initially corrected for physical and instrument variables and then subjected to filtration using Fourier Transformation before being back projected to generate the tomographic image. These processes are performed using dedicated computer hardware interfaced to a general-purpose computer.

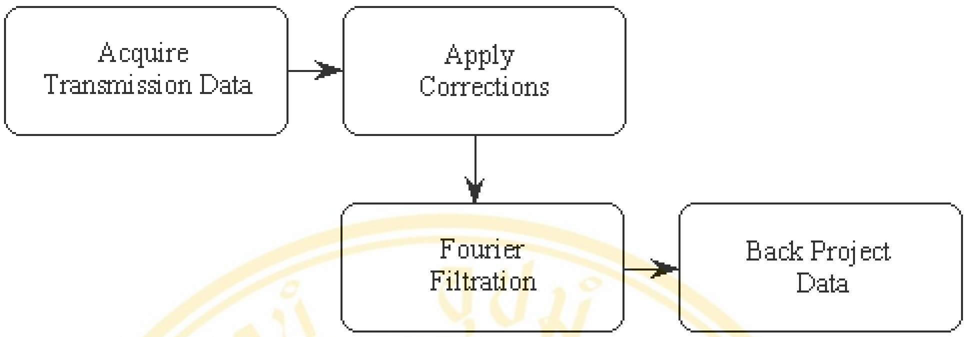


Figure 2-9 Flow chart depicting steps in the Filtered Back Projection process.

(http://www.life.rmit.edu.au/mrs/subject/mr100/xrayct.html)

The original concept developed by Radon and used initially by Hounsfield used simple back projection. Figure 2-10 is a representation of how back projection works. The basic premise is that any attenuation of the X-ray beam is assumed to have occurred uniformly along the entire ray path. Thus, the result of the back projection of the first profile, P_1 is to put the values 7 and 9 in both elements of the first and second rows, respectively. The second profile, P_2 adds a 4 to the top right element, 1 to the bottom left element and 11 to the other two elements when back projected. The other profiles are treated in similar fashion. Following subtraction of an offset (16 in this case) and renormalisation (division by 3 in this case) of the data set, the final image is obtained.

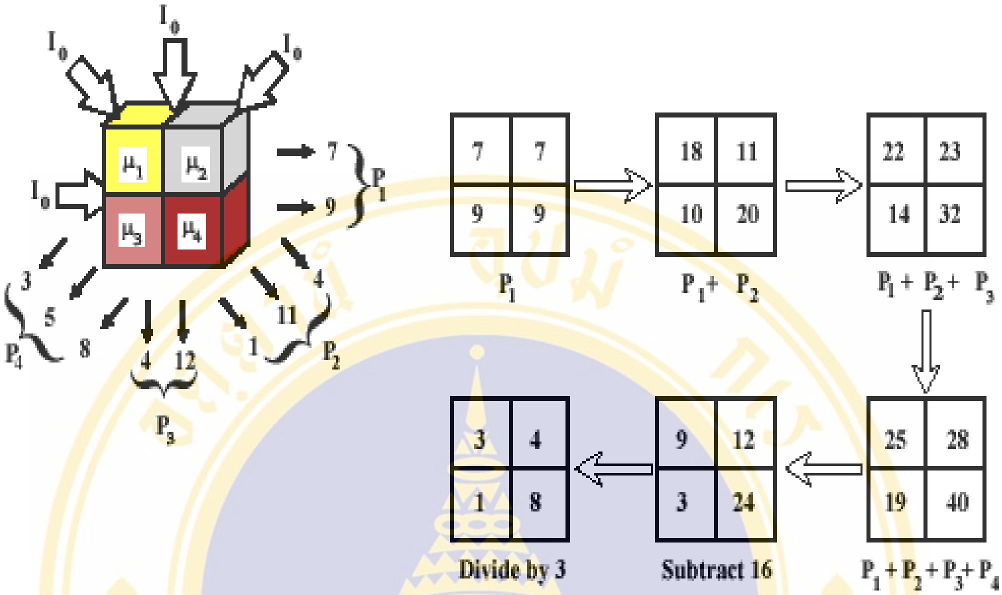


Figure 2-10 Representation of back projection.

The representation in Figure 2-11 demonstrates the principle in more detail. A single profile is back projected to give a dark stripe across the entire image plane (Figure 2-11(a)). As we scan the phantom from many directions and back project the ray profiles onto the image plane (Figure 2-11(b)), an image of the radio-dense dot, albeit a poor one, begins to emerge (Figure 2-11(c)). As the number of projections increases, the quality improves but there will always remain spoking or blurring in the image. This blurring can be removed using what is known as Filtered Back Projection (Figure 2-11(d)).

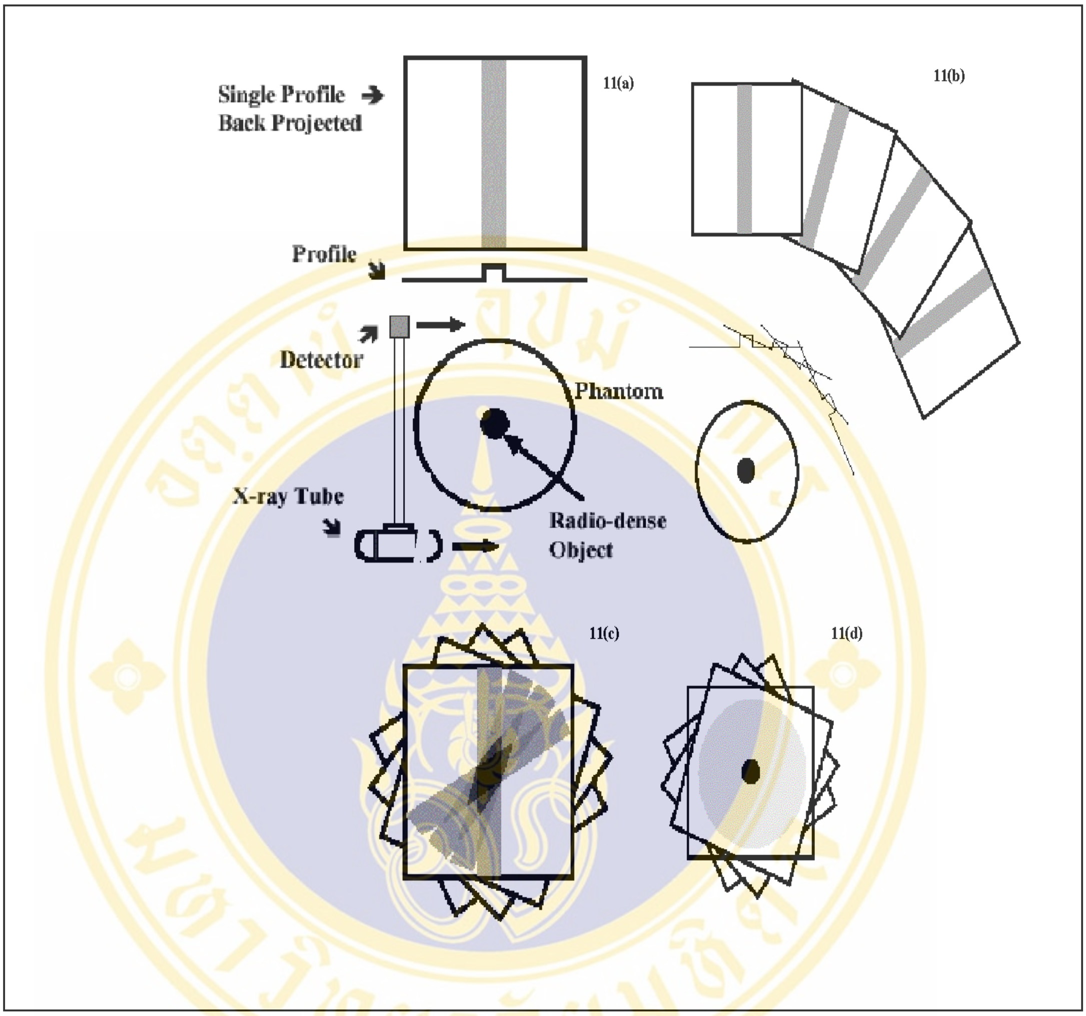


Figure 2-11 Demonstration of simple back projection: (a) An X-ray tube scans a phantom, consisting of a radio-dense object in an otherwise uniform container, and generates the profile as shown for the back projection process. (b) Four profiles generated by scanning at slightly different angles around the phantom. (c) The image reconstructed from just four projections. (d) The image reconstructed using filtered back projection.

2.3.2 CT number

After a CT scanner reconstructs an image, the relative pixel values represent the relative linear attenuation coefficients because the process of reconstruction is not conductive to the calculation of the absolute values of the attenuation coefficients. However, it is valuable to quantify the pixel value so that the physician can compare the composition of one tissue with that of another. A CT numbering system that relates a CT number to the linear attenuation coefficients of x-ray was devised and is given by

$$\text{CT number} = \frac{K(\mu - \mu_w)}{\mu_w} \qquad (4)$$

μ_w is the attenuation coefficients of the water.

μ is the attenuation coefficients of the pixel in question.

K is the factor scale (K = 1000)

In honor of Godfrey Hounsfield, the inventor of CT scanning, the CT units are named Hounsfield units (HU) (29). Attenuation values for various body and fluids show in table 2-6. Using HUs, water is 0 HU and air is -1000 HU. Fat is about -90 HU, un-enhanced soft tissue about 50 HU and cortical bone 1000 to 2000 HU. The human visual system cannot distinguish between the subtle differenced in attenuation CT can detect when the full range of values is displayed. Therefore contrast and brightness are altered when the image data is displayed to accentuate attenuation differences in the range of interest (10).

Table 2-6. Attenuation values for various body and fluids (31).

Tissue Types	Standard Value (HU)	Scatter(HU)
Bone (compact)	> 250	
Bone (spongy)	130 ± 100	
Thyroid	70 ± 10	
Liver	65 ± 5	45 - 75
Muscle	45 ± 5	35 - 50
Spleen	45 ± 5	35 - 55
Lymphoma	45 ± 10	40 - 60
Pancreas	40 ± 10	25 - 55
Kidney	30 ± 10	20 - 40
Fat	-65 ± 10	-80 - (-100)

Fluids	Standard Value (HU)
Blood (coagulated)	1130 ± 100
Blood (venous whole blood)	30 ± 100
Plasma	130 ± 100
Exudate (>30 g protein/l)	130 ± 100
Transudate (<30 g protein/l)	130 ± 100
Ringer solution	130 ± 100

2.3.3 Densitometry

The arrangement of detectors on a scanning gantry facilitates quantitative density measurements in regions of interest (ROI). The CT number represents the arithmetic mean of all attenuation values measured in an individual volume element. The gray-scale display of a scanned object alone provides some information on the relative density of a structure on the image. Upon comparison with the arounding tissue, the structure may be described as isodense (same density), hypodense (low density) or hyperdense (high density).

2.3.4 Technical Realization

Methods of obtaining the necessary ray projections for a CT scan require an x-ray source, detectors, and associated electronics all mounted on gantry, or frame, that mechanically moves to produce the scan. Such instruments have been designd along three generation lines since their introduction by Godfrey Hounsfield in 1972 (32). The translate-rotate mechanical motion was the type originally developed by Hounsfield, and instruments using this original design are referred to as first generation scanners.

Most X-ray CT scanners in use today employ a large fan beam such that the patient is completely encompassed by it. The number of elements in the detector array is of the order of 750 - 900. They are aligned along the arc of a circle centred on the focus of the X-ray tube (Figure 2-12). The X-ray tube and detector array rotate through 360^{o} during which time transmission data is accumulated.

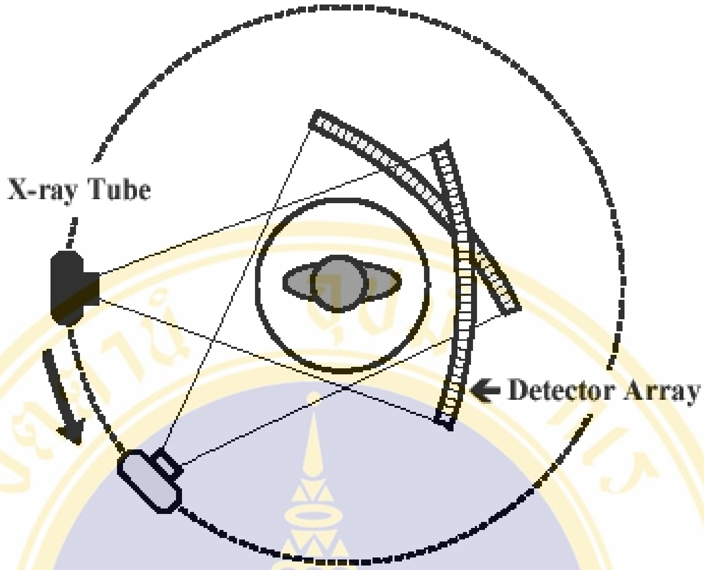


Figure 2-12 The X-ray tube and detector array rotate continuously about the patient.

Attenuation is measured by detectors which are aligned behind the patient, opposite to the x-ray source. There are basically five different types of CT scanning systems.

First generation *(Single Detector Rotate-Translate Systems);* the first successful clinical CT scanner was based on a translate-rotate gantry geometry (33). The intensity of the beam is measured by individual contralateral detector elements. In this type of system the x-ray is collimated down to the desired slice thickness and a narrow slit. The resulting x-ray pattern is referred to as a pencil beam. It is component by one x-ray tube and one detector. A fine x-ray beam scans the body through 180 step of 1 º. After each angular increment, a translation is made as the beam transversrs the body. A total of 5 $^{1}/_{2}$ to 6 minutes are required for scanning.

Second generation *(Multiple Detectors Rotate-Translate Systems);* A detector array with 5 to 50 elements is located contralateral to the x-ray tube. A fan beam reduces the number of angular increments required for scanning. Scan is made at steps of 10º, which corresponds to the angle of the fan beam. The minimum scan time ranges from 6 to 20 seconds.

Third generation *(Rotation Scanner with Movable Detector);* Most scanners even today are of this (third generation) type. A typical scanner (Figure 2-13) employs a large fan beam such that the patient is completely encompassed by the fan. The number of detector elements is in the hundreds, e.g.

- the GE Hispeed Advantage has 852 elements 1.0 mm apart;
- the Siemens Somatom Plus 4 has 768 elements 1.1 mm apart; and
- the Toshiba Xpress/SX has 896 elements 1.03 mm apart.

The detector elements are aligned along the arc of a circle centred on the focus of the X-ray tube.

The X-ray tube and detector array rotate as one through 360 degrees during which accumulation of several hundred discrete profiles are obtained. Depending on the scanner design, the X-ray beam may be pulsed or continuous. Both solid state detectors and pressurised xenon gas ionisation chambers are used for the detection process.

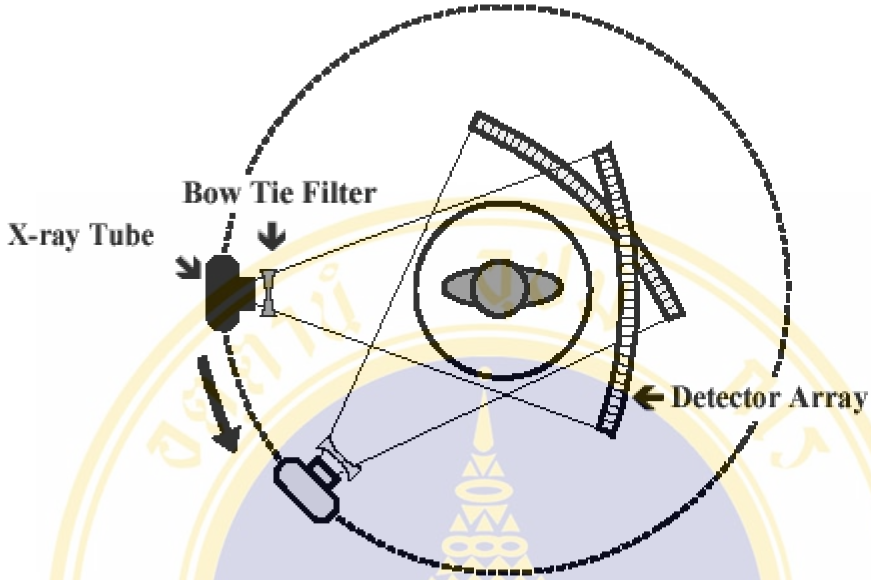


Figure 2-13 Third generations CT scanner.

The X-ray tube and detector array rotate as one about the patient. The number of profiles recorded depends on the chosen scan parameters but is at least a few hundred and may be in excess of a thousand. Scan times can be as low as a second. Although the dynamic range of the detectors is very high, some manufacturers have overcome partially the effect of excessive variations in signal strength by using special bow tie shaped filters chosen to suit the body or head shape. The filter attenuates the peripheral part of the fan to a greater extent than the central part. It also helps overcome the effects of beam hardening and helps minimise patient skin dose in the peripheral part of the field of view.

Variations in X-ray output intensity with time can be accounted for by normalising the data at each view by sampling the signal from a number of reference detectors located at the extremes of the fan array. They are able to continuously monitor the unattenuated X-ray beam. However, the individual detector elements in the fan have to be calibrated prior to any patient studies, usually once a day to minimise ring artifacts which is a potential problem with third generation scanners and is caused by unequal detector element efficiencies. Another feature of third generation scanners is pre-detector anti-scatter collimation between adjacent detector elements.

Helical scanning: Recent innovations in slip-ring technology have enabled the X-ray tube to rotate continuously in the same direction which overcomes problems of interscan delays. When the continuous motion of the X-ray tube is combined with a continuous advance of the patient table along the axis of the scanner we have helical or spiral scanning, as illustrated in Figure 2-14. Typical table velocities are 1 - 10 mm/s; a complete 360 degree rotation may be achieved in 0.5 s and the nominal fan beam thickness is 1 mm or greater.

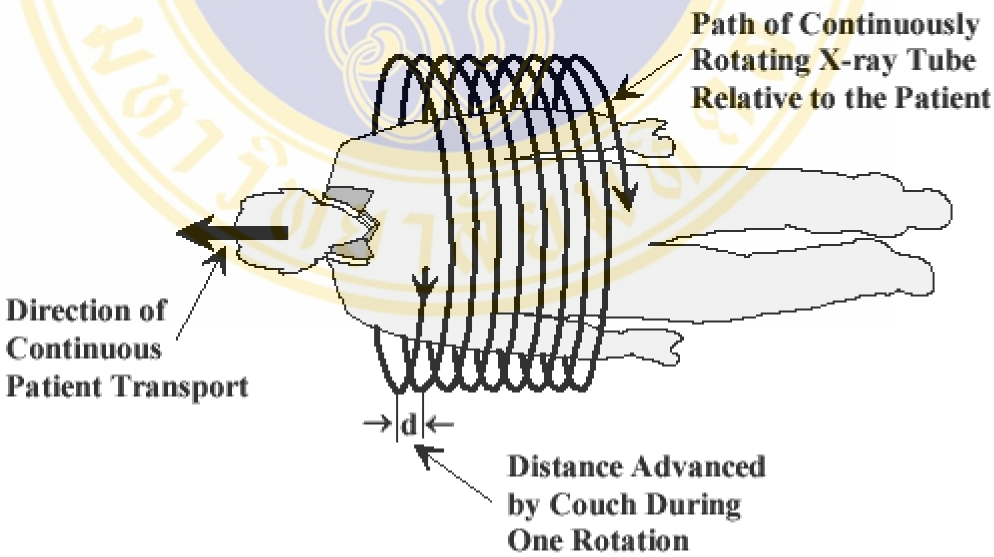


Figure 2-14 Illustration of helical scanning.

In the context of helical scanning a new parameter called the pitch is frequently employed. The pitch is defined as the: ratio of the table movement distance in one rotation to the nominal slice thickness.Thus, for a couch advance of 10 mm and a nominal slice width (as defined by the collimators) of 10 mm the pitch is 1. Typically, pitch values in the range of 1 to 2 are utilised depending on what spatial resolution is desired in the direction of couch motion.

A significant reduction in examination time's results from helical scanning because large volumes can be scanned contiguously without any gaps and with little influence from patient motion. The Somatom Plus-4A allows up to 80 slices to be scanned contiguously in 60 seconds of non-stop scanning. Thus, single breathhold scanning is now possible and reconstruction, with minimal loss of spatial resolution, of sagittal, coronal and 3D images is now feasible. Within the scanned volume, images can be calculated at arbitrary positions and at arbitrary spacing with effective slice widths of 1 mm or greater. One important difference is that the position, spacing and thickness of the successive slices chosen for reconstruction can be made retrospectively without the need to re-scan the patient.

Multi-slice CT: It was inevitable that the demand for increased speed would produce technical advances such as multi-slice scanning. El Scint was the first manufacturer to offer this technology when they provided the option of simultaneous dual focus/dual detector geometry with their helical CT scanner. In effect, the operator had the opportunity to either halve the scan time for a particular volume of interest or improve the spatial resolution along the patient axis.

Since then there has been a massive commitment by most manufacturers to achieve multi-slice capability. In essence, all CT manufacturers now offer multi-slice capability in which between 2 and 4 slices of thickness between 0.5 mm and 10 mm may be imaged simultaneously. This is achieved by having a detector array with a length along the Z-axis of 20-32 mm (Figure 2-15). Minimum scanner rotation times are usually half a second, so that this technology has the potential to offer fast volume acquisitions. It is anticipated that manufacturers will introduce scanners with 8 and 16 slice capabilities in the near future.

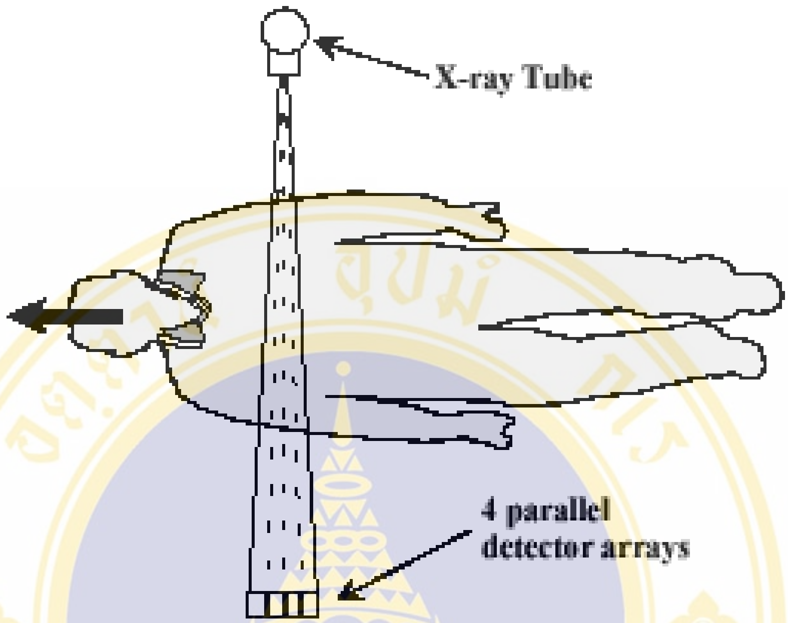


Figure 2-15 A generic multi-slice CT system.

Electron beam CT: Imatron first marketed A novel approach in the quest for speed in 1983. The device is illustrated in Figure 2-16 and for reasons that will become obvious is referred to as Electron Beam CT. In essence, mechanical movement has been eliminated by incorporating the target of the X-ray tube as a circular arc of approximately 210 degrees. The patient is placed above and at the centre of this arc and the tomographic motion is achieved by electronic steering of the electron beam of about 600 mA around the circumference of the target. At any instant the X-ray beam is collimated to a small fan of angle 30 degrees and width 2 cm. The HVL of the beam is approximately 10.5 mm Al with the X-ray tube operated at 130 kVp, which implies a somewhat harder beam than that routinely encountered in conventional CT machines.

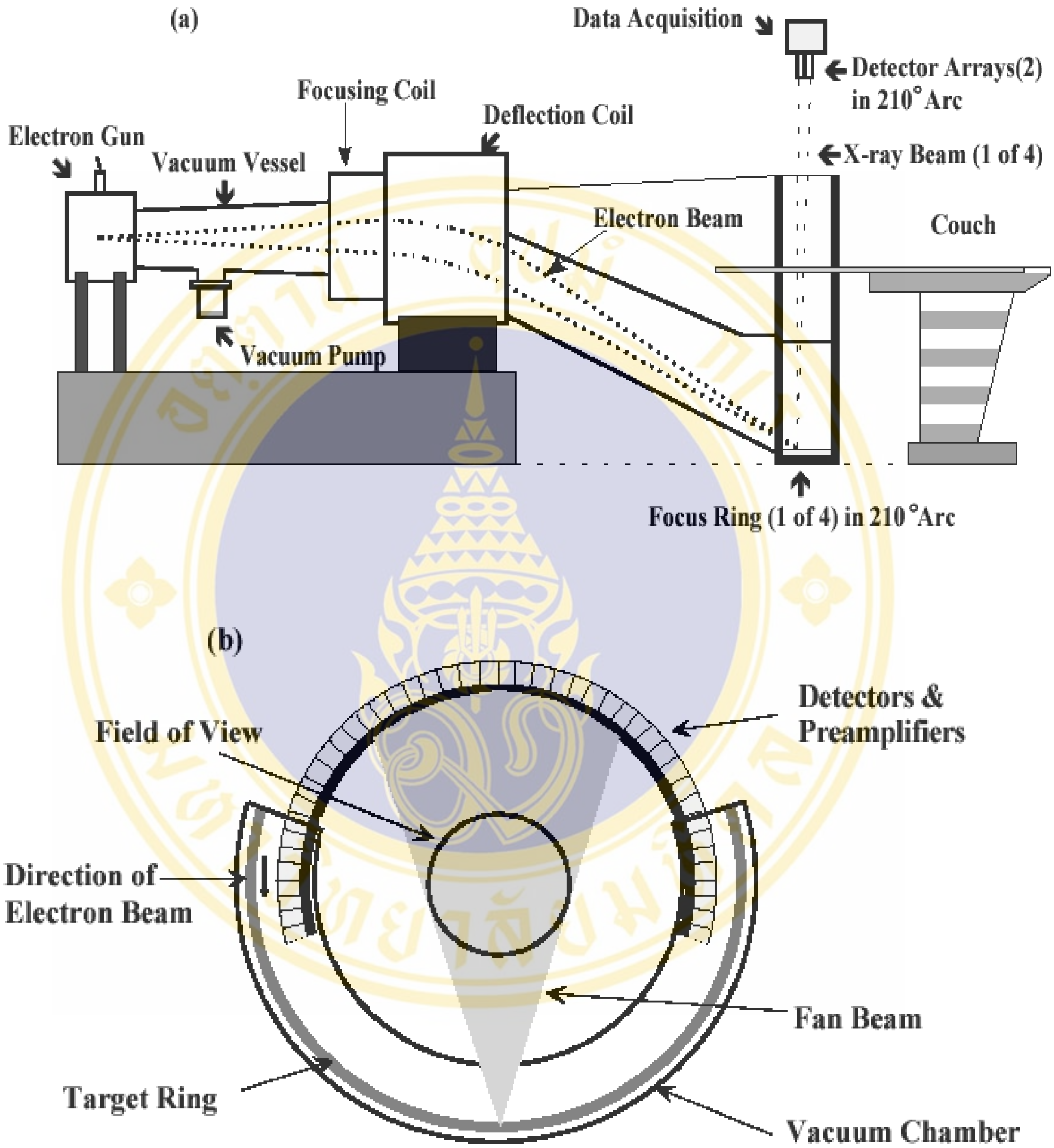


Figure 2-16 Simplified schematic of the Imatron CT scanner in (a) longitudinal view and (b) end on.

Advantages of CT

- Spatial ambiguity is completely overcome.
- In lung; the shape, margin and relationship to other structures can be outlined.
- Images produced can show tiny changes in density. Particularly, contrast between fat and other tissues define the mediastinal contents.
- A unique position can be identified for needle biopsy.

Below: Representative pairs of CT images look very much like anatomic cross sections. There is no structural overlap. The CT scanner gives every picture element (262,144 in these images) a density value on a 4096 unit hounsfield scale. Tissues with large density difference such as air and bone are best seen in displays showing a wide range of values (such as images of lung on the right). Tissues with small density differences are best seen on displays of a small range of values (such as the images of the mediastinum on the left). Each pair of images below came from the same digital data set, only display parameters are different.

2.3.5 Technical standards for CT of the chest. (11,18)

The following are technical criteria that should be met for adequate CT evaluation in lung cancer.

1. Third or foueth generation CT equipment with slice scanning times of 2 s or less.

2. Maximum slices thickness and slice interval of 10 mm. Obtain 1-2 mm slices through the nodule to look for calcifications.

3. Scan area to include from above the apices of the lungs through the adrenal glands.

4. The field of view should include the contiguous chest wall.

5. Printed hard copies should have appropriate lung and mediastinal windows.

2.3.6 Image Display of CT

A wide range in CT density is present on any CT scan of thorax. The density differences among chest wall, mediastinum, and lung parenchyma requier viewing of the image that least at two-window setting. Both the window level and window width must be manipulated to achieve optimum density for evaluation of the thorax. Specific window settings are often referring to be they are designed to display. Foe example, lung windows, soft tissue windows, or bone windows. Standard window width and window level for CT of the chest very among institutions, but some generalization can be made: for soft tissues of mediastimum and chest wall a window width of 300 to 500 HU and a window level of 40 HU are appropriate. For the lung are photographed at window width between 1000 and 1500 HU or more at window level of approximately –600 HU. For skeletal structures the widest possible window setting at a window level of 30 HU is the best (14).

CT images are typically printed on to lazer film, but they are increasingly being reviewed and interpreted on cathode ray tube (CRT) displays. Such soft copy viewing coupled with picture archive and communication systems (PACS) allows simultaneous and remote viewing and image manipulation.

2.4 Contrast Media

The comparison between normal and altered anatomical structures is the basis of the evaluation of an image obtained by CT. In some situations the high resolution of CT is able to identify pathological areas without the aid of contrast enhancement (CE).However CE is frequently needed to increase the sensitivity and specificity of the investigation. Contrast media are used in CT with the aim of obtaining different attenuation values between tissue and therefore making tissue identification and characterisation easier (27, 34).

Intravenous contrast, although seldom required for the evaluation of the lung, can help determine or exclude the vascular nature of a lesion in selected case. Enhance scan may help in distinguishing between malignant and benign lesions (10, 3).

Swensen SJ, et al. (35) reported that malignant neoplasms enhanced significantly more than glanulomas and benign neoplasms. With 15 HU as the threshold, the sensitivity was 98%, the specificity was 58%, and the accuracy was 77%.

IV contrast material varies in its concentration and composition. Non-ionic or low osmolality contrast agents are associated with less discomfort and a low incident of allergic reactions but the more expensive than ionic contrast media. Non-ionic contrast is preferred in patients with drug allergies, a pior contrast reaction, or history of asthma, heart disease, or sickle cell disease, as well as in debilitated patients. IV contrast should be avoided in patients with creatinine above 2.0. Diabetic patients taking Glucophaeg should discontinue that medication for 2 day and have close diabetic monitoring following IV contrast administration. Contrast is requirement and can be administered at 2-4 cc per second through an antecubital vein (3, 10, 36). In CT of the chest the use of bolus injection technique is recommended: 50 – 120 ml of non-ionic contrast medium 300-350 mgI/ml. (34, 36).

2.5 Characterize lung cancer by CT imaging dependent on its morphologic features.

2.5.1 Size: Zerhouni EA, et al.(37) reported .that a nodule size > 3 cm is associated with malignancy in 93-99% of case.

2.5.2 Cavitation: All lung cancers may potentially form cavities: overall, approximately 16% of peripheral cancers show cavitation (38). Squamous cell cancer cavitates most frequently, with adenocarcinoma and large carcinoma cavitating less so. Cavitating in small cell is distinctly uncommon. Cavity may be seen in any size tumor, including fairly small tumors; the wall of cavitated tumor nodule is typical irregular, especially in larger tumors. The walls of the cavity are usually thick, approaching 1 cm or more (38).

2.5.3 Calcification: The probability that the nodule will be benign rises proportionally with the degree of calcification. The cross sectional area of malignant tumors normally contains less than 10% calcification (31). Central area of calcification (especially popcorn or dumbbell shaped calcification and ringlike peripheral calcification) indicate benign growth. So do finely plaqued, stipple areas of calcification that are distributed evenly throughout the nodule. Eccentric, fine calcification that is found predominantly along the periphery is sign of malignancy, especially when found in nodules that are larger than 3 cm (31).

Calcifications are sign of benign lesions, but they may be seen in malignant tumors. Calcification in malignant tumors may occur owing to tumor production, dystrophic calcification in tumor necrosis, or engulfment of pre-exiting benign calcification by tumor. Characteristic benign calcifications are described as diffuse punctate, central dense, popcorn, or laminar (bull's-eye) types with in the nodule. All solitary pulmonary nodules with out such characteristic calcification or demonstrated stability in size require a tissue diagnosis. As many as 40% of determinate nodules prove to be malignant at biopsy (8). Figure 2-17 showed benign and malignant pattern of SPN calcifications.

Webb WR. (39) Reported that only characteristic patterns of calcification such as central, diffuse, laminar or popcorn are indicative of benignity.

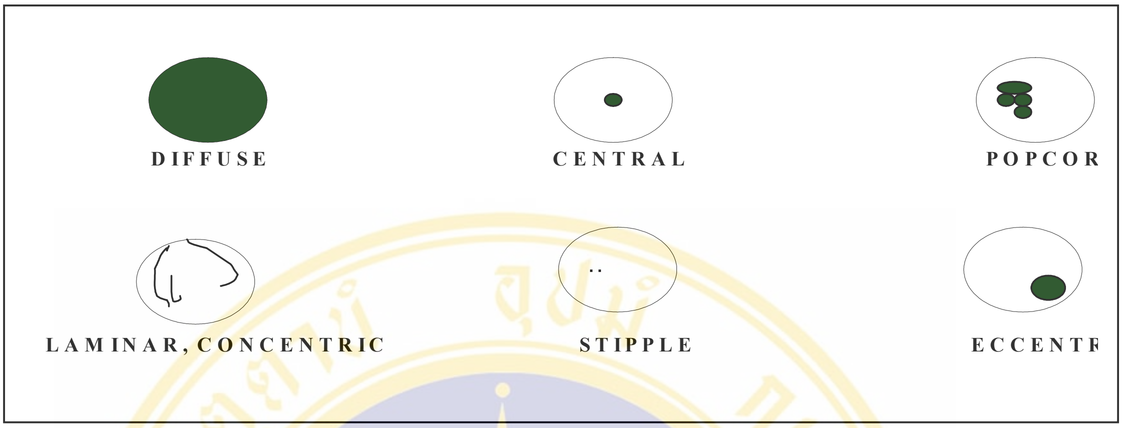


Figure 2-17 Benign and malignant pattern of SPN calcifications. A, B, C and D illustration shows the typical appearances of calcifications with in pulmonary nodules caused by benign disease. E and F represent nonspecific pattern of calcification within the SPN that carry a potential diagnosis of either benign granuloma or malignant pulmonary nodule with calcification (From Aisner J, Arriagada R, Green RM, Martini N, Perry CM. Comprehensive Textbook of Thoracic Oncology. Baltimore: William & Wilkins; 1996:129)

2.5.4 Edges: Stanley S.Siegelman et al (40) reported that 65.1% of malignancies had edges some irregular undulations or slight speculation or grossly irregular with speculation primary.

2.6 CT imaging features of lung cancer

The imaging appearances of lung cancer are considered in the following framework

Peripheral tumor *(tumors arising beyond the hilum)*

- Approximately 40 % of lung cancer arises beyond segmental bronchi.
- Usual shapes or oval.

- A corona radiata (distort surrounding vessels) is nearly specific for bronchial carcinoma.

- Edge is usually lobular or irregular.

- Cavity is seen in 16% of case on plain chest radiographs and more frequency on (14).

- CT demonstrates calcification with in 6-10% .(37, 41)

Central tumors *(tumors arising at or close to the hilum)*

The cardinal imaging signs of a central tumor are collapse and consolidation of lung beyond the tumor and the presence of hilar enlargement, signs that may be seen in isolation or in conjunction with one or another (14).

2.7 CT imaging patterns of lung cancer based on cell type

2.7.1 Squamous cell carcinomas

The lesion is usually located centrally. It is most likely to cavitate. Squamous cell carcinomas grow intraluminally and are least likely to metastasis distantly (< 20% of case at presentation). These are usually slow growing, with late metastasis predominately to the liver, adrenal glands, kidneys, and bones. The mode of spread is direct extension into the local lymph nodes, the chest wall or mediastinum with bone destruction, superior vena cava syndrome, and phrenic or recurrent laryngeal nerve paralysis have been reported (42, 43, 44). Squamous cell carcinomas may attain grate size. Sat Sharma et al. (3) reported that radiologic findings by tumor histologic type (Table 2-7).

Sider L. (42), Theros EG. (45) and Heitzman ER. (46) reported that tumors usually range in size from 1 to 10 cm. They are typically found in the central bronchi; although one third occur beyond the segmental bronchi.

Squamous cell carcinoma most frequency arise as masses in central bronchi. Superior sulcus tumors, so-called Pancoast's tumors, are usually squamous cell carcinoma (8).

Sider L. (42) and Byrd RB, Carr DT, Miller WE, et al. (47) reported that squamous cell carcinoma cavitates in 10 to 20% of cases.

Table 2-7 Radiologic finding by tumor histologic type.

Radiologic symptom	Squamous cell carcinomas (%)	Adenocarci-noma (%)	Small cell carcinoma (%)	Large cell carcinoma (%)
Hilar tumor	40	78	18	32
Peripheral tumor	27	29	71	59
Peripheral tumor >4 cm	18	26	8	41
Apical tumor	3	2	1	4
Multiple tumors	0	1	2,4	2
Atelectasis	36	17	10	13
Pneumonia	15	22	15	23
Liquefaction	7	0	2	4
Mediastinal lymph nodes	1	13	2	10

2.7.2 Adenocarcinoma

It is typically classified as acinar, papillary, solid, and bronchioloalveolar varieties. Adenocarcinoma typically presents as a small (often < 4 cm), peripheral, round or oval, smoothly marginated, solitary pulmonary nodule. Occasionally, a more central location or spiculation and irregular margins are noted. Some lesions distort surrounding vessels (corona radiata) or cause retraction of the adjacent pleura ("pleuroparenchymal tail"), but these features also may be seen with benign abnormalities (42, 45, 48). The lesion is located peripherally in approximately one half of cases, it rarely cavitates, and an eccentric pattern of calcification may be evident. Calcification is rarely seen in lung cancer on chest radiographs, but is seen small proportion of case on CT.

Filderman et al. (49) and Woodring et al. (50) reported that eccentric or amorphous calcification has been reported in up to 6% of cases at CT. Calcification at times represent engulfment of a preexisting granuloma.

Theros EG. (45), Byrd RB, Carr DT, Miller WE, et al. (47) and Woodring JH, Stelling CB (50) reported that adenocarcinoma, lymphadenopathy is seen in 40% and 27% of hilar and mediastinal lymph nodes, respectively.

An early propensity is noted of metastases to the lymph nodes, pleura, adrenal glands, central nervous system (CNS), and bone (3, 11). It occurs most often as a peripheral pulmonary nodule, unrelated to bronchi (8).

2.7.3 Large cell carcinoma

The majority present as a large (average size > 7 cm), peripheral mass,with poorly defined margins. Cavitation and calcification are uncommon (6%). Hilar and mediastinal adenopathy are seen in 30% and 10% of cases, respectively.Rapid growth with early lymphatic and hematogenous metastases occurs frequently (3, 8, 51).

2.7.4 Small cell lung cancer

SCLC mostly originates in the proximal airways such as the lobar bronchi or main bronchi. The tumors are usually located centrally (75 to 90% of cases), and mediastinal extension is common and often extensive with encasement of mediastinal structures and tracheobronchial compression (Figure 2-18 and Figure 2-19). The less-commonly described peripheral. SCLC is often associated with hilar adenopathy, and atelectasis secondary to main stem bronchus compression. Pleural effusions are reported in 5 to 50% of cases.

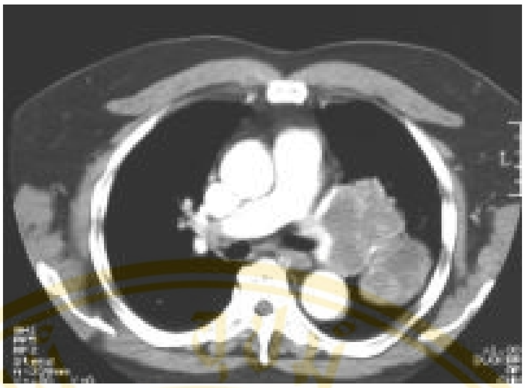


Figure 2-18. Small cell lung cancer. Contrast-enhanced CT scan of the chest shows a large left lung and a hilar mass, with invasion of the left pulmonary artery.(from http://www.emedicine.com/radio/topic405.htm)

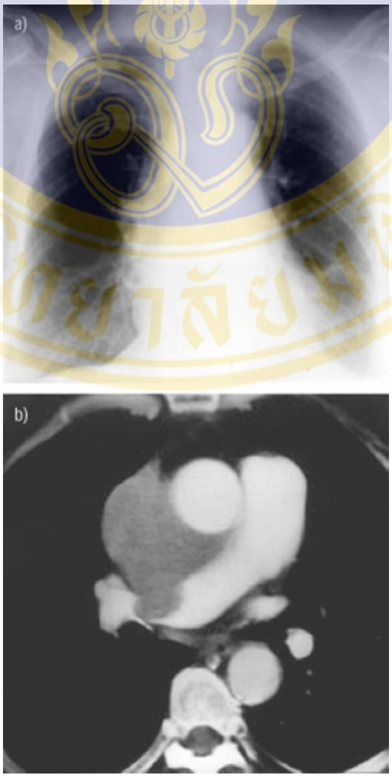


Figure 2-19 Selected radiographic images (x-ray and CT) from a patient with small cell lung carcinoma. (from http://www.emedicine.com/radio/topic405.htm).

The primary lesion may be small or not even visible on radiograph studies, but early extrathoracic metastases are common and even present prior to the development of pulmonary symptoms.Liver, bone marrow, adrenal glands (Figure 2-20), and brain are frequent sites of metastatic disease (3, 51).

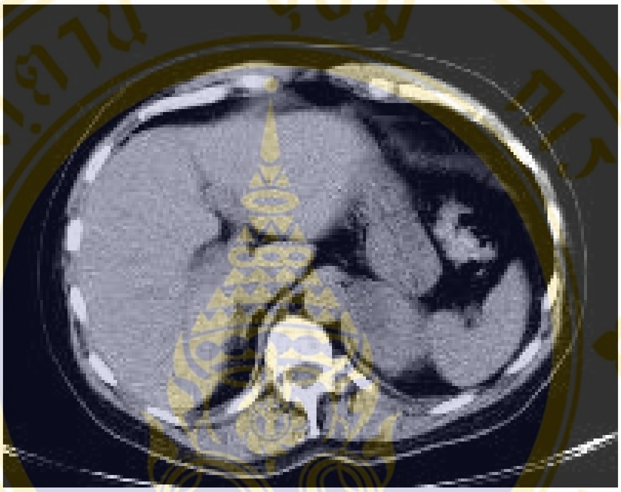


Figure 2-20. Small cell, lung cancer. Nonenhanced CT scan of the abdomen at the level of adrenal gland shows a large adrenal mass on the left side. The high attenuation values on this image and the large size of the adrenal mass suggest a malignant lesion. The adrenal glands are a common site for metastatic small-cell lung cancer.

(from http://www.emedicine.com/radio/topic405.htm)

CHAPTER III

MATERIALS AND METHODS

3.1 Materials

We study on 333 patients with pathological proven primary lung cancer in any 4-cell types, for instance squamous cell carcinoma, adenocarcinoma, large cell carcinoma and small cell carcinoma. Since 1995 to 2000 in Siriraj hospital.

Criteria for inclusions into the study were:

(1) A preoperative complete CT scan of the chest was available for review.

(2) CT imaging of the chest with pre and post contrast media injected.

(3) Scan area to include from above the apices of the lungs through the adrenal glands.

(4) The field of view should include the contiguous chest wall.

(5) Hard or soft copies of the CT scans were contained at both mediastinal and lung windows display.

Sixty-seven patients (54 male and 13 female) ranging in age from 29 to 84 years (mean ± Standard Deviation, 63 ± 10 years) fulfilled the inclusion criteria. There were comprised 28 squamous cell carcinoma, 23 adenocarcinoma, 7 large cell carcinoma and 9 small cell carcinoma (Table 3-1).

Table 3-1 Frequency of pathologic results.

Pathologic cell type of lung cancer	No. of patients
Squamous cell carcinoma	28(41.8%)
Adenocarcinoma	23(34.3%)
Large cell carcinoma	7(10.4%)
Small cell carcinoma	9(13.4%)
Total	67

3.2 Methods

Two observers who were unaware of the pathologic results independently reviewed each CT imaging. Observers recorded a characteristic of the tumor including location and present or absent of a variety of margin and internal characteristics. Discrepancies in interpretation between observers were resolved by consensus.

All CT examination was reviewed for the following finding:

(1) Location of the tumor by lobe and within a specific lobe was recorded. Tumor located within arising beyond the hilum at CT was arbitrarily considered to be peripheral (Figure3-1). Those within arising at or close to the hilum were considered central (Figure3-2).

(2) The present of infiltration of the lung parenchyma (Figure3-3).

(3) Size was recoded. The diameter was measured within short and long axis diameters at mediastinal window setting on transverse CT imaging.

(4) Edges were recorded. The edges were classified as regular if the tumor was sharply and distinctly separated from surrounding lung parenchyma. In the present of hazy or distinct margins, the tumor was considered to be irregular.

(5) Internal characteristics of tumor attenuation was noted be either

homogeneous or inhomogeneous density at pre and post contrast injected, if inhomogeneous, the present or absence of cavitation (Figure 3-4) and calcification of the tumor were recorded (Figure3-5).

(6) The present or absent of pleural effusion (Figure 3-6).

(7) The present or absent of mediastinal lymph node enlargement (Figure 3-7).

(8) Chest wall invasion (Figure 3-8).

(9) Metastases to the liver (areas of low attenuation that did not appear to be cysts in portions of liver was recorded (Figure 3-9).

(10) Metastases to the adrenal gland (thickness> 1cm) (Figure 3-10).

(11) Metastases to the contra or ipsilateral lung were recorded (Figure11 and Figure 3-12).

(12) The observers interpretation that patient have any cell type in lung cancer. Discrepancies in interpretation between observers were resolved by consensus.

Each case was classified as squamous cell carcinoma, adenocarcinoma, large cell carcinoma and small cell carcinoma.

(12.1) The criteria for a squamous cell carcinoma were (a) central

lesion (b) localize in upper lobe (c) cavitations lesion.

(12.2) The criteria for a adenocarcinoma were (a) peripheral lesion

(b) tumor size is smaller than 4 cm.

(12.3) The criteria for a large cell carcinoma were (a) peripheral lesion

(b) tumor size is larger than 7 cm (c) presence of pleural effusion.

(12.4) The criteria for a small cell carcinoma were(a) central lesion (b) mediastinum / hilar LN enlargement (c) intrathoracic or extrathoracic metastasis.

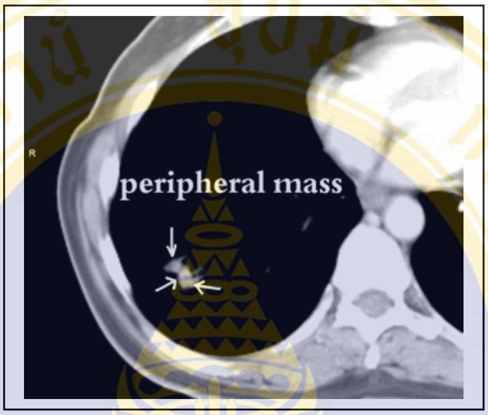


Figure 3-1 A 47 years old female with peripheral mass.

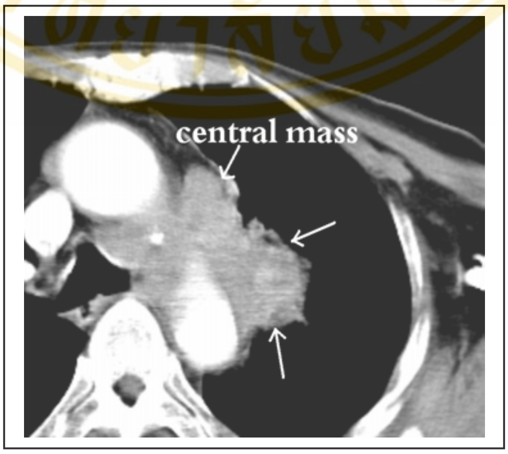


Figure 3-2 A 77 years old male with central mass.

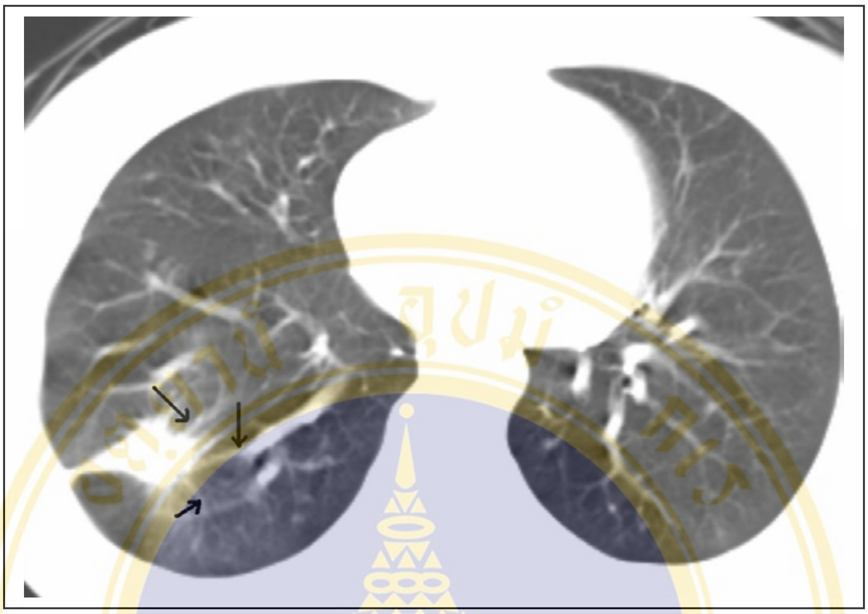


Figure 3-3 Adenocarcinoma: A 47 years old female with infiltration mass at right peripheral.

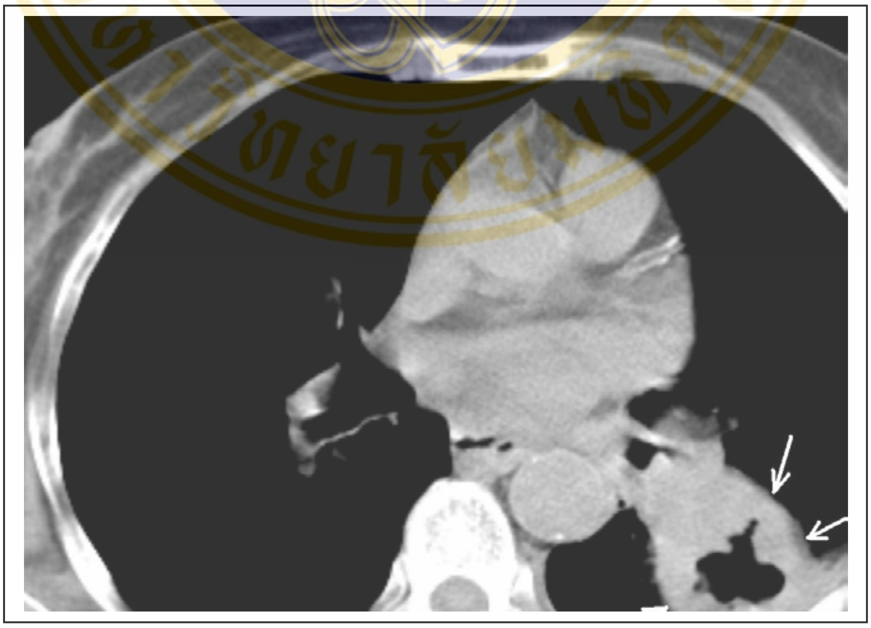


Figure 3-4 Adenocarcinoma: A 60 years old male with cavitating mass at left lower lobe.

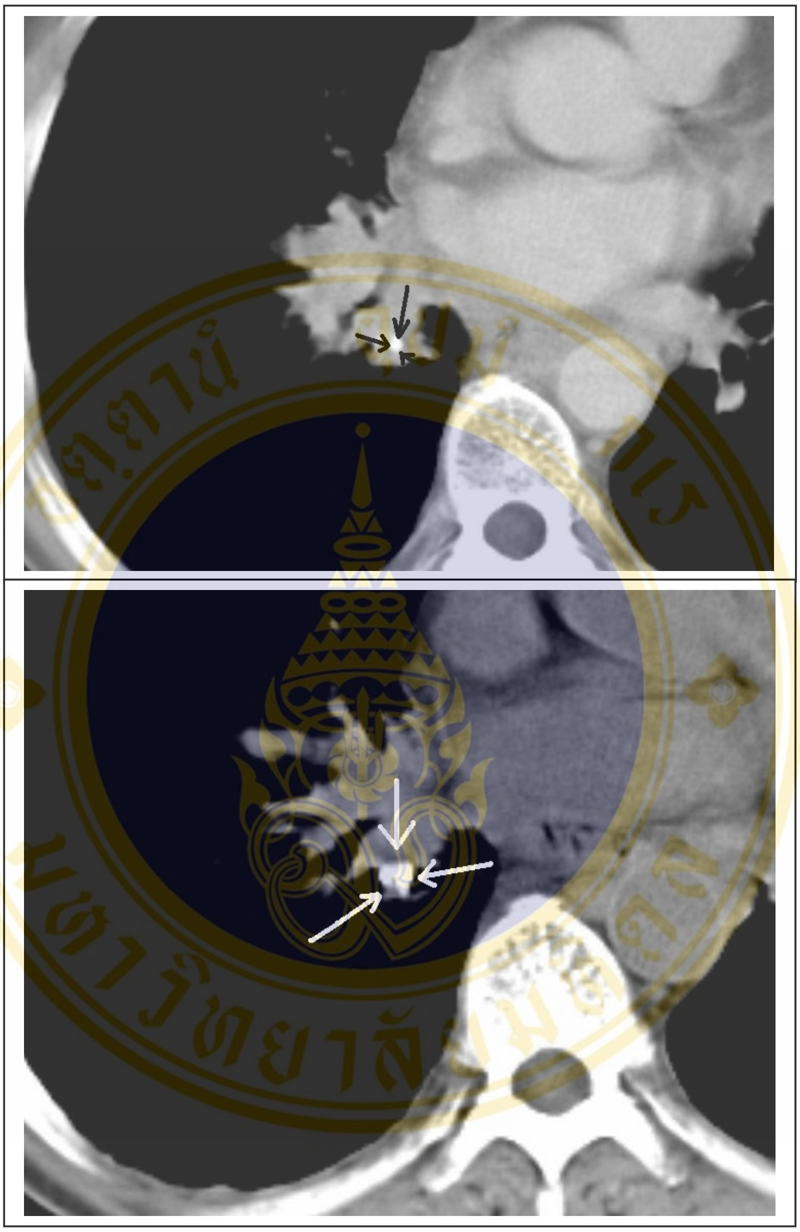


Figure 3-5 Adenocarcinoma: A 57 years old male with central mass presented calcification.

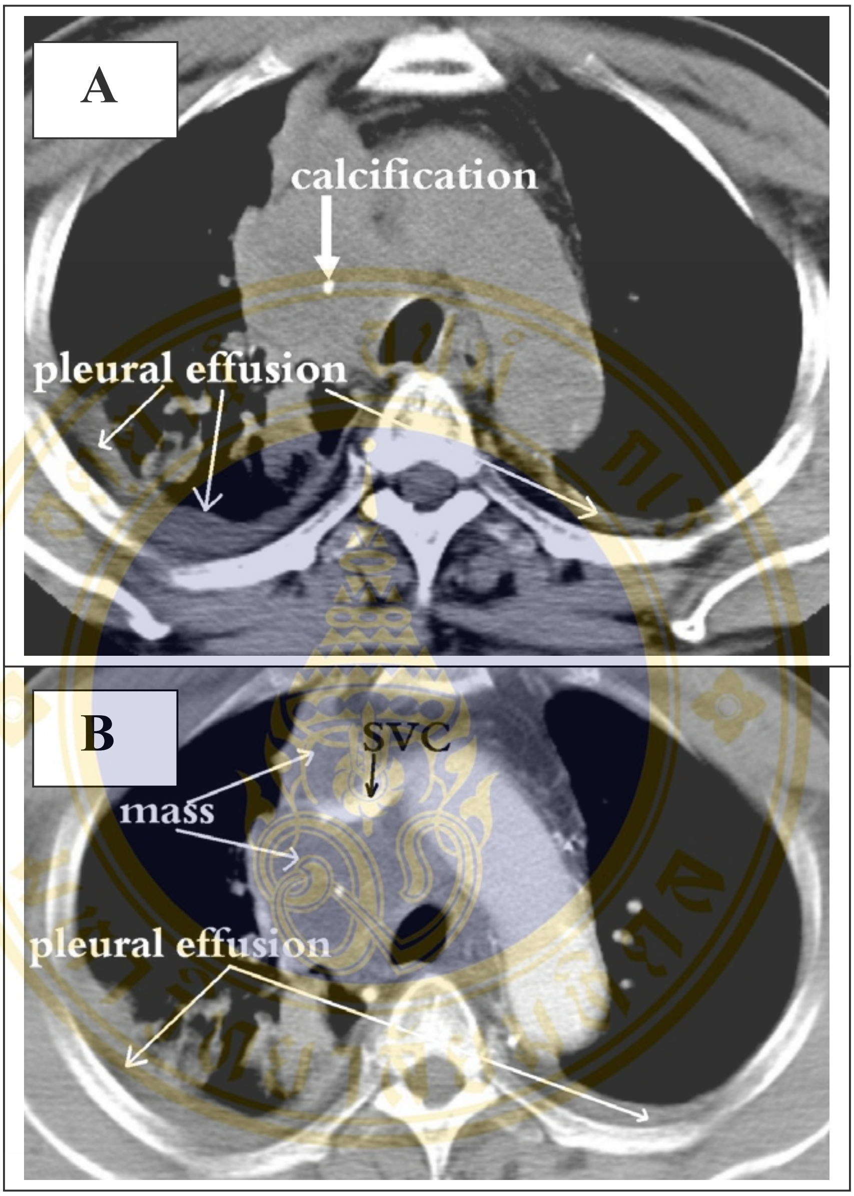


Figure 3-6 Pleural effusions in both lungs of a 72 years old male with right upper lobe tumor. A tumor compresses the superior vena cava (SVC). An apical lung tumor, also known as a Pancoast tumor.

(A) Tumor attenuation was inhomogeneous density at pre-contrast injected.

(B) Tumor attenuation inhomogeneous density and increase enhancement at post-contrast injected.

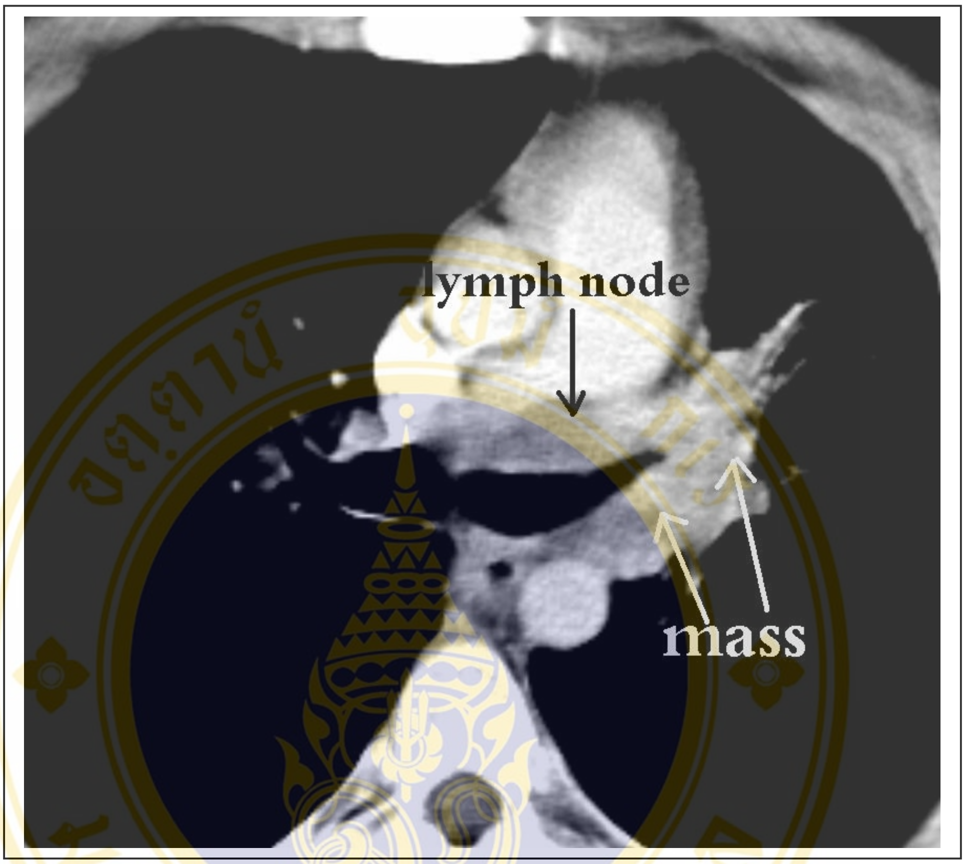


Figure 3-7 Mediastinal lymph node enlargements. A 29 years old male with irregular mass at left upper lobe. CT showing paratrachial lymph node enlargement.

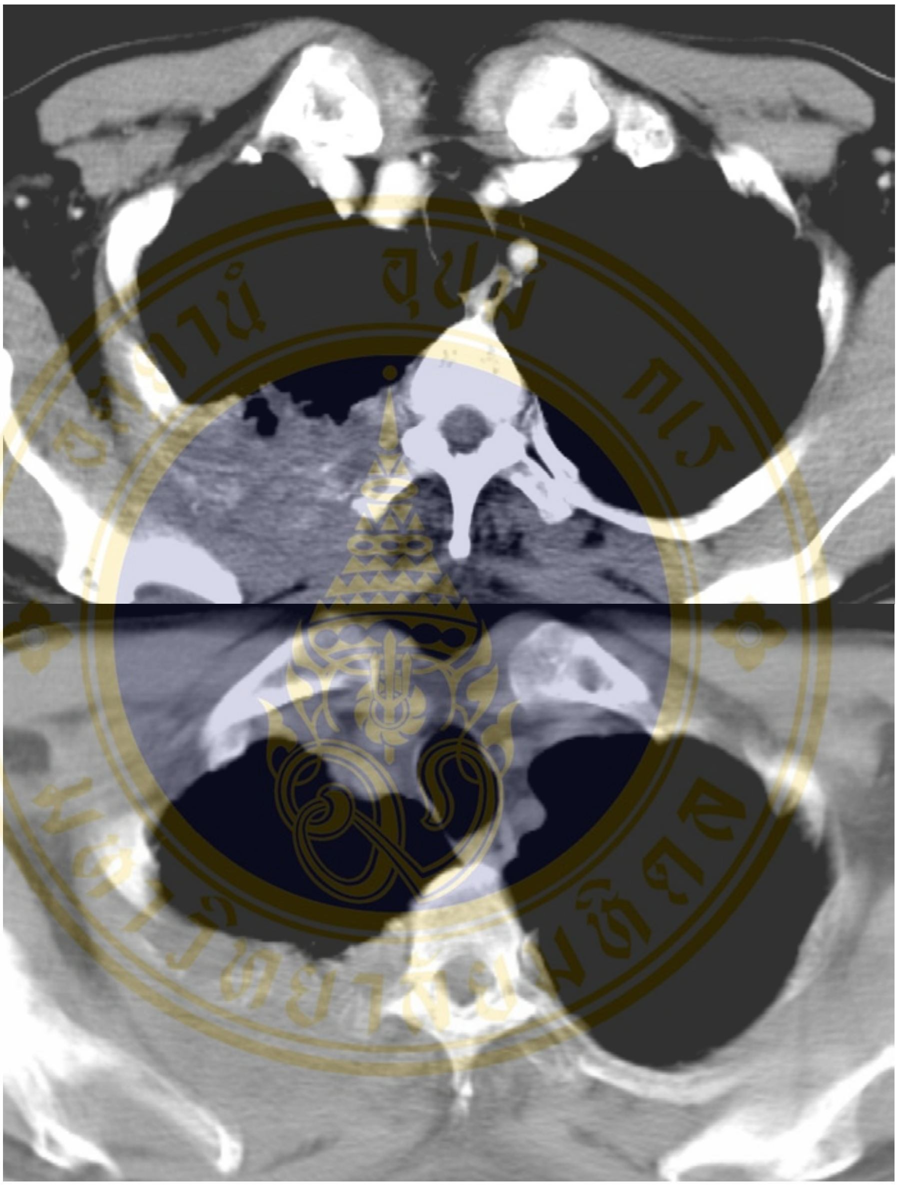


Figure 3-8 Adenocarcinoma: A 69 years old male with frank chest wall invadsion by large tumor at posterior right upper lobecavitating mass at left lower lobe.

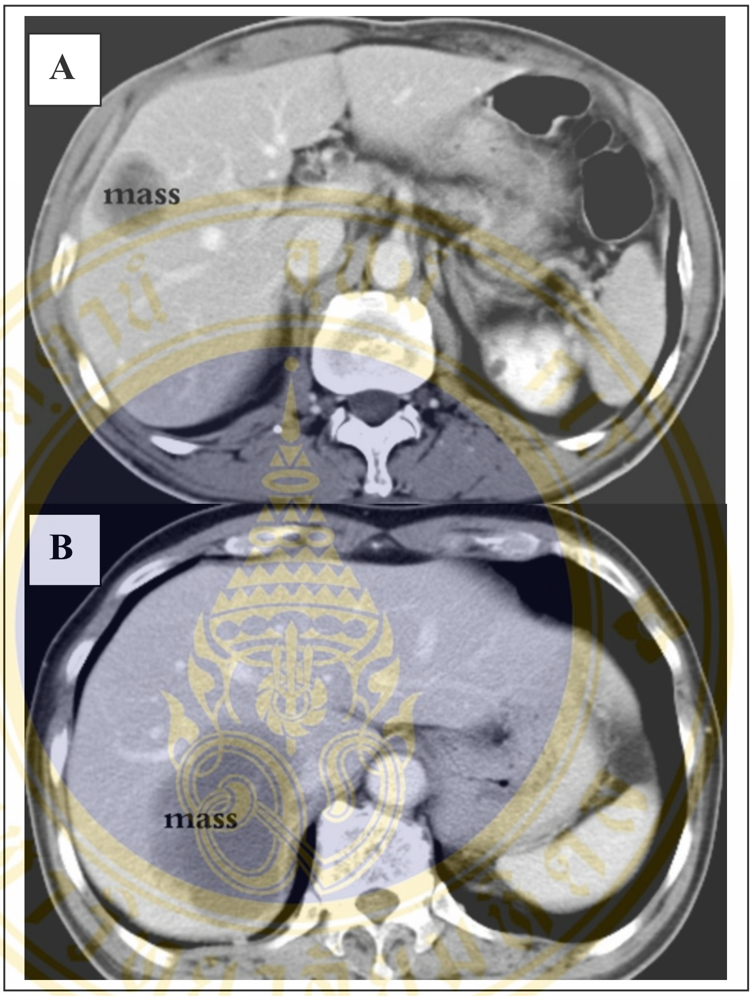


Figure 3-9 (A) A 60 years old male with liver metastasis.

(B) A 69 years old male with liver metastasis.

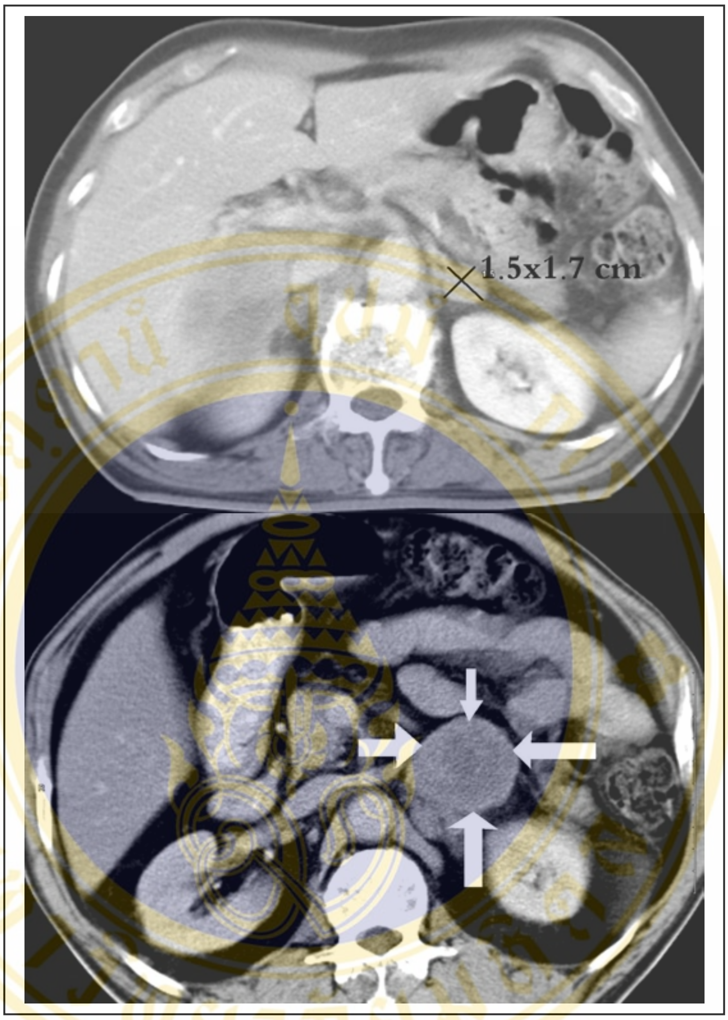


Figure 3-10 (A) Adenocarcinoma: A 69 years old male with left adrenal gland metastasis. (B) Small cell carcinoma: A 73 years old female with left adrenal gland metastasis.

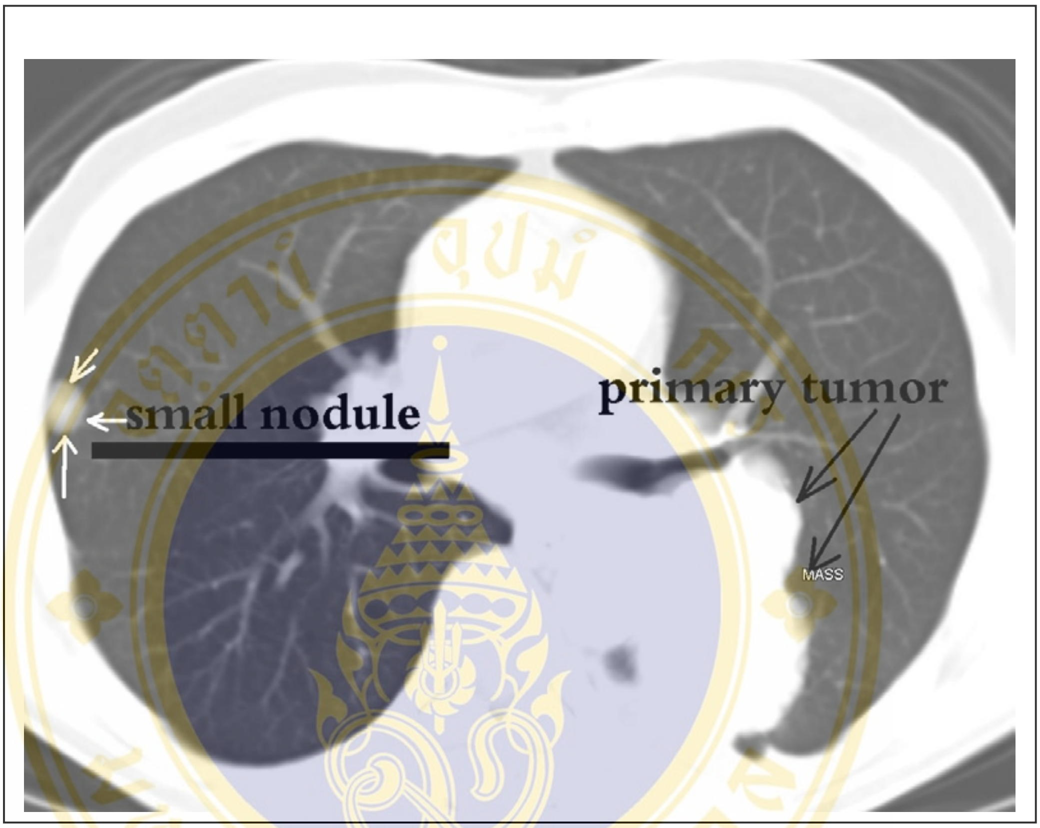


Figure 3-11. A 29 years old male with a adenocarcinoma at left lower lobe and metastasis to the contralateral at right lower lobe.

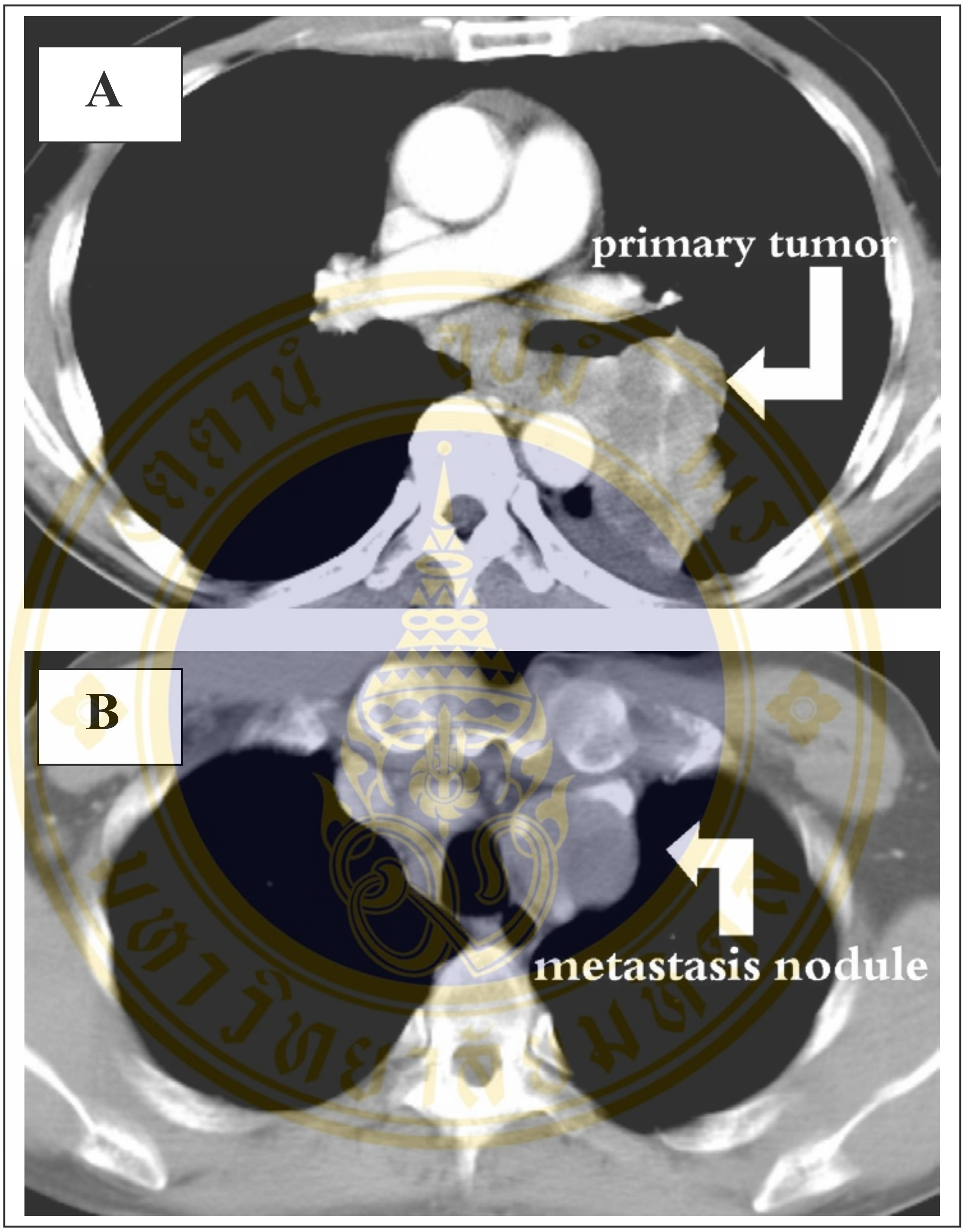


Figure 3-12 (A) A 51 years old male with a primary mass at left lower lobe

(B) Metastasis to the ipsilateral lung at left upper lobe

3.2 Statistical Analysis

3.1 Average size of the primary lung cancer was presented as mean ± standard deviation.

3.2 Association between pathologicalcell type and characteristic pattern in CT imaging was calculated with Pearson's chi square.

3.3 Agreement between observers; Agreement between interpretation of the two reviewers was calculated with the Kappa test of concordance. Concordance between observers was consider fair ($0.05 < K \leq 0.6$), good ($0.6 < K \leq 0.8$), or excellent ($K > 0.8$).

3.4 Accuracy and predictive values with 95% Confidence Interval was used to estimate the evaluation pathologic cell type of primary lung cancer disease by Computer Tomography imaging of the chest.

CHAPTER IV
RESULTS

4.1 Population

The distribution of lung cancer in 4-cell type is presented in table 4-1. The encountered lung cancer among the 28 cases (21 male and 7 female; mean age ± SD, 68 ± 11 years; age range 47-84 years) were squamous cell carcinoma, 23 cases (18 male and 5 female; mean age ± SD, 58 ± 9 years; age range 29-73 years), were adenocarcinoma, 7 cases (7 male and 0 female; mean age 59 ± 9 years; age range 43-68 years) were large cell carcinoma and 9 cases (8 male and 1 female; mean age 65 ± 6 years; age range 56-73 years) were small cell carcinoma (Chart 4-1).

4.2 Tumor size

Over all, the mean ± standard deviation diameter was 6.5 ± 2.9 cm, minimum and maximum diameters were 1.5 cm and 14.0 cm, respectively. The mean ± standard deviation diameter of squamous cell carcinoma, adenocarcinoma, large cell carcinoma, and small cell carcinoma were 6.5 ± 2.8 cm (minimum diameter was 2.2 cm and maximum diameter was 13.5 cm), 5.3 ± 2.3 cm (minimum diameter was 1.5 cm and maximum diameter was 10.0 cm), 9.0 ± 3.1 cm (minimum diameter was 4.0 cm and maximum diameter was 13.0 cm), and 7.9 ± 3.4 cm (minimum diameter was 1.5 cm and maximum diameter was 14.0 cm), respectively (Table 4-1).

Table 4-1 The distribution of lung cancer in 4 cell type by sex, age, and size.

	Pathology			
	Squamous cell carcinoma (n=28)	Adenocarcinoma (n=23)	Large cell carcinoma (n=7)	Small cell Carcinoma (n=9)
Sex				
Male	21(75%)	18(78%)	7(100%)	8(89%)
Female	7(25%)	5(22%)	-	1(11%)
Age(yrs)				
Mean ± SD	68±11	59 ± 9	59 ± 9	65 ± 6
Meadian	70	60	58	66
Rang	47-84	29-73	43-68	56-73
Size(cm)				
Mean ± SD	6.5±2.8	5.3±2.3	9.0±3.1	6.5±2.9
Meadian	5.9	5.0	8.7	6.0
Rang	2.2-3.5	1.5-10.0	4.0-13.0	1.5-14.0

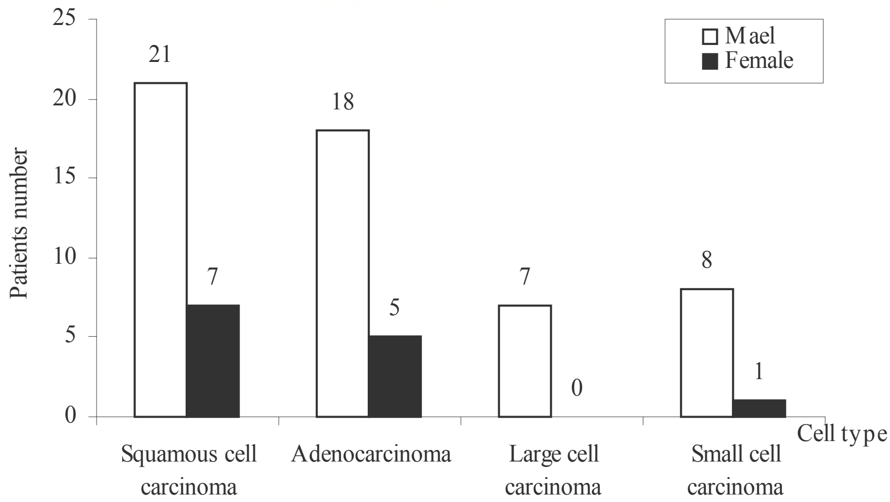


Chart 4-1 The distribution of lung cancer in 4 cell type by sex.

4.3 Location

4.3.1 Location (central, peripheral)

Seven lesions (25%) of squamous cell carcinoma were localized in peripheral region and twenty-one lesions (75%) to the central region of the lung. Twelve lesions (52%) of adenocarcinoma were localized in peripheral region and eleven lesions (48%) to central region. Two lesions (27%) of large cell carcinoma were localized in peripheral region and four lesions (57%) to the central region. But one lesion of large cell carcinoma has very large size, so both observe can not be evaluate to the location of this lesion. Then, they resolve that lesion was localized in the whole lobe. Two lesions (22%) of small cell carcinoma were localized in peripheral region and seven lesions (78%) to the central region of the lung (Chart 4-2). Pearson's chi square test showed a good significant association between pathology (squamous cell carcinoma and adenocarcinoma) and location (central and peripheral) ($p<0.05$), as shown in table 4-2.

4.3.2 Lobe (right, left)

Eighteen lesions (64%) of squamous cell carcinoma were located in right lobe and ten lesions (36%) in left lobe. Twelve lesions (52%) of adenocarcinoma were located in right lobe and eleven lesions (48%) in left lobe. Four lesions (57%) of large cell carcinoma were located in right lobe and three lesions (43%) in left lobe. Five lesions (56%) of small cell carcinoma were located in right lobe and four lesions (44%) in left lobe (Chart 4-3). For association between pathology (squamous cell carcinoma and adenocarcinoma) and lobe (right and left), Pearson's chi square test showed no statistically differences ($p>0.05$), as shown in table 4-2.

4.3.3 Lobe (upper, lower)

Thirteen lesions (46%) of squamous cell carcinoma were located in upper lobe and fifteen lesions (54%) in lower lobe. Thirteen lesions (57%) of adenocarcinoma were located in upper lobe and ten lesions (43%) in lower lobe. Five lesions (71%) of large cell carcinoma were located in upper lobes, one lesion (14%) in lower and one lesion (14%) in whole of left lobe. Five lesions (55%) of small cell carcinoma were located in upper lobes and four lesions (44%) in lower lobe (Chart 4-4). For association between pathology (squamous cell carcinoma and adenocarcinoma) and lobe (upper and lower), Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-2.

4.3.4 Lobe (RUL, RLL, LUL, LLL, Whole lobe)

Seven lesions (25%) of squamous cell carcinoma were located in right upper lobe; eleven lesions (39%) in right lower lobe, seven lesions (25%) were located in the left upper lobe and three lesions (11%) in left lower lobe. Six lesions (26%) of adenocarcinoma were located in right upper lobe; six lesions (26%) in right lower lobe, seven lesions (30%) were located in the left lower lobe and four lesions (17%) in left lower lobe. Four lesions (57%) of large cell carcinoma were in right upper lobe and one lesion (14%) in left upper lobe. But one lesion of large cell carcinoma has very large size, so both observe can not be evaluate to the location of this lesion. Then, they resolve that lesion was localized in the whole lobe. Four lesions (44%) of small cell carcinoma were located in right upper lobe, one (11%) lesion in right lower lobe, one (11%) lesion left upper lobe and three lesions (33%) in left lower lobe (Chart 4-5). For association between pathology (squamous cell carcinoma and adenocarcinoma) and lobe (RUL, RLL, LUL, and LLL), Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-2.

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Table 4-2 The distribution of lung cancer in 4 cell type by location and lobe.

	Histology				
	Squamous cell carcinoma (n=28)	Adenocarci-noma (n=23)	Large cell carcinoma (n=7)	Small cell Carcinoma (n=9)	p-value
Location					
Peripheral	7(25%)	12(52%)	2(29%)	2(22%)	0.046@
Central	21(75%)	11(48%)	4(57%)	7(78%)	
Whole lobe	-	-	1(14%)	-	
(Left/Right)Lobe					
Right	18(64%)	12(52%)	4(57%)	5(56%)	0.382©
Left	10(36%)	11(48%)	(%43)3	4(44%)	
(Lower/Upper)beLo					
Upper	13(46%)	13(57%)	5(72%)	5(56%)	0.473Θ
Lower	15(54%)	10(43%)	1(14%)	4(44%)	
Whole of left lobe	-	-	1(14%)	-	
Lobe					
RUL	6(21%)	7(30%)	4(57%)	4(44%)	0.750®
RLL	12(43%)	5(22%)	-	1(11%)	
LUL	7(25%)	6(26%)	2(29%)	1(11%)	
LLL	3(11%)	5(22%)	-	3(33%)	
Whole Left lobe	-	-	1(14%)	-	

@ Association between pathology (squamous cell carcinoma and adenocarcinoma) and location (peripheral and central).

© Association between pathology (squamous cell carcinoma and adenocarcinoma) and lobe (right and left).

Θ Association between pathology (squamous cell carcinoma and adenocarcinoma) and lobe (upper and lower).

® Association between pathology (squamous cell carcinoma and adenocarcinoma) and lobe (RUL, RLL, LUL, and LLL).

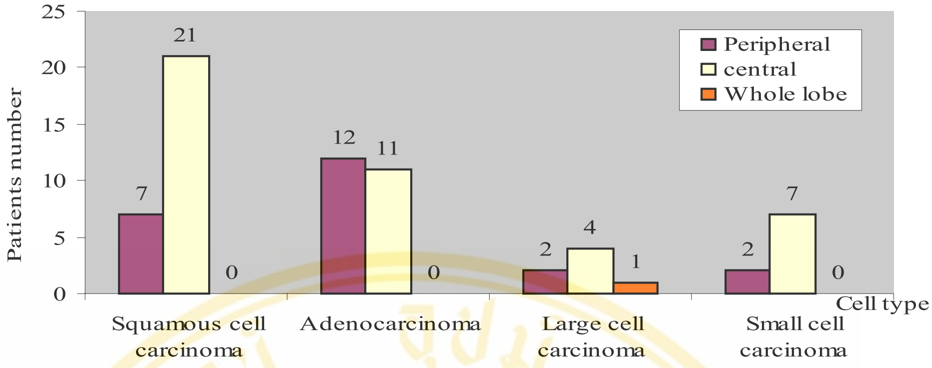

Chart 4-2 The distribution of lung cancer in 4 cell type by location.

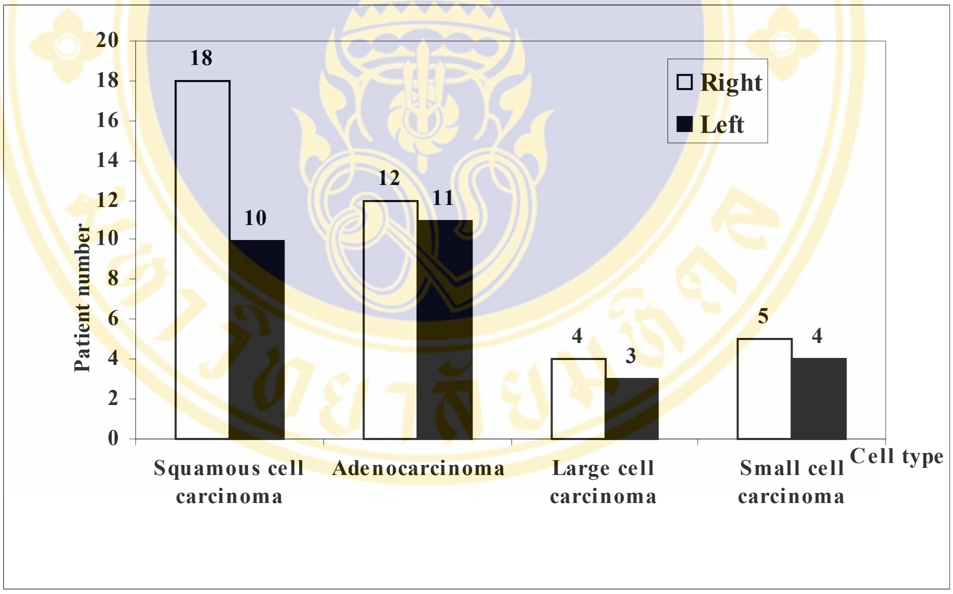

Chart 4-3 The distribution of lung cancer in 4 cell type by lobe (Right, Left).

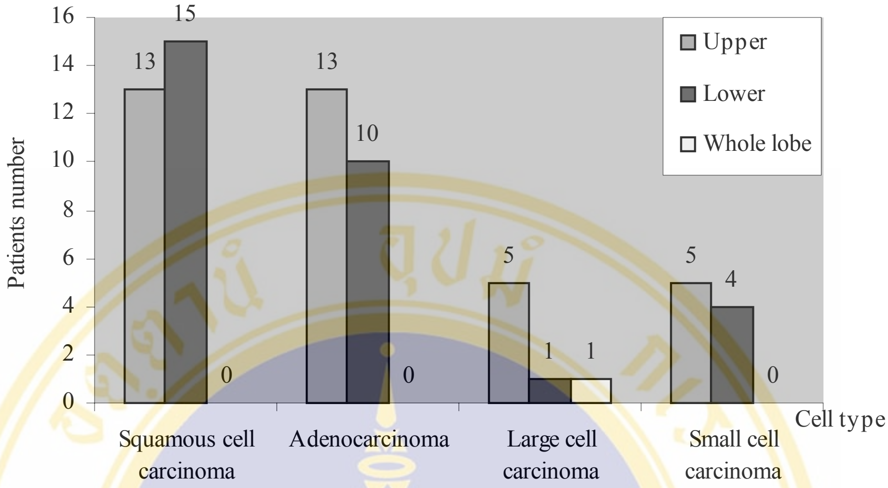

Chart 4-4 The distribution of lung cancer in 4 cell type by lobe (Upper, Lower, Whole lobe).

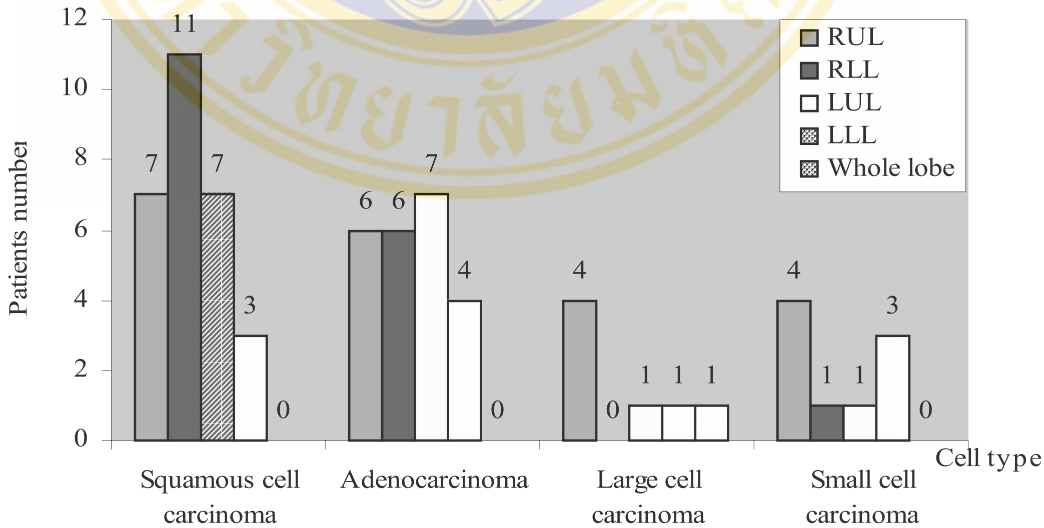

Chart 4-5 The distribution of lung cancer in 4 cell type by lobe (RUL, RLL, LUL, and LLL).

4.4.1 Edge

Five lesions (18%) of squamous cell carcinoma were regular edge and twenty-three lesions (82%) were irregular edge. Four lesions (17%) of adenocarcinoma were regular edge and nineteen lesions (83%) were irregular edge. One lesion (14%) of large cell carcinoma was regular edge and six lesions (86%) were irregular edge. One lesion (11%) of small cell carcinoma was regular edge and eight lesions (89%) were irregular edge (Chart 4-6). For association between pathology (squamous cell carcinoma and adenocarcinoma) and edge, Pearson's chi square test showed no statistically differences ($p>0.05$), as shown in table 4-3.

4.4.2 Infiltration

Twenty-five lesions (90%) of squamous cell carcinoma were present infiltration and three lesions (11%) were absent infiltration. Nineteen lesions (83%) of adenocarcinoma were present infiltration and four lesions (17%) were absent infiltration. Four lesions (57%) of large cell carcinoma were present infiltration and three lesions (43%) were absent infiltration. Seven lesions (78%) of small cell carcinoma were present infiltration and two lesions (22%) were absent infiltration (Chart 4-7). For association between pathology (squamous cell carcinoma and adenocarcinoma) and infiltration, Pearson's chi square test showed no statistically differences ($p>0.05$), as shown in table 4-3.

4.4.1 Edge / infiltration

Three lesions (11%) of squamous cell carcinoma were present regular edge with out infiltration, two lesions (7%) were present regular edge with infiltration, three lesions (11%) were present irregular edge with out infiltration and twenty lesions (71%) were present irregular edge with infiltration. One lesion (4%) of adenocarcinoma was present regular edge with out infiltration, three lesions (13%) were present regular edge with infiltration, three lesions (13%) were present irregular edge with out infiltration and sixteen lesions (70%) were present irregular edge with infiltration. One lesion (14%) of large cell carcinoma was present regular edge with infiltration, two lesions (29%) were present irregular edge with out infiltration and four lesions (57%) were present irregular edge with infiltration. One lesion (11%) of small cell carcinoma was present regular edge with infiltration, two lesions (22%) were present irregular edge with out infiltration and six lesions (67%) were present irregular edge with infiltration (Chart 4-8). For association between pathology (squamous cell carcinoma and adenocarcinoma) and edge with infiltration, Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-3.

4.5 Pleural effusion

Twelve cases (43%) of squamous cell carcinoma were demonstrate pleural effusion and sixteen cases (57%) not seen the pleural effusion. Six cases (26%) of adenocarcinoma were demonstrate pleural effusion and seventeen cases (74%) not seen the pleural effusion. Four cases (57 %) of large cell carcinoma were demonstrate pleural effusion and three cases (43%) not seen the pleural effusion. Four cases (44%) of small cell carcinoma were demonstrate pleural effusion and five cases (56%) not seen the pleural effusion (Chart 4-9). For association between pathology (squamous cell carcinoma and adenocarcinoma) and pleural effusion, Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-3.

Table 4-3 The distribution of lung cancer in 4 cell type by edge, infiltration and pleural effusion.

	Histology				
	Squamous cell carcinoma (n=28)	Adenocar-cinoma (n=23)	Large cell carcinoma (n=7)	small cell carcinoma (n=9)	p-value
Edge					
Regular	5(18%)	4(17%)	1(14%)	1(11%)	1.000*
Irregular	23(82%)	19(83%)	6(86%)	8(89%)	
Infiltrat					
Present	25(90%)	19(83%)	4(57%)	7(78%)	0.718+
Absent	3(11%)	4(17%)	3(43%)	2(22%)	
Infiltration/Edge					
Regular edge with infiltration	3(11%)	1(4%)	-	-	1.000†
Regular edge without infiltration	2(7%)	3(13%)	1(14%)	1(11%)	
Irregular edge without infiltration	3(11%)	3(13%)	2(29%)	2(22%)	
Irregular edge with infiltration	20(71%)	16(70%)	4(57%)	6(67%)	
Pleural effusion					
Present	12(43%)	6(26%)	4(57%)	4(45%)	0.212^
Absent	16(57%)	17(74%)	3(43%)	5(55%)	

* Association between pathology (squamous cell carcinoma and adenocarcinoma) and edge (regular, irregular).

+ Association between pathology (squamous cell carcinoma and adenocarcinoma) and infiltration (present, absent).

† Association between pathology (squamous cell carcinoma and adenocarcinoma) and edge / infiltration (regular edge with infiltration, regular edge without infiltration, irregular edge with infiltration, and irregular edge without infiltration).

^ Association between pathology (squamous cell carcinoma and adenocarcinoma) and Pleural effusion (present, absent).

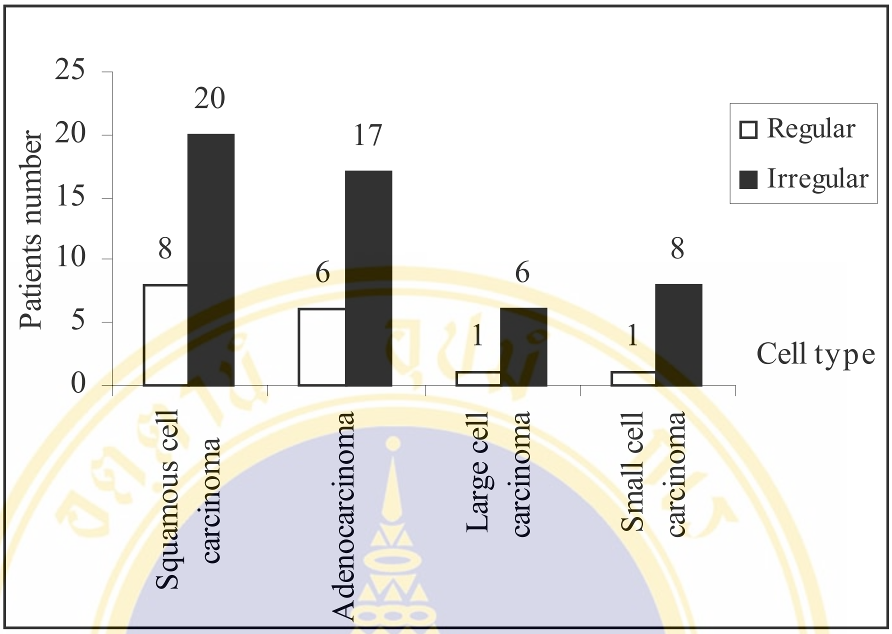

Chart 4-6 The distribution of lung cancer in 4 cell type by edge.

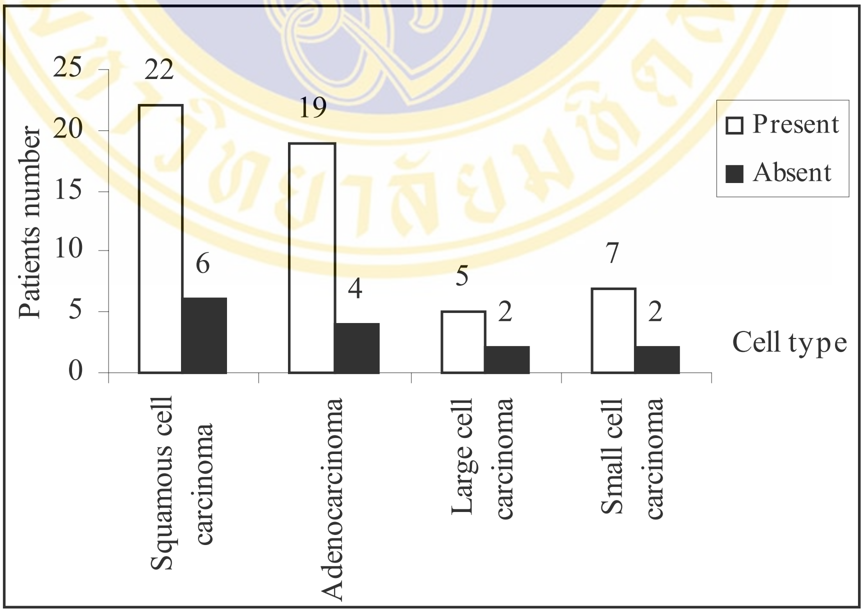

Chart 4-7 The distribution of lung cancer in 4 cell type by infiltration.

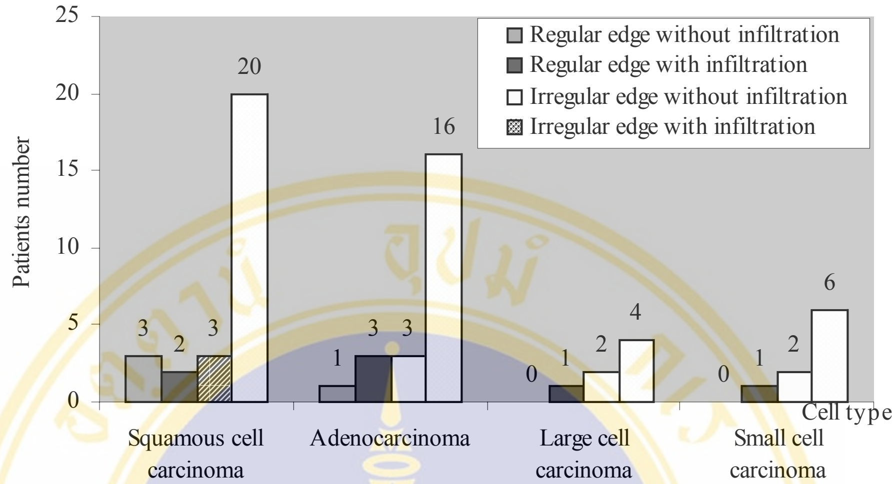

Chart 4-8 The distribution of lung cancer in 4 cell type by edge and infiltration.

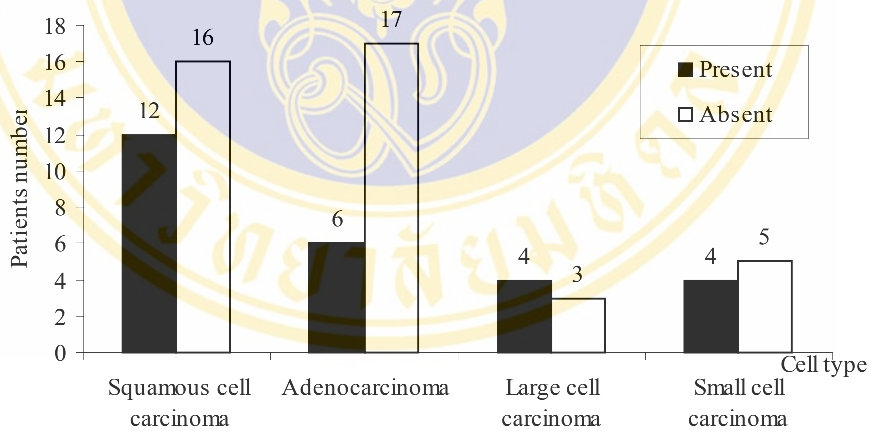

Chart 4-9 The distribution of lung cancer in 4 cell type by pleural effusion.

4.6 Internal characteristics of tumors

4.6.1 Attenuation at pre contrast media injection

Ten lesions (36%) of squamous cell carcinoma demonstrated homogeneous attenuation and eighteen lesions (64%) demonstrated inhomogeneous attenuation on CT imaging. Ten lesions (44%) of adenocarcinoma demonstrated homogeneous attenuation and thirteen lesions (57%) demonstrated inhomogeneous attenuation. Three lesions (43%) of large cell carcinoma demonstrated homogeneous attenuation and four lesions (57%) demonstrated inhomogeneous attenuation. One lesion (11%) of small cell carcinoma demonstrated homogeneous attenuation and eight (89%) demonstrated inhomogeneous attenuation (Table 4-4).

4.6.2 Attenuation at post contrast media injection

Distribution of primary lung cancer by attenuation within the tumor at pre and post contrast media as shown in table 4-4. Six lesions (21%) of squamous cell carcinoma demonstrated homogeneous attenuation on CT imaging and twenty-two lesions (79%) demonstrated inhomogeneous attenuation. Seven lesions (30%) of adenocarcinoma demonstrated homogeneous attenuation and sixteen lesions (70%) demonstrated inhomogeneous attenuation. Two lesions (29%) of large cell carcinoma demonstrated homogeneous attenuation and five lesions (71%) demonstrated inhomogeneous attenuation. All of small cell carcinoma (nine lesions) demonstrated inhomogeneous attenuation at post contrast media injected (Chart 4-10).

Table 4-4 Distribution of primary lung cancer by attenuation within the tumor at pre and post contrast media.

Attenuation within the tumors	Pathology							
	Squamous cell carcinoma (n=28)		nocarcinomaAde (n=23)		Large cell Carcinoma (n=7)		Small cell carcinoma (n=9)	
	Pre contrast	Post contrast	Pre contrast	Post contrast	Pre contrast	Post Contrast	Pre contrast	Post contrast
Homogeneous	10(36%)	6(21%)	10(44%)	7(30%)	3(43%)	2(29%)	1(11%)	-
Inhomogeneous	18(64%)	22(79%)	13(56%)	16(70%)	4(57%)	5(71%)	8(89%)	9(100%)

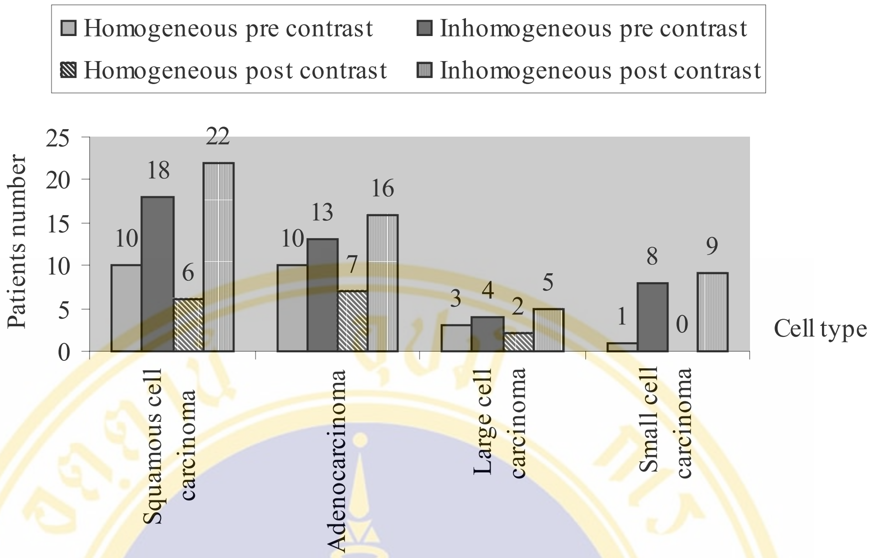

Chart 4-10 Distribution of primary lung cancer by attenuation within the tumor at pre and post contrast media.

Increment of attenuation after contras media injection were twenty-five lesions (89%) of squamous cell carcinoma, twenty-one lesions (91%) of adenocarcinoma, six lesions (86%) of large cell carcinoma and nine lesions (100%) of small cell carcinoma (Chart 4-11). For association between pathology (squamous cell carcinoma and adenocarcinoma) and attenuation after contras media injection (No increase enhancement, increase enhancement), Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-5.

4.6.3 Cavitation

The presence of cavitation in squamous cell carcinoma was eight lesions (29%), three lesions (13%) in adenocarcinoma, and one lesion (14%) in large cell carcinoma, but not found cavitation in small cell carcinoma (Chart 4-12). For association between pathology (squamous cell carcinoma and adenocarcinoma) cavitation, Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-5.

4.6.4 Calcification

Calcification was observed in two lesions of squamous cell carcinoma (7%), two lesions of adenocarcinoma (9%), two lesions of large cell carcinoma (28%), and two lesions (22%) of small cell carcinoma (Chart 4-13). For association between pathology (squamous cell carcinoma and adenocarcinoma) and calcification, Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-5.

4.6.5 Cavitation with Calcification

Present of calcification with calcification was observed in only one lesion (14%) of large cell carcinoma (Chart 4-14). For association between pathology (squamous cell carcinoma and adenocarcinoma) and cavitation with calcification, Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-6.

4.7 Location with cavitation

Central lesion with cavitation shown in five lesions (18%) of squamous cell carcinoma and one lesion (4%) of adenocarcinoma. Periphery lesion with cavitation shown in three lesions (11%), two lesions (9%), and 1 lesion (14%) of squamous cell carcinoma, adenocarcinoma, and large cell carcinoma, respectively (Chart 4-15). For association between pathology (squamous cell carcinoma and adenocarcinoma) and location with cavitation, Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-6.

Table 4-5 The distribution of lung cancer in 4 cell type by enhancement, cavitation and calcification.

	Pathology				
	Squamous cell carcinoma (n=28)	Adenocar cinoma (n=23)	Large cell carcinoma (n=7)	small cell carcinoma (n=9)	p-value
Enhancement					
No increase enhancement	4(14%)	3(13%)	1(14%)	-	1.000∀
Increase enhancement	24(86%)	20(87%)	6(86%)	9(100%)	
Cavitation					
Present	8(29%)	3(13%)	1(14%)	-	0.180⊕
Absent	20(71%)	20(87%)	6(86%)	9(100%)	
Calcification					
Present	2(7%)	2(9%)	2(28%)	2(22%)	1.000⊗
Absent	26(93%)	21(91%)	5(72%)	7(78%)	

∀ Association between pathology (squamous cell carcinoma and adenocarcinoma) and enhancement (increase, no increase enhancement).

⊕ Association between pathology (squamous cell carcinoma and adenocarcinoma) and cavitation (present, absent).

⊗ Association between pathology (squamous cell carcinoma and adenocarcinoma) and calcification (present, absent).

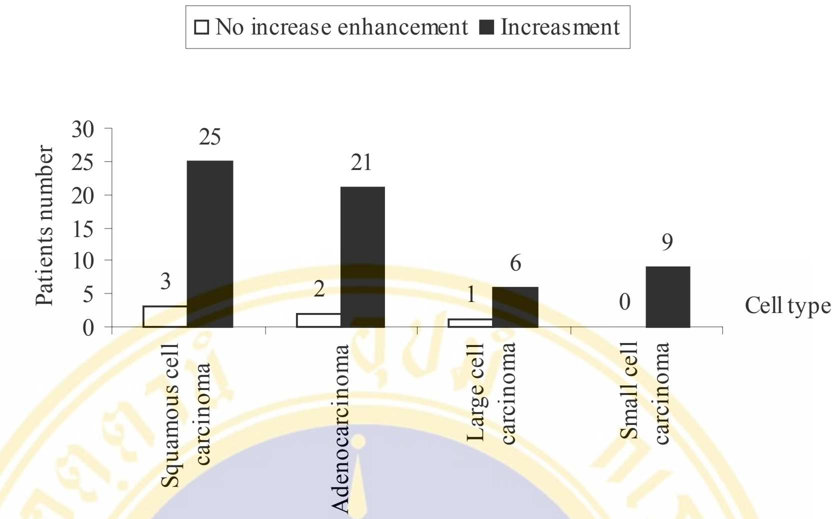

Chart 4-11 Distribution of primary lung cancer in 4 cell type by enhancement.

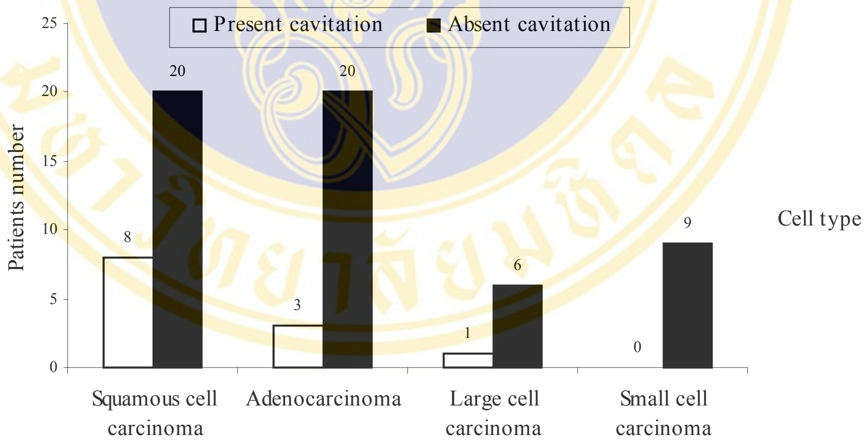

Chart 4-12 The distribution of lung cancer in 4 cell type by cavitation.

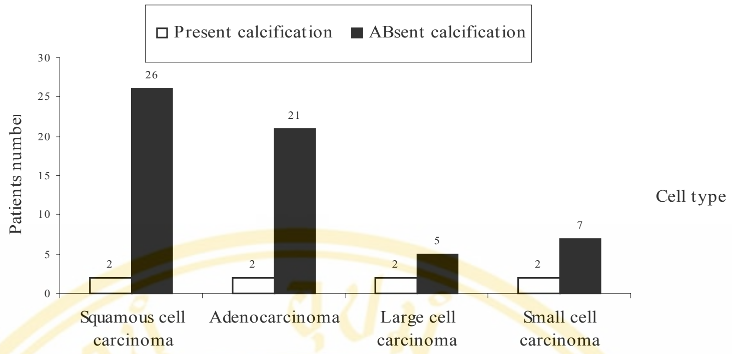

Chart 4-13 The distribution of lung cancer in 4 cell type by calcification.

Table 4-6 The distribution of lung cancer in 4 cell type cavitation with calcification, and location with cavitation.

	Pathology				
	Squamous cell carcinoma (n=28)	Adenocarcinoma (n=23)	Large cell carcinoma (n=7)	small cell carcinoma (n=9)	p-value
Cavitation ficationwith calci					1.000э
Absent cavitation and calcification	18(64%)	18(78%)	5(72%)	2(22%)	
Absent cavitation and present calcification	2(7%)	2(9%)	1(14%)	7(78%)	
Present cavitation and absent calcification	8(29%)	3(13%)	-		
Present cavitation with calcification	-	-	1(14%)		
Location with cavitation					1.000∞
Central lesion with absent cavitation	16(57%)	10(43%)	1(14%)	2(22%)	
Peripheral lesion with absent cavitation	4(14%)	10(43%)	5(72%)	7(78%)	
Central lesion with present cavitation	5(18%)	1(4%)	-	-	
Peripheral lesion with present cavitation	3(11%)	2(9%)	1(14%)	-	

э Association between pathology (squamous cell carcinoma and adenocarcinoma) and cavitation with calcification.

∞ Association between pathology (squamous cell carcinoma and adenocarcinoma) and location with cavitation.

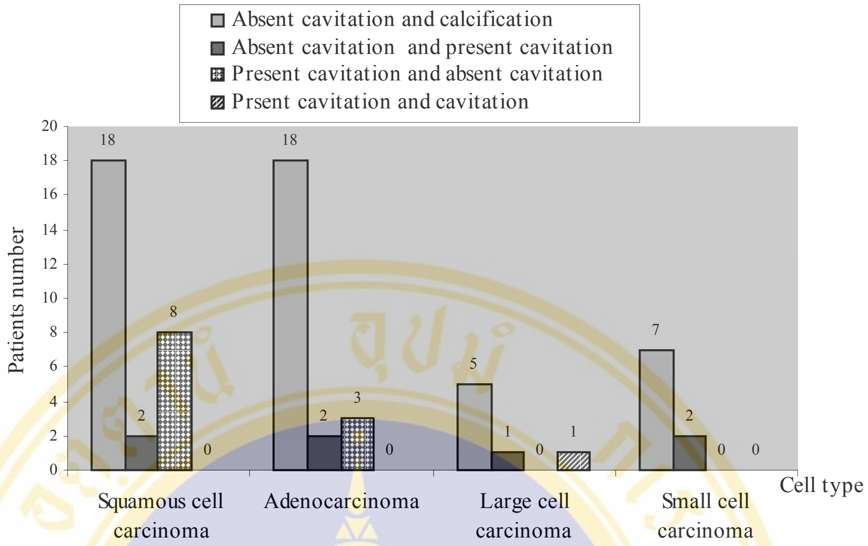

Chart 4-14 The distribution of lung cancer in 4 cell type by cavitation with calcification.

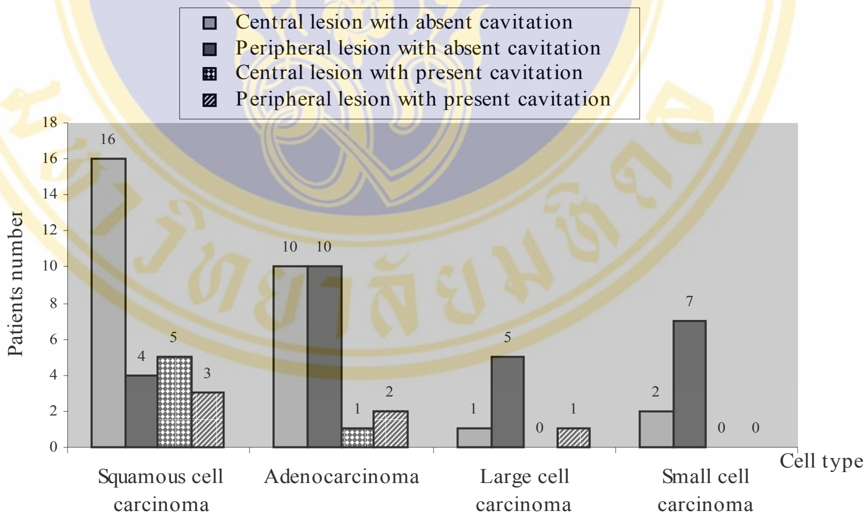

Chart 4-15 The distribution of lung cancer in 4 cell type by location with cavitation.

4.8 Lymph node enlargement

Lymph node enhancement was found in twenty two cases (79%), seventeen cases (74%), six cases (86%), and eight cases (89%) of squamous cell carcinoma, adenocarcinoma, large cell carcinoma, and small cell carcinoma, respectively (Figure 4-16). For association between pathology (squamous cell carcinoma and adenocarcinoma) and lymph node enlargement, Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-7.

Lymph node enhancement with pleural effusion was found in eight cases (29%), five cases (22%), four cases (57%), and four cases (44%) of squamous cell carcinoma, adenocarcinoma, large cell carcinoma, and small cell carcinoma, respectively (Figure 4-17). For association between pathology (squamous cell carcinoma and adenocarcinoma) and lymph node enlargement with pleural effusion, Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-8.

4.9 Intrathoracic Metastases

4.9.1 Metastasis to ipsilateral /contralateral of the lung.

Metastasis to the contralateral associate with ipsilateral lung was found in three cases (11%), four cases (17%) and two cases (22%) of squamous cell carcinoma, adenocarcinoma, and small cell carcinoma, respectively. But not found in large cell carcinoma. Metastasis to the only contralateral lung was found in three cases (7%), two cases (9%), two cases (29%), and one case (11%) of squamous cell carcinoma, adenocarcinoma, large cell carcinoma and small cell carcinoma, respectively. Three cases (11%), two cases (9%), nd two cases (29%) of squamous cell carcinoma, adenocarcinoma, and small cell carcinoma were metastasis to the only ipsitralateral lung (Chart 4-18). For association between pathology (squamous cell carcinoma and adenocarcinoma) and metastasis to ipsilateral with contralateral lung, Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-9.

4.9.2 Metastasis to chest wall

Three cases (13%) of adenocarcinoma and two cases (22%) of small cell carcinoma were metastasis to the chest wall. Not found metastasis to chest wall from squamous cell carcinoma and small cell carcinoma (Chart 4-19). For association between pathology (squamous cell carcinoma and adenocarcinoma) and chest wall metastasis, Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-7.

4.10 Extrathoracic Metastases

4.10.1 Metastasis to the liver

Metastasis to the liver was found in two cases (7%), three cases (13%), one case (14%) and one case (11%) of squamous cell carcinoma, adenocarcinoma, large cell carcinoma and small cell carcinoma, respectively (Chart 4-20).. For association between pathology (squamous cell carcinoma and adenocarcinoma) liver metastasis, Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-7.

4.10.2 Metastasis to the adrenal gland

Metastasis to the adrenal gland was found in one case (4%), two cases (9%), one case (14%) and two cases (22%) of squamous cell carcinoma, adenocarcinoma, large cell carcinoma and small cell carcinoma, respectively (Chart 4-21). For association between pathology (squamous cell carcinoma and adenocarcinoma) and adrenal gland metastasis, Pearson's chi square test showed no statistically differences (p>0.05), as shown in table 4-7.

Table 4-7 The distribution of lung cancer in 4 cell type by lymph node enlargement, metastasis to chest wall, liver, and adrenal gland.

	Pathology				
	Squamous cell carcinoma (n=28)	Adenocar-cinoma (n=23)	Large cell carcinoma (n=7)	Small cell carcinoma (n=9)	p-value
Lymph node enlargement					
Presence	22(79%)	17(74%)	6(86%)	8(89%)	0.696$^{\Omega}$
Absence	6(21%)	2(26%)	1(14%)	1(11%)	
Metastasis to chest wall					
Presence	-	3(13%)	2(29%)	-	0.170$^{\phi}$
Absence	28(100%)	20(87%)	5(71%)	9(100%)	
Metastasis to liver					
Presence	2(7%)	3(13%)	1(14%)	1(11%)	0.817$^{\vee}$
Absence	26(93%)	20(87%)	6(86%)	8(89%)	
Metastasis to adrenal gland					
Presence	1(4%)	2(9%)	1(14%)	2(22%)	0.860$^{\Diamond}$
Absence	27(96%)	21(91%)	6(86%)	7(78%)	

Ω Association between pathology (squamous cell carcinoma and adenocarcinoma) and lymph node enlargement (present, absent).

ϕ Association between pathology (squamous cell carcinoma and adenocarcinoma) and metastasis to chest wall (present, absent).

∨ Association between pathology (squamous cell carcinoma and adenocarcinoma) and metastasis to liver (present, absent).

◊ Association between pathology (squamous cell carcinoma and adenocarcinoma) and metastasis to adrenal gland (present, absent).

Table 4-8 The distribution of lung cancer in 4 cell type by lymph node enlargement .and pleural effusion

Lymph node enlargement	Pleural effusion	Histology Squamous macell carcino (n=28)	Adenocar cinoma (n=23)	Large cell carcinoma (n=&)	small cell carcinoma (n=9)	p-value
-	-	2(7%)	5(22%)	1(14%)	1(11%)	1.000♣
-	+	4(14%)	1(4%)	-	-	
+	-	14(50%)	12(52%)	2(29%)	4(44%)	
+	+	8(29%)	5(22%)	4(57%)	4(44%)	

♣ Association between pathology (squamous cell carcinoma and adenocarcinoma) and ..lymph node enlargement with pleural effusion

Table 4-9 The distribution of lung cancer in 4 cell type by metastasis to ipsilateral with metastasis to contralateral lung.

Metastasis to ipsilateral	Metastasis to contralateral	Pathology Squamous cell carcinoma (n=28)	Adenocar carcinoma (n=23)	Large cell carcinoma (n=7)	small cell carcinoma (n=9)	p-value
-	-	20(71%)	15(65%)	5(71%)	5(56%)	1.000♠
-	+	3(11%)	2(9%)	2(29%)	1(11%)	
+	-	2(7%)	2(9%)	-	1(11%)	
+	+	3(11%)	4(17%)	-	2(22%)	

♠ Association between pathology (squamous cell carcinoma and adenocarcinoma) and metastasis to ipsilateral with metastasis to contralateral lung.

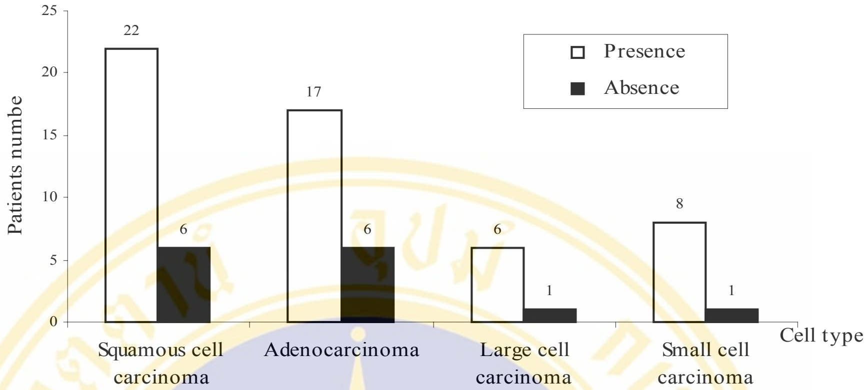

Chart 4-16 The distribution of lung cancer in 4 cell type by lymph node enlargement.

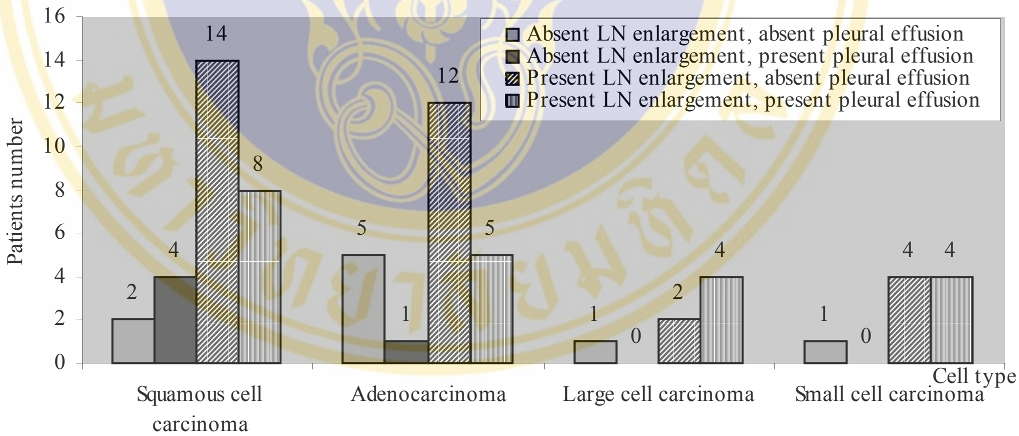

Chart 4-17 The distribution of lung cancer in 4 cell type by lymph node enlargement with pleural effusion.

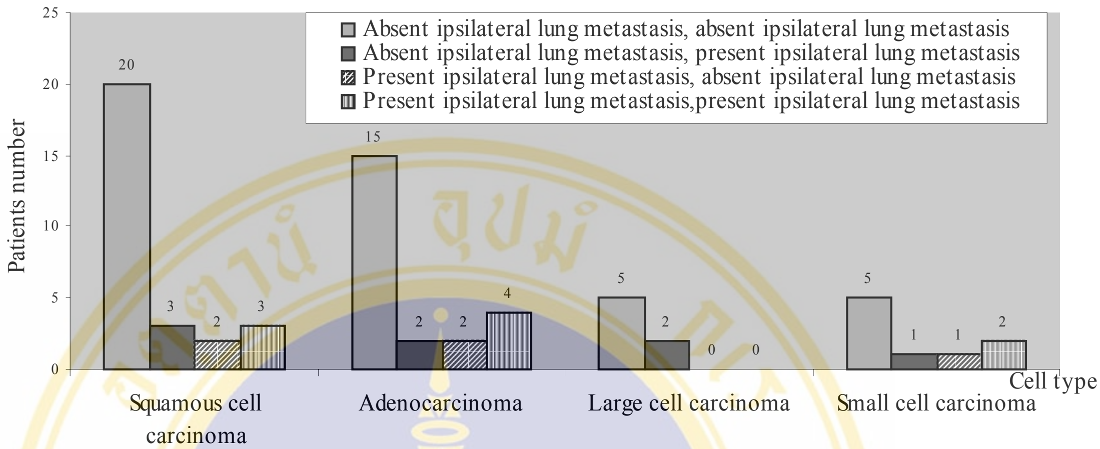

Chart 4-18 The distribution of lung cancer in 4 cell type by metastasis to ipsilateral with metastasis to contralateral lung.

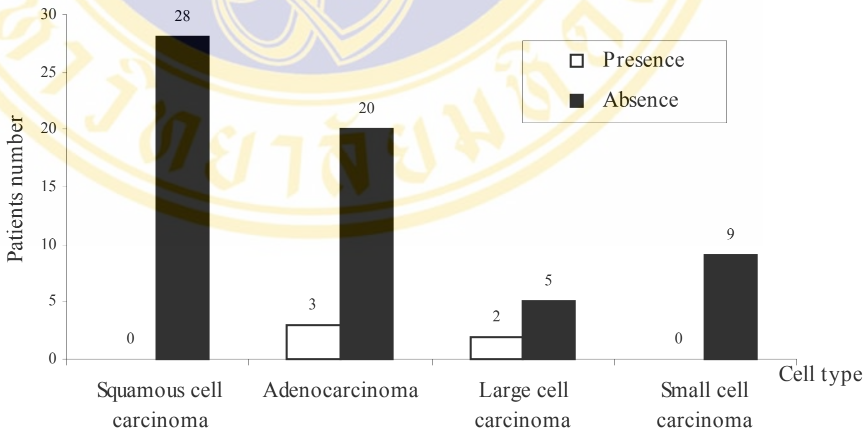

Chart 4-19 The distribution of lung cancer in 4 cell type by metastasis to chest wall.

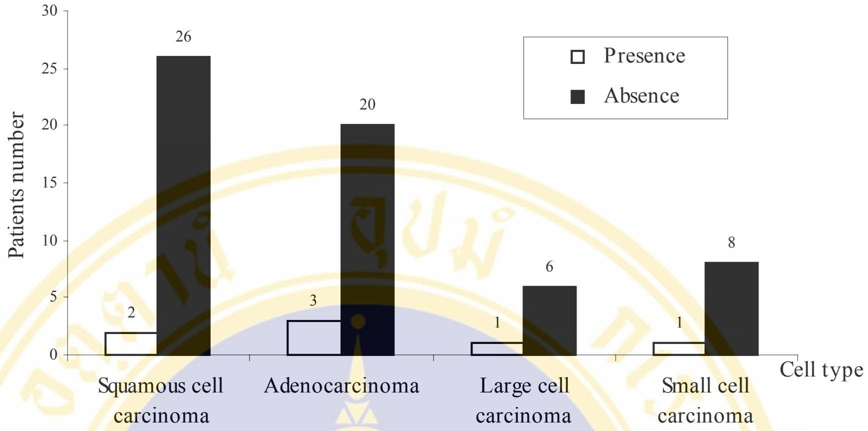

Chart 4-20 The distribution of lung cancer in 4 cell type by metastasis to liver.

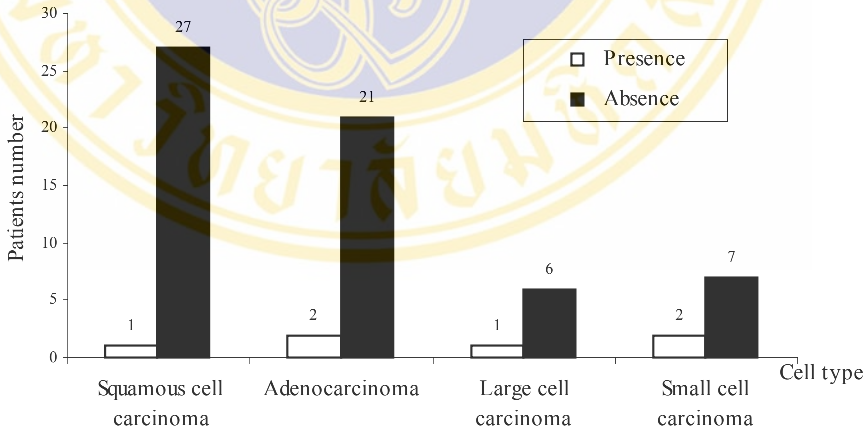

Chart 4-21 The distribution of lung cancer in 4 cell type by metastasis to adrenal gland.

4.10 Inter observe agreement

Agreement between CT chest interpretation of the two observes was calculated with Kappa test of concordance. Concordance for the CT chest interpretation between observers was fair (K = 0.247) (Table 4-10).

Table 4-10 Agreement between interpretations of two observers.

Observer 2	Observer 1				Total
	Squamous cell carcinoma	Adenocarcinoma	Large cell carcinoma	small cell carcinoma	
Squamous cell lung cancer	19	5	2	8	34
Adenocarcinoma	5	13	0	3	21
cinomaLarge cell car	1	0	0	0	1
Small cell carcinoma	7	1	0	3	11
Total	32	19	2	14	67

Kappa index = 0.247

4.11 Accuracy and predictive value

After consensus, Accuracy of CT for the diagnosis squamous cell carcinoma, adenocarcinoma, large cell carcinoma and small cell carcinoma were 82%, 65%, 0%, 44%, Predictive value were 64%, 65%, 0%, 57%, respectively (Table 4-11 and figure 4-20).

Table 4-11 Interpretation from CT by consensus.

Interpretation from CT	Pathology				
	Squamous cell carcinoma	Adenocar cinoma	Large cell carcinoma	small cell carcinoma	Total
Squamous cell lung cancer	23	6	5	2	36
Adenocarcinoma	3	15	2	3	23
Large cell carcinoma	1	0	0	0	1
Small cell carcinoma	1	2	0	4	7
Total	28	23	7	9	67

Accuracy: Squamous cell lung cancer = 82%, (95%CI = 68-96)
Adenocarcinoma = 65%, (95%CI = 46-84)
Large cell carcinoma = 0%
Small cell lung cancer = 44%, (95%CI = 12-76)

Predictive value: Squamous cell lung cancer = 64%, (95%CI = 46-82)
Adenocarcinoma = 65%, (95%CI = 46-84)
Large cell carcinoma = 0%
Small cell lung cancer = 57%, (95%CI = 25-89)

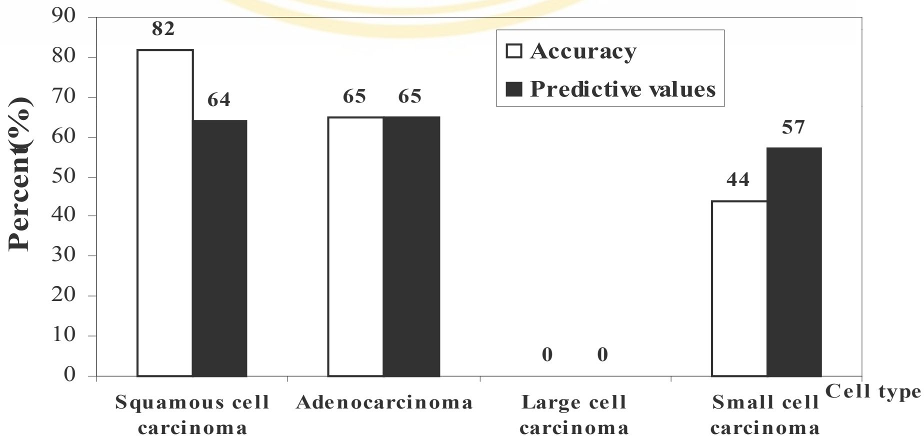

Chart 4-22 The accuracy and predictive value of interpretation from CT imaging.

CHAPTER V

DISCUSSION

Lung cancer continues to major health problem. It is the most common malignancy in wold wide and Thailand. Unfortunately, because most patients have advance disease at presentation, treatment options are limited. So diagnostic for lung cancer is important to treatment planning. At present, CT imaging is the one diagnostic imaging modality in that it provides information about primary tumor, thoracic lymph nodes, pleura, chest wall and upper abdomen.

The aim of this study to concentrate the evaluation in CT imaging patterns of lung cancer based on cell type. Two observers reviewed and interpreted of CT imaging. The patterns and any sign from lung cancer in CT imaging were recorded. We study in 67 cases, An amount of squamous cell carcinoma, adenocarcinoma, large cell carcinoma and small cell carcinoma were 28, 23, 7 and 9 cases, respectively. The means of tumor size were approximately in any cell type of lung cancer. The smallest size was adenocarcinoma and small cell carcinoma (1.5 cm). The largest size found in small cell carcinoma (14 cm). In this study we found that mainly of lung cancer were central lesions and located in right lobe. There was significant location of squamous cell carcinoma in central and adenocarcinoma in pheripheral ($p<0.05$). The most common location of squamous cell carcinoma and small cell lung cancer were central. We found that adenocarcinoma and large cell carcinoma were approximately in central and peripheral location and we can not indict the location in one case of large cell carcinoma. In addition to this study, we found that a great number of adenocarcinoma was in central and 2 in 9 of small cell carcinoma were in peripheral. The most common of squamous cell carcinoma were located in right and often found in right lower lobe. Frequently of adenocarcinoma, large cell carcinoma and small cell carcinoma were located in right upper lobe. Present of lymph node enlarge associate with pleural effusion was found in large cell carcinoma more than other cell type.

There was considerable overlap in infiltration and edge characteristic of each cell type of lung cancer, the majority of each cell type were irregular edge and had infiltration of lung parenchyma.

In this study, we not found differentiation of each cell type about internal characteristic (attenuation, cavitation and calcification). About attenuation at pre and post contrast media injection, the most common of every cell type were inhomogeneous densities. The highest incident of cavitations was found in squamous cell carcinoma (27%). None of the small cell carcinoma had recognizable cavitations. Strang and Simpson (1953), in a study of 1,930 cases of lung cancer, found radiographic evidence of cavitations in 4%, and 36 of 44 tumors showing cavitations proved to be squamous cell carcinoma (52).

The calcification was found in a few percent in all most cell type (23% in squamous cell carcinoma, 13% in adenocarcinoma and 14% in large cell carcinoma). None of the small call carcinoma had recognizable calcification.

The highest incidence of pleural effusion was found in large cell carcinoma (71%) but the incident in other cell type was resembled (54% in squamous cell carcinoma, 52% in adenocarcinoma and 44% in small cell carcinoma). We found that the highest incident of lymph node enlargement in every cell type.

Metastasis to chest wall or rib destruction was found to occur in peripheral tumor, being present in 13% of adenocarcinoma and 29% of large cell carcinoma. Incidence of metastasis to ipsilateral and/or contra lateral lung was found in all cell type. These incidences was found to occur most often in association with small cell carcinoma, occurring in 44% of case, and other cell type such as adenocarcinoma, large cell carcinoma and squamous cell carcinoma were 35%, 29% and 29%, respectively.

Thus in 67 consecutive patients with lung cancer routine computed tomography of abdomen before surgery showed that 12 cases had extra thoracic deposits. The incidence of metastasis to the liver showed in large cell carcinoma, adenocarcinoma, small cell carcinoma and squamous cell carcinoma were 14%, 13%, 11% and 7%, respectively. We found occur the abnormally about adrenal gland that had a larger more than normal size, occurring in 22% of small cell carcinoma, 14% of large cell carcinoma, 9% of adenocarcinoma, and 4% of squamous cell carcinoma.

Concordance for the agreement between observers was fair (Kappa index = 0.247). After consensus, accuracy and predictive values were calculated. The accuracy sequences from high to low be squamous cell carcinoma (82%), adenocarcinoma (65%), small cell carcinoma (44%) and large cell carcinoma (0%). Predictive value from high to low is adenocarcinoma (65%), squamous cell carcinoma (64%), small cell carcinoma (57%), and large cell carcinoma (0%).

CHAPTER VI
CONCLUSION

CT imaging has the advantage in lung; the shape, margin and relationship to other structures can be outlined. CT chests display several of characteristic in lung cancer. Some characterized can help the radiologist to predicted about some cell type of lung cancer, such as most of central lesion were sqamous cell carcinoma or small cell carcinoma, and most of peripheral lesion was adenocarcinoma, but in large cell carcinoma was indistinct. Central lesions with cavitating have possibility to squamous cell carcinoma. Present of lymph node enlarge associate with pleural effusion was found in large cell carcinoma more than other cell type. At least for the differentiation of characteristic presenting in CT imaging (such as size, edge, infiltration, lymph node enlarge, pleural effusion, metastasis to other organ, attenuation pre and post contrast media injection) not evaluated cell type of lung cancer, there is a reason able consensus as to which imaging studies.

In our study, the interpretation criteria of Computed Tomography imaging for evaluated pathologic cell type of lung cancer have usefulness in squamous cell carcinoma and adenocarcinoma. But we can not resume about this criteria in large cell carcinoma and small cell carcinoma, because of the small sample size in these cell type. We believe that pathologic resulted should be an appropriate procedure to differentiate in any cell type of lung cancer in Siriraj Hospital. But CT has necessary to assess and treatment planning for patients who have lung cancer because CT imaging presented about the margin, internal characteristic of tumors and relationship to other structures. Our study is a pilot study for the usefulness of Computed Tomographic imaging of the chest in evaluation pathologic cell type of primary lung cancer. Prospective study with more sample size is suggested.

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