Sudan University of Science & Technology

College of Graduate Studies

Faculty of Engineering

Biomedical Engineering MSc.

Bath(5)

COMPUTER AIDED DIAGNOSIS SYSTEM FOR THE DETECTION OF PULMONARY NODULES ON CT SCANS

This thesis for the Master of Biomedical Engineering Degree

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Dedication

My heartfelt thanks go to all of my family members and especially my parents, whose sacrifice, support, love, caring inspired me to overcome all the difficulties throughout my academic life. This dissertation processes would not be successful without having their patience, love, and dedication.

Acknowledgment

Thanks to God first and foremost for his generosity and grace on me in the completion of this thesis. Then I would like to express my sincere appreciation to my thesis main advisor, Dr. Zeinab Adam Mustafa, for the encouragement, guidance, critics, advices, motivation, idea, and his patience from the beginning to the end of this thesis.

I would like to deeply thank the Dean of the Department of medical engineering (UST), DR. Mohammed Albasheer , during my undergraduate studies . for his continuous and great support on both the technical and the psychological levels and kept me motivating for this depart .

I am really indebted to many of my colleagues , friends , sisters and hospitals who never let me down in any quick technical or administrative advice I sought from them.

For all without having his continual support and interest, this thesis would not have been the same as present here.

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Glossary

CT	Computed tomography
ANN	Artificial neural net work
GUI	Graphical User Interface
NSCLC	Non-small Cell Lung Cancer
SCLC	Small Cell Lung Cancer
CAT	Computed Axial Tomography
PET	Positron Emission Tomography
MRI	Magnetic Resonance Imaging
MATLAB	Matrix Laboratory
ROI	Region Of Interest
NN	Neural Network
BP	Back-Propagation
CAD	Computer Aid Diagnoses System
SOM	Self Organizing Map
SE	Sensitivity
SP	Specificity
PPV	Positive Predictive Value
NPV	Negative Predictive Value
TP	True Positives
TN	True Negatives
FP	False Positives
FN	False Negatives
(COPD)	chronic obstructive pulmonary disease

ABSTRACT

Lung cancer is the most common cause of death due to cancer in both men and women throughout the world. Statistics from the American Cancer Society estimated that in 2014 about 224,000 new cases of lung cancer in the U.S. occurred and about 159,000 deaths were due to the disease. According to the U.S. National Cancer Institute, approximately one out of every 14 men and women in the U.S. will be diagnosed with cancer of the lung at some point in their lifetime.

Pulmonary nodules can be an indication for primary lung cancer , CT offers better contrast , detect smaller, earlier stage nodules with a higher sensitivity .

CAD is technologies to improve the quality and productivity of radiologists' tasks by improving the accuracy and consistency of radiological diagnoses and also by reducing the image reading time and miss.

The objective of this study is identifying all nodules from the chest CT lung images and classifying these nodules into tumor and non-tumor nodules, to reduce the false positive rate using Image processing and Neural Network techniques.

The results obtained from proposed CAD system are good compared to existing CAD systems. The sensitivity and specificity of the image were 100% , 96% respectively and achieved accuracy of 98.2%.

Chapter One

Introduction

Pulmonary nodules are among the most common focal pulmonary lesions .
The presence or absence of pulmonary nodules can be of great value in the differential diagnosis of lung diseases .
Pulmonary nodules are often benign, or may be metastases from various cancer types, but they can also be an indication for primary lung cancer. Cancer of the lung and bronchus, referred to below simply as ‘lung cancer’, is the second most common cancer type. However, due to its aggressiveness, lung cancer is the number one cause of all cancer-related deaths, with more than 150 000 deaths in the USA each year .[1]

The early detection of lung nodules is crucial, either for close observation or biopsy to differentiate between benign or malignant nodules, or for timely therapy. The detection and diagnosis of pulmonary nodules in CT data sets of the thorax has therefore become a standard procedure in radiological practice.
CT offers better contrast than chest X-ray between nodule and background with no overlapping structures, and several studies have shown that CT can detect smaller, earlier stage nodules with a higher sensitivity than chest X-ray.[2]

CAD has generally been defined by diagnosis made by a physician who takes into account the computer output based on quantitative analysis of radiological images. The goal of CAD is to improve the quality and productivity of radiologists’ tasks by improving the accuracy and consistency of radiological diagnoses and also by reducing the image reading time.[3]

Artificial Neural Network (ANN) is proposed for the classification of lung cancer in CT images. An ANN was developed to differentiate the cancerous nodules from other suspected nodule areas in the CT images.[4]

1.1Objectives:-

To design a computer aided detection (CAD) software to aid in detection pulmonary nodule and normal features of lung using artificial neural net work.

1.2 Problem Statement:-

The goal of this dissertation is the investigation of the various components and development of an automated CAD system to assist radiologists in the classification (characterization) of lung nodules on CT scans. Therefore, early and accurate detection of a lung is critical to plan appropriate care and improving life for further survival.

1.3 Significant of study:-

A computer aided diagnosis (CAD) system would be to enable the scans of patients in third world regions that lack experienced radiologists to be analyzed quickly and reliably. Additionally, in recent years large pulmonary studies that involve the collection of multiple CT scans from thousands of patients have been funded. Each of these scans needs to be analyzed by a radiologist, and the analysis of these scans can be prohibitively expensive and time consuming.

1.4 Thesis layout

Chapter I: Provides an introductory view of the thesis, problem statement, the concerned objectives, and significant of the study.

Chapter II: Provides some anatomical and physiological, a quick overview of all the concerned topics and general talking of technique for uses in this research.

Chapter III: Is a brief recollection of the various works of image processing and enhancement and pattern recognition and classification of lung.

Chapter IV: Includes a detailed assembly of the various algorithms and methodologies that have been manipulated and implemented for the achievement of the research objectives.

Chapter V: Demonstrates the gathering of results, the respective discussions for the created systems and the evaluation of the efficacy of the results obtained.

Chapter VI: Provides the overall conclusions drawn up from the thesis and some directions that could present as useful suggestions for future work.

Chapter two

BACKGROUND

2.1 The Human Lungs

Lungs are the organs of respiration. Humans have two lungs, a right lung and a left lung. The right lung consists of three lobes while the left lung is slightly smaller consisting of only two lobes (the left lung has a "cardiac notch" allowing space for the heart within the chest).

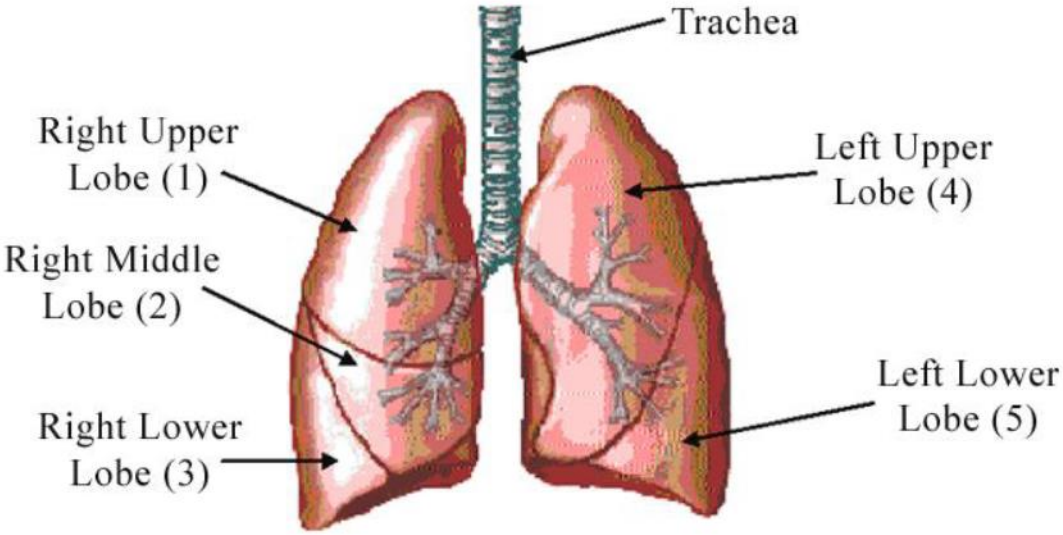

Figure (2.1) right and left lung

The lungs are located within the thoracic cavity, on either side of the heart and close to the backbone. They are enclosed and protected by the ribcage. [5]
[4]

The left lung has a lateral indentation which is shaped to accommodate the position of the heart. The right lobe is a little shorter than the left lung and this is to accommodate the positioning of the liver. Both lungs have broad bases enabling them to rest on the diaphragm without causing displacement.[5]

2.2 Breathing

Breathing is a combination of many factors. These factors are integrated and controlled by the nervous system.(mechanics of breathing) The lungs can be expanded and contracted by downward and upward movement of the diaphragm to lengthen or shorten the chest cavity and by elevation and depression of the ribs to increase and decrease the anteroposterior diameter of the chest cavity.

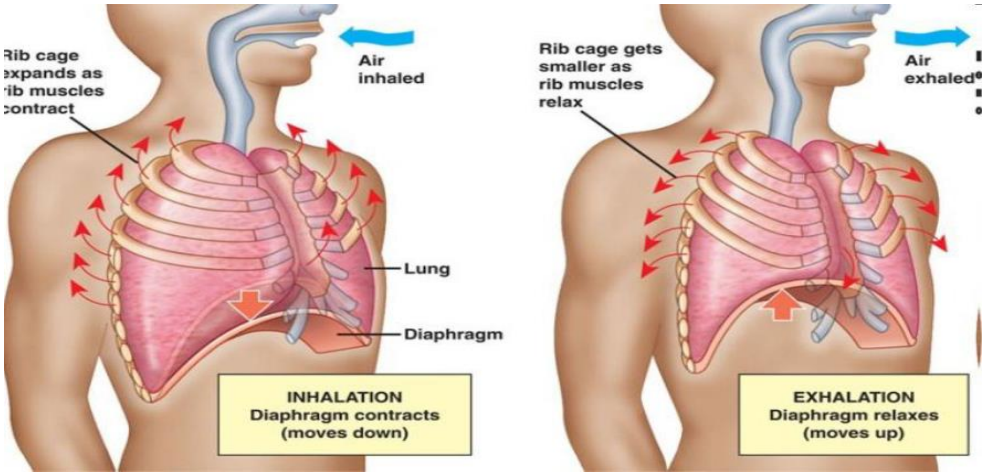

Figure (2.2) mechanics of breathing

Surrounding each lung individually is a serous cavity, called the pleural cavity. The minute quantity of serous fluid in the cavity serves as a lubricant. This serves to minimize friction for the expansion and contraction of the lungs during breathing.[6]

There are essentially two blood supplies for the lungs--nutrient blood and functional blood. Nutrient blood is carried by the bronchial arteries from the thoracic aorta. Nutrient blood provides nourishment and oxygen to the tissues of the lung.

Functional blood is actually involved in the respiratory exchange of gases between the alveoli and the capillaries. Functional blood is brought to and from the lungs by the pulmonary cycle of the cardiovascular system.[7]

2.3 Lung cancer [8]

Lung cancer is the uncontrolled growth of abnormal cells in one or both of the lungs. While normal cells reproduce and develop into healthy lung tissue, these abnormal cells reproduce faster and never grow into normal lung tissue. Lumps of cancer cells (tumors) then form and grow. Besides interfering with how the lung functions, cancer cells can spread from the tumor into the bloodstream or Lymphatic system where they can spread to other organs.

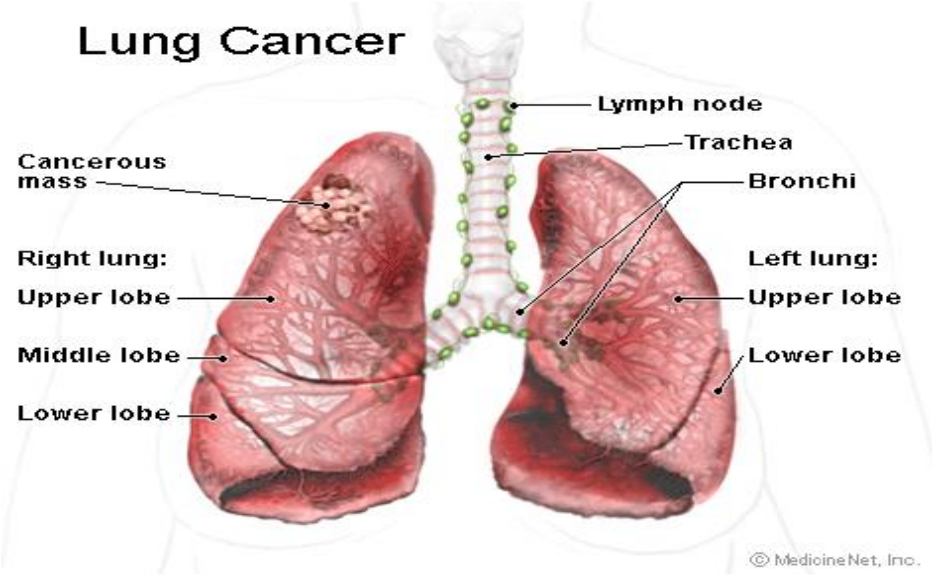

Figure (2.3) several forms of lung cancer

Lung cancer is the most common cause of death due to cancer in both men and women throughout the world. Statistics from the American Cancer Society estimated that in 2014 about 224,000 new cases of lung cancer in the U.S. occurred and about 159,000 deaths were due to the disease. According to the U.S. National Cancer Institute, approximately one out of every 14 men and women in the U.S. will be diagnosed with cancer of the lung at some point in their lifetime.

2.4 Lung diseases [8]

The presence of certain diseases of the lung, notably chronic obstructive pulmonary disease (COPD), is associated with an increased risk (four- to six-fold the risk of a nonsmoker) for the development of lung cancer even after the effects of concomitant cigarette smoking are excluded. Pulmonary fibrosis (scarring of the lung) appears to increase the risk about seven-fold, and this risk does not appear to be related to smoking.

2.5 Prior history of lung cancer [8]

Survivors of lung cancer have a greater risk of developing a second lung cancer than the general population has of developing a first lung cancer. Survivors of non-small cell lung cancers (NSCLCs, see below) have an additive risk of 1%-2% per year for developing a second lung cancer. In survivors of small cell lung cancers (SCLCs, see below), the risk for development of second lung cancers approaches 6% per year.

2.6 Air pollution [8]

Air pollution from vehicles, industry, and power plants can raise the likelihood of developing lung cancer in exposed individuals. Up to 1% of lung cancer deaths are attributable to breathing polluted air, and experts believe that prolonged exposure to highly polluted air can carry a risk for the development of lung cancer similar to that of passive smoking.

2.7 Causes lung cancer [8]

2.7.1Smoking : about 90% of lung cancers arising as a result of tobacco use.

2.7.2 Passive smoking : Research has shown that nonsmokers who reside with a smoker have a 24% increase in risk for developing lung cancer when compared with nonsmokers who do not reside with a smoker.

2.7.3 Asbestos fibers: are silicate fibers that can persist for a lifetime in lung tissue following exposure to asbestos.

2.7.4 Radon gas : is a known cause of lung cancer, with an estimated 12% of lung-cancer deaths in the U.S.

2.7.5 Familial predisposition : individual genetic susceptibility, may play a role in the causation of lung cancer.

2.8 Types of lung cancer [8]

Lung cancers, also known as bronchogenic carcinomas, are broadly classified into two types:

small cell lung cancers (SCLC) and non-small cell lung cancers (NSCLC). This classification is based upon the microscopic appearance of the tumor cells themselves. These two types of cancers grow and spread in different ways and may have different treatment options, so a distinction between these two types is important.

2.8.1 small cell lung cancers (SCLC) :-

SCLC comprise about 20% of lung cancers and are the most aggressive and rapidly growing of all lung cancers. SCLC are strongly related to cigarette smoking, with only 1% of these tumors occurring in nonsmokers. SCLC metastasize rapidly to many sites within the body and are most often discovered after they have spread extensively. Referring to a specific cell appearance often seen when examining

samples of SCLC under the microscope, these cancers are sometimes called oat cell carcinomas.

2.8.2 non-small cell lung cancers (NSCLC) :-

NSCLC are the most common lung cancers, accounting for about 80% of all lung cancers. NSCLC can be divided into three main types that are named based upon the type of cells found in the tumor:

- **Adenocarcinomas** are the most commonly seen type of NSCLC in the U.S. and comprise up to 50% of NSCLC. While adenocarcinomas are associated with smoking, like other lung cancers, this type is observed as well in nonsmokers who develop lung cancer. Most adenocarcinomas arise in the outer, or peripheral, areas of the lungs.
- **Bronchioloalveolar carcinoma** is a subtype of adenocarcinoma that frequently develops at multiple sites in the lungs and spreads along the preexisting alveolar walls.
- **Squamous cell carcinomas** were formerly more common than adenocarcinomas; at present, they account for about 30% of NSCLC. Also known as epidermoid carcinomas, squamous cell cancers arise most frequently in the central chest area in the bronchi.
- **Large cell carcinomas**, sometimes referred to as undifferentiated carcinomas, are the least common type of NSCLC.
- **Mixtures** of different types of NSCLC are also seen. **Other types of cancers** can arise in the lung; these types are much less common than NSCLC and SCLC and together comprise only 5%-10% of lung cancers:
  - **Bronchial carcinoids** account for up to 5% of lung cancers. These tumors are generally small (3 cm-4 cm or less) when diagnosed and occur most commonly in people under 40 years of age. Unrelated to cigarette smoking, carcinoid tumors can metastasize, and a small proportion of these tumors secrete hormone-like substances that may cause specific symptoms related to

the hormone being produced. Carcinoids generally grow and spread more slowly than bronchogenic cancers, and many are detected early enough to be amenable to surgical resection.

- **Cancers of supporting lung tissue** such as smooth muscle, blood vessels, or cells involved in the immune response can rarely occur in the lung.

  As discussed previously, metastatic cancers from other primary tumors in the body are often found in the lung. Tumors from anywhere in the body may spread to the lungs either through the bloodstream, through the lymphatic system, or directly from nearby organs. Metastatic tumors are most often multiple, scattered throughout the lung, and concentrated in the peripheral rather than central areas of the lung.

2.9 Lung cancer diagnose [8]

Procedures and tests to diagnose lung cancer include the following:

- The **history and physical examination** may reveal the presence of symptoms or signs that are suspicious for lung cancer. In addition to asking about symptoms and risk factors for cancer development such as smoking, doctors may detect signs of breathing difficulties, airway obstruction, or infections in the lungs. Cyanosis, a bluish color of the skin and the mucous membranes due to insufficient oxygen in the blood, suggests compromised function due to chronic disease of the lung. Likewise, changes in the tissue of the nail beds, known as clubbing, also may indicate chronic lung disease.

- The **chest X-ray** is the most common first diagnostic step when any new symptoms of lung cancer are present. The chest X-ray procedure often involves a view from the back to the front of the chest as well as a view from the side. Like any X-ray procedure, chest X-rays expose the patient briefly to a small amount of radiation. Chest X-rays may reveal suspicious areas in the lungs but are unable to determine if these areas are cancerous. In particular, calcified nodules in the lungs or benign tumors called hamartomas may be identified on a chest X-ray and mimic lung cancer.

- **CT (computerized tomography, computerized axial tomography, or CAT) scans** may be performed on the chest, abdomen, and/or brain to examine for both metastatic and lung tumors. A CT scan of the chest may be ordered when X-rays do not show an abnormality or do not yield sufficient information about the extent or location of a tumor. CT scans are X-ray procedures that combine multiple images with the aid of a computer to generate cross-sectional views of the body. The images are taken by a large donut-shaped X-ray machine at different angles around the body. One advantage of CT scans is that they are more sensitive than standard chest X-rays in the detection of lung nodules, that is, they will demonstrate more nodules. Sometimes intravenous contrast material is given prior to the scan to help delineate the organs and their positions. A CT scan exposes the patient to a minimal amount of radiation. The most common side effect is an adverse reaction to intravenous contrast material that may have been given prior to the procedure. This may result in itching, a rash, or hives that generally disappear rather quickly. Severe anaphylactic reactions (life-threatening allergic reactions with breathing difficulties) to contrast material are rare. CT scans of the abdomen may identify metastatic cancer in the liver or adrenal glands, and CT scans of the head may be ordered to reveal the presence and extent of metastatic cancer in the brain.

- A technique called a **low-dose helical CT scan** (or spiral CT scan) is recommended for use annually in current and former smokers between ages 55 and 80 with at least a 30 pack-year history of cigarette smoking who have smoked cigarettes within the past 15 years per the USPSTF recommendations. The technique appears to increase the likelihood of detection of smaller, earlier, and more curable lung cancers. Three years of low-dose CT scanning in this group reduced the risk of lung cancer death by 20%. Use of models and rules for analyzing the results of these tests are decreasing the need for testing to evaluate detected nodules when the likelihood is high the nodule is not cancerous

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- **Magnetic resonance imaging** (MRI) scans may be appropriate when precise detail about a tumor's location is required. The MRI technique uses magnetism, radio waves, and a computer to produce images of body structures. As with CT scanning, the patient is placed on a moveable bed which is inserted into the MRI scanner. There are no known side effects of MRI scanning, and there is no exposure to radiation. The image and resolution produced by MRI is quite detailed and can detect tiny changes of structures within the body. People with heart pacemakers, metal implants, artificial heart valves, and other surgically implanted structures cannot be scanned with an MRI because of the risk that the magnet may move the metal parts of these structures.

- **Positron emission tomography** (PET) scanning is a specialized imaging technique that uses short-lived radioactive drugs to produce three-dimensional colored images of those substances in the tissues within the body. While CT scans and MRI scans look at anatomical structures, PET scans measure metabolic activity and the function of tissues. PET scans can determine whether a tumor tissue is actively growing and can aid in determining the type of cells within a particular tumor. In PET scanning, the patient receives a short half-lived radioactive drug, receiving approximately the amount of radiation exposure as two chest X-rays. The drug accumulates in certain tissues more than others, depending on the drug that is injected. The drug discharges particles known as positrons from whatever tissues take them up. As the positrons encounter electrons within the body, a reaction producing gamma rays occurs. A scanner records these gamma rays and maps the area where the radioactive drug has accumulated. For example, combining glucose (a common energy source in the body) with a radioactive substance will show where glucose is rapidly being used, for example, in a growing tumor. PET scanning may also be integrated with CT scanning in a technique known as PET-CT scanning. Integrated PET-CT has been shown to improve the accuracy of staging (see below) over PET scanning alone.

- **Bone scans** are used to create images of bones on a computer screen or on film. Doctors may order a bone scan to determine whether a lung cancer has metastasized to the bones. In a bone scan, a small amount of radioactive material is injected into the bloodstream and collects in the bones, especially in abnormal areas such as those involved by metastatic tumors. The radioactive material is detected by a scanner, and the image of the bones is recorded on a special film for permanent viewing.

- **Sputum cytology**: The diagnosis of lung cancer always requires confirmation of malignant cells by a pathologist, even when symptoms and X-ray studies are suspicious for lung cancer. The simplest method to establish the diagnosis is the examination of sputum under a microscope. If a tumor is centrally located and has invaded the airways, this procedure, known as a sputum cytology examination, may allow visualization of tumor cells for diagnosis. This is the most risk-free and inexpensive tissue diagnostic procedure, but its value is limited since tumor cells will not always be present in sputum even if a cancer is present. Also, noncancerous cells may occasionally undergo changes in reaction to inflammation or injury that makes them look like cancer cells.

- **Bronchoscopy**: Examination of the airways by bronchoscopy (visualizing the airways through a thin, fiberoptic probe inserted through the nose or mouth) may reveal areas of tumor that can be sampled (biopsied) for diagnosis by a pathologist. A tumor in the central areas of the lung or arising from the larger airways is accessible to sampling using this technique. Bronchoscopy may be performed using a rigid or a flexible fiberoptic bronchoscope and can be performed in a same-day outpatient bronchoscopy suite, an operating room, or on a hospital ward. The procedure can be uncomfortable, and it requires sedation or anesthesia. While bronchoscopy is relatively safe, it must be carried out by a lung specialist (pulmonologist or surgeon) experienced in the procedure. When a tumor is visualized and adequately sampled, an accurate cancer diagnosis usually is possible.

Some patients may cough up dark-brown blood for one to two days after the procedure. More serious but rare complications include a greater amount of bleeding, decreased levels of oxygen in the blood, and heart arrhythmias as well as complications from sedative medications and anesthesia.

- **Needle biopsy**: Fine-needle aspiration (FNA) through the skin, most commonly performed with radiological imaging for guidance, may be useful in retrieving cells for diagnosis from tumor nodules in the lungs. Needle biopsies are particularly useful when the lung tumor is peripherally located in the lung and not accessible to sampling by bronchoscopy. A small amount of local anesthetic is given prior to insertion of a thin needle through the chest wall into the abnormal area in the lung. Cells are suctioned into the syringe and are examined under the microscope for tumor cells. This procedure is generally accurate when the tissue from the affected area is adequately sampled, but in some cases, adjacent or uninvolved areas of the lung may be mistakenly sampled. A small risk (3%-5%) of an air leak from the lungs (called a pneumothorax, which can easily be treated) accompanies the procedure.

- **Thoracentesis**: Sometimes lung cancers involve the lining tissue of the lungs (pleura) and lead to an accumulation of fluid in the space between the lungs and chest wall (called a pleural effusion). Aspiration of a sample of this fluid with a thin needle (thoracentesis) may reveal the cancer cells and establish the diagnosis. As with the needle biopsy, a small risk of a pneumothorax is associated with this procedure.

- **Major surgical procedures**: If none of the aforementioned methods yields a diagnosis, surgical methods must be employed to obtain tumor tissue for diagnosis. These can include mediastinoscopy (examining the chest cavity between the lungs through a surgically inserted probe with biopsy of tumor masses or lymph nodes that may contain metastases) or thoracotomy (surgical opening of the chest wall for removal or biopsy of a tumor).

With a thoracotomy, it is rare to be able to completely remove a lung cancer, and both mediastinoscopy and thoracotomy carry the risks of major surgical procedures (complications such as bleeding, infection, and risks from anesthesia and medications). These procedures are performed in an operating room, and the patient must be hospitalized.

- **Blood tests**: While routine blood tests alone cannot diagnose lung cancer, they may reveal biochemical or metabolic abnormalities in the body that accompany cancer. For example, elevated levels of calcium or of the enzyme alkaline phosphatase may accompany cancer that is metastatic to the bones. Likewise, elevated levels of certain enzymes normally present within liver cells, including aspartate aminotransferase (AST or SGOT) and alanine aminotransferase (ALT or SGPT), signal liver damage, possibly through the presence of tumor metastatic to the liver. One current focus of research in the area of lung cancer is the development of a blood test to aid in the diagnosis of lung cancer. Researchers have preliminary data that has identified specific proteins, or biomarkers, that are in the blood and may signal that lung cancer is present in someone with a suspicious area seen on a chest X-ray or other imaging study.

- **Molecular testing**: For advanced NSCLCs, molecular genetic testing is carried out to look for genetic mutations in the tumor. For example, testing may be done to look for mutations or abnormalities in the epithelial growth factor receptor (EGFR) and the anaplastic lymphoma kinase (ALK) genes. Other genes that may be mutated include MAPK and PIK3. Targeted therapies are available that may be administered to patients whose tumors have alterations in these genes

2.10 Treatment for lung cancer [8]

Treatment for lung cancer can involve surgical removal of the cancer, chemotherapy, or radiation therapy, as well as combinations of these treatments. The decision about which treatments will be appropriate for a given individual must take into account the location and extent of the tumor as well as the overall health status of the patient.

As with other cancers, therapy may be prescribed that is intended to be curative (removal or eradication of a cancer) or palliative (measures that are unable to cure a cancer but can reduce pain and suffering). More than one type of therapy may be prescribed. In such cases, the therapy that is added to enhance the effects of the primary therapy is referred to as adjuvant therapy. An example of adjuvant therapy is chemotherapy or radiotherapy administered after surgical removal of a tumor in an attempt to kill any tumor cells that remain following surgery.

- **Surgery**: Surgical removal of the tumor is generally performed for limited-stage (stage I or sometimes stage II) NSCLC and is the treatment of choice for cancer that has not spread beyond the lung. About 10%-35% of lung cancers can be removed surgically, but removal does not always result in a cure, since the tumors may already have spread and can recur at a later time. Among people who have an isolated, slow-growing lung cancer removed, 25%-40% are still alive five years after diagnosis. It is important to note that although a tumor may be anatomically suitable for resection, surgery may not be possible if the person has other serious conditions (such as severe heart or lung disease) that would limit their ability to survive an operation. Surgery is less often performed with SCLC than with NSCLC because these tumors are less likely to be localized to one area that can be removed.

  The surgical procedure chosen depends upon the size and location of the tumor. Surgeons must open the chest wall and may perform a wedge resection of the lung (removal of a portion of one lobe), a lobectomy (removal of one lobe), or a pneumonectomy (removal of an entire lung). [16]

Sometimes lymph nodes in the region of the lungs also are removed (lymphadenectomy). Surgery for lung cancer is a major surgical procedure that requires general anesthesia, hospitalization, and follow-up care for weeks to months. Following the surgical procedure, patients may experience difficulty breathing, shortness of breath, pain, and weakness. The risks of surgery include complications due to bleeding, infection, and complications of general anesthesia.

- **Radiation**: Radiation therapy may be employed as a treatment for both NSCLC and SCLC. Radiation therapy uses high-energy X-rays or other types of radiation to kill dividing cancer cells. Radiation therapy may be given as curative therapy, palliative therapy (using lower doses of radiation than with curative therapy), or as adjuvant therapy in combination with surgery or chemotherapy. The radiation is either delivered externally, by using a machine that directs radiation toward the cancer, or internally through placement of radioactive substances in sealed containers within the area of the body where the tumor is localized. Brachytherapy is a term used to describe the use of a small pellet of radioactive material placed directly into the cancer or into the airway next to the cancer. This is usually done through a bronchoscope.
  Radiation therapy can be given if a person refuses surgery, if a tumor has spread to areas such as the lymph nodes or trachea making surgical removal impossible, or if a person has other conditions that make them too ill to undergo major surgery. Radiation therapy generally only shrinks a tumor or limits its growth when given as a sole therapy, yet in 10%-15% of people it leads to long-term remission and palliation of the cancer. Combining radiation therapy with chemotherapy can further prolong survival when chemotherapy is administered. External radiation therapy can generally be carried out on an outpatient basis, while internal radiation therapy requires a brief hospitalization. A person who has severe lung disease in addition to a lung cancer may not be able to receive radiotherapy to the lung since the radiation can further decrease function of the lungs. A type of external radiation therapy called the "gamma knife" is sometimes used to treat single brain metastases.

In this procedure, multiple beams of radiation coming from different directions are focused on the tumor over a few minutes to hours while the head is held in place by a rigid frame. This reduces the dose of radiation that is received by noncancerous tissues.

For external radiation therapy, a process called simulation is necessary prior to treatment. Using CT scans, computers, and precise measurements, simulation maps out the exact location where the radiation will be delivered, called the treatment field or port. This process usually takes 30 minutes to two hours. The external radiation treatment itself generally is done four or five days a week for several weeks.

Radiation therapy does not carry the risks of major surgery, but it can have unpleasant side effects, including fatigue and lack of energy. A reduced white blood cell count (rendering a person more susceptible to infection) and low blood platelet levels (making blood clotting more difficult and resulting in excessive bleeding) also can occur with radiation therapy. If the digestive organs are in the field exposed to radiation, patients may experience nausea, vomiting, or diarrhea. Radiation therapy can irritate the skin in the area that is treated, but this irritation generally improves with time after treatment has ended.

- **Chemotherapy**: Both NSCLC and SCLC may be treated with chemotherapy. Chemotherapy refers to the administration of drugs that stop the growth of cancer cells by killing them or preventing them from dividing. Chemotherapy may be given alone, as an adjuvant to surgical therapy, or in combination with radiotherapy. While a number of chemotherapeutic drugs have been developed, the class of drugs known as the platinum-based drugs have been the most effective in treatment of lung cancers.

  Chemotherapy is the treatment of choice for most SCLC, since these tumors are generally widespread in the body when they are diagnosed. Only half of people who have SCLC survive for four months without chemotherapy.

With chemotherapy, their survival time is increased up to four- to fivefold. Chemotherapy alone is not particularly effective in treating NSCLC, but when NSCLC has metastasized, it can prolong survival in many cases.

Chemotherapy may be given as pills, as an intravenous infusion, or as a combination of the two. Chemotherapy treatments usually are given in an outpatient setting. A combination of drugs is given in a series of treatments, called cycles, over a period of weeks to months, with breaks in between cycles. Unfortunately, the drugs used in chemotherapy also kill normally dividing cells in the body, resulting in unpleasant side effects. Damage to blood cells can result in increased susceptibility to infections and difficulties with blood clotting (bleeding or bruising easily). Other side effects include fatigue, weight loss, hair loss, nausea, vomiting, diarrhea, and mouth sores. The side effects of chemotherapy vary according to the dosage and combination of drugs used and may also vary from individual to individual. Medications have been developed that can treat or prevent many of the side effects of chemotherapy. The side effects generally disappear during the recovery phase of the treatment or after its completion.

- **Prophylactic brain radiation**: SCLC often spreads to the brain. Sometimes people with SCLC that is responding well to treatment are treated with radiation therapy to the head to treat very early spread to the brain (called micrometastasis) that is not yet detectable with CT or MRI scans and has not yet produced symptoms. Brain radiation therapy can cause short-term memory problems, fatigue, nausea, and other side effects.
- **Treatment of recurrence**: Lung cancer that has returned following treatment with surgery, chemotherapy, and/or radiation therapy is referred to as recurrent or relapsed. If a recurrent cancer is confined to one site in the lung, it may be treated with surgery. Recurrent tumors generally do not respond to the chemotherapeutic drugs that were previously administered. Since platinum-based drugs are generally used in initial chemotherapy of lung cancers,

these agents are not useful in most cases of recurrence. A type of chemotherapy referred to as second-line chemotherapy is used to treat recurrent cancers that have previously been treated with chemotherapy, and a number of second-line chemotherapeutic regimens have been proven effective at prolonging survival. People with recurrent lung cancer who are well enough to tolerate therapy also are good candidates for experimental therapies (see below), including clinical trials.

- **Targeted therapy**: Molecularly targeted therapy involves the administration of drugs that have been identified to work in subsets of patients whose tumors have specific genetic changes. For example, the drugs erlotinib (Tarceva) and gefitinib (Iressa) are so-called targeted drugs, which may be used in certain patients with NSCLC who are no longer responding to chemotherapy. Targeted therapy drugs more specifically target cancer cells, resulting in less damage to normal cells than general chemotherapeutic agents. Erlotinib and gefitinib target a protein called the epidermal growth factor receptor (EGFR) that is important in promoting the division of cells. This protein is found at abnormally high levels on the surface of some types of cancer cells, including many cases of non-small cell lung cancer.

  Other attempts at targeted therapy include drugs known as antiangiogenesis drugs, which block the development of new blood vessels within a cancer. Without adequate blood vessels to supply oxygen-carrying blood, the cancer cells will die. The antiangiogenic drug bevacizumab (Avastin) has also been found to prolong survival in advanced lung cancer when it is added to the standard chemotherapy regimen. Bevacizumab is given intravenously every two to three weeks. However, since this drug may cause bleeding, it is not appropriate for use in patients who are coughing up blood, if the lung cancer has spread to the brain, or in people who are receiving anticoagulation therapy ("blood thinner" medications). Bevacizumab also is not used in cases of squamous cell cancer because it leads to bleeding from this type of lung cancer. Ramucirumab (Cyramza) is another angiogenesis inhibitor that can be used to treat advanced non-small cell lung cancer.

Cetuximab is an antibody that binds to the epidermal growth factor receptor (EGFR). In patients with NSCLC whose tumors have been shown to express the EGFR by immunohistochemical analysis, the addition of cetuximab may be considered for some patients. Other targeted therapies include ALK tyrosine kinase inhibitor drugs (for example, crizotinib, ceritinib) that are used in patients whose tumors have an abnormality of the ALK gene.

- **Photodynamic_therapy (PDT)**: One newer therapy used for different types and stages of lung cancer (as well as some other cancers) is photodynamic therapy. In photodynamic treatment, a photosynthesizing agent (such as a porphyrin, a naturally occurring substance in the body) is injected into the bloodstream a few hours prior to surgery. During this time, the agent is taken up in rapidly growing cells such as cancer cells. A procedure then follows in which the physician applies a certain wavelength of light through a handheld wand directly to the site of the cancer and surrounding tissues. The energy from the light activates the photosensitizing agent, causing the production of a toxin that destroys the tumor cells. PDT has the advantages that it can precisely target the location of the cancer, is less invasive than surgery, and can be repeated at the same site if necessary. The drawbacks of PDT are that it is only useful in treating cancers that can be reached with a light source and is not suitable for treatment of extensive cancers. The U.S. Food and Drug Administration (FDA) has approved the photosensitizing agent called porfimer sodium (Photofrin) for use in PDT to treat or relieve the symptoms of esophageal cancer and non-small cell lung cancer. Further research is ongoing to determine the effectiveness of PDT in other types of lung cancer.

- **Radiofrequency ablation** (RFA): Radiofrequency ablation is being studied as an alternative to surgery, particularly in cases of early stage lung cancer. In this type of treatment, a needle is inserted through the skin into the cancer, usually under guidance by CT scanning. Radiofrequency (electrical) energy is then transmitted to the tip of the

needle where it produces heat in the tissues, killing the cancerous tissue and closing small blood vessels that supply the cancer. RFA usually is not painful and has been approved by the U.S. Food and Drug Administration for the treatment of certain cancers, including lung cancers. Studies have shown that this treatment can prolong survival similarly to surgery when used to treat early stages of lung cancer but without the risks of major surgery and the prolonged recovery time associated with major surgical procedures.

- **Experimental therapies**: Since no therapy is currently available that is absolutely effective in treating lung cancer, patients may be offered a number of new therapies that are still in the experimental stage, meaning that doctors do not yet have enough information to decide whether these therapies should become accepted forms of treatment for lung cancer. New drugs or new combinations of drugs are tested in so-called clinical trials, which are studies that evaluate the effectiveness of new medications in comparison with those treatments already in widespread use. Experimental treatments known as immunotherapies are being studied that involve the use of vaccine-related therapies or other therapies that attempt to utilize the body's immune system to fight cancer cells. Vaccine therapies against lung cancer are another area in which research is ongoing, and lung cancer treatment vaccines are also being studied in clinical trials.

2.11 Pulmonary nodules

A lung nodule is defined as a “spot” on the lung that is 3 cm (about 1 ½ inches) in diameter or less. If an abnormality is seen on an x-ray of the lungs that is larger than 3 cm, it is considered a “lung mass” instead of a nodule, and is more likely to be cancerous. Lung nodules usually need to be at least 1 cm in size before they can be seen on a chest x-ray.[1]

Pulmonary nodules are often benign, or may be metastases from various cancer types, but they can also be an indication for primary lung cancer. Cancer of the lung and bronchus, referred to below simply as ‘lung cancer’, is the second most common cancer type. However, due to its aggressiveness, lung cancer is the number one cause of all cancer-related deaths, with more than 150 000 deaths in the USA each year . [2]

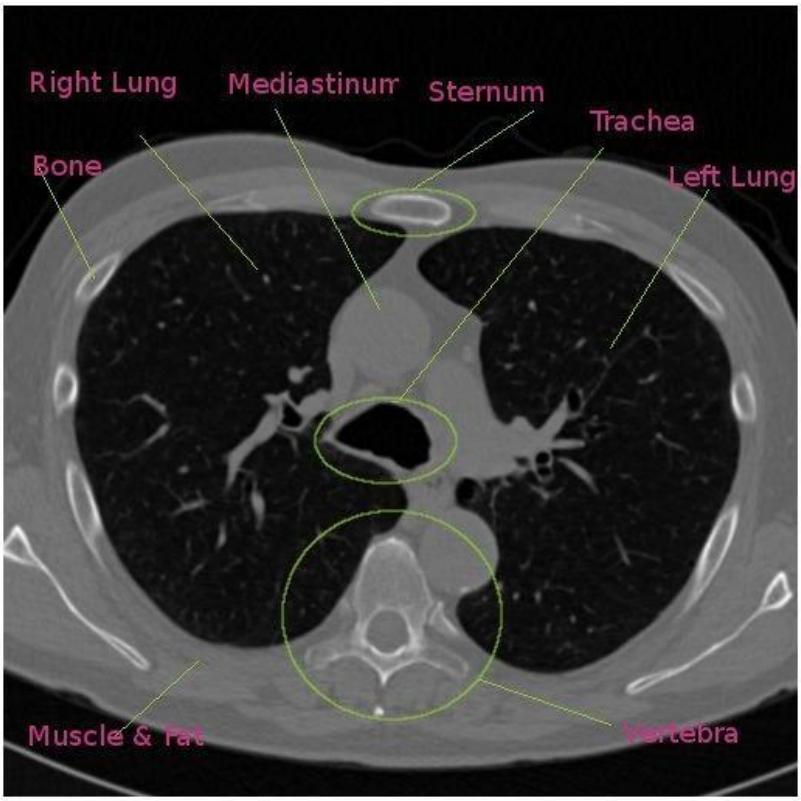
2.11.1 Pulmonary nodules on CT Scan

The early detection of lung nodules is crucial, either for close observation or biopsy to differentiate between benign or malignant nodules, or for timely therapy. The most common methods used to detect pulmonary nodules include chest X-ray and CT. Fiber-optic bronchoscopy is also used, but has limited value for finding nodules other than those in the larger airways.

The detection and diagnosis of pulmonary nodules in CT data sets of the thorax has therefore become a standard procedure in radiological practice.

CT offers better contrast than chest X-ray between nodule and background with no overlapping structures, and several studies have shown that CT can detect smaller, earlier stage nodules with a higher sensitivity than chest X-ray.

Recently, CT technology has undergone a major evolution with the introduction of multislice technology with multislice CT, a full-lung, thin-slice (< 1 mm) scan can be done within a single breath-hold. It is hoped that, with the high-resolution CT data available from multislice CT scanners, cancerous nodules can be recognized while still small and in an early stage of lung cancer. [2]



Figure(2.11)Lung CT

Many researchers assume that this down-staging effect achieved by early detection of lung cancer will ultimately improve the survival rate .

Moreover, it is hoped that lung cancer screening of high-risk patient groups may significantly increase the rate of lung cancer cases which are diagnosed before the cancer has metastasized. These propositions will be investigated during a large-scale randomized 9-year trial conducted by the US National Cancer Institute (NCI). The currently starting National Lung Screening Trial (NLST) will enroll 50 000 current or former smokers and will take place at a total of 30 sites throughout the USA .The NCI is also forming a consortium to build up a lung image database This could possibly be used to validate computer aided detection software . [2]

2.12 Computer-aided diagnosis (CAD) [3]

Recently, computer-aided diagnosis (CAD) has become one of the major research subjects in medical imaging and diagnostic radiology . Over the last 3 years, at the Annual Meetings of the Radiological Society of North America (RSNA) in Chicago, which is one of the major meetings in the field of diagnostic radiology, the number of papers presented on subjects related to CAD has increased by approximately 50% per year, from 55 in 2000, to 86 in 2001, to 134 in 2002, and 191 in 2003. Many different types of CAD schemes are being developed for detection and/or characterisation of various lesions in medical imaging, including conventional projection radiography, computed tomography (CT), magnetic resonance imaging (MRI) and ultrasound. Organs currently being subjected to research for CAD includes the breast, chest, colon, brain, liver, kidney, and the vascular and skeletal systems. The basic concept of CAD is to provide a computer output as a ‘‘second opinion’’ to assist radiologists’ image readings .

Therefore, for development of a successful CAD scheme it is necessary not only to develop computer algorithms, but also to investigate how useful the computer output would be for radiologists in their diagnoses, how to quantify the benefits of the computer output for radiologists, and how to maximize the effect of the computer output on their diagnoses.

Thus, large scale observer performance studies on radiologists using a reliable methodology such as receiver operating characteristic (ROC) analysis are equally as important as the development of computer algorithms in the field of CAD. Therefore, the research and development of CAD has involved a team effort by investigators with different backgrounds such as physicists, radiologists, computer scientists, engineers, psychologists and statisticians.

CAD has generally been defined by diagnosis made by a physician who takes into account the computer output based on quantitative analysis of radiological images. This definition is clearly distinct from automated computerized diagnosis , which was attempted in the 1960s and 1970s, replacing radiologists by computers. However, our serious investigation of CAD at the University of Chicago began in the 1980s with a clear goal in mind of assisting radiologists by use of a computer.

The goal of CAD is to improve the quality and productivity of radiologists' tasks by improving the accuracy and consistency of radiological diagnoses and also by reducing the image reading time. The general approach for CAD is to find the location of a lesion and also to determine an estimate of the probability of a disease; these correspond to CAD for detection of a lesion and CAD for differential diagnosis.

The basic technologies involved in CAD schemes are: (1) image processing for detection and extraction of abnormalities; (2) quantitation of image features for candidates of abnormalities; (3) data processing for classification of image features between normals and abnormals (or benign and malignant); (4) quantitative evaluation and retrieval of images similar to those of unknown lesions; and (5) observer performance studies using ROC analysis.

Because the concept of CAD is broad, CAD can be applied to all imaging modalities, including projection radiography, CT, MRI, ultrasound and nuclear medicine imaging, used for all body parts such as the skull, thorax, heart, abdomen and extremities, and all kinds of examinations including skeletal imaging, soft tissue imaging, functional imaging and angiography.

However, the majority of CAD schemes developed in the past include the detection of breast lesions on mammograms , the detection of lung nodules in chest radiographs and thoracic CT , and the detection of polyps in CT colonography . Therefore, the current results obtained from basic research and clinical applications of CAD may be considered the tip of an iceberg, and thus a major impact of CAD on medical imaging and diagnostic radiology may be expected in the future. [3]

2.13 Role of CAD with pulmonary nodules:-

CAD systems can aid radiologists by providing a “second opinion” and may be used in the first stage of examination in the near future , the main role of using a CAD with pulmonary nodules lies in three main applications:

- Improve nodule detection by the radiologists
- Quantify nodule volume and number
- Assess change over time in nodule number and diameter, which could be used in the assessment of the efficiency of the treatment [9]

2.14 Digital Image Processing

digital Image An image may be defined as a two-dimensional function, f(x, y), where x and y are spatial (plane) coordinates, and the amplitude of f at any pair of coordinates (x, y) is called the intensity or gray level of the image at that point. When x, y, and the amplitude values of f are all finite, discrete quantities, we call the image a digital image.

digital image processing digital images by means of a digital computer. Note that a digital image is composed of a finite number of elements, each of which has a particular location and value. These elements are referred to as picture elements, image elements, pels, and pixels. [10]

Image Sensing and Acquisition is the types of images in which we are interested are generated by the combination of an “illumination” source and the reflection or absorption of energy from that source by the elements of the “scene” being imaged.We enclose illumination and scene in quotes to emphasize the fact that they are considerably more general than the familiar situation in which a visible light source illuminates a common everyday 3-D (three-dimensional) scene.[10]

Sampling is the process of representing a continuous time or continuous space signal on a discrete grid, with samples that are separated by (usually) uniform intervals.

Quantization is the process of representing the values of a sampled signal or image using a finite set of allowed values.[11]

2.15 Image Enhancement [10]

2.15.1 Gray Level Transformation

Image enhancement techniques by discussing gray-level transformation functions.

These are among the simplest of all image enhancement techniques.

gray-level transformations, consider which shows three basic types of functions used frequently for image enhancement:

- linear (negative and identity transformations)
- logarithmic (log and inverse-log transformations),
- power-law (nth power and nth root transformations).

The identity function is the trivial case in which output intensities are identical to input intensities. It is included in the graph only for completeness.

2.15.2 Histogram Processing

Histograms are the basis for numerous spatial domain processing techniques Histogram manipulation can be used effectively for image enhancement, as shown in this section. In addition to providing useful image statistics, we shall see in subsequent chapters that the information inherent in histograms also is quite useful in other image processing applications, such as image compression and segmentation. Histograms are simple to calculate in software and also lend themselves to economic hardware implementations, thus making them a popular tool for real-time image processing.

2.15.3 Spatial Filtering

The mechanics of spatial filtering are the process consists simply of moving the filter mask from point to point in an image. The response of the filter at that point is calculated using a predefined relationship. For linear spatial filtering the response is given by a sum of products of the filter coefficients and the corresponding image pixels in the area spanned by the filter mask.

Include **Smoothing filters** : are used for blurring and for noise reduction. Blurring is used in preprocessing steps, such as removal of small details from an image prior to (large) object extraction, and bridging of small gaps in lines or curves. Noise reduction can be accomplished by blurring with a linear filter and also by nonlinear filtering. And **Sharpening Spatial Filters** : The principal objective of sharpening is to highlight fine detail in an image or to enhance detail that has been blurred, either in error or as a natural effect of a particular method of image acquisition. Uses of image sharpening vary and include applications ranging from electronic printing and medical imaging to industrial inspection and autonomous guidance in military systems.[10]

2.16 Feature extraction

In the present study, image feature extraction is very important stage of computer based system. Feature extraction provides certain parameters, on the basis of which computer system takes decision.

After the segmentation is performed on lung region, the features can be obtained from it and the diagnosis rule can be designed to detect nodules in the lung.

The entire feature which are calculated from the image, convey some information regarding lung nodule. This information is very helpful in detecting lung nodule[12]

In this paper After extracting the region of interest, determine whether all the extracted regions are nodules or not. We have to analyze the features of each nodule to distinguish true nodules from the false positive nodules. Many features, such as variance, location, , sum entropy, energy, entropy, contrast , homogeneity , etc, are applied in detection .
We analyzed these features on CT images to found that are nodules or not by using Artificial Neural Network (ANN) classification .

2.17 Artificial Neural Network (ANN)

An Artificial Neural Network (ANN) is a mathematical model that tries to simulate the structure and functionalities of biological neural networks. Basic building block of every artificial neural network is artificial neuron, that is, a simple mathematical model (function). Such a model has three simple sets of rules: multiplication, summation and activation. At the entrance of artificial neuron the inputs are weighted what means that every input value is multiplied with individual weight. In the middle section of artificial neuron is sum function that sums all weighted inputs and bias. At the exit of artificial neuron the sum of previously weighted inputs and bias is passing through activation function that is also called transfer function [3]

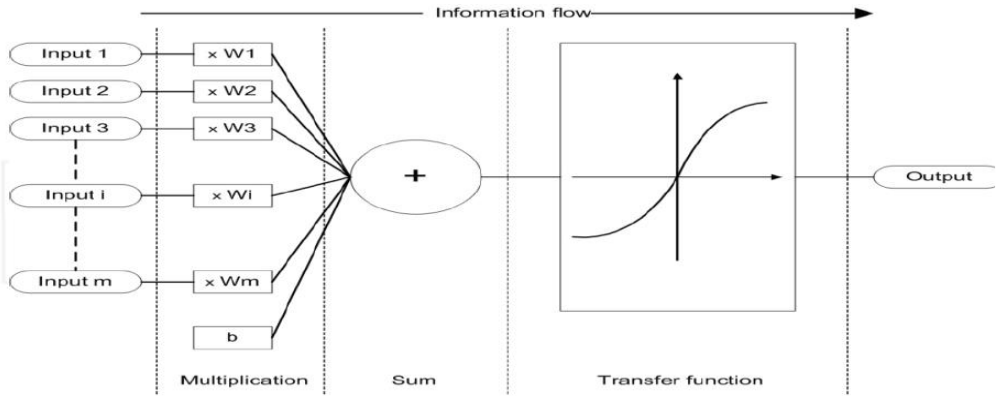


Figure (2.17) Working principle of an artificial neuron.

2.18 Artificial neuron

Artificial neuron is a basic building block of every artificial neural network. Its design and functionalities are derived from observation of a biological neuron that is basic building block of biological neural networks (systems) which includes the brain, spinal cord and peripheral ganglia. Similarities in design and functionalities can be seen in Fig.2.18. where the left side of a figure represents a biological neuron with its soma, dendrites and axon and where the right side of a figure represents an artificial neuron with its inputs, weights, transfer function, bias and outputs.

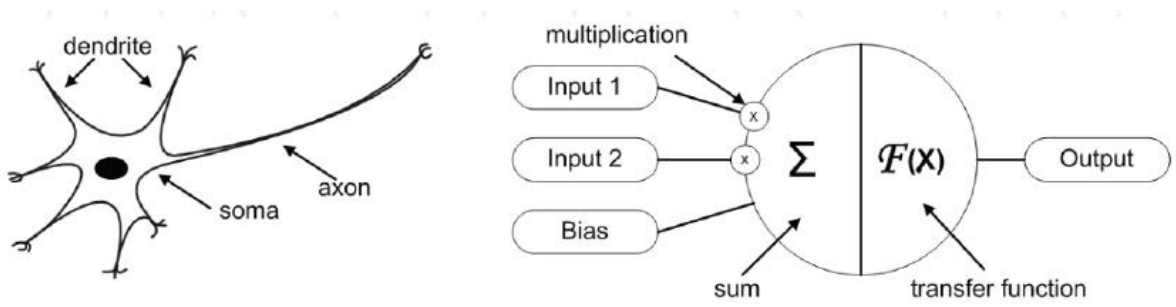


Figure (2.18) Biological and artificial neuron design.

In case of biological neuron information comes into the neuron via dendrite, soma processes the information and passes it on via axon. In case of artificial neuron the information comes into the body of an artificial neuron via inputs that are weighted (each input can be individually multiplied with a weight). The body of an artificial neuron then sums the weighted inputs, bias and “processes” the sum with a transfer function. At the end an artificial neuron passes the processed information via output(s). [3]

2.19 Type Of Artificial Neural Networks [3]

When combining two or more artificial neurons we are getting an artificial neural network. If single artificial neuron has almost no usefulness in solving real-life problems the artificial neural networks have it. In fact artificial neural networks are capable of solving complex real-life problems by processing information in their basic building blocks (artificial neurons) in a non-linear, distributed, parallel and local way. The way that individual artificial neurons are interconnected is called topology, architecture or graph of an artificial neural network. The fact that interconnection can be done in numerous ways results in numerous possible topologies that are divided into two basic classes:-

- simple feed forward topology (acyclic graph) where information flows from inputs to outputs in only one direction

- simple recurrent topology (semicyclic graph) where some of the information flows not only in one direction from input to output but also in opposite direction.

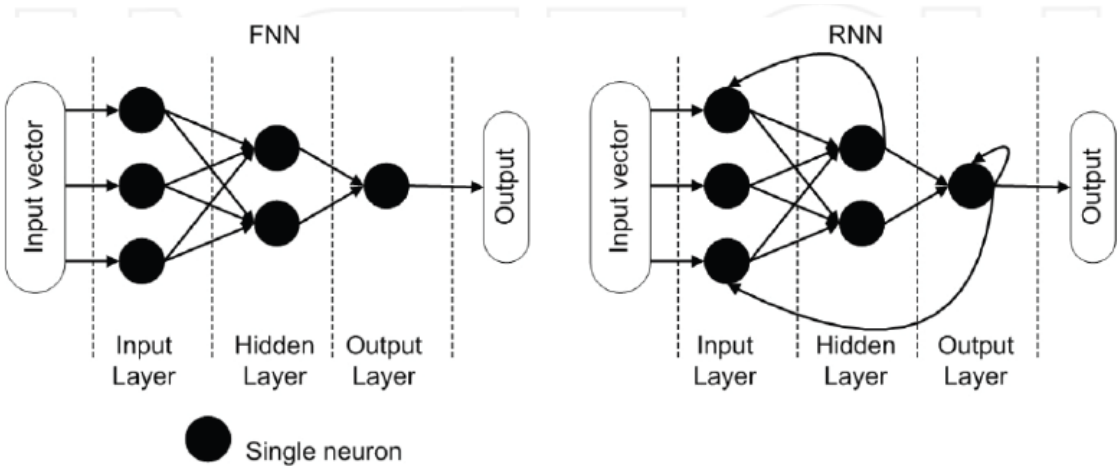


Figure (2.19) Feed-forward (FNN) and recurrent (RNN) topology of an artificial neural network.

2.19.1 Feed-forward Artificial Neural Networks

Artificial neural network with feed-forward topology is called Feed-Forward artificial neural network and as such has only one condition: information must flow from input to output in only one direction with no back-loops. There are no limitations on number of layers, type of transfer function used in individual artificial neuron or number of connections between individual artificial neurons. The simplest feed-forward artificial neural network is a single perceptron that is only capable of learning linear separable problems.

2.19.2 Recurrent Artificial Neural Networks

Artificial neural network with the recurrent topology is called Recurrent artificial neural network. It is similar to feed-forward neural network with no limitations regarding backloops. In these cases information is no longer transmitted only in one direction but it is also transmitted backwards. This creates an internal state of the network which allows it to exhibit dynamic temporal behaviour. Recurrent artificial neural networks can use their internal memory to process any sequence of inputs.

2.19.3 Hopfield Artificial Neural Network

A Hopfield artificial neural network is a type of recurrent artificial neural network that is used to store one or more stable target vectors. These stable vectors can be viewed as memories that the network recalls when provided with similar vectors that act as a cue to the network memory. These binary units only take two different values for their states that are determined by whether or not the units' input exceeds their threshold. Binary units can take either values of 1 or -1, or values of 1 or 0.

2.19.4 Elman and Jordan Artificial Neural Networks

Elman network also referred as Simple Recurrent Network is special case of recurrent artificial neural networks. It differs from conventional two-layer networks in that the first layer has a recurrent connection. It is a simple three-layer artificial neural network that has back-loop from hidden layer to input layer trough so called context unit .

This type of artificial neural network has memory that allowing it to both detect and generate time-varying patterns.The Elman artificial neural network has typically sigmoid artificial neurons in its hidden layer, and linear artificial neurons in its output layer. This combination of artificial neurons transfer functions can approximate any function with arbitrary accuracy if only there is enough artificial neurons in hidden layer. Being able to store information Elman artificial neural network is capable of generating temporal patterns as well as spatial patterns and responding on them.

2.19.5 Long Short Term Memory

Long Short Term Memory is one of the recurrent artificial neural networks topologies. In contrast with basic recurrent artificial neural networks it can learn from its experience to process, classify and predict time series with very long time lags of unknown size between important events. This makes Long Short Term Memory to outperform other recurrent artificial neural networks, Hidden Markov Models and other sequence learning methods. Long Short Term Memory artificial neural network is build from Long Short Term Memory blocks that are capable of remembering value for any length of time. This is achieved with gates that determine when the input is significant enough remembering it, when continue toremembering or forgetting it, and when to output the value.

2.19.6 Bi-directional Artificial Neural Networks (Bi-ANN)

Bi-directional artificial neural networks are designed to predict complex time series. They consist of two individual interconnected artificial neural (sub) networks that performs direct and inverse (bidirectional) transformation. Interconnection of artificial neural sub networks is done through two dynamic artificial neurons that are capable of remembering their internal states. This type of interconnection between future and past values of the processed signals increase time series prediction capabilities. As such these artificial neural networks not only predict future values of input data but also past values. That brings need for two phase learning; in first phase we teach one artificial neural sub network for predicting future and in the second phase we teach a second artificial neural sub network for predicting past.

2.19.7 Self-Organizing Map (SOM)

Self-organizing map is an artificial neural network that is related to feed-forward networks but it needs to be told that this type of architecture is fundamentally different in arrangement of neurons and motivation. Common arrangement of neurons is in a hexagonal or rectangular grid. Self-organizing map is different in comparison to other artificial neural networks in the sense that they use a neighbourhood function to preserve the topological properties of the input space. They uses unsupervised learning paradigm to produce a low-dimensional, discrete representation of the input space of the training samples, called a map what makes them especially useful for visualizing low-dimensional views of high-dimensional data. Such networks can learn to detect regularities and correlations in their input and adapt their future responses to that input accordingly.

2.20 Stochastic Artificial Neural Network

Stochastic artificial neural networks are a type of an artificial intelligence tool. They are built by introducing random variations into the network, either by giving the network's neurons stochastic transfer functions, or by giving them stochastic weights. This makes them useful tools for optimization problems, since the random fluctuations help it escape from local minima. Stochastic neural networks that are built by using stochastic transfer functions are often called Boltzmann machine.[3]

2.21 Physical Artificial Neural Network

Most of the artificial neural networks today are software-based but that does not exclude the possibility to create them with physical elements which base on adjustable electrical current resistance materials. History of physical artificial neural networks goes back in 1960’s when first physical artificial neural networks were created with memory transistors called memistors. Memistors emulate synapses of artificial neurons. [3]

2.22 Modes of Operation ANN

There are two modes of operation in a neural network: training mode and operating mode. Once we complete the training of the network, we test it with sample data different from the training data.

2.22.1 Training mode

Depending on the training algorithm used, we can classify the neural networks into three categories: fixed-weight networks, unsupervised networks, and supervised networks. There is no training required for fixed weight networks, and a training mode is supervised or unsupervised. In supervised training, the training data consists of many pairs of source/target training patterns. The network processes the source inputs and compares its resulting outputs against the target outputs, using the results to adjust its weights. In unsupervised or adaptive learning networks, the training set Consists of input training patterns only. Weight updates in these networks often involve moving selected weight vectors closer to the input training vector [13].

2.22.2 Operating mode

The main difference between training and operating mode is that weights change in training mode but not in the operating mode. We test the neural network in its operating mode.

2.22.3 Testing

A testing set tests the performance of the neural network. The testing set is generally not part of the training set but a representation of the general types of inputs the ANN is expected to receive in practice. Apply each testing input to the ANN in operating mode and compare the resultant output to the target output. If the network performs well on the testing set, it can be expected to perform well on the general case. The round robin method (leave one out method) is a good example of training and testing procedure used to evaluate the performance of an ANN. In this method we train the ANN with all the cases except for one in the database.

We apply this case for testing the ANN with the trained computer scheme[13].

2.23 Usage of Artificial Neural Networks

One of the greatest advantages of artificial neural networks is their capability to learn from their environment. Learning from the environment comes useful in applications where complexity of the environment (data or task) make implementations of other type of solutions impractical. As such artificial neural networks can be used for variety of tasks like classification, function approximation, data processing, filtering, clustering, compression, robotics, regulations, decision making, etc. Choosing the right artificial neural network topology depends on the type of the application and data representation of a given problem.

When choosing and using artificial neural networks we need to be familiar with theory of artificial neural network models and learning algorithms. Complexity of the chosen model is crucial; using to simple model for specific task usually results in poor or wrong results and over complex model for a specific task can lead to problems in the process of learning.

Complex model and simple task results in memorizing and not learning. There are many learning algorithms with numerous tradeoffs between them and almost all are suitable for any type of artificial neural network model. Choosing the right learning algorithm for a given task takes a lot of experiences and experimentation on given problem and data set.

When artificial neural network model and learning algorithm is properly selected we get robust tool for solving given problem.[3]

Chapter three

LITERATURE REVIEW

Maki et al (1999) The past 20 years has witnessed a renaissance in pulmonary imaging. The development of both CT and MRI has revolutionized imaging of the lungs, and advances in nuclear medicine such as positron emission tomography (PET) have opened the door to noninvasive characterization of lesions that previously was not possible. Furthermore, the development of digital chest radiography is rapidly replacing more traditional methods to acquire, transmit, and view chest radiographs. In addition, computer-aided diagnosis (CAD) is now becoming feasible.

Although CAD is promising, there is still inadequate scientific literature to support the efficacy of this procedure, at this time.[14]

Deus Technologies received FDA premarket approval for its RapidScreen CAD system in July 2001. Its intended use is “To identify and mark regions of interest on digital or digitized frontal chest radiographs. It identifies features associated with solitary pulmonary nodules from 9–30 mm in size, which could represent early-stage lung cancer. The device is intended for use as an aid only after the physician has performed an initial interpretation of the radiograph. The device is of little value when used for patients who are not at high risk for lung cancer.”[14]

Sharsishi et al. (2003) examined the effect of a high sensitivity in CAD for lung nodules in chest radiographs when extremely subtle cases were presented to radiologists. The chest radiographs used in this study consisted of 36 normal images and 54 abnormal images containing solitary lung nodules, of which 25 were extremely subtle and 29 were very subtle. None of 306 computer-false positives were incorrectly regarded as a nodule by all radiologists; 63 false positives were incorrectly identified by 1 or more radiologists.[14]

These investigators concluded that the accuracy of radiologists in the detection of some extremely subtle solitary pulmonary nodules can be improved significantly when the sensitivity of a CAD scheme can be made to be at an extremely high level. However, all of the 6 radiologists failed to identify some nodules (about 10 %), even with the correct output of the CAD.[14]

In February 2004, the FDA approved the R2 Technology Image Checker® CT CAD Software System as a technique to assist in the detection of lung nodules on multi detector CT scans of the chest. This system is the first CAD system to receive an approval for computer-aided detection of solid lung nodules during review of multi detector CT (MDCT) chest exams. Early lung cancer often presents as nodules and can be difficult to detect in its early stages.[14]

Böröczky et al. (2005) performed a study based on genetic algorithms to improve the performance of false positive reduction in lung nodule computer-aided detection (CAD). The performance of the CAD was tested using a lung nodule database (52 true nodules and 443 false ones) acquired by multislice CT scans. Testing showed significant improvement achieved by a system incorporating the CAD over a system without it. This approach can be also applied to other machine learning problems; e.g. computer-aided diagnosis of lung nodules.[14]

Doi (2005) Computer-aided diagnosis (CAD) has become one of the major research subjects in medical imaging and diagnostic radiology. The basic concept of CAD is to provide a computer output as a second opinion to assist radiologists' image interpretation by improving the accuracy and consistency of radiological diagnosis and also by reducing the image reading time. In this article, a number of CAD schemes are presented, with emphasis on potential clinical applications. These schemes include: (1) Detection and classification of lung nodules on digital chest radiographs; (2) Detection of nodules in low dose CT; (3) Distinction between benign and malignant nodules on high resolution CT; (4) Usefulness of

similar images for distinction between benign and malignant lesions; (5) Quantitative analysis of diffuse lung diseases on high resolution CT; and (6) Detection of intracranial aneurysms in magnetic resonance angiography. Because CAD can be applied to all imaging modalities, all body parts and all kinds of examinations, it is likely that CAD will have a major impact on medical imaging and diagnostic radiology in the 21st century.[14]

Computer-aided detection (CAD) systems for digital chest radiographs, software that subtracts one lung from another to reveal subtle asymmetric opacities, and temporal subtraction of prior chest x-rays from the current exam are all topics under investigation to improve the performance of the chest x-ray in detecting lung cancer (Lobrano, 2006).[14]

Shiraishi et al. (2006) Completed a study by combining two independent CAD schemes for the detection and classification of lung nodules into one new CAD scheme by use of a database of 150 chest images, including 108 cases with solitary pulmonary nodules and 42 cases without nodules. The selection included forty-eight chest images, including 24 lung cancers, 12 benign nodules, and 12 cases without nodules, from the database to investigate radiologist performance in the detection of lung cancers. Performance of the CAD scheme indicated that sensitivity in detecting lung nodules was 80.6%, with 1.2 false-positive results per image, and sensitivity and specificity for classification of nodules by use of the same database for training and testing the CAD scheme were 87.7% and 66.7%, respectively. In summary, this type of CAD scheme, which includes two functions, namely detection and classification, seems to improve radiologist accuracy in the diagnosis of lung cancer.[14]

Shiraishi et al. (2007) developed a computerized scheme for detection of lungcnodules in the lateral views of chest radiographs, in order to improve the overall performance in combination with the computer-aided diagnostic (CAD)

scheme for posterior-anterior (PA) views; one hundred six pairs of PA and lateral views of chest radiographs (122 lung nodules) for development of the CAD scheme were used. In the CAD scheme for lateral views, initial candidates of lung nodules were identified by use of a nodule enhancement filter based on the edge gradients. Thirty-four image features extracted from the original and the nodule-enhanced images were used for the rule-based scheme and for artificial neural networks for removal of some false-positive candidates. For PA views, we used the existing CAD scheme, which was trained with one-half of 924 chest images and then tested with the remaining images. When the CAD scheme was applied only to PA views, the sensitivity in the detection of lung nodules was 70.5%, with 4.9 false positives per image.

Although the performance of the computerized scheme for lateral views was relatively low (60.7% sensitivity with 1.7 false positives per image), the overall sensitivity (86.9%) was improved (6.6 false positives per two views), because 20 (16.4%) of the 122 nodules were detected only on lateral views. The CAD scheme by use of lateral-view images has the potential to improve the overall performance for detection of lung nodules on chest radiographs when combined with a conventional CAD scheme for standard PA views.[14]

Matvey V. Sprindzuk, M.D. Alekseevich Kovalev V., Ph.D.Snezhko E. Vitalévich, Ph.D.and Kharuzhyk S. Anatolévich, M.D., Ph.D Lung Cancer 2009. Early the modern concepts of computer-aided diagnosis (CAD), themethods of pulmonary nodule detection, Several issues in lung cancer (LC) epidemiologyand early diagnosis are discussed. Analysis of research done so far showsevidence that various CAD systems can be successfully applied to chest radiographs , computed tomography (CT), magnetic resonance imaging (MRI),and positron emission tomography (PET). Thesemodalities can serve asuseful potential alternative tools available to practicing medical professionalsperforming routine diagnostics.[15]

Sudha.V, Jayashree.P December 2012.This study aims to develop an efficient lung nodule detection system by performing nodule segmentation through thresholding and morphological operations. The proposed method has two stages: lung region segmentation through thresholding and then segmenting the lung nodules through thresholding and morphological operations.[16]

In summary, in recent years, particularly with the development of surveillance programs, which tend to detect tumors at a smaller size, debate continues to occur as to whether detection and treatment of small tumors, which seem to be earlierstage lung cancers, translates into improved mortality. While CAD for chest radiographs may be potentially useful in screening for lung cancer, the clinical value needs to be established by additional, larger, randomized controlled trials. There is a lack of published peer-reviewed evidence from prospective clinical studies regarding the impact of this test on the management and long-term outcomes of patients, as well as the efficacy of this additional testing. At the present time, computer-aided detection of chest radiographs for lung cancer screening is investigational and therefore not medically necessary.[14]

Chapter four

METHODOLOGY

The researcher CAD system involve following steps as shown in the Computer Aided Diagnosis system .The methods of lung cancer diagnostic involve The first stage of the entire system concerns loading the image, processing and enhancement In the second stage, enhanced CT images that contain abnormal masses and normal masses were passed into a segmentation stage where a variable window size for the region of interest (ROI) was taken from the CT images in order to select a dataset of features for the process of feature extraction. The resulting features were then used to train classifier known as the feedforward backpropapgation network in order to discriminate the pattern recognition of the masses into two classes; benign and malignant. The methods of lung cancer diagnostic involve loading lung image, noise removal, features extraction and Neural Network Techniques for image classification. The output can be used for cancer classification.

Then The MATLAB graphical user interface (GUI) was used to create and represent the entire system.

4.1 Flow chart:-

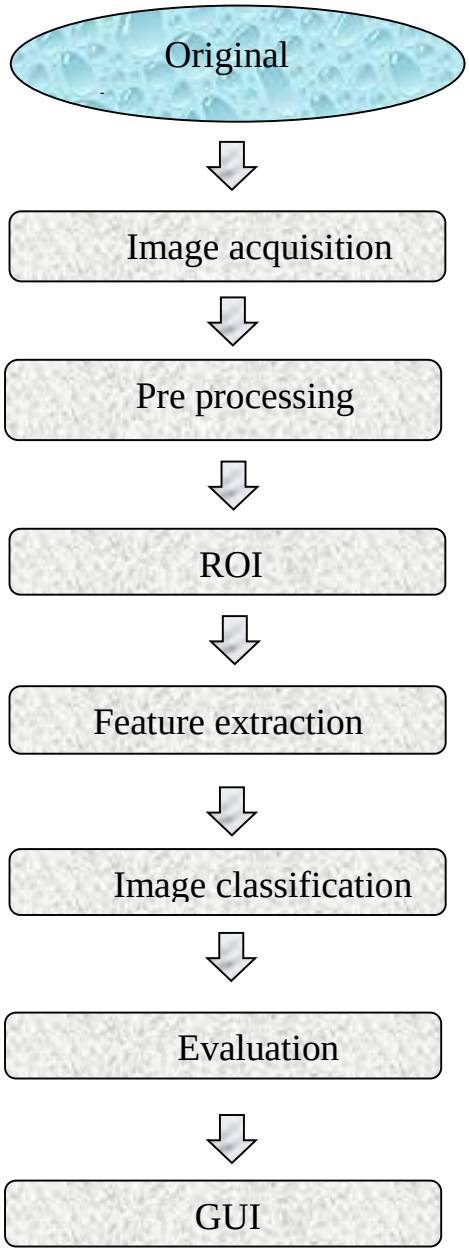


Figure (4.1) Block diagram for proposed technique

4.1.1 Stage I (Data acquisition)

At the beginning were collected group of CT scan images of the lung provided from al shaab hospital & al amal national hospital . the images were diagnosed by two doctors to determine whether the images were normal or abnormal. The dataset consists of digitized lung images. The database group of images with 25 normal, and 30 images abnormal .

4.1.2 Stage II (Image Processing and Enhancement):-

The quality of the image can be enhanced in order to increase the intensity and thus can be proper for feature extraction. Generally, the quality of image is affected by different artifacts due to non-uniform intensity, variations, motions, shift, and noise. all the image have been undergoing several pre-processing process in order to standardize all the image characteristics.

Image pre-processing processes involved are, Resizing the image to 512 X 512 pixels so that it has the specified number of rows and column , performs median filtering and contrast enhancement using histogram equalization to enhance image .Before any procedures made, all the images have been converted into gray scale images as to facilitate intensity analysis.

This process occurs for a single image loaded into the GUI system to classify the images.

4.1.3 Stage III (ROI))

Segmentation is done in order to separate the (ROI) from the background. Image segmentation has found wide applications in the field of medical and biomedical imaging.

Some of these methods can be broadly classified as: edge detection, model based, thresholding, neural networks and other artificial intelligence based techniques. CT scan image segmentation is strongly influenced by the quality of data. There are characteristic artifacts, noise and unrelated region. Further complications arise as

the contrast between areas of interest is often low. Hence forth the image had to be segmented effectively for better diagnosis.

4.1.4 Stage V (Features Extraction)

After the segmentation is performed on lung region, the features can be obtained from it and the diagnosis rule can be designed to exactly detect the cancer nodules in the lungs. This diagnosis rules can eliminate the false detection of cancer nodules resulted in segmentation and provides better diagnosis.

4.1.5 Stage VI (Pattern Recognition and Classification)

This stage of the study concerned with the detection of masses and their classification into either, normal or abnormal Therefore, a total of 55CT images comprising 25normal and 30 abnormal cases were taken into consideration.

4.1.6 Classification using ANN

Artificial Neural Network is developed for diagnosis and classification of candidate nodules obtained from application of diagnostic rules. ANN work by training and testing process applied to it. The ANN net work consist of three main layers input layer, hidden layer, output layer. The network is trained using Back propagation (BP) algorithm. The idea of BPA is to reduce error produced by the difference between actual output and expected result Initially the best optimized ANN is obtained by varying various parameters of network like hidden nodes , training percentage for training ANN, number of epochs. After the successful net work have been developed it is then ready for classification process. The following Table shows the result obtained from classification process of selected candidate nodule.

4.1.7 Design of Graphical user interface (GUI)A graphical user interface

provides the user with a familiar environment in which to work. As shown on figure(4.2) this environment contains pushbuttons, toggle buttons, lists, menus, textboxes, and so forth, all of which are already familiar to the user, so that he or she can concentrate on using the application rather than on the mechanics involved

in doing things. However, GUIs are harder for the programmer because a GUI-based program must be prepared for mouse clicks (or possibly keyboard input) for any GUI element at any time. Such inputs are known as events, and a program that responds to events is said to be event driven. The three principal elements required to create a MATLAB Graphical User Interface are:

Components:- Each item on a MATLAB GUI (pushbuttons, labels, edit boxes, etc.) is a graphical component. The types of components include graphical controls (pushbuttons, edit boxes, lists, sliders, etc.), static elements (frames and text strings), menus, and axes. Graphical controls and static elements are created by the function uicontrol, and menus are created by the functions uimenu and uicontextmenu. Axes, which are used to display graphical data, are created by the function axes

Figures:- The components of a GUI must be arranged within a figure, which is a window on the computer screen. In the past, figures have been created automatically whenever we have plotted data. However, empty figures can be created with the function figure and can be used to hold any combination of components.

Callbacks.:- Finally, there must be some way to perform an action if a user clicks a mouse on a button or types information on a keyboard. A mouse click or a key press is an event, and the MATLAB program must respond to each event if the program is to perform its function. For example, if a user clicks on a button, that event must cause the MATLAB code that implements the function of the button to be executed. The code executed in response to an event is known as a call back. There must be a callback to implement the function of each graphical component on the GUI .

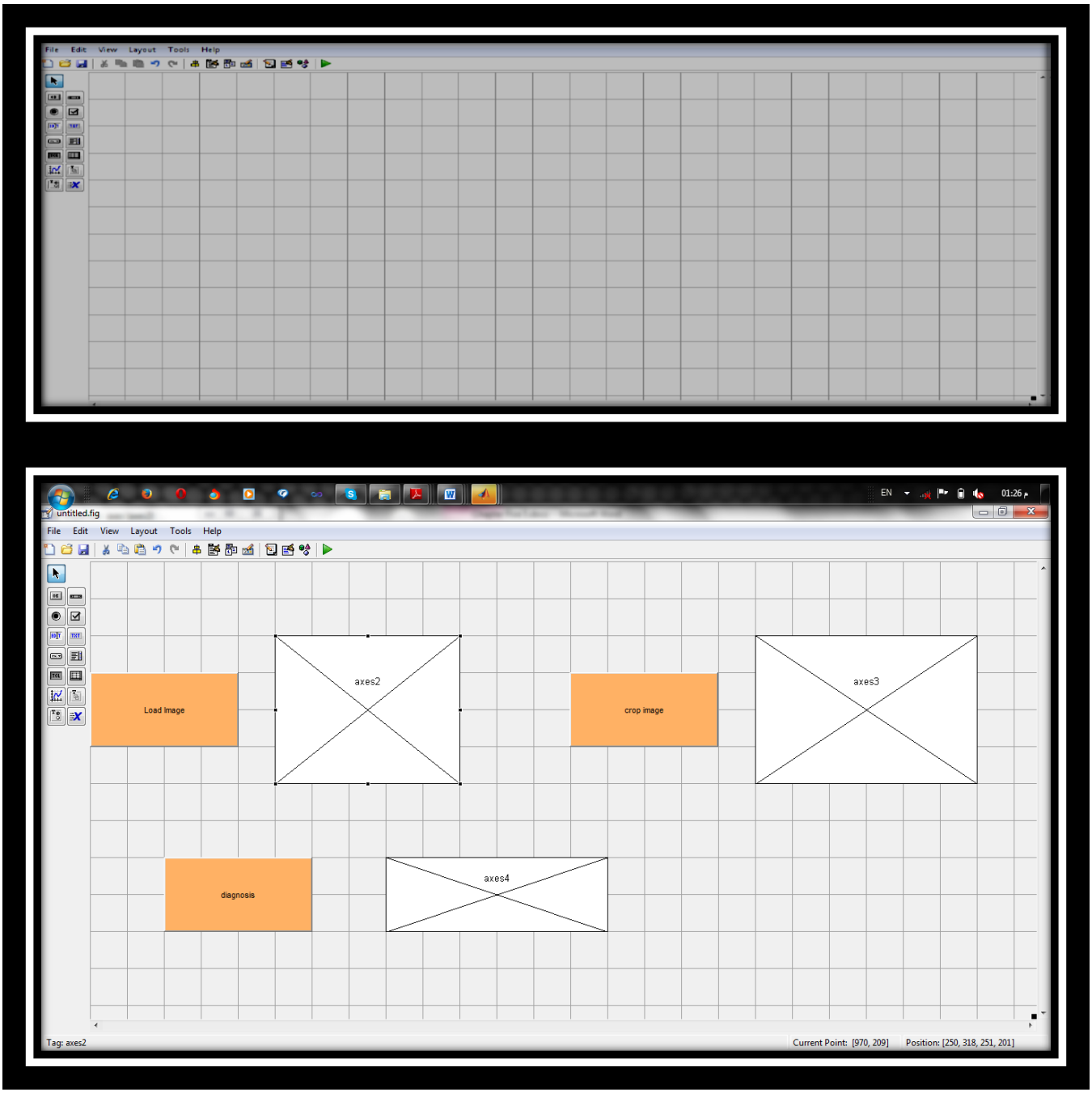


Figure (4.2) : GUI builder

Chapter Five

Result AND desiccation

5.1 Results:-

The first stage of the entire system concerns loading the image, processing and enhancement. In the second stage, enhanced CT images that contain masses and without masses were passed into a segmentation stage where a variable window size for the region of interest (ROI) was taken from the CT images in order to select a dataset of features for the process of feature extraction. The resulting features were then used to classifier known as the feed forward back propagation network in order to discriminate the pattern recognition of the masses into two classes; tumor and without tumor . With the lung cancer system fully developed using MATLAB, the means to evaluate the efficacy of the methods and algorithms used, is crucial. A total of 55samples of CT lung images containing masses have been compiled for this project. 30 lung images which contain tumor cases,25 lung images which contain without tumor cases.

5.2 Results for stage I(Image acquisition and preprocessing)

In this research The data base is composed by 55 pulmonary nodules chest radiographs that were selected from routine cases at the Radio diagnostic Service. The second step processing and enhancement in this image .convert all image to gray image . The enhancement techniques chosen correspond to some of the most commonly used enhancement methodologies

on lung images and are furthermost suitable to enhance the characteristics of such images .then histogram ,histogram equalization using because to stretching image to limit problem of image and using filter (adaptive filter) to remove noise and birthing of edge . , illustrates in Figure (5.1)

original image

(a)

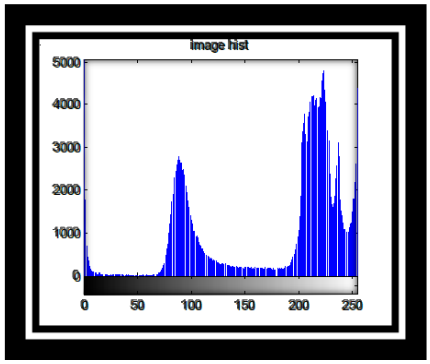
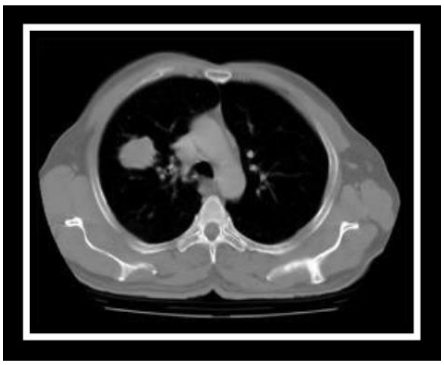


image hist
5000
4000
3000
2000
1000
0
0
50
100
150
200
250

(b)



(C)

(d)

(e)

(f)

Figure (5.1): Enhancement technique of image (a) original image (b)histogram of image,(c)gray image (d)resizing image ,(e)adaptive Filter (f) histogram Equalization

The CT scan image is converted into Gray scale image for further processing as shown in fig. Then the preprocessing steps are carried out, which are required for further post-processing.

Then the lung ROI and lung outline region is detected using and finally using spatial characteristics we differentiate the nodules from blood vessels, which may have the similar values as nodules. And we get the pulmonary nodules.

5.3 stage II (Pattern Recognition and Classification)

5.3.1 Segmentation

This involves a GUI that allows the radiologist to import the enhanced CT image onto the detection window. Once loaded, the radiologist according to his/her expertise is allowed to focus onto the suspicious area by using the imcrop tool. This process delineates the rest of the lung image which is of no use and focuses the window only on the selected region

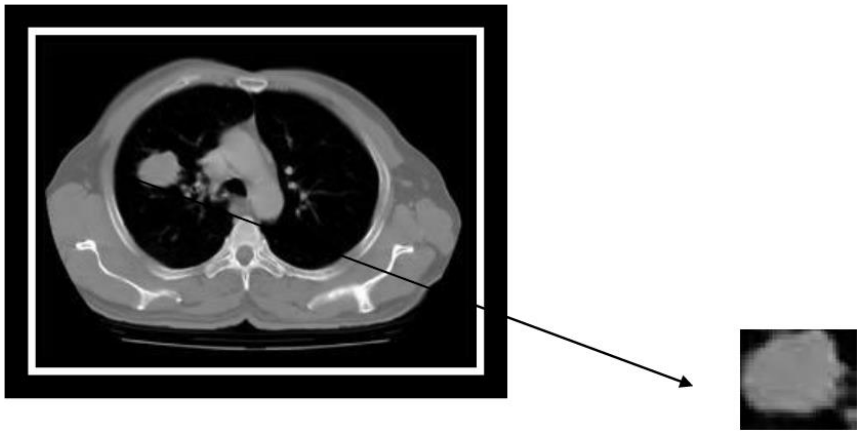


Figure (5.2) : segmentation (ROI)

5.3.2 Classification

The final procedure of the proposed system is to confirm the suspicious region and determine if it is a true nodule utilizing features obtained from previous stages Neural networks(NN).

The Artificial Neural Networks (ANN) Feed-forward back propagation network is good for binary classification.

5.3.2.1 Performance measures

Sensitivity (SE) : The sensitivity of a test is the ability of the test to identify correctly the affected individuals Proportion of persons testing positive among affected individuals

$$SE = TP/FP + FN \qquad (5.1)$$

Specificity (SP): The specificity of a test is the ability of the test to identify correctly non-affected individuals Proportion of persons testing negative among non-affected individuals

$$SP = TN/FN + TN \qquad (5.2)$$

Positive Predictive Value (PPV) : Is the proportion of Abnormal cases

correctly identified

$$\mathbf{PPV = TP/FP + FP} \qquad (5.3)$$

Negative Predictive Value (NPV): Is the proportion of benign cases correctly identified

$$\mathbf{NPV = TN/FN + TN} \qquad (5.4)$$

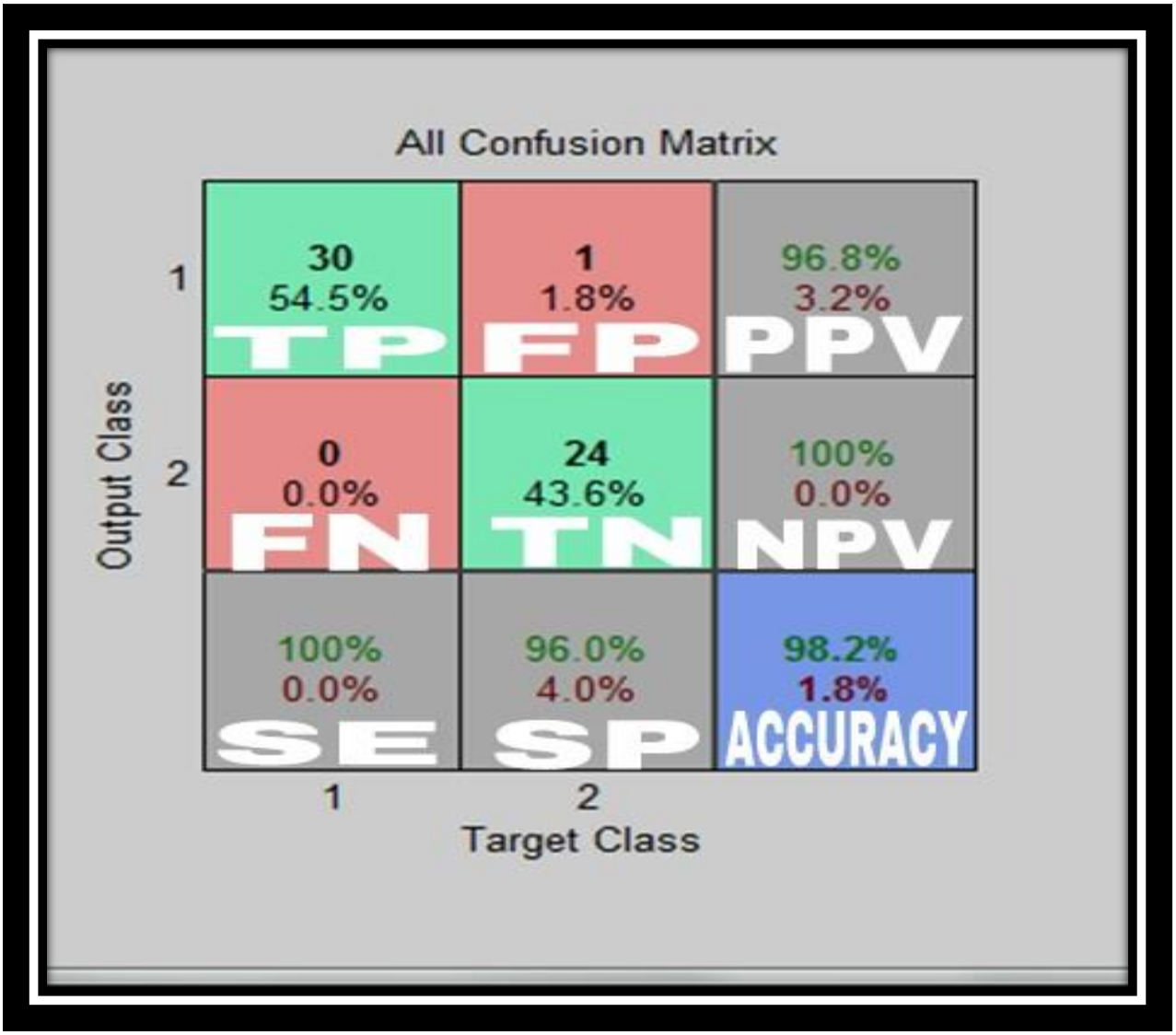


Figure (5.3): classification of images using ANN

The accuracy in Figure 5.3 is the overall evaluation of the classifier for the pattern recognition and classification of the tumors. Therefore, the proposed system has successfully been able to discriminate between Abnormal and normal tissue with a precision level of 98.2%.

Table 5.1: Summary of classification performance

Sensitivity	Specificity	Overall accuracy
100%	96%	98.2%

5.4 Result of Graphical User Interface (GUI) of the system

Figure 5.4, 5.5 show the designed Graphical User Interfaces (GUI) that elucidates the major outcomes and the implementation of the algorithm software.

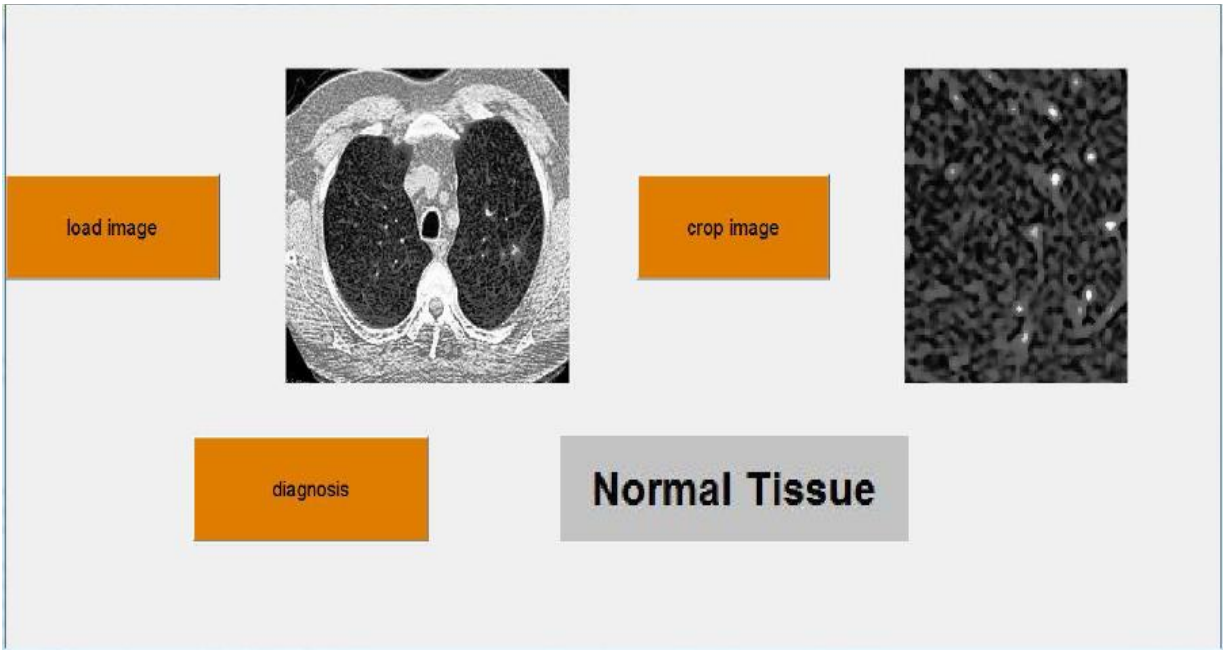


Figure 5.4: GUI of lung cancer diagnosis system with the illustration of normal mass in lung image being segmented and classified.

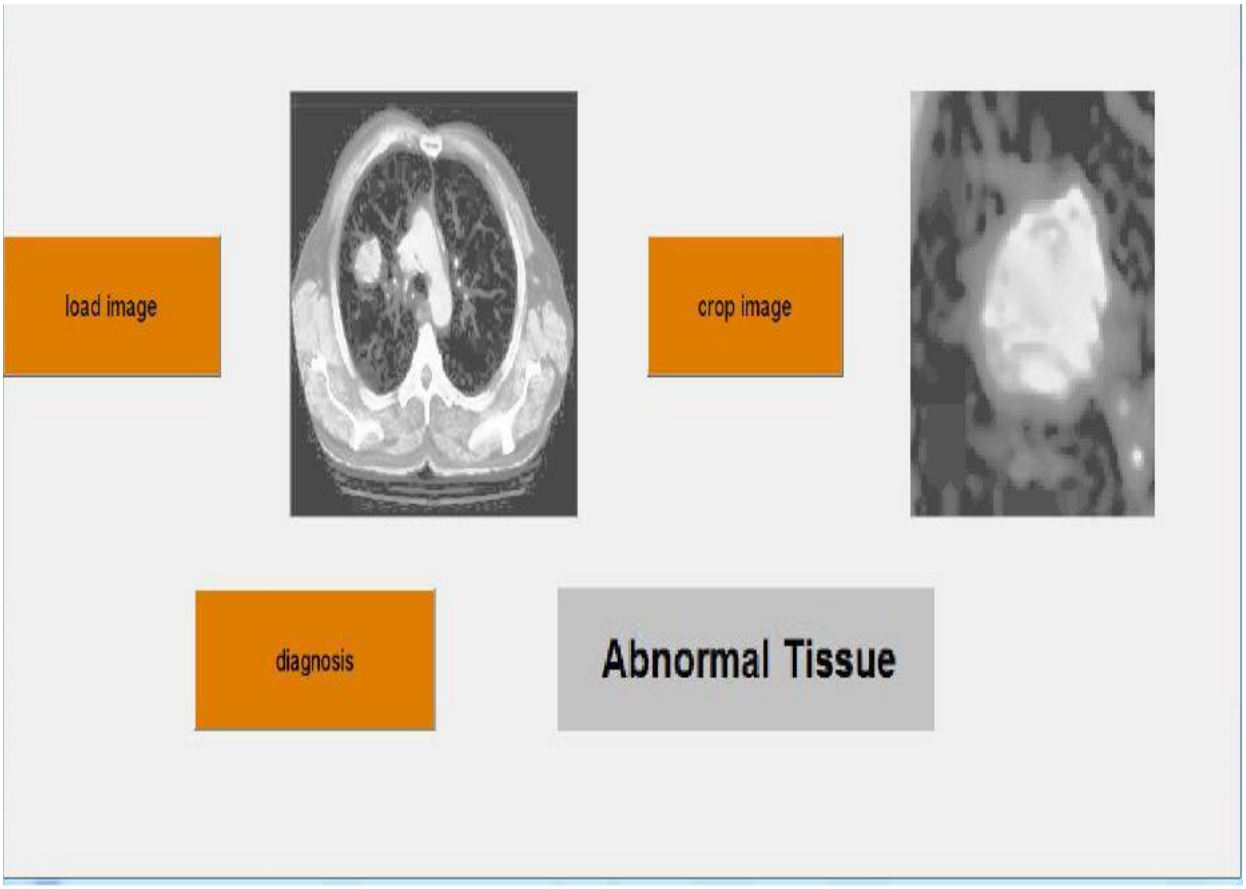


Figure 5.5: GUI of lung cancer diagnosis system with the illustration of Abnormal mass in lung image being segmented and classified.

Chapter SIX

CONCLUSION AND FUTUREWORK

6.1 Conclusion

Lung cancer is a major cause of cancer-related deaths; it can be detected early by detecting the lung nodules. Early detection can improve the survival rate of lung cancer patients. The main idea of this study is to detect lung nodule and to classify nodules as normal and abnormal using artificial neural network (ANN) technique. Thus the lung CT image is subjected to various processing steps and features are extracted for a set of images. The processing steps include thresholding, and feature extraction. By using these steps the nodules are detected and segmented and some features are extracted. The extracted features are tabulated for future classification.

6.2 Future work

The future work of this project is to identify the effective features for further classification. Artificial neural net work Classifier will be used for classification of lung CT images as cancerous or non-cancerous malignant or beginning by using the identified effective features.

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