BUSE UĞUR

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LUNG TUMOR SEGMENTATION USING OTSU THRESHOLDING

A THESIS SUBMITTED TO THE GRADUTE SCHOOL OF APPLIED SCIENCES OF NEAR EAST UNIVERSITY

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In Partial Fulfillment of the Reguirements for the Degree of Master of Science in Biomedical Engineering

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I hereby declare that all information in this document has been obtained and presented in accordance with academic rules and etical conduct. I also declare that, as required by these rules and conduct, I have fully cited and referenced all material and results that are not original to this work.

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ABSTRACT

Lung cancer is one of the most common diseases and main cause of deaths in many countries due its malignancy. The thesis is a development of an algorithm based medical image processing to segment the lung tumor in CT images due to the lack of such algorithms and approaches used to detect tumor where most of researches involve machine learning to solve such segmentation problem. The work involves different image processing tools which successfully achieved the required goals when combined and successively applied.

The segmentation system comprises of different stages to finally reach its target which is to segment the lung tumor. Image pre-processing takes place first where some enhancement techniques are used to enhance and reduce noise in images. The next stage is where the different parts in the images are seperated to be able to segment the tumor in later stages. In this phase threshold was selected automatically which assures the right selection of all images since the tumor have different gray-levels intensities in each image. Another technique was also used here to remove the tumor from the thresholded image. Finally, the lung tumor is accurately segmented by subtracting the thresholded and the other image. The developed segmentation algorithm was tested on 70 tumor and non-tumor images which shows a high accuracy of segmenting tumor of 97.14%. Moreover, the system shows a high sensitivity and specificity of 100% and 96% respectively.

Keywords: Accuracy; image enhancement; image processing techniques; lung tumor; segmentation; sensitivity; specificity; thresholding

ÖZET

Kanser günümüzde en çok rastlanan sonu ölümle sonuçlanan hastalıklardan birisidir. Akciğer kanseri ise en sık karşılaşılan ve tedavisi olmayan kanser türlerindendir. Bu çalışmada, medikal alanda kullanılmak üzere görüntü işleme teknikleri içeren ve tomografi görüntülerinde tümörün saptanması hedef alınarak geliştirilen algoritma kullanılmıştır. Bu çalışmada kullanılan farklı görüntü işleme teknikleri başarıyla sonuca ulaşıp amacını elde etmiştir. Akciğerde bulunan tümörü ayırabilmek için farklı aşamalarda oluşan segmentasyon sistemi uygulanmıştır. Öncelikle görüntü ön işleme alınarak iyileştirme dahteknikleri kullanıldı. Görüntülerdeki gürültüler azaltılarak daha iyi bir görüntü elde edildi.

Daha sonra tümörün saptanabilmesi için görüntü farklı kısımlara bölünmüştür. Bu aşamada ise eşik değeri otomatik olarak seçilerek görüntülerde bulunan tümörlerin farklı gri seviyedeki yoğunluklarından meydana gelen çeşitliliği doğru bir şekilde seçilmesi sağlanmıştır. Eşiklenen görüntüye uygulanan bir başka teknikle tümör yok edilmiştir. Son olarak ise elde edilen bu görüntülerden eşiklenen görüntüler çıkartılarak tümör başarıyla elde edilmiştir. Segmentasyon algoritmasında toplamda 70 adet olmak üzere tümörlü ve tümörsüz akciğer görüntüleri test edilerek %97.14 oranında başarı sağlanmıştır. Ayrıca, buna ek olarak sistemde duyarlılık %100 ve özgüllük ise %96 olarak hesaplanmıştır. Bu sistemle, onkologlara ve radyologlara erken tanıda yardımcı olmak hedeflenmiştir

Anahtar Kelimeler: Akciğer tümörü; başarı; eşik; görüntü işleme teknikleri; görüntü iyileştirme; hassasiyet; özgüllük; segmentasyon

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LIST OF ABBREVIATIONS

NSCLC	Non-small cell lung cancer
SCLC	Small cell lung cancer
MRI	Magnetic resonance imaging
CT	Computerized tomography
CO2	Carbon Dioxide
COPD	Chronic obstructive pulmonary disease
CFTR	Cystic fibrosis trans membrane conductance regulator
U.S	United States
%	Percentage
ACTH	Adrenocorticotrophic hormone
PET	Positron emission tomography
FNA	Fine needle aspiration
PDT	Photodynamic therapy
RFA	Radiofrequency ablation
LIDC	Lung Image Database Consortium
GLCM	Gray-Level Co-occurrence Matrix

CHAPTER ONE
INTRODUCTION

This chapter makes a present of an overall introduction of the lung cancer. It discusses the structure of the lung cancer, moreover types of it consisting benign and malignant tumors. In this chapter, aims of the thesis are also described. In addition to this, the contributions of the proposed work are discussed, as well as, the thesis overview and structure.

Cancer is the name given to a collection of related diseases. In all types of cancer, some of the body's cells begin to divide without stopping and spread into surrounding tissues. Cancer can start almost anywhere in the human body, which is made up of trillions of cells. In a wide range of cancer, some portion of the body's cells, start to separate without halting and spread into encompassing tissues. Tumor can begin anywhere within these cells. In general the human cells develop and separate to form new cells as required by the body. When cells are old, new cells usually substitute them, however when cancer occurs, this process does not operate as it supposed to. The old cells do not die and the new cells are formed without necessity. The cells keep on dividing without any restrictions and forms outgrowths in the body called tumors. (Som et al., 2011)

Tumors are usually solid and are strong masses of tissue. Malignancies of the blood, for example, leukaemia, by and large do not shape strong tumors. The cancerous tumors can spread into, or attack the tissues close to them, these are called malignant. In addition, as these tumors grow, some cancer cells can break off and travel to distant places in the body through the blood or the lymph system and form new tumors far from the original tumor, but benign tumors are not like malignant tumors, they do not spread or attack the tissues surrounding them, or the tissues close to them. After removal either by surgery or by other treatment procedures, benign tumors do not grow back. This is unlike malignant tumors, which sometimes grow back after removal (Sayar et al., 2004).

Generally, benign tumors are not life threatening, except for the benign tumors that occur in the brain. The brain benign tumors can be risky and can even be the cause of death of a person.

Cancer cells differ from normal cells in many ways that allow them to grow out of control and become invasive.The imperative contrast is that disease cells are not as specialized as normal human cells in the body. Normal human cells can grow into cells performing particular functions in the body but carcinogenic cells cannot. This causes them to spread widely without a halt. The body uses a mechanism called programmed cell death also called as apoptosis, where it does away with unwanted cells (Travis et al., 2013).

The cancer cells do not listen to signals sent by the body to stop dividing. The area around tumor cells in some cases, like the non-carcinogenic human cells, blood vessels, gets affected. This area is called microenvironment. The cancer cells can affect the normal cells in such a way that they are forced to create blood vessels to feed the tumors and can get rid of the excreta from the tumors.

The immune system, which is a system of organs and concentrated cells that shields the body from diseases and different conditions are frequently dodged by the cancer cells.Tumors can also use the immune system to stay alive and grow. For example, with the help of certain immune system cells that normally prevent a runaway *immune response,* cancer cells can actually keep the immune system from killing cancer cells (Lin and Yan, 2002).

The lungs are the parts of our body that we use to breathe. They supply oxygen to the organs and tissues of the body. The lungs are divided into areas called lobes. The right lung has three lobes and the left lung has two. Lung cancer is the type of cancer which unchecks the growth of unusual cells either in one or in both the lungs. These anomalous cells do not perform the functions of healthy human cells and do not mature into normal cells. This abnormality affects the proper regular functioning of the lung of supplying oxygen to the human body through blood. All though there are many advances in treatment procedures, the lung cancer which is at an advanced stage or late stage is not often easily curable (Gould et al., 2013).

There are two main types of primary lung cancer which one is known as the most common type, Non-small cell lung cancer (NSCLC) and the other one is Small cell lung cancer (SCLC) .The treatment of these two types of lung cancers is quite different as they behave in different ways and respond to treatments differently. The most common known of lung tumor is non-small cell lung cancer (NSCLC), as one of genuine ailments bringing on death for human beings.Computer-aided diagnosis and survival prediction of NSCLC is of great sign of cancer in diagnosis and treatment of people suffering from lung cancer (Wang et al., 2014). The prognosis of lung malignancy is poor, in many nations only 10 percent of survival rate for about five-year. Two major types of NSCLC are adenocarcinoma (including bronchi alveolar carcinoma) which is about 40% and squamous cell carcinoma about 25 - 30% (Wang et al., 2014).

Adenocarcinoma is a type of cancer that forms in mucus-secreting glands throughout the body. It can occur in many different places in the body. Diagnostic tests vary according to where the cancer is located. When diagnosing adenocarcinoma, some kind of tests may be carried out. First one is biopsy which is the removal of a sample of abnormal tissue in the body. Once the tissue is removed, a pathologist can examine it under a microscope to determine whether cancer is present. If cancer is present, a biopsy can determine whether the cancer originated at the biopsied site or in another part of the body. Secondly, computerized tomography is an X-ray procedure that uses a computer to take detailed, three-dimensional pictures of abnormal tissue in the body. CT scans are also performed during treatment to check the effectiveness of current treatment and the last one is magnetic resonance imaging (MRI) uses radiofrequency waves to create detailed cross-sectional images of different parts of the body. Treatment for adenocarcinoma varies depending on where it grows in the body, but may include. Usually the treatment for adenocarcinoma varies depending on where it grows on the body (Ung et al., 2007). But generally the treatment procedures include;

Surgery is one of the treatment option which is adenocarcinoma is often treated with surgical removal of cancerous glandular tissue, as well as some surrounding tissue. Minimally invasive surgical treatment methods can help to reduce healing time and minimize the risk of infection after surgery.

Radiation therapy is typically used in combination with surgery and/or chemotherapy. Advanced radiation therapies make use of image guidance before and during treatment to target adenocarcinoma tumors, while sparing healthy tissues and surrounding organs.

Chemotherapy treats adenocarcinoma with drugs that destroy cancer cells, either throughout the whole body, or in a specific area. In some cases, chemotherapy may be used in combination with other forms of adenocarcinoma treatment, such as radiation therapy or surgery (Anagnostou et al., 2012).

Squamous cell Carcinoma is found centrally in the lung and is generally linked to smoking. This type of lung cancer is responsible for about 30 percent of all non-small cell lung cancers. It is found centrally in the lung where the larger bronchi join the trachea to the lung or in one of the main airway branches. This sort of lung tumor usually stays inside the lungs. The cancer spreads though the lymph nodes and creates cavities. Squamous cell carcinoma is usually found in the regions of the body affected by UV rays from the sun.
The squamous cell carcinoma of the lungs can be classified into 4 stages of cancer. In stage 1, the cancer is present within the lung and has not yet spread to other parts and lymph nodes. In stage 2, the tumor already affected the nearby lymph nodes or is in a particular part of the bronchi. In stage 3, the lungs are already affected by the carcinoma and In stage 4, other regions of the body get affected.

The usual symptoms of squamous cell carcinoma are coughing up blood, constant cough. They usually show symptoms at very early stage as compared to other forms of lung cancer. They usually obstruct the airways of the lungs causing infections like pneumonia and damage part of the lung. There is a syndrome called Pancoast syndrome. The syndrome starts at the beginning of the lungs and move on to other parts of the body adjacent to them, is mostly caused by Squamous cell carcinoma. People with squamous cell carcinoma are likewise more inclined to encounter a raised calcium level (hypercalcemia) which can bring about weak muscles and other issues. Hypercalcemia is one of the side effects of paraneoplastic disorder, and is created by a tumor which secrets a hormone-like substance that brings the calcium level up in the blood.

The first step of detection of squamous cell carcinoma is through X-rays. If there is any abnormalities in the lungs. The other diagnostic methods are The computed tomography of the chest aids pathologists visualize the lungs and vessels inside them through non-invasive imaging techniques. The technique also involves injecting a dye known as contrast dye into the veins before scanning, so as to enable pathologists to clearly view the lungs. The second one is Positron Emission Tomography test is a radiology test which is commonly used alongside other diagnosis measures like CT scan. And the last one is Bronchoscopy which is a process in which large tube is inserted in the passage of mouth or through the nose in order to view the airways under medical supervision.

This thesis is a development of an image processing algorithm for accurate segmentation of the lung tumor. The developed approach is purely image processing where it uses different iimage preparing tools to reach its target: lung tumor segmentation. The segmentation system can be mainly divided into three main stages. During the first stage, the CT images are smoothed and enhanced using some image enhancement techniques such as median filtering and image erosion. This helps in reducing the noise in an image and clearly smoothes its edges. Secondly, the image is to be partitioned so that each part of it is separated from the other. This is achieved by using thresholding which eliminated the intensities which are lower than an automatically selected threshold. As a result of thresholding, an image of tumor and clavicles is remained. The thresholded image also undergoes a technique which helps in removing all parts in the image keeping only the tumor. The third part of the segmentation system is to extract the tumor by subtracting the thresholded image from the cleaned image which results in an image that contains only a tumor. Experimentally, the system is tested using many tumor and non-tumor lung images it outperforms the related systems listed in the state of art (Senthilkumaran and Vaithegi, 2016).

Overall, the developed segmentation system showed a great efficiency, accuracy, sensitivity, and specificity in segmenting tumor present in a CT lung images

1.1 Contribution of Thesis

This thesis is a contribution to the international carcinoma diagnosis and early detection researches around the world using image processing techniques in software programming.

It is a part of these ongoing researches to detect and diagnose lung cancer that purposes to decrease the rate of presence of that disease and detect it in its earlier stages instead of treating it prior to its growth and development. It can also help radiologists and doctors to follow the condition of diseases at early stages.

However, the thesis provides different and additional methods and techniques to reach the desired purpose which is to detect the tumor located in the lung, and then remove it from the original image.

1.2 Aim of Thesis

The aim of this study is to develop an image processing algorithm for lung tumor detection on CT Images. Proposed system is to ensure that oncologists and radiologists can easily diagnose the illness and begin treatment as soon as possible.

Most of medical researchers appraised the analysis of sputum cells for early diagnosis of lung cancer. Ultimate research relay on quantitative information for instance, the shape, size and the ratio of the affected cells

1.3 Limitations of Thesis

The proposed image processing lung nodules detection system aims to detect the tumor in the lungs image. However, the image contains many structures including the tumor. Therefore, it was a bit though to segment the tumor where it is directly attached to the lungs. Moreover, another limitation of the work is to get enough number of images to test and evaluate the performance of system. Such databases are usually private for some hospitals and research centers. Eventually one database is obtained and used for testing purposes.

1.4 Thesis Overview

In this thesis; chapter one gives a brief introduction, aim of thesis and thesis overview. Chapter two will discuss the related studies; Anatomy of lung, lung tumor and lung cancer. Chapter three discusses the image processing fundamentals that includes; Image Acquisition, Image Enhancement, Image Segmentation and Image Classification. Chapter four discusses and explains the methodology that apply to detect lung tumor from CT images. Chapter five introduces the obtained results from the proposed system designed, discussions of the analysis results. Finally, in chapter six will talk about conclusion of the thesis.

CHAPTER TWO
ANATOMY OF THE LUNG AND LUNG CANCER

In this chapter we will have a quick overview on the anatomy of the lungs, which is very important to understand many of the structures we will see while interpreting the lung CT. We will also have a quick look on the respiratory system, which will help in understanding the internal structure of the lung. Then, we will cover some of the most common lung diseases. Lastly, we will talk about lung cancer, the core disease we are working in developing a system to diagnose.

2.1 Anatomy of the Lungs and the Respiratory System

The right lung consists of three lobes, while the left has only two lobes. Each lung has two layers of pleura, which is filled in with a fluid called pleural fluid produced by the pleurae to lubricate the surfaces of the pleura. The main entrance of the trachea into the lung is called the primary bronchus, which is subdivided into secondary bronchi, then to tertiary bronchi, and so on. The last end of the wind track are the alveoli, which are the final branchings of the respiratory tree and act as the primary gas exchange units of the lung (Ries et al., 2002).

2.2 The Gas Exchange System

The alveolar sacs consist of many alveoli and are composed of a single layer of epithelial tissue. There are about 300 million alveoli in the adult lung. The alveoli are considered the functional unit of the lung. In the spaces between the alveoli of the lungs is elastic connective tissue which is important for exhalation. The alveoli are surrounded by a network of pulmonary capillaries. These capillaries are made of simple squamous epithelium, therefore there are only two cells between the air in the alveoli and the blood in the pulmonary capillaries which permits efficient diffusion of gases. It is through the moist walls of both the alveoli and the capillaries that rapid exchange of CO_2 and O_2 occurs.

Carbon dioxide diffuses from the red blood cells through the capillary walls, into the alveoli. CO_2 leaves the alveoli, exhaled through the nose and mouth. The opposite process occurs with O2, which diffuses from the alveoli into the capillaries, and from there into the red blood cells (Ichinose et al., 2001).

2.3 The Breathing Process

The diaphragm divides the body cavity into the *abdominal cavity*, which contains the viscera (e.g. stomach and intestines) and the *thoracic cavity*, which contains the heart and lungs.

The inner surface of the thoracic cavity and the outer surface of the lungs are lined with *pleural membranes* which adhere to each other. If air is introduced between them, the adhesion is broken and the natural elasticity of the lung causes it to collapse. This can occur from trauma. And it is sometimes induced deliberately to allow the lung to rest. In either case, reinflation occurs as the air is gradually absorbed by the tissues. Because of this adhesion, any action that increases the volume of the thoracic cavity causes the lungs to expand, drawing air into them. Inhalation is also called inspiration and is the movement of air into the lungs. Changes in the shape and size of the thoracic cavity result in changes in the air pressure within that cavity and in the lungs. The difference in air pressure causes the movement of air into and out of the lungs. Air moves from an area there pressure is high to area where pressure is lower. Respiratory muscles are responsible for changes in the shape of the thoracic cavity that cause the air movements involved in breathing (Tanaka et al., 2001).

- During inspiration (inhaling),
    - The external intercostal muscles contract, lifting the ribs up and out.
    - The diaphragm contracts, drawing it down.

- During expiration (exhaling), these processes are reversed and the natural elasticity of the lungs returns them to their normal volume. At rest, we breathe 15-18 times a minute exchanging about 500 ml of air.
    - In more vigorous expiration,
    - The internal intercostal muscles draw the ribs down and inward
    - The wall of the abdomen contracts pushing the stomach and liver upward.

Under these conditions, an average adult male can flush his lungs with about 4 liters of air at each breath. This is called *the vital capacity*. Even with maximum expiration, about 1200 ml of *residual air* remain.

2.4 Common Lung Diseases

Common lung diseases are mentioned below.

2.4.1 Pneumonia

Pneumonia is an infection of the alveoli. It can be caused by many kinds of both bacteria (e.g., Streptococcus pneumoniae) and viruses. Tissue fluids accumulate in the alveoli reducing the surface area exposed to air. If enough alveoli are affected, the patient may need supplemental oxygen (Martini et al., 1992).

2.4.2 Asthma

In asthma, periodic constriction of the bronchi and bronchioles makes it more difficult to breathe in and, especially, out. Attacks of asthma can be:

- triggered by airborne irritants such as chemical fumes and cigarette smoke
- airborne particles to which the patient is *allergic*

2.4.3 Emphysema

In this disorder, the delicate walls of the alveoli break down, reducing the gas exchange area of the lungs. The condition develops slowly and is seldom a direct cause of death. However, the gradual loss of gas exchange area forces the heart to pump ever-larger volumes of blood to the lungs in order to satisfy the body's needs. The added strain can lead to heart failure.

The immediate cause of emphysema seems to be the release of proteolytic enzymes as part of the inflammatory process that follows irritation of the lungs. Most people avoid this kind of damage during infections, etc. by producing an enzyme inhibitor (a serpin) called *alpha-1 antitrypsin*. Those rare people who inherit two defective genes for alpha-1 antitrypsin are particularly susceptible to developing emphysema (Izbichi et all., 1995).

2.4.4 Chronic bronchitis

Any irritant reaching the bronchi and bronchioles will stimulate an increased secretion of mucus. In chronic bronchitis the air passages become clogged with mucus, and this leads to a persistent cough. Chronic bronchitis is usually associated with cigarette smoking (Velzen et al., 1997).

2.4.5 Chronic obstructive pulmonary disease (COPD)

Irritation of the lungs can lead to asthma, emphysema, and chronic bronchitis. And, in fact, many people develop two or three of these together. This constellation is known as *chronic obstructive pulmonary disease (COPD).*

Among the causes of *COPD* are

- cigarette smoke (often)
- cystic fibrosis (rare)

2.4.6 Cystic fibrosis

It is a genetic disorder caused by inheriting two defective genes for the *cystic fibrosis trans-membrane conductance regulator (CFTR)*, a trans-membrane protein needed for the transport of Cl^- ions out of the epithelial cells of the lung thus enabling water to follow by osmosis. Diminished CFTR function reduces the water content of the fluid in the lungs making it more viscous and difficult for the ciliated cells to move it up out of the lungs. The accumulation of mucus plugs the air ways interfering with breathing and causing a persistent cough. Cystic fibrosis is the most common inherited disease in the U.S. white population (Riquet et al., 1999).

2.5 Lung Cancer

Tumors can be benign or malignant; when we speak of “cancer” we refer to those tumors that are considered malignant. Benign tumors can usually be removed and do not spread to other parts of the body. Malignant tumors, on the other hand, grow aggressively and invade other tissues of the body, allowing entry of tumor cells into the bloodstream or lymphatic system and then to other sites in the body. This process of spread is termed *metastasis*; the areas of tumor growth at these distant sites are called metastases. Since lung cancer tends to spread or metastasize very early in its course, it is a very life-threatening cancer and one of the most difficult cancers to treat. While lung cancer can spread to any organ in the body, certain organs -- particularly the adrenal glands, liver, brain, and bone -- are the most common sites for lung-cancer metastasis. The lung is also a very common site for metastasis from tumors in other parts of the body. Tumor metastases are made up of the same type of cells as the original, or primary, tumor. For example, if prostate cancer spreads via the bloodstream to the lungs, it is metastatic prostate cancer in the lung and is not lung cancer (Goldman and Schafer, 2011).

Lung cancer is the most common cancer and the most common cause of cancer deaths in U.S. males. Although more women develop breast cancer than lung cancer, since 1987 U.S. women have been dying in larger numbers from lung cancer than from breast cancer.
Lung cancer, like all cancer, is an uncontrolled proliferation of cells. There are several forms of lung cancer, but the most common (and most rapidly increasing) types are those involving the epithelial cells lining the bronchi and bronchioles. Ordinarily, the lining of these airways consists of two layers of cells.

Chronic exposure to irritants causes the number of layers to increase. This is especially apt to happen at forks where the bronchioles branch. The ciliated and mucus-secreting cells disappear and are replaced by a disorganized mass of cells with abnormal nuclei. If the process continues, the growing mass penetrates the underlying basement membrane. At this point, malignant cells can break away and be carried in lymph and blood to other parts of the body where they may lodge and continue to proliferate. It is this metastasis of the primary tumor that eventually kills the patient (Ung et al., 2007).

2.6 Causes of Lung Cancer

Most cases of lung cancer are caused by smoking, although people who have never smoked can also develop the condition. The causes of are lung cancer is described below**.**

2.6.1 Smoking

The incidence of lung cancer is strongly correlated with cigarette smoking, with about 90% of lung cancers arising as a result of tobacco use. The risk of lung cancer increases with the number of cigarettes smoked over time; doctors refer to this risk in terms of pack-years of smoking history (the number of packs of cigarettes smoked per day multiplied by the number of years smoked). For example, a person who has smoked two packs of cigarettes per day for 10 years has a 20 pack-year smoking history. While the risk of lung cancer is increased with even a 10-pack-year smoking history, those with 30-pack-year histories or more are considered to have the greatest risk for the development of lung cancer. Among those who smoke two or more packs of cigarettes per day, one in seven will die of lung cancer (Stewart and Kleihues, 2003).

Pipe and cigar smoking can also cause lung cancer, although the risk is not as high as with cigarette smoking. While someone who smokes one pack of cigarettes per day has a risk for the development of lung cancer that is 25 times higher than a non-smoker, pipe and cigar smokers have a risk of lung cancer that is about five times that of a non-smoker.

Tobacco smoke contains over 4,000 chemical compounds, many of which have been shown to be cancer-causing, or carcinogenic. The two primary carcinogens in tobacco smoke are chemicals known as nitrosamines and polycyclic aromatic hydrocarbons. The risk of developing lung cancer decreases each year following smoking cessation as normal cells grow and replace damaged cells in the lung. In former smokers, the risk of developing lung cancer begins to approach that of a non-smoker about 15 years after cessation of smoking (Johnson et al., 2001).

2.6.2 Passive smoking

Passive smoking, or the inhalation of tobacco smoke from other smokers sharing living or working quarters, is also an established risk factor for the development of lung cancer. Research has shown that non-smokers who reside with a smoker have a 24% increase in risk for developing lung cancer when compared with other non-smokers. An estimated 3,000 lung cancer deaths occur each year in the U.S. that are attributable to passive smoking (Whincup et al., 2004)

2.6.3 Asbestos fibers

Asbestos fibers are silicate fibers that can persist for a lifetime in lung tissue following exposure to asbestos. The workplace is a common source of exposure to asbestos fibers, as asbestos was widely used in the past as both thermal and acoustic insulation. Today, asbestos use is limited or banned in many countries, including the U.S. Both lung cancer and mesothelioma (cancer of the pleura of the lung as well as of the lining of the abdominal cavity called the peritoneum) are associated with exposure to asbestos.

Cigarette smoking drastically increases the chance of developing an asbestos-related lung cancer in exposed workers. Asbestos workers who do not smoke have a fivefold greater risk of developing lung cancer than non-smokers, and those asbestos workers who smoke have a risk that is 50 to 90 times greater than non-smokers (Dostert et al., 2008).

2.6.4 Radon gas

Radon gas is a natural, chemically inert gas that is a natural decay product of uranium. Uranium decays to form products, including radon, that emit a type of ionizing radiation. Radon gas is a known cause of lung cancer, with an estimated 12% of lung-cancer deaths attributable to radon gas, or 15,000-22,000 lung cancer-related deaths annually in the U.S., making radon the second leading cause of lung cancer in the U.S. As with asbestos exposure, concomitant smoking greatly increases the risk of lung cancer with radon exposure. Radon gas can travel up through soil and enter homes through gaps in the foundation, pipes, drains, or other openings. The U.S. Environmental Protection Agency estimates that one out of every 15 homes in the U.S. contains dangerous levels of radon gas. Radon gas is invisible and od or less, but it can be detected with simple test kits (Field et al., 2000).

2.6.5 Familial predisposition

While the majority of lung cancers are associated with tobacco smoking, the fact that not all smokers eventually develop lung cancer suggests that other factors, such as individual genetic susceptibility, may play a role in the causation of lung cancer. Numerous studies have shown that lung cancer is more likely to occur in both smoking and non-smoking relatives of those who have had lung cancer than in the general population. Recent research has localized a region on the long (q) arm of human chromosome number 6 that is likely to contain a gene that confers an increased susceptibility to the development of lung cancer in smokers (Flynn et al., 2005).

2.6.6 Lung diseases

The presence of certain diseases of the lung, notably chronic obstructive pulmonary disease (COPD), is associated with an increased risk (four to six times the risk of a non-smoker) for the development of lung cancer even after the effects of concomitant cigarette smoking are excluded.

2.6.7 Prior history of lung cancer

Survivors of lung cancer have a greater risk than the general population of developing a second lung cancer. Survivors of non-small cell lung cancers (NSCLCs) have an additive risk of 1%-2% per year for developing a second lung cancer. In survivors of small cell lung cancers (SCLCs), the risk for development of second cancers approaches 6% per year (Miller et al., 2004).

2.6.8 Pollution

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 Types of Lung Cancer

Lung cancers, also known as bronchogenic carcinomas (carcinoma is another term for cancer), 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 (Travis et al., 2013).

2.7.1 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 non-smokers. SCLC 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 (Pataer et al., 2012).

2.7.2 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 non-smokers 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 (Schild et al., 2017).

2.7.3 Bronchial carcinoids

They account for up to 5% of lung cancers. These tumors are generally small (3-4 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 (Sevastos et al., 2007).

2.8 The Signs and Symptoms of Lung Cancer

Symptoms of lung cancer are varied depending upon where and how widespread the tumor is. Warning signs of lung cancer are not always present or easy to identify. A person with lung cancer may have the following kinds of symptoms:

2.8.1 No symptoms

In up to 25% of people who get lung cancer, the cancer is first discovered on a routine chest X-ray or CT scan as a solitary small mass sometimes called a coin lesion, since on a two-dimensional X-ray or CT scan, the round tumor looks like a coin. These patients with small, single masses often report no symptoms at the time the cancer is discovered (Travis et al., 1999).

2.8.2 Symptoms related to the cancer

The growth of the cancer and invasion of lung tissues and surrounding tissue may interfere with breathing, leading to symptoms such as cough, shortness of breath, wheezing, chest pain, and coughing up blood (hemoptysis). If the cancer has invaded nerves, for example, it may cause shoulder pain that travels down the outside of the arm (called Pancoast's syndrome) or paralysis of the vocal cords leading to hoarseness. Invasion of the esophagus may lead to difficulty swallowing (dysphagia). If a large airway is obstructed, collapse of a portion of the lung may occur and cause infections (abscesses, pneumonia) in the obstructed area.

2.8.3 Symptoms related to metastasis

Lung cancer that has spread to the bones may produce excruciating pain at the sites of bone involvement. Cancer that has spread to the brain may cause a number of neurologic symptoms that may include blurred vision, headaches, seizures, or symptoms of stroke such as weakness or loss of sensation in parts of the body (Grippi, 1990).

2.8.4 Paraneoplastic symptoms

Lung cancers frequently are accompanied by symptoms that result from production of hormone-like substances by the tumor cells. These paraneoplastic syndromes occur most commonly with SCLC but may be seen with any tumor type. A common paraneoplastic syndrome associated with SCLC is the production of a hormone called adrenocorticotrophic hormone (ACTH) by the cancer cells, leading to over secretion of the hormone cortisol by the adrenal glands (Cushing's syndrome). The most frequent paraneoplastic syndrome seen with NSCLC is the production of a substance similar to parathyroid hormone, resulting in elevated levels of calcium in the bloodstream.

2.8.5 Nonspecific symptoms

Nonspecific symptoms seen with many cancers, including lung cancers, include weight loss, weakness, and fatigue. Psychological symptoms such as depression and mood changes are also common (Andersen and Prakash, 1982).

2.9 Diagnosing Lung Cancer

Doctors use a wide range of diagnostic procedures and tests to diagnose lung cancer. These include;

- 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, that suggests compromised function of the lung. Likewise, changes in the tissue of the nail beds, known as clubbing, may also indicate 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 minimum 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 (Strauss et al., 2008).

- *CT (computerized axial tomography scan, or CAT scan) scans* may be performed on the chest, abdomen, and/or brain to examine for both metastatic and primary tumor. 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. One advantage of CT scans is that they are more sensitive than standard chest X-rays in the detection of lung nodules. Sometimes intravenous contrast material is given prior to the procedure 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. There may be resulting 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 (Miller et al., 2004).

- A technique called a *low-dose helical CT scan* (or spiral CT scan) is sometimes used in screening for lung cancers. This procedure requires a special type of CT scanner and has been shown to be an effective tool for the identification of small lung cancers in smokers and former smokers.

- 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. (Tsubamoto et al., 2002).

- 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 functioning of tissue. 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 and receives approximately the amount of radiation exposure as two chest X-rays. The drug discharges particles known as positrons from wherever they are taken up and used in the body. 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 is located. 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 (Quekel et al., 2001).

- *Bronchoscopy,* examination of the airways by bronchoscopy (visualizing the airways through a thin, fiber optic 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, fiber optic 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 (Vansteenkiste et al., 1999).

- *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 (Burry et al., 1998).

- *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 (Veselle et al., 2002).

- *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 (Murray et al., 2002).

- *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 metastatic tumor (Rangdaeng et al., 2002).

2.10 Staging of Lung Cancer

The stage of a cancer refers to the extent to which a cancer has spread in the body. Staging involves both evaluation of a cancer's size as well as the presence or absence of metastases in the lymph nodes or in other organs. Staging is important for determining how a particular cancer should be treated, since lung-cancer therapies are geared toward specific stages. Staging of a cancer is also critical in estimating the prognosis of a given patient, with higher-stage cancers generally having a worse prognosis than lower-stage cancers. Doctors may use several tests to accurately stage a lung cancer, including laboratory (blood chemistry) tests, X-rays, CT scans, bone scans, and MRI scans. Abnormal blood chemistry tests may signal the presence of metastases in bone or liver, and radiological procedures can document the size of a cancer as well as possible spread to other organs (Kiernan et al., 2002).

I. NSCLC are assigned a stage from I to IV in order of severity:

- In stage I, the cancer is confined to the lung.
- In stages II and III, the cancer is confined to the chest (with larger and more invasive tumors classified as stage III).
- Stage IV cancer has spread from the chest to other parts of the body.

II. SCLC are staged using a two-tiered system:

- Limited-stage SCLC refers to cancer that is confined to its area of origin in the chest.
- In extensive-stage SCLC, the cancer has spread beyond the chest to other parts of the body (Graeter et al., 2003).

2.11 Treatment of Lung Cancer

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 localization 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 order to be certain that all tumor cells are killed (Bach et al., 2001).

2.11.1 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. Surgery may not be possible if the cancer is too close to the trachea or if the person has other serious conditions (such as severe heart or lung disease) that would limit their ability to tolerate an operation. Surgery is less often performed with SCLC because these tumors are less likely to be localized to one area that can be removed (Schroen et al., 2000).

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). Sometimes lymph nodes in the region of the lungs are also 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 (Silvestri et al., 1998).

2.11.2 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 regimens), 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 (Laroche et al., 1998).

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 increase the chances of 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. 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 are focused on the tumor over a few minutes to hours while the head is held in place by a rigid frame.

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 over 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) can also 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 (Field et al., 2000).

2.11.3 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 have metastasized, it can prolong survival in many cases (Pataer et al., 2012).

Chemotherapy may be given as pills, as an intravenous infusion, or as a combination of the two. Chemotherapy treatments are usually 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 (Schild et al., 2017).

2.11.4 Brain prophylactic 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 micro-metastasis) 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.

2.11.5 Treatment of recurrence

Lung cancer that has returned following treatment with surgery, chemotherapy, and/or radiation therapy is called recurrent or relapsed. If a recurrent cancer is confined to one site in the lung, it may be treated with surgery. Relapsed 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 are also good candidates for experimental therapies, including clinical trials (Dostert et al., 2008).

2.11.6 Targeted therapy

One alternative to standard chemotherapy is the drug erlotinib (Tarceva) which may be used in patients with NSCLC who are no longer responding to chemotherapy. It is a so-called targeted drug, a drug that more specifically targets cancer cells, resulting in less damage to normal cells. Erlotinib targets a protein called the epidermal growth factor receptor (EGFR) that helps cells to divide. 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. Erlotinib is taken by mouth in pill form.

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 oxygenated blood, the cancer cells will die. The antiangiogenic drug bevacizumab (Avastin) has recently 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 is also not used in cases of squamous cell cancer, because it leads to bleeding from this type of lung cancer (Flynn et al., 2005).

2.11.7 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 deposits itself selectively 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. Research is ongoing to further determine the effectiveness of PDT in lung cancer (Sevastos et al., 2007).

2.11.8 Radiofrequency ablation (RFA)

Radiofrequency ablation is being studied as an alternative to surgery, particularly in cases of early stage lung cancer. In this newer 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 (Tannehill et al., 1997).

2.11.9 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 (Komaki et al., 2001).

2.12 The Prognosis (outcome) of Lung Cancer

The prognosis of lung cancer refers to the chance for cure or prolongation of life (survival), and is dependent upon where the cancer is localized, the size of the cancer, the presence of symptoms, the type of lung cancer, and the overall health status of the patient.

SCLC has the most aggressive growth of all lung cancers, with a median survival time of only two to four months after diagnosis when untreated. (That is, by two to four months, half of all patients have died.) However, SCLC is also the type of lung cancer most responsive to radiation therapy and chemotherapy. Because SCLC spreads rapidly and is usually disseminated at the time of diagnosis, methods such as surgical removal or localized radiation therapy are less effective in treating this tumor type. However, when chemotherapy is used alone or in combination with other methods, survival time can be prolonged four- to fivefold; however, of all patients with SCLC, only 5%-10% are still alive five years after diagnosis. Most of those who survive have limited-stage SCLC (Travis et al., 2013).

In non-small cell lung cancer (NSCLC), results of standard treatment are generally poor in all but the most localized cancers that can be surgically removed. However, in stage I cancers that can be completely removed, five-year survival approaches 75%. Radiation therapy can produce a cure in a small minority of patients with NSCLC and leads to relief of symptoms in most patients. In advanced-stage disease, chemotherapy offers modest improvements in survival time, although overall survival rates are poor.

The overall prognosis for lung cancer is poor when compared with some other cancers. Survival rates for lung cancer are generally lower than those for most cancers, with an overall five-year survival rate for lung cancer of about 16% compared to 65% for colon cancer, 89% for breast cancer, and over 99% for prostate cancer (O'Leary et al., 2017)

CHAPTER THREE
IMAGE PROCESSING

This chapter discusses a brief and general introduction of the image processing, since the proposed system is based completely on image processing techniques and methods. It briefly presents the history of image processing and how it has developed through years. Moreover, this chapter explains the main image processing techniques that are used in each image analysis system such as image enhancement and mage filtering. It also discusses some applications of image processing in medicine and explains the image fusion.

3.1 Introduction

Image processing is a method to convert an image into digital form and perform some operations on it, in order to get an enhanced image or to extract some useful information from it. It is a type of signal dispensation in which input is image, like video frame or photograph and output may be image or characteristics associated with that image. Usually Image Processing system includes treating images as two dimensional signals while applying already set signal processing methods to them.

It is among rapidly growing technologies today, with its applications in various aspects of a business. Image Processing forms core research area within engineering and computer science disciplines too (Andrew, 2008). Image processing basically includes the following three steps.

- Importing the image with optical scanner or by digital photography.
- Analyzing and manipulating the image which includes data compression and image enhancement and spotting patterns that are not to human eyes like satellite photographs.
- Output is the last stage in which result can be altered image or report that is based on image analysis.

In parallel with space applications, digital image processing strategies started in the late 1960s and mid-1970s to be utilized as a part of restorative imaging, remote Earth assets perceptions, and astronomy. The innovation in the mid-1970s of modernized hub tomography (CAT), additionally called automated tomography (CT) for short, is a standout amongst the most essential occasions in the use of image processing in restorative judgment. Automated hub tomography is a procedure in which a ring of identifiers surrounds an article (or quiet) and a X-beam source, concentric with the indicator ring, turns about the object. The X-beams go through the item and are gathered at the inverse end by the relating identifiers in the ring. As the source turns, this technique is repeated. (Chaudhary and Singh, 2012)

Tomography comprises of calculations that utilize the sensed information to develop a picture that speaks to a "cut" through the item. Movement of the item in a bearing opposite to the ring of identifiers delivers an arrangement of such cuts, which constitute a three-dimensional (3-D) version of within the article. Tomography was concocted freely by Sir Godfrey N. Hounsfield and Professor Allan M. Cormack, who imparted the 1979 Nobel Prize in Medicine for their creation. It is intriguing to note that X-beams were found in 1895 by Wilhelm Conrad Roentgen, for which he got the 1901 Nobel Prize for Physics. These two creations, about 100 years separated, prompted a percentage of the most dynamic application ranges of image processing today (Gonzalez and woods, 2004).

Medical image analysis is shifting from the visual analysis of planar images to the computerized quantitative analysis of volumetric images. It is important to have high performance computing power to handle the extra computation necessary for volumetric images (Warfield et al., 1998).

3.1.1 Purpose of image processing

The purpose of image processing is divided into 5 groups. They are:

1. Visualization - Observe the objects that are not visible.
2. Image sharpening and restoration - To create a better image.
3. Image retrieval - Seek for the image of interest.
4. Measurement of pattern – Measures various objects in an image.
5. Image Recognition – Distinguish the objects in an image.

3.1.2 Types

The two types of methods used for Image Processing are Analog and Digital Image Processing. Analog or visual techniques of image processing can be used for the hard copies like printouts and photographs. Image analysts use various fundamentals of interpretation while using these visual techniques. The image processing is not just confined to area that has to be studied but on knowledge of analyst. Association is another important tool in image processing through visual techniques. So analysts apply a combination of personal knowledge and collateral data to image processing (Sharma and Jindal, 2011).

Digital Processing techniques help in manipulation of the digital images by using computers. As raw data from imaging sensors from satellite platform contains deficiencies. To get over such flaws and to get originality of information, it has to undergo various phases of processing. The three general phases that all types of data have to undergo while using digital technique are Pre- processing, enhancement and display, information extraction (Assefa et al., 2013).

3.2 Image Processing Basics

In the wake of changing over picture data into a cluster of numbers, the picture can be controlled, prepared, and showed by PC. PC transforming is utilized for picture upgrade, rebuilding, division, portrayal, distinguishment, and coding, remaking, change.

The general electronic picture changing system may be separated into three sections: The information device (or digitizer), the mechanized processor, and the yield contraption (Stefanescu et al., 2004).

The digitizer changes more than a perpetual tone and spatially persevering sparkle spread f [x, y] to a discrete bunch (the propelled picture) fq [n, m], where n, m, besides fq are numbers.

- The modernized processor chips away at the propelled picture fq [n, m] to make an alternate mechanized picture gq [k, c], where k, c, and gq are numbers. The yield picture may be identified with in another heading system, in this way the use of various records k and c.

- The picture showcase changes over the propelled yield picture gq [k, c] afresh into a ceaseless tone moreover spatially steady picture g [x, y] for audit. It should be recognized that a couple of structures may not oblige a showcase (e.g., in machine vision and fake insight applications); the yield may be a touch of information. For example, a modernized imaging system that was expected to answer the request, Is there confirmation of a ruinous tumor in this x-bar picture ideally would have two possible yields (YES or NO), i.e., a singular bit of information (Teramato and Fujita, 2013).

3.3 Image Analysis Strategies

Image analysis involves the conversion of features and objects in image data into quantitative information about these measured features and attributes. Microscopy images in biology are often complex, noisy, artifact-laden and consequently require multiple image processing steps for the extraction of meaningful quantitative information (Korfiatis et al., 2014).

An outline of a general strategy for image analysis is presented below:

1) The starting point in image analysis typically involves a digital image acquired using a CCD camera. Raw microscopy images obtained on digital CCD cameras are subject to various imperfections of the image acquisition setup, such as noise at low light levels, uneven illumination, defective pixels, etc…We often need to first process the image to correct for such defects and also to enhance the contrast to accentuate features of interest in the image for subsequent analysis. In section II, we introduce various image transformation and spatial filtering techniques that can be used for this purpose (Milan et al., 1998).

2) Having corrected artifacts and enhanced contrast in the images, we can apply various computational techniques to extract features and patterns from the images. In the following section, we describe various tools of morphological image processing and image segmentation that can be used for this purpose (Dai et al., 2015).

3) After biological important features have been segmented from images, we can then derive quantitative information from these features and objects. MATLAB provides a set of tools that can be used to measure the properties of regions; the matrix representation of images in MATLAB also allows for easy manipulation of data and calculation of quantities from microscopy images (Suzuki et al., 2005).

3.4 Image Processing Applications

The field of digital image has rapidly expanded in the recent years. The usefulness of this technology is clear in many different disciplines and areas (Andrew, 2008; Van et al., 2001).

The fields of image processing are:

- Robotics
- Medical imaging
- Machine vision
- Digital camera images

3.4.1 Medical image processing

Restorative imaging has been experiencing an insurgency in the previous decade with the coming of quicker, more precise, and less obtrusive gadgets. This has driven the requirement for relating programming improvement which thusly has given a noteworthy catalyst to new calculations in sign and picture transforming (Zhou et al., 2014).

In particular, in therapeutic imaging we have four key issues:

1. Segmentation - automated methods that create patient-specific models of relevant anatomy from images;

2. Registration - automated methods that align multiple data sets with each other;

3. Visualization - the technological environment in which image-guided procedures can be displayed;

Imaging innovation in Medicine made the specialists to see the inside parts of the body for simple determination. It likewise helped specialists to make keyhole surgeries for coming to the inside parts without truly opening excessively of the body. CT Scanner, Ultrasound and Magnetic Resonance Imaging assumed control x-beam imaging by making the specialists to take a gander at the body's subtle third measurement. With the CT Scanner, body's inside can be uncovered with straight forwardness and the unhealthy territories can be distinguished without bringing about either uneasiness or torment to the patient. X-ray grabs signals from the body's attractive particles turning to its attractive tune and with the assistance of its intense PC, changes over scanner information into uncovering pictures of inward organs. Image processing strategies produced for breaking down remote sensing information may be altered to dissect the yields of therapeutic imaging frameworks to get best preference to break down indications of the patients without any difficulty (Rao and Rao, 2004).

3.5 Computerized Image Processing Requirements for Medical Applications

• Interfacing Analog yields of sensors for example, magnifying lens, endoscopes, ultrasound and so forth, to digitizers and thusly to Computerized Image Processing frameworks (Paryeen and Kayitha, 2013).

- Image upgrades.
- Changing thickness element scope of B/W images.
- Color redress in shading images.
- Manipulating of hues inside an image.
- Contour discovery.
- Area estimations of the cells of a biomedical picture.
- Display of picture line profile.
- Restoration of images.
- Smoothing of images.
- Registration of different images.
- Construction of 3-D images from 2-D images.
- Generation of negative images.
- Zooming of images.
- Pseudo shading.
- Point to point estimations.
- Getting help impact.

3.6 Image Enhancements

Image enhancement is basically improving the interpretability or perception of information in images for human viewers and providing ‘better’ input for other automated image processing techniques. The principal objective of image enhancement is to modify attributes of an image to make it more suitable for a given task and a specific observer. During this process, one or more attributes of the image are modified. The choice of attributes and the way they are modified are specific to a given task. Moreover, observer-specific factors, such as the human visual system and the observer’s experience, will introduce a great deal of subjectivity into the choice of image enhancement methods (Kumar and Saini, 2013).

There exist many techniques that can enhance a digital image without spoiling it. The enhancement methods can broadly be divided in to the following two categories:

1. Spatial Domain Methods
2. Frequency Domain Methods

In spatial domain techniques, we directly deal with the image pixels. The pixel values are manipulated to achieve desired enhancement. In frequency domain methods, the image is first transferred in to frequency domain. It means that, the Fourier Transform of the image is computed first. All the enhancement operations are performed on the Fourier transform of the image and then the Inverse Fourier transform is performed to get the resultant image. These enhancement operations are performed in order to modify the image brightness, contrast or the distribution of the grey levels. As a consequence the pixel value (intensities) of the output image will be modified according to the transformation function applied on the input values (Gonzalez and woods, 2001).

Image enhancement simply means, transforming an image f into image g using T. (Where T is the transformation. The values of pixels in images f and g are denoted by r and s, respectively. As said, the pixel values r and s are related by the expression,

$$s = T(r) \tag{3.1}$$

where T is a transformation that maps a pixel value r into a pixel value *s*. The results of this transformation are mapped into the grey scale range as we are dealing here only with grey scale digital images.

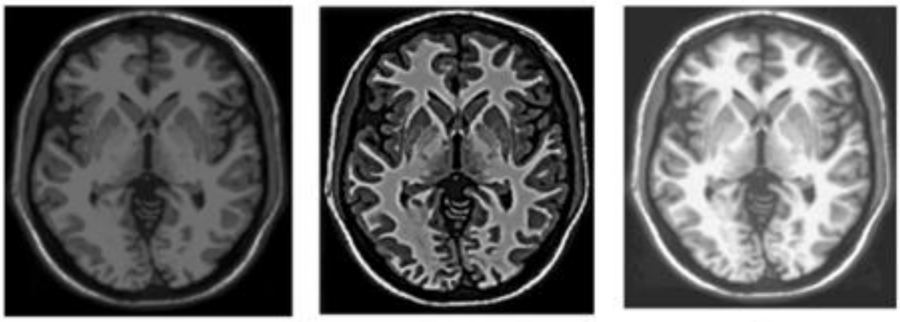


Figure 3.1: Example of image enhancement (Fan et al., 2002).

3.7 Data Compression and Data Redundancy

Data compression is defined as the process of encoding data using a representation that reduces the overall size of data. This reduction is possible when the original dataset contains some type of redundancy. Digital image compression is a field that studies methods for reducing the total number of bits required to represent an image. This can be achieved by eliminating various types of redundancy that exist in the pixel values. In general, three basic redundancies exist in digital images that follow. Psycho-visual Redundancy: It is a redundancy corresponding to different sensitivities to all image signals by human eyes. Therefore, eliminating some less relative important information in our visual processing may be acceptable (Javed et al., 2013).

Inter-pixel Redundancy: It is a redundancy corresponding to statistical dependencies among pixels, especially between neighboring pixels.

***Coding Redundancy*:** The uncompressed image usually is coded with each pixel by a fixed length. For example, an image with 256 gray scales is represented by an array of 8-bit integers. Using some variable length code schemes such as Huffman coding and arithmetic coding may produce compression. There are different methods to deal with different kinds of aforementioned redundancies. As a result, an image compressor often uses a multi-step algorithm to reduce these redundancies.

3.7.1 Compression methods

During the past two decades, various compression methods have been developed to address major challenges faced by digital imaging (Wallace, 1991).

These compression methods can be classified broadly into lossy or lossless compression. Lossy compression can achieve a high compression ratio, 50:1 or higher, since it allows some acceptable degradation. Yet it cannot completely recover the original data. On the other hand, lossless compression can completely recover the original data but this reduces the compression ratio to around 2:1. In medical applications, lossless compression has been a requirement because it facilitates accurate diagnosis due to no degradation on the original image. Furthermore, there exist several legal and regulatory issues that favor lossless compression in medical applications.

- *Lossy compression methods*

Generally most lossy compressors (Figure 3.2) are three-step algorithms, each of which is in accordance with three kinds of redundancy mentioned above.

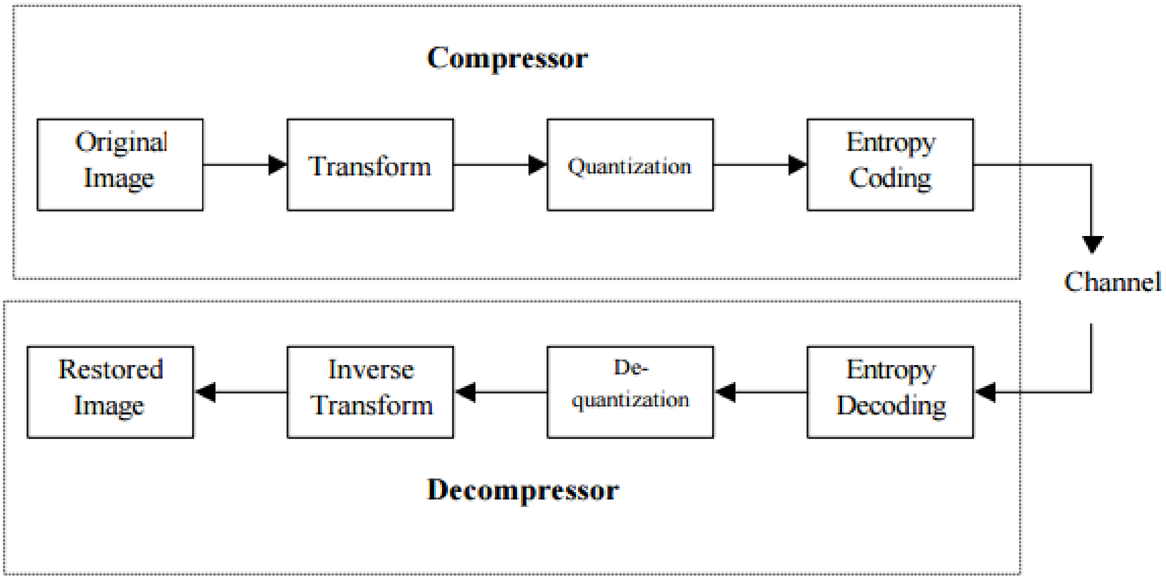


Figure 3.2: Lossy compression (Wallace, 1991)

The first stage is a transform to eliminate the inter-pixel redundancy to pack information efficiently. Then a quantizer is applied to remove psycho-visual redundancy to represent the packed information with as few bits as possible. The quantized bits are then efficiently encoded to get more compression from the coding redundancy.

- *Lossless compression methods*

Lossless compressors (Figure 3.3) are usually two-step algorithms. The first step transforms the original image to some other format in which the inter-pixel redundancy is reduced. The second step uses an entropy encoder to remove the coding redundancy. The lossless decompressor is a perfect inverse process of the lossless compressor (Zhou et al., 2014).

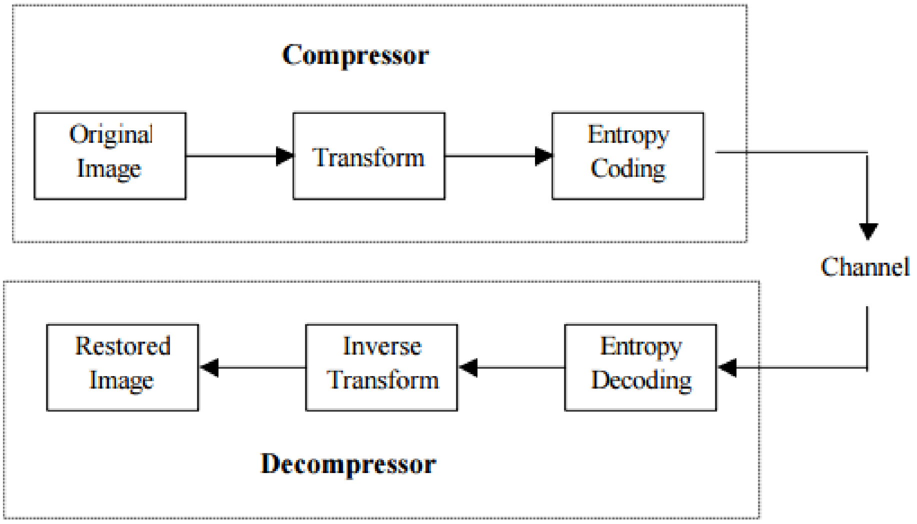


Figure 3.3: Lossless compression (Wallace, 1991)

3.8 Image Segmentation

Image segmentation is the division of an image into regions or categories, which correspond to different objects or parts of objects. Every pixel in an image is allocated to one of a number of these categories. A good segmentation is typically one in which:

- pixels in the same category have similar grayscale of multivariate values and form a connected region,
- neighbouring pixels which are in different categories have dissimilar values.

Segmentation is often the critical step in image analysis: the point at which we move from considering each pixel as a unit of observation to working with objects (or parts of objects) in the image, composed of many pixels. If segmentation is done well then all other stages in image analysis are made simpler. But, as we shall see, success is often only partial when automatic segmentation algorithms are used. However, manual intervention can usually overcome these problems, and by this stage the computer should already have done most of the work (Zhang et al., 2010).

Segmentation algorithms may either be applied to the images as originally recorded, or after the application of transformations and filters. After segmentation, methods of mathematical morphology can be used to improve the results. The segmentation results will be used to extract quantitative information from the images.

There are three general approaches to segmentation, termed thresholding, edge-based methods and region-based methods.

- *In thresholding,* pixels are allocated to categories according to the range of values in which a pixel lies.
- *In edge-based segmentation*, an edge filter is applied to the image, pixels are classified as edge or non-edge depending on the filter output, and pixels which are not separated by an edge are allocated to the same category.
- *Region-based segmentation algorithms* operate iteratively by grouping together pixels which are neighbours and have similar values and splitting groups of pixels which are dissimilar in value (Mansoor et al., 2014).

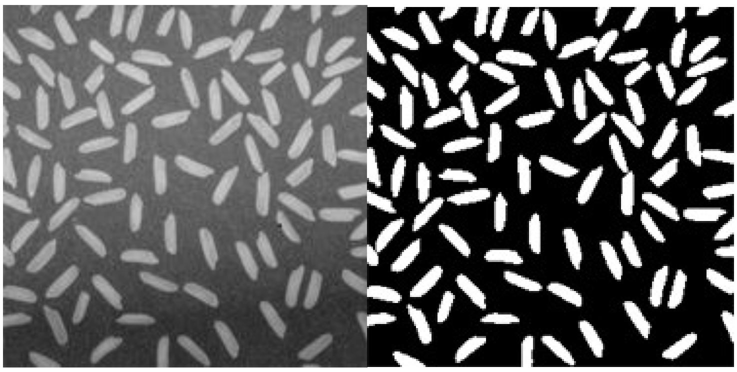


Figure 3.4: Threshold based segmentation (Saif et al., 2012)

3.8.1 Thresholding

This method converts a gray value image into a binary image. If a voxel has a value within a certain threshold range it is assigned the value one, otherwise zero, where $T1$ and T2 represent the upper and lower bounds of the threshold interval. Often only $T1$ is specified, assuming $T2$ to be the highest intensity value in the image.

Instead of using a fixed threshold range, an optimal threshold procedure can be used, where for each input image the optimal threshold interval is determined. In (Hu et al., 2001) for example, an iterative procedure is used to select the optimal threshold:

$$T^{i+1} = \frac{\mathrm{Vb} + \mathrm{Vn}}{2} \qquad \text{until} \quad T^{i+1} = T^{i} \tag{3.2}$$

In this equation T^i represents the threshold at step i, T^{i+1} represents the threshold at step i+1. Two types of voxels are distinguished: body voxels, belonging to the object, and non-body or background voxels. The values ν_b and ν_n represent the mean gray level of the body voxels and non-body voxels after segmentation with threshold T^i. The iteration is initialized with a selected threshold T^0 (Bhargavi and Jyothi, 2014).

CHAPTER FOUR
DESIGNED LUNG TUMOR SEGMENTATION SYSTEM

In this chapter segmentation of tumors within the lung using image processing techniques will be proposed. Introducing main features and goals of the developed lung tumor segmentation system will be discussed in this chapter. Furthermore, developed algorithms of lung tumor segmentation by listing and explaining the methods used for the detection process will be clarified. Database of the images which used for this research and demonstrate some examples of the medical image processing system will be discussed.

4.1 Methodology

This section describes basic steps of lung tumor segmentation.

4.1.1 Proposed system

In this thesis, a Lung Tumor Segmentation System is designed. The system is a model which found in image processing that combines different image processing techniques to accomplish its goal that is the segmentation of the lung tumors placed into the lung and segment them on the original image using threshold. The system is implemented and simulated using Matlab programing language (Matlab 2013Ra, software tools).

Lung Tumor Segmentation System is based upon different image processing techniques used for segmenting the lung tumor into a lung. The lung image database is an on-line CT image dataset available for the researchers in the field of digital image processing. Firstly, removing the noise from images, erosion and median filter are applied to the system respectively. Afterwards, thresholding is applied to the filtered image which is one of the most common techniques used in CT images. Threshold value is a specific value that turns a grayscale image into a binary image due to thresholding method. Then, binary areas are opened to remove small objects from threshold images. In last method, in order to create tumor cells alone, difference between filtered image and small objects removed from the images are taken into account

4.1.2 Flowchart

Flowchart of the proposed system is given below.

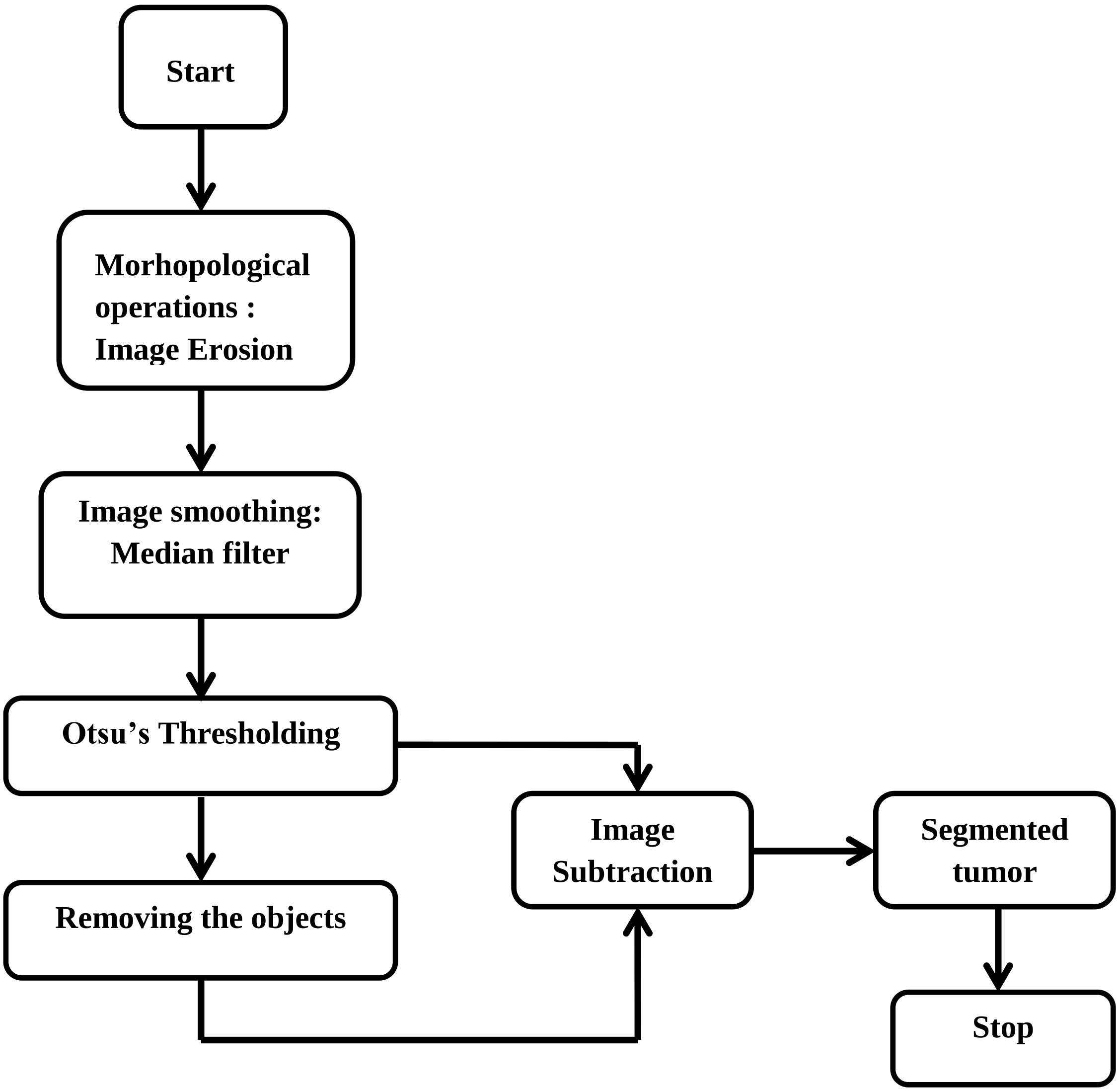


Figure 4.1: Flowchart of the proposed system

4.2 Proposed System Procedure

Many methods and techniques have been used in this system instead of segmenting the lung tumor in a lung. These steps which used in the proposed system are creating database, erosion which is known as morphological operations, image filtering, segmentation using threshold, object removing and image subtraction.

4.2.1 Database

Computed tomography (CT) scan images are preferred to be used in this research, due to low noise and better clarity compared to X-Ray and MRI images. The lung image database has been chosen randomly from NIH/NCI Lung Image Database Consortium (LIDC) which is an on-line CT image dataset available in the "Cancer Imaging Archieve" (Cancer Imaging Archieve, 2014) for the researchers in the field of digital image processing. The images used within this research are in .jpg format. Figure 4.2 shows samples of original CT images. It converts original DICOM images which are in grey color to JPEG format by removing the tint and saturation information while maintaining the luminance. The original size of the images was 512*512 and then it converted to 256*256 to get better quality. Then database is created by own system. There is 70 images which 50 of them has tumor and 20 of them has non tumor in total. This number is enough since the designed system is an image analysis and processing system.

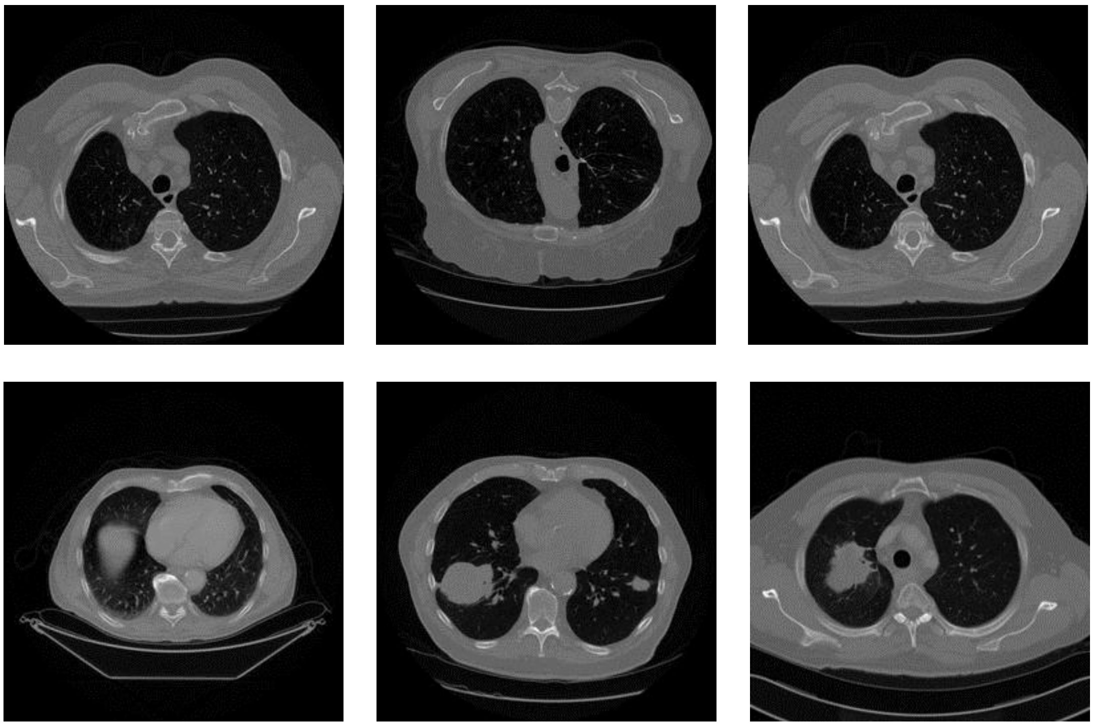
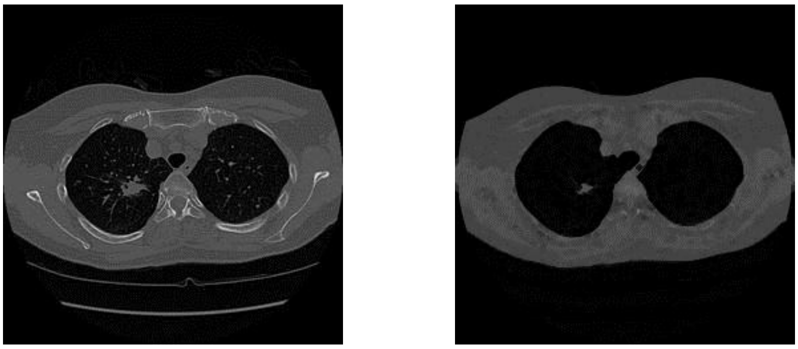


Figure 4.2: Samples of original CT images

4.2.2 Morphological operations

Morphology operations can be characterized as a gathering of image processing procedures that process images taking into account shapes. These morphological operations are taking into account applying an organizing component to an input image keeping in mind the end goal to make a yield image of the same size. In such operation, the estimation of every pixel in the yield image is taking into account an examination of the comparing pixel in the information picture with its neighbors. This is carried out by picking the size and state of the area. At that point, we can build up a morphological operation that is delicate to particular shapes in the input image (AKalaivani et al., 2013).

The structure element is a matrix consists of 0’s and 1’s, where the 1’s are called the neighbors. The value of each pixel in the output image is set according to a comparison of the corresponding pixel in the input image with its neighbors. It has many shapes according to its application. The most common and basic morphological operations are dilation and erosion. Dilation is to add pixels to the boundaries of objects in an image, while erosion is to remove pixels on object boundaries. The number of pixels that are added or even removed from the structure in an image depends on the size and shape of the structuring element that is used to process that image. In these morphological operations (dilation and erosion), the condition of any given pixel in the output image can be determined by applying a rule to the studied pixel and its neighbors in the input image (Gonzalez and Woods, 2004).



(a) original image (b) eroded image

Figure 4.3: Erosion for abnormal images

The figure above shows the erosion of the input original grayscale image which contains tumor. It shows that the erosion helped in margining the tumor and also shrinking it to be separated from other tissues which help in later processing of the tumor.

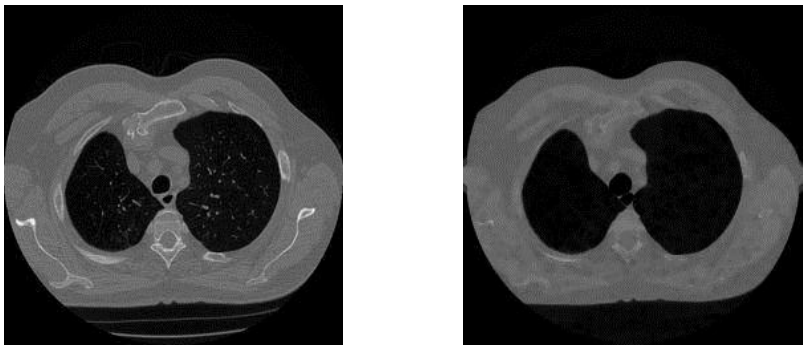
- *Dilation*

It is a morphological operation used to remove or add a pixel at object boundary based on the shape and radius of its corresponding structuring element. During dilation, the value of the output pixel is the maximum value of all the pixels in the input pixel of the set neighborhood (Radha and Lakshman, 2013).

- *Erosion*

This can be considered as a dual to dilation; it can be defined as dilation by set complementation and vice versa. Thus, to erode an image we should dilate the complement of it, while dilating an image can be accomplished by eroding the complement of the image. In other words, we can say that the dilation can be used to expand foreground of the image and shrinks its background, while erosion is used to shrink the image foreground and expands its background (Radha and Lakshman, 2013).

In this work, only erosion was used to shrink the images. In our case, or system, the "diamond" structure element with a "radius" of 2 is used to extract the background of the image (Sahoo et al., 1988).



(a) original image (b) eroded image

Figure 4.4: Erosion for normal images

The image above shows a non-tumor image that undergoes erosion using the proposed system.

4.2.3 Image filtering

Smoothing is an image processing technique used in order to reduce the noise in an image to produce less pixelated and clearer image. Most smoothing techniques are based on low pass linear filters. It is mostly based on the averaging technique of the input image or the middle (median) value technique (Eng and Malek, 2001).

To perform a smoothing operation we will apply a filter to our image. The most common type of filters is the linear filters such as median filter which is used in our proposed system. This filter is used to reduce impulsive noise or the salt-and pepper in an image with preserving the useful features and image edges. Median filtering is a linear process in which the output of the being processed pixel is found by calculating the median of a window of pixels that surrounds that studied pixel (Eng and Malek, 2001). In other words, the median filter goes through each element of the image and replaces each pixel with the median of its neighboring pixels which are located in a square neighborhood (kernel) of 5*5 pixels around the evaluated pixel.

What effect does this have on the boundary values? There are other approaches that have different properties that might be preferred in particular circumstances:

- Avoid processing the boundaries, with or without cropping the signal or image boundary afterwards.
- Fetching entries from other places in the signal. With images for example, entries from the far horizontal or vertical boundary might be selected.
- Shrinking the window near the boundaries, so that every window is full.

An example of a median filter:

	6	3	4	
	5	2	5	
	4	5	9	

3-by-3 adjacent block valuels:

6, 3, 4, 5, 2, 5, 4, 5, 9

Values after sorting process:

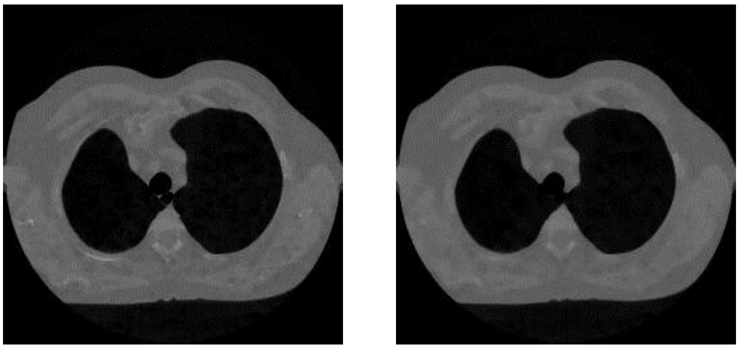
2, 3, 4, 4, 5, 5, 5, 6, 9

Median value:

5

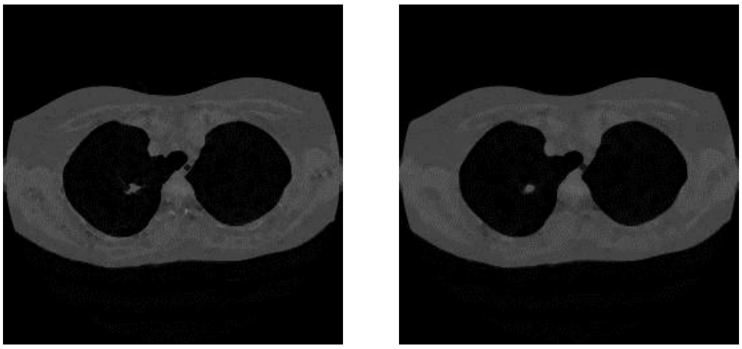
Figure 4.5: Filtration process

Figure above illustrates an example of a median filter and its mechanism to reduce the noise in an image by setting a kernel or window that goes through the whole matrix and find an output for the processed pixel by calculate the median of the pixels in the window (Church et. al, 2008). For figure 4.6 and 4.7; (a) is the eroded image, (b) is the median filtered image.



(a) eroded image (b) median filtered image

Figure 4.6: Median filtering for normal images



(a) eroded image (b) median filtered image

Figure 4.7: Median filtering for abnormal images

It can be seen that the median filter helped in setting and smoothing the edges of the tumor which makes it easy to be segmented in later techniques and also this filter helped to reduce impulsive noise or the salt-and pepper in the image which is clear in the Figure 4.7 (a) with preserving the useful features and image edges by going through each element of the image and replace each pixel with the median of its neighboring pixels which are located in a square neighborhood (kernel) around the evaluated pixel.

4.2.4 Threshold segmentation

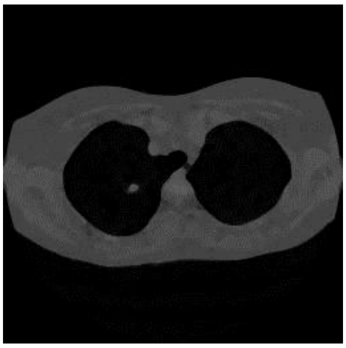
Thresholding is an important technique in image segmentation applications. The basic idea of thresholding is to select an optimal gray-level threshold value for separating objects of interest in an image from the background based on their gray-level distribution. While humans can easily differentiate an object from complex background and image thresholding is a difficult task to separate them (Gonzalez and Woods, 2007).

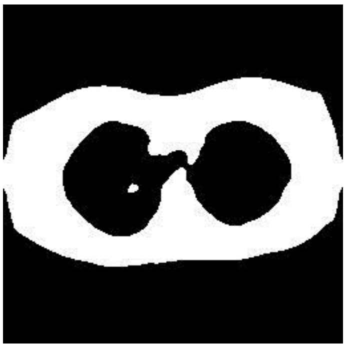
Image segmentation by thresholding is a simple but powerful approach for segmenting images having light objects on dark background. Thresholding technique is based on image space regions i.e. on characteristics of image. Thresholding operation convert a multilevel image into a binary image i.e., it choose a proper threshold T, to divide image pixels into several regions and separate objects from background.The gray-level histogram of an image is usually considered as efficient tools for development of image thresholding algorithms. Thresholding creates binary images from grey-level ones by turning all pixels below some threshold to zero and all pixels above that threshold to one. If g(x, y) is a threshold version of f(x, y) at some global threshold T, it can be defined as (Kang et al., 2009).

$$\begin{aligned} g(x, y) &= 1 \text{ if } f(x, y) \geq T \\ &= 0 \text{ otherwise.} \end{aligned} \tag{4.1}$$

Most common threshold methods are described below:

- Simple thresholding
- Otsu thresholding





(a) median filetered image (b) thresholded image

Figure 4.8: Thresholding for abnormal images

Figure 4.8 shows the thresholding process of a tumor images. (a) shows the median filtered image, (b) is the image after thresholding. It is noticeable that the tumor was correctly separated from other parts such as lungs and the other structure in the image. This technique allows the detection of the tumor as a separate object in the image. After this technique the tumor is easier to be segmented since it is a standalone object in an image of three structures or parts: lungs, cage, and tumor.

Simple thresholding

Threshold is one of the widely used methods for image segmentation. It is useful in discriminating foreground from the background. By choosing an adequate threshold value T, the gray level image can be transform in to binary image. The binary image must contain required information about the position and shape of the objects of interest (foreground) (Jain, 1986).

The advantage of obtaining first a binary image is that it reduces the complexity of the data and simplifies the process of recognition and classification. The most usual way to convert a gray-level image to a binary image is to select a single threshold value (T). Then all the gray level values below this T will be classified as black (0), and those above T will be white (1). The segmentation problem becomes one of selecting the proper value for the threshold T.

Otsu thresholding

Otsu is an automatic threshold selection region based segmentation method. Another way of accomplishing similar results is to set the threshold so as to try to make each cluster as tight as possible, thus minimizing their overlap. Obviously, we can't change the distributions, but we can adjust where we separate them (the threshold). As we adjust the threshold one way, we increase the spread of one and decrease the spread of the other (Qu and Hang, 2010)

Otsu method is of type global thresholding in which threshold value depends only on gray value of the image. Otsu method was proposed by Scholar Otsu in 1979. Otsu method is global thresholding selection method, which is widely used because it is simple and effective (Gonzalez and Woods, 2007).

The Otsu method requires computing a gray level histogram before running. However, because of the one-dimensional which only consider the gray-level information, it does not give better segmentation result. Otsu's method was one of the better threshold selection methods for general real world images with regard to uniformity and shape measures. But this method does not work well with non-uniform illumination.

Considering, the pixels of a given picture be represented in L gray levels [1, 2,…, L]. The number of pixels at level i is denoted by n_i and the total number of pixels by N = n_1 + n_2 + + n_L. In order to simplify the discussion, the gray-level histogram is normalized and regarded as a probability distribution (Otsu, 1979):

$$pi \ = \ ni/N, \quad pi > 0 \sum_{i=1}^{L}, \ Pi = 1 \qquad (4.2)$$

We divide the pixels into two classes CO and C1 (background and objects, or vice versa) by a threshold at level k; CO denotes pixels with levels [1, , k], and C1 denotes pixels with levels [k + 1,…. , L]. Then the probabilities of class occurrence and the class mean levels, respectively, are given by

$$\omega_0 = \Pr(Co) = \sum_{i=1}^{k} pi = \omega(k) \tag{4.3}$$

$$\omega_1 = \Pr(C1) = \sum_{i=K+1}^{L} pi = 1 - \omega(k) \tag{4.4}$$

and

$$\mu_0 = \sum_{i=1}^{k} i \Pr(i|C_0) = \frac{\mu(k)}{\omega(k)} \tag{4.5}$$

$$\mu_1 = \sum_{i=k+1}^{L} i \Pr(i|C_1) = \mu_T - \mu(k)/1 - \omega(k) \tag{4.6}$$

where

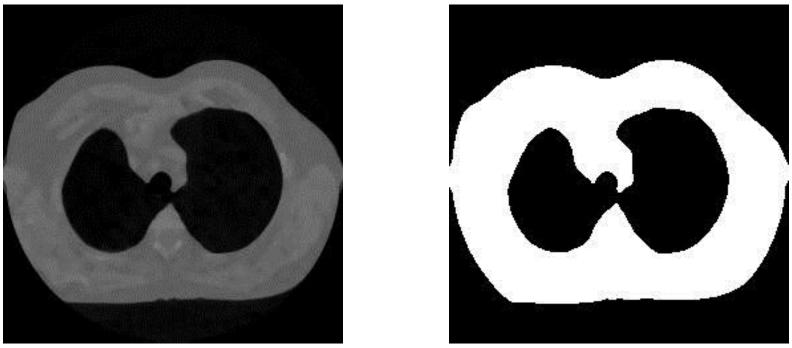
$$\omega(k) \sum_{i=1}^{k} Pi \tag{4.7}$$

and

$$\mu(k) = \sum_{i=1}^{k} ip_i \tag{4.8}$$

which are the zeroth and the first-order increasing moments of the histogram up to kth level.

For this thesis, Otsu thresholding was used due to its simplicity and the difference in graylevels intensities which requires different threshold different images. Therefore, the threshold was selected automatically for different images using Ostu thresholding.



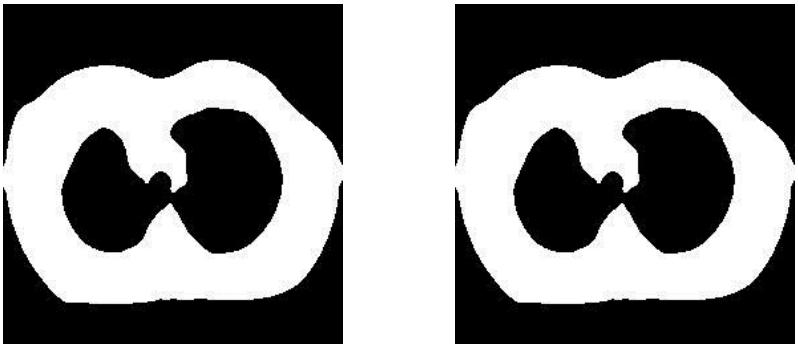
(a) median filtered image (b) thresholded image

Figure 4.9: Thresholding for normal images

The figure above shows the thresholding process of a median filtered non-tumor image. It can be seen that the image edges were correctly detected after this technique which allows the separation of the lungs and the other parts in the image.

4.2.5 Small objects removal

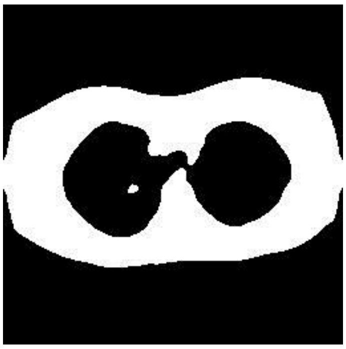
The images then undergo an operation called as area opening. This technique is used to remove the un-wanted components into an image. This technique is to remove form a binary image all the connected components (objects) that have pixels lower than than a set value (Al Mahmud et al., 2015). After applying this technique we could get a result image showing the segmented region of interest (tumor region) for abnormal images and an full black image representing the normal image (Fig.4.10).



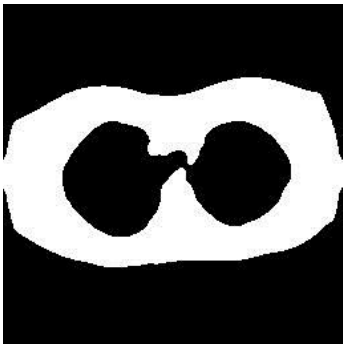
(a) Thresholded image (b) object removed image

Figure 4.10: Object removal for normal images

Figure 4.10 shows the application of the function that removes connected components to a tumor which are uselss. We see no change in image (a) and (b) because the image has no tumor therefore, there should be no elimination of any object in the image; there are no useless parts in the image.



(a) Thresholded image



(b) Object removed image

Figure 4.11: Object removal for abnormal images

Figure 4.11 shows the results of applying a technique or function the removes the objects that are connected to a tumor in order to make it easier to segment it. Usually this technique is used to remove the components connected to a tumor which are not related to it. However, in this thesis this technique is used to remove tumor to keep only the other parts in the image. In later techniques this image will be subtracted from the one which has tumor in addition to other parts. As results the tumor will be obtained as a segmented image.

4.2.6 Image subtraction

The pixel subtraction operator takes two images as input and produces as output a third image whose pixel values are simply those of the first image minus the corresponding pixel values from the second image. It is also often possible to just use a single image as input and subtract a constant value from all the pixels. Some versions of the operator will output the absolute difference between pixel values rather than the signed output. The subtraction of two images is performed straight forwardly in a single pass. The output pixel values are given by

$$R(m,n) = P(m,n) - Q(m,n) \tag{4.9}$$

Or if the operator computes absolute differences between the two input images, then:

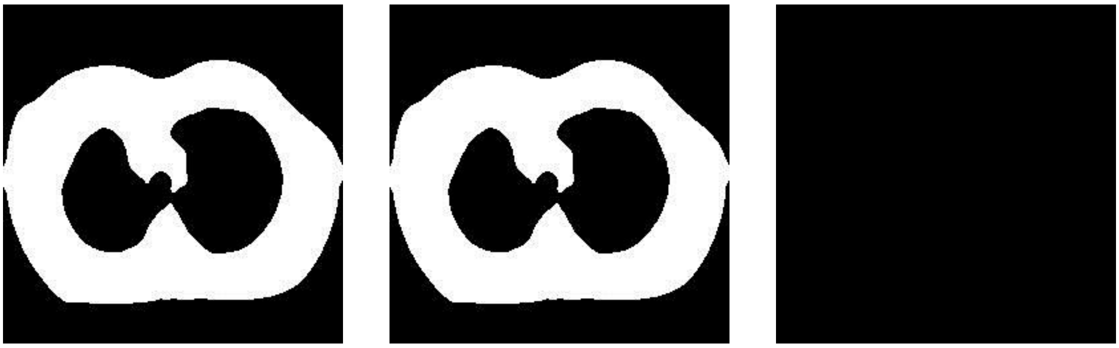
$$R(m,n) = |P(m,n) - Q(m,n)| \tag{4.10}$$

Or if it is simply desired to subtract a constant value C from a single image, then:

$$R(m,n) = P(m,n) - C \tag{4.11}$$

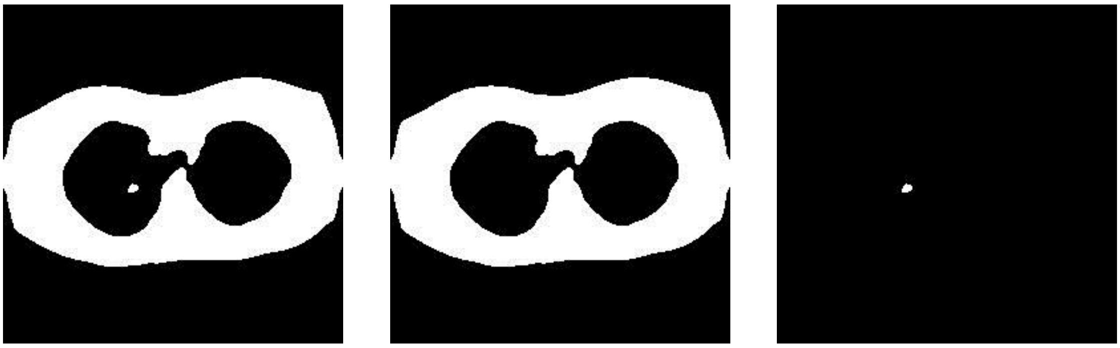
If each pixel value corresponds to an n-tuple instead of a number (for instance, the color image would have each pixel as a vector of three values corresponding to red, blue, and green components), then such pixels are operated on by subtraction at each corresponding vector element to produce the output value.

If the operator calculates absolute differences and the two input images use the same pixel value type, then it is impossible for the output pixel values to be outside the range that may be represented by the input pixel type, and so this problem does not arise. This is one good reason to use absolute differences (Qidwai and Chen, 2009).



(a) Thresholded image (b) Object removed image (c) Resultant image

Figure 4.12: Image subtraction for normal images



(a) Thresholded image (b) Object removed image (c) Resultant image

Figure 4.13: Image subtraction for abnormal images

The figure 4.13 shows the subtraction of the cleaned image (b) from the thresholded image (a). As a result of this subtraction operation, the tumor is obtained and segmented in (c). Similarly figure 4.12 is a subtraction of (b) from (a). However, the result image is black since both images has no tumor and mathematically are equal so the result must be zero which is a black image.

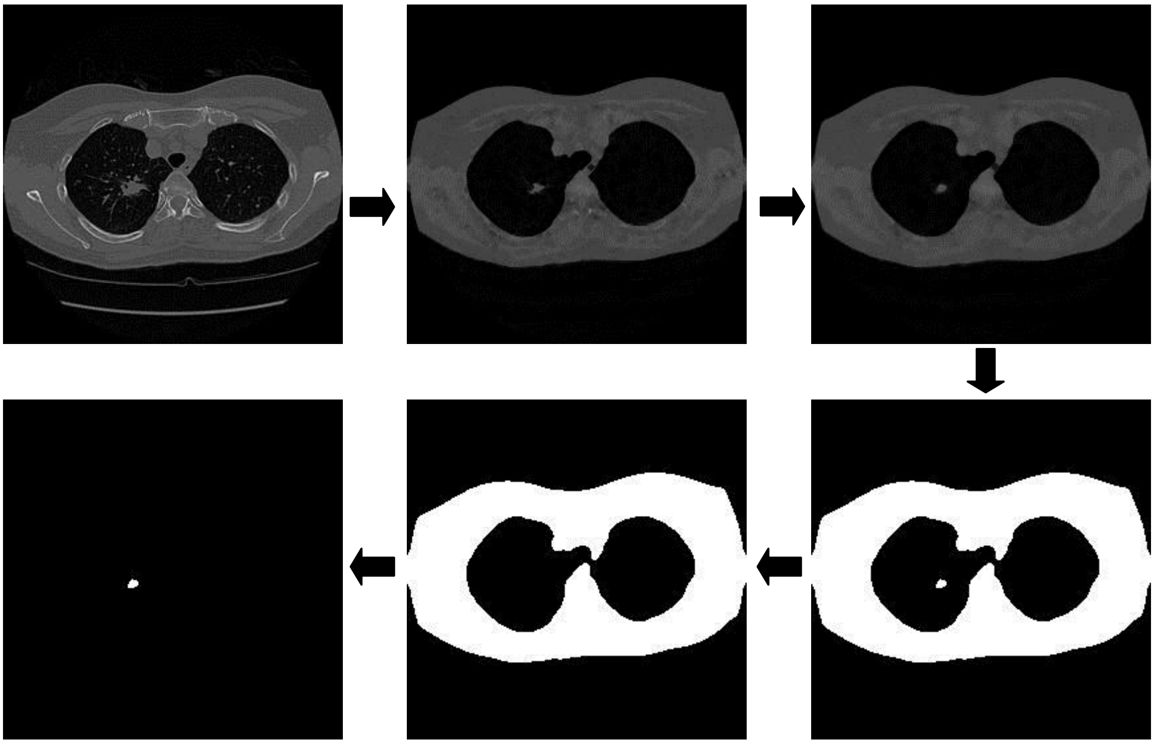


Figure 4.14: Steps of the processing sytstem

Figure 4.14 shows an image of lungs with tumor that was processed using the developed system for the lung tumor segmentation. The image undergoes different techniques until the tumor is segmented. First the image is eroded to separate the tumor from other objects, then the eroded image is filtered to remove the noise. The image is also threshold automatically in order to be converted to binary image and to detect the tumor. After thresholding the tumor was removed from image. Later on the image with no tumor is subtracted from the one that has a tumor to get the segmented tumor alone in one image.

CHAPTER FIVE
RESULTS AND DISCUSSION

This chapter discusses the testing stage of the developed system and the source of the images that are used in the system are mentioned. Designed system performance is also represented here, in which the overall segmentation accuracy, sensitivity and specificity are calculated, and compared, to other researches. These are also shown as tables. Also illustrated are some figures that present the whole process of the system, when undergoing both tumor, and non tumor, lung images.

5.1 System Performance

The developed system will automatically segment any lung tumor in a lung image which contains many other components, or structures, such as clavicles and lungs. Thus, the images were pre-processed first before starting the segmentation process. This allows the tumors to be separated from other components in images. This then makes it easier to segment tumors using thresholding, and some other image processing operations. To test the system we had to apply some images containing tumors and others with no tumor. 50 lung tumor images and 20 with no tumor images were used to evaluate the effectiveness of the system. The measurements that were used for evaluating the developed system are the accuracy, sensitivity, and specificity.

Accuracy is the total number of correctly segmented tumors over the total number of images

$$\mathrm{ACC} = \frac{\mathrm{CS}}{\mathrm{T}} \tag{5.1}$$

Where CS is the number of corrected segmented images, and T is the total number of images. ACC is the accuracy of the system

Sensitivity was also used as a measure to evaluate the segmentation system. It can be defined as a measure of true positive which are the correctly identified areas.

It can be defined as the following:

$$\text{Senitivity} = \frac{\text{TP}}{\text{TP} + \text{FN}} * 100 \tag{5.2}$$

Where TP is true positive this represents the images that they were segmented and that they have tumor.

FN represents the images that were segmented and they have no tumor.

Another parameter was used for system performance evaluation is the specificity. It can be defined as:

$$\text{Specificity} = \frac{\text{TN}}{\text{TN} + \text{FP}} * 100 \tag{5.3}$$

TN are the images that have no tumor and they were segmented correctly.

FP are the images that were not segmented and they have tumors.

Table 1 & 2 show the system performance, where the accuracy achieved is 97% as a total accuracy obtained after testing the system by tumor and non-tumor images. The sensitivity and specificity of the system were 100% and 87% respectively.

Table 1: The segmentation ratio of the system

	Number of images	**Correct segmented images**	**Segmentation ratio**
Non Tumor	20	20/20	100%
Tumor	50	48/50	96%
Total	70	68/70	97%

Table 2: The performance ratio of the system

	Number of images	Accuracy	Sensitivity	Specificity
Total	70	97.14%	96%	100%

5.2 Result Discussion

This thesis is to develop a new image processing approach for the segmentation of the lung tumor compared to other studies. In this thesis different image processing techniques are used.

Firstly, images where are enhanced by using image smoothing techniques like erosion and median filtering. Then, the tumor is segmented by using Otsu thresholding. This techniques was used because of the difference in Gray-levels intensities of images which require different thresholds for different images. The useless connected pixels were removed from threshold image to make it ready for the last technique.

The last step is the extraction of the tumor which is the main part of the system. The threshold images, which contain tumor, and other lung structures and the other images which only contain lung structures without tumor. This non tumor image which is clean was subtracted from the threshold images in order to extract tumor.

Many challenges were encountered when developing this system. One of them is the selection of the right technique for the final tumor extraction. Thresholding was first selected to be used in which different thresholds were used to segment different areas of the image. This technique had some advantages, however some tumors were not segmented using it. In addition some images were detected to have tumor but actually they don’t which decreases the accuracy and sensitivity of the system. The reason for this incorrect segmentation was the difference in intensities of tumor and other parts in each image. Thus, Otsu’s thresholding was used where the threshold is set automatically depending on each image intensity.

This technique was definitely good in segmenting an image, by keeping the tumor and clavicle in an image since they have almost the same intensities. Therefore, another technique was used to remove the tumor from the images keeping only the clavicle. After that the two images were subtracted and the tumor was segmented.

Experimentally, the developed approach showed a great efficiency in segmenting tumors in a CT image using the above discussed technique. This developed lung tumor segmentation approach outperforms many of the researches listed in the state of art in terms of accuracy, sensitivity, and specificity.

5.3 Result Comparison

Many researches have been carried out for the purpose of lung tumor segmentation and detection. However, most of these researches were meant to classify the tumor malignancy rather than segmenting it. These classification systems used some intelligent classifier which showed their efficiency in classifying the lung tumor malignancy by distinguishing both benign and malignant tumor features. Few researches used only image processing techniques to segment the lung tumor. Therefore, this work was meant to develop a new easy and simple approach for segmenting the lung tumor using some image processing techniques.

An approach for extracting lung cancer nodule features from CT images was implemented by Tun et al., 2014. This work involves a method for using Otsu's thresholding and marker-controlled Watershed segmentation to segment the lung tumor. In their system, the authors used feature extraction technique to extract the significant features of a tumor. The Gray-Level Co-occurrence Matrix (GLCM) technique and the physical dimensional measure are applied for such task. Experimentally, the authors tested their system and it performed well with accuracy of 91%.

Sakthi et al., 2016 presented also a system for the segmentation of lung tumor using image processing techniques. Different image processing techniques were used to detect first and then segment the tumor in a lung. Their system consists of pre-processing phase where images were smoothed using mean and median filters. In addition, images were enhanced by increasing their pixels intensity by adjusting them and reducing the difference in intensity between the adjacent pixels. For the next segmentation phase, the authors used technique called Marker-Controlled Watershed Segmentation. This is an important technique in image processing where the goal is to detect first and then separate foreground pixels from the background of image. Marker-controlled watershed technique has two types: external one which is related to the background, however, the other one is the internal one and it is related with the foreground. This segmentation technique based watershed can segment unique edges in an image. In addition to watershed segmentation the authors also used Otsu's thresholding where the image is divided into two regions; background and foreground. This division is based on a selected threshold where the pixels are converted to one if they are above this threshold, however, the pixels below this selected threshold are converted to zero. The experimental results of this system proposed by Sakthi et al., 2016 shows a good performance in segmenting the lung tumor with accuracy of 91%.

Similarly, our proposed system based image processing techniques was implemented to segment lung using thresholding and image subtraction. Our system consists of pre-processing techniques such as erosion and median filter where the lung images were smoothed and the edges were defined as well as the intensity of images was increased. After image enhancement, the segmentation of the lung tumor in an image takes place. For this purpose, Otsu's thresholding was used to divide image into foreground and background regions where the tumor is in the foreground part. Otsu thresholding was used due to its simplicity and the difference in gray-levels intensities which requires different thresholds and different images. A threshold was selected in such a way where the tumor is preserved in the images together with the lung clavicles. This image is then cleaned so that the tumor is removed from the threshold image. A subtraction operation takes place then between the two images of this operation the lung tumor is extracted. Experimentally, the developed system outperforms the state of arts in segmenting the lung tumor with accuracy of 97.14%.

Table 3: Comparion of the system

Paper Title	Authors	Methods used	Recognition Rate
Implementation of Lung Cancer Nodule Feature Extraction using Threshold Technique	Sakthi et al., 2016	Marker-controlled watershed segmentation & Otsu thresholding	91%
Implementation of Lung Cancer Nodule Feature Extraction Using Digital Image Processing	Tun et al., 2014	GLCM & Marker-controlled watershed segmentation approach	91 %
Proposed System Detection Rate	Author	Morhphological operations & Otsu thresholding	97.14%

CHAPTER SIX
CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

Early cancer detection and researches on early detection solutions play vital roles for human health. Computed tomography images (CT) are widely used in radiotherapy planning because they provide electronic densities of tissues of interest which are mandatory to a correct dose computation. Furthermore, the good spatial resolution and soft/hard tissues contrast allow precise target delineation. Also, CT techniques are preferred compared to X-Ray and MRI images. Image processing techniques have started to become popular in use of CT images.

In this thesis, a new approach for the segmentation of lung tumors, especially to the carcinoma patients, was developed. Image processing techniques were implemented for this segmentatıon task. The used image processing techniques are easy to use and simple but play an important role in the medical field in terms of automatic segmentation of lung tumors in CT ımages. The motivation behind the proposed system is due to the lack of simple and effective systems for segmenting the lung tumors. Thus, in the designed system, significant image processing methods used in huge machines such as thresholding and implement them into a simple and easy use system to help in detecting the tumors.

The developed system was tested by many affected and non-affected images collected from an online database. The testing aimed to show the capability of the proposed system in extracting the lung tumor automatically preparing it for segmentation.

The system starts by pre-processing the images so that the tumor may be separated from the other parts of image. Therefore, images were smoothed using median filter which reduces the noise in an image and defines its edges. The images were then eroded in order to define the region of interest “tumor” by shrinking it and clearing its edges.

Thus, thresholding was selected to be automatic due to the difference in tumor intensities for each image. This allows the detection of tumor regardless of its intensity. The thresholding technique used here for the purpose of segmenting tumor and the clavicles. As a result of thresholding we get image of tumor and clavicles only. The longest connected components are then eliminated from image to keep only the tumor. These two images undergo subtraction operation which yields to an image of segmented tumor.

The experimental results show that the techniques used in this system were efficient enough to segment the tumor in many images since they consider the image's intensities variance separately for each image.

Overall, it can be stated that the developed system was capable of segmenting tumors of different tumor and non-tumor images of the used database by achieving high accuracy of 97.14% which outperforms the state of art methods discussed in chapter one.

6.2 Recommendations

For future work many techniques for enhancing and segmenting the lung tumor can recommended:

Classifying the lung images having tumors or non tumors by using artificial intelligence approaches such as neural network and support vector machine. Finally, for more advanced researches, artificial neural networks propose a quite different approach to problem solving. Considering the proposed system in this thesis as a solution, neural networks, or support vector machine and their interrelated analysis can be combined with this proposed system as future work.

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APPENDICES

APPENDIX A
SOURCE CODE

```
clear;
clear all;
clc;


for k = 1:50                                                    % for abnormal images

myFolder = ‘C:\Users\ahmet\Dropbox\New folder\buse program\lung\Lung-thesis Matlab
code\Lung-Tumors’;                                              % reading directory

filePattern = fullfile(myFolder, ‘*.jpg’);
jpegFiles = dir(filePattern);
baseFileName = jpegFiles(k).name;                     % read jpg files from directory
fullFileName = fullfile(myFolder, baseFileName);
im = imread(fullFileName);

a = im;

imwrite(a,strcat(‘C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\saved images\Tumor\(step1)Original\’, ‘Original’,num2str(k),’.jpg’))

se = strel(‘diamond’,2);                                                 % Erosion
b = imerode (a,se);

imwrite(b,strcat(‘C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\saved images\Tumor\(step2)Erosion\’, ‘Erosion’,num2str(k),’.jpg’))

c = medfilt2(b,[5 5]);                                              % Median filter

imwrite(c,strcat(‘C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\saved images\Tumor\(step3)Median\’, ‘Median’,num2str(k),’.jpg’))

level = graythresh (c);
d = im2bw (c,level);                                            % Otsu threshold

imwrite(d,strcat(‘C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\saved images\Tumor\(step4)Threshold\’, ‘Threshold’,num2str(k),’.jpg’))

e = bwareaopen (d,1000);                     % remove unwanted objects on image

imwrite(e,strcat(‘C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\saved images\Tumor\(Step5)Bwopen\’, ‘Bwopen’,num2str(k),’.jpg’))

f = d - e;                                                 % Image Subtraction

imwrite(f,strcat(‘C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\saved images\Tumor\(step6)Tumor\’, ‘Tumor’,num2str(k),’.jpg’))
end
```

```
for k = 1:20;                                               % for normal images

MyFolder = 'C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\Lung-NonTumor';

filePattern = fullfile(MyFolder, '*.jpg');
jpegFiles = dir(filePattern);
baseFileName = jpegFiles(k).name;
fullFileName = fullfile(MyFolder, baseFileName);
im = imread(fullFileName);

a = im;

imwrite(a,strcat('C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\saved images\Non-Tumor\(step1)Original\', 'Original',num2str(k),'.jpg'))

se = strel('diamond',2);
b = imerode (a,se);

imwrite(b,strcat('C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\saved images\Non-Tumor\(step2)Erosion\', 'Erosion',num2str(k),'.jpg'))

c = medfilt2(b,[5 5]);

imwrite(c,strcat('C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\saved images\Non-Tumor\(step3)Median\', 'Median',num2str(k),'.jpg'))

level = graythresh (c);
d = im2bw (c,level);

imwrite(d,strcat('C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\saved images\Non-Tumor\(step4)Threshold\', 'Threshold',num2str(k),'.jpg'))

e = bwareaopen (d,1000);

imwrite(e,strcat('C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\saved images\Non-Tumor\(step5)Bwopen\', 'Bwopen',num2str(k),'.jpg'))

f = d - e;

imwrite(f,strcat('C:\Users\ahmet\Dropbox\New folder\buse-program\lung\Lung-thesis Matlab
code\saved images\Non-Tumor\(step6)Non-Tumor\', 'Non-Tumor',num2str(k),'.jpg'))
end


% Calculations

% Total image = 70

% True positive (TP): the diagnostic system yields positive test
% result for the sample and the sample actually has the disease.

% False positive (FP): the diagnostic system yields positive
% test result for the sample but the sample does not actually
```

```
% have the disease.

% True negative (TN): the diagnostic system yields negative
% test result for the sample and the sample does not actually
% have the disease.

% False negative (FN): the diagnostic system yields negative
% test result for the sample but the sample actually has the
% disease.

% TP: True Positive: Tumor Present and true detected
% TN: True Negative: Tumor not present and not detected
% FP: False Positive: Tumor not present and detected
% FN: False Negative: Tumor present and false detected

TP = 48;
TN = 20;
FP = 2;
FN = 0;

% 1) Accurarcy (verimlilik)

Accuarcy = (TP+TN) / (TP+TN+FP+FN) * 100

% 2) Sensitivity

Sensitivity = TP / (TP+FN) * 100

% 3) Specificity

Specificity = TN / (TN+FP) * 100
```

APPENDIX B
DATABASE