CHAPTER 1

INTRODUCTION TO COMPUTER AIDED DIAGNOSIS

1.1 INTRODUCTION

The aim of this work is to develop Computer Aided Diagnosis (CAD) system for the detection of brain tumor by using metaheuristic Algorithms. Brain tissue has a complex structure and its segmentation is an important step for deriving the computerized anatomical atlases as well as pre and intra operative guidance for therapeutic intervention (Hanley 1989). The accurate quantification of disease patterns in medical images allows the radiologists to track the status of the disease. Image analysis is still performed manually which is often a difficult and time consuming task. As a result, there is an increasing need for computerized analysis to facilitate image based diagnosis. Many investigators have carried out basic studies and clinical applications toward the development of modern computerized schemes called CAD system for detection and characterization of lesions in images of brain, chest, colon, breast, liver, kidney and the vascular and skeletal systems. The early detection is the most effective way to reduce mortality (Chan et al., 1995, 1998 and Leaster 1984).

Most of the radiologists achieve this goal with the process of image perception to recognize the unique image pattern to identify the relationship between the perceived patternd the possible diagnosis. But both detection and characterization processes depend heavily on the radiologists' empirical knowledge, memory, intuition and diligence. So, there are chances for well documented errors and variations in the human interpretation of clinical images. Indeed, the estimates indicate that between 10% and 30% of tumors are missed by the radiologists during the routine screening (Vannier et al., 1988). The widespread availability of the suitable detectors has aided the rapid development of new technologies for monitoring and diagnosis as well as the treatment of patient's. The intension of the intelligent system is not to replace the radiologists but to provide them with a second opinion on a lesion diagnosis to achieve high accuracy and save human lives.

1.2 BRAIN TUMOR

The brain is the most fascinating and the least understood organ in the human body. It is a soft, delicate, non-replaceable and spongy mass of tissues .For centuries, scientists and philosophers have pondered over the relationship among behavior, emotion, memory, thought, consciousness and the physical body. Healthy brain tissues can generally be classified into three broad tissue types on the basis of an MRI brain image. Gray Matter (GM), White Matter (WM) and Cerebro-Spinal Fluid (CSF) are the three important types.

Brain tumor is one of the major causes for the increase in mortality among children and adults. In India, nearly 80,000 people are affected annually by various types of tumor. Brain tumors are a diverse group of diseases characterized by the abnormal and uncontrolled growth of tissues either in the brain itself or in blood vessels, in cranial nerves, in the brain envelopes, in skull, in pituitary and pineal gland or spread from tumors in other organs. Brain tumors can directly destroy brain cells or they may indirectly damage cells by producing inflammation compressing other parts of the brain. As the tumor grows, it induces brain swelling and causing increased pressure within the skull.

Brain tumors can either be benign (without tumor cells) or malignant (tumor cells).The complex brain tumors can be classified into two general categories depending on the tumor origin, the growth pattern and malignancy. They are primary brain tumors and secondary or metastatic brain tumors. Brain tumors can occur at any age.

1.2.1 Benign Brain Tumor

Benign brain tumors do not contain tumor cells which can easily be removed and they seldom grow back. Cells from benign tumors neither invade tissues around them nor spread to other parts of the body. Benign brain tumors have clearly defined edges and contain cells that look healthy, just like normal cells (Zijdenbos et al., 1994 and Set and Leith, 1994). They can press on sensitive areas of the brain and cause serious health hazards. Unlike benign tumors in other parts of the body, those in the brain can be life-threatening. At times, a benign brain tumor may become malignant.

1.2.2 Malignant Brain Tumor

Malignant brain tumors contain tumor cells. They are generally more dangerous and life-threatening. This type of tumor is likely to grow rapidly and invade the surrounding healthy brain tissues. In certain cases, tumor cells may break away from a malignant brain tumor and spread to other parts of the brain and to other parts of the body (Zijdenbos et al., 1994 and Michelson set and Leith, 1994). The spread of tumor is called metastasis.

1.2.3 Primary Brain Tumor

Brain tumors that begin in brain tissues are known as primary brain tumors. These tumors are named according to the type of cells or the parts of the brain in which they begin. The most common primary brain tumors are gliomas which begin in glial cells.

1.2.4 Secondary Brain Tumor

Secondary brain tumors may originate in any other part of the body. When tumor spreads from its original place to other parts of the body, the new tumor will have the same kind of abnormal cells and the same name as the primary tumor. Tumor that spreads to the brain from other parts of the body is different from a primary brain tumor. Secondary tumors in the brain are far more common than primary brain tumors. Table 1.1 explains brain tumor types, its descriptions and victim rates.

Table 1.1 Brain Tumor Types and Victim Rates

Types of Brain Tumor	Description	Victim Rate
Acoustic Neurinoma	Benign tumor occurring in the acoustic nerve between the Pons and the cerebellum.	2.31%
Astrocytoma	A type of brain tumor that begins in the brain or spinal cord in small, star-shaped cells called Astrocytes.	10.04%
Ependymoma	Tumor arising from the Ependymal cells found along the ventricles and central canal of the spinal cord.	5.02%
Glioblastoma Multiforme(GBM)	A type of brain tumor that forms from glial (supportive) tissue of the brain. It grows very quickly and it has cells that look very different from normal cells .It is also called grade IV Astrocytoma.	25.37%
Meningioma	A type of tumor that occurs in the meninges, the membranes that cover and protect the brain and spinal cord.	7.06%
Metastatic Tumor	Tumor formed by tumor cells that spread to the brain from elsewhere in the body.	16.55%
Mixed Glioma	Tumor containing astrocytic and neuronal elements as well as oligodendroglial cells.	3.80%
Oligodendroglioma	Tumor arising from oligodendrocytes, a type of supportive brain tissue.	8.28%
Pineal region Tumor	Tumor occurring in the area of the pineal gland.	2.08%
Other type of Benign Brain Tumor	This is the non cancerous one. It occurs from the brain cells.	12.08%
Other type of Malignant Tumor	The tumor that invades and destroys the tissue where it originates from and which can spread to other tissues in the body.	9.50%

1.3 CAUSES OF BRAIN TUMOR

The exact causes of brain tumor are being investigated. The doctors can seldom explain why one person gets brain tumor and another person does not. However, brain tumor research has shown that people with certain risk factors are more likely to develop brain tumor than others. A risk factor is anything that increases a person's chances of developing a disease. Specific risk factors for developing a primary brain tumor are given below.

- Family history of prior brain tumor.
- Exposure to radiation from nuclear industry.
- Exposure to certain chemicals like formaldehyde, vinyl chloride and acrylonitrile.
- Brain tumors occur more often in Caucasians than in people of other races.
- Brain tumors are more common in males than in females. However, most of the time meningiomas occur only in females.
- Most brain tumors are detected in people who are 70 years of age or older. However, brain tumors are the second most common tumors in children. Leukemia is the most common childhood tumor which occurs below the age of 8.
- Scientists are currently investigating cell phones and head injuries as possible causes of brain tumors.

1.4 BRAIN TUMOR SYMPTOMS

The symptoms of brain tumor depend on their size, type and their location in the brain. Table 1.2 gives the details of brain tumor symptoms and victim rate.

Table 1.2 Brain Tumor Symptoms and Victim Rate

Basic Symptoms	Victim Rate
Headaches	76.80%
Changes in mood, personality, or ability to concentrate	43.55%
Muscle jerking or twitching	32.97%
Hearing problems	34.46%
Numbness or tingling in the arms or legs	41.93%
Nausea or vomiting	36.50%
Problems with vision	46.00%
Problems with sensation in hands	22.80%
Strange smell felt	18.72%

1.5 BRAIN TUMOR SURVIVAL RATE

On an average, the survival rate for an individual with malignant brain tumor is only one or two years. Overall survival rates are 33 percent, while average life expectancy ranges between 6 months to 1 year after diagnosis. More importantly, patients suffering from benign brain tumor show better survival rates than their counterparts with a malignant tumor. Several factors play a vital role in determining whether the particular person will survive with brain tumor or not. These factors include:

- Type of brain tumor
- Size and location of the tumor
- Stage of the tumor
- Grade of the tumor
- General health of the person

Table 1.3 Age Factor and Survival Rate of Brain Tumor

Age	Survival Rate (%)
< 14	73
14 - 44	55
45 - 64	16
> 65	5

Table 1.3 describes that, as the age of the patient increases, the survival rate continues to depreciate. The brain cancer survival rate in children is 70 to 80%, if the cancer has not spread and a complete surgical resection is feasible. However, if the cancerous cells have spread to other parts, the survival rate drops down to 30% to 40%. This means that the brain tumor survival rate in children is relatively better than the others.

1.6 BRAIN TUMOR DIAGNOSIS

Brain tumors are diagnosed by the doctors based on the results of a medical history, physical examination and results of a variety of specialized tests of the brain and nervous system. The medical history includes questions about the patient's habits, occupational history and a family history of any medical conditions, past illness and treatments. By Physical examination the doctor will check up for general signs of health and signs of disease such as lumps or anything else that seems unusual. Check up for alertness, muscle strength, coordination, reflex, eye swelling and response to pain are also essential. The treatment of the brain tumor depends on its type, location and size of the tumor as well as the age and health of the patient.

1.6.1 Medical Imaging Systems

Medical imaging is an essential tool for improving the diagnoses and understanding and treating a large variety of diseases. Over the last century, technology has advanced from the discovery of x-rays to a variety of medical imaging tools such as MRI (Magnetic Resonance Imaging), CT (Computer Tomography), PET (Positron Emission Tomography) and Ultrasonography. These medical imaging techniques can provide detailed information about diseases and can identify many pathologic conditions.

The techniques used to examine the brain tumor are:

- CT and PET taken by an x-ray machine that is linked to a computer which tends to take a series of detailed pictures of the head.
- MRI which uses powerful magnetic fields.
- Angiogram in which a dye is injected into the bloodstream that flows into the blood vessels in the brain to make them show up on an x-ray.
- Skull x-ray: some brain tumor causes calcium deposits in the brain or changes in the bones of the skull. An x-ray of the skull can be used to checkup these changes.
- Spinal tap that uses a long, thin needle to remove cerebrospinal fluid from the spinal column.

1.6.2 Magnetic Resonance Imaging

MRI is one of the best technologies currently being used for diagnosing brain tumor. Haney et al., 2001 has found that MRI method has higher resolution which is approximately 100 microns. At present MRI is the method of choice for early detection of brain tumor in human brain. MRI is an advanced medical imaging technique used to produce high-quality images of the parts of brain and the nerve tissues in multiple planes without obstruction by overlying bones. From these high resolution images, one can derive detailed anatomical information to examine the development of human brain tumor and discover abnormalities. Brain tumor is diagnosed at the earliest stages with the help of the MRI image.

Brain MRI is the most opted procedure mainly for the brain disorders. It provides clear images of the brainstem and posterior brain which are difficult to view on a CT scan. It is also useful in the diagnosis of demyelinating disorders. Further the evaluation of flow of blood and flow of Cerebrospinal Fluid (CSF) is possible with this non-invasive procedure. MRI can distinguish tumors, inflammatory lesions and other pathologies from the normal brain anatomy. However, MRI scans are used to avoid the dangers of interventional procedures like angiography and of repeated exposure to radiation as required for CT and other X-ray examinations.

1.7 AIM OF THE RESEARCH

- To develop the system, that generates disease specific atlas which reflects a particular clinical group for a large set of images.
- To design a system that can incorporate the disease specific atlas and a segmentation scheme.
- To develop a stable system that detects the tumor at the earliest stage.

- To develop CAD system for automatic detection of brain tumor through MRI system that can provide the valuable outlook and accuracy of the earlier brain tumor detection which assists the radiologists.
- To extract and analyze the characteristics of benign and malignant lesions.
- To reduce the number of false detections.
- To develop a novel segmentation technique using metaheuristic algorithms to detect the suspicious region.
- To increase sensitivity and specificity in tumor diagnosis.

1.8 CAD SYSTEM

Early detection being a key factor in producing successful results, it is of important role to improve the ability of identifying tumors at the earliest stage. CAD system uses computers to find out the suspicious areas helping the radiologist to achieve diagnostic accuracy (Chan et al., 1999) .With the help of the digital image obtained by scanning, the radiologist can examine the suspicious areas and decide if a biopsy or any further evaluation is needed.

It is difficult to interpret brain images, as the probability of encountering an abnormality is low and the information of the patient is limited. It takes a trained radiologist to segment the suspicious region without missing any abnormality. In the development of CAD system, it is the computer that essentially acts as a second reader and so a large number of cases can be examined without an increase in cost. Furthermore, it can help to get better sensitivity, cost effectiveness and less time-consumption.

The CAD system can provide the valuable outlook and accuracy of earlier brain tumor detection. The two key steps involved in the implementation of CAD system are segmentation and classification of suspicious region. Segmentation algorithm has two stages: (i) Bilateral registration segmentation (ii) Single image segmentation. In addition the classification is based on Pixel Similarity Index (PSI).

1.9 NEED FOR METAHEURISTIC ALGORITHM

Segmentation of medical images is challenging due to the poor image contrast and artifacts that result in missing or diffuse organ and tissue boundaries. The manual segmentation is not only tedious and time consuming, sometimes it is also inaccurate. Therefore optimization of an appropriately defined objective function is essential. The objective function is usually complex, multimodal, discontinuous, and cannot be described in a closed mathematical form that can be analytically solved and hence the application of several classical techniques becomes limited. Heuristic methods that are not bound by the stringent restrictions of classical methods gain importance in such situations. In this regard, application of a search and optimization method that is capable of handling huge, complicated and multimodal search spaces is appropriate and natural (Bandyopadhyay et al., 2007). In this work the overall performance of the CAD system is improved by developing an automated method of choosing optimized feature which is achieved by using Markov Random Field - Maximum A Posteriori -Parallel Ant Colony Optimization (MRF- MAP-PACO) technique to segment the normal tissue from tumor tissue. The performance of the developed algorithms is evaluated by Receiver Operating Characteristics (ROC) curve.

1.10 CONTRIBUTION OF THE THESIS

The contribution of this work is to optimize the CAD system thereby improving accuracy. The generation of disease specific area is the main aspect of this work and it is useful to segment and classify the input images. The area is obtained from the selected set of input images having similar evolution of a disease. The images are segmented and classified in the brain tumor area. The segmentation is done using two methods using metaheuristic algorithms. The first one is bilateral image segmentation and the second one is single image segmentation. The plan is implemented using Mat lab 7.0. The CAD system has developed a new segmentation methodology and a new code is generated for the registration segmentation and metaheuristic segmentation. The detection of brain tumor is performed in four phases namely Image acquisition and pre-processing, Enhancement, Segmentation, Feature extraction and Classification.

1.10.1 Image Acquisition and Pre-Processing

Accessing the real medical images from different imaging devices like MRI, PET and CT scan for research purpose is very complex because of privacy and legal issues along with heavy technical complications. Among these systems, the 0.5T intra-operative magnetic resonance scanner offers the possibility to acquire 256*256*58 (0.86mm, 0.86mm, 2.5 mm) T1 weighted images with the fast spin echo protocol (TR=400,TE=16 ms, FOV=220*220 mm) in 3 minutes and 40 seconds. The real time MRI brain images are obtained from Kovai Medical Center and Hospital (KMCH, Signa SP, and GE Medical Systems), Primal Hitech MRI and CT Scan Center and kovai scan center.

Image pre-processing indicates whether the same tissue type has a different scale of signal intensities for different images or not. In this research work pre-processing is done in two stages. In the first stage film artifacts such as labels and X-ray marks from the MRI Image are removed using Tracking algorithm. In the second stage the non - brain skull portion is removed by using another efficient Dual Threshold-Morphological (DTM) skull stripping algorithm. It is also called as modified skull stripping algorithm.

1.10.2 Enhancement of MRI Brain Image

The pre-processed MRI brain image is further enhanced by two stages namely contrast enhancement and de-noising. Contrast enhancement is done by employing point operations and histogram manipulations. The validation of enhancement is subjective as the visual assessment is enough to evaluate the enhancement performance. However in this work Peak Signal to Noise Ratio (PSNR) value is used as a performance metric. The enhanced image still contains a high intensity salt and pepper noise which appears due to the presence of gray scale variations in the image which is removed by applying suitable smoothing or de-noising techniques and performing normalization. In this work de-noising is done using neighborhood operations. The performance evaluation of de-noising techniques is estimated in terms of PSNR value. The implemented Adaptive Centered Weighted Median (ACWM) filter has achieved high PSNR value of 23.65 dB. The advantage of using the ACWM filter is that it removes the noise without disturbing the edges.

1.10.3 Segmentation of Suspicious Region

Segmentation is an important process to extract information from complex medical images. It has wide application in the medical field. The main objective is to partition an image into mutually exclusive and exhausted region so that each Region of Interest (ROI) is spatially contiguous and the pixels within the regions are homogeneous with respect to a predefined criterion. In the proposed system, the segmentation is performed using two methods. The first method is bilateral segmentation using registration segmentation technique with GA and the second one is single image segmentation using metaheuristic algorithms.

1.10.3.1 Bilateral Registration Segmentation

In bilateral registration segmentation technique, the normal image (referred as reference image) is compared with the patient image (referred as target image). The segmentation is performed by two effective methods namely Rigid Registration Segmentation (RRS) with GA and Non-Rigid Registration Segmentation (NRRS) with GA. Segmentation by RRS method is based on similarity measures which quantify the degree of similarity between intensity patterns in normal image and target image. Non Rigid registration is defined as a deformation field that gives a translation or mapping for every pixel in the image. These registrations are capable of locally warping the target image to align with the reference image. Non rigid transformations include radial basis functions, physical continuum models (viscous fluids), and large deformation models. Segmentation by NRRS is block based. Hence suspicious region is segmented using two algorithms namely RRS -GA and NRRS -GA.

1.10.3.2 Single Image Segmentation by Metaheuristic Algorithm

Single image segmentation is performed using MRF- MAP-PACO technique. Ant Colony Optimization (ACO) is a population based metaheuristic approach and is inspired by the observation of real ants' colony. In this work MRF- MAP-PACO algorithm is implemented to select the global optimum label by reducing MAP estimate. Hence the pixels having this optimum label are extracted from the original brain image and form the segmented image. Performance evaluation is made and computational result indicates that MRF-MAP-PACO improves the performances of the segmentation and can find the optimum solution faster than the other methods.

1.10.4 Classification of Suspicious Region

In the fourth phase classification has been performed. Classification aims in finding the best class of segmentation. In this work, classification is planned at finding correlation between the proposed system results and the radiologist results based on PSI.

In performance evaluation, ROC curve is used as performance indicator. Performance evaluations determine how well a system performs relative to some requirement. It is determined through PSI methods namely pixel accuracy, position accuracy and overall accuracy.

New CAD System is developed for verification and comparison of brain tumor detection algorithm. The proposed system is tested on real time MRI brain images and also on simulated brain images to detect and verify the classification accuracy. MRF-MAP-PACO automatically determines the optimal intensity value of given image. In all the proposed approaches, the influence of MRF-MAP-PACO technique overlaps 96.89% of the specified region and hence it is computationally more efficient. The flow diagram of the proposed System is shown in Figure 1.1.

Based on this CAD framework, the paper entitled" Structural Modeling and Analysis of CAD System: A Graph Theoretic Approach ", is published in the International Journal of Computer Science and Applications, Vol. 2, pp.5-8, 2009. (ISSN: 0974-9667).

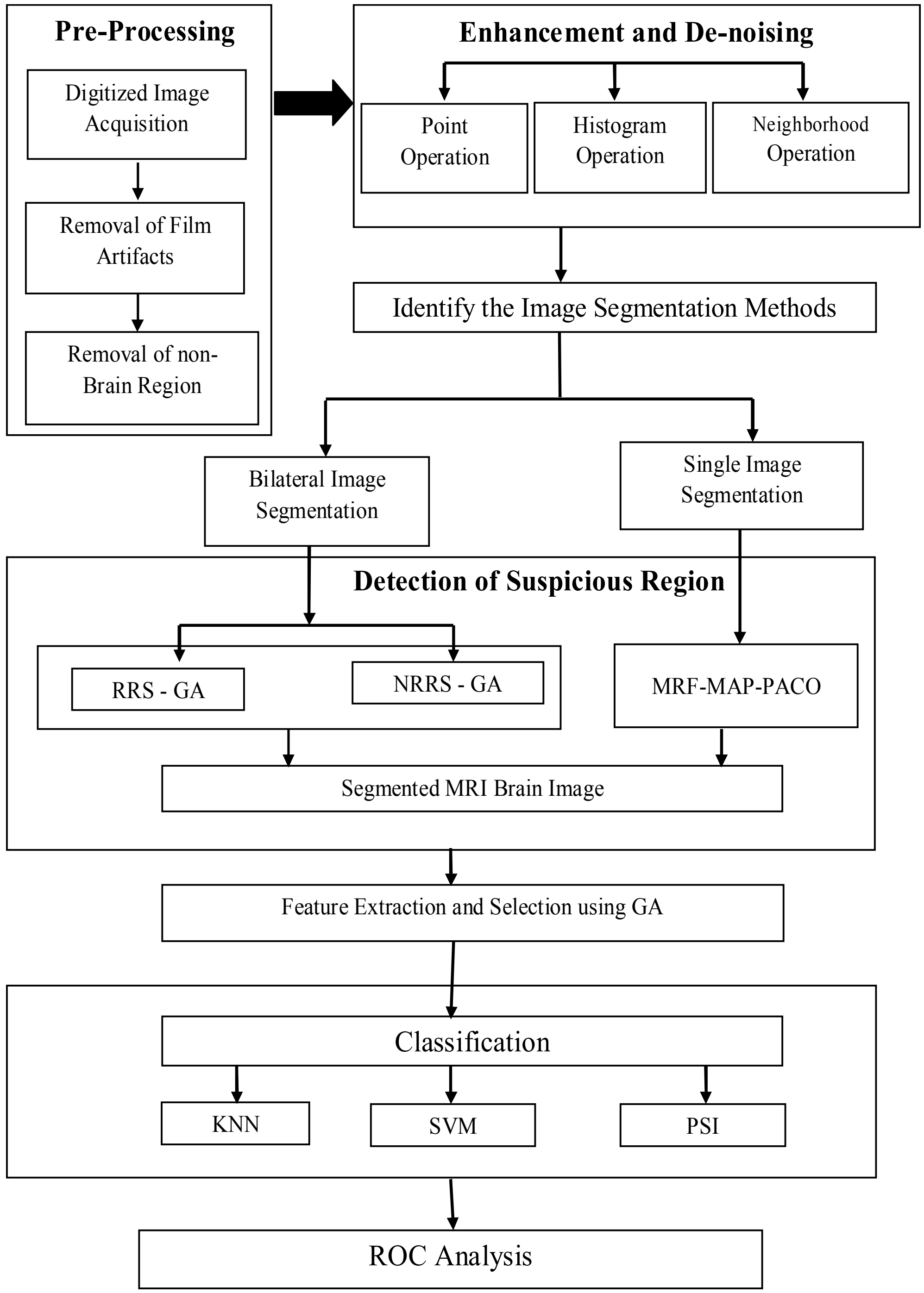

Figure 1.1 Flow Diagram of the Proposed CAD System for Brain Tumor

1.11 ORGANIZATION OF THE THESIS

The proposed CAD system consists of four subsystems namely image acquisition and pre-processing, enhancement, segmentation and classification subsystems. In this thesis, RRS-GA, NRRS-GA, and MRF-MAP- PACO methods are proposed for image segmentation. The thesis is organized with six chapters as follows:

Chapter 1 deals with the introduction to brain tumor and CAD system. An outline of medical imaging techniques of brain tumor and the need of metaheuristic algorithms for CAD system is briefed.

Chapter 2 describes the pre-processing and enhancement details. Tracking algorithm and skull stripping algorithm have been proposed for pre-processing the images. Conventional spatial domain enhancement techniques such as point processing and neighborhood processing are discussed and a new ACWM filter is implemented and the simulation results are compared with the existing techniques.

Chapter 3 illustrates bilateral image segmentation using registration segmentation algorithms. Registration segmentation is done by RRS-GA and NRRS-GA. The performance analysis has been evaluated.

Chapter 4 discusses the single image segmentation by MRF- MAP-PACO. The computational results are compared with the existing techniques.

Chapter 5 deals with the classification using PSI technique which analyses the pixel similarity between segmented results with the Radiologist's report. The performance evaluation of the CAD system is done by ROC.

Chapter 6 summarizes the work presented in the Thesis. The main contribution of the Thesis is highlighted and suggestions are made for future work.