CHAPTER 1
INTRODUCTION

1.1. Introduction

Computers have been successfully applied to various fields of medical sciences such as biochemical analysis, drug development and recognition of diseases from medical images. Visual interpretations of medical images are used for the early detection and diagnosis of diseases. The decision based on visual interpretations depends on the ability of the physicians to distinguish certain patterns or shape of the image. Diagnostic accuracy can be improved by providing additional information, generated by computational methods that cannot be obtained by simple visual interpretations. As a result, Computer Aided Diagnosis (CAD) has become one of the major research subjects in medical imaging and diagnostic radiology.

Successful identification of lung cancer, brain tumor is possible with the existing CAD. However, little research has been focused on liver because of the difficulties in segmenting liver from other adjacent abdominal organs such as kidney, stomach and gall bladder using abdominal images due to gray level similarities of adjacent organs. The most common medical imaging studies for early detection and diagnosis of liver diseases include Ultra Sonography (US), Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) [1].

A CAD can assist radiologist and physicians in detecting lesions and in differentiating benign and malignant lesions on medical images. The results obtained from CAD can be used as a "second opinion" by radiologists in their interpretations which improve diagnostic accuracy [2]. A number of CAD schemes have been developed for detection and classification of lesions in medical images. Performance studies indicate that the computer
output helped radiologists to improve their diagnostic accuracy. As, CAD can be applied to all imaging modalities, all body parts and all kinds of examinations, it is likely that CAD will have a major impact on medical imaging and diagnostic radiology in the 21st century [3].

1.2. Problem Statement

The study and development of Neural Networks for medical image analysis to characterize diffused liver diseases like fatty and cirrhosis and focal liver diseases like benign (hepato cellular adenoma, hemangioma) and malignant (hepato cellular carcinoma, cholangio carcinoma) tumors is reported in this work. Neural networks are chosen for recognizing diseases from the features extracted from the liver images as there is no need to provide a specific explicit technique on how to identify the diseases. The neurons and networks supposed to learn from examples and store this knowledge in a distributed way among the connection weights for recognizing diseases. Preprocessing of liver images, the region of interest identification, segmentation, feature extraction and feature selection are done using image processing techniques.

Adaptive threshold decision based on histogram analysis, morphological operations, Fuzzy C Means clustering and biorthogonal wavelet based texture analysis are used for processing the liver images. Extracted features are optimized by Sequential Backward Search (SBS), Sequential Forward Search (SFS), Sequential Forward Floating Search (SFFS) and Genetic Algorithm (GA) to reduce the cost of qualifier. Neural networks used for classification are Probabilistic Neural Network (PNN), Learning Vector Quantization (LVQ) Neural Network and Back Propagation Neural Network (BPN).

As a part of this research work, a prototype was developed for identifying diffused liver diseases like fatty and cirrhosis and focal liver diseases like hepato cellular carcinoma,
cholangio carcinoma, hemangioma and hepato cellular adenoma using liver images with satisfactory performance. The end product is typically aimed to provide physicians with a reliable second opinion during their medical decision process and improves diagnostic accuracy. Since neural networks excel in statistical pattern recognition tasks [4] a broad bottom up approach to the problem was adopted.

The computer analyzes the images with computer vision techniques specially designed for diseases. At the same time the radiologist also examines the images and evaluates the likelihood of the diseases. The radiologist then compares the two results and makes a final decision. If there is a big difference between the radiologist’s judgement and computer’s diagnosis, the patient can be called back for a second look. Computer is not going to replace the radiologist entirely, but the technology is meant to complement the radiologist’s judgement.

1.3. Motivation

Liver diseases are taken seriously, because liver is vital important to the life of a patient. Liver is one of the largest organ in the human body located in the upper right portion of the abdomen. The liver has many important functions, like clearing toxins from the blood, metabolizing drugs, blood proteins and produce bile which assists digestion [5]. Liver can be permanently damaged due to different reasons which include virus infections, reaction due to drugs or alcohol, tumors, hereditary conditions and problem with the body's immune system. Liver diseases constitute a major medical problem of worldwide proportions. Approximately 50% of the people [6] are affected by liver diseases.
Liver diseases are mainly classified into diffused liver diseases (Table 1.1.) and focal liver diseases (Table 1.2.) based on the dispersion in the pathology [7,8]. Diffused liver diseases are distributed throughout the whole liver volume whereas focal liver diseases are concentrated in small spots in one or both of the liver lobes while the rest of the liver tissues remain normal.

Table 1.1. Diffused Liver Diseases

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Disease Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fatty Liver</td>
</tr>
<tr>
<td>2</td>
<td>Cirrhosis Liver</td>
</tr>
<tr>
<td>3</td>
<td>Steatosis</td>
</tr>
<tr>
<td>4</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>5</td>
<td>Jaundice</td>
</tr>
<tr>
<td>6</td>
<td>Acute Liver Failure</td>
</tr>
<tr>
<td>7</td>
<td>Drug induced liver disease</td>
</tr>
</tbody>
</table>

Table 1.2. Focal Liver Diseases

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Disease Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Malignant Tumor (cancerous)</td>
</tr>
<tr>
<td>a.</td>
<td>Hepato cellular carcinoma</td>
</tr>
<tr>
<td>b.</td>
<td>Cholangio carcinoma</td>
</tr>
<tr>
<td>2</td>
<td>Benign Tumor</td>
</tr>
<tr>
<td>a.</td>
<td>Hepato cellular adenoma</td>
</tr>
<tr>
<td>b.</td>
<td>Hemangioma</td>
</tr>
<tr>
<td>c.</td>
<td>Focal nodular hyperplasia</td>
</tr>
<tr>
<td>3</td>
<td>Metastatic Disease</td>
</tr>
<tr>
<td>4</td>
<td>Ascites</td>
</tr>
<tr>
<td>5</td>
<td>Cysts</td>
</tr>
<tr>
<td>a.</td>
<td>Simple Hepatic cysts</td>
</tr>
<tr>
<td>b.</td>
<td>Congenital Hepatic cysts</td>
</tr>
<tr>
<td>c.</td>
<td>Polycystic Liver disease</td>
</tr>
</tbody>
</table>

Fatty and cirrhosis are the common diffused diseases. Fatty liver is an accumulation of fat cells in the liver which is common in diabetic patients or patients suffering from obe
weight. Cirrhosis is a group of chronic liver diseases in which normal liver cells are
damaged and replaced by scar tissue, decreasing the amount of normal liver tissue.
This is characterized by fibrosis and nodule formation. Fatty liver is highly attenuating and
echogenic, but cirrhosis liver has normal attenuation and echogenicity [9].

Focal liver lesions range from benign cysts to extremely aggressive hepato cellular
carcinomas and cholangio carcinomas. Liver tumor is also an example of focal liver disease.
Tumor is a growth of tissue in which the tissue cells multiply in an uncontrolled
fashion. Tumors can be either benign (non cancerous) or malignant (cancerous).
The most common benign tumors of the liver are hemangioma, hepato cellular adenoma
and focal nodular hyperplasia. The malignant tumors are hepato cellular carcinoma
and cholangio carcinoma.

A doctor may diagnose a disease on the basis of symptoms, laboratory test results,
patient’s medical history, physical examinations and scan reports. For example, during
physical examination, the doctor may notice that the liver is harder or larger than usual
and order blood tests that can show whether the disease is present. The doctor can ask
for a scan if it is needed. Focal liver lesions are frequently detected in patients undergoing
abdominal investigations. The liver tumors constitute a major diagnostic challenge for
radiological imaging, especially when cancer patients are involved.

Most benign tumors are found by chance on an imaging study of the liver,
such as ultrasound or CT scan. Occasionally, a biopsy may be required to make the
diagnosis of hepato cellular adenoma. Malignant tumors may be detected by screening
high risk patients or by chance on an imaging study of the abdomen performed for
another reason or may be detected because of symptoms such as abdominal pain. In
patients, who suffer from more advanced hepatocellular carcinoma, weight loss, periodic severe pain and other generalized symptoms may occur. The diagnosis of hepatocellular carcinoma is typically made by liver imaging tests such as abdominal ultrasonound and CT scan in combination with the measurement of blood levels of alphafeto protein. According to studies [10], it was found that statistically, the hepatoma, a malignant tumor is usually more coarse grained, while the hemangioma, a benign tumor, has more homogeneous textures, though the texture difference in these two types of disease images may not be easily observed by human eyes. In addition, the hemangioma usually has higher gray level intensity and contrast than hepatoma. The final diagnosis is confirmed by biopsy, which is typically performed by a radiologist who can direct the biopsy needle to the exact position of the tumor. It is very difficult even for an experienced clinician to perform the diagnosis about the existence, type, and the level of a disease.

Ultrasonography is inexpensive and non invasive. It can distinguish interfaces among soft tissue structures of different acoustic densities. It is an excellent test to screen the liver for bilary obstruction or gall bladder disease and to assess vascular patency. It is highly sensitive at differentiating a cyst from a solid liver lesion. However, it is not as sensitive as CT or MRI at detecting focal liver lesions [11]. CT offers the best spatial resolution and the ability to study the entire liver in a single breath hold. MRI has emerged as the best imaging test for liver lesion detection and characterization, because this modality provides high lesion to liver contrast and does not use ionizing radiation. The main drawbacks of MRI include its high cost, a long procedure time and the need for the patient to hold his breath for longer periods [12].
A liver biopsy is a simple, rapid method of obtaining a sample of liver tissues for analysis. It provides important information for evaluating and treating liver disorders. Although liver biopsy is considered to be the golden test for diagnosis in terms of accuracy, it has the disadvantage of being invasive and more importantly, it poses a risk of cancer spreading if it cuts through a localized cancer area [13, 14].

When several tests are involved, the ultimate diagnosis may be difficult to obtain, even for a medical expert during image interpretation because of their non-systematic search patterns and the presence of structure noise that camouflages the normal anatomic background. In addition, the vast amounts of data generated by some imaging devices makes detection of potential disease a burdensome task and may cause errors. Also, similar characteristics of some normal and abnormal lesions, as well as overlap in clinical information, may cause interpretational errors. Developments in computer vision and artificial intelligence in medical image interpretation have shown the potential for computers as providers of a “second opinion” in image interpretation. CAD systems leave the final diagnosis regarding the possible presence of disease and patient care to the radiologist [15]. Therefore, a method that is robust, fully automatable and capable of routine use in a clinical setting is desirable.

Research into potential applications of computational intelligence to the medical diagnostic process has blossomed over the last few decades. Early decision tree structures such as the expert system MYCIN for the diagnosis of blood infections, have been followed by the application of even more sophisticated statistical tools such as neural networks [16]. Medical diagnostic imaging applications date from early in this period with work by R.P.Kruger et al. [17] on automated diagnosis of pneumoconiosis being of particular
significance, and have been the focus of great activity in recent times. Commercial exploitation of this research has been comparatively slow. Some of the commercial devices and the date of patent registration given within brackets are AutoPop (9/95), Neuro Medical Systems Popnet (11/95), cervical cytology slide readers (6/98), R2 Technology Image Checker Screening Mammogram image analysis system (6/98), Logicon RDA carrier detection for diagnosis dental caries (9/98) and Deus Technologies Chest X Ray Medical Image Analyzer (10/2000).

Accordingly, this study motivated to develop a CAD system for diagnosing liver diseases such as fatty liver, cirrhosis liver, hepato cellular carcinoma, cholangio carcinoma, hepato cellular adenoma and hemangioma using liver images such as Ultrasonic liver images and CT abdominal images which are easily available in clinical routine.

1.4. Thesis Structure

An introduction to Computer Aided Diagnosis is given in Chapter 1. The Problem Statement and Motivation for developing the prototype is also discussed.

Surveys related to the research work and their findings are included in Chapter 2 to know the current status of the work. Also, it describes the Liver diseases considered in this work. Diagnostic Methods for investigating liver diseases including liver images, various Wavelet Transforms, Texture Description Methods, Feature Selection Methods like Sequential feature selection algorithms and Genetic Algorithm and Neural Network classifiers like PNN, LVQ and BPN are also discussed.

Chapter 3 portrays the System Outline of the proposed System and the methodology for liver extraction from CT abdominal images, tumor extraction from liver images, ROI selection
from Ultrasonic Liver Images, Biorthogonal Wavelet Based Statistical Texture Feature Extraction, Feature Selection and Classification of liver images.

Performance evaluation based on the classification using the parameters like Sensitivity, Specificity and ROC analysis is discussed in Chapter 4. The results are also evaluated with the help of radiologists.

Chapter 5 presents the results of the ROI segmentation. It illustrates the results of the Feature Selection, lists the investigations of the application of the PNN, LVQ, BPN neural networks and Minimum Distance Classifier for classifying liver diseases and shows the results of the performance measures. Also it summarizes the findings of the work.

Chapter 6 suggests that a much easier hardware implementation of tissue analysis functions can be provided in image acquisition machines like CT scanner and Ultrasound scanner in the future. The proposed system can be extended for the diagnosis of other types of liver diseases like cysts, ascites, and steotosis and also for other organs and medical images like MRI and PET.