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# CHAPTER ONE: INTRODUCTION

## Background to the study

The liver is the largest organ in the human body. It is responsible for all metabolic functions within the body from the conversion of nutrients within the diet into usable body substances to storing these substances and then supplying them to the cells when required. It is also responsible for the conversion of toxic substances into harmless substances. Other vital functions of the liver include bile production, protein production, storing and releasing glucose, processing haemoglobin, blood cleaning, immune factor production, clearing bilirubin, etc. Thus, it is the primary and most crucial body organ, and the maintenance of its health is essential for improved overall health. But the fact is that people generally overlook it in the case of health. Due to unhealthy lifestyle routines, most of the population across the globe are suffering from acute to severe liver problems. About 10 percent of the World’s population is affected by liver disease and around 5 percent leads to mortality (H. Devarbharvi, 2023).

Cirrhosis of the liver is a condition where the liver is scarred and permanently damaged; the healthy tissue of the liver has been replaced with scar tissue and impairs the functioning of the liver (NIDDK, 2023). It is commonly referred to as end-stage liver failure which has a high mortality rate. Cirrhosis of the liver in its early stages is hard to detect as it presents as asymptomatic but later stages of cirrhosis is categorized by redness of the urine, vomiting, sleep disorders, jaundice among a plethora of other symptoms. Some of the causal factors include excessive alcohol use, nonalcoholic fatty liver disease (buildup of fat in the liver), chronic infection of Hepatitis B and C etc.

The current methods used to identify the onset of liver cirrhosis include physical examination; checking for enlargement of the liver, the presence of hand tremors, and tenderness in the abdomen among other things; blood tests to determine the amount of liver enzymes present in the liver, the blood count of the individual to determine anemia and blood infection from internal bleeding, the presence of Hepatitis B and C by testing for viral infections; imaging tests such as Magnetic Resonance Imaging (MRI), computed tomography (CT), x-rays among others.

Current methods put in place, effective as they are, are time-intensive, expensive and do not indicate the onset of cirrhosis until the latter, less manageable stages. As technology advances, the need for earlier detection of cirrhosis will prove essential in reducing the mortality rates associated with liver disease. Early detection plays a pivotal role in improving the prognosis and increasing treatment success rates.

This study aims to introduce a system to detect in the early stages, liver scarring, indicative of liver disease aiding in the diagnostic process of patients, reducing the risk for higher complications, improving the quality of life of the affected, reduce the effect of type 2 errors during the diagnosis of patients and facilitate the easy management of affected patients.

The diagnosis of early stage liver cirrhosis using conventional means poses a risk of misdiagnosis in patients who do not present normal symptoms of liver Cirrhosis, which in turn worsens the risk of liver disease and ultimately liver failure. On account of this, the development of a detection system for this becomes essential.

## 1.2 Aim and Objectives

This project is geared towards the development of a web-based detection system for early stage liver cirrhosis detection using Convolutional Neural Network (CNN) model.

The specific objectives of these research are to:

1. Develop a machine learning based detection system to identify early stage liver cirrhosis
2. Implement risk predictions using identifiable qualities
3. Develop a liver disease classification
4. Implement of a simple, explanatory user interface to explain the results of the predictions
5. Generate an expected timeline of progression of the disease based off of historical data presented it.

## 1.3 Methodology

The methodology stated in this section delineates a structured and procedural approach to the development of a machine learning based liver cirrhosis detection system.

The machine learning based liver cirrhosis detection system will make use of computer vision. These techniques allow for processing of the image ensuring that images are scaled properly and allow for accurate predictions and classifications of diseases.

ReactJS will be used to develop a user-centric interface and allow consistent display of screens of different resolutions without compromise of user experience. The prediction and classification algorithms will be developed using the Python programming language owing to its simplicity in use, scalability and robust array of programming packages.

The Application Programming Interfaces (APIs) will be developed using Python’s FastAPI library and tested extensively using Postman and SwaggerDocs.

## 1.4 Scope of study

The scope of this study is tailored to address the needs of hospitals in the early stage diagnosis of cirrhosis, including low-budget medical facilities that may lack access to advanced imaging tools such as Magnetic Resonance Imaging (MRI), Computed Tomography (CT), Ultra-sonography (US), Elastography (FibroScan) and Magnetic Resonance Elastography (MRE).

Instead, these low budget medical facilities rely on x-rays for cirrhosis prognosis. By developing a web-based system accessible through common web browsers on mobile devices and a stable internet connection, we aim to enable easier prediction and classification of images obtained from the X-ray, MRI, CT, US and MRE.

This research will involve the utilization of processed datasets obtained from the kaggle platform

## 1.5 Methodology

The scope of this research project covers the design and implementation of a machine learning based liver cirrhosis detection system. The implemented system will be able to run on any mobile device with the presence of a web browser.

This project is geared towards medical institutions especially community and rural medical centers where medical instrumentation is almost absent and there’s a high prevalence individuals at risk of having the ailment without knowledge. It also aims to be a tool in the diagnosis of multiple liver conditions set on as a result of liver scarring.

## 1.6 Significance of the study

An importance of this study which cannot be overstated is the development of a predictive service which utilizes historical data to estimate the risk of liver cirrhosis in a particular individual. This feature will not only aid the early detection of liver scarring, which in turn may mitigate the risk of other underlying health conditions in those who do not have the facilities to carry out specialized liver biopsies. It also aims to allow the direct treatment of early stage cirrhosis in order to mitigate its impact.

## 1.7 Justification of the study

This significant contributions to the existing body of knowledge are to:-

1. Implement a test-based binary classification system that can detect if a person has liver cirrhosis using the images obtained from imaging tools like: X-ray, MRI, CT, US
2. Build a robust web-based system that can be accessible to medical facilities for early diagnosis of liver cirrhosis

## 1.8 Definition of Terms

1. **Liver Cirrhosis**: This is a condition in which the liver is scarred and permanently damaged. Scar tissue replaces healthy liver tissue and prevents the liver from working normally.
2. **Liver Cirrhosis Detection System:** A software program or platform that makes the detection of liver cirrhosis and allows for the detection of liver cirrhosis.
3. **Anemia:** This is a condition in which the body does not have enough healthy red blood cells.
4. **Machine Learning:** Machine learning is a subfield of artificial intelligence that uses algorithms trained on data sets to create models that enable machines to perform tasks that would otherwise only be possible for humans, such as categorizing images, analyzing data, or predicting price fluctuations (Coursera, 2023)
5. **Prognosis:** Prognosis is a term used in science and medicine which refers to determining the predicted or probable level of improvement in function, and the amount of time needed to reach that level of improvement in a health condition.
6. **Classification:** Classification is a supervised machine learning method where the model tries to predict the correct label of a given input data. In classification, the model is fully trained using the training data, and then it is evaluated on test data before being used to perform prediction on new unseen data.(Datacamp, 2022)
7. **Prediction:** Machine learning prediction, or prediction in machine learning, refers to the output of an algorithm that has been trained on a historical dataset.

## 1.9 Organization of Chapters

**Chapter 1:** This chapter has successfully examined the conceptual introduction of the design and implementation of a machine learning based liver cirrhosis detection system. This chapter also identified the need for carrying out this study and highlighted the major objectives of the study under review, as well as the proposed methodology.

**Chapter 2:** This chapter briefly discusses major concepts and theories associated with the implementation of a machine learning based liver cirrhosis detection system as well as the approaches adopted in related and existing systems alongside examples of similar systems already in place. It also discusses the limitations of the stated systems.

**Chapter 3:** This chapter discusses the system analysis and design as they are applied to this project. The chapter analyses the current system and proposed system as well as methods of implementation.

**Chapter 4:** This chapter discusses the processes used to implement the system design software solution and management of other developmental constraints.

**Chapter 5:** This chapter is the last and serves as the conclusion. It includes a summary of the entire project, results, findings and recommendations for further study.



# CHAPTER TWO: LITERATURE REVIEW



## Introduction

The early identification of liver cirrhosis plays a pivotal role in enhancing patient prognosis and managing the disease effectively. In recent years, the integration of machine learning (ML) into medical research has shown remarkable potential for revolutionizing diagnostic processes. Specifically, in the context of liver health, Machine Learning algorithms offer a unique capability to discern intricate patterns within vast datasets, presenting an opportunity for detecting subtle indicators of cirrhosis at its nascent stages. This literature review delves into the current body of research dedicated to employing ML techniques in the early diagnosis of liver cirrhosis. By examining the methodologies, datasets, and outcomes of previous studies, this review aims to provide a comprehensive understanding of the landscape, thereby establishing the foundation for the present research endeavor and the identification of potential pitfalls of the previous systems.

## Historical Background of research

The liver regulates most chemical levels in the blood and excretes a product called bile. This helps carry away waste products from the liver. All the blood leaving the stomach and intestines passes through the liver. The liver processes this blood and breaks down, balances, and creates the nutrients and also metabolizes drugs into forms that are easier to use for the rest of the body or that are nontoxic. More than 500 vital functions have been identified with the liver. Some of the more well-known functions include the following:

1. Production of bile, which helps carry away waste and break down fats in the small intestine during digestion

2. Production of certain proteins for blood plasma

3. Production of cholesterol and special proteins to help carry fats through the body

4. Conversion of excess glucose into glycogen for storage (glycogen can later be converted back to glucose for energy) and to balance and make glucose as needed

5. Regulation of blood levels of amino acids, which form the building blocks of proteins

6. Processing of hemoglobin for use of its iron content (the liver stores iron)

7. Conversion of poisonous ammonia to urea (urea is an end product of protein metabolism and is excreted in the urine)

8. Clearing the blood of drugs and other poisonous substances.

Cirrhosis is a recognized liver disease that poses a threat to people globally. According to (S. Khan & Saxena, 2020) Cirrhosis of the liver is the late stage of liver disease in which healthy liver tissue has been gradually replaced with scar tissue. Cirrhosis is the final stage attained by various chronic liver diseases after years or decades of slow progression as mentioned by (Younossi et al., 2020). (Agbim & Asrani, 2019) emphasized that Liver cirrhosis is the final pathological result of various chronic liver diseases, and fibrosis is the precursor of cirrhosis. While liver fibrosis is the first stage of liver scarring and can be reversible, liver Cirrhosis is the terminal stage of liver scarring and it’s non-reversible. The common risk factors of Liver Cirrhosis include:

1. Chronic hepatitis B.

2. Chronic hepatitis C.

3. Chronic excessive alcohol intake.

4. Fatty liver disease (non-alcoholic steatohepatitis)

5. Autoimmune liver disease (autoimmune hepatitis, primary biliary cirrhosis or primary sclerosing cholangitis)

Cirrhosis often has no symptoms until the liver damage is severe. At the early of liver damage, patients may experience fatigue, weakness and weight loss(Yoshiji et al., 2021). During later stages, patients may develop jaundice (yellowing of the skin), gastrointestinal bleeding: this is a sign of disorder in the digestive tract, abdominal swelling and confusion.

### **Early diagnosis of Liver Cirrhosis**

After conducting 500 autopsies, the process of detecting organ diseases through the study of abnormal changes or diseases that affect specific organs within the human body was identified by the first anatomist pathologist, Giovanni Battista Morgagni (1682-1771) in his 1761 seminal mechanistic book, *De sedibus et causis morborum per anatomen indagatis*(Mousa & Kamath, 2021a)*.* Furthermore, in 1819, the name Cirrhosis was concocted by Rene Theophile-Hyacinthe Laennec (1781-1826), a French man and the inventor of stethoscope. Although he wasn’t the first to discover this end-stage terminal liver disease but he was the originator of the term Cirrhosis, which was coined from the Greek word “cirrhosis” meaning tawny, referring to the yellow nodules associated with this liver disease(Mousa & Kamath, 2021b).

Unfortunately, the deadly liver disease known as “Cirrhosis” has been in existence since the 17th century till date. During the ancient times, the Cirrhosis terminology was not very clear which caused confusion in interpreting early abnormalities associated with the liver. Hard liver, associated with Jaundice during the 17th century was known as a bad sign. Jaundice is a symptom of Cirrhosis characterized with the yellowing of the skin, eyes, mucous membranes and secretions, indicating liver dysfunction. During the Greek classical times, Hippocrates, who was a Greek physician and also known as the father of medicine would diagnose medicine for this Jaundice disease which led to hard liver for the Greeks and Romans (Mousa & Kamath, 2021c). Later on, in 1851, Addison and Gull at Guy's Hospital Report, wrote a report on the study titled, "*On a certain affectation of skin-vitiligoiedea-alpha plana-beta tuberosa*(Addison T, 1851)". This study included early description and understanding of clinical manifestations and skin findings associated with what is now known as Primary Biliary Cholangitis (PBC).

In 1930, seventy-one years later, Hans Poper(1903-1988), the known father of modern hepatology, including early researchers proposed the initial explanation for the development of the Cirrhosis condition: a sequence involving tissue degeneration, regeneration and scarring as mentioned by (Kaiser et al., 2020), which is now recognized in the recent years as (1) Injury: The liver experiences damage, (2) Degeneration: The liver cells starts to break down , (3) Fibrosis: Scar- like tissue forms in the liver, (4) Formation of Fibro-Vascular Membranes: Supportive structure similar to thin membranes develop, (5) Parenchymal dissection into nodules: Liver tissue breaks into small, separate nodules or groups, (6) Rearrangement of blood circulation: Blood flow through the liver adjusts and changes, (7) Cirrhosis: The liver undergoes significant changes and becomes scarred. (Ignat et al., 2020) called this process a “self-perpetuating irreversible process”. (Ahrens et al., 1950) coined the term Biliary Cirrhosis which was changed in 2014 to Primary biliary Cholangitis (PBC)(Blesl & Stadlbauer, 2021). PBC occurs when the body’s immune system mistakenly attacks its own cells, in this case the bile duct. It is a chronic liver disease that damages small bile ducts within the liver. The bile ducts are essential for the transport of bile, which aids in the digestion of fats. In PBC, inflammation in the bile ducts leads to the destruction of the bile ducts, causing bile to accumulate in the liver and leading to liver scarring or damage over time.

After early pioneers like Giovanni Battista Morgagni (1682-1771), Rene Theophile-Hyacinthe Laennec (1781-1826), Hans Poper (1903-1988) and the other medical inclined researchers, laid the foundation for the liver diseases diagnosis when it was still in its infancy stage, years passed and medical practitioners and researchers began to develop their understanding and knowledge of liver diseases, paving the way for development of diagnostic methods that can detect this deadly disease. The collaboration of medical practitioners with engineers has brought about the advent of different computer imaging methods that are classified based on how images are produced. It was the invention of these traditional imaging methods that has led to the transformative shift in the prognosis, diagnosis and treatment planning of the liver cirrhosis.

The introduction of traditional methods, including liver biopsy, a known gold standard (Neuberger et al., 2020) which has not just resulted in false negative misdiagnosis (Elastography Wikipedia, n.d.) but also necessitated blood transfusions or surgical intervention to stop the bleeding at the affected site in the patient (Neuberger et al., 2020) and also imaging studies through computer aided liver diagnosis systems such as: Computed Tomography (CT), Ultra-sonography (US), magnetic resonance imaging (MRI) and Elastography, have played crucial roles in the diagnosis of liver cirrhosis. The 2000s saw the introduction of a transient Elastography-based method for quantifying liver stiffness, particularly useful for fibrosis and cirrhosis assessment. Magnetic Resonance Elastography (MRE) emerged in the same period as an advanced MRI-based technique, providing accurate evaluations of liver fibrosis. Ultrasound Elastography, including shear wave and strain Elastography, gained prominence from the 2010s onwards for real-time assessment of liver fibrosis.

In recent years, there has been a decline in the number of liver biopsies due to the development of highly effective treatments for common indications such as viral hepatitis B and C (Jain et al., 2021). The accuracy of liver cirrhosis diagnosis has been significantly improved by various painless and non-invasive computer aided techniques that assist in structural analysis of the region of interest (ROI) (R. A. Khan et al., 2022). This computer aided diagnostic methods include, Ultra-sonography (US), Computed Tomography, Magnetic Resonance Imaging (MRI), and Elastography. Each of these imaging methods also known as modalities has contributed to the advancement of liver cirrhosis diagnosis in distinct ways. Firstly, CT, which combines x-rays and computer-processing, has facilitated the creation of detailed cross-sectional images of the body, enabling the detection of liver nodules and lesions (abnormalities)(Moghbel et al., 2018). Secondly, Ultra-sonography utilizes sound waves to generate real-time images of the liver, making it a preferred diagnostic tool. It is also employed to guide procedures like liver biopsies, ensuring precise targeting and minimizing risks (Mancini et al., 2018). Thirdly, MRI employs radio waves to produce detailed liver tissue images and assists in the identification and staging of liver fibrosis (Hoffman et al., 2020).

Elastography techniques, offer a non-invasive alternative to liver biopsy for assessing the degree of fibrosis by creating a visual map of the elastic properties and stiffness of the soft tissue, thereby reducing patient discomfort and associated risks (Agbim & Asrani, 2019). While Computed Tomography (CT), Magnetic Resonance Imaging (MRI) and Ultra-sonophraphy (US) are unable to offer any insight into the elasticity or stiffness in the liver’s tissue and the different stages of liver fibrosis, particularly in mild and early cases (Li et al., 2018), the advent of Magnetic Resonance Imaging system, a system particularly used in providing detailed information on soft tissues like the liver, integrated with Elastography has significantly enhanced our ability to identify and classify liver cirrhosis even in its fibrosis stage. Magnetic Resonance Elastography an advanced MRI-based technique, providing a non-invasive imaging modality, was first introduced and documented at Mayo Clinic by (Muthupillai et al., 1995). MRE is a form of Elastography that effectively utilizes magnetic resonance images (MRI ) to accurately measure and subsequently depict the physical attributes that is, the elasticity or stiffness of soft tissue in the body(Smith, 2022).

The implementation of Elastography across a considerable number of 2000 Magnetic Resonance Imaging (MRI) systems on a global scale, has granted MRE a Category I CPT code by the American Medical Association(Ehman, 2022). This acknowledgement is predicated on the clinical accessibility and reliability of MRE. MRE now serves as a secure, more agreeable and substantially less costly substitute to liver biopsy in the diagnosis of liver fibrosis, a precursor of liver cirrhosis. Again, despite these advancements, the MRE, challenges remain. For instance, Quality of images can be affected by factors such as background noises and metallic substance worn by the patient undergoing examination, causing the imaging acquisition method to produce blurry images. Additionally, the quality of images and measurements can be influenced by the operator's skill and experience, especially in the case of Ultrasonography and Elastography (Moga et al., 2018).

In light of these persistent challenges, the application of predictive models in identifying and assessing liver diseases to aid in early diagnosis, prognosis, and treatment planning emerges as a promising solution. These models utilize diverse data sources, including clinical information, imaging studies, and laboratory results, to enhance accuracy and efficiency.

### **Application of Machine Learning models**

Research using machine learning techniques to detect early stages of liver cirrhosis has developed against the backdrop of advances in medical diagnostics and artificial intelligence. Cirrhosis is a chronic liver disease characterized by the replacement of healthy liver tissue with scar tissue, and there are often no symptoms in the early stages. Therefore, early detection is critical for effective intervention and treatment. CT, MRI and US as previously mentioned are filled with several limitations due to the inability to detect the elasticity and rigidness of the diseased liver, however a powerful tool like MRE, a non-invasive, cost-effective and an alternative to liver biopsy emerged, revolutionizing clinicians ability to detect and classify diseases even at its fibrosis stage. As we delve deeper into this subject, it will be of interest to explore how these medical imaging techniques intersect with machine learning, a branch of Artificial Intelligence and an intelligent software that has the ability to learn through data, statistics and experimentation in order to perform complex tasks at a much faster pace(Raschka et al., 2020).

Machines, inherently devoid of inherent intelligence, were initially engineered for specific functions such as analyzing financial data, diagnosing medical conditions, processing natural language, predicting weather patterns, and recognizing speech. Their ability to execute these tasks with unparalleled speed and precision has significantly simplified and improved various aspects of our lives. Machine learning, a branch of artificial intelligence, is dedicated to imbuing machines with the capability to perform these tasks a deptly through intelligent software.

At the heart of intelligent software or machines lie statistical learning methods, serving as the cornerstone for the development of machine intelligence. Since machine learning algorithms rely on data for effective learning, a close connection with the field of databases is imperative. Concepts like Knowledge Discovery from Data (KDD), data mining, and pattern recognition are commonplace, prompting exploration of the broader context wherein these connections become evident**.**

The utilization of different machine learning techniques in the evaluation of liver cirrhosis using historical data has significantly enhanced the prompt detection of liver cirrhosis in an individual. Machine learning models including, (1) Non-Linear Machine models like Decision trees, Random forest, (2) Deep-neural machine like Convolutional Neural Networks, Recurrent Neural Networks models and (3) Support Vector machines applied in image classification, medical diagnosis in classifying patients based on data, are used in (1) Preprocessing: The removal of unwanted elements like background noises in images and segmentation of region of interest in images, (2) Attribute analysis: The assessment of texture properties and (3) Classification analysis: Identifying and grouping region of interest to according to the type the specific region of interest fall on respectively(Meza et al., 2019).

Imaging-based predictive models, like radiomics and texture analysis, examine patterns within medical images (CT, MRI) that may not be visible to the human eye. They offer quantitative data for liver lesion or abnormalities characterization and assist in early identification and treatment response assessment. Genetic risk scores evaluate an individual's genetic predisposition to liver diseases, aiding in early intervention. Serum biomarkers (e.g., Alpha-fetoprotein antigen (AFT), Alanine Aminotransferase (ALT)) combined with clinical data create risk prediction models for diseases such as hepatocellular carcinoma (HCC).

Integration of multiple data sources, through multimodal predictive models, enhances overall accuracy by combining clinical, imaging, genetic, and biomarker data. These models contribute to a comprehensive assessment of liver diseases.

Population health models, including epidemiological and demographic models, predict disease prevalence and distribution in specific populations. They support public health planning and resource allocation for prevention and intervention programs.

The use of predictive models in liver disease identification continues to evolve. Ongoing research focuses on refining algorithms, incorporating new data sources, and enhancing interpretability, contributing to more personalized and effective approaches in liver disease management. Despite significant advances, the need for large and diverse datasets, ensuring model interpretability, and the use of machine learning for medical diagnosis. Challenges remain, including consideration of ethical considerations when using it.

Ongoing and future research may include improving existing models, exploring new biomarkers, and incorporating real-world clinical data to improve the robustness of early cirrhosis detection.

In summary, the historical development of research on early detection of liver cirrhosis using machine learning techniques has been shown to improve diagnostic accuracy, reduce invasiveness, and improve patient care by integrating advanced technologies in the field of hepatology reflects continued efforts to improve outcomes.

## Overview of existing system

1. **Title**: Machine learning improves early detection of liver fibrosis by quantitative ultrasound radiomics

**Publication Date**: October 2022

**Authors**: Maryam Al-Hasani, Laith R Sultan, Hersh Sagreiya, Theodore W Cary, Mrigendra B Karmacharya, Chandra M Sehgal

**Methodology:** The methodology used in the study involved the collection of ultrasound images of the liver from patients with varying degrees of fibrosis. The images were then analyzed using quantitative ultrasound radiomics, which involved the extraction of features such as echo intensity, heterogeneity, and entropy. Machine learning algorithms, such as logistic regression, naïve Bayes and multilayer perceptron, were then used to classify the images into early and advanced fibrosis groups based on the extracted features.

**Result Obtained:** The results obtained from the study showed that the use of quantitative ultrasound radiomics and machine learning algorithms improved the early detection of liver fibrosis. The study found that first-order histograms including echo intensity and heterogeneity were significantly higher in advanced vs. early stage fibrosis groups. The measure of variance, heterogeneity, also increased over time, likely corresponding to the generalized formation of collagen septate. The study also found that entropy, which represents the complexity of texture in images, showed a significant difference between the two groups.

The results indicated that logistic regression models with non-contrast (NC) images normalized using Gamma correction with γ = 1.5 performed best for fibrosis detection. The study also identified Boruta as the best radiomic feature selection method and highlighted the effectiveness of energy, kurtosis, and skewness as prominent features for fibrosis detection. The logistic regression models achieved mean test AUCs of 0.7549 and 0.7166 on biopsy-based and non-biopsy ROIs, respectively, outperforming baseline and best models found during the initial study.

**Gaps found**: -There was lack of independence between sequential images, there was controlled imaging protocol, not representative of clinical settings.

1. **Title**: A Comprehensive Study of Radiomics-based Machine Learning for Fibrosis Detection

**Publication date**: November 2022

**Authors:** Jay J. Yoo, Khashayar Namdar, Chris McIntosh, Farzad Khalvati, Patrik Rogalla

**Methodology**: The methodology used in the paper involves the extraction of radiomic features from CT images, followed by the selection of relevant features using a machine learning algorithm. The selected features are then used to train a classifier to distinguish between mild liver fibrosis and normal liver tissue.

**Result Obtained:** The results indicated that logistic regression models with non- contrast (NC) images normalized using Gamma correction with γ = 1.5 performed best for fibrosis detection. The study also identified Boruta as the best radiomic feature selection method and highlighted the effectiveness of energy, kurtosis, and skewness as prominent features for fibrosis detection. The logistic regression models achieved mean test AUCs of 0.7549 and 0.7166 on biopsy-based and non-biopsy ROIs, respectively, outperforming baseline and best models found during the initial study.

**Gaps found:** The paper highlights some gaps in knowledge and vulnerabilities in radiomic signature development. The authors note that the performance of radiomic signature-based models can be affected by factors such as image acquisition parameters, image preprocessing, and feature selection methods. They also point out that the lack of standardization in radiomic feature extraction and analysis can lead to inconsistencies in results. The authors suggest the need for safeguards to ensure the reproducibility and generalizability of radiomic signature-based models.

1. **Title:** A Deep Learning for Detecting Liver Cirrhosis form volatomic analysis of exhaled breath.

**Publication date:** February 2022

**Authors:** Mikolaj Wieczorek, Alexander Weston, Matthew Ledenko, Jonathan Nelson Thomas, Rickey Carter and Tushar Patel

**Methodology:** The methodology used in the study involves the application of a deep learning model (1D Convolutional Neural Networks) to detect the presence of liver cirrhosis in volatolomic profiles obtained from the analysis of exhaled breath samples from patients using Thermal Desorption-Gas Chromatography-Field Asymmetric Ion Mobility Spectrometry (TD-GC-FAIMS) and Thermal Desorption-Gas Chromatography-Mass Spectrometry (TD-GC-MS). The model's performance was evaluated, showing an Area under Curve (AUC) of 0.90 and a sensitivity of 100% at the patient level. Additionally, Shapely Additive Explanation (SHAP) analysis was employed to identify unique peaks associated with both positive and negative predictions, with 64% of the top 10 peaks being reproducible across multiple independently trained models.

**Result obtained:** The results obtained from the study demonstrate the feasibility of a non-invasive clinical screening exam for diagnosing and monitoring liver cirrhosis from non-invasive breath samples without the need for invasive detection and characterization methods.

**Gaps found:** The study also highlights certain gaps in knowledge. Further experimental work is needed to identify the specific compounds identified by the peaks, and ongoing subject recruitment focuses on the collection of additional samples to support the initial dataset and justify the recruitment of additional patient participants.

1. **Title:** Analysis of Vision-based Abnormal Red Blood Cell Classification

**Date of publication:**  May 2021

**Authors:** Annika Wong , Nantheera Anantrasirichai , Thanarat H. Chalidabhongse , Duangdao Palasuwan , Attakorn Palasuwan , David Bull

**Methodology:** The methodology used in the analysis involves the implementation of classification models such as Support Vector Model (SVM) and TabNet, as well as the semantic segmentation network U-Net. The models were trained using batch normalization to enable the use of higher learning rates, adaptive learning rate optimization using the Adam optimizer, and a stochastic method with a minibatch size of 4 due to memory constraints. Five-fold cross-validation was employed for all models, and due to memory constraints, only a portion of the augmented images could be used for the five-class model, while no augmented images could be used for the nine-class model.

**Results obtained:** The analysis highlights the need for alternative performance evaluation metrics due to the imbalance in the dataset, as high accuracy scores can be achieved by classifying all cells as normal in extreme cases.

**Gaps found:** The gaps in knowledge include the impact of memory constraints on the use of augmented images and the need for alternative approaches to address imbalanced datasets in the context of abnormal red blood cell classification

1. **Title:** Machine Learning with Abstention (LWA) for Automated Liver Disease Diagnosis

**Publication date:** November 2018

**Authors:** Kanza Hamid, Amina Asif, Wajid Arshad. Abbasi, Durre Sabih, Fayyaz-ul- Amir Afsar Minhas

**Methodology**: The methodology used in the study involves comparing the performance of the Learning with Absentation (LWA) method with conventional classification techniques, such as SVM and nearest neighbor classifiers, using a specific dataset and evaluation protocol.

**Result obtained**: The results obtained from the study indicate that the LWA approach is effective in comparison to conventional techniques, as it automatically detects low confidence in predicting certain examples and abstains from misclassifications. The paper also presents the implementation details of the LWA classifier, highlighting its efficiency in terms of processing time on a standard laptop.

**Gaps found:** Based on the findings, potential areas for further investigation could include the scalability of the LWA method to larger datasets, the generalizability of the approach to different domains, and the exploration of additional diagnostic techniques for cases where both the LWA method and medical experts find classification challenging.

1. **Title:** Prediction of chronic liver disease patients using integrated projection based statistical feature extraction with machine learning algorithms

**Publication date:** December 2022

**Authors:** Ruhul Amin, Rubia Yasmin, Sabba Ruhi , Md Habibur Rahman, Md Shamim Reza.

**Methodology:** The study compares the performance of various classifiers on the Indian Liver Patient Dataset (ILPD) and introduces a new method for prediction. The methodology involves the use of machine learning algorithms such as Logistic Regression, K-Nearest Neighbors, Random Forest, Support Vector Machine, Multi- Layer Perceptron, and Ensemble methods.

**Result Obtained:** The results obtained from the study show that the proposed method achieved an accuracy of 55.40% with Logistic Regression, 67.90% with K-Nearest Neighbors, 88.10% with Random Forest, 67.90% with Support Vector Machine, 83.53% with Multi-Layer Perceptron, and 82.09% with Ensemble methods. The study also includes a comparison of the proposed method with recent studies, showing that the Random Forest classifier achieved the highest accuracy of 88.10% and the highest AUC of 88.20% among all the classifiers tested.

**Gaps found:** The gaps in knowledge in this paper could include the need for further validation of the proposed method on larger and more diverse datasets to assess its generalizability. Additionally, the paper could benefit from discussing the limitations of the study, such as potential biases in the dataset, the interpretability of the machine learning models, and the clinical implications of the findings.



## Review of related works

The reviewed literature encompasses a range of articles focusing on the development of machine learning based methods for liver disease detection. Each article, published in different years and authored by various experts in the field, contributes unique perspectives and methodologies to advance the understanding and implementation of these technologies and as such aid in the facilitation for development of novel systems.

In ‘Machine learning improves early detection of liver fibrosis by quantitative ultrasound radiomics’ (Al-Hasani et al., 2022), the methodology entails the use of analyzed ultrasound images of the liver to extract features that were then used for classification. This paper, however, does not take into consideration the deployment of the model and variations in the quality of ultrasound.

In ‘A Comprehensive Study of Radiomics-based Machine Learning for Fibrosis Detection’ (Yoo et al., 2022), the methodology entails the use of radiomic features from CT images were used to train a classifier to distinguish between mild liver fibrosis and normal liver tissue. The study highlighted the impact of factors such as image acquisition parameters and feature selection methods on model performance. It also emphasized the need for standardization in radiomic feature extraction and analysis to ensure reproducibility and generalizability of models.

In ‘Deep Learning for Detecting Liver Cirrhosis from Volatolomic Analysis of Exhaled Breath’ (Wieczorek et al., 2022). A deep learning model was applied to detect the presence of liver cirrhosis in volatolomic profiles obtained from the analysis of exhaled breath samples. The study emphasized the need for further experimental work to identify specific compounds in the breath samples and to address memory constraints in image analysis

In ‘Analysis of Vision-based Abnormal Red Blood Cell’(Wong et al., 2021), an automated process was presented using machine learning to detect abnormalities in red blood cells. It analyzes the performance of three different machine learning technologies and addresses the issue of imbalanced datasets. The findings indicate promising methods for automating RBC abnormality detection.

In ‘Machine Learning with Abstention (LWA) for Automated Liver Disease Diagnosis’(Hamid et al., 2017), the proposed model (Nearest Neighbor identifier model uses a LWA method) can detect when its prediction is likely to be incorrect and the proposed model also offers the state of art classification performance.

In ‘Prediction of chronic liver disease patients using integrated projection based statistical feature extraction with machine learning algorithms’(Amin et al., 2023), the paper proposes an integrated feature extraction approach using machine learning algorithms to predict chronic liver disease patients. The proposed technique yielded better results compared to the latest existing studies, with improvements ranging from 0.10% to 18.5%.

## Strength and Weakness of existing system

1. **Title:** : Machine learning improves early detection of liver fibrosis by quantitativeultrasound radiomics

**Strength:**

* Logistic regression, naïve Bayes, and multi-class perceptron have been used as machine learning models, with high diagnostic performance observed for all three methods
* The system proposes to use machine-learning based approaches in utilizing quantitative Ultra-sonogram (US) radiomics to enhance sensitivity of B-mode US for early detection of liver fibrosis.
* Logistic regression models with NC images normalized using Gamma correction with γ = 1.5 performed best for fibrosis detection.
* The Boruta algorithm was the best radiomic feature selection method.

**Weakness:**

* No weakness was found in the proposed system

1. **Title:** A Comprehensive Study of Radiomics-based Machine Learning for Fibrosis Detection

**Strength:**

* The logistic regression models with Non-Contrast images normalized using Gamma correction with γ = 1.5 performed best for fibrosis detection.
* The Boruta algorithm was the best radiomic feature selection method.

**Weakness:**

* The performance of radiomic signature-based models used by the proposed system can be affected by factors such as image acquisition parameters, image preprocessing, and feature selection methods.
* The authors point out that the lack of standardization in radiomic feature extraction and analysis can lead to inconsistencies in results produced by the proposed system.

1. **Title:** A Deep Learning for Detecting Liver Cirrhosis form volatomic analysis of exhaled Breath

**Strength:**

* The system utilizes breath analysis to detect liver disease, specifically cirrhosis, using volatile organic compounds (VOCs) present in breath samples**.**
* The studies utilize different techniques such as thermal desorption-gas chromatography-mass spectrometry (TD-GC-MS), thermal desorption-gas chromatography-field asymmetric ion mobility spectroscopy (TD-GC-FAIMS), and deep learning approaches to analyze breath samples and identify biomarkers.
* The identified biomarkers show promise in distinguishing between healthy individuals and those with cirrhosis, as well as correlating with disease severity and blood metrics of liver function.
* A set of 29 breath Volatile Organic Compounds (VOC) differed significantly between cirrhosis and healthy controls with a sensitivity of 88-92% and specificity of 75%

**Weakness:**

* The proposed system has an accuracy with a sensitivity of 88-92% and specificity of 75%which means there is room for more improvement

1. **Title:** Analysis of Vision-based Abnormal Red Blood Cell Classification.

**Strength:**

* There was increased capacity and standardization of cell abnormality detection
* It presented promising method in automating Red blood cells (RBC) abnormality detection

**Weakness:**

* Highly imbalanced datasets used in the system was prone to affect the efficacy of machine learning processes used
* There were impact of unknown cells on semantic segmentation

1. **Title:** Machine Learning with Abstention (LWA) for Automated Liver Disease Diagnosis

**Strength:**

* The proposed model used (Nearest Neighbor Classifier) can detect when it’s prediction is likely to be incorrect
* The authors aim to extend this method to multi-class classification and evaluate its performance on a large independent test set with Elastography data.
* The authors also plan to build a publicly accessible webserver implementation of their method.

**Weakness:**

* The nearest neighbor classifier has low Area Under the Receiver Operating Characteristic Curve (AUC-ROC) and accuracy (57 and 82, respectively). AUC-ROC is a performance metric used to evaluate the accuracy of a binary classification model with the value ranging from 0 (means low) to 1 (means high).
* The proposed Learning with Abstention (LWA) classifier's performance is not mentioned.

1. **Title:** Prediction of chronic liver disease patients using integrated projection based statistical feature extraction with machine learning algorithms

**Strength:**

* The proposed technique yielded better results compared to the latest existing studies, with improvements ranging from 0.10% to 18.5%.
* The system achieved an accuracy of 88.10%, a precision of 85.33%, a recall of 92.30%, an F1 score of 88.68%, and an AUC score of 88.20% in predicting liver diseases. The F1 score ranges from 0 to 1, with a higher value indicating better performance.
* The system is based on the rapid advancement in artificial intelligence and machine learning algorithms, which have the potential to improve the lifespan of patients with chronic liver disease in the early stages.
* The authors also plan to build a publicly accessible webserver implementation of their method.
* The system can be used as a supplement to a physician's diagnosis of liver disease, enhancing the accuracy and effectiveness of the diagnosis

**Weakness:**

* The feature extraction stage using projection-based methods does not produce desired results.
* The proposed system has an accuracy of 88.10%, which suggests room for improvement.

## General Comments

The existing systems have applied different machine models and techniques to develop a non-invasive approach that would detect early stages of liver cirrhosis through the application of (1) radiomics features extracted from computed tomography (CT) images and ultrasound images and optimize early stages fibrosis detection, (2) machine learning models for automated diagnosis, (3) Volatomic Organic Compounds as a non-invasive approach of early diagnosis of liver cirrhosis and many more systems that aim to create an approach that wouldn’t affect the health of patient in the future and also cause discomfort for the patient during examination. However, despite all these creative approaches, there are gaps and shortcomings our system proposes to fill through the design and development of a web-based system that automatically uses predictive models to automatically segment and classify early signs and symptoms of liver cirrhosis that are not visible to the normal eyes utilizing patients historical data and images generated from the computer imaging method e.g. CT, MRI, MRE

**References**

Addison T, G. W. (1851). On a certain affection of the skin-vitilgoidea- α-plana β-tuberosa. In *Guys Hosp Rept* (Vol. 7, pp. G265-277).

Al-Hasani, M., Sultan, L. R., Sagreiya, H., Cary, T. W., Karmacharya, M. B., & Sehgal, C. M. (2022). Machine learning improves early detection of liver fibrosis by quantitative ultrasound radiomics. *IEEE International Ultrasonics Symposium:[Proceedings]. IEEE International Ultrasonics Symposium*, *2022*.

Amin, R., Yasmin, R., Ruhi, S., Rahman, M. H., & Reza, M. S. (2023). Prediction of chronic liver disease patients using integrated projection based statistical feature extraction with machine learning algorithms. *Informatics in Medicine Unlocked*, *36*, 101155.

Blesl, A., & Stadlbauer, V. (2021). The gut-liver axis in cholestatic liver diseases. In *Nutrients* (Vol. 13, Issue 3, pp. 1–32). https://doi.org/10.3390/nu13031018

Ehman, R. L. (2022). Magnetic resonance elastography: from invention to standard of care. *Abdominal Radiology*, *47*(9), 3028–3036. https://doi.org/10.1007/s00261-022-03597-z

Hamid, K., Asif, A., Abbasi, W., & Sabih, D. (2017). Machine learning with abstention for automated liver disease diagnosis. *2017 International Conference on Frontiers of Information Technology (FIT)*, 356–361.

Ignat, S.-R., Dinescu, S., Hermenean, A., & Costache, M. (2020). Cellular interplay as a consequence of inflammatory signals leading to liver fibrosis development. *Cells*, *9*(2), 461.

Kaiser, S., Sziranyi, J., & Groß, D. (2020). The hepatopathologist Hans Popper (1903–1988). *Der Pathologe*, *41*(1), 30–38. https://doi.org/10.1007/s00292-019-0619-y

Meza, J. K. S., Yepes, D. O., Rodrigo-Ilarri, J., & Cassiraga, E. (2019). Predictive analysis of urban waste generation for the city of Bogotá, Colombia, through the implementation of decision trees-based machine learning, support vector machines and artificial neural networks. *Heliyon*, *5*(11).

Mousa, O. Y., & Kamath, P. S. (2021a). A History of the Assessment of Liver Performance. In *Clinical Liver Disease* (Vol. 18, Issue S1, pp. 28–48). https://doi.org/10.1002/cld.1100

Mousa, O. Y., & Kamath, P. S. (2021b). An Official Learning Resource of AASLD review a History of the assessment of liver Performance. *28 | CliniCal Liver Disease*, *18*, 1. https://doi.org/10.1002/cld.1100/suppinfo

Raschka, S., Patterson, J., & Nolet, C. (2020). Machine learning in python: Main developments and technology trends in data science, machine learning, and artificial intelligence. *Information*, *11*(4), 193.

Smith, D. R. (2022). *Mechanical evaluation of structure and function in fibrous soft tissue using MR elastography*. University of Delaware.

Wieczorek, M., Weston, A., Ledenko, M., Thomas, J. N., Carter, R., & Patel, T. (2022). A deep learning approach for detecting liver cirrhosis from volatolomic analysis of exhaled breath. *Frontiers in Medicine*, *9*, 992703.

Wong, A., Anantrasirichai, N., Chalidabhongse, T. H., Palasuwan, D., Palasuwan, A., & Bull, D. (2021). Analysis of vision-based abnormal red blood cell classification. *ArXiv Preprint ArXiv:2106.00389*.

Yoo, J. J., Namdar, K., McIntosh, C., Khalvati, F., & Rogalla, P. (2022). A Comprehensive Study of Radiomics-based Machine Learning for Fibrosis Detection. *ArXiv Preprint ArXiv:2211.14396*.

Yoshiji, H., Nagoshi, S., Akahane, T., Asaoka, Y., Ueno, Y., Ogawa, K., Kawaguchi, T., Kurosaki, M., Sakaida, I., & Shimizu, M. (2021). Evidence-based clinical practice guidelines for liver cirrhosis 2020. *Journal of Gastroenterology*, *56*(7), 593–619.

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