

Ultrasound-based tissue characterization and classification of fatty liver disease: A screening and diagnostic paradigm



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ABSTRACT

Fatty Liver Disease (FLD) is a progressively prevalent disease that is present in about 15% of the world population. Normally benign and reversible if detected at an early stage, FLD, if left undetected and untreated, can progress to an irreversible advanced liver disease, such as fibrosis, cirrhosis, liver cancer and liver failure, which can cause death. Ultrasound (US) is the most widely used modality to detect FLD. However, the accuracy of US-based diagnosis depends on both the training and expertise of the radiologist. US-based Computer Aided Diagnosis (CAD) techniques for FLD detection can improve accuracy, speed and objectiveness of the diagnosis, and thereby, reduce operator dependability. In this paper, we first review the advantages and limitations of different diagnostic methods which are currently available to detect FLD. We then review the state-of-the-art US-based CAD techniques that utilize a range of image texture based features like entropy, Local Binary Pattern (LBP), Haralick textures and run length matrix in several automated decision making algorithms. These classification algorithms are trained using the features extracted from the patient data in order for them to learn the relationship between the features and the end-result (FLD present or absent). Subsequently, features from a new patient are input to these trained classifiers to determine if he/she has FLD. Due to the use of such automated systems, the inter-observer variability and the subjectivity of associated with reading images by radiologists are eliminated, resulting in a more accurate and quick diagnosis for the patient and time and cost savings for both the patient and the hospital.

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Abbreviations: ALT, Alanine Aminotransferase; AHP, Analytic Hierarchy Process; ASM, Angular Second Moment; ANN, Artificial Neural Network; CBR, Case-Based Reasoning; CART, Classification And Regression Tree; CWT, Continuous Wavelet Transforms; CAD, Computer-Aided Diagnosis; CT, Computed Tomography; DT, Decision Trees; DWT, Discrete Wavelet Transform; FFS, Far-Field Slope; FLD, Fatty Liver Disease; FDTA, Fractal Dimension Texture Analysis; FSC, Fuzzy Sugeno Classifier; GLCM, Gray Level Co-occurrence Matrix; GLDS, Gray Level Difference Statistics; RUNL, Gray Level Run Length Statistics; HOS, Higher Order Spectra; k-NN, k-Nearest Neighbor Classifier; LBP, Local Binary Pattern; MRI, Magnetic Resonance Imaging; MGL, Mean Gray Level; NAFLD, Non-Alcoholic Fatty Liver Disease; RBF, Radial Basis Function; SGLDM, Spatial Gray Level Dependence Matrices; SVM, Support Vector Machine; US, Ultrasound; WPD, Wavelet Packet Decomposition.

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1. Introduction

Fatty Liver (Steatosis) or Fatty Liver Disease (FLD) indicates accumulation of triglycerides (fat) in the liver. Fatty liver can occur with or without the intake of alcohol. In 1980, Ludwig et al. [76] named it as Non-Alcoholic Fatty Liver Disease (NAFLD) when the fatty liver condition is independent of alcohol intake. FLD has been associated to metabolic syndrome [127], and hence it leads to several diffuse and prevalent pathologies, such as diabetes mellitus, insulin resistance, hypertension, and dyslipidemia. The accumulation of fat in the liver may eventually lead to inflammation, condition called as alcoholic or non-alcoholic steatohepatitis (ASH or NASH) and finally to cirrhosis (which describes large scale liver degeneration associated with an increased risk of hepatocellular carcinoma [95,116,19]). Studies revealed that the prevalence of

FLD depends on sex [99], ethnicity [37], and age [52]. Overall, FLD affects about 15% of the world population [37,98]), and it is the most common reason for elevated liver enzymes and chronic liver disease in developed countries [18]. Early diagnosis of FLD is of paramount importance to prevent its degeneration into irreversible liver diseases, such as liver cancer [117] and acute liver failure [146]. FLD is also a major risk factor for heart attacks and stroke [138,139]. Furthermore, advanced liver diseases result in higher health care utilization, which implies higher cost for the health care provider [14].

Even though detection of FLD is easy, the differential diagnosis of FLD is difficult [149]. In fact, FLD might be linked to different factors, such as infections, inflammations, and drug or toxin-related injuries. Hepatic steatosis is usually categorized as macrovesicular or microvesicular [149]. Macrovesicular steatosis is a common occurrence in ambulatory patients, and microvesicular steatosis is associated with severe mitochondrial injury and acute hepatic dysfunction [149]. Therefore, liver biopsy is the preferred diagnostic technique for FLD detection [100]. However, biopsy is invasive, and it causes anxiety and discomfort to patients due to pain and the possibility of bleeding/hemorrhage [80]. These complications occur in at least 1.3% of all cases and the mortality ranges from 0.1% to 0.5% [17]. Given the relatively high prevalence of FLD in the general population, minimal invasive procedures have been developed for FLD diagnosis and the assessment of its degree of severity. Among all noninvasive techniques, Ultrasound (US) is the most common and widely used imaging modality for FLD diagnosis, because it is (a) inexpensive, (b) emits no harmful radiation, (c) is widely available and (d) has high sensitivity. A major downside of this imaging modality is the operator dependability [135]. Computer Aided Diagnosis (CAD) systems have been and are being developed as adjunct techniques to reduce operator dependability and to get reproducible results [30,39,113,125,49,144]. Therefore, developing CAD systems that detect early stage FLD is of utmost importance to: (a) save patients from unwanted anxiety, (b) increase the chance of recovery and (c) reduce the cost associated with providing treatments for advanced liver diseases [7].

In this paper, we first review the advantages and limitations of current modalities that are used for FLD detection (Section 2). Subsequently, we discuss the structure of an US-based CAD system and briefly describe the features that are extracted from the US images and the commonly used classification algorithms (Section 3). We then review the methodology and evaluation results of several CAD systems proposed in the literature (Section 4). In these techniques, first informative features are extracted from the US images. The features are used as input to train automated decision making systems. Coupling feature extraction with automated classification provides a way to evaluate the features in a practical setting, i.e. it is a way to find out how useful these features are for a working radiologist. After careful analysis of the literature, we found that the US-based CAD techniques for FLD can improve accuracy, speed and objectiveness of the diagnosis, and thereby, reduce operator dependability. We conclude the paper in Section 5.

2. Literature review

2.1. Liver

The liver is the heaviest and the largest glandular organ in the human body and it is absolutely crucial to life [12]. The liver performs vital functions: synthesis of proteins, fats and fatty acids, metabolism and storage of carbohydrates, and bile production and excretion. It maintains both volume and quality of blood by filtering potentially harmful biochemical products from the blood. One of these harmful products is bilirubin, which forms during

the breakdown of old blood cells [134]. Another harmful product is ammonia, which forms during the breakdown of proteins [75]. The human body produces both bilirubin and ammonia constantly. The liver is also responsible for filtering harmful substances from external sources, such as drugs, alcohol and environmental toxins. Thus, any disturbance to these detoxifying functions leads to poor health.

2.2. Liver disease

Liver disease can be due to infection, injury, drug exposure, toxin presence, autoimmune processes, or genetic defects that result in the accumulation of iron or copper. Liver disease results in inflammation, scarring, fibrosis, obstructions, clotting abnormalities, and liver failure [132]. A common example of liver disease, which is gaining increasing recognition worldwide, is FLD [78].

2.3. Fatty Liver Disease (FLD)

FLD is a spectrum of conditions, which are predominantly characterized by hepatic steatosis, the accumulation of fat-containing vacuoles within hepatocytes [28]. This accumulation of triglyceride fats happens through a process of steatosis, whereby there is an abnormal retention of lipids within cells [117,94]. Chronic alcohol abuse is one of the main causes of FLD. About 90% of individuals who drink more than 60 g of alcohol a day develop FLD [25]. Other causes of FLD include insulin resistance and all forms of the metabolic syndrome, such as obesity, Type 2 diabetes, arterial hypertension, and hyperlipidemia [1]. Based on the causes, there are two FLD types: Alcoholic Steatosis and Non-Alcoholic Fatty Liver Disease (NAFLD). The term FLD can indicate asymptotic steatosis, with elevated or normal aminotransferases to steatohepatitis, cirrhosis with liver function complications, and even hepatocellular carcinoma [11]. For milder forms of FLD, the accumulation of excess fats in the liver is usually benign and fully reversible [101]. Left untreated, the disease is likely to progress further to irreversible advanced forms.

2.4. Diagnosis of Fatty Liver Disease (FLD)

Early and accurate diagnosis of FLD is of significant clinical importance, because disease incurred damage can often be reduced or reversed with proper treatment. It also helps health care providers by reducing the number of subjects with advanced liver diseases. Hence, the overall healthcare cost comes down. The diagnosis of FLD requires evidence of fatty liver tissues. Currently, a range of methods is used to obtain this information. These methods are classified as invasive [101] and noninvasive [95,20,41,86,128,104]. We briefly describe these diagnosis methods in the following paragraphs, and present a summary of these methods along with their advantages and limitations in Table 1.

2.4.1. Blood tests

Liver function blood tests are one of the most commonly performed analysis steps during routine medical checkups. The blood drawn from a patient undergoes centrifuge treatment and the resultant blood serum is then subjected to a battery of tests. These tests can assess basic liver functions, liver injury and liver diseases, like FLD. For example, the presence of certain enzymes (proteins) in the blood indicates liver damage or liver disease [114]. Usually, these enzymes are present within the liver cells. In the event of liver damage, due to disease or injury, these enzymes spill into the blood stream where they can be detected by routine blood tests. Among these blood tests, aminotransferase is the most sensitive detector of FLD [63], and the related tests are called Aspartate Aminotransferase (AST) test and Alanine Aminotransferase (ALT)

Table 1
Summary of the clinical examinations used for the assessment of fatty liver disease.

Technique	Advantages	Limitations
Blood tests	<ul style="list-style-type: none"> - Assessment of basic liver functions - High sensitivity to increased levels of AST and ALT 	<ul style="list-style-type: none"> - Poor specificity - No correlation with the degree of liver damage
Biopsy	<ul style="list-style-type: none"> - Correlates with degree of liver damage - Examination with prognostic value 	<ul style="list-style-type: none"> - Invasiveness - Potential complications, such as bleeding/hemorrhage and pain - Operator dependent
Computed Tomography	<ul style="list-style-type: none"> - Depicts steatosis by lower liver intensity - Quantitative measurement 	<ul style="list-style-type: none"> - Poor sensitivity for early steatosis - Inter-equipment variability - Use of ionizing radiation
Magnetic Resonance Imaging	<ul style="list-style-type: none"> - Good quantification of the fat content of the liver - Possibility of spectroscopy analysis 	<ul style="list-style-type: none"> - Fat quantification inaccuracies in the presence of high iron concentration - High cost of examination
Ultrasound	<ul style="list-style-type: none"> - Prescribed for initial diagnosis - Low cost, non-invasive, safe - High specificity for fat accumulation higher than 33% 	<ul style="list-style-type: none"> - Unsuitable for subjects with implanted electronic devices - Operator dependent - Unsuitable for subjects with high Body Mass Index (BMI) - Intra-operator variability

test. The normal range of AST is between 5 and 40 units per liter of serum, and the range of ALT is between 7 and 56 units per liter of serum.

Limitation of blood tests – even though AST and ALT are sensitive indicators of liver damage, there are several limitations. In general, higher than normal enzyme levels do not automatically equate to liver disease or damage. The interpretation of elevated enzyme levels depends largely on the clinical evaluation of the individual. The reason which underpins the need for this holistic assessment comes from the fact that elevated enzyme levels can also be caused by other factors like chronic use of alcohol and underlying diseases like chronic hepatitis B and C. Certain medication, like common pain killers and antibiotics, can also cause an abnormal amount of liver enzymes in the blood. Moreover, enzyme levels do not correlate well with the extent of liver damage or disease. These considerations establish that blood tests are subjective, i.e. they are influenced by the experience of the physician.

For FLD diagnosis, no single blood test is specific. Serum enzymes are insensitive measures of steatosis when FLD is in the initial stage. The early stage of hepatic steatosis, when it is not accompanied with liver damage or necrosis, is only indicated by modestly elevated values of AST and ALT. Even though patients with FLD have slightly elevated AST and ALT levels, such levels could also be normal, at least intermittently normal. Indeed, blood tests provide a clue that FLD is present, but such liver function tests are not conclusive. Therefore, methods, such as liver biopsy (invasive) and abdominal imaging techniques (noninvasive), are required to aid and confirm the diagnosis.

2.4.2. Liver biopsy

Liver biopsy is currently the most commonly prescribed diagnostic standard for steatosis assessment [116]. In general, state of the art noninvasive tests have low sensitivity and specificity for diagnosing FLD [15]. Liver biopsy provides information about the degree of liver damage, changes in the overall architecture of the organ, and the degree of inflammatory activity and fibrosis [85]. Based on this information, it is possible to predict the disease progression that allows the physicians to improve disease management [102,9,145]. During the biopsy, a small liver sample is collected and examined under a microscope for signs of disease or damage. In most cases, liver biopsy is performed after blood tests, to confirm the disease and to estimate the degree of liver damage. A minimum of 5–10%, by weight, of steatosis is considered as being a strong indicator for FLD [97]. A common technique for collecting liver samples is percutaneous liver biopsy [83]. A hollow needle (usually a 1.4–1.6 mm diameter needle with a suction system) is inserted, through the abdomen, into the liver, where tissue is collected inside the needle.

Limitations of liver biopsy – even though liver biopsy is the commonly used standard for FLD diagnosis, it has several important limitations. It is an invasive method which is stressful for both patient and their physician. Furthermore, it is associated with potentially significant complications, such as bleeding/hemorrhage and pain. Complications occur in more than 1.3% of all cases [111] and the mortality through bleeding is estimated to be in the range from 0.1% to 0.5% [84,70]. Therefore, it cannot be used for screening a disease that occurs in about 15% of the population. There is also evidence that a liver biopsy is subject to significant sampling variability, because the evaluated tissue sample is only a small part of the entire liver (about 1/50,000 of the total liver mass), and this sample may not represent the complete organ [116,89,55]. Studies found that liver biopsy is prone to sampling errors, which result from a small sample size and a lack of homogeneity in the fat distribution. Hence, the accuracy of the procedure is questionable [141,136,64]. Another limitation is that the histological analysis of the steatosis degree of the liver sample remains subjective because the diagnosis is dependent on the training and capability of the pathologist [150]. The results are influenced by the skill and experience of the reading pathologist [150].

Despite being the gold standard for the evaluation of liver histology [22], liver biopsy has serious side effects, is expensive and the results are subjective. Hence, there is a need to develop reliable, noninvasive and cost efficient methods for assessing the liver fat content. Noninvasive techniques, such as imaging with high accuracy and sensitivity, are crucial to FLD screening.

2.4.3. Computed Tomography (CT)

CT is a noninvasive medical diagnosis tool that uses multiple X-ray images to produce tomographic models of specific areas of the human body. CT was introduced in the early 1970s, and since then CT based FLD diagnosis has been evaluated in multiple studies [34,106,61]. CT provides accurate high contrast images of the entire liver; so the common patterns of FLD such as diffuse fat accumulation, diffuse fat accumulation with focal sparing, and focal fat accumulation can be accurately diagnosed [36].

Steatosis of the liver is better visible in images from unenhanced CT than from enhanced CT, because steatosis is differentiable with lower attenuation values due to the inverse relationship between hepatic fat content and the corresponding attenuation [59,112,72]. Images from unenhanced CT show the normal liver with a slightly higher attenuation when compared to spleen and blood. Furthermore, intra-hepatic vessels are visible and appear hypo-attenuated. In contrast, images of fatty liver show the liver more attenuated than the spleen, and the intra-hepatic vessels are not so distinguishable [88]. Various studies show that parameters, such as contrast agent injection rate and measurement delays

influence the attenuation values, and this directly affects the evaluation threshold of hepatic steatosis [62,65].

There are three predominant attenuation measurements that are carried out in order to assess the liver fat content with unenhanced CT. These measurements are analyzed in terms of Hounsfield Units (HU) and the parameters include: absolute attenuation of the liver, difference in the attenuation values between liver and spleen and liver-to-spleen attenuation ratio [54,87]. Average absolute attenuation values of a healthy liver are higher than 50 HU, and normally 8–10 HU higher compared to values from the spleen [112]. FLD is diagnosed when the absolute attenuation is less than 40 HU or 10 HU lower compared to values obtained from the spleen [45,107]. Liver-to-spleen CT attenuation values ratio greater than 1:1 suggest moderate hepatic steatosis [54]. In the case of higher degree of hepatic steatosis (>30%), unenhanced CT has been found to have a detection sensitivity of 82% and specificity of 100% [107].

Limitations of CT – despite the fact that unenhanced CT images show attenuation values that correlate well with hepatic steatosis, this modality is inaccurate when the percentage of fatty infiltration is low [45]. The attenuation values vary significantly when tested with scanners from different manufacturers, with different generations of scanners and even with different combinations of scanning and computing equipment [16]. Another major disadvantage is that the image measurement involves harmful radiation, and this restricts it from being used in repeated studies and in children [128]. Attenuation values could also be altered due to an underlying diffuse liver disease causing false positive FLD diagnoses. Fig. 1 shows the typical normal and FLD CT images.

2.4.4. Magnetic Resonance Imaging (MRI)

MRI is an imaging modality which uses the property of nuclear magnetic resonance in cells to capture body images. MRI provides images which have a good contrast between different tissues. Therefore, it is useful in imaging soft tissues within the body, such as brain, heart and muscles. MRI based liver fat quantification is possible, because there are characteristic differences in the resonant frequency of fat and water [121]. MRI techniques use these differences to generate in-phase and out-of-phase images. Unlike US, MRI is operator independent, therefore, the inter-observer variation is lower [103].

There are many types of Magnetic Resonance (MR) imaging techniques. The most widely used technique to determine the liver fat content is dual chemical-shift gradient-echo. This method generates images based on the difference between in-phase images and out-of-phase images. MR images are acquired with two echo times, so water and fat proton resonance signals are captured

in-phase or out-of-phase. In in-phase images, the signal intensities of water and fat, within a voxel, are additive and they are at a maximum. For out-of-phase images, the signal intensities are subtractive and they are at a minimum [121]. The decrease of signal intensity from an in-phase to an out-of-phase image indicates the presence of liver fat. The amount of fat is calculated by measuring the total decrease of signal intensity [128].

Another MR technique, called proton magnetic resonance spectroscopy (^1H MR Spectroscopy), was proven to be safe and accurate. Georgoff et al. [40] determined that the diagnostic accuracy of ^1H -MRS for hepatic steatosis was high with an area under the receiver operating characteristic curve of 0.94. Using the ^1H spectra of liver tissue, it is possible to differentiate the water signal from the signal of methylene protons of fatty acids. Even more detailed information can be obtained from MR spectroscopy which generates up to 3 dimensional matrices [115,131]. Such information, obtained from ^1H MR spectroscopy, allows physicians to reach a very accurate FLD diagnosis. This technique overcomes the fat-water ambiguity problem of the chemical-shift method, but the technique is very time consuming. It takes at least three times longer to obtain results than other MRI techniques.

Limitations of MRI – High hepatic iron concentrations can result in localized inhomogeneity in the magnetic field, and this leads to a loss of signal intensity during the measurement. This decrease of signal intensity affects the accuracy when quantifying the presence of liver fat [51,42]. Another limitation of MRI comes from the fact that the resolution, and therefore, the image accuracy, depends on the magnetic field strength H [153,118]. Unfortunately, there are physical limits for this field strength and getting close to these limits is very costly. Therefore, the availability of the equipment for ^1H MR Spectroscopy is limited and most MRI machines in the market do not come with that capability.

Even though MRI techniques have the ability to quantify FLD with a high degree of accuracy, MR imaging techniques are relatively costly, and hence, they are not widely available. In addition, MR imaging relies on a strong magnetic field, therefore it is not recommended for patients with implanted electronic devices or ferromagnetic metal implants. Fig. 2 shows the typical normal and FLD MRI images.

2.4.5. Ultrasound (US)

US is a commonly used modality to generate images in studies of fetus, muscles, joints, heart, blood vessels, abdominal and pelvic organs [105,38]. In the diagnosis of FLD, US is widely used for initial screening as it is low-cost, noninvasive, radiation free and readily available [105,120,122,140,90]. B-mode US is generally used for an initial evaluation and classification of the liver [46].

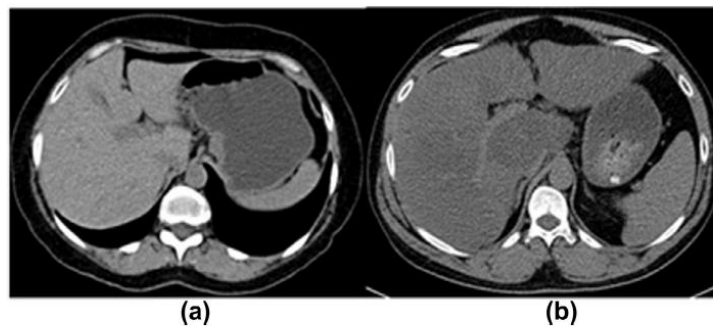


Fig. 1. Typical CT liver images (a) normal (b) FLD. Steatosis changes the intensity of the liver tissue, making it appear darker.

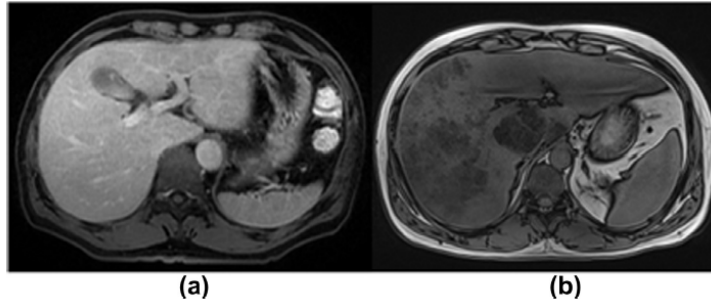


Fig. 2. Typical MRI liver images (a) normal (b) FLD. This MRI image was acquired by using a fat suppression sequence. It is possible to notice that steatosis darkens the appearance of the liver tissue.

In US images, steatosis appears as a diffuse increase in echogenicity caused by an increase in the parenchymal reflectivity which results from the intracellular accumulation of fat-containing vacuoles. The echogenicity of the normal liver is generally equal to or slightly higher than that of the renal cortex or spleen [148]. The presence of FLD is detected by an increase in the liver echogenicity compared to the renal cortex, and spleen and US signal attenuation, loss of definition of the diaphragm, and poor delineation of intrahepatic architecture [59,57]. The degree of liver steatosis can be evaluated based on echogenicity, attenuation masking of portal vein or gall bladder [143]. Despite being widely used, sensitivity and specificity of US in detecting FLD are still the topic of debate [126,58,124,82,8,145]. Reported sensitivities range from 60% to 94% and reported specificities range from 75% to 100% [58,123,44] when detecting fat accumulation of more than 33%. These numbers drop with increasing BMI [29,91]. Most studies use a three or more point scoring system for tabulating the disease severity, with regard to the hyperechogenic liver tissue, the increased echo amplitude between the liver and the renal cortex as well as the loss of echo from the walls of the portal system [123,44].

Limitations of US – one major downside of US for diagnosing FLD is its operator dependability. Strauss et al. [135] studied inter- and intra-observer variability of US imaging. Three experienced radiologists evaluated the extent of liver steatosis in 168 patients independently. After one month, the evaluation was repeated under the same conditions, but blinded with respect to the initial reading. After both evaluations, inter- and intra-observer variabilities were measured and the agreement percentages were captured. The mean inter-observer and intra-observer agreement percentages, for the presence of fatty liver, were 72% and 76% respectively. Intra-observer agreement for the degree of severity of fatty liver was between 55% and 68%. The results of this study demonstrate the subjectivity associated with the interpretation of ultrasound images making, as a consequence human based US interpretation for FLD diagnosis is unreliable.

Even though the sensitivity and specificity of US in detecting FLD is acceptable [50], the weakness of this screening modality is in reproducibility and reliability in detecting steatosis [110]. Fig. 3 shows the typical normal and FLD ultrasound images.

3. Computer Aided Diagnostic (CAD) technique workflow

In this section, we present a few of the commonly used processing methods which extract informative features from US images. These features can be used in automated classification algorithms for FLD detection. Fig. 4 shows a typical system block diagram

which depicts both data flow and algorithms which act on the data. The following sections provide a short discussion of these algorithms.

3.1. Image pre-processing

Image pre-processing reduces unwanted image details such as the US image graph axis, and it ensures that all images, used as input to the CAD system, are similar in terms of color and size. Most feature extraction algorithms work with grayscale images, and therefore, pre-processing algorithms also convert the acquired images to grayscale. In general, conversion to grayscale ensures image data uniformity, which improves image analysis results.

3.2. Feature extraction

In this step, features based on texture and Higher Order Spectra (HOS) are extracted from the image. This section provides a brief description of these measures.

3.2.1. Texture features

Texture analysis identifies spatial variations in pixel intensities and quantifies them into numerical features [77]. There are different methods for identifying the spatial variations in pixel intensities. *Structural approaches* depict texture with well-defined primitives and a hierarchy of spatial arrangements of those primitives [81]. This method provides a good symbolic description of the image, and therefore, it is useful for synthesis. However, the description could be ill-defined for natural textures which have no well-defined micro-texture or macro-texture. *Statistical approaches* make use of descriptive properties and the relationships between the gray levels in an image [133]. They are based on a set of statistics which is used to analyze the spatial distribution of gray values. *Model based approaches* employ on models that are used to describe and even synthesize textures. These models describe the image as probability or linear combination of basic functions. In a first step, the model parameters are estimated and they are used for image analysis. *Transform based approaches* include methods such as Fourier, Gabor and Wavelet transforms [81]. In the following sections, we briefly describe few commonly used statistical approaches (Entropy, Local Binary Pattern, Gray Level Co-occurrence Matrix (GLCM), and Run Length Matrix) and transform based approaches (Wavelet transform).

3.2.1.1. Wavelet transform. Wavelet theory describes a method which models the signal in terms of basic components by comparing it with special functions [93]. These functions are created by scaling and translating a so called mother wavelet. Wavelet transforms, like Continuous Wavelet Transforms (CWT), Discrete Wavelet

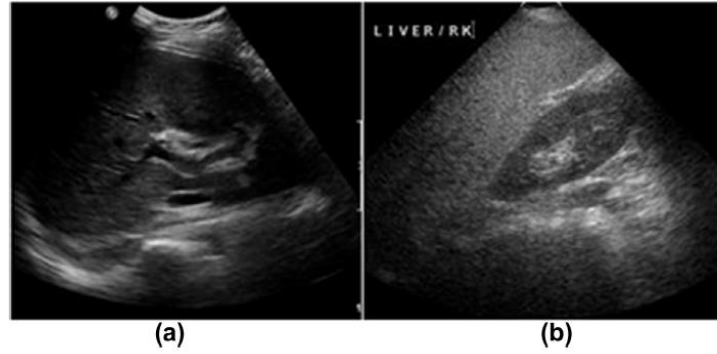


Fig. 3. Typical US liver images (a) normal (b) FLD. Normal liver is usually homogeneous and characterized by a dark and neat granular pattern, whereas an FLD affected liver appears brighter and smoother.



Fig. 4. Overview block diagram of FLD CAD systems.

Transform (DWT), and Wavelet Packet Decomposition (WPD), determine specific wavelet coefficients that adequately describe the image. The advantage of using wavelets is that there is a wide range of mother wavelets each of which has distinct analytical properties. Hence, the best suited transform for a given image analysis problem can be chosen.

3.2.1.2. Entropy. Entropy is a measure of uncertainty which is associated with the randomness of the measured entity. Let the image $I(x,y)$ have N_i distinct gray values, where $i=0, 1, \dots, L_i-1$. The normalized histogram for a region of interest of size $(A \times B)$ is defined as:

$$F_i = \frac{N_i}{AB} \quad (1)$$

Shannon Entropy is given by [130]:

$$S_n = -\sum_{i=0}^{L-1} F_i \log_2 F_i \quad (2)$$

Yager's entropy can be calculated by [130]:

$$Y = \frac{\sum_{i=0}^{L-1} |2F_i - 1|}{|A \times B|} \quad (3)$$

Kapur's entropy can be calculated by [130]:

$$K_{\alpha,\beta} = \frac{1}{\beta - \alpha} \log_2 \frac{\sum_{i=0}^{L-1} F_i^\alpha}{\sum_{i=0}^{L-1} F_i^\beta} \quad (4)$$

where $\alpha \neq \beta, \alpha > 0, \beta > 0$.

Renyi's entropy is given by [130]:

$$R = \frac{1}{1-\alpha} \log_2 \sum_{i=0}^{L-1} F_i^\alpha \quad (5)$$

3.2.1.3. Local Binary Pattern. Local Binary Pattern (LBP) is a textural measure of local neighborhood [96]. Consider P circular neighborhood pixel points on a circle of radius R . Let G_c indicate the center pixel's gray value and G_p be the corresponding gray value of the

neighborhood pixels for $p=0, 1, \dots, P-1$. Depending on G_c , circular points P are converted into a binary pattern. The local texture is defined as:

$$T = t(G_c, G_0, \dots, G_{P-1}) \quad (6)$$

The LBP for center pixel is given by:

$$LBP_{P,R} = \sum_{p=0}^{P-1} F(G_p - G_c) 2^p \quad (7)$$

$$\text{where } F(x) = \begin{cases} 1, & x \leq 0 \\ 0, & \text{otherwise} \end{cases}$$

Various entropy and energy features of the LBP image can be formed for $R=1, 2$, and 3 with the corresponding pixel count P being $8, 16$, and 24 , respectively.

3.2.1.4. Gray Level Co-occurrence Matrix (GLCM). Haralick was the first to introduce GLCM and textural features for image classification in 1973 [48]. For an image of size of M by N pixels, GLCM is defined as:

$$C_d(i,j) = \left| \left\{ \begin{array}{l} (p,q), (p+\Delta x, q+\Delta y) : I(p,q) = i, \\ I(p+\Delta x, q+\Delta y) = j \end{array} \right\} \right| \quad (8)$$

where $(p,q), (p+\Delta x, q+\Delta y) \in M \times N, d = (\Delta x, \Delta y)$ and $|\cdot|$ denotes the cardinality of a set. Given a gray level i in an image, the probability that the gray level of a pixel at a $(\Delta x, \Delta y)$ distance away is j is:

$$P_d(i,j) = \frac{C_d(i,j)}{\sum C_d(i,j)} \quad (9)$$

The texture features are then defined using Eq. (9).

3.2.1.5. Run Length Matrix. The run length approach extracts higher order statistical features from the image texture. The run length matrix, P_θ , contains all the elements where the gray level value i has the run length j continuous in direction θ [142]. The direction for θ is often set as $0^\circ, 45^\circ, 90^\circ$, and 135° .

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