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A Comprehensive Review of Medical Image Analysis Techniques for Liver Disorders

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***Abstract*—** Recently, medical image analysis is considered an essential step in the early detection, diagnosis, and treatment of liver disorders. After diagnosis, medical image analysis methods are used within the treatment course to track the recovery process. In addition, medical imaging analysis techniques are used to build a 3D computer model for body organs. This will help in reducing surgical medical errors by providing tools for advanced surgical aids, preoperative planning, and rehearsal. This paper presents a comprehensive review of the current work on liver disorders' analysis using medical image analysis techniques. It discusses the existing medical imaging modalities, their characteristics, advantages and drawbacks. It also describes the recent liver lesions segmentation methods and makes a comparison between them in terms of their complexity, speed, noise sensitivity, advantages, and limitations. Moreover, this paper elucidates liver computer-aided diagnosis (CAD) systems and shows how they are used in accurate diagnosis of different liver disorders. On top of that, challenges facing the medical images' analysis are introduced and future research trends in this area are discussed and analyzed.

***Keywords*—** Liver disorders; Medical image analysis; Computer-aided diagnosis; Liver tumour segmentation; Lesions classification; Magnetic resonance imaging; Positron emission tomography.

1. INTRODUCTION

Medical imaging modalities are techniques used to create an image for internal body organs and tissues. Acquired images are clinically used to pre-diagnose several diseases such as liver tumor. To increase the efficiency of acquired images for better diagnosis and treatment, medical image processing techniques are used. For soft tissues such as the liver, the most used modality is computed tomography (CT). CT modality is considered the best choice to detect and classify liver lesions into benign or malignant. This is because of its ability to acquire an image in a relatively short time; i.e., 0.4 s [1]. Reducing acquisition time can be beneficial in minimizing resulting noise from body movement or breathing; i.e., high signal to noise ratio.

On the other hand, the liver is responsible of at least 500 essential functions for the human body. According to the American Cancer Society's (ACS), around 42030 adults were diagnosed with primary liver cancer in the US in 2019 divided as 29480 men and 12550 women [2]. The morbidity of liver cancer has increased three times when compared to 1980. Through the past decade, the percentage increased by about 3%. Liver cancer is expected to be responsible for about 31780 deaths (21600 men and 10180 women). It is considered the fifth most common death caused by cancer in men, and the seventh in women [2].

Chronic liver disease (CLD) development is identified in many phases. Each has its physiological and pathological features. The early phase of liver cancer starts when increased fats in hepatocytes appear. This phase is called fatty liver infiltration or steatosis [3]. In the

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liver damage phase, fibrosis appears. The evolution of fibrosis relies on the source of hepatic failures such as chronic hepatitis. The late phase of CLD is cirrhosis, and it refers to a deficiency of liver functionality due to long-term damage. Cirrhosis is classified into two categories, namely decompensated and compensated cirrhosis. Compensated cirrhosis is identified by an asymptomatic phase which is succeeded in the liver dysfunction phase, called decompensated cirrhosis. When cirrhosis reaches late phases, the patient is diagnosed with primary liver cancer or hepatocellular carcinoma (HCC).

The staging and detection of CLD are done using medical imaging modalities with the aid of artificial intelligence (AI) systems called computer-aided diagnosis (CAD) systems. CAD systems are computer methods that extract hidden knowledge from acquired medical images to enhance the accuracy of disease diagnosis. For liver cancer diagnosis, CT imaging modality is used. CAD has been considered one of the hottest research topics in the medical field [3]. CAD liver system is mainly concerned with developing methodologies and techniques for enhancing the quality of medical images, improving the diagnosis accuracy, and detecting or segmenting liver lesions.

The typical CAD system consists of five stages. The first stage is image acquisition using one of the medical imaging modalities such as CT scan. The second stage is the pre-processing stage which is mainly concerned with enhancing the quality of the acquired image by enhancing the contrast. In the third stage, features are extracted. The features extraction stage is considered an essential stage of the CAD system because the accuracy of lesions detection is built upon it. The lesions identification process is the fourth stage of the CAD system and is referred to as the lesion segmentation stage. Liver lesions refer to any abnormal structure in the liver. An injury or disease causes these lesions. The most common method to identify liver lesions is to calculate pixel intensity differences for different liver regions in the CT image. In the CAD system, the segmentation stage means the detection of lesion regions from the liver regions based on the extracted features [4]. However, the segmentation stage is very tricky and can be done either manually or automatically. The task of manually segmenting CT images is considered complex and consumes much time. Although automatic segmentation is supposed to solve manual segmentation problems, it stills a very challenging task [5]. This is mainly because of many reasons including a CT scan of the liver is a combination of 150 cross-sectional images (i.e., slices), unlimited shaped of liver lesions, and sometimes the intensity between lesions and liver tissues are quite similar. Automatic segmentation methods are built on the top of a common method such as region-growth, thresholding, texture-based, Bayesian, or entropy-based techniques [6]. The final stage of a liver CAD system is the diagnosis stage at which lesions are classified into benign or malignant. Generally, the classification process is implemented by passing the features of the segmented lesion to a binary classifier such as support vector machines (SVM) [7].

This paper discusses different AI liver segmentation and diagnosis techniques. Section 2 discusses the existing medical imaging modalities. Section 3 describes liver segmentation methods. Liver CAD systems are discussed in section 4. Section 5 elucidates existing research challenges. Future research trends are presented in section 6. Conclusions are covered in section 7.

2. MEDICAL IMAGING MODALITIES

Medical imagining modalities refer to the different acquisition devices being used to capture an image for human body organs or tissues. The imaging modality selection depends on what disease or abnormalities to be imaged and on the area where the disease or abnormalities is caused. The primary imaging modalities used in diagnosing liver are the CT, positron emission tomography (PET), magnetic resonance imaging (MRI), and ultrasound.

2.1. CT

CT scan is an imaging method that uses X-ray beams, and by rotating X-ray source around the body, it produces cross-sectional (i.e., slices) of the imaged body organ. After the collection of sufficient number of successive slices, the CT scanner computer forms a 3D image of the body by stacking together collected slices. Unlike X-ray scanners, CT scanners use detectors' arrays instead of single X-ray film. The position of the detectors depends on the generation of the used CT scanner. Usually, they are placed in the opposite direction to the beam source as shown in Fig. 1. CT imaging modality is the best choice in case of detecting any possible lesions in soft tissues such as the brain, heart, liver, and lung [8].

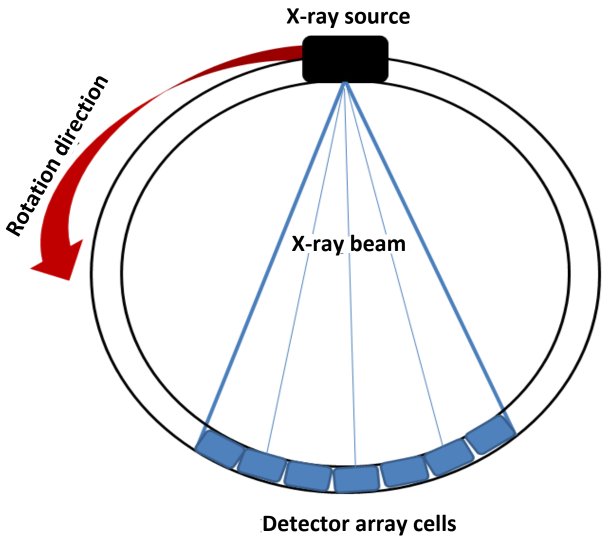


Fig. 1. The working theory of the CT scanner, the continuous rotation of the detectors, allows the collection of full projection data sets for the CT subsystems.

2.1.1. Liver Lesions CT Scan

The detection of liver lesions in the CT images depends on the differentiation between pixels intensity in lesions and normal liver regions. After the completion of lesions' detection, lesions are classified based on some characteristics. If the lesion is not growing and tending to have sharp boundaries and homogeneous structure with intensity colors different from liver intensity colors, then it is classified as a cyst as shown in Fig. 2. If the lesion is growing peripherally or nodular, then it could be a haemangioma. Haemangioma is considered the most common liver tumor. If the lesion is neither haemangioma nor cyst, then the lesion is further classified into either hyper-vascular or hypo-vascular lesions. Further classification is generally depends on several factors such as lesion growth patterns, patient history, and pathological features; i.e., presence of calcifications, fat, blood pressure, cystic or fibrotic components [9].

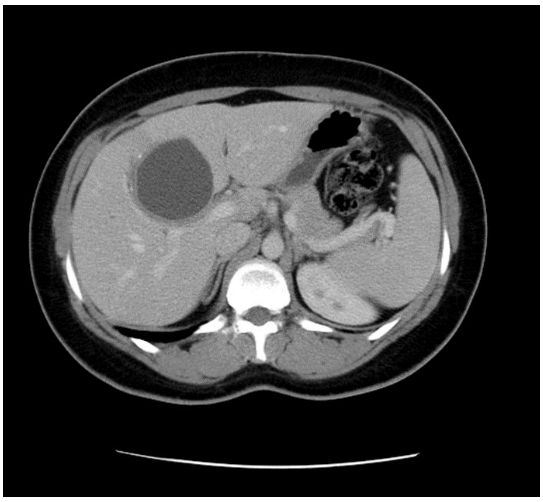


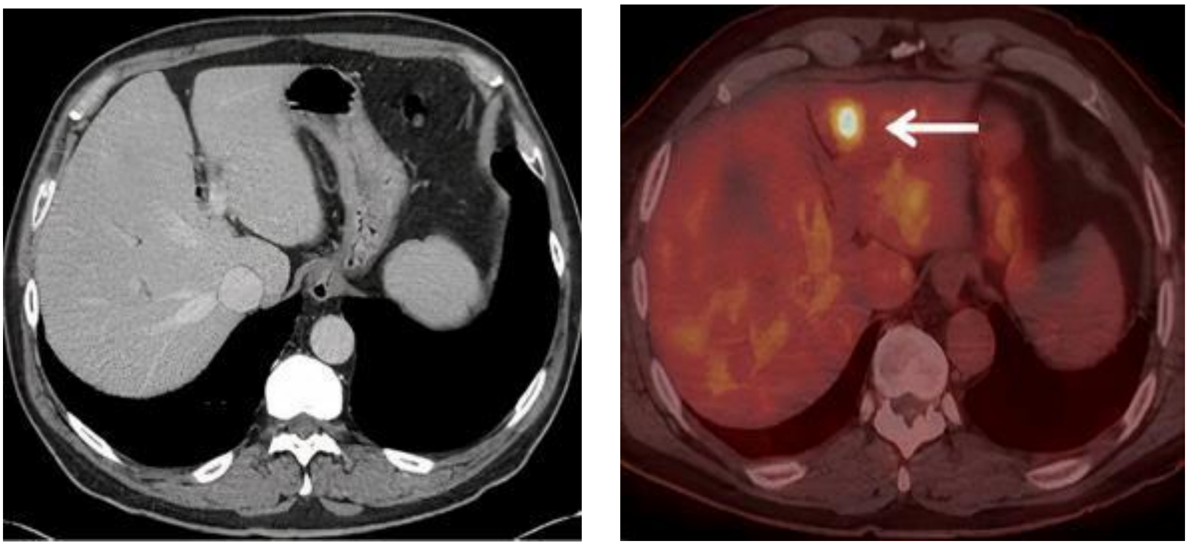
Fig. 2. Hepatic cyst lesion on contrast-enhanced CT scan [10].

2.2. PET

PET is used to evaluate the physical state and functionality of body tissues. PET scan mainly depends on radioactive tracer (drug) and PET scanner. Tracer drugs may be inhaled, injected, or swallowed depending on the tissues to be imaged. As the tracer is traveling through the body, it is getting collected by body tissues with higher chemical activity levels. Chemical activities are shown as “hot spots” for higher activities or “cold spots” for lower activities. PET scanner detects radiation that is emitted by a radiotracer. Compared to healthy cells, lesion cells are always very active, so a radiotracer made them bright in the PET image as shown in Fig. 3. The analysis of liver lesions “hot spots” is considered a difficult task. This is mainly because liver size may attenuate the lesion signal. To deal with this problem, signal amplification and quantification methods are used to enhance the interpretation of hepatic lesions. The lesion-to-benign tissue (L/B ratio) is used to analyze PET scans [11]. PET scans are mostly used to evaluate neurological diseases, cancers, and heart diseases [12]. PET scans are usually used combined with CT or MRI scans to help in more effective diagnosis.

2.2.1. Liver Lesion PET Scan

PET scan can be used to diagnose liver lesions when lesions are either lymphoma or metastases. Primary hepatic lymphoma (PHL) is a very rare case. Even though, it has been delineated in the hepatitis C virus (HCV) positive patients. Typically, it appears as a single hepatic mass. However, multiple masses with diffuse shapes are also delineated. PHL is represented as homogenously hypoechoic lesions on an ultrasound scan. On CT scan, PHL is shown as a hypoattenuating lesion (i.e., low-intensity area indicating lesion location). PHL patterns enhancement is a variant task since 50% of PHL lesions cannot be enhanced, 33% may have patchy enhancement, and 16% may have ring enhancement. This will result in a misdiagnosis of PHL lesions and they will be diagnosed either as HCC or metastases. Since PHL absorbed radiotracer drug is emitted in PET scan, PET is considered superior for analyzing PHL. Since PHL disease is considered a rare disease, the number of researchers made to evaluate PHL PET scans is limited [13].



(a) (b)

Fig. 3. A liver lesion: a) lesion is invisible on CT scan; b) lesion is emitting on PET scan [14].

2.3. MRI

MRI is a non-invasive imaging modality that produces a 3D detailed anatomical image of body organs and tissues. MRI uses a magnetic field to realign protons within that field. In other words, MRI detects the change in proton rotational direction. When a radio frequency pulse passes through the human body, the atom's protons are energized and spin out of their equilibrium state. When the magnetic field is turned off, protons realign to their original equilibrium state. This realignment produces a radiofrequency field (i.e., energy), which is later detected by MRI sensors. The consumed time during the realignment phase and the strength of radio frequency field power emitted are relying on the surrounding medium and the chemical nature of the atoms. Radiologists use the different magnetic characteristics of tissues to distinguish between lesions and typical regions [15]. MRI scans are often used to detect and diagnose several diseases such as abnormal tissues in blood vessels and chest and abdomen injuries.

2.3.1. Liver Lesion MRI Scan

Hepatic cysts lesions (HCL) - even those lesions with no pathological significance - can be easily detected using an ultrasound scan. However, in some rare states, an MRI scan is used as an additional scan to detect non-complicated hepatic cysts. HCL evaluation can become complex and complicated by the presence of abscesses, haemorrhage, hematomas cystadenomas, and cystadenocarcinomas. HCL can be benign or malignant. If HCL is complicated by the presence of severe haemorrhage and severe hematomas, diagnosis and detection can be easily made using an MRI image with no enhancement [16]. The most difficult task is to distinguish between HCL lesions caused by cystadenomas or cystadenocarcinomas. This is because they cannot be detected using an un-enhanced image, and the lesions may not be segmented as shown in Fig. 4. The likelihood of malignant HCL increases when the thickness of the lesion increases. This can only be visible when an enhanced MRI scan is used.

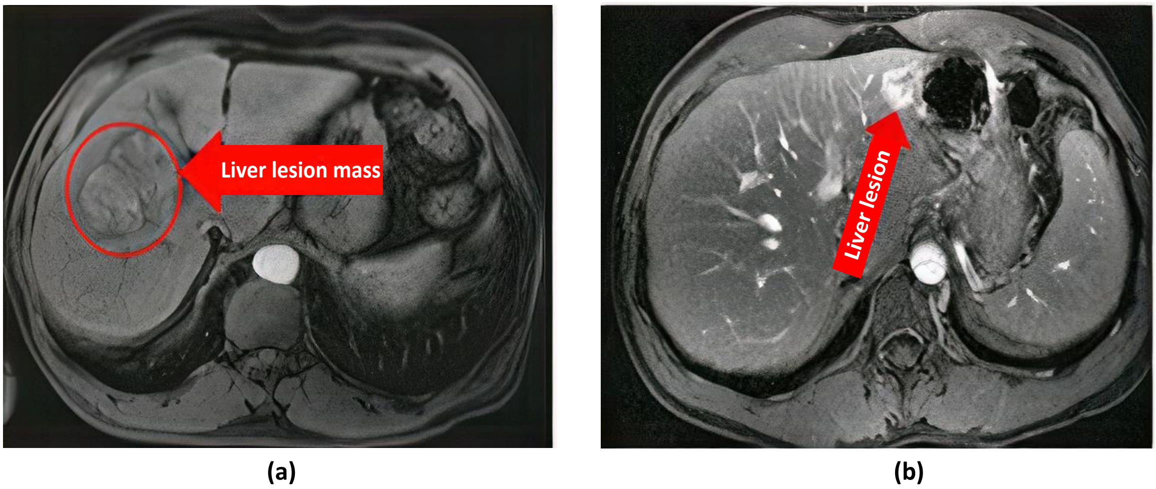


Fig. 4. An MRI scan for liver lesions: a) pre-MRI scan (lesion is invisible on un-enhanced MRI scan); b) post-MRI scan (lesion is visible on enhanced MRI scan) [17].

2.4. Ultrasound

Ultrasound or ultrasonography (US) is a non-invasive diagnostic technique to image body tissues and organs. US imaging modality uses transducers or probes to produce US waves above 20 kHz and collects reflected US echoes. When reflected echoes hit the transducer, an electrical signal is generated. As the US beam penetrates a medium, the beam is attenuated or loses energy. As a beam penetrates tissue, some of the beams are reflected, refracted, or absorbed as heat generation. The amount of penetration will determine the depth of the scanning area. Penetration is directly related to wavelength. Smaller wavelengths are more easily reflected or refracted in the superficial tissues than longer wavelengths. As the wavelength is increased (or frequency decreased), the US will penetrate deeper. As the wavelength is decreased (or frequency is increased), the US beam will have a shallower penetration. Low-frequency US has superior penetration. Resolution and penetration are the primary criteria for the image quality of diagnostic US. In theory - and usually in practice - the maximum depth of imaging in a tissue increases as the power (pressure) increases. Alternatively, at a particular effective penetration, an increased power may be used to allow a higher US frequency for higher resolution and tissue contrast. The US scanner then collects this signal. The speed of US waves and the time consumed until echo reflection are used by the scanner to calculate the distance from the transducer to the organ's edges. Calculated distances are then used to produce a 2D US image of the organs [18]. Transducers are usually placed on the skin. However, produced image quality can be optimized when transducers are placed inside the body via the gastrointestinal tract, vagina, or blood vessels.

2.4.1. Liver Lesion US Scan

US scan is mostly used to detect liver fibrosis. When US waves pass through the liver, liver tissues move. This movement is very clear in the center of the liver. The resulted electricity of wave reflection is calculated to distinguish between normal liver tissues and fibrotic lesion tissues [19]. This is because fibrotic lesions respond more to waves (i.e., move to a greater degree than the rest of liver tissue). Hence, it produces larger electrical signals. Fig. 5 illustrates US scans for different types of tumors.

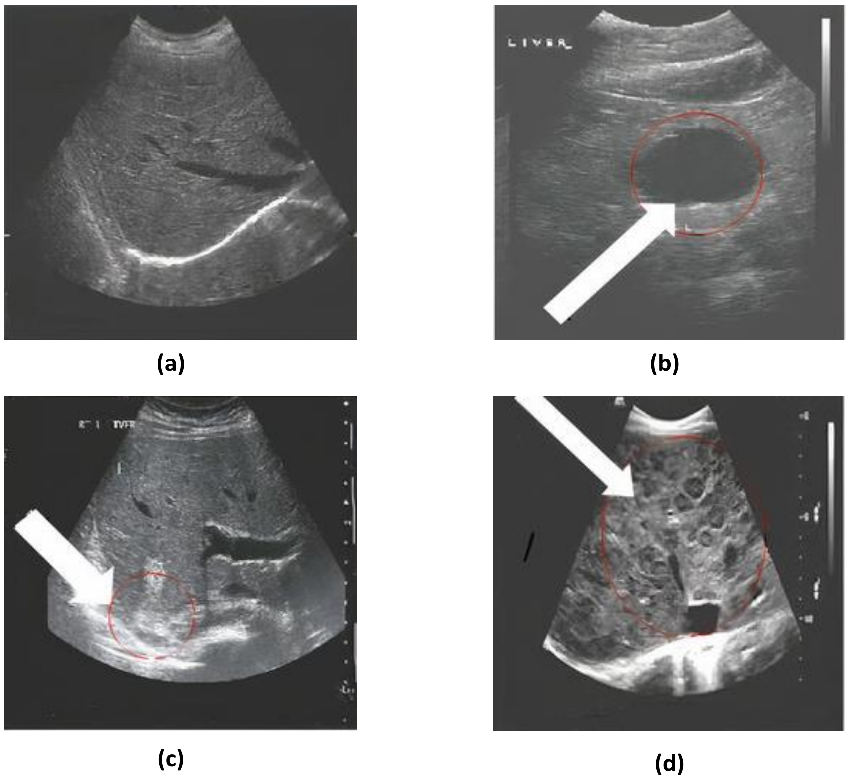


Fig. 5. US scans for different liver diseases: a) normal; b) cyst; c) benign; d) metastases [19].

2.5. Comparison between Different Liver Imaging Modalities

Table 1 compares mostly used liver imaging modalities in terms of their cost, complexity, sensitivity, advantages, and limitations.

Table 1. The imaging modalities for liver disorders.

Criteria	CT	US	PET	MRI
Cost	Cheap	Cheap	High	High
Complexity	Simple	Simple	Complex	Complex
Sensitivity	Low sensitivity	Low specify	Low sensitivity	-
Advantages	- Produces a 3D image of a liver - Can identify liver lesions size - Real-time monitoring	- Absence of ionizing radiations - Real-time liver vascularity visualization	- Wide anatomical coverage - Functional imagining	- High lesion-to-liver contrast - Absence of ionizing radiations - High spatial resolution
Limitations	- High radiation dose - Lesions with size < 1 cm cannot be identified.	- High operator and patient dependency - Lesions with size < 1 cm cannot be identified. - Low specificity.	- Low spatial resolution - False positive uptake in normal structure or benign tumours.	- High cost - Time-consuming method - Requires that the patient hold the breath for a relatively long time.

3. LIVER LESION SEGMENTATION

Segmentation aims to contour the desired region of interest (i.e., liver lesions). Segmentation of liver lesions is required to analyze lesions accurately and thus, accurately identify the staging and evaluation of the lesions. Segmentation methods can be classified - based on the automation level - into two classes: fully automatic and semi-automatic. Liver segmentation methods are built on the top of basic segmentation methods such as region-based/contour-based segmentation methods, thresholding methods, model-based approach, level-based, and graph cut methods. Lesion segmentation is usually implemented in five steps: i) identification of liver region, ii) noise reduction to enhance lesion to liver contrast, iii) identification of lesion seed point to identify other points with the same intensity which will be labeled as the lesion, iv) lesion detection improvement by the usage of localized contouring method, and v) lesions are rendered in a 3D space to display position, volume, and growth of the lesions within the liver. Lesion volume is calculated by counting the number of comprised voxels in the lesion area [20]. The following subsections discuss the liver segmentation methods.

3.1. Region-Based Segmentation

Region-based segmentation methods always depend on the intensity values between neighbor pixels (i.e., group pixels with similar intensity values into a region). This method archives good results with contrast-enhanced images. Region-based methods are divided into two classes: region growing and region splitting. Region growing methods start with seed points and pixels with similar values as seed are grouped. Region growing continues iteratively until all homogeneous neighbors as the seed points are obtained. The limitations of this method are the seed point choice is a dependable user process, and the method will be inefficient in the case of heterogeneous regions.

The basic requirements of any region growing method are the following: i) segmentation process stops when each pixel belongs to a region, ii) pixels in the same region must be connected, iii) generated regions must be unique, iv) properties and criteria of the region must be satisfied by the pixels to be segmented in that region, and v) the properties of each region must be unique.

Evaluation of region splitting algorithms was built on larger sets of pixels rather than single pixels (i.e., seed point). Zhou et al. [21] provided a performance benchmark study for three semi-automatic liver lesions-segmentation methods. Those three methods involved region growing with knowledge-based rules, propagational learning for lesion pixels classification, and region growing based on the Bayesian rules. The results showed the superiority of the first two methods over the third. Pohle et al. [22] proposed an adaptive region growing technique. This method had the advantage of being able to acquire knowledge about the homogeneity criterion from segmented region characteristics automatically. However, this method was inefficient if the segmented region is heterogeneous, and it led to under segmentation.

Ruskó et al. [23] proposed the choice of seed region based on the density of pixels in the CT gray level image. This was advantageous in dealing with heterogeneous regions' problems. The liver region was identified with the help of anatomical characteristics of the liver. Then, they applied their enhanced region growing method version to segment the image. Their results showed under-segmentation near the right lung lobe which had been solved using some post-processing techniques. Their method was a high-speed method when compared to other region-growing methods. However, it suffered from complexity and resulted in under-segmentation when the liver intensity level was heterogeneous due to the presence of a huge lesion.

Kumar et al. [24] proposed a method to use the largest connected region centroid as the initial seed point, and a gaussian model determines the region growing threshold. Post-processing techniques were implemented to deal with the liver under segmentation by fixing gaps and connection with other neighborhood tissues. This method showed lower time consuming with reasonable outputs. Huang et al. [25] proposed to transform the liver CT scan image into a projection plane using the ray casting algorithm, and then use region growing for segmentation.

Kuar et al. [26] proposed an algorithm that used k- means clustering with region growing method to enhance liver cyst area segmentation. K-mean clustering was unable to separate cysts cluster from the rest of the image clusters. To deal with this problem, region growing was used to further segment cyst lesions based on their morphological characteristics. This method proofed its superiority over the standard k-means method.

3.2. Threshold Based Methods

Threshold-based segmentation algorithms were used for rough segmentation and identifying lesions regions or seed points as pre-processing. All threshold-based methods had the same implementation as following: i) contrast enhancement of the initial input image, ii) liver and lesion region identification using intensity histogram analysis and knowledge-based constraints, or iii) rough segmentation of liver lesion using threshold values. The simplest formula for thresholding segmentation was as follows: when pixel $p\ (x, y)$ value is greater than a threshold $\boldsymbol{\tau}$, set the pixel $p\ (x, y)$ to *0*, this means for each pixel in the segmented image, if the pixel was greater than a specified threshold, then pixel value will be 0. For multilevel thresholding, more than one segmentation rule with multiple thresholds was used as following: whenever the pixel $p\ (x, y)$ value is less than a threshold $\boldsymbol{\tau 1}$, then set $p\ (x, y)$ value to 255, also when pixel $p\ (x, y)$ value is greater than or equals threshold $\boldsymbol{\tau 1}$ but less than threshold $\boldsymbol{\tau 2}$, then set $p\ (x, y)$ value to 128. If no condition is validated, $p\ (x, y)$ is *0.* Multilevel thresholding segmentation was considered complex and hard to be implanted when compared to a single threshold approach.

In general, threshold-based segmentation showed poor performance with parenchyma lesions. However, it showed good performance when the contrast between the lesion and surrounding normal tissues is high. Abdel- Messiah et al. [27] proposed an enhanced threshold-based method for liver lesion segmentation on CT scans. They first enhanced the gray level intensity contrast of the input image. The threshold ability to segment lesion region out of liver tissues was enhanced by increasing lesion to liver contrast. The contrast was increased by adding an enhanced image to itself. This method suffered from being noise sensitive. Accuracy was enhanced, and false detections were reduced through roundness and neighboring slices information.

3.3. Graph Cut Methods

Graph cut methods re-represent the original image using an undirected weighted graph. Each image pixel is represented using a graph node. Two adjacent pixels are connected with an edge. Edge's weights represent the gray level similarity between pixels. The segmentation process here means to cut out a subgraph where the intensity level's similarity is the maximum. Recently, graph cut methods had the advantages of having unique implementation steps (i.e., not iterative), and it could maximize the minimization of some energy function. The energy function was calculated as:

$$\alpha\,(1-\delta\,(li-lintial\;i)+\beta\,\sum\;(1-\delta\,(li,(i))),(i) \qquad (1)$$

where α refers to the change factor for each pixel label, β refers to the change in pixel label and neighboring pixels, N(i) refers to a neighborhood of pixel i, and δ is the Kronecker delta function. The graph cut algorithm is classified under a semi-automatic segmentation approach. This because the selection of the seed point was full- dependable upon the user.

The easiest application of graph cut in liver segmentation was when vessels or lesions were segmented from the homogeneous background (i.e., liver). On the other hand, when the graph cut was implemented to segment liver parenchyma where the background was heterogeneous, the selection of seed point was quite difficult. For this reason, Yang et al. [28] proposed a method to automate seed point selection. They implemented CT liver lesions rough segmentation by utilizing mathematical morphology with fast marching. However, this method showed poor performance in segmentation parenchyma lesions when other imaging modalities were used.

Fang et al. [29] proposed an enhanced graph cut to segment lesions from enhanced MRI images. This method was built upon the optimal tree metrics approach. Primarily, the feature set was generated based on the multi-phase contrast-enhanced MRI image. Spatial-temporal MRI information was extracted using color-space mapping. Then, optimal global labeling was obtained using tree-metrics graph cut algorithms. Classification of lesions was simplified by applying the tree-pruning method. The tree pruning method has the following three elements as inputs: i) MRI enhanced image, ii) original classifier labels, and iii) smoothness factor $\lambda \geq 0$. Then, a new reduced label set was produced with agglomerative classification based on the extracted dynamic features. This method had the advantage of consuming less computational power by avoiding iterations, and of its ability to be applied to different imaging modalities with different organs.

3.4. Texture Based Methods

Unlike other segmentation algorithms, existing texture-based algorithms focused on segmenting objects based on their textural characteristics rather than its boundaries. The basic flow of all texture-based methods is: i) extraction of textural features of the object, ii) features classification into desired texture and undesired textural features, and iii) smoothing of the segmented region using post-processing techniques. Different methods for liver/tumor segmentation with different texture features were proposed. Huang et al. [30] proposed the usage of neighbor pixels mean, variance, Law's texture, Unser's sum, and difference histograms as the main features to segment lesions from CT scans.

Ji et al. [31] proposed the usage of structure and context properties to segment lesions from surrounding liver tissues in 3D CT scans. This method had the advantages of: i) automatically acquire implicit lesions shape characteristics using the autocontext model (ACM) method, ii) good segmentation performance due to its ability to combine multiple atlas scans which enhanced segmentation accuracy, iii) classification improvement by the usage of enhanced mean shift method, and iv) segmentation time reduction. However, this method required ground truth to be specified manually by the user.

Danciu et al. [32] proposed the usage of lesion volume, diameter and size to region ratio as the main texture features. This segmentation method selected lesions features based on the concept of minimum redundancy/maximum relevance. This helped in the selection of unique textural features with lower redundancy as possible. Also, the dependency of extracted features was maximized. Luo et al. [33] used discrete wavelet transform (DWT) on CT image and then used transform coefficients as a basis to identify characteristics of the liver and its surrounding tissues. Luo et al. [34] proposed a method that put both global and local texture into consideration. They enhanced lesion segmentation by using anatomical, morphological, and some high order statistical texture features which then passed to the SVM classifier.

3.5. Comparison of Liver/Lesion Segmentation Methods

Table 2 summarizes previously discussed liver segmentation research work - discussed in sections 3.1, 3.2, 3.3 and 3.4 - in terms of methods contributions, advantages, limitations, and results. Table 3 compares mostly used liver lesions (i.e., tumors) segmentation methods in terms of methods complexity, speed, noise sensitivity, advantages, and limitations.

Table 2. Liver segmentation methods' related work.

Author(s)	Contribution	Advantages	Limitations	Results
Zhou et al. [21]	Performance benchmark study for three semi-automatic liver lesions in segmentation methods.	Good quantitative results	- Over or under segmentation - High user dependency	Lesions contour with subtle details
Pohle et al. [22]	An adaptive region growing technique.	This method had the advantage of being able to acquire knowledge about the homogeneity criterion from segmented region characteristics automatically.	- Inefficient if the segmented region is heterogeneous - Under segmentation.	- Reliable if the target region is homogeneous - Simple but robust, hence produce reasonable segmentation quality even when some model rules were not met.

Table 2. Liver segmentation methods' related work -Continued(1)

Author(s)	Contribution	Advantages	Limitations	Results
Ruskó et al. [23]	A technique to choose a seed region depending on the density of pixels in the CT scan image.	- This method was able to deal with the heterogeneous region's problem. - Low time consumption	- Cannot deal with large liver lesions	This method suffered from complexity and resulted in under-segmentation when liver intensity level was heterogeneous due to the presence of a huge lesion.
Kumar et al. [24]	Used largest connected region centroid as the starting seed point and the threshold is determined by a Gaussian model.	Low time consumption	- It can deal with the liver under segmentation by fixing gaps and connecting with other neighbourhood tissues.	The average error for the segmented region was 1.93%.
Huang et al. [25]	Enhanced lesions localization by transforming the liver CT scan image into a projection plane using a ray casting algorithm and then use region growing for segmentation.	No over segmentation	- Threshold choice. - Over-segmentation and segmentation shortfalls.	Segmentation accuracy is not very precise.
Kuar et al. [26]	Enhanced liver cyst area segmentation by combining k- means clustering with region growing method.	Low complexity	Implementation quality was dependent on the choice of cluster's initial centroids.	This method proved its superiority over the standard k-means method (i.e., standard k-mean clustering was unable to separate cysts cluster from the rest of image clusters).
Abdel-Massieh et al. *[27]*	An enhanced threshold-based method for liver lesion segmentation on CT scans.	Can segment lesions very accurately in case of a single large lesion.	This method suffered from being noise sensitive.	The sensitivity score was 79%.

Table 2. Liver segmentation methods' related work -Continued(2)

Author(s)	Contribution	Advantages	Limitations	Results
Yang et al. [28]	A method to automate seed point selection.	Accurate lesions segmentation from CT scans.	Poor performance in segmentation parenchyma lesions when other imaging modalities were used.	Experiments have been executed on human liver CT data and obtain results in less time compared to the implementation with CPU.
Fang et al. [29]	An enhanced graph cut to segment lesions from enhanced MRI images.	- Low computational cost. - Achieved global optimization in labelling tree metrics. - Not iterative.	- The tree structure was not optimal. - Smoothing parameter choice.	Enhanced performance when compared to existing approaches in terms of lesions visualization and size measurement.
Huang et al. [30]	Segmented liver lesions based on statistical features such as pixels mean, variance, Law's texture, Unser's sum and difference histograms.	No prior knowledge about liver texture, place, or orientation was needed.	It can not segment large lesions.	Reasonable segmentation quality for liver parenchyma lesions.
Ji et al. [31]	Used lesions structure, shapes, and context properties to segment lesions from surrounding tissues in three dimensions CT scans.	- Automatically acquire implicit lesions shape characteristics using the ACM method. - Good segmentation performance due to its ability to combine multiple atlas scans, which enhanced segmentation accuracy. - Classification improvement by the usage of enhanced mean shift method. - Segmentation time reduction.	This method required ground truth to be specified manually by the user.	Results were similar to results reported in liver segmentation benchmark work with an average surface of 1.5 cm and average volume overlap error of 8.3%.

Table 2. Liver segmentation methods' related work -Continued(3)

Author	Contribution	Advantages	Limitations	Results
Danciu et al. [32]	Used lesion volume, diameter and size to region ratio as the main texture features.	Selected features were unique textural features with lower redundancy and high dependency.	May result in over or under segmentation.	Results showed noticeable feature reduction and lower computational overhead.
Luo et al. [33]	Used DWT transform on CT image and then used transform coefficients as a basis to identify characteristics of the liver and its surrounding tissues.	- DWT coefficients resulted in satisfactory classification performance with SVMs. - Liver volume was accurately contoured, by combining structural features pixel-wised SVM.	High time consumption.	Results showed sensitivity as 94.1% for untrained data set, and 96.3% for partially trained data set.

Table 3. A comparison between the lesion segmentation methods.

Criteria	Fuzzy C Means (FCM)	Thresholding	Watershed (texture-based)	Region growing
Complexity	Simple	Simple	Moderate	Complex
Speed	Fast	Fast	Moderate	Slow
Sensitivity to noise	Sensitive	Sensitive	Sensitive	Sensitive
Advantages	Efficient method with reasonable coverage.	- Useful in greyscale images and for image linearization. - Prior image information is not required.	Classify the pixels of images based on their intensities.	- Provide an exact image with clear edges. - A small number of seed points are required. - Multiple criteria at the same time.
Limitations	- The output depends on the segmentation partitions. - Fuzzy members identification is difficult.	- It does not work on all MRI images because of the intensity variation. - Threshold selection: critical and difficult.	The usage of pixels' intensities for pixels separations may lead to the over-segmentation.	- This algorithm may lead to a gradient problem. - The local method with no global views.
Notes	Better than K-Means	Used in real-time applications		Separates the image into regions with the same properties based on the given criteria.

4. LIVER CAD

CAD systems were used as technological solutions to assist disease diagnosis using medical image analysis. CAD systems had two main subcategories, namely computer-aided detection (CADe) and computer-aided diagnosis (CADx). CADe systems are used to detect and segment abnormalities in organ tissues, while CADx schemes used to tell if the lesion is malignant or not. CAD systems had the advantage of being able to reduce medical errors and intra- and inter- radiologists' variability. Hameed et al. [35] proposed an enhanced CAD system to assist the classification of lesions into malignant or benign on CT images. Grey level co-occurrence matrix (GLCM) was used to segment the liver from the rest of the abdominal CT scan. GLCM outputted features set in terms of pixels homogeneity, contrast and correlation with statistical features such as variance and mean. Those features were passed into a probabilistic neural network (PNN) classifier to tell if the segmented lesion was malignant or benign. This method was unable to deal with high order features.

Chen et al. [36] proposed a method to diagnose liver with cirrhosis lesions. This method mainly focused on how liver and spleen texture changes can point to liver cirrhosis. They enhanced classification performance by constructing statistical shape models (SSM) for the liver, spleen, and their joint. Alahmer et al. [37] used FCM clustering in order to detect benign and malignant liver lesions in CT scans. They divided the region of interest into inner and outer lesion regions. To enhance the accuracy of the segmentation process, they put intensity, texture and shape properties into consideration. When features set is constructed successfully, the features set is served as input to SVM to be classified either as benign and malignant. The experimental results showed an enhancement in the classification accuracy using multiple region on interest (ROI) technique compared to the accuracy using a single ROI.

Edwin et al. [38] proposed dividing the initial image into sub-images and implementing segmentation on the sub-images and then merging them to enhance lesion identification. This method first computed the segmentation function, and then it computes foreground markers. In the next step, the system computed the background markers. Further modifications were then implemented. At the end, it colors the output images of the watershed method as purple, green and red. Malar et al. [39] proposed a CAD method based on region growing for image segmentation. In this method, it will grow from the seed and further compared with the neighborhood values. This will result in liver region identification. After feature extraction and selection phases, the selected features are passed to the Hidden Markov Model (HMM) for classification.

Das et al. [40] proposed a CAD system for cancer tissue detection on CT scans. Their proposed system was integrating adaptive thresholding to segment lesions with spatial fuzzy clustering to label segmented lesions. Adcock et al. [41] proposed a method to classify different liver lesions namely cysts, metastases, haemangiomas, hepatocellular, carcinomas, focal nodules, abscesses, and neuroendocrine neoplasms. Their proposed CAD system integrated 2D persistent homology, bottleneck matching, and SVM. The output of this method had the advantage of being suitable to be passed to machine learning algorithms. However, this method suffered from difficulties presented when large lesion pixels were normalized. This led to misclassifications.

Dankerl et al. [42] proposed a technique to identify lesions on CT scans based on lesions histological characteristics. At first, lesion regions were identified by radiologists. The system then acquires knowledge about histological features of identified lesions. When a new lesion was presented to the system, previous histological knowledge was retrieved, and the input lesion was then classified in comparison with that knowledge. Lesions were classified based on density and volume into benign/malignant. Then lesions were further classified into cyst, metastases, haemangiomas. Abd-Elaziz et al. [43] used the region growing method segmentation. In the beginning, seed point properties were compared with the neighboring pixels. Iteratively, the location of the lesion was specified.

Li et al. [44] proposed a hybrid method to solve the classification issue for haptic lesions. This method starts with some prior knowledge (a radiologist identified lesion region on the CT scan images). This will fasten and ease the process of feature extraction. Features include spatial grey scale metrics such as dependency, run length, and different metrics. Multiclass SVM is used to classify haptic tissue into primary hepatic carcinoma, haemangioma, and normal tissue using one against all and one against one comparison.

Huang et al. [45] proposed a technique to categorize lesions into either benign or malignant. The lesion region was segmented using the FCM Clustering method. Features were extracted using ast discrete curvelet transform from the segmented lesions. Feed forward classification method is then used to label lesions either to benign and malignant. Safdari et al. [46] proposed a method based on FCM to segment hepatic lesions. After segmentation, they used properties like lesions size, location, circularity, and the shortest distance from the liver border to lesions as features. Classification is implemented using a Naïve classifier, and lesions were labeled into either normal or abnormal slices. Entezarimaleki et al. [47] proposed an automatic lesion segmentation technique from the CT images. They used a sequential backward selection technique for feature selection and probabilistic neural networks to label lesions as hepatocellular carcinoma, cholangiocarcinoma, hemangioma, or hepatoadenoma. Table 4 summarizes the discussed CAD systems in terms of the contributions they offer, their advantages, limitations, and results.

Table 4. Recent research works on liver CAD systems.

Author	Contribution	Advantages	Limitations	Results
Hameed et al. [35]	An enhanced CAD system to assist the classification of lesions into malignant or benign on CT images.	More adaptable and can classify lesions accurately when compared to the standard neural network.	Unable to deal with high order features.	Results showed a sensitivity of 84% when the PNN classifier was used, and 87% when PCNN was used.
Chen et al. [36]	A CAD system to diagnose liver with cirrhosis lesions.	- Can achieve an accurate normal/abnormal classification - Can estimate the proceeding stage of cirrhotic cases.	Unable to deal with large data sets.	Results showed a classification accuracy of 88% in the case of a healthy liver, and 90% for the abnormal liver.

Table 4. Recent research works on liver CAD systems –Continued.

Author	Contribution	Advantages	Limitations	Results
Alahmer et al. [37]	Used FCM clustering to detect benign and malignant liver lesions in CT scans.	Higher classification accuracy when multiple regions of interest are used.	This method was classifying limited types of liver lesions.	Classification accuracy was 98%.
Edwin et al. [38]	Enhanced lesion identification by partitioning original image and segmenting the sub-images and merging them.	Simple, reliable and accurate method to segment the liver tumour from abdominal CT image	- Threshold value choice. - Over/under segmentation.	Results showed a sensitivity of 93%.
Malar et al. [39]	A CAD method based on region growing and HMM for image segmentation.	- Low time consumption - Enhanced diagnosis of confidence.		Results showed a sensitivity of 96.5%.
Das et al. [40]	A CAD system that integrated adaptive thresholding to segment lesions with spatial fuzzy clustering to label segmented lesions.	No need for user intervention.		Results showed an accuracy of 89.15% and 95.02% for MLP and C4.5 classifiers, respectively.
Adcock et al. [41]	A method to classify liver lesions: cysts, metastases, haemangiomas, hepatocellular, carcinomas focal nodules, abscesses, and neuroendocrine neoplasms	The output of this method had the advantage of being suitable to be passed to machine learning algorithms.	Cannot handle lesions with large size.	Results showed lesions identification precision as 91.5%.
Dankerl et al. [42]	A method to identify lesions on CT scans based on lesions histological characteristics.	Less processing time with reasonable confidence rates.	Cannot handle lesions with large size.	Results showed 95.5% accuracy for lesions identification.
Abd-Elaziz et al. [43]	A method to localize lesions based on region growing segmentation.	Low segmentation time.	Cannot handle lesions smaller than 1 cm.	Results showed specificity > 99%.
Li et al. [44]	A hybrid method to solve the classification issue for haptic lesions.	- Flexible initialization - Low time consumption during convergence process - Robust segmentation.		Area overlap error was in the range of 6.99-12.75%.

5. CHALLENGES

Despite the huge development in liver medical image analysis, there are some challenges which remain unsolved. The key challenges are related to either diagnosis or surgery medical field in terms of [48-53]:

- CAD systems are sensitive to noise and fail to contour lesions accurately. They may also need long computational time with high implementation complexity. Also, creating an automatic segmentation method is still quite challenging. This is because the structure of the 2D liver CT scan differs from slice to another. The only common thing among all slices is that the liver is connected with many organs. Those organs make the process of segmenting the liver automatically complex and difficult since they may have the intensities of the same pixels as the liver.
- Image enhancement: existing methods are sensitive to noise and fail to preserve the weak texture on an image. Those weak features can help to improve the detection of some liver lesions such as HCC by 40% [54].
- Features extraction method: none of the existing feature extraction algorithms guaranteed the expected accuracy with less computation (i.e., the accuracy increases when computation increases).
- Registration: providing systems that can fuse liver scans from different modalities automatically is still challenging. Those systems will be advantageous to assist liver lesion diagnosis more accurately when one modality is not enough to identify lesion type.
- Classification: all existing classification methods are using a supervised learning approach (i.e., the region of interest/ lesion is labeled in advance by the radiologist). Hence, the need for unsupervised classifier to be used in the absence of training samples is still a challenging task.

6. FUTURE RESEARCH TRENDS

The current research trends are focusing on: i) enhancing acquired liver scans, ii) providing high-performance automatic lesion segmentation system that can identify lesion area accurately and without consuming much time, iii) providing classification methods based on unsupervised learning methods, and classification methods that can classify all existing liver lesions, iv) providing features extraction methods that can provide unique and reasonable features which can best characterize liver lesions with lower computational time, v) providing segmentation methods that can handle features with high order, and vi) proposing segmentation methods that can segment large lesions (i.e., lesions size > 1 cm) without resulting in over/under segmentation.

7. CONCLUSIONS

This paper discussed different medical imaging modalities such as CT, MRI, PET, and US. It also declared which modality is the best choice with what lesions in Section 2. The liver segmentation process aims to divide the medical image into the background (i.e., liver) and foreground (i.e., lesions). The diagnosis step aims to extract dominant features from a lesion in the segmented image, and then classify those lesions into different disease classes such as cyst and HCC. A comparison between segmentation related work was provided with a general comparison of available techniques. Liver lesions CAD systems were discussed, and a comparison among provided CAD methods was presented. Moreover, challenges facing the medical images' analysis were introduced and futures research trends in this area were discussed.

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