8th International Conference on
Combinatorics, Cryptography, Computer Science and Computation
November. 15-16, 2023

Deep Learning Techniques for Liver Cancer: A Survey on Early Prediction, Detection, and Prognosis of Metastasis and Survival

Arefe Pourmajidian
Mazandaran University of Science and Technology, Department of Computer Engineering
Babol, Iran
arefe.pourmajidian@gmail.com

Javad Vahidi
Iran University of Science and Technology, Department of Computer Science
Tehran, Iran
jvahidi@iust.ac.ir

ABSTRACT

Background: The liver, an essential organ for digestion and removing toxins, is vulnerable to conditions such as liver cancer. Frequently, these ailments aren't identified until they've progressed significantly due to their understated initial symptoms. Although contemporary imaging techniques occasionally overlook these preliminary indications, the advent of advanced tech solutions is increasingly recognized as pivotal. The urgency of early detection is underscored by the severe repercussions of liver cancer. While traditional diagnostic measures have their limitations, nascent technologies, notably Deep Learning (DL) and especially Convolutional Neural Networks (CNN), are exhibiting remarkable diagnostic prowess, occasionally outpacing human expertise. Leveraging these DL methodologies and state-of-the-art tools has the potential to revolutionize early liver cancer detection, thus mitigating patient mortality rates and subsequently trimming both the costs and duration of treatments.

Methodology: This survey assessed 84 notable articles from top journals over the last five years. Selection prioritized articles showcasing precise computations with evaluable outcomes. Our focus was on the potential of DL in early detection of precancerous liver lesions, liver cancer diagnosis, and survival rate predictions.

Results: DL proved highly effective in early lesion detection and liver cancer diagnosis, achieving near-perfect accuracy of 100% in specific datasets. Prognoses concerning metastasis and survival reached an accuracy of 89.1%.

Conclusion: Our survey highlights the advantage of merging neural networks with other techniques for better image classification. However, data-related constraints limit its wider application, especially due to the lack of a global standard for AI in biomedical imaging. Collaborative efforts are needed to curate extensive datasets, and more research is essential on precancerous lesions and liver cancer prognosis.

KEYWORDS: Artificial Intelligence, Deep Learning, Early Detection, Liver Cancer, Prediction, Prognosis

1 INTRODUCTION

The liver, a pivotal organ exclusive to vertebrates, nestles under the ribs on the right side of the abdomen. Functioning as a crucial digestive aid and a detoxifier, it efficiently processes nutrients and expels toxins. Despite its resilience, the liver is susceptible to a range of diseases, both inherited and acquired, often stemming from factors like viruses, alcohol consumption, obesity, and unhealthy dietary choices.

Over prolonged periods, such afflictions can exacerbate, leading to cirrhosis—a debilitating condition where healthy liver tissue is supplanted by scar tissue, thus impeding regular liver function. When left unchecked, such deteriorations can escalate to liver failure and the formidable adversary—liver cancer. A primary challenge posed by liver diseases is their covert nature. Many remain undetected until advanced stages due to a dearth of early symptoms. Traditional imaging techniques can occasionally miss or misinterpret liver abnormalities, underscoring the imperative need for a harmonious fusion of advanced technology and medical diagnostics in liver ailment treatment.

Currently, while ultrasounds are routine in liver disease screenings, CT scans remain the mainstay diagnostic tool, furnishing clearer insights compared to their ultrasound counterparts. In situations fraught with diagnostic ambiguity, such as differentiating between liver cancer and benign regenerative nodules, the utility of contrast-enhanced ultrasounds (CEUS) becomes evident. Emerging at the nexus of technology and liver diagnostics are computer-aided diagnosis (CAD) tools. These cutting-edge innovations enhance CT image clarity, distinguish liver from neighbouring organs, categorize liver lesions, furnish measurements of the liver and tumours, and provide intricate 3D visualizations of the liver and its intricate architecture. Augmenting the CAD toolkit are machine learning methodologies, especially adept at tumour classification, drawing insights from tumour-centric liver features.

Recent shifts in global lifestyles have amplified liver-related maladies, with statistics sounding the alarm bells. The American Cancer Society's 2023 report reveals an estimated 41,210 new cases and 29,380 deaths from liver and intrahepatic bile duct cancers combined, highlighting the magnitude of the crisis [1]. An additional concern is the potential metastasis to the liver seen in over half the patients diagnosed with colorectal cancer (CRC). Amid these challenges, the silver lining emerges in the form of ultrasound-guided percutaneous thermal ablation (US-PTA), which has demonstrated undeniable efficacy in treating both primary and secondary liver cancers [2].

Colorectal cancer stands as the third most common cancer in Western countries, with a concerning 50% of patients either presenting with or later developing metastases, predominantly in the liver. This results in a sombre 5-year survival rate of just 15%. Curative liver metastasis resection, though beneficial, is applicable for only about 25% of CRC patients. The necessity to identify those at heightened risk becomes evident. Historically, body mass index (BMI) served as the go-to metric, but it's now seen as inadequate in capturing a patient's genuine physical health. In contrast, CT image-based markers, which detail body composition, offer a more comprehensive view. Earlier techniques, while insightful, were manual and not conducive to regular clinical routines. However, the dawn of DL now permits automated and precise evaluations from 3D CT scans, offering not only insights into body composition but also the geometry of metastases, critical for survival predictions. Leveraging this technology, our aim has been to devise a prediction model that melds seamlessly with routine care, ushering in a new era of personalized treatment strategies [3].

2 METHODOLOGY

For this survey, a comprehensive search of the literature was performed, focusing on the top published works from reputed journals. A total of 84 preeminent articles published within the last five years were meticulously selected from notable databases such via Pubmed, Nature, IEEE, Science Direct (Elsevier), Springer, and John Wiley Library. The search spanned a reference period of 5 years, starting from January 2019 up to November 2023. The selection criteria for these articles were based on specific metrics used within each paper. Emphasis was given to those articles that demonstrated precise calculations, yielding results that were both evaluable and comparable.

By adopting this approach, the survey ensures a systematic and comprehensive examination of the transformative potential of DL in early detection of precancerous liver lesions, diagnosis of liver cancer, and prognosis of survival rates and the likelihood of metastasis in liver cancer using DL algorithms.

3 LITERATURE SURVEY

In the comprehensive review of the literature, articles are systematically organized in chronological order based on the progression stages of the disease, segmented into three distinct sections.

3.1 Deep Learning-Assisted Early Detection of Precancerous Liver Lesions

The early detection of precancerous lesions of the liver and recognition of initial symptoms of the disease are paramount in modern healthcare. Recognizing these early warning signs can significantly reduce the progression to full-blown liver cancer, a condition associated with high mortality rates. Early diagnosis not only provides a higher chance of successful treatment but also considerably decreases the financial burden associated with prolonged and advanced medical interventions. Moreover, treatments initiated in the early stages of the disease are less invasive, leading to fewer side effects and complications for the patient. Importantly, early detection and intervention drastically reduce the risk of death, emphasizing the need for regular screenings and heightened awareness among both medical professionals and the general population. Zhao et al. [4] undertook a retrospective study spanning January 2010 to May 2019, where they harnessed CEUS images to construct a DL model for predicting early recurrence (ER) following thermal ablation of CRC liver metastasis. The dataset comprised 207 patients with a total of 13,248 slice images. This DL model was not only trained but also enhanced by weaving in significant clinical markers such as preoperative chemotherapy, lymph node metastasis, and T stage. When combined, this DL-C model exhibited remarkable prediction accuracy, achieving 0.72 in the internal test cohort and 0.76 in the external test cohort. The fusion of DL with these pivotal clinical attributes heralds a promising trajectory for refining prognostic methodologies in the realm of CRC liver metastasis treatments.

Liang et al. [5] introduced PathFinder, an interpretable, human-centric, DL-guided framework designed to aid pathologists in identifying new tissue biomarkers from whole slide images. Utilizing sparse multi-class tissue spatial distribution information, PathFinder excels in localizing, characterizing, and verifying potential biomarkers, offering state-of-the-art prognostic performance. The framework revealed the significant prognostic value of the spatial distribution of necrosis in liver cancer, leading to the proposal of two clinically independent prognostic indicators related to necrosis. Testing the framework across different datasets, the proposed PaSegNet model achieved impressive multi-class tissue classification accuracy: 94.8% on the QHCG dataset, 95.6% on the TCGA dataset, and 94.1% on the PAIP dataset, with corresponding AUCs of 0.9980, 0.9984, and 0.9974, respectively. In prognosis prediction, MacroNet outperformed other networks, demonstrating robust generalizability and achieving a concordance index (C-Index) of 0.754 on the QHCG dataset and superior performance in survival analysis.

Han et al. [6] have developed an innovative approach for the early detection of complex diseases like hepatocellular carcinoma (HCC) by integrating Dynamic Network Biomarkers (DNB) with Graph Convolutional Neural Networks (GCN). Their model, DNB-GCN, constructed using transcriptomic data and gene expression levels as node features, was trained using a mouse model for HCC. The DNB analysis alone identified a critical transition point at 7 weeks, which histological examinations could not detect. When coupled with GCN, the DNB-GCN model excelled, achieving 100% accuracy in distinguishing between healthy and cancerous mice, and it accurately predicted the health status of newly introduced mice samples. This synergy of DNB and DL through GCNs suggests a promising direction for overcoming the limitations of traditional biomarker discovery, providing a more nuanced and precise method for early disease detection and paving the way for advancements in personalized precision medicine. Further development and validation of this method could significantly enhance early diagnosis and treatment of complex diseases such as HCC.

Table 1 presents detailed overview on the performance of DL in early detection of precancerous liver lesions studied in this survey along with their results.

Table 1 Deep learning in early detection of precancerous liver lesions

Author	Data	Proposed Method	Results
Zhao et al. [4]	CEUS	DL-C	Accuracy of internal test cohort = 72% Accuracy of external test cohort: 76% AUC = 78%
Liang et al. [5]	QHCG dataset	PaSegNet	Accuracy: 94.8% AUC = 99.80%
Han et al. [6]	Transcriptomic data and gene expression levels	DNB-GCN	Accuracy = 100%

3.2 Deep Learning-Assisted Diagnosis of Liver Cancer

The implementation of artificial intelligence (AI) in liver cancer detection offers a plethora of advantages that address several challenges in the medical field. Firstly, AI-powered diagnostic tools can significantly reduce the cost of diagnosis, offering a more economical alternative to traditional methods that often involve expensive equipment and specialist consultations. Moreover, despite the expertise of medical professionals, human error is inevitable; AI systems, with their consistent data processing capabilities, can drastically reduce diagnostic errors. This is especially crucial in regions where there's a shortage of specialist doctors or where patients face difficulties accessing expert care due to geographical or economic constraints. Poor image quality and noise can lead to mistakes in image diagnosis. As a result, many studies focus on improving image quality and removing noise before further processing. Chen et al. [7] conducted a study exploring the impact of deep learning reconstruction (DLR) on the image quality and diagnostic performance of liver diffusion-weighted imaging (DWI) at 3 Tesla. It was found that DLR significantly enhanced the qualitative image quality, with sharper lesion boundaries and higher signal-to-noise ratios (SNR) and contrast-to-noise ratios (CNR) compared to non-DLR images. Despite the observation that DLR reduced the apparent diffusion coefficient (ADC) values of malignant tumours, this decrease did not translate into a diminished ability to differentiate malignant from benign liver lesions. The diagnostic performance of ADC values remained consistent between the DLR and non-DLR groups. The phantom study within the research confirmed that DLR causes a reduction of ADC values, particularly in images with low resolution and more so in heterogeneous structures. Additionally, the study reported a sensitivity of 93.7%, specificity of 84%, and an overall accuracy of 94.3%.

Khan et al. [8] have developed a cutting-edge multi-modal deep neural network (DNN) tailored for multi-class malignant liver diagnosis that integrates both portal venous computed tomography (CT) scans and pathology data. This novel network employs a deep dilated CNN to identify key features from CT scans, with residual connections to mitigate vanishing gradient issues, and a wide and deep network for learning pathological features, combining memorization with generalization. The model then concatenates down-scaled hierarchical features from both CT scans and pathology data for the classification of liver cancer variants. Utilizing transfer learning from pre-trained layers, the network adeptly manages the challenges posed by insufficient and imbalanced datasets. The finely tuned model boasts a remarkable average accuracy of 96.06% and an Area Under the Curve (AUC) of 0.832 for predicting three classes of liver cancer variants. Similarly, Manjunath et al. [9] have proposed a novel DL model specifically designed for the detection and classification of liver disease tumours from CT images, focusing on distinguishing between Metastasis and Cholangiocarcinoma. Their modified Unet-60 classifier has demonstrated superior performance over other existing classifiers, achieving remarkable results with a high accuracy rate of 98.61%, a sensitivity of 97.22%, a specificity of 100%, and an impressive Dice similarity coefficient of 98.59%. These metrics underscore the model's effectiveness in adapting to different datasets and

outperforming other classifiers in terms of accuracy and precision. Looking ahead, they aim to reduce the model's training time and examine a greater variety of labeled CT images depicting various liver diseases. They also plan to extend their work to include 3D volumetric analysis of the liver and to consider multinomial classification to differentiate among types of liver diseases.

In the study by Sridhar et al. [10], an innovative DL-based system is introduced for accurately segmenting tumours from liver images, utilizing a novel approach of incorporating user interaction and a Coot Optimization Algorithm (COA) to optimize the Extreme Learning Model (ELM) parameters. The system marks an advancement over traditional interactive segmentation methods and current CNN-based approaches by achieving a higher segmentation accuracy. The proposed geodesic distance encoding method allows for enhanced initial segmentation with minimal additional user input. Subsequently, the optimized ELM classifier demonstrates superior performance with an accuracy of 87.09%, significantly outperforming other methods such as DNN-GF (80%) and HI-DNN (83%). When combined with COA, the model's accuracy further improves, reaching up to 96%, with sensitivity and specificity nearing 99%.

Bhattacharyya et al. [11] conducted a study on liver cancer, a leading cause of death globally, using medical images to detect the disease. The research utilized adaptive thresholding with watershed transform for image segmentation, while the Gray Level Matrix and the Local Binary Pattern helped in feature extraction from a dataset of 225 images. Various classifiers, including neural networks and DNNs, categorized the cancers. The watershed Gaussian-based DL algorithm showed promise for liver cancer diagnosis. Among the methods, the DNN classifier outperformed others, achieving an impressive accuracy of 99.25%.

Trivedi et al. [12] conducted research to predict the progression of HCC, a prevalent type of liver cancer. The study utilized various machine learning methods, including KNN, SVM, SGD, Neural Networks, Naïve Bayes, and Logistic regression, on a public dataset to assess their predictive capabilities. Among the tested models, the neural network demonstrated superior performance, achieving a remarkable classification accuracy of 98.8%. This research underscores the potential of machine learning, particularly neural networks, in the early diagnosis of liver cancer, with plans to further enhance accuracy by extracting more dataset features and exploring broader machine learning and DL techniques.

In a study by Sirćo et al. [13], liver cancer, a prominent global health concern, was diagnosed using CT scans. The research utilized DL techniques, specifically ResNet models, to segment the liver and tumour from CT scans. Among the models tested (ResNet-18, ResNet-34, ResNet-50, and ResNet-101) the ResNet-34 model demonstrated the highest accuracy at 99.2%. Although ResNet-101 was found to be the most efficient, ResNet-18 was the quickest. In addition, Rahman et al. [14] proposed an efficient method for segmenting liver and tumours from CT image volumes using a hybrid ResUNet model, which combines the ResNet and UNet models. The primary purpose of this model was to segment the liver and assess the region of interest (ROI) in CT volume slices of patients with liver tumours. This innovative approach was evaluated on the public 3D dataset IRCADB01. The experimental results revealed an impressive accuracy for liver segmentation, with true value accuracy rate of 98.16%. Additionally, the dice coefficient authentication rate increased, underscoring the model's robustness and readiness for liver tumour detection.

In a study by Chen et al. [15], the differentiation levels of liver cancer were explored, which can be categorized as poorly differentiated, moderately differentiated, and well differentiated. Differentiation levels are pivotal for determining patient survival rates and treatment durations. Traditional methods of classifying histopathological images, which are considered the gold standard for liver cancer diagnosis, can be time-consuming and labor-intensive. This research introduced the SENet DL model for the intelligent classification of these histopathological images and compared its performance with four other models: VGG16, ResNet50, ResNet_CBAM, and SKNet. Results highlighted the SENet model's superiority in classification, achieving the highest accuracy rate of 95.27%.

Das et al. [16] proposed a novel approach for the detection of cancer genes, utilizing DL models to analyze DNA sequences. Their method involved digitizing gene sequences using three numerical mapping techniques and then analyzing these sequences in two forms: as one-dimensional signals using a custom CNN model, and as two-dimensional spectrogram images using two different 2D CNN models. The first 2D CNN model employed feature extraction with VGG16 followed by classification with an SVM,

achieving an accuracy of 98.86%. The second model added new layers to VGG16 and applied fine-tuning, which resulted in a perfect accuracy rate of 100%. These models, especially the fine-tuned VGG16, demonstrated a highly effective feature extraction capability for distinguishing between liver cancer and normal liver gene sequences. The study suggests potential for expanding the approach to larger datasets and various types of cancer, highlighting the method's readiness for broader testing and its superiority over traditional machine learning methods that require manual feature extraction.

A novel DL framework named "LiverNet" was introduced for multi-class cancer classification of liver HCC tumour histopathology images by Aatresh et al. [17]. The framework drew inspiration from the BreastNet architecture, with enhancements including the addition of atrous spatial pyramid pooling (ASPP) blocks for capturing multi-scale features. The research aimed to classify liver histopathology data into four distinct classes: non-cancerous, low sub-type liver HCC tumour, medium sub-type liver HCC tumour, and high sub-type liver HCC tumour. LiverNet was tested on two datasets, KMC and TCGA-LIHC. The results showed that LiverNet surpassed other state-of-the-art frameworks in terms of classification quality and computational efficiency, achieving an accuracy of 90.93% on the KMC dataset and 97.72% on the TCGA-LIHC dataset.

In a study by Cheng et al. [18], a nanoplasmonics biosensing chip (NBC) was introduced, designed for point-of-care testing (POCT) of liver cancer. This innovative NBC, comprising silver nanoparticle-decorated ZnO nanorods on cellulose filter paper, enables one-drop blood tests using surface-enhanced Raman spectroscopy (SERS) detection. Leveraging this NBC in combination with a DNN model, the team established a serological detection platform capable of automatically identifying liver cancer in mere minutes. The DNN model, trained on 1140 serum SERS spectra from both HCC patients and healthy individuals, achieved an impressive identification accuracy of 91% on an external validation set comprising 100 spectra. This groundbreaking platform, merging the biosensing chip with DNN, holds promise for swift cancer screenings and potential broader applications in detecting various cancer types.

Lal et al. [19] introduced NucleiSegNet, a novel DL network designed for the accurate segmentation of nuclei in H&E stained liver cancer histopathology images. This architecture incorporates three key components: a robust residual block for efficient extraction of high-level semantic maps, a bottleneck block, and an attention decoder block with a new attention mechanism to enhance object localization and minimize false positives. When tested on two datasets, including the newly introduced KMC liver dataset, NucleiSegNet consistently outperformed other state-of-the-art nuclei segmentation models. Specifically, the proposed model achieved an F1 score of 81.363 and a JI score of 68.883, showcasing its superior performance and potential applicability in other image segmentation domains.

Early prediction of liver cancer in patients with viral hepatitis is a critical area of medical research, focusing on identifying those at high risk before the disease fully manifests. Viral hepatitis, particularly hepatitis B and C, is a known major risk factor for liver cancer, also known as HCC. Advances in medical imaging, blood tests for tumour markers like alpha-fetoprotein (AFP), and genetic profiling have significantly improved the ability to detect liver cancer at an early stage in these patients. Regular surveillance is recommended for those with chronic hepatitis, as early-stage liver cancer can often be treated more effectively, leading to better outcomes. Additionally, understanding the molecular and genetic changes in the liver caused by viral hepatitis can provide insights into the mechanisms of cancer development, potentially leading to new preventative strategies and therapies. Phan et al. [20] explored the utility of DL models to facilitate the early prediction of liver cancer in patients with viral hepatitis, drawing from a vast dataset of 1 million random samples from the National Health Insurance Research Database of Taiwan collected between 2002 and 2010. They observed an overall increase in the annual prevalence of hepatitis with an average annual percentage change of 5.8%, yet interestingly, a decrease in prevalence among the younger demographic. Applying DL techniques, the team discovered that a CNN model excelled in forecasting liver cancer cases within the hepatitis cohort, achieving a noteworthy accuracy of 98% and an area under the receiver operating characteristic curve (AUC) of 0.886.

Dong et al. [21] introduced the Hybridized Fully Convolutional Neural Network (HFCNN) tailored for the segmentation of liver tumours in CT images. This DL model amalgamates features from Inception combined with residual structures and pre-trained weights. Particularly aimed at discerning between liver

metastases of CRC and benign cysts in abdominal CT images, the algorithm manifests a commendable accuracy, delivering liver volume measurements of 97.22%. Furthermore, the segmentation method exhibited an average Dice coefficient of 0.92, emphasizing the efficacy of the HFCNN in addressing liver cancer analysis and demonstrating its potential in enhancing the precision of medical image detection. Working on CT images mainly, Yang et al. [22] developed a deep convolutional neural network for ultrasound imaging (DCNN-US) to differentiate malignant from benign focal liver lesions. Their study with 2143 patients showed that the DCNN-US matched the accuracy of contrast-enhanced CT at 84.7%, although it was slightly less accurate than contrast-enhanced MRI, which had an accuracy of 87.9%. This highlights the potential of DCNN-US to aid radiologists, especially less experienced ones, and underscores its viability for future clinical testing.

The classification of liver cancer histopathological images is a complex task, challenged by the intricate and subtle features characteristic of different cancer stages and types. These images contain a wealth of information, including variations in cell morphology, tissue architecture, and staining patterns, which are crucial for accurate diagnosis and treatment planning. However, the complexity of these features often makes manual classification time-consuming and prone to variability among pathologists. Moreover, the development of automated classification systems, such as those using machine learning and DL algorithms, is hindered by the scarcity of annotated training images. High-quality, well-annotated histopathological images are essential for training these models, but acquiring such datasets is challenging due to the sensitive nature of medical data, privacy concerns, and the need for expert annotation. This scarcity of data leads to difficulties in training robust models that can generalize well across different cases and institutions. Therefore, enhancing the availability of annotated datasets and improving algorithmic approaches to handle intricate histopathological features are key to advancing the classification of liver cancer from histopathological images. Sun et al. [23] introduced a novel DL approach for the classification of liver cancer histopathological images, addressing the challenges of intricate features and the scarcity of annotated training images. Instead of relying on detailed cancer region annotations, the method capitalizes on global labels, extracting patch features which are then fully harnessed. Utilizing transfer learning for patch-level feature extraction and combining it with multiple-instance learning for image-level feature extraction, this methodology adeptly handles the processing of large-scale images. Impressively, it achieved a classification accuracy of 0.98, an F1-score of 0.99, and a recall of 1, distinguishing liver histopathological images as either abnormal or normal.

Classifying liver tumours using both enhanced and unenhanced Magnetic Resonance (MR) images represents a significant advancement in diagnostic radiology. Enhanced MR images, obtained after the administration of contrast agents, provide detailed information about the vascularity of liver lesions, which is critical in distinguishing benign from malignant tumours. Unenhanced MR images, on the other hand, offer essential baseline data about the liver's anatomy and the intrinsic characteristics of the tumours. The integration of these two types of MR images allows for a more comprehensive assessment of liver tumours. By analyzing the contrast uptake patterns, growth characteristics, and the signal intensity of the lesions in both enhanced and unenhanced images, radiologists can more accurately classify liver tumours. This dual approach improves diagnostic accuracy, aids in the determination of the most appropriate treatment strategy, and can significantly impact patient outcomes. Zhen et al. [24] developed a DL system (DLS) using CNNs to classify liver tumours based on enhanced and unenhanced MR images, coupled with clinical data. The DLS was trained on a dataset of 31,608 images from 1,210 patients and validated on 6,816 images from 201 patients. The system exhibited an impressive performance, comparable to experienced radiologists. Specifically, using only unenhanced images, the CNN differentiated malignant from benign tumours with an AUC of 0.946. Combining unenhanced images with clinical data further elevated the DLS's performance, notably classifying malignancies such as HCC (AUC, 0.985) and metastatic tumours (AUC, 0.998), with an accuracy surpassing 90%. The results suggest that the DLS can effectively utilize unenhanced sequences to make accurate diagnoses, presenting a potential cost-effective alternative for diagnosing liver tumours, especially for high-risk patients, while mitigating the risks associated with contrast agents.

Chen et al. [25] utilized the inception V3 architecture, a CNN, to classify HCC using histopathological H&E images from the Genomic Data Commons Databases. This neural network comprises multiple convolution filters, pooling layers, and fully connected layers. Specifically, the inception V3 employs inception modules, combining different kernel sizes in its convolutions and a max-pooling layer. It starts with five convolution nodes linked to two max-pooling operations and continues with 11 stacks of these inception modules. A fully connected layer was added to the architecture's end, allowing for the refinement of parameters. The concluding softmax layer classifies by assigning a probability to each category, with the highest probability dictating the final prediction. The model's performance was noteworthy, aligning closely with a pathologist with 5 years of experience. It achieved an accuracy of 96.0% for benign and malignant classification, and 89.6% for tumour differentiation levels. Additionally, the model predicted four out of ten significant mutated genes in HCC from the histopathology images.

Kiani et al. [26] developed a DL model to assist pathologists in differentiating between HCC and cholangiocarcinoma using whole-slide images. The densely-connected convolutional neural network (DenseNet) achieved an accuracy of 0.842 on an independent test set. When implemented, the model significantly impacted the diagnostic decisions of pathologists, especially enhancing accuracy when its predictions were correct and decreasing it when incorrect.

Yamakawa et al. [27] are working on a CADx system that leverages an ultrasound image database being constructed by the Japan Society of Ultrasonics in Medicine (JSUM). This database consists of B-mode images of liver and breast tumours. Using a portion of this database, the researchers developed a CNN-based CADx system, grounded in the VGGNet architecture, to classify four types of liver tumours. The 4-class classification system achieved an accuracy rate of 88.0%, with individual accuracies of 98.1% for cysts, 86.8% for hemangiomas, 86.3% for HCC, and 29.2% for metastatic liver cancer. They also introduced a CADx system for determining if a liver tumour is benign or malignant, boasting an accuracy of 94.8%, a sensitivity of 93.8%, and a specificity of 95.2%.

Das et al. [28] introduced an automated system for liver cancer detection using CT images. Their proposed method, termed the watershed Gaussian based deep learning (WGDL) technique, initially segments the liver using marker-controlled watershed segmentation. The cancer lesions are then delineated using the Gaussian mixture model (GMM) algorithm. After segmenting the tumour, texture features are extracted and input into a DNN classifier to automatically categorize three types of liver cancer: hemangioma (HEM), HCC, and metastatic carcinoma (MET). Using this approach, they achieved a remarkable classification accuracy of 99.38%, a Jaccard index of 98.18%, and a negligible validation loss of 0.062 after 200 epochs with the DNN classifier.

Table 2 presents detailed overview on the performance of DL in liver cancer detection studied in this survey along with their results.

Table 2 Deep learning in liver cancer detection

Author	Data	Proposed Method	Results
Chen et al. [7]	MRI	ADC	Accuracy 94.3% Sensitivity 93.7% Specificity 84%
Khan et al. [8]	CT scans and pathology	Transfer learned & fine-tuned neural network	Average accuracy = 96.06% AUC = 83.2%
Manjunath et al. [9]	CT scans	Unet-60 classifier	Accuracy = 98.61% Aensitivity = 97.22% Specificity = 100% Dice similarity coefficient = 98.59%

Sridhar et al. [10]	CT scans	COA optimized with ELM	Accuracy = 96% F1-Score = 96% Precision = 99% Recall (Sensitivity) = 99% Sensitivity = 99% Specificity: 99% with COA
Bhattacharyya et al. [11]	CT scans	DNN	Accuracy = 99.25%
Trivedi et al. [12]	Medical data	Neural Network	Accuracy = 98.8% Precision = 98.8% Recall = 98.8% F1 = 98.8% CA = 98.8% AUC = 99.1%
Sirćo et al. [13]	CT scans	ResNet-34	Accuracy = 99.2%
Rahman et al. [14]	CT scans	ResUNet	Accuracy = 98.16% Precision = 99.9%
Chen et al. [15]	Histopathological images	SENet	Accuracy = 95.27%
Das et al. [16]	2D spectrogram images	Tuned VGG16	Accuracy = 100%
Aatresh et al. [17]	Histopathology images	LiverNet	KMC dataset: Accuracy = 90.93% IoU = 83.60% TCGA-Liver dataset Accuracy = 97.72% IoU = 95.61%
Cheng et al. [18]	Surface-enhanced Raman spectroscopy (SERS)	NBC combined with DNN	Accuracy = 91%
Lal et al. [19]	Histopathology images	NucleiSegNet	F1 score = 81.363% JI score = 68.883%
Phan et al. [20]	National Health Insurance Research Database (NHIRD)	CNN	Accuracy = 98% AUC = 88.6%
Dong et al. [21]	CT scans	HFCNN	Accuracy = 97.22%
Yang et al. [22]	Ultrasound imaging	DCNN	Accuracy of contrast-enhanced CT = 84.7% Accuracy of contrast-enhanced MRI = 87.9% AUC of 92.4% Sensitivity = 86.5% Specificity = 85.5%
Sun et al. [23]	WSI	CNN	Accuracy = 98% F1-score = 99%

			Recall = 100%
Zhen et al. [24]	MRI	CNN	Accuracy = 90%
Chen et al. [25]	Histopathology H&E images	Inception V3	Benign and malignant classification: Accuracy = 96.0% Tumour differentiation levels: Accuracy = 89.6%
Kiani et al. [26]	WSI	DenseNet	Accuracy = 84.2%
Yamakawa et al. [27]	B-mode ultrasound images	VGGNet-based CNN	4-class classification: CADx accuracy = 88.0% 2-class classification: CADx accuracy = 94.8%
Das et al. [28]	CT scans	WGDL	Accuracy = 99.38% Jaccard index = 98.18%

3.3 Deep Learning-Assisted Prognoses of Metastasis and Survival of Liver Cancer

Liver metastases, which most frequently arise from CRC, present a complex challenge in oncology due to the intricate interactions between tumour cells and the hepatic microenvironment. This dynamic interplay, which involves various cell types within the liver, is essential for tumour engraftment, survival, and progression, unfolding through four distinct phases: microvascular, pre-angiogenic, angiogenic, and growth. The detection and diagnosis of liver metastases rely heavily on imaging techniques such as ultrasonography, CT, MRI, and PET scans. While surgical resection offers the primary potential cure for resectable liver metastases, the management of this condition often requires a multidisciplinary approach, encompassing a variety of treatments tailored to the disease's extent and origin. Tsilimigras et al. [29] emphasize the importance of early detection for effective treatment, which may include resection, ablation, locoregional treatments, systemic chemotherapy, and targeted therapies. They also note the emerging role of genetic testing in refining clinical decision-making and improving prognostic predictions for patients with liver metastases.

Bevacizumab, a monoclonal antibody targeting the vascular endothelial growth factor (VEGF), is used in combination with chemotherapy to inhibit tumour growth and improve the resectability of liver metastases. The challenge lies in identifying biomarkers or clinical parameters that can accurately forecast patient response to this treatment. Factors such as the genetic profile of the tumour, molecular markers, and the patient's overall health status may influence the effectiveness of Bevacizumab. Additionally, imaging techniques, such as MRI and CT scans, are used to assess the tumour’s response to therapy. Predicting response to Bevacizumab is crucial for optimizing treatment plans, avoiding unnecessary side effects in non-responders, and improving overall survival rates. Zhou et al. [30] developed a multi-modal deep learning model named DERBY to predict the efficacy of bevacizumab in patients with initially unresectable colorectal cancer liver metastases (CRLM) using baseline PET/CT, clinical data, and colonoscopy biopsy specimens. The model extracted PET/CT features with DNNs and combined them with relevant clinical factors. They later enhanced this model, creating DERBY+, by integrating histopathological biomarkers. In external validation, DERBY+ demonstrated robust accuracy with an AUC of 0.83, a sensitivity of 80.4%, and specificity of 76.8%.

The obesity epidemic has had a profound impact on the field of liver transplantation, particularly concerning the availability and viability of donor livers. Obesity, often leading to conditions such as nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH), can compromise the health of a donor liver, making it less suitable for transplantation. This reduction in the pool of healthy donor livers comes at a time when the demand for liver transplants is increasing, partly due to liver diseases linked to obesity. Furthermore, the transplantation of fatty livers, which are more common in obese donors, is associated with a higher risk of complications post-transplant, including graft dysfunction and a lower

survival rate of the transplanted organ. This scenario poses a significant challenge for transplant programs, necessitating more stringent evaluation of donor livers and innovative approaches to improve the viability of fatty livers. Zhang et al. [31] explored the potential of using steatotic donor livers (SDLs) as a way to address the increasing demand for donor livers due to the obesity epidemic and rising prevalence of nonalcoholic fatty liver disease. Using data from the U.S. organ procurement and transplantation network, the researchers employed deep survival learning predictive models to assess the survival outcomes of accepting an SDL versus waiting for a non-steatotic donor liver (non-SDL). The models considered 20,000 simulated scenarios. The study found that deep survival learning was more effective than both the Cox proportional hazards and Random Survival Forest (RSF) models in predicting post-transplant survival. The results showed that in 25% to 30% of the simulations, candidates who accepted an SDL had a higher 3-year survival rate compared to those who waited for a non-SDL. The difference in 3-year survival post-decision was only 1.43% when comparing accepting an SDL immediately to waiting an average of 260 days for a non-SDL. The study suggests that SDLs, when used appropriately, could effectively expand the donor pool and offer recipients significant long-term survival benefits.

Jensen et al.'s [32] study demonstrated that the highest accuracy for small lesion (≤5mm) characterization was achieved using SECT with DL image reconstruction (DLIR), recording an 89.1% accuracy rate. DECT, on the other hand, showed a slightly lower accuracy of 84.8% for the same metric. Overall, DECT required a higher DLIR strength to match the image noise level of SECT, but the detection and characterization of liver metastases were comparable between the two techniques. Moreover, the application of DECT with spectral HU curves specifically improved the characterization of indeterminate lesions, suggesting an advantage in using DECT for detailed lesion analysis.

Foda et al. [33] focused on improving the detection of HCC, a prevalent cause of cancer mortality, particularly in individuals at high risk due to conditions like cirrhosis and viral hepatitis. The study leveraged whole-genome cell-free DNA (cfDNA) fragmentome analysis across a diverse cohort of 724 individuals from the United States, the European Union, and Hong Kong. They developed two machine learning models: a Gradient Boosting Machine for high-risk individuals and a penalized logistic regression for the average-risk population, both incorporating features from the Mathios et al. study as well as cfDNA fragmentation patterns linked to transcription factor binding sites. These models demonstrated high sensitivity and specificity: 88% sensitivity at 98% specificity in average-risk individuals, and 85% sensitivity at 80% specificity in high-risk individuals. Furthermore, the study conducted Monte Carlo simulations to compare the DELFI cfDNA-based screening to traditional methods, proposing better adherence rates and potentially improved screening outcomes.

Heinemann et al. [34] developed an automated DL method to evaluate non-alcoholic fatty liver disease (NAFLD) more precisely and reproducibly than current pathology-based assessments. This method was trained and validated on 296 human liver biopsies, and tested against a separate set of 171 biopsies with known pathologist scores, achieving quadratic weighted Cohen’s kappa values of 0.66 for steatosis, 0.24 for inflammation, 0.43 for ballooning, 0.62 for fibrosis, and 0.52 for the NAFLD activity score (NAS). Mean absolute errors were low across the board, indicating a high level of accuracy in comparison to the pathologist's scores. The DL architecture utilized modified Inception-V3 CNNs trained on annotated image tiles to predict scores for steatosis, inflammation, ballooning, and fibrosis on a continuous scale, which were then aggregated by an artificial neural network (ANN) to produce a single score per biopsy.

In a study by Bertsimas et al. [35], employing AI techniques from the Massachusetts Institute of Technology, the optimal surgical margin width for KRAS-variant CRC liver metastases (CRLM) was investigated. Data from 2000 to 2017 on 1843 patients from international centers were analyzed. The study utilized optimal policy trees (OPTs) based on random forest (RF) models to individualize margin width recommendations. With an AUC of 0.76, the RF model effectively predicted optimal margins between 6 to 12 mm for different patient subgroups, commonly suggesting 7 mm as the optimal width. This finding was substantiated by an external cohort validation using a new RF model with an AUC of 0.78, which supported the association of a 7 mm margin with extended survival. At the same time, Ranjan et al. [36] studied various cancers, including Lung, Kidney, Liver, Brain, and Breast cancers, were investigated. The malignancy of these cancers was classified using proposed models: RF Classifier, CNN, and ResNet50.

The CNN achieved the highest accuracy of 99% on the Lung Cancer Prediction dataset, sourced from Kaggle. Additionally, CNN secured a 96% accuracy rate for Breast Cancer, while the RF classifier attained an accuracy of 88.09% for Kidney Cancer and 75.75% for Liver Cancer. For the Brain Cancer dataset, ResNet50 showed an accuracy of 81%.

Han et al. [37] developed a sophisticated AI model to predict liver metastasis (LM) in T1 CRC patients by integrating data from the Surveillance Epidemiology and End Results (SEER) database and Xijing hospital. The model, which utilized various machine learning techniques, demonstrated exceptional predictive power, with the stacking bagging model achieving an AUC of 0.9631, the highest among the models tested. This model accurately identified all eight LM cases in an external validation cohort of 326 T1 patients and showed excellent performance in predicting LM for tumours ranging from one to 50 mm in size (AUC=0.956).

The response to chemotherapy in colorectal liver metastases is a critical factor in determining patient prognosis and guiding treatment strategies. CRC often metastasizes to the liver, and the effectiveness of chemotherapy in these cases can significantly influence the feasibility of surgical resection, the most definitive treatment option. Chemotherapeutic regimens, typically involving drugs like oxaliplatin, irinotecan, fluorouracil, and targeted agents such as bevacizumab or cetuximab, aim to shrink the metastases, making them operable. The response varies widely among patients due to factors like the genetic and molecular characteristics of the tumour, the patient’s overall health, and previous treatments. Imaging studies, such as CT and MRI scans, are used to monitor the response, with a focus on changes in the size and number of metastatic lesions. A favourable response not only opens the possibility for surgery but also indicates a better overall prognosis. Wei et al. [38] developed a DL-based radiomics model to predict chemotherapy response in colorectal liver metastases (CRLM) that outperforms traditional models. Utilizing contrast-enhanced multidetector computed tomography (MDCT) images, their ResNet10-based model, when combined with the clinical factor of carcinoembryonic antigen (CEA) levels, reached a maximum area under the receiver operating characteristic curve (AUC) of 0.935 in the training cohort.

Liver transplantation (LT) is a leading treatment for patients with cirrhosis and HCC. The procedure removes both the tumour and the damaged liver, reducing the risk of new tumours. A new AI system combines radiologic and pathologic images with clinical data. Using advanced techniques like natural language processing and DL, it assesses the risk of tumour recurrence after LT. Traditionally, the Milan criteria guided doctors in selecting patients for LT based on tumour size. However, with changes in medical practices and new research, there's a need for updated criteria. Many new methods show promise in predicting patient outcomes more accurately. As we adapt to these changes, it's crucial to update computer models to include more factors related to HCC, ensuring better patient selection and outcomes in liver transplantation. He et al. [39] developed a convergent AI strategy called i-RAPIT, an image omics-based, multi-network DL model that utilizes multi-scale image and clinical datasets to predict recurrence-free survival in liver transplantation recipients with HCC. The model was trained and validated on patient data from a major liver transplant centre in Houston, Texas. It incorporates clinical features, MRI scans, and histopathologic images. Of the models tested, the combination of clinical, MRI, and pathology features showed the highest accuracy. The model achieved a total accuracy of 82%, with 80% recall and 89% precision. i-RAPIT aims to assist physicians in making better-informed decisions regarding liver transplantation based on comprehensive data rather than just tumour size, potentially expanding the number of HCC patients eligible for transplantation. However, further multi-center studies are planned to assess the model's scalability and generalizability.

Table 3 presents detailed overview on the performance of DL in prognoses of metastasis and survival of liver cancer studied in this survey along with their results.

Table 3 Deep learning in prognosis of metastasis and survival of liver cancer

Author	Data	Proposed Method	Results

Zhou et al. [30]	PET/CT scans	DERBY+	AUC = 83% Sensitivity = 80.4% Specificity = 76.8%
Jensen et al. [32]	SECT and DECT images	DLIR	Accuracy = 89.1%
Foda et al. [33]	Whole-genome cell-free DNA	Gradient Boosting Machine and penalized logistic regression	average-risk individuals: sensitivity = 88% specificity = 98% high-risk individuals: sensitivity = 85% specificity = 80%
Bertsimas et al. [35]	Medical data	RF	AUC = 76%
Ranjan et al. [36]	HCC Liver Cancer dataset	RF	Accuracy = 75.75%
Han et al. [37]	SEER database	Bagging	AUC = 96.31%
Wei et al. [38]	MDCT images	ResNet10	AUC = 93.5%
He et al. [39]	MRI and histological images	i-RAPIT	Accuracy = 82% Recall = 80% Precision = 89%

4 DISCUSSION

The application of AI in liver cancer detection and diagnosis has demonstrated promising potential. However, several limitations persist. A fundamental challenge is the restricted dataset size in many studies, hindering the generalizability of results. Even in studies boasting substantial accuracy like the one employing Res-UNet, the dataset's limited scope can obscure potential model shortcomings. Overcoming such limitations may necessitate broader data collection, varied preprocessing techniques, or extended training epochs. Often, the neural network's robustness is questionable with a smaller sample size, making results susceptible to overfitting and less reliable in diverse clinical scenarios.

The data quality and access barriers also pose significant challenges. Not only is there a need for extensive labelled datasets to train DL models efficiently, but ensuring these datasets represent diverse populations worldwide is crucial. This diversity accounts for varying anatomy, genetics, and lifestyles across races and regions. While image enhancement techniques like denoising can refine the quality, they can't compensate for an initial lack of representation.

Moreover, the limited focus of most studies on binary outcomes—healthy or cancerous—oversimplifies the multifaceted nature of liver cancer, which has various stages, each demanding different treatment. Properly classifying the disease's stage is vital for optimizing patient care, minimizing treatment costs, and reducing potential side effects. This level of detail requires high-quality biomedical imaging and precise stage diagnosis from medical specialists.

Beyond technical aspects, practical and economic challenges also loom. Despite DL's potential, the adoption of these systems in real-world medical environments remains low, largely due to concerns about their reliability. For AI models to gain widespread trust, they must not only be accurate but also transparent, offering understandable insights into their decision-making processes. Furthermore, economic disparities and variable access to medical facilities worldwide can limit the reach of advanced AI tools. Efforts to create low-hardware-demand software aim to bridge this gap, ensuring broader global accessibility.

5 CONCLUSION

In this survey, we undertook an in-depth analysis comparing a spectrum of DL methodologies aimed at early detection of precancerous liver lesions, diagnosis of liver cancer, and prognostic estimations concerning survival rates and potential metastasis in liver cancer patients. Our findings accentuate the benefits of merging neural networks with alternative methods, whether for refining classification or enhancing image quality. However, the journey from research to real-world medical utility is hindered by existing constraints, especially those linked to dataset availability and quality. The absence of a globally accepted protocol for AI's usage of biomedical images, combined with varying international standards for patient privacy and image storage, necessitates a unified effort. We strongly advocate for a worldwide collaboration, with liver disease specialists from diverse regions contributing to an enriched and comprehensive dataset. Moreover, it's imperative for future studies to delve deeper into advanced image pre-processing methodologies to achieve top-tier images. It's important to note that this was a survey, and our aspiration is that this contribution aids the broader research community. However, we emphasize that there's a pressing need for more focused research on precancerous lesions, metastasis, and survival prognosis in the realm of liver cancer.

6 ACKNOWLEDGEMENTS

The authors declare no conflict of interest.

REFERENCES

[1] R. L. Siegel, K. D. Miller, N. S. Wagle and A. Jemal, "Cancer statistics, 2023," *A Cancer Journal for Clinicians*, pp. 17-48, 2023.

[2] S. Qin, G.-J. Liu, M. Huang, J. Huang, Y. Luo, Y. Wen, Y. Wang and L. Chen, "The local efficacy and influencing factors of ultrasound-guided percutaneous microwave ablation in colorectal liver metastases: a review of a 4-year experience at a single center," *International Journal of Hyperthermia*, vol. 36, no. 1, pp. 36-43, 2019.

[3] J. Keyl, R. Hosch, A. Berger, O. Ester, T. Greiner, S. Bogner, J. Treckmann, S. Ting, B. Schumacher, D. Albers, P. Markus, M. Wiesweg, M. Forsting, F. Nensa, M. Schuler, S. Kasper and J. Kleesiek, "Deep learning-based assessment of body composition and liver tumour burden for survival modelling in advanced colorectal cancer," *Journal of Cachexia, Sarcopenia and Muscle*, vol. 14, no. 1, pp. 545-552, 2022.

[4] Q.-x. Zhao, X.-l. He, K. Wang, Z.-g. Cheng, Z.-y. Han, F.-y. Liu, X.-l. Yu, Z. Hui, J. Yu, A. Chao and P. Liang, "Deep learning model based on contrast-enhanced ultrasound for predicting early recurrence after thermal ablation of colorectal cancer liver metastasis," *European Radiology*, no. 3, 2023.

[5] J. Liang, W. Zhang, J. Yang, M. Wu, Q. Dai, H. Yin, Y. Xiao and L. Kong, "Deep learning supported discovery of biomarkers for clinical prognosis of liver cancer," *Nature Machine Intelligence*, pp. 408-420, 2023.

[6] Y. Han, J. Akhtar, G. Liu, C. Li and G. Wang, "Early warning and diagnosis of liver cancer based on dynamic network biomarker and deep learning," *Computational and Structural Biotechnology Journal*, vol. 21, pp. 3478-3489, 2023.

[7] Q. Chen, S. Fang, Y. Yuchen, R. Li, R. Deng, Y. Chen, D. Ma, H. Lin and F. Yan, "Clinical feasibility of deep learning reconstruction in liver diffusion-weighted imaging: Improvement of

image quality and impact on apparent diffusion coefficient value," *European Journal of Radiology*, vol. 168, 2023.

[8] R. A. Khan, M. Fu, B. Burbridge, Y. Luo and F.-X. Wu, "A multi-modal deep neural network for multi-class liver cancer diagnosis," *Neural Networks*, vol. 165, pp. 553-561, 2023.

[9] R. V. Manjunath, A. Ghanshala and K. Kwadiki, "Deep learning algorithm performance evaluation in detection and classification of liver disease using CT images," *Springer Link*, 2023.

[10] K. Sridhar, K. C, W.-C. Lai and B. P. Kavin, "Detection of Liver Tumour Using Deep Learning Based Segmentation with Coot Extreme Learning Model," *Biomedicines*, 2023.

[11] D. Bhattacharyya, N. S. Joshua, N. T. Rao, A. Kumar, M. Bhushan, J. A. Galindo, L. Garg and Y.-C. Hu, "Liver Cancer Classification With Using Gray-Level Co-Occurrence Matrix Using Deep Learning Techniques," in *Machine Intelligence, Big Data Analytics, and IoT in Image Processing: Practical Applications*, Scrivener Publishing LLC, 2023.

[12] N. K. Trivedi, R. G. Tiwari, A. Anand, V. Gautam, D. Witarsyah and A. Misra, "Application of Machine Learning for Diagnosis of Liver Cancer," in *International Conference Advancement in Data Science, E-learning and Information Systems (ICADEIS)*, 2022.

[13] A. Sirco, A. Almisreb, N. M. Tahir and J. Bakri, "Liver Tumour Segmentation based on ResNet Technique," in *IEEE 12th International Conference on Control System, Computing and Engineering (ICCSCE)*, 2022.

[14] H. Rahman, T. F. Naik Bukht, A. Imran, J. Tariq, S. Tu and A. Alzahrani, "A Deep Learning Approach for Liver and Tumour Segmentation in CT Images Using ResUNet," *Bioengineering*, 2022.

[15] C. Chen, C. Chen, M. Ma, X. Ma, X. Lv, X. Dong, Z. Yan, M. Zhu and J. Chen, "Classification of multi-differentiated liver cancer pathological images based on deep learning attention mechanism," *BMC Medical Informatics and Decision Making*, 2022.

[16] B. Das and S. Toraman, "Deep transfer learning for automated liver cancer gene recognition using spectrogram images of digitized DNA sequences," *Biomedical Signal Processing and Control*, vol. 72, 2022.

[17] A. A. Aatresh, K. Alabhya, S. Lal, J. Kini and P. P. Saxena, "LiverNet: efficient and robust deep learning model for automatic diagnosis of sub-types of liver hepatocellular carcinoma cancer from H&E stained liver histopathology images," *International Journal of Computer Assisted Radiology and Surgery*, 2021.

[18] N. Cheng, J. Fu, D. Chen, S. Chen and H. Wang, "An antibody-free liver cancer screening approach based on nanoplasmonics biosensing chips via spectrum-based deep learning," *NanoImpact*, vol. 21, 2021.

[19] S. Lal, D. Das, K. Alabhya, A. Kanfade, A. Kumar and J. Kini, "NucleiSegNet: Robust deep learning architecture for the nuclei segmentation of liver cancer histopathology images," *Computers in Biology and Medicine*, vol. 128, 2021.

[20] D.-V. Phan, C.-L. Chan, A.-H. A. Li, T.-Y. Chien and V.-C. Nguyen, "Liver cancer prediction in a viral hepatitis cohort: A deep learning approach," *International Journal of Cancer (IJC)*, vol. 147, no. 10, pp. 2871-2878, 2020.

[21] X. Dong, Y. Zhou, L. Wang, J. Peng, Y. Lou and Y. Fan, "Liver Cancer Detection Using Hybridized Fully Convolutional Neural Network Based on Deep Learning Framework," *IEEE Access*, vol. 8, pp. 129889 - 129898, 2020.

[22] Q. Yang, J. Wei, X. Hao, D. Kong, X. Yu, T. Jiang, J. Xi, W. Cai, Y. Luo, X. Jing, Y. Yang, Z. Cheng, J. Wu, H. Zhang, J. Liao, P. Zhou, Y. Song, Y. Zhang, Z. Han, W. Cheng, L. Tang, F. Liu, J. Dou, R. Zheng, J. Yu, J. Tian and P. Liang, "Improving B-mode ultrasound diagnostic

performance for focal liver lesions using deep learning: A multicentre study," *EBioMedicine,* vol. 56, 2020.

[23] C. Sun, A. Xu, D. Liu, Z. Xiong, F. Zhao and W. Ding, "Deep Learning-Based Classification of Liver Cancer Histopathology Images Using Only Global Labels," *IEEE Journal of Biomedical and Health Informatics,* vol. 24, no. 6, 2019.

[24] S.-h. Zhen, M. Cheng, Y.-b. Tao, Y.-f. Wang, S. Juengpanich, Z.-y. Jiang, Y.-k. Jiang, Y.-y. Yan, W. Lu, J.-m. Lue, J.-h. Qian, Z.-y. Wu, J.-h. Sun, H. Lin and X.-j. Cai, "Deep Learning for Accurate Diagnosis of Liver Tumour Based on Magnetic Resonance Imaging and Clinical Data," *Cancer Imaging and Image-directed Interventions,* vol. 10, 2020.

[25] M. Chen, B. Zhang, W. Topatana, J. Cao, H. Zhu, S. Juengpanich, Q. Mao, H. Yu and X. Cai, "Classification and mutation prediction based on histopathology H&E images in liver cancer using deep learning," *npj precision oncology,* 2020.

[26] A. Kiani, B. Uyumazturk, P. Rajpurkar, A. Wang, R. Gao, E. Jones, Y. Yu, C. P. Langlotz, R. L. Ball, T. J. Montine, B. A. Martin, G. J. Berry, M. G. Ozawa, F. K. Hazard, R. A. Brown, S. B. Chen, M. Wood, L. S. Allard, L. Ylagan, A. Y. Ng and J. Shen, "Impact of a deep learning assistant on the histopathologic classification of liver cancer," *npj precision oncology,* 2020.

[27] M. Yamakawa, T. Shiina, N. Nishida and M. Kudo, "Computer aided diagnosis system developed for ultrasound diagnosis of liver lesions using deep learning," in *IEEE Symposium (IUS) Ultrasonics*, Glasgow, UK, 2019.

[28] A. Das, U. R. Acharya, S. S. Panda and S. Sabut, "Deep learning based liver cancer detection using watershed transform and Gaussian mixture model techniques," *Cognitive Systems Research,* vol. 54, pp. 165-175, 2019.

[29] D. I. Tsilimigras, P. Brodt, P.-A. Clavien, R. J. Muschel, M. I. D'Angelica, I. Endo, R. W. Parks, M. Doyle, E. d. Santibañes and T. M. Pawlik , "Liver metastases," *National Library of Medicine,* 2021.

[30] S. Zhou, D. Sun, W. Mao, Y. Liu, W. Cen, L. Ye, F. Liang, J. Xu, H. Shi, Y. Ji, L. Wang and W. Chang, "Deep radiomics-based fusion model for prediction of bevacizumab treatment response and outcome in patients with colorectal cancer liver metastases: a multicentre cohort study," *eClinicalMedicine,* vol. 65, 2023.

[31] X. Zhang, M. Dutton, R. Liu, A. A. Ali and F. Sherbeny, "Deep Learning–Based Survival Analysis for Receiving a Steatotic Donor Liver Versus Waiting for a Standard Liver," *Transplantation Proceedings,* 2023.

[32] C. T. Jensen, V. K. Wong, N. A. Wagner-Bartak, X. Liu, R. P. Nair Sobha, J. Sun, G. S. Likhari and S. Gupta, "Accuracy of liver metastasis detection and characterization: Dual-energy CT versus single-energy CT with deep learning reconstruction," *European Journal of Radiology,* vol. 168, 2023.

[33] Z. H. Foda, A. V. Annapragada, K. Boyapati, D. C. Bruhm, N. A. Vulpescu, J. E. Medina, D. Mathios, S. Cristiano, N. Niknafs, H. T. Luu, M. G. Goggins, R. A. Anders, J. Sun, S. H. Meta, D. L. Thomas, G. D. Kirk, V. Adleff, J. Phallen, R. B. Scharpf, A. K. Kim and V. E. Velculescu, "Detecting Liver Cancer Using Cell-Free DNA Fragmentomes," *Cancer Discovery,* 2023.

[34] F. Heinemann, P. Gross, S. Zeveleva, H. S. Qian, J. Hill, A. Höfer, D. Jonigk, A. M. Diehl, M. Abdelmalek, M. C. Lenter, S. S. Pullen, P. Guarnieri and B. Stierstorfer, "Deep learning-based quantification of NAFLD/NASH progression in human liver biopsies," *Scientific Reports,* 2022.

[35] D. Bertsimas, G. A. Margonis, S. Sujichantararat, T. Boerner, Y. Ma, J. Wang, C. Kamphues, K. Sasaki, S. Tang, J. Gagniere, A. Dupré, M. I. Løes, D. Wagner, G. Stasinos, A. Macher-Beer, R. Burkhart, D. Morioka, K. Imai, V. Ardiles, J. M. O'Connor, T. M. Pawlik, G. Poultsides, H. Seeliger, K. Beyer, K. Kaczirek, P. Kornprat, F. N. Aucejo, E. d. Santibañes, H. Baba, I. Endo, P. E. Lønning, M. E. Kreis, M. J. Weiss, C. L. Wolfgang and M. D'Angelica, "Using Artificial

Intelligence to Find the Optimal Margin Width in Hepatectomy for Colorectal Cancer Liver Metastases," *JAMA Surgery*, 2022.

[36] M. Ranjan, A. Shukla, K. Soni, S. Varma, M. Kuliha and U. Singh, "Cancer Prediction Using Random Forest and Deep Learning Techniques," in *International Conference on Communication Systems and Network Technologies (CSNT)*, Indore, India, 2022.

[37] T. Han, J. Zhu, X. Chen, R. Chen, Y. Jiang, S. Wang, D. Xu, G. Shen, J. Zheng and C. Xu, "Application of artificial intelligence in a real-world research for predicting the risk of liver metastasis in T1 colorectal cancer," *Cancer Cell International*, vol. 22, 2022.

[38] J. Wei, J. Cheng, D. Gu, F. Chai, N. Hong, Y. Wang and J. Tian, "Deep learning-based radiomics predicts response to chemotherapy in colorectal liver metastases," *Medical Physics*, 2021.

[39] T. He, J. N. Fong, L. W. Moore, C. F. Ezeana, D. Victor, M. Divatia, M. Vasquez, M. Ghobrial and S. T. Wong, "An imageomics and multi-network based deep learning model for risk assessment of liver transplantation for hepatocellular cancer," *Computerized Medical Imaging and Graphics*, vol. 89, 2021.