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Enhancing ultrasonographic detection of hepatocellular carcinoma with artificial intelligence: current applications, challenges and future directions

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ABSTRACT

Hepatocellular carcinoma (HCC) remains a leading cause of cancer-related mortality worldwide, with early detection playing a crucial role in improving survival rates. Artificial intelligence (AI), particularly in medical image analysis, has emerged as a potential tool for HCC diagnosis and surveillance. Recent advancements in deep learning-driven medical imaging have demonstrated significant potential in enhancing early HCC detection, particularly in ultrasound (US)-based surveillance. This review provides a comprehensive analysis of the current landscape, challenges, and future directions of AI in HCC surveillance, with a specific focus on the application in US imaging. Additionally, it explores AI's transformative potential in clinical practice and its implications for improving patient outcomes. We examine various AI models developed for HCC diagnosis, highlighting their strengths and limitations, with a particular emphasis on deep learning approaches. Among these, convolutional neural networks have shown notable success in detecting and characterising different focal liver lesions on B-mode US often outperforming conventional radiological assessments. Despite these advancements, several challenges hinder AI integration into clinical practice, including data heterogeneity, a lack of standardisation, concerns regarding model interpretability, regulatory constraints, and barriers to real-world clinical adoption. Addressing these issues necessitates the development of large, diverse, and high-quality data sets to enhance the robustness and generalisability of AI models. Emerging trends in AI for HCC surveillance, such as multimodal integration, explainable AI, and real-time diagnostics, offer promising advancements. These innovations have the potential to significantly improve the accuracy, efficiency, and clinical applicability of AI-driven HCC surveillance, ultimately contributing to enhanced patient outcomes.

SUMMARY BOX

⇒ Conventional ultrasound-based hepatocellular carcinoma (HCC) surveillance has limited sensitivity, particularly for early-stage tumors, and remains highly operator-dependent, leading to variability in detection accuracy.

⇒ Artificial intelligence (AI), especially deep learning models, enhances the detection and characterization of HCC through imaging techniques, such as ultrasound, CT, and MRI.

⇒ AI-driven systems integrate imaging data with clinical and laboratory findings, enabling a more comprehensive risk assessment and personalized surveillance strategies.

⇒ Despite its promise, the adoption of AI in HCC surveillance faces challenges, including data heterogeneity, algorithm standardization, and ethical considerations, necessitating further validation in real-world settings.

INTRODUCTION

Hepatocellular carcinoma (HCC) is a major global health concern, being the most common primary liver cancer and the second leading cause of liver-related deaths worldwide.[1] In 2015, the Asia-Pacific region accounted for 72.7% of HCC-related deaths,[2] followed by 67% of new cases in 2019[3] and 63% of global cases in 2021.[1] Key risk factors include chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, excessive alcohol use, metabolic dysfunction-associated steatotic liver disease (MASLD), and aflatoxin B1 exposure.[4] These vary geographically. In Western nations, the HCC aetiological landscape is shifting, with alcohol-associated liver disease projected to become the leading cause, and MASLD surpassing HCV.[5]

Surveillance is crucial for early HCC detection, improving curative treatment chances and long-term survival.[6] International liver societies recommend surveillance for

patients with cirrhosis and those at risk of non-cirrhotic chronic HBV infection.[7–11] Abdominal ultrasound (US) is the preferred surveillance tool due to its affordability and non-invasive nature,[12 13] though its accuracy declines in patients with obesity or MASLD.

Artificial intelligence (AI) is revolutionising HCC surveillance by improving imaging-based detection. Deep learning (DL) models, especially convolutional neural networks (CNNs), excel at analysing US, CT, and MRI scans for early lesion identification.[14] AI reduces variability and improves sensitivity and specificity, thereby enhancing early detection. It can integrate multimodal data—including imaging, clinical history, and laboratory results—for comprehensive risk stratification in patients at high HCC risk. Given these advancements, this review provides an overview of AI's role in enhancing HCC surveillance.

CURRENT TOOLS AND BENEFITS OF HCC SURVEILLANCE

HCC surveillance enables early detection of liver lesions, facilitating timely treatment and improved outcomes. Imaging modalities, such as US, CT, and MRI, are crucial for HCC surveillance,[15 16] particularly for individuals at high risk, including those with cirrhosis, chronic HBV, HCV, or other underlying liver diseases.[12 17 18]

Ultrasound as a primary tool

B-mode US remains the primary imaging modality for HCC surveillance due to its cost-effectiveness, non-invasiveness, and ability to provide real-time diagnostic information.[5] It is typically used to continuously monitor at-risk patients to detect the emergence or progression of liver lesions. US is recommended by leading liver societies, including the American Association for the Study of Liver Diseases (AASLD)[18] and the European Association for the Study of the Liver (EASL),[19] for surveillance in high-risk populations. Major guidelines recommend US-based surveillance every 6 months in these individuals. However, the effectiveness of US can be influenced by several factors, including equipment quality, operator skill, and patient characteristics. For instance, obesity or advanced cirrhosis may limit the visualisation of hepatic lesions, reducing diagnostic accuracy. In cases where US findings are inconclusive or require a more detailed assessment, CT and MRI are preferred due to their higher sensitivity in detecting small lesions.[12 17 18]

In addition to conventional B-mode imaging, contrast-enhanced US (CEUS) expands diagnostic effectiveness further by using microbubble-based contrast agents. They are typically composed of low-solubility gases, such as sulfur hexafluoride or perfluorocarbons surrounded by a shell.[20] Intravenous injection increases the visualisation of blood circulation and enhances the signal-to-noise ratio of B-mode images. CEUS also uses non-linear oscillations at harmonic frequencies, with significantly improved contrast-to-tissue ratio and dynamic imaging by arterial, portal venous, and late phases.[21] Hypoenhancement at this stage can image malignant lesions due to reduced Kupffer cell density, representing a valuable tool in discriminating between benign and metastatic liver lesions. CEUS is thus a valuable and now generally accepted modality in the diagnosis of focal liver lesions (FLLs) and is particularly valuable when conventional US yields suboptimal images. However, CEUS is not currently recommended as a routine surveillance of HCC due to limited generalisability, need for special contrast agents, and its dependence on skilled radiologists.[22]

CT and MRI for detailed assessment

CT and MRI are valuable tools for detailed assessment of liver lesions suspected to be HCC. These modalities offer superior contrast and spatial resolution compared with US, allowing for better differentiation between benign and malignant growths.[13] They are particularly useful for identifying small tumours and distinguishing HCC from other types of liver nodules. CT can visualise both the arterial and venous phases of liver perfusion, providing critical insights into hepatic blood flow and abnormalities associated with HCC. Meanwhile, MRI, particularly with contrast agents, exhibits enhanced sensitivity in detecting small lesions.[17] Additionally, MRI is often preferred over CT in certain cases as it does not involve radiation exposure.[23]

Challenges in imaging interpretation

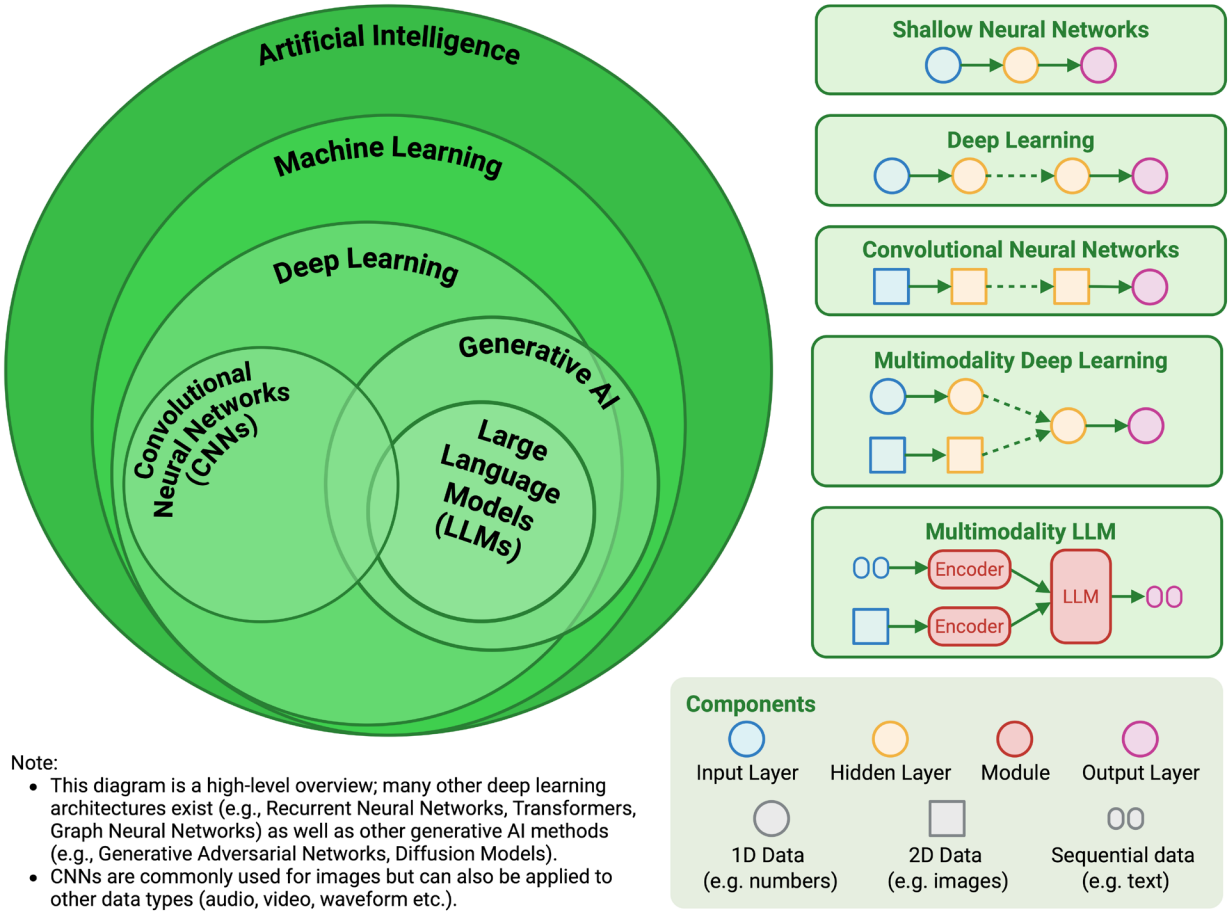
Interpreting imaging results poses significant challenges due to variations in lesion appearance and the presence of underlying liver conditions, such as cirrhosis or steatosis, which can obscure malignant features.[24] These underlying conditions can significantly alter the liver architecture, making it difficult to differentiate between malignant and benign lesions. The accuracy of surveillance imaging relies heavily on the experience and expertise of the radiologist, particularly when dealing with complex cases or patients with underlying liver conditions.[25] Small HCCs are especially difficult to detect, particularly in cirrhotic livers, where fibrosis and regenerative nodules can obscure tumour visualisation. US, in particular, may be unable to detect liver nodules <1 cm in size. While MRI offers high sensitivity for detecting small HCCs, it carries the risk of false positives, particularly in cirrhotic livers, where non-malignant lesions can mimic HCC.[26]

OVERVIEW OF AI IN HEALTHCARE

AI is revolutionising healthcare by enhancing medical diagnoses, improving treatment strategies, and optimising clinical workflows.[27–29] AI algorithms can process and learn from vast amounts of complex data, leading to more accurate diagnoses, precise measurements, and improved predictions of disease progression and treatment outcomes.[27]

AI terminology

AI is a multidisciplinary field dedicated to developing computational systems capable of performing tasks that



Note:
- This diagram is a high-level overview; many other deep learning architectures exist (e.g., Recurrent Neural Networks, Transformers, Graph Neural Networks) as well as other generative AI methods (e.g., Generative Adversarial Networks, Diffusion Models).
- CNNs are commonly used for images but can also be applied to other data types (audio, video, waveform etc.).

Figure 1 Overview of the hierarchical relationship among key concepts in artificial intelligence (AI). The outermost circle represents AI, encompassing all methodologies that enable machines to imitate human intelligence. Machine learning (ML), a subarea of AI, focuses on algorithms that learn patterns from data without explicit programming. Deep learning (DL), a specialised part of ML, leverages multilayer neural networks such as convolutional neural networks (CNNs) to extract complex details from high-dimensional data, including medical images. Generative AI and large language models (LLMs) extend these capabilities by generating new data and understanding structured and unstructured data, including text and images (multimodal processing). The right side of the diagram illustrates different neural networks, from simple to complex systems that process multiple types of data and LLMs designed for advanced multimodal applications.

traditionally require human cognitive functions, such as learning, reasoning, and problem-solving.[27–29] As illustrated in figure 1, machine learning (ML) is a subset of AI that involves algorithms learning patterns from data to make data-driven decisions. An important subset of ML is neural networks (NNs), which are computational models inspired by the biological structure and function of the human brain. As NNs increase in complexity, they form the foundation of deep learning, which uses a multilayered architecture to autonomously extract hierarchical features from data.[30] Among DL techniques, CNNs have proven to be particularly efficient in processing visual data. CNNs are widely used in medical imaging, where they perform important tasks, such as classification (distinguishing tissue types or lesion features), detection (localising anomalies in images), and segmentation (delineating structures such as lesions or organs).

Recent advances include multi-modal systems that integrate diverse data sources, such as imaging, clinical records, genomics, and laboratory results, to create a unified diagnostic perspective tailored to individual risk profiles.[31] The next frontier is the incorporation of foundation models and large language models, pretrained on extensive multimodal data sets to offer even deeper insights, thereby enabling personalised healthcare delivery by analysing and synthesising complex information into targeted clinical recommendations.[32]

Benefits of AI for HCC surveillance

DL models, particularly CNNs, have shown considerable promise in analysing medical images and detecting abnormalities in modalities such as X-rays, US, CT and MRI.[28 30] These models increasingly support clinicians in decision-making, thereby improving diagnostic accuracy and efficiency.[28–30] Beyond diagnostics, AI techniques improve image quality, reduce noise, and reconstruct images from lower-dose scans or different imaging modalities. Additionally, AI facilitates precise

measurements and quantitative assessments of anatomical structures or lesions, aiding in tumour size tracking and volume estimation over time.[33] This enables more accurate disease staging and better treatment planning. Furthermore, AI models integrate imaging with clinical variables to predict disease progression and treatment outcomes.

In diagnosing liver diseases, AI can be used to detect liver fibrosis, differentiate FLLs, predict the prognosis of chronic liver diseases, and diagnose MASLD.[34–36] AI can assist in assessing the severity of liver fibrosis in chronic liver diseases, including viral hepatitis, using US, thereby identifying patients at a higher risk of disease progression and prioritising those requiring closer monitoring or more aggressive treatment.[34 36] Additionally, AI can locate and classify liver lesions as benign or malignant using CEUS and other imaging techniques. These insights help guide biopsy indications, inform interventional planning, and improve diagnostic accuracy in HCC cases.[35–37] Therefore, AI plays a crucial role in diagnosing and assessing MASLD, which is essential for early detection and timely treatment to prevent the progression of severe liver disease.[36 38]

Several studies have shown that AI systems outperform clinicians in interpreting imaging data.[14 33 35 37 39 40] One of AI's major advantages in healthcare is its ability to minimise diagnostic variability.[37 41] Human interpretation of medical images is influenced by various factors, such as clinician experience and patient-specific variables. AI enables consistent and objective analysis of imaging data, contributing to more reliable diagnoses.[34]

AI algorithms have been explored for HCC detection using various imaging modalities, including US, CT, and MRI.[35 38] Each modality is suited to different clinical scenarios.[17] CT and MRI generally offer higher sensitivity and specificity for detecting HCC than US.[12 13 35] US is often the first-line imaging modality due to its cost-effectiveness and real-time diagnostic capabilities. However, detecting HCC via US can be challenging, especially in the presence of cirrhosis or other liver diseases that alter the liver structure. Additionally, obesity and technical limitations—such as US equipment quality and operator experience—can affect US sensitivity.[42] Studies have shown that AI algorithms improve the detection of HCC in US images, which is a key factor in early cancer diagnosis and improved patient outcomes.[14 35 37 41 42] CT scans provide detailed cross-sectional images of the liver, allowing for better visualisation of the fine details of liver anatomy and pathology than US.[35] Research has shown that AI can detect HCC on CT scans with high accuracy, even in early stages, facilitating timely interventions and potentially curative treatments.[14 35 43] MRI, known for its superior soft-tissue contrast, is particularly beneficial for characterising liver lesions.[35 39] AI models applied to MRI data can detect and differentiate complex liver lesions—including HCC, cysts, and metastatic tumours—improving diagnostic accuracy, particularly in patients with cirrhosis or steatosis.[38]

AI algorithms can analyse electronic health record data to identify individuals at high risk of HCC, thereby enhancing surveillance strategies.[44] These algorithms can be trained to recognise specific risk factors associated with HCC by analysing historical trends compared with clinical guidelines.[14] In patients with chronic HBV infection, AI models can predict the risk of developing HCC by integrating specific-related patient characteristics, antiviral treatment data, and imaging features.[14] This allows healthcare providers to detect HCC at an earlier, more treatable stage, ultimately improving patient outcomes.

AI is a supportive tool that aids clinicians in making accurate and timely decisions. For example, AI enhances the diagnostic accuracy of radiologists by highlighting potential abnormalities and providing quantitative assessments, ultimately leading to more informed diagnoses.[35]

Applications of AI in the diagnosis of HCC

US is a standard imaging modality for HCC surveillance, as recommended by both the AASLD and EASL. Several studies have highlighted the potential of AI models in detecting and classifying FLLs, including HCC. Although these studies employed different data sets and evaluation protocols—making direct comparisons challenging—their consistent performance underscores the potential of AI in clinical practice. The integration of AI into clinical workflows could significantly enhance early detection, inform treatment decisions, and improve overall patient outcomes (see online supplemental figure 1 in Additional file 1).[14 39]

Benign and malignant classification

AI models have demonstrated significant potential in differentiating benign from malignant liver tumours. Online supplemental table 1 (Additional file 1) summarises key studies investigating this classification. Several studies have specifically focused on this challenge. Xi *et al*[45] developed a DL model to distinguish benign from malignant tumour lesions using a data set of 596 patients, which included 911 images (535 malignant and 376 benign). Their algorithm analysed the region of interest (ROI) of FLLs—manually cropped by radiologists—and classified them into two categories: benign and malignant. Using ResNet50, the model achieved an area under the curve (AUC) of 83%, a sensitivity of 87% (95% CI: 74% to 94%), and a specificity of 78% (95% CI: 61% to 89%). The model's performance was comparable to that of expert radiologists. Mao *et al*[46] investigated the use of US radiomics to differentiate primary from metastatic liver cancers in a data set of 114 patients. The ROIs of the liver lesions were delineated by expert radiologists, and the algorithm extracted 1409 radiomics features from each image. Using logistic regression, the algorithm achieved an AUC of 81.6%, a sensitivity of 76.8%, and a specificity of 88.0%.

Several studies have also examined the role of AI-assisted CEUS, reporting AUC values ranging from 0.74 to 0.957, sensitivity between 74% and 94%, specificity

from 63.3% to 100%, and accuracy between 82% and 98.9%.[47–54] These findings suggest that CEUS, when combined with AI techniques, offers promising diagnostic performance for distinguishing benign and malignant liver lesions.

Tumour subtype classification

Several studies have expanded beyond the binary classification of benign and malignant tumours by further differentiating tumour subtypes. Table 1 summarises studies investigating tumour subtype classification, with a focus on HCC outcomes. Schmauch *et al*[55] developed an AI algorithm to identify FLLs in full-frame still US images and classified them as angiomas, cysts, metastases, HCC, or focal nodular hyperplasia (FNH). The model was trained on a data set of 367 liver samples and tested on a separate data set of 177 patients. The algorithm achieved an AUC of 89.1% for classifying FLLs into subtypes and an AUC of 93.1% specifically for classifying HCC. Chen *et al*[56] developed a DL model to preoperatively differentiate among three types of liver cancer: HCC, intrahepatic cholangiocarcinoma (ICC), and combined HCC-ICC. This study used full-field B-mode US images from 465 patients with primary liver cancer. Overall, the model achieved an AUC of 92.4% (95% CI: 86.3% to 98.4%), an accuracy of 84.6%, a sensitivity of 78.3%, and a specificity of 92.7%. For HCC, the model achieved an AUC of 93.7% (95% CI: 84.0% to 99.0%). These findings demonstrate that AI can effectively distinguish between primary liver cancer subtypes. Tangruangkiat *et al*[57] investigated a pretrained DL model for classifying the ROI of FLLs in US images as non-FLL, cyst, focal fat sparing, haemangioma, or HCC. The model was developed and validated using a data set comprising 581 US images. Overall, it achieved an accuracy of 87.0%, a sensitivity of 81.0%, and a specificity of 89.0%. For HCC, the model attained an accuracy of 87.2%, a sensitivity of 80.7%, and a specificity of 81.2%. Nishida *et al*[40] trained an AI model to classify the ROI of liver tumours into four categories—cyst, haemangioma, HCC, and metastasis—using a large data set of over 70 950 images. The overall diagnostic accuracy across all tumour types was 91.1%. When comparing the accuracy of AI models to that of physicians, the correct diagnosis rate for AI was 89.1%. The authors observed that model performance improved with increasing data set size, with AI models outperforming expert physicians. Nakata and Siina[58] investigated the effectiveness of ensemble techniques in improving the AI accuracy for classifying the ROI of hepatic masses in US images into four categories: benign liver tumours, liver cysts, metastatic liver cancer, and primary liver cancer. The study observed that ensemble learning consistently improved classification accuracy, with the weighted average voting method achieving the highest performance, yielding a sensitivity of 78.3%, a specificity of 92.8%, and an accuracy of 78.3%. These findings underscore the robustness of ensemble learning approaches in liver tumour classification.

Certain recent research has explored AI-aided CEUS models for tumour subtype classification and indicated favourable diagnostic performance. Urhut *et al* evaluated a DL model with CEUS data of 59 FLLs and achieved an accuracy of 69.9%, sensitivity of 86.9%, and specificity of 56.2%.[54] Li *et al* applied the classic ML models—gradient-boosted decision trees, random forest, and generalised linear models—to a large CEUS data set of 3210 patients and achieved an accuracy of 83%, sensitivity of 77.3%, and specificity of 88.6%.[59] Feng *et al* used a DL approach with 1,241 CEUS video frames and achieved an AUC of 89% and sensitivity, specificity, and accuracy of 83%, 82%, and 83%, respectively.[60] Wan *et al* used a DL network trained with 174 CEUS cases and achieved an AUC of 87.9%, accuracy of 88.4%, sensitivity of 86.2%, and specificity of 90.1%.[61] Recently, Ding *et al* also achieved one of the highest performances with DL on a CEUS database of 3725 FLLs with 1250 HCC lesions (training) and 685 lesions (test), where they achieved test set AUCs of 87–91%, accuracy of 91–96%, and specificity of 96–98%.[62] These findings demonstrate the value of CEUS with AI models in enhancing tumour subtype discrimination and offer a solid foundation for future integration of CEUS-based algorithms in clinical applications.

Tumour detection and segmentation

Further studies have investigated the localisation of FLLs in US images through detection or segmentation techniques. Table 2 summarises research on the localisation of FLLs, particularly in relation to HCC outcomes. Tiyarattanachai *et al*[63] developed a model that achieved an overall detection rate of 75% (95% CI: 71.7% to 78.3%), a sensitivity of 84.9% (95% CI: 81.6% to 88.2%), and a specificity of 97.1% (95% CI: 96.5% to 97.6%) when tested on an external data set. The model demonstrated strong diagnostic performance for HCC, though it exhibited limitations in detecting smaller lesions or those with atypical features. Ryu *et al*[64] developed a system capable of simultaneously segmenting liver lesion boundaries in US images and classifying lesions into four types: cyst, haemangioma, metastasis, or HCC. The system was trained and validated using a US data set of 3873 patients. For segmenting liver lesions, the model achieved an intersection-over-union (IoU) score of 68.5%. In differentiating benign from malignant lesions, the model achieved an AUC of 97%, a sensitivity of 86%, and a specificity of 95%. For classifying the four hepatic lesion types, the model attained an AUC of 94.7%, a sensitivity of 86.7%, and a specificity of 89.7%. The authors demonstrated that their approach outperformed traditional segmentation and classification systems. Dadoun *et al*[65] investigated the effectiveness of different DL models in the detection, localisation, and classification of FLLs. Using a large multicentre data set comprising US images from 1025 patients, their system first detected FLLs in a US image before classifying them into two broad categories—benign and malignant—further subclassifying benign lesions as cyst, angioma, FNH, and adenoma,

Table 1 Performance comparison of studies assessing HCC outcomes

Study	Data type	Data set		Model	HCC outcome			
		Total	HCC cases		AUC (%)	Acc (%)	Sen (%)	Spc (%)
Schmauch *et al*[55]	B-mode	367 images from 177 patients	6 images	ResNet50	93.1	79.2	–	–
Chen *et al*[56]	B-mode	465 patients	264 patients	ResNet18	93.7 (84.0–99.0)	–	–	–
Tangruangkiat *et al*[57]	B-mode	581 images	54 images	ResNet50	–	87.2±2.2	80.7±6.8	81.2±3.7
Nishida *et al*[40]	B-mode	70950 images from 23756 cases	1750 images	VGG	–	93.40	67.50	96
Urhut *et al*[54]	CEUS	59 lesions	24 lesions	Deep learning	–	69.93 (66.12–74.59)	86.91 (80.85–92.57)	56.22 (49.69–92.57)
Li *et al*[59]	CEUS	3210 patients	2811 patients	Classical (gradient-boosted, RF, generalised linear model)	–	83	77.3	88.6
Feng *et al*[60]	CEUS	1241 videos	667	Deep learning	89	83	82	83
Wan *et al*[61]	CEUS	174 patients	105	Deep learning	87.9	88.4	86.2	90.1
Ding *et al*[62]	CEUS	3725 lesions	1250 lesions (training set) 685 (test set)	Deep learning	87–91 (test set)	91–96	–	96–98

Acc, accuracy; AUC, area under the curve; CEUS, contrast-enhanced ultrasound; HCC, hepatocellular carcinoma; ResNet18, Residual Neural Network 18; ResNet50, Residual Neural Network 50; RF, random forest; Sen, sensitivity; Spc, specificity; VGGNet, Visual Geometry Group Network.

Table 2 Performance comparison of studies focused on tumour detection and segmentation

Study	Data set		Model	HCC outcome			
	Total	HCC cases		Det (%)	Acc (%)	Sen (%)	Spc (%)
Tiyarattanacha *et al*[63]	20 432 FLL images from 3487 patients	2516 FLL images	RetinaNet	–	–	73.6* (64.3–82.8)	97.8* (96.7–98.9)
				–	–	81.5† (74.2–88.8)	94.4† (92.8–96.0)
Ryu *et al*[64]	4309 images of 3873 patients	874 images	FCN	–	67.2	–	–
Tangruangkiat *et al*[66]	2208 images	543 images	YOLO4	–	–	72.0	–
Chaiteerakij *et al*[67]	26288 images from 5444 patients	1635 FLLs	YOLOv5	82.30 (77.1–87.5)	94.82 (93.8–95.8)	78.10 (72.5–83.7)	97.03 (96.2–97.9)

*Internal test set.
†External validation set.
Acc, accuracy; Det, detection; FCNs, fully convolutional networks; FLL, focal liver lesion; HCC, hepatocellular carcinoma; RetinaNet, retinal neural network; Sen, sensitivity; Spc, specificity; YOLO4, You Only Look Once V.4; YOLOv5, You Only Look Once V.5.

and malignant lesions as metastasis and HCC. To localise FLLs, the model achieved an IoU score of 69.0%±12.0. In classifying FLLs as benign or malignant, the best model achieved an accuracy of 81% (95% CI: 68.0% to 94.0%), a sensitivity of 82% (95% CI: 62.0% to 100.0%) and a specificity of 81% (95% CI: 67.0% to 91.0%). When classifying FLLs into six categories, the highest-performing model achieved an accuracy of 76% (95% CI: 62.0% to 91.0%), a sensitivity of 65% (95% CI: 50.0% to 80.0%), and a specificity of 94% (95% CI: 90.0% to 98.0%). Tangruangkiat *et al*[66] proposed a two-stage method for HCC screening using B-mode US images, comprising an object detector for FLL localisation and a classifier for differentiating among three distinct FLL types. The study was developed and validated using a data set of 2208 US images. Overall, object detection achieved a mean average precision of 76%. The two-stage method demonstrated an accuracy of 86%, a precision of 88%, and a recall of 84% in identifying suspicious FLLs. Chaiteerakij *et al*[67] developed and evaluated an AI-assisted US system for FLL detection and classification. Using a data set of 5444 patients to classify seven FLL types, the model achieved an overall detection rate of 84.8%, with an HCC detection rate of 82.3% (95% CI: 77.1% to 87.5%). Additionally, the model differentiated malignant from benign FLLs with both a sensitivity and specificity of 97.0%.

Integration with clinical data

Several studies have examined the integration of imaging features with clinical data to enhance the diagnostic accuracy of AI models (table 3). Yang *et al*[68] developed an AI model to classify the ROI of FLLs in US images as benign or malignant. The model initially segmented the liver and FLL within a US image. Incorporating clinical data, the model then classified these features as benign or malignant, achieving an AUC of 92.4% on an external validation data set. Compared with radiologists possessing ≥15 years of experience, the model demonstrated better diagnostic accuracy, sensitivity, and specificity. Zhao *et al*[69] developed USC-ENet, an AI model leveraging EfficientNet to extract imaging features from an FLL ROI in US images and integrate them with clinical data for enhanced classification of benign versus malignant liver lesions. This study analysed data from 542 patients with liver tumours, improving sensitivity, specificity, and AUC from 81.8% to 91.5%, 80.3% to 88.0%, and 82.5% to 95.6%, respectively. Xu *et al*[70] developed a DL pipeline that incorporated a mass-guided strategy and clinical factors to segment and classify liver malignancies. The model, trained and validated on a data set of 11 468 patients, was evaluated using two external data sets. In the first data set, it detected liver metastases with an AUC of 94.5%, a sensitivity of 86.7%, and a specificity of 92.7%. It also classified liver masses as malignant or benign with an AUC of 92.8%, a sensitivity of 82.7%, and a specificity of 92.7%. In the second data set, the model classified liver masses as malignant or benign, with an AUC of 88.5%, a sensitivity of 85.4%, and a specificity of

Table 3 Performance comparison of studies integrating AI with clinical data

Study	Clinical data	Data set	Model	Target	Outcome		
					AUC (%)	Sen (%)	Spc (%)
Yang *et al*[68]	7 clinical factors including age, gender, hepatitis history, and AFP	24 343 images from 2143 patients	ResNet18 and LR	Malignancy	92.4 (88.9–95.9)	86.5	85.5
Zhao *et al*[69]	33 clinical variables including age, gender, family history, hepatitis history, history of alcoholism, AFP, lesion characteristics, and others	2168 images from 542 patients	USC-ENet	Malignancy	95.6	91.5	88.0
Xu *et al*[70]	12 clinical factors including age, sex, AFP, ALB, GGT, AST, HBsAg, ALP, ALT, CEA, TBIL, and DBIL.	43 746 images from 10 997 patients	LMC-Net	Malignancy	96.7 (95.5–97.9)	88.1	91.9
				HCC	79.6 (76.3–82.8)	–	–

AFP, alpha-fetoprotein; AI, artificial intelligence; ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AUC, area under the curve; CEA, carcinoembryonic antigen; DBIL, direct bilirubin; GGT, gamma-glutamyl transferase; HBsAg, hepatitis B surface antigen; HCC, hepatocellular carcinoma; LMC-Net, Liver Malignancy Classification Network; LR, logistic regression; ResNet18, Residual Neural Network 18; Sen, sensitivity; Spc, specificity; TBIL, total bilirubin; USC-ENet, Ultrasound Classification EfficientNet.

77.8%. For subtype classification, the model differentiated HCC from other subtypes with an AUC of 69.2%. Its sensitivity was comparable to that of mid-level radiologists.

A clear trend is emerging toward integrating imaging, clinical, laboratory, and genomic data to improve HCC risk prediction and early detection. Instead of relying solely on the US, newer AI models incorporate patient demographics, laboratory results (eg, liver function tests and viral load), and medical history alongside imaging.[71] Such multimodal systems offer comprehensive risk scores and diagnostic assessments.[72] Although these multimodal AI systems remain in the prototype stage, initial applications in preliminary research indicate that they exhibit superior predictive power compared with single-modality algorithms.

BRIDGING RESEARCH TO CLINICAL PRACTICE

Several studies have examined the real-world applicability of AI-assisted systems in clinical practice (online supplemental table 2). Tiyarattanachai *et al*[73] investigated the feasibility of an AI-based US system to detect FLLs in US videos. The AI system was developed and trained using a two-stage process. The model was trained on US snapshots and further refined using difficult frames extracted from full-length US videos where the initial model struggled to recognise FLLs. This approach addresses the challenge of detecting FLLs, even in cases where they are difficult to visualise. Overall, the performance of the AI system was compared with that of radiologists and non-radiologist physicians, demonstrating significantly higher detection rates (89.8% vs 70.9% and 29.1%, respectively). Notably, the AI system functions in real-time, underscoring its clinical practicality. Tiyarattanachai *et al*[74] conducted a randomised controlled trial (RCT) investigating an AI-assisted system for real-time FLL detection in 260 patients. This study compared the performance of expert and non-expert ultrasonographers with and without AI support. The AI system significantly improved FLL detection rates among non-expert ultrasonographers, demonstrating its potential utility in resource-limited settings where trained specialists are scarce.

AI models show strong potential in detecting and classifying HCC and other liver lesions. However, variability in data sets and evaluation protocols limits direct comparisons. Nonetheless, the consistent performance of AI across different applications highlights its promise for clinical practice. Integrating AI into clinical workflows could significantly impact early detection, treatment decisions, and overall patient outcomes.

Recently, the US Food and Drug Administration approved numerous AI-enabled medical devices, though only a few are directly intended for HCC surveillance, and just three devices involve US.[75] This indicates that US-based AI applications for HCC surveillance remain in the early stages of regulatory approval. Regulatory agencies are actively developing frameworks to ensure the safety and efficacy of AI-based technologies. In Europe, the Conformité Européenne (CE) marking is a mandatory requirement for clinical AI systems under medical

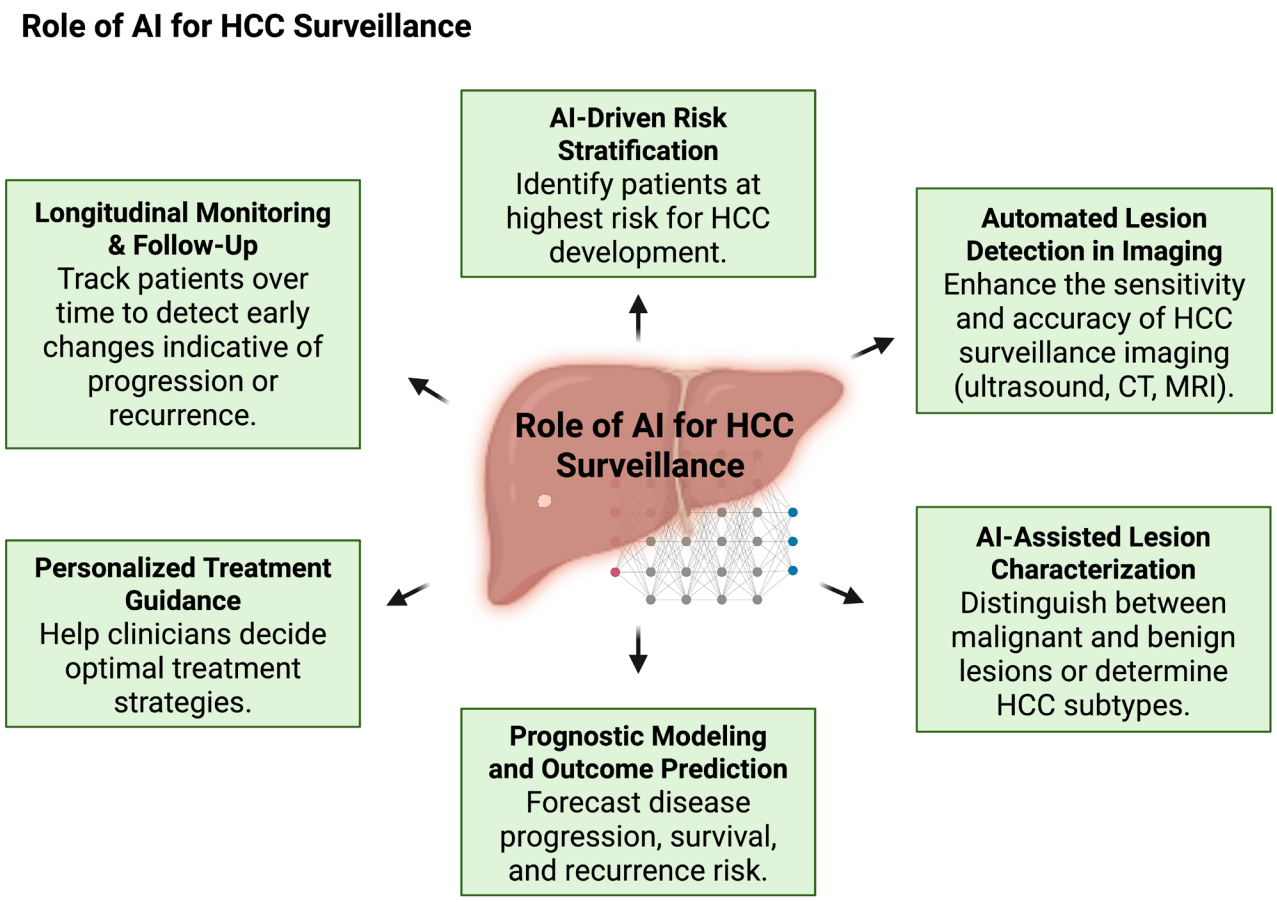


Figure 2 Role of artificial intelligence (AI) in hepatocellular carcinoma (HCC) surveillance This diagram illustrates the various applications of artificial intelligence (AI) in HCC surveillance, including AI-driven risk stratification, automated lesion detection, AI-assisted lesion characterisation, prognostic modelling, personalised treatment guidance, and longitudinal monitoring.

device regulations. However, no CE-marked AI tools for HCC US screening have been formally recognised.[76] Authorities in various countries are in the process of establishing guidelines that will shape the integration of AI in healthcare, which could influence the deployment of HCC surveillance protocols in these regions.

Major liver disease guidelines have begun to recognise AI; however, none have formally incorporated it into standard HCC surveillance protocols. The International Liver Cancer Association and other bodies have published white papers calling for further research and the eventual integration of AI as the evidence matures.[11] Regulatory and policy bodies have also emphasised the need for standardisation (eg, common performance benchmarks) before AI can be fully used for HCC screening.

CONCLUSIONS

AI is reshaping HCC surveillance by enhancing diagnostic accuracy, risk stratification, and clinical decision-making (figure 2). Recent progress—from accurate DL models and initial RCTs to evolving regulatory frameworks—underscores the potential of AI to enhance image interpretation, enabling earlier detection and improved patient outcomes. However, challenges remain, including the need for standardised AI algorithms, diverse and robust training data, real-world validation, and broader clinical adoption. Future research should address these limitations while exploring the AI's potential role in real-time diagnostics and personalised surveillance strategies. In the coming years, further results from clinical trials may pave the way for AI integration into standard HCC screening and treatment guidelines, thereby ushering in a new era of technology-enabled surveillance. With continued innovation and integration into clinical workflows, AI could significantly improve detection, reduce mortality, and enhance healthcare efficiency.

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