Review

Advancements in Imaging and Medical AI for the Management of Liver Disease — Applications and Challenges in Personalized Care —

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Review

Advancements in Imaging and Medical AI for the Management of Liver Disease—Applications and Challenges in Personalized Care

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Abstract: Liver disease can significantly impact life expectancy, making early diagnosis and therapeutic intervention critical challenges in medical care. Imaging diagnostics play a crucial role in diagnosing and managing liver diseases. Recently, the application of artificial intelligence (AI) in medical imaging analysis has become indispensable for healthcare. AI, trained on vast datasets of medical images, has sometimes demonstrated diagnostic accuracy that surpasses human experts. AI-assisted imaging diagnostics are expected to contribute significantly to the standardization of diagnostic quality. Furthermore, AI has the potential to identify image features imperceptible to humans, thereby playing an essential role in clinical decision-making. This capability enables physicians to formulate more accurate diagnoses and develop effective treatment strategies, ultimately improving patient outcomes. Additionally, AI is anticipated to become a powerful tool in personalized medicine. By integrating individual patient imaging data with clinical information, AI can propose optimal treatment plans, making it an essential component in providing the most appropriate care for each patient. Current reports highlight the advantages of AI in managing liver diseases. As AI technology continues to evolve, it is expected to further advance personalized diagnostics and treatments, contributing to overall improvements in healthcare quality.

Keywords: artificial intelligence; deep learning; liver disease; hepatocellular carcinoma; imagining; diagnosis; treatment; personalized medicine

1. Introduction

Imaging diagnostics are indispensable in the diagnosis and treatment of liver diseases, with a large volume of medical imaging data accumulating daily. Since most medical images are standardized in the Digital Imaging and Communications in Medicine (DICOM) format, they provide a substantial advantage as training data for artificial intelligence (AI). AI, trained on lesion-specific imaging features, can offer valuable information not only for disease diagnosis but also for estimating disease progression and predicting prognosis, thereby enhancing disease management. This paper outlines the current state of AI development in medical imaging for liver diseases and its societal implementation, focusing primarily on deep learning models.

2. Advantages of AI in medical imaging diagnostics

Liver diseases, such as cirrhosis and malignant liver tumors, significantly impact prognosis, making early diagnosis and timely therapeutic intervention crucial. Imaging diagnostics, including ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI), are vital in diagnosing and managing liver diseases. However, the large volume of imaging data often overwhelms clinical capacity, making it challenging to review and interpret results within the required time frame. AI, trained on extensive image datasets labeled by specialists, has demonstrated diagnostic accuracy that, in some cases, surpasses that of human experts. This enhances the standardization of imaging diagnostic quality [1–5]. Moreover, AI systems can process large amounts

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of data rapidly, significantly reducing the time required for diagnosis. Recently, AI has been developed to perform tasks previously considered extremely difficult for humans. For instance, an AI model trained on 32,537 whole slide images (WSI) of hematoxylin-eosin (HE) stained specimens has been developed to predict the origin of tumors, extracting features to diagnose cancers of unknown primary origin [6]. The ability of AI to identify image features unrecognizable by humans proves its potential to play a crucial role in clinical decision-making [7,8].

3. Training of AI models using imaging data of liver disease

Common imaging modalities for liver diseases include US, CT, MRI, and pathological tissue images [9]. US examinations provide real-time images and are often used for the initial diagnosis of liver lesions. If a lesion is suspected, further examinations such as CT or MRI are typically conducted. Given the widespread availability of US diagnostic equipment, a large number of images can be obtained for AI training. However, in US imaging, US waves are directed at a target object and the reflected echoes are processed into image data, making issues such as artifacts common. Therefore, quality control of training images is crucial for effective AI development [2,10,11]. In contrast, CT and MRI scans offer high spatial resolution and allow for comprehensive imaging of the liver, enabling three-dimensional reconstruction of its structure. These modalities provide more uniform image quality, making radiomics data more readily available compared to US examinations. Additionally, well-established classification and segmentation training datasets exist for CT and MRI images [2]. Nonetheless, caution is required when using such images for training due to potential issues such as hepatic deformation from interventions such as liver atrophy due to cirrhosis or partial surgical resection.

Pathological examination remains the gold standard for diagnosing many liver diseases. The advent of digital pathology scanners has made it easier to obtain WSIs for AI training. However, image quality issues may arise when using stored specimens from older cases due to sample degradation. While WSIs are often divided into patches for AI training, annotating images at the cellular level is labor-intensive. Therefore, careful consideration of the AI's intended purpose and functionality is essential to ensure appropriate annotation.

3.1 Supervised learning for imaging data

In supervised learning, AI is trained using expert-labeled data provided by specialists to match its final output with the correct labels. Traditional methods quantify features such as the shape, extent, and contrast of lesions, which are used to train machine learning algorithms like support vector machines, logistic regression, and multilayer perceptron for lesion classification and prediction [12,13]. In the development of AI models for CT and MRI, radiomics features are commonly applied. When humans manually select features, the results are often easier to interpret. In contrast, deep learning automatically determines numerous features while simultaneously training the model using multi-layered neural networks. Each layer of the network extracts features from the previous layer, transforming them progressively until the final output aligns with the correct label. Convolutional neural networks (CNNs) are commonly used in image analysis [2]. CNNs use specific coefficients, or kernels, to process pixels within a defined range, thereby extracting diverse image features. By automatically adjusting kernel coefficients and sizes, CNNs can capture various image features. This approach consolidates information within a set range of pixels, making it less influenced by minute positional relationships, and ensuring stable, unbiased learning. Some models trained on time-series data from different stages of the same case have been applied to distinguish malignant liver tumors. However, preparing a large number of expert-level labels for training data is often challenging due to the significant time, effort, and cost required for annotation. To address this, innovative approaches, such as collectively labeling datasets to assess overall disease conditions, are necessary, particularly for complex annotations such as patch images of WSI in pathological tissue [3,14].

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3.2. Unsupervised learning for imaging data

Unsupervised learning aims to detect specific patterns within data without the need for labeled training data. This approach includes techniques such as clustering, which groups subjects based on data features, and dimensionality reduction, which extracts key information that characterizes the data. One advantage of unsupervised learning is that it requires less effort in preparing training data since no labels are required. However, even if new patterns are discovered, interpreting such classifications can be challenging, and AI-generated classifications may not always be clinically useful. Since unsupervised learning lacks labels, it cannot perform differential diagnoses or predict diagnostic probabilities, limiting its application in clinical practice. Clustering techniques, such as K-means and spectral clustering, are used for classifying liver MRI and CT images based on distances derived from sample features [15]. Other applications include autoencoders, which transform images into vectors that retain important information while removing irrelevant details. Generative adversarial networks (GANs) are also employed, where a generator creates artificial images and a discriminator attempts to differentiate between real and generated images. This technique can be used to generate new artificial data, which may serve as training data for AI [1,16].

3.3. Transfer learning for imaging data

Transfer learning is commonly employed to address the lack of labeled image data [17]. It involves using a pre-trained AI model, initially developed for a specific purpose, as a starting model for performing similar tasks. This method simplifies the construction of models compared to training AI from scratch. For instance, there are reports of using a pre-trained AI model for contrast-enhanced US images to develop an AI model for diagnosing lesions in B-mode US using a smaller dataset [18]. Additionally, transfer learning has been applied to develop models for classifying liver fibrosis by using a pre-trained AI model on B-mode US images [19].

4. AI-aided imaging diagnosis and its clinical application

AI plays a significant role in clinical practice, aiding in the diagnosis and risk prediction of diseases and serving as a powerful tool for personalized medicine [5,20]. However, developing versatile AI systems requires the collection of large-scale medical data. Many reports on AI in medical imaging highlight issues such as small and homogenous training cohorts and a lack of validation with external datasets [11]. Despite these challenges, AI is expected to contribute to various aspects of disease management, including the early detection of lesions, accurate differentiation of malignant lesions, and the prediction of disease progression and complications. AI not only supports current medical practices by reducing human error and variability among clinicians but also has the potential to identify features in images that are undetectable by humans, applying these features as morphological biomarkers in clinical settings.

Intervention to improve the disease prognosis, particularly for malignant tumors, can be categorized into three stages: ① disease prevention, ② early detection, and ③ the selection of effective treatments (Table 1). For instance, lifestyle improvements such as reducing alcohol consumption can prevent the onset of certain diseases and reduce deaths related to alcohol use. AI-based applications that encourage behavior changes, such as reducing alcohol intake, could be effective tools for disease prevention. Early detection is another key factor in improving prognosis. AI can help by identifying high-risk populations and developing screening methods. A recent AI model, trained on a large dataset from Denmark and the USA, successfully predicted the occurrence of pancreatic cancer within 36 months [21]. Since pancreatic cancer is difficult to detect early and has a poor prognosis, an AI system that identifies high-risk individuals could greatly contribute in early detection and improved outcomes. Many AI systems assist in diagnosing medical images at this stage, such as those that estimate the stages of liver fibrosis and steatosis, effectively narrowing down high-risk populations for liver cancer. Alternatively, AI systems that assist in image diagnosis is also expected to be effective in reducing misdiagnosis and aiding early detection. AI has also been shown to support the diagnosis of pancreatic cancer from plain CT images [22]. In liver disease, AI models

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supporting the diagnosis of liver tumors from US and CT images have been reported, and these systems are expected to reduce human error and improve diagnostic accuracy.

Selecting effective treatments is also crucial for improving disease prognosis. AI models that estimate treatment outcomes and prognoses are increasingly important. For example, an AI system using image-based diagnostics has been reported to estimate and compare survival outcomes between surgery and radiofrequency ablation (RFA) for early liver cancer [23].

Table 1. Stage of medical care and AI application required in each step.

	Prevention	Diagnosis	Treatment
Actions required	Improvement of lifestyle	Narrowing down high-risk populations Examination with high accuracy	Selection of effective treatments
AI support	Encouraging behavior and lifestyle change	Screening assistance and diagnostic support	Prediction of treatment outcomes

For the prevention of the disease, improvement of lifestyle is necessary, and AI application may help promote behavior and lifestyle change. For the diagnosis of the disease, AI can support disease screening and diagnosis for narrowing down high-risk populations and examination with high accuracy. For the treatment, prediction of treatment outcome by AI should be helpful for selection of most effective treatments in each patient.

4.1. Prediction of staging and diagnosis of lesions

Liver fibrosis and cirrhosis are well-established high-risk factors for developing hepatocellular carcinoma (HCC). The non-invasive, accurate assessment of liver fibrosis is crucial not only for the early diagnosis of HCC but also for managing its life-threatening complications. Wang et al. developed a deep learning model based on shear wave elastography (SWE) imaging, which visualizes tissue elasticity and accurately stages fibrosis in a multicenter study [24]. Additionally, automated systems have been developed to stage fibrosis from CT images [25], predict variceal bleeding in hepatitis B-related cirrhosis [26], and detect cirrhosis and portal hypertension using AI [27]. Liu et al. utilized radiomics data from CT and MRI images to non-invasively detect portal hypertension in cirrhosis [28]. Hamm et al. designed a CNN-based model that classified six types of liver lesions from multiphase MRI images [29].

In the clinical setting, B-mode US is frequently recommended for screening cirrhotic patients for HCC. Differentiating benign from malignant lesions is crucial for early HCC detection [30–32]. Guo et al. demonstrated improved diagnostic accuracy for malignancy using AI trained on contrast-enhanced US images [33]. Similarly, our AI system has been trained on over 100,000 B-mode US images to differentiate HCC, metastatic liver cancer, hemangiomas, and cysts [34]. Because US diagnosis relies on the operator's experience, an AI-aided system is useful for the standardization of US examination quality. Moreover, Chiang et al. demonstrated that AI can outperform human experts in detecting early HCC using a multivariate logistic regression model based on clinical features and imaging data [35].

4.2. Risk prediction of liver disease

Predicting the risk of liver disease progression, such as liver decompensation, malignancy potential, or liver cancer prognosis, presents major challenges (Table 2). Imaging markers, such as spleen volume have been utilized to predict liver decompensation risk [36]. Additionally, Yu et al. developed a model that estimates the hepatic venous pressure gradient from contrast-enhanced CT

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images to diagnose portal hypertension [37]. Other models related to portal hypertension include those that estimate the hepatic venous pressure gradient in cirrhotic cases from CT angiography [38], including models that predict portal hypertension from CT and MRI through hepatic venous pressure gradient measurements [27], and models that detect subclinical hepatic encephalopathy, a complication of cirrhosis, from functional brain MRI [39].

Table 2. AI trained with imaging data for predicting treatment outcomes and prognosis in hepatocellular carcinoma.

Imaging modality and prediction	Number of the training cases *	Findings	References
Ultrasonography			
HCC: Prediction of RFS after MWA	513 cases *	2-year RFS after MWA (C-index = 0.72)	Wu, *et al*., 2022 [66]
HCC: Prediction of recurrences after RFA or MWA	318 cases *	Recurrence beyond 2 years after RFA or MWA (C-index = 0.77)	Ma, *et al*., 2021 [67]
HCC (early stage): Prediction of RFS after RFA or surgery	214 cases for RFA*, 205 cases for surgery*	Recurrence beyond 2 years after treatment (C-index = 0.73)	Liu, *et al*., 2020 [23]
HCC: Prediction of treatment outcome after TACE	130 cases *	Response for TACE AURUC = 0.93	Liu, *et al*., 2020 [59]
CT			
HCC (intermediate stage): Prediction of treatment outcome after TACE	543 cases	Time to progression after TACE (C index = 0.70)	Wang, *et al*., 2022 [68]
HCC: Prediction of treatment outcome after TACE	313 cases *	Response for TACE AURUC = 0.92	Peng, *et al*., 2022 [69]

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HCC: Prediction of treatment outcome after TACE	111 cases*	Response for TACE AURUC = 0.91	Bai, *et al*., 2022 [70]
HCC: Prediction of treatment outcome after TACE	48 cases	Response for TACE AURUC = 0.90	Li, *et al*., 2022 [71]
HCC: Prediction of treatment outcome after TACE	248 cases*	Response for TACE AURUC = 0.87	Li, *et al*., 2022 [72]
HCC: Prediction of recurrence after liver transplantation	88 cases	Tumor recurrence/progression after transplantation AURUC = 0.87	Ivanics, *et al*., 2021 [73]
HCC (intermediate stage): Prediction of treatment outcome after TACE	310 cases	Response for TACE AURUC = 0.99	Peng, *et al*., 2021 [74]
HCC: Prediction for TACE ineligibility	256 cases*	Emergence of extrahepatic metastasis and vascular invasion after TACE. AURUC = 0.91	Jin, *et al*., 2021 [75]
HCC: Prediction of treatment outcome after TACE	789 cases	Response with 4-class classification (CR, PR, SD, PD) Accuracy = 85.1%	Peng, et al., 2020 [56]

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HCC: Prediction for TACE ineligibility	243 cases*	Response for TACE AURUC = 0.90	Liu, *et al.*, 2020 [57]
HCC: Prediction of treatment outcome after TACE	105 cases*	Response for TACE accuracy = 0.742	Morshid, *et al.*, 2019 [55]
Prediction of radiation-induced liver injury	125 cases (including 36 HCC cases)	Emergence of radiation-induced liver injury AUROC = 0.85	Ibragimov, et al., 2018 [60]
MRI			
HCC: PFS after MWA	149 cases*	2-year RFS (C-index = 0.73)	Peng, et al., 2023 [76]
HCC: Prediction of treatment outcome after TACE	140 cases*	Response for TACE AURUC = 0.81	Liu, et al., 2022 [77]
HCC: Prediction of treatment outcome after TACE	252 lesions	Response for TACE (3-class classification、accuracy = 93.2%)	Svecic, *et al.*,2021 [78]
HCC (solitary, 2～5cm in size): RFS after surgery	167 cases	Model with trained with images 3-mm peritumoral border extension of tumor showed comparable performance with that of the postoperative clinicopathologic model.	Kim, *et al.*, 2019 [44]
HCC: Prediction of microvascular invasion	110 cases	Presence of microvascular invasion	Feng, *et al.*, 2019 [43]

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		sensitivity = 0.90、specificity = 0.75、accuracy = 0.83	
HCC: Prediction of treatment outcome after TACE	36 cases *	Response for TACE accuracy = 78%、sensitivity = 62.5%, specificity = 82.1%	Abajian, *et al*., 2018 [54]
Pathology			
HCC: Prediction of survival after surgery	The discovery set, 194 images, The validation set, 328 images (whole slide image)	C-index = 0.75～0.78	Saillard, *et al*., 2020 [50]
HCC: Prediction of survival after surgery	The Zhongshan cohort, 2,451 images, The TCGA cohort, 320 images (whole slide image) and multi-omics data	A 'tumor risk score (TRS)' was established to evaluate patient outcomes. The predictive ability of TRS was superior to and independent of clinical staging systems.	Shi, *et al*., 2021 [51]

* Report of the models using image data along with clinical and blood test data for training. * Report of the models using image data along with clinical and blood test data for training. HCC: hepatocellular carcinoma, RFS: recurrence-free survival, DL: deep learning, MWA: microwave ablation, RFA: radiofrequency ablation, machine learning, TACE: transarterial chemoembolization, AURUC: Area Under the Receiver Operator Characteristic curve, CR: complete response、 PR: partial response、 SD: stable disease、 PD: progressive disease. TCGA: The Cancer Genome Atlas.

For liver cancer risk prediction, AI models have been reported that assess the risk of postoperative liver cancer recurrence by combining tumor shape and radiomics features with serum markers such as alpha-fetoprotein and albumin-bilirubin grade (ALBI grade) [40]. Moreover, AI systems have been developed to predict microvascular invasion, cytokeratin 19 expression associated with malignancy, and early tumor recurrence from CT and MRI images [41,42]. Feng et al. used gadolinium-ethoxybenzyl (EOB)-diethylenetriamine-enhanced MRI (EOB-MRI) images, combined with pathological findings of resected specimens as training data, to estimate microvascular invasion preoperatively in resectable HCC cases, outperforming radiologists in some cases [43]. Other studies have applied random forest models to predict recurrence-free survival after surgery from EOB-MRI features in solitary HCC cases [44]. For the prediction of early recurrence, an AI model using preoperative EOB-MRI feature including the area 3 mm outside of the tumor edge demonstrated performance equivalent to an AI model trained with clinicopathological findings of resected specimens [44].

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In liver cancer prognosis, genetic mutations play a key role [45–47]. Studies in non-small cell lung cancer have shown that prognostic imaging features can be derived from genetic expression data [48]. Similarly, for liver cancer, efforts have been made to estimate specific genetic mutations, tumor immune microenvironments, and survival from images of HE specimens [49–51] (Table 2). In the future, multimodal AI models integrating imaging with genomic and transcriptomic data could provide even more accurate risk estimations for liver diseases [4,52].

4.3 Application to personalized medicine for the management of liver cancer

By training AI models on quantitative imaging data, it becomes possible to accurately predict individual responses to various treatments, thereby enabling appropriate therapeutic approaches for liver cancer, significantly contributing to cost reduction. The ability of AI to predict the efficacy of local therapies, pharmacotherapies, and radiotherapies offers significant value in personalized medicine [53]. A summary of AI-based models trained on imaging data to predict treatment outcomes and prognosis in liver cancer is shown in Table 2. Several studies have demonstrated AI's potential in predicting the response to transarterial chemoembolization (TACE) using CT, MRI, and US images. For example, multimodal AI models, which integrate clinical and imaging data, have been used to predict TACE outcomes [54–58]. CNN-based models trained on CT images and random forest models using MRI data are examples of AI systems developed for this purpose [54,55]. Additionally, AI models that analyze contrast agent inflow dynamics in contrast-enhanced US (CEUS) images have also been used to predict TACE effectiveness [59]. AI systems trained on preoperative CEUS images can predict post-operative progression-free survival for early-stage liver cancer patients undergoing RFA or surgery, allowing physicians to adjust treatment strategies based on AI predictions, potentially leading to better tumor control [23]. Ibragimov et al. developed a CNN-based model using 3D-CT images of HCC before radiotherapy to predict radiation-induced liver injury [60]. Similarly, Müller et al. used AI-based segmentation to calculate spleen volume from CT images and identified it as a predictive marker for immunotherapy response in liver cancer [61]. In liver transplantation, particularly in cases with large tumor volumes, multimodal risk assessment systems that incorporate imaging data have also been reported [8]. AI's ability to recognize subtle changes in imaging features that may not be apparent to human observers allows for more precise monitoring of treatment response, predicting disease progression, and forecasting outcomes. For instance, Taylor et al. highlighted the advantage of AI over traditional histology-based staging in evaluating liver fibrosis progression, particularly in cases of non-alcoholic steatohepatitis (NASH), where fibrosis staging can be heterogeneous [62]

The treatment landscape for liver cancer is diverse, with significant improvements in survival rates for advanced-stage cases. However, the therapeutic framework has become increasingly complex, with multiple treatment options available for the same stage of HCC depending on patient-specific factors [63,64]. Despite this, appropriate biomarkers to guide treatment decisions are still lacking. As a result, determining the optimal therapeutic approach remains challenging, and conducting numerous prospective clinical trials and omics analyses for biomarker development to address these uncertainties requires substantial effort [65]. However, AI's predictive capabilities can address these challenges by estimating treatment outcomes and disease progression based on historical data, offering a powerful tool for optimizing clinical decision-making.

5. Conclusions

The application of AI in liver imaging diagnostics is promising but still in its early stages. Challenges remain, particularly in ensuring the quality of image data and the accuracy of ground truth labels. The effectiveness of AI models relies heavily on the quality and volume of training data, making it essential to collect large, high-quality, and accurately labeled datasets to support further AI development. Additionally, AI models that integrate multimodal data, combining medical imaging with pathological, genomic, epigenomic, and transcriptomic information, show great potential for advancing personalized medicine [4,14,65]. With continued development, AI is poised to revolutionize the diagnosis and treatment of liver diseases.

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