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REVIEW

An Artificial Intelligence Pipeline for Hepatocellular Carcinoma: From Data to Treatment Recommendations

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Abstract: Hepatocellular carcinoma (HCC) poses significant clinical challenges, including difficulties in early diagnosis and the complexity of treatment options. Artificial intelligence (AI) technologies are emerging as powerful tools to address these issues through a unified AI pipeline. This pipeline begins with data ingestion and preprocessing, integrating multimodal data such as imaging, genomic and clinical records. Machine learning and deep learning techniques are then applied to analyze these data, improving tumor detection, characterization, and early diagnosis. The pipeline extends to personalized treatment planning, where AI integrates diverse data types to predict patient responses to various therapies. In drug development, AI accelerates the discovery of new treatments through virtual screening and molecular modeling, while also identifying potential new uses for existing drugs. AI further enhances patient management through remote monitoring and intelligent support systems, enabling real-time data analysis and personalized care. In research, AI improves big data analysis and clinical trial design, uncovering new biomarkers and optimizing patient recruitment and outcome prediction. However, challenges such as data quality, standardization, and privacy remain. Future developments in multimodal data integration and edge computing promise to further enhance AI's impact on HCC diagnosis, treatment, and research, leading to improved patient outcomes and more effective management strategies.

Keywords: hepatocellular carcinoma, artificial intelligence, machine learning, deep learning, personalized treatment

Introduction

Liver cancer ranks as the sixth most commonly diagnosed cancer and the third leading cause of cancer-related deaths worldwide, with hepatocellular carcinoma (HCC) accounting for approximately 90% of all liver cancer cases.[1] According to the Global Burden of Disease Study 2021, there were over 529,000 new cases and 483,000 deaths attributed to liver cancer in 2021 alone.[2] Over the past two decades, the incidence of liver cancer has increased by 53.7%, while mortality rates have risen by 48.0%, reflecting a growing global health challenge.[3] The clinical management of HCC is fraught with challenges, particularly due to difficulties in early diagnosis and the complexity of treatment options.[4] Early-stage HCC often remains asymptomatic, leading to late detection when the disease has already progressed to an advanced stage, limiting therapeutic options and worsening the prognosis.[5] Moreover, the heterogeneity of liver cancer—both at the molecular and clinical levels—complicates treatment decisions, which may include surgical resection, liver transplantation, locoregional therapies, and systemic treatments.[6] These complexities underscore the need for advanced tools to aid in the diagnosis and treatment of this disease.

In recent years, artificial intelligence (AI) has emerged as a transformative technology in medicine, offering new solutions to these challenges.[7] AI, which encompasses machine learning, deep learning, natural language processing, and computer vision, has shown significant potential in addressing the complexities of HCC. For example, deep learning models have been trained on vast datasets of imaging studies to identify liver tumors with a level of accuracy that rivals,

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and in some cases surpasses, human radiologists.[8,9] These AI models can detect subtle changes in imaging data that may be indicative of early-stage HCC, thereby enabling earlier interventions that could be life-saving.

Additionally, AI is being leveraged to personalize treatment strategies for HCC patients.[10] By integrating and analyzing data from various sources, including genetic profiles, imaging studies, and clinical histories, AI can help predict how individual patients will respond to different treatments.[11] This allows for the design of personalized treatment plans that maximize efficacy while minimizing side effects. For instance, machine learning algorithms can analyze patient genetic and molecular data to predict their response to targeted therapies or immunotherapies, thus guiding oncologists in selecting the most appropriate treatment course.[12,13]

In research, AI is accelerating the discovery of novel biomarkers and therapeutic targets. Natural language processing tools are being used to sift through vast amounts of biomedical literature and electronic health records, extracting relevant data that can lead to new insights into the mechanisms of HCC.[14] Furthermore, AI-driven drug discovery platforms are being employed to predict the efficacy of new compounds in treating HCC, significantly reducing the time and cost associated with traditional drug development processes.[15]

This review aims to explore the current applications of AI in the diagnosis, treatment, and research of HCC. By examining how AI is being used to enhance diagnostic accuracy, optimize treatment strategies, and drive research advancements, this paper seeks to highlight the transformative potential of AI in improving outcomes for HCC patients. Additionally, the review will discuss the challenges associated with integrating AI into clinical practice, including issues related to data quality, model interpretability, and the ethical implications of AI in healthcare. By addressing these challenges and exploring future directions, this review hopes to provide a comprehensive understanding of AI's role in the ongoing fight against HCC.

Overview of Artificial Intelligence Technologies in Hepatocellular Carcinoma Management

AI encompasses a range of technologies that are revolutionizing various aspects of medicine, including the diagnosis and treatment of complex diseases such as HCC.[16] Core AI technologies, including machine learning, deep learning, computer vision, and natural language processing, play crucial roles in advancing medical practice.[17]

Machine Learning and Deep Learning

Machine learning and deep learning are foundational to AI's capability in data analysis and pattern recognition. Machine learning algorithms, which learn from data and make predictions or decisions, are extensively used to identify patterns in large datasets. In the context of HCC, machine learning models can analyze clinical and imaging data to detect early signs of HCC, predict patient outcomes, and assist in tailoring individualized treatment plans. Deep learning, a subset of machine learning, employs neural networks with multiple layers to model complex patterns in data. This technology excels in tasks requiring high-level abstraction, such as classifying images of liver scans. For instance, deep learning algorithms can enhance the accuracy of tumor detection and characterization in CT and MRI scans, potentially surpassing traditional methods in sensitivity and specificity.[18,19]

Computer Vision

Computer vision, another key AI technology, focuses on enabling machines to interpret and process visual information.[20] In medical imaging, computer vision algorithms are applied to analyze and interpret data from imaging modalities like ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). By automating the detection of tumors and other abnormalities, computer vision can significantly improve diagnostic accuracy and efficiency.[21] For example, computer vision systems can automatically segment liver tumors from surrounding tissues in imaging studies, facilitating more precise assessment and treatment planning.[22]

Natural Language Processing

Natural language processing is used to process and analyze human language data, which is particularly useful in handling unstructured information in healthcare.[23] Natural language processing tools can extract relevant information from

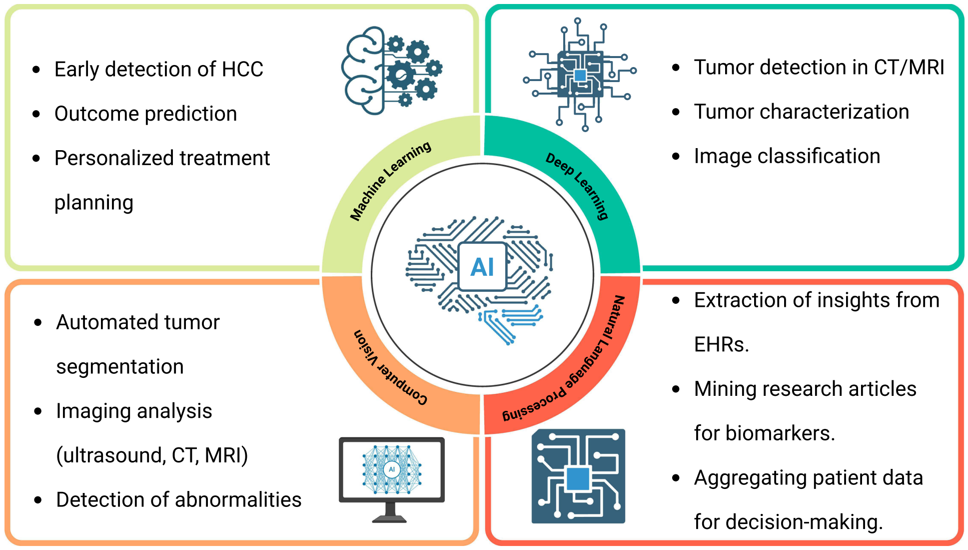

Figure 1 Taxonomy of Artificial Intelligence Technologies in Hepatocellular Carcinoma Management. Created in BioRender. Yuan, X. (2025) https://BioRender.com/q0gvbv2.

medical literature, electronic health records (EHRs), and clinical notes, transforming this data into actionable insights. In HCC management, natural language processing can be employed to identify key clinical findings from EHRs, mine research articles for emerging biomarkers, and aggregate patient data to support decision-making and personalized treatment approaches.[24,25]

Together, these AI technologies are driving significant advancements in the management of hepatocellular carcinoma. By enhancing data analysis, improving imaging interpretation, and facilitating the extraction of actionable insights from diverse data sources, AI holds the potential to transform the landscape of HCC diagnosis, treatment, and research (Figure 1).

Applications of Artificial Intelligence in Hepatocellular Carcinoma Diagnosis

Imaging Analysis

AI, particularly deep learning, has revolutionized the image analysis for HCC diagnosis, significantly enhancing tumor detection, characterization, and segmentation.[26,27] Convolutional neural networks (CNNs) are pivotal in this domain, designed to automatically learn and extract features from medical images through layered convolutional operations.[28] Trained on large datasets of CT, MRI, and ultrasound images, CNNs demonstrate high precision in identifying liver tumors. For instance, a study by Said et al[29] evaluated CNNs for semiautomated HCC segmentation on MRI in 292 patients. The CNNs excelled in single-slice segmentation, particularly on diffusion-weighted imaging (DWI) and pre-contrast T1-weighted imaging (T1WI pre) sequences, with accuracy correlating with tumor size. While single-slice segmentation showed strong results, volumetric segmentation requires further refinement. Beyond segmentation, CNN-based systems significantly improve tumor localization, characterization (distinguishing benign from malignant lesions), and assessment of stage and grade,[30,31] automating detection to enhance diagnostic accuracy and speed, enabling earlier intervention and improved outcomes.[32]

The U-Net architecture, proposed by Ronneberger et al in 2015,[33] is a deep learning model specifically designed for medical image segmentation, offering unique advantages over traditional CNNs in the diagnosis and treatment planning of HCC.[34] In HCC diagnosis, U-Net excels at accurately segmenting the liver and associated tumors from imaging modalities such as CT and MRI, which is critical for optimizing treatment strategies like surgical resection, radiotherapy, and transplantation. For example, a U-Net variant with residual connections demonstrated robust performance across diverse patient populations and imaging conditions, achieving segmentation accuracy ranging from 0.81 to 0.93 on annotated CT datasets.[35] Beyond U-Net, innovative approaches like the Successive encoder-decoder (SED) framework further enhance segmentation capabilities. The SED framework, consisting of two encoder-decoder networks connected in series, first removes irrelevant voxels and organs to extract liver locations from CT images and then segments the lesions. This staged processing achieves a Dice score of 0.92 for liver segmentation and 0.75 for tumor prediction, while its ability to reconstruct 3D images from individual CT scans provides a practical solution for improving clinical diagnosis and therapeutic procedures in HCC.[36] Together, these advancements underscore U-Net's pivotal role in automating and improving HCC diagnosis, enabling earlier intervention and better patient outcomes.

Significant progress in segmentation and prognostic assessment is also demonstrated by DeepLab V3+.[37] This deep learning model excels in semantic image segmentation and has been effectively applied to automate HCC segmentation on MRI. In a study of 209 patients with HCC, DeepLab V3+ model achieved high segmentation accuracy and reliable feature extraction. Integrating these features into a decision fusion model improved microvascular invasion (MVI) prediction, while combining it with a nomogram enhanced early recurrence prediction post-surgery, aiding clinical decision-making and improving patient outcomes.[38]

The AI models discussed herein, including CNNs, U-Net, and DeepLab V3+, each offer distinct capabilities for HCC imaging analysis. CNNs provide versatile foundational architectures for tumor detection and characterization, while U-Net variants excel in generalizable organ and lesion segmentation. The SED framework addresses complex multi-stage segmentation tasks through its successive refinement approach, and DeepLab V3+ demonstrates superior precision in prognostic marker identification such as MVI. Selection of an optimal model depends on the clinical objective: U-Net and SED are prioritized for treatment planning requiring anatomical delineation, whereas DeepLab V3+ is ideal for outcome prediction tasks. Future work should focus on harmonizing these architectures into unified pipelines to leverage their complementary strengths (Table 1).

Table 1 Comparative Analysis of AI Models in HCC Imaging Diagnosis

Architecture	Specific Model	Application	Performance Highlights	Key Advantages	Major Limitations	Ref.
CNN Variants	DCNN-US	Ultrasound	a. Acc: 84.7% b. Sen: 86.5% c. Spec: 85.5% d. AUC: 0.924	Cost-effective alternative to contrast-enhanced CT	Inferior to contrast-enhanced MRI	[39]
	DCCA-MKL	CEUS	a. Acc: 90.4% b. Sen: 93.6% c. Spec: 86.9% d. AUC: 0.953	Superior multi-phase image analysis	Requires three-phase CEUS imaging	[40]
	CNN (Two-Input)	CT	a. Acc: 61.0% b. Sen: 75.0% c. Spec: 88.0% d. AUC: 0.870	Integrates tumor marker data	Suboptimal overall accuracy	[41]
	Extremely Randomized Trees	MRI	a. Acc: 88% b. Sen: 75.0% c. Spec: 56.0% d. AUC: 0.910	Differentiates 5 lesion types	Limited HCC specificity	[42]
U-Net Variants	U-Net (Residual)	CT	a. Acc: 81–93%	High anatomical detail capture	Needs robustness validation	[35]
	SED	CT	a. Dice: 0.92 (Liver), 0.75 (Tumor)	Automated 3D segmentation pipeline	Moderate tumor segmentation performance	[36]

(*Continued*)

Table 1 (Continued).

Architecture	Specific Model	Application	Performance Highlights	Key Advantages	Major Limitations	Ref.
DeepLab	DeepLab V3+ + Fusion	MRI	a. AUC-MVI: 0.968, b. AUC-ER: 0.69 (Val)	Accurate microvascular invasion detection	Retrospective validation only	[38]

Abbreviations: Acc, Accuracy; Sen, Sensitivity; Spec, Specificity; AUC, Area Under Curve; CEUS, Contrast-Enhanced Ultrasound; ER, Early Recurrence; Val, Validation set performance.

Early Screening

AI is transforming early HCC screening by addressing the limitations of traditional guideline-recommended methods which include ultrasound with suboptimal sensitivity and serum alpha-fetoprotein (AFP) that remains negative in nearly two-thirds of early-stage HCC patients.[43,44] AI overcomes these challenges by integrating diverse data sources, including demographic information, medical history, and laboratory results, to identify high-risk individuals. For instance, a randomized trial by Kristina et al demonstrated that AI-supported mammography screening detected a similar number of cancers as radiologists while reducing workload by 44.3%, highlighting AI's potential to enhance efficiency without compromising accuracy.[45] Similarly, machine learning models can prioritize patients for further diagnostic testing, enabling timely interventions and improving outcomes.[46]

Beyond improving screening efficiency, recent advancements in deep learning have further elevated AI's role in HCC screening. A proposed deep learning model based on B-mode ultrasound images, Xception, achieved an AUC of 93.68% in identifying AFP-negative HCC in hepatitis B virus-infected patients, outperforming other models like MobileNet and Resnet50.[47] With high sensitivity (96.08%) and specificity (76.92%), this model offers a robust tool for early detection. Additionally, a gradient-boosting machine algorithm developed for chronic hepatitis B patients demonstrated superior predictive performance (c-index 0.79) compared to traditional risk scores like PAGE-B and REACH-B.[48] It identified a minimal-risk group with less than 0.5% HCC risk over 8 years, suggesting potential for less intensive surveillance. These AI-driven approaches not only improve diagnostic accuracy but also reduce workload and enable personalized risk stratification, paving the way for more effective HCC screening strategies.

Biomarker Analysis

In addition to imaging, AI is increasingly being used to analyze genetic and proteomic data to identify novel biomarkers.[49] High-dimensional data from gene expression profiles and proteomic studies can be challenging to interpret using traditional methods. AI algorithms, such as machine learning models and neural networks, can process these complex datasets to uncover patterns associated with liver cancer.[50] For example, Haoran et al studied MVI in HCC using multi-transcriptomics data. They identified a malignant cell subtype linked to MVI, enriched in the MYC pathway and interacting via the MIF signaling pathway.[51] Their newly developed prognostic model, based on MVI-related genes, showed superior accuracy compared to existing models, providing valuable insights and support for HCC management.[51] Similarly, AI can be used to analyze protein expression data to identify proteins that are differentially expressed in liver cancer, which may serve as diagnostic or prognostic markers. These AI-driven approaches can facilitate the development of more accurate and reliable biomarkers for early detection and personalized treatment of HCC.

While tissue biopsy remains the gold standard for mutational profiling in HCC, AI-enabled liquid biopsy approaches show promise as alternatives, including circulating tumor cells (CTC) and circulating tumor DNA (ctDNA).[52,53] As ctDNA represents the tumor's total genomic landscape, its role in determining clinical outcomes is gaining significant attention, particularly in advanced and unresectable HCC.[54] In a larger cohort study of 121 advanced HCC patients, mutational analysis of ctDNA revealed alterations in the most common HCC-associated driver oncogenes and tumor suppressor genes, including TERT promoter, TP53, PTEN, ARID2, KMT2D, and TSC2.[55] This technique enabled the identification of predictive mutational signatures associated with response to systemic therapy with tyrosine kinase inhibitors. Despite the proven value of ctDNA as a tumor biomarker, its limitations in early detection sensitivity, lack of standardized protocols, and inability to capture tumor spatial heterogeneity suggest that multiparametric approaches are needed to enhance its utility for HCC diagnosis.[56] Consequently, AI-based profiling currently serves as a complementary tool for unresectable cases, not a biopsy replacement, pending validation through large-scale prospective trials (Table 2).

Applications of Artificial Intelligence in Hepatocellular Carcinoma Treatment

Personalized Treatment Planning

AI has become a pivotal tool in developing personalized treatment plans for HCC. Traditional treatment strategies often rely on general protocols that may not be optimal for every patient due to the heterogeneous nature of liver cancer. AI addresses this by integrating various data sources—genomic, imaging, and clinical—to predict how individual patients will respond to different therapies.[57]

One key application is the prediction of treatment responses based on genomic data. Machine learning algorithms analyze patients' genetic profiles, including mutations and gene expression patterns, to identify biomarkers that indicate how a tumor might respond to specific therapies. For example, AI models can process data from next-generation sequencing to identify mutations associated with sensitivity or resistance to targeted therapies. This allows for more precise selection of treatments such as tyrosine kinase inhibitors or immune checkpoint inhibitors, tailored to the genetic makeup of each patient's tumor.[58,59]

Additionally, AI can enhance decision-making by integrating imaging data with genetic and clinical information.[60] For instance, deep learning algorithms analyze pre-treatment imaging scans to assess tumor characteristics such as size, shape, and texture.[61] By combining these insights with genomic data, AI models can predict which treatment options are likely to be most effective. This personalized approach helps to avoid fewer effective treatments and reduces the likelihood of adverse side effects, thereby improving patient outcomes and quality of life.[62]

Table 2 Applications of Artificial Intelligence in Hepatocellular Carcinoma Diagnosis

Application	Area	Description	AI Contribution
Imaging Analysis	CNNs for Tumor Detection	CNNs are used to analyze CT, MRI, and ultrasound images for liver tumors.	CNNs improve tumor detection and segmentation, enhancing accuracy and speed, and identifying subtle patterns missed by radiologists.
	Segmentation Performance	Evaluation of CNNs on MRI data for HCC showed high precision in single-slice segmentation, especially on DWI and T1WI pre sequences.	CNNs demonstrated strong results in segmentation, though volumetric segmentation needs further refinement.
Early Screening	AI-supported Screening	AI integrates various data sources to identify high-risk individuals for HCC early screening.	AI can reduce workload in screening while maintaining detection rates, as shown in mammography comparisons.
	Example Tool: LiverColor	"LiverColor" uses image analysis and machine learning to assess hepatic steatosis.	Achieved 85% accuracy and an ROC curve of 0.82, outperforming traditional methods and improving liver assessment.
Biomarker Analysis	Genetic and Proteomic Data	AI analyzes high-dimensional genetic and proteomic data to identify biomarkers associated with liver cancer.	AI uncovers patterns in gene expression and protein data, aiding in the development of accurate and reliable biomarkers.
	Prognostic Models	AI-based models analyze multi-transcriptomics data to identify malignant cell subtypes and prognostic markers.	Provided superior accuracy in prognostic modeling compared to existing methods, offering valuable insights for HCC management.

Optimizing Radiation Therapy

In radiation therapy for HCC, optimizing treatment plans is crucial for targeting tumors while protecting healthy tissues. Deep learning algorithms analyze 3D imaging data from CT or MRI scans to create detailed anatomical models of the liver and tumor. These models help simulate and optimize radiation dose distribution, predicting effective doses and angles based on the tumor's size, shape, and location, as well as the surrounding healthy tissues. To address the challenges in liver tumor segmentation, recent advancements have introduced an auto-segmentation method that combines a Gaussian filter with the nnU-Net architecture. This approach aims to enhance accuracy in distinguishing between tumors and cysts. Utilizing 130 cases from the LiTS2017 dataset for training and validation, and testing on additional 14 cases from the 3D-IRCADb and 25 clinical cases, the nnU-Net model achieved average dice similarity coefficients (DSC) of 0.86 and 0.82 for validation and public testing sets, respectively. In clinical testing, the DSC improved from 0.75 to 0.81 after applying the Gaussian filter, demonstrating its effectiveness in refining segmentation accuracy.[63]

Furthermore, treatment plans can be adjusted dynamically as therapy progresses. This is particularly beneficial when tumors shrink or change shape during treatment. By continuously updating imaging data, the system ensures that radiation remains accurately targeted throughout the treatment, reducing side effects and improving overall effectiveness.[64]

Surgical Assistance

Advanced navigation and robotic assistance technologies are transforming surgical interventions for HCC. Precise preoperative planning and intraoperative guidance are essential for successful liver surgeries, where the goal is to remove tumors while preserving healthy tissue.[65] These technologies utilize 3D imaging data to create detailed virtual models of the liver and tumor, enhancing visualization of the tumor's location relative to critical structures like blood vessels and bile ducts.[66] For instance, Khaled et al conducted a feasibility study to automate the Liver Imaging Reporting and Data System (LI-RADS) for HCC diagnosis using a deep learning algorithm. They trained a U-Net-based deep CNNs on multiphasic MRI data from 174 patients to automatically segment the liver and detect HCC. The model achieved high accuracy, with mean DSC of 0.91 for liver and 0.68 for HCC lesions, and reduced false positives through postprocessing. This study suggests a more efficient and clinically practical implementation of LI-RADS for HCC diagnosis.[67]

During surgery, robotic systems integrate real-time imaging with preoperative models to guide surgical instruments with high accuracy.[68] This facilitates precise incisions and complex maneuvers, reducing the risk of complications and improving outcomes. Additionally, real-time feedback and predictive analytics from intraoperative data help identify potential issues such as excessive bleeding or changes in tumor position, supporting effective decision-making.[69]

Overall, these advancements in technology are significantly improving the treatment of HCC by personalizing therapy, optimizing radiation planning, and enhancing surgical precision, ultimately leading to better patient outcomes and reduced risks (Table 3).

Applications of Artificial Intelligence in Hepatocellular Carcinoma Drug Development

Drug Discovery and Design

AI is transforming the process of drug discovery and design, particularly for complex diseases like HCC. Traditional drug development is a time-consuming and costly process, often taking years to identify promising compounds and advance them through clinical trials. AI accelerates this process through advanced techniques such as virtual screening and molecular modeling.[70]

One of the primary applications of AI in drug discovery is AI-driven virtual screening.[71] This involves using machine learning algorithms to predict the interaction between small molecules and target proteins associated with HCC. By analyzing large datasets of chemical compounds and their known interactions, AI models can identify potential drug candidates that might interact effectively with specific cancer-related targets. For example, deep learning models can

Table 3 Applications of Artificial Intelligence in Hepatocellular Carcinoma Treatment

Aspect	Focus Area	Details	AI Contributions
Personalized Treatment	Genomic Data	AI uses genetic profiles, including mutations and gene expression, to tailor treatment plans.	Machine learning models identify mutations linked to treatment responses, enabling targeted therapies.
	Imaging Data Integration	AI combines imaging data with genomic and clinical information to optimize treatment choices.	Deep learning algorithms evaluate tumor characteristics to refine treatment options and reduce side effects.
Radiation Therapy	3D Imaging	AI analyzes 3D imaging data to create models for optimizing radiation dose distribution.	Models predict optimal radiation doses and angles, improving targeting accuracy and protecting healthy tissue.
	Segmentation Accuracy	New techniques enhance tumor and cyst differentiation in imaging data.	nnU-Net with Gaussian filter achieved high accuracy in segmentation, improving the precision of tumor delineation.
	Adaptive Treatment	AI adjusts radiation plans based on real-time changes in tumor size or shape.	Continuous updates ensure precise targeting throughout treatment, enhancing effectiveness and minimizing side effects.
Surgical Assistance	Preoperative Planning	AI creates detailed virtual models of liver and tumor for surgical planning.	3D imaging enhances visualization, aiding in accurate tumor removal and preserving healthy tissue.
	Robotic Guidance	Robotic systems use real-time imaging to guide surgical instruments during operations.	Real-time feedback helps in performing precise maneuvers and addressing issues like bleeding or tumor movement.
	Automated LI-RADS	AI automates the Liver Imaging Reporting and Data System (LI-RADS) for HCC diagnosis.	Deep learning models improve accuracy in liver segmentation and HCC detection, reducing false positives.

analyze databases of chemical libraries to predict which compounds are most likely to inhibit the growth of liver cancer cells or block key signaling pathways involved in tumor progression.[15]

Molecular modeling, another crucial aspect of AI in drug development, uses computational techniques to simulate the behavior of molecules and predict their binding affinities to target proteins.[72] AI algorithms can generate detailed 3D models of drug molecules and their target proteins, allowing researchers to visualize how these compounds fit into their targets' active sites. This approach helps in optimizing drug design by predicting which modifications to a molecule might enhance its efficacy or reduce potential side effects. For instance, AI-driven molecular docking simulations can identify the most promising candidates for further development and testing, significantly speeding up the initial phases of drug discovery.[73]

Drug Repurposing

AI is also making significant contributions to drug repurposing, a strategy that involves finding new uses for existing drugs. Drug repurposing can be a more efficient and cost-effective approach compared to developing new drugs from scratch, as it leverages compounds that have already undergone extensive testing for safety and efficacy.[74]

Data mining and machine learning techniques are central to AI-driven drug repurposing efforts. By analyzing large volumes of biomedical data, including clinical trial results, EHRs, and scientific literature, AI can identify existing drugs that might have therapeutic potential for HCC. For example, the role of microRNAs (miRNAs) in the imbalance between cell proliferation and apoptosis in cancer was systematically explored. A miRNA-gene regulatory network was constructed, and a shortest path-based method was used to assess the impact of miRNAs on cell fate genes. Results from breast and liver cancer datasets confirmed that differentially expressed miRNAs significantly affected cell fate genes and were associated with cancer progression and drug sensitivity, offering insights for potential therapeutic applications.[75]

AI can also integrate multi-omics data (such as genomics, proteomics, and metabolomics) to identify existing drugs that target pathways or biomarkers associated with HCC.[76] Recent studies have demonstrated the efficacy of machine learning tools like MDeePred in drug repurposing for HCC. MDeePred leverages datasets from the Open Targets Platform, UniProt, ChEMBL, and Expasy databases to predict drug-target interactions (DTIs). Through enrichment analyses, MDeePred identified 6 out of 380 DTIs as promising candidates for HCC treatment. These candidates exhibited favorable drug-like properties, including physicochemical characteristics, lipophilicity, water solubility, and medicinal chemistry profiles, comparable to approved HCC drugs such as lenvatinib, regorafenib, and sorafenib. Additionally, molecular docking studies confirmed the binding efficacy of these compounds to HCC-associated targets, highlighting their potential for further experimental validation.[77] This integrated approach underscores the utility of AI in accelerating the discovery of repurposed drugs for HCC, expanding therapeutic options for this challenging disease (Figure 2).

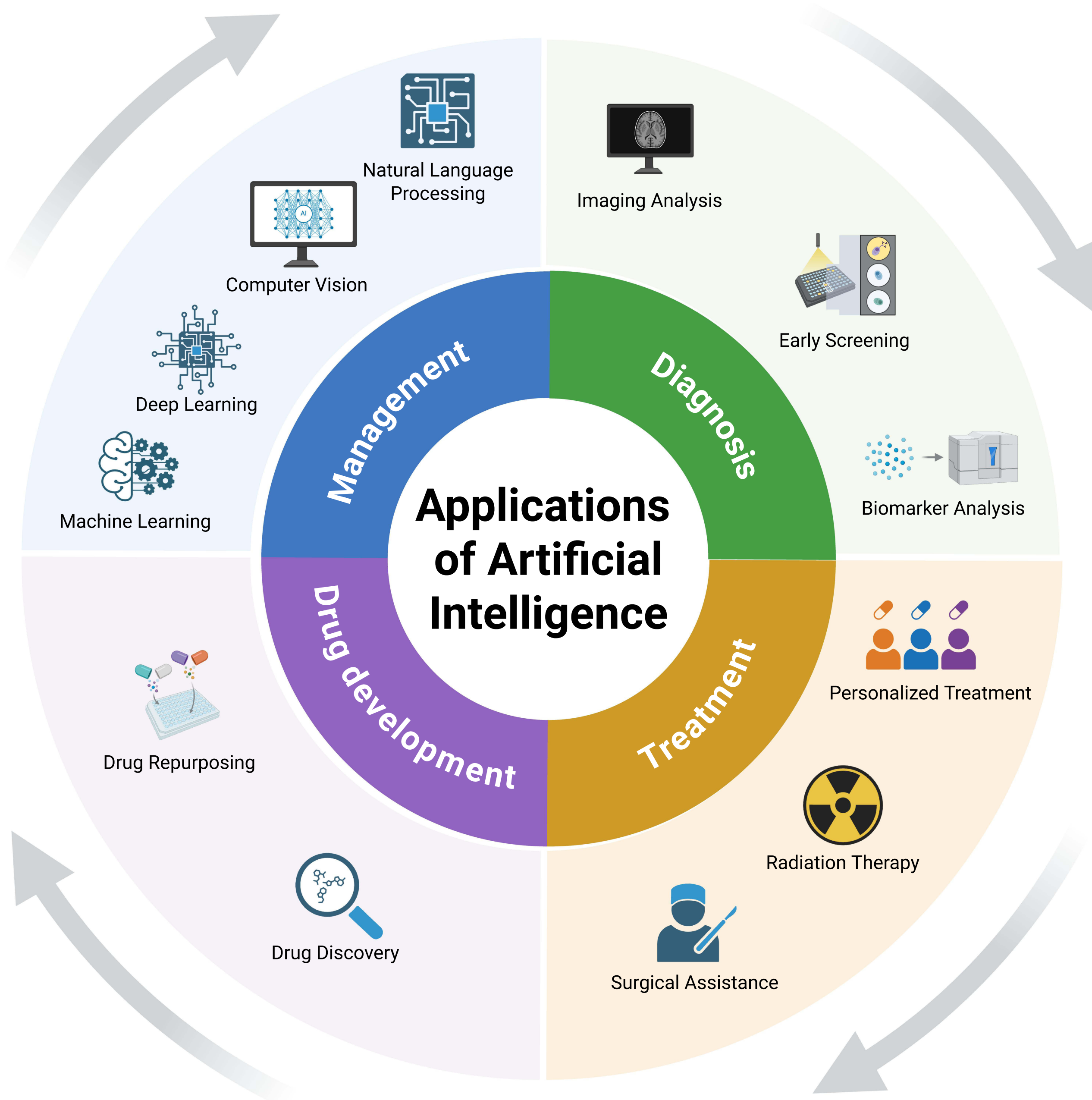

Figure 2 Applications of Artificial Intelligence in Hepatocellular Carcinoma. Created in BioRender. Yuan, X. (2025) https://BioRender.com/n0ddab8.

Clinical Challenges and Future Perspectives

Clinical Challenges

The integration of AI in HCC management faces significant challenges, particularly in data quality and standardization. AI models rely on diverse data sources, such as imaging, genomic, and clinical records, but these often suffer from heterogeneity in formats, protocols, and standards.[78] For example, imaging data from different machines or institutions may vary in resolution, contrast, and acquisition techniques, thereby complicating the creation of unified datasets.[79] Similarly, clinical data from EHRs may be inconsistent due to variations in data entry practices, incomplete records, and missing values. Handling missing data is particularly challenging, as incomplete datasets can introduce biases and inaccuracies into AI models.[80,81] Although advanced imputation techniques are necessary, they add complexity to data preprocessing and may impact model performance. Additionally, data privacy and security are crucial concerns, requiring careful balancing of ethical and legal considerations when anonymizing and protecting patient data for AI training. The performance of AI in HCC diagnosis is evaluated through false-positive and false-negative rates, critical for clinical decisions. Factors like image quality and lesion characteristics influence these rates. Strategies such as multi-modal data integration and human-AI collaboration are essential to minimize errors and enhance model accuracy in future research and clinical applications.

To enhance the robustness of AI models in HCC management, distributed learning techniques like cyclical weight transfer (CWT) and fairness-aware methods are critical. CWT optimizations, such as proportional local training iterations, improve model adaptability to heterogeneous data, while fairness constraints and adversarial debiasing mitigate biases from imbalanced datasets.[82] Additionally, explainable AI ensures transparency, and federated learning addresses data privacy concerns. Collaborative efforts among researchers, clinicians, and regulators are essential to establish standardized protocols and regulatory frameworks, ensuring AI models are reliable, equitable, and applicable across diverse clinical settings.[83,84]

Bias in AI models and regulatory hurdles are critical challenges in HCC management. Bias often stems from imbalanced datasets, such as those predominantly from development regions, which underrepresent ethnic groups, socioeconomic classes, and geographical areas.[85,86] For instance, hepatitis B virus-related HCC is more prevalent in Asian populations, while hepatitis C virus and alcohol-related HCC dominate in Western countries, leading to disparities in diagnostic accuracy and treatment recommendations.[87] Socioeconomic disparities in access to advanced imaging further exacerbate bias, as models trained on data from tertiary centers may underperform in resource-limited settings.[88] Gender and age-related biases have also been identified, affecting screening and treatment decisions.[89] Addressing these issues requires diverse datasets, fairness-aware machine learning, and rigorous validation. Simultaneously, regulatory challenges hinder AI adoption, as tools must undergo rigorous evaluation for safety and efficacy. Regulatory frameworks by agencies like the Food and Drug Administration and European Commission are evolving but remain complex, particularly for adaptive AI models that require ongoing oversight.[90,91] Collaborative efforts among researchers, clinicians, and regulators are essential to establish clear pathways for AI integration, ensuring patient safety, model reliability, and fairness in algorithmic outcomes.

Future Perspectives

Clinicians can implement AI tools in HCC management today by integrating them into existing workflows. For instance, AI-based imaging tools for lesion detection can be embedded into Picture Archiving and Communication Systems (PACS), providing real-time insights to enhance diagnostic accuracy.[92] Additionally, AI-driven risk prediction models, which combine imaging, genomic, and clinical data, are increasingly integrated into EHRs, offering decision support during consultations.[93] To ensure successful implementation, healthcare institutions should provide targeted training for clinicians on interpreting AI outputs and integrating them into daily workflows. Ongoing technical support and interdisciplinary collaboration between AI developers, clinicians, and IT teams are essential to optimize tool use and address operational challenges. By leveraging these existing solutions, clinicians can enhance HCC diagnosis, treatment planning, and patient outcomes today, bridging the gap between AI innovation and clinical practice.

Looking to the future, several promising directions can enhance AI's role in HCC research and management, offering transformative potential for personalized and effective healthcare solutions. First, multimodal data integration, which

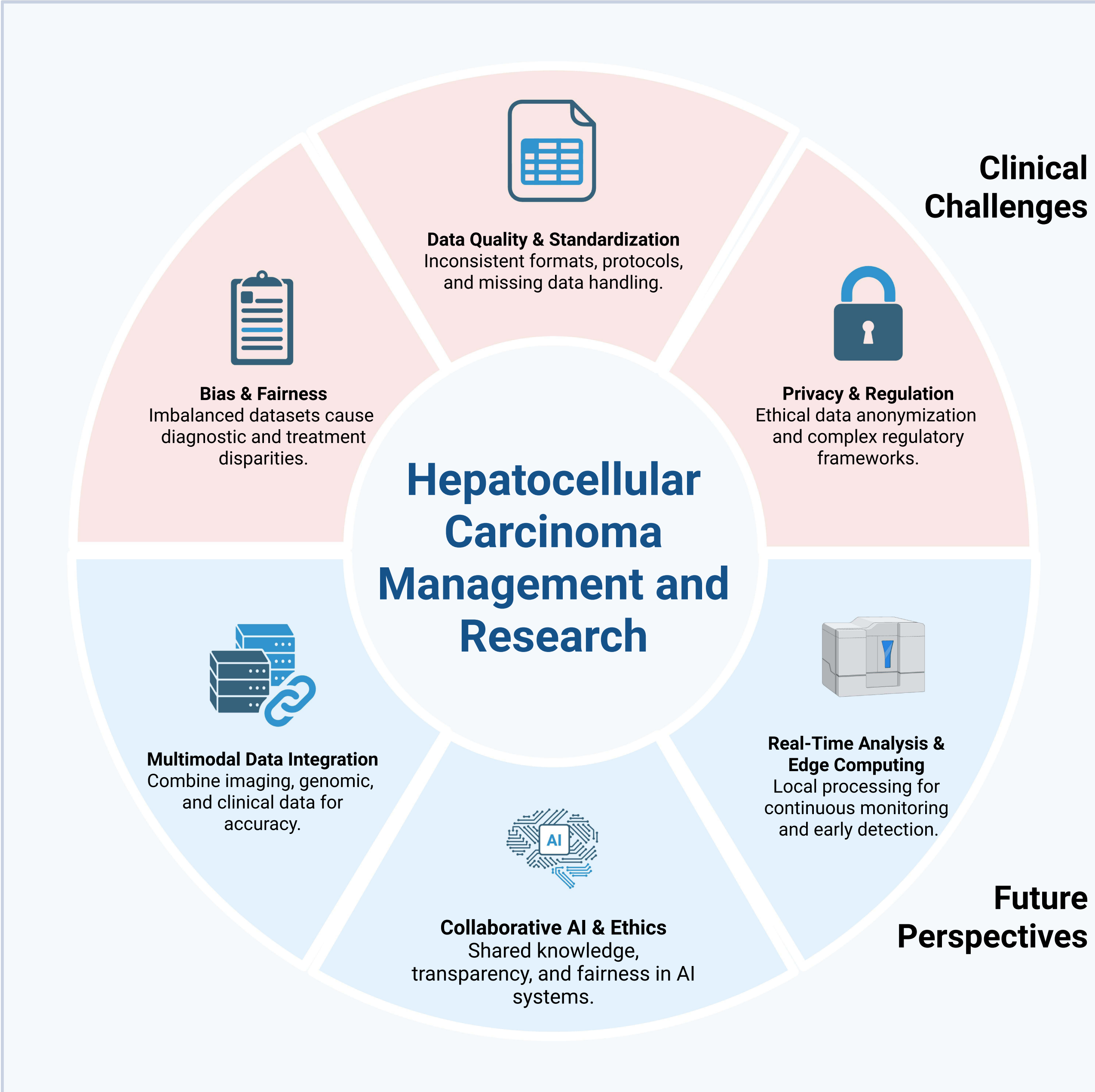

Figure 3 Challenges and Future Perspectives of Artificial Intelligence in Hepatocellular Carcinoma. Created in BioRender. Yuan, X. (2025) https://BioRender.com/sif344o.

combines diverse sources such as imaging, genomic, and clinical records, can significantly improve model accuracy by leveraging complementary insights.[94] This approach enables a holistic understanding of HCC, particularly when genomic data is paired with imaging results to enhance tumor profiling and tailor personalized treatment strategies.[16] Additionally, AI and edge computing, which processes data locally on devices or within healthcare systems, facilitates real-time analysis and decision-making, minimizing delays and data transfer.[95] This is especially beneficial for chronic conditions like HCC, where wearable devices equipped with AI algorithms can continuously monitor patient data, detect early signs of disease progression, and provide immediate feedback, while also addressing critical privacy concerns.[96] Furthermore, advanced AI algorithms, such as deep learning, reinforcement learning, and transfer learning, which are designed to handle the complexities and variabilities of HCC data, can improve model robustness and generalizability, leading to more accurate predictions and tailored treatments.[97,98]

Moreover, collaborative AI systems, which integrate inputs from multiple healthcare providers and institutions, can enhance collective knowledge and decision-making by fostering the sharing of best practices and innovative approaches.[99] This collaborative framework not only improves patient outcomes but also accelerates the adoption of AI-driven solutions across diverse healthcare settings. Finally, establishing robust ethical and regulatory frameworks, which ensure transparency, accountability, and fairness in AI algorithms, is essential to gaining trust and promoting responsible use in healthcare.[91] These frameworks must address concerns such as algorithmic bias, data privacy, and the ethical implications of AI-driven decisions. By exploring these interconnected directions, the research community can significantly advance AI's role in HCC management, paving the way for more effective, personalized, and equitable healthcare solutions that address the unique challenges of this complex disease (Figure 3).

Conclusion

In summary, while there are notable challenges in integrating AI into HCC research and management—particularly related to data quality, standardization, and privacy—there are also exciting opportunities for advancement. Future developments in multimodal data integration and edge computing hold the potential to greatly enhance the accuracy, efficiency, and personalization of HCC diagnosis and treatment, ultimately leading to improved patient care and outcomes.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interest in this work.

References

1. Llovet JM, Kelley RK, Villanueva A, et al. Hepatocellular carcinoma. *Nat Rev Dis Primers*. 2021;7(1):6. doi:10.1038/s41572-020-00240-3
2. Danpanichkul P, Suparan K, Tothanarungroj P, et al. Epidemiology of gastrointestinal cancers: a systematic analysis from the Global Burden of Disease Study 2021. *Gut*. 2024;74(1):26–34. doi:10.1136/gutjnl-2024-333227
3. Hwang SY, Danpanichkul P, Agopian V, et al. Hepatocellular carcinoma: updates on epidemiology, surveillance, diagnosis and treatment. *Clin Mol Hepatol*. 2025;31(Suppl):S228–S254. doi:10.3350/cmh.2024.0824
4. Omata M, Cheng AL, Kokudo N, et al. Asia-Pacific clinical practice guidelines on the management of hepatocellular carcinoma: a 2017 update. *Hepatol Int*. 2017;11(4):317–370. doi:10.1007/s12072-017-9799-9
5. Vogel A, Meyer T, Sapisochin G, Salem R, Saborowski A. Hepatocellular carcinoma. *Lancet*. 2022;400(10360):1345–1362. doi:10.1016/S0140-6736(22)01200-4
6. Li L, Wang H. Heterogeneity of liver cancer and personalized therapy. *Cancer Lett*. 2016;379(2):191–197. doi:10.1016/j.canlet.2015.07.018
7. Yang Y, Wang H, Ji C, Niu Y. Artificial intelligence-driven diagnostic systems for early detection of diabetic retinopathy: integrating retinal imaging and clinical data. *SHIFAA*. 2023;2023:83–90. doi:10.70470/SHIFAA/2023/010
8. Poirion OB, Jing Z, Chaudhary K, Huang S, Garmire LX. DeepProg: an ensemble of deep-learning and machine-learning models for prognosis prediction using multi-omics data. *Genome Med*. 2021;13(1):112. doi:10.1186/s13073-021-00930-x
9. Chaudhary K, Poirion OB, Lu L, Garmire LX. Deep learning-based multi-omics integration robustly predicts survival in liver cancer. *Clin Cancer Res*. 2018;24(6):1248–1259. doi:10.1158/1078-0432.CCR-17-0853
10. Yang X, Yang C, Zhang S, et al. Precision treatment in advanced hepatocellular carcinoma. *Cancer Cell*. 2024;42(2):180–197. doi:10.1016/j.ccell.2024.01.007
11. Guo W, Strouse C, Mery D, et al. A risk stratification system in myeloma patients with autologous stem cell transplantation. *Cancers*. 2024;16(6):1116. doi:10.3390/cancers16061116

12. Wang B, Yu H, Gao J, et al. Machine learning deciphers the significance of mitochondrial regulators on the diagnosis and subtype classification in non-alcoholic fatty liver disease. *Heliyon*. 2024;10(9):e29860. doi:10.1016/j.heliyon.2024.e29860
13. Yuan X, Yang L, Gao J, Mao X, Zhang Y, Yuan W. Identification of a novel matrix metalloproteinases-related prognostic signature in hepatocellular carcinoma. *Aging*. 2024;16(10):8667–8686. doi:10.18632/aging.205832
14. Chen D, Liu J, Zang L, et al. Integrated machine learning and bioinformatic analyses constructed a novel stemness-related classifier to predict prognosis and immunotherapy responses for hepatocellular carcinoma patients. *Int J Biol Sci*. 2022;18(1):360–373. doi:10.7150/ijbs.66913
15. Song Q, Li M, Li Q, et al. DeepAlloDriver: a deep learning-based strategy to predict cancer driver mutations. *Nucleic Acids Res*. 2023;51(W1): W129–W133. doi:10.1093/nar/gkad295
16. Nam D, Chapiro J, Paradis V, Seraphin TP, Kather JN. Artificial intelligence in liver diseases: improving diagnostics, prognostics and response prediction. *JHEP Rep*. 2022;4(4):100443. doi:10.1016/j.jhepr.2022.100443
17. Hamet P, Tremblay J. Artificial intelligence in medicine. *Metabolism*. 2017;69S:S36–S40. doi:10.1016/j.metabol.2017.01.011
18. Jiang B, Guo N, Ge Y, Zhang L, Oudkerk M, Xie X. Development and application of artificial intelligence in cardiac imaging. *Br J Radiol*. 2020;93 (1113):20190812. doi:10.1259/bjr.20190812
19. Owens C, Hindocha S, Lee R, Millard T, Sharma B. The lung cancers: staging and response, CT, (18)F-FDG PET/CT, MRI, DWI: review and new perspectives. *Br J Radiol*. 2023;96(1148):20220339. doi:10.1259/bjr.20220339
20. Hashimoto DA, Rosman G, Rus D, Meireles OR. Artificial Intelligence in Surgery: promises and Perils. *Ann Surg*. 2018;268(1):70–76. doi:10.1097/SLA.0000000000002693
21. Jiang Y, Yang M, Wang S, Li X, Sun Y. Emerging role of deep learning-based artificial intelligence in tumor pathology. *Cancer Commun*. 2020;40 (4):154–166. doi:10.1002/cac2.12012
22. Egger J, Schmalstieg D, Chen X, Zoller WG, Hann A. Interactive outlining of pancreatic cancer liver metastases in ultrasound images. *Sci Rep*. 2017;7(1):892. doi:10.1038/s41598-017-00940-z
23. Li C, Zhang Y, Weng Y, Wang B, Li Z. Natural language processing applications for computer-aided diagnosis in oncology. *Diagnostics*. 2023;13 (2):286.
24. Oh JH, Tannenbaum A, Deasy JO. Improved prediction of drug-induced liver injury literature using natural language processing and machine learning methods. *Front Genet*. 2023;14:1161047. doi:10.3389/fgene.2023.1161047
25. Karimi YH, Blayney DW, Kurian AW, et al. Development and use of natural language processing for identification of distant cancer recurrence and sites of distant recurrence using unstructured electronic health record data. *JCO Clin Cancer Inform*. 2021;5:469–478. doi:10.1200/CCI.20.00165
26. Harding-Theobald E, Louissaint J, Maraj B, et al. Systematic review: radiomics for the diagnosis and prognosis of hepatocellular carcinoma. *Aliment Pharmacol Ther*. 2021;54(7):890–901. doi:10.1111/apt.16563
27. Cinar U, Cetin Atalay R, Cetin YY. Human hepatocellular carcinoma classification from H&E stained histopathology images with 3D convolutional neural networks and focal loss function. *J Imaging*. 2023;9(2):25. doi:10.3390/jimaging9020025
28. Harada S, Akita H, Tsubaki M, et al. Dual graph convolutional neural network for predicting chemical networks. *BMC Bioinformatics*. 2020;21 (Suppl 3):94. doi:10.1186/s12859-020-3378-0
29. Said D, Carbonell G, Stocker D, et al. Semiautomated segmentation of hepatocellular carcinoma tumors with MRI using convolutional neural networks. *Eur Radiol*. 2023;33(9):6020–6032. doi:10.1007/s00330-023-09613-0
30. Saraiva MM, Ribeiro T, Ferreira JPS, et al. Artificial intelligence for automatic diagnosis of biliary stricture malignancy status in single-operator cholangioscopy: a pilot study. *Gastrointest Endosc*. 2022;95(2):339–348. doi:10.1016/j.gie.2021.08.027
31. Incir R, Bozkurt F. Improving brain tumor classification with combined convolutional neural networks and transfer learning. *Knowl-Based Syst*. 2024;299:111981. doi:10.1016/j.knosys.2024.111981
32. Jabbour S, Fouhey D, Shepard S, et al. Measuring the impact of AI in the diagnosis of hospitalized patients: a randomized clinical vignette survey study. *JAMA*. 2023;330(23):2275–2284. doi:10.1001/jama.2023.22295
33. Ronneberger O, Fischer P, Brox T. U-Net: convolutional networks for biomedical image segmentation. In: *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2015*. Cham: Springer International Publishing; 2015:234–241.
34. Chen W-F, Ou H-Y, Lin H-Y, et al. Development of novel Residual-Dense-Attention (RDA) U-net network architecture for hepatocellular carcinoma segmentation. *Diagnostics*. 2022;12:1916. doi:10.3390/diagnostics12081916
35. Brunese MC, Rocca A, Santone A, Cesarelli M, Brunese L, Mercaldo F. Explainable and robust deep learning for liver segmentation through U-net network. *Diagnostics*. 2025;15(7):878. doi:10.3390/diagnostics15070878
36. Chen WF, Ou HY, Liu KH, et al. In-series U-net network to 3D tumor image reconstruction for liver hepatocellular carcinoma recognition. *Diagnostics*. 2020;11(1):11. doi:10.3390/diagnostics11010011
37. Sharma N, Gupta S, Elkamchouchi DH, Bharany S. Encoder-decoder variant analysis for semantic segmentation of gastrointestinal tract using UW-Madison dataset. *Bioengineering*. 2025;12(3):309. doi:10.3390/bioengineering12030309
38. Huang Z, Pan Y, Huang W, et al. Predicting microvascular invasion and early recurrence in hepatocellular carcinoma using DeepLab V3+ segmentation of multiregional MR habitat images. *Acad Radiol*. 2025;32(6):3342–3357. doi:10.1016/j.acra.2025.02.006
39. Yang Q, Wei J, Hao X, et al. Improving B-mode ultrasound diagnostic performance for focal liver lesions using deep learning: a multicentre study. *EBioMedicine*. 2020;56:102777. doi:10.1016/j.ebiom.2020.102777
40. Guo LH, Wang D, Qian YY, et al. A two-stage multi-view learning framework based computer-aided diagnosis of liver tumors with contrast enhanced ultrasound images. *Clin Hemorheol Microcirc*. 2018;69(3):343–354. doi:10.3233/CH-170275
41. Nakai H, Fujimoto K, Yamashita R, et al. Convolutional neural network for classifying primary liver cancer based on triple-phase CT and tumor marker information: a pilot study. *Jpn J Radiol*. 2021;39(7):690–702. doi:10.1007/s11604-021-01106-8
42. Jansen MJA, Kuijf HJ, Veldhuis WB, Wessels FJ, Viergever MA, Pluim JPW. Automatic classification of focal liver lesions based on MRI and risk factors. *PLoS One*. 2019;14(5):e0217053. doi:10.1371/journal.pone.0217053
43. Yang J, Xu R, Wang C, Qiu J, Ren B, You L. Early screening and diagnosis strategies of pancreatic cancer: a comprehensive review. *Cancer Commun*. 2021;41(12):1257–1274. doi:10.1002/cac2.12204
44. European Association for the Study of the L. EASL Clinical Practice Guidelines on the management of hepatocellular carcinoma. *J Hepatol*. 2025;82(2):315–374. doi:10.1016/j.jhep.2024.08.028

45. Lang K, Josefsson V, Larsson AM, et al. Artificial intelligence-supported screen reading versus standard double reading in the Mammography Screening with Artificial Intelligence trial (MASAI): a clinical safety analysis of a randomised, controlled, non-inferiority, single-blinded, screening accuracy study. *Lancet Oncol*. 2023;24(8):936–944. doi:10.1016/S1470-2045(23)00298-X
46. Oliveira W, Albuquerque Santos M, Burgardt CAP, Anjos Pontual ML, Zanchettin C. Estimation of human age using machine learning on panoramic radiographs for Brazilian patients. *Sci Rep*. 2024;14(1):19689. doi:10.1038/s41598-024-70621-1
47. Zhang WB, Hou SZ, Chen YL, et al. Deep learning for approaching hepatocellular carcinoma ultrasound screening dilemma: identification of alpha-fetoprotein-negative hepatocellular carcinoma from focal liver lesion found in high-risk patients. *Front Oncol*. 2022;12:862297. doi:10.3389/fonc.2022.862297
48. Kim HY, Lampertico P, Nam JY, et al. An artificial intelligence model to predict hepatocellular carcinoma risk in Korean and Caucasian patients with chronic hepatitis B. *J Hepatol*. 2022;76(2):311–318. doi:10.1016/j.jhep.2021.09.025
49. Guo W, Zhan Y, Mery D, et al. Prognostic value of ferritin in ASCT MM patients: integration with GEP models and ISS series systems. *Blood Cancer J*. 2024;14(1):30.
50. Ma M, Gu W, Liang Y, et al. A novel model for predicting postoperative liver metastasis in R0 resected pancreatic neuroendocrine tumors: integrating computational pathology and deep learning-radiomics. *J Transl Med*. 2024;22(1):768. doi:10.1186/s12967-024-05449-4
51. Huang H, Wu F, Yu Y, et al. Multi-transcriptomics analysis of microvascular invasion-related malignant cells and development of a machine learning-based prognostic model in hepatocellular carcinoma. *Front Immunol*. 2024;15:1436131. doi:10.3389/fimmu.2024.1436131
52. Méhes G. Liquid biopsy for predictive mutational profiling of solid cancer: the pathologist's perspective. *J Biotechnol*. 2019;297:66–70. doi:10.1016/j.jbiotec.2019.04.002
53. Gerratana L, Davis AA, Foffano L, et al. Integrating machine learning-predicted circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA) in metastatic breast cancer: a proof of principle study on endocrine resistance profiling. *Cancer Lett*. 2025;609:217325. doi:10.1016/j.canlet.2024.217325
54. Bartolomucci A, Nobrega M, Ferrier T, et al. Circulating tumor DNA to monitor treatment response in solid tumors and advance precision oncology. *NPJ Precis Oncol*. 2025;9(1):84. doi:10.1038/s41698-025-00876-y
55. von Felden J, Craig AJ, Garcia-Lezana T, et al. Mutations in circulating tumor DNA predict primary resistance to systemic therapies in advanced hepatocellular carcinoma. *Oncogene*. 2021;40(1):140–151. doi:10.1038/s41388-020-01519-1
56. Maravelia P, Silva DN, Rovesti G, et al. Liquid biopsy in hepatocellular carcinoma: opportunities and challenges for immunotherapy. *Cancers*. 2021;13(17):4334. doi:10.3390/cancers13174334
57. Gerratana L, Davis AA, Polano M, et al. Understanding the organ tropism of metastatic breast cancer through the combination of liquid biopsy tools. *Eur J Cancer*. 2021;143:147–157. doi:10.1016/j.ejca.2020.11.005
58. Chen S, Zhang Z, Wang Y, et al. Using quasispecies patterns of hepatitis B virus to predict hepatocellular carcinoma with deep sequencing and machine learning. *J Infect Dis*. 2021;223(11):1887–1896. doi:10.1093/infdis/jiaa647
59. Jayakrishnan TT, Sangwan N, Barot SV, et al. Multi-omics machine learning to study host-microbiome interactions in early-onset colorectal cancer. *NPJ Precis Oncol*. 2024;8(1):146. doi:10.1038/s41698-024-00647-1
60. Magazzu G, Zampieri G, Angione C. Clinical stratification improves the diagnostic accuracy of small omics datasets within machine learning and genome-scale metabolic modelling methods. *Comput Biol Med*. 2022;151(Pt A):106244. doi:10.1016/j.compbiomed.2022.106244
61. Kamireddy RR, Kandala R, Dhuli R, et al. Brain MRI detection and classification: harnessing convolutional neural networks and multi-level thresholding. *PLoS One*. 2024;19(8):e0306492. doi:10.1371/journal.pone.0306492
62. Ding GY, Tan WM, Lin YP, et al. Mining the interpretable prognostic features from pathological image of intrahepatic cholangiocarcinoma using multi-modal deep learning. *BMC Med*. 2024;22(1):282. doi:10.1186/s12916-024-03482-0
63. Lin H, Zhao M, Zhu L, et al. Gaussian filter facilitated deep learning-based architecture for accurate and efficient liver tumor segmentation for radiation therapy. *Front Oncol*. 2024;14:1423774. doi:10.3389/fonc.2024.1423774
64. Fallahpoor M, Nguyen D, Montahaei E, et al. Segmentation of liver and liver lesions using deep learning. *Phys Eng Sci Med*. 2024;47(2):611–619. doi:10.1007/s13246-024-01390-4
65. Gong XQ, Tao YY, Wu YK, et al. Progress of MRI radiomics in hepatocellular carcinoma. *Front Oncol*. 2021;11:698373. doi:10.3389/fonc.2021.698373
66. Wei H, Zheng T, Zhang X, et al. MRI radiomics based on deep learning automated segmentation to predict early recurrence of hepatocellular carcinoma. *Insights Imaging*. 2024;15(1):120. doi:10.1186/s13244-024-01679-8
67. Bousabarah K, Letzen B, Tefera J, et al. Automated detection and delineation of hepatocellular carcinoma on multiphasic contrast-enhanced MRI using deep learning. *Abdom Radiol*. 2021;46(1):216–225. doi:10.1007/s00261-020-02604-5
68. Alip SL, Kim J, Rha KH, Han WK. Future platforms of robotic surgery. *Urol Clin North Am*. 2022;49(1):23–38. doi:10.1016/j.ucl.2021.07.008
69. Abraham J, Meng A, Montes de Oca A, et al. An ethnographic study on the impact of a novel telemedicine-based support system in the operating room. *J Am Med Inform Assoc*. 2022;29(11):1919–1930. doi:10.1093/jamia/ocac138
70. Sarkar C, Das B, Rawat VS, et al. Artificial intelligence and machine learning technology driven modern drug discovery and development. *Int J Mol Sci*. 2023;24(3):2026. doi:10.3390/ijms24032026
71. Gryniukova A, Kaiser F, Myziuk I, et al. AI-powered virtual screening of large compound libraries leads to the discovery of novel inhibitors of Sirtuin-1. *J Med Chem*. 2023;66(15):10241–10251. doi:10.1021/acs.jmedchem.3c00128
72. Kant S, Deepika, Roy S. Artificial intelligence in drug discovery and development: transforming challenges into opportunities. *Discov Pharm Sci*. 2025;1(1):7. doi:10.1007/s44395-025-00007-3
73. Sadaqat M, Qasim M, Tahir Ul Qamar M, et al. Advanced network pharmacology study reveals multi-pathway and multi-gene regulatory molecular mechanism of Bacopa monnieri in liver cancer based on data mining, molecular modeling, and microarray data analysis. *Comput Biol Med*. 2023;161:107059. doi:10.1016/j.compbiomed.2023.107059
74. Tanoli Z, Vaha-Koskela M, Aittokallio T. Artificial intelligence, machine learning, and drug repurposing in cancer. *Expert Opin Drug Discov*. 2021;16(9):977–989. doi:10.1080/17460441.2021.1883585
75. Xu P, Wu Q, Lu D, et al. A systematic study of critical miRNAs on cells proliferation and apoptosis by the shortest path. *BMC Bioinformatics*. 2020;21(1):396. doi:10.1186/s12859-020-03732-x

76. Issa NT, Stathias V, Schurer S, Dakshanamurthy S. Machine and deep learning approaches for cancer drug repurposing. *Semin Cancer Biol*. 2021;68:132–142. doi:10.1016/j.semcancer.2019.12.011
77. Baser T, Rifaioglu AS, Atalay MV, Atalay RC. Drug repurposing approach to identify candidate drug molecules for hepatocellular carcinoma. *Int J Mol Sci*. 2024;25(17):9392. doi:10.3390/ijms25179392
78. Willemink MJ, Koszek WA, Hardell C, et al. Preparing medical imaging data for machine learning. *Radiology*. 2020;295(1):4–15. doi:10.1148/radiol.2020192224
79. Geras KJ, Mann RM, Moy L. Artificial intelligence for mammography and digital breast tomosynthesis: current concepts and future perspectives. *Radiology*. 2019;293(2):246–259. doi:10.1148/radiol.2019182627
80. Chen S, Xu C. Handling high-dimensional data with missing values by modern machine learning techniques. *J Appl Stat*. 2023;50(3):786–804. doi:10.1080/02664763.2022.2068514
81. Emmanuel T, Maupong T, Mpoeleng D, Semong T, Mphago B, Tabona O. A survey on missing data in machine learning. *J Big Data*. 2021;8(1):140. doi:10.1186/s40537-021-00516-9
82. Balachandar N, Chang K, Kalpathy-Cramer J, Rubin DL. Accounting for data variability in multi-institutional distributed deep learning for medical imaging. *J Am Med Inform Assoc*. 2020;27(5):700–708. doi:10.1093/jamia/ocaa017
83. Saranya A, Subhashini R. A systematic review of Explainable Artificial Intelligence models and applications: recent developments and future trends. *Decis Anal J*. 2023;7:100230. doi:10.1016/j.dajour.2023.100230
84. Keir G, Hu W, Filippi CG, Ellenbogen L, Woldenberg R. Using artificial intelligence in medical school admissions screening to decrease inter- and intra-observer variability. *JAMIA Open*. 2023;6(1):ooad011. doi:10.1093/jamiaopen/ooad011
85. Hasanzadeh F, Josephson CB, Waters G, Adedinsewo D, Azizi Z, White JA. Bias recognition and mitigation strategies in artificial intelligence healthcare applications. *NPJ Digit Med*. 2025;8(1):154. doi:10.1038/s41746-025-01503-7
86. Ciro C, Alessio Q, Marcello M, et al. The application of artificial intelligence-based tools in the management of hepatocellular carcinoma: current status and future perspectives. *Hepatoma Res*. 2025;11:4.
87. Jafri W, Kamran M. Hepatocellular Carcinoma in Asia: a Challenging Situation. *Euroasian J Hepatogastroenterol*. 2019;9(1):27–33. doi:10.5005/jp-journals-10018-1292
88. Karia A, Zamani R, Akrami M. Socio-economic disparities in access to diagnostic neuroimaging services in the United Kingdom: a systematic review. *Int J Environ Res Public Health*. 2021;18(20):10633. doi:10.3390/ijerph182010633
89. Chu CH, Donato-Woodger S, Khan SS, et al. Age-related bias and artificial intelligence: a scoping review. *Humanit Soc Sci Commun*. 2023;10(1):510. doi:10.1057/s41599-023-01999-y
90. Zaidan E, Ibrahim IA. AI governance in a complex and rapidly changing regulatory landscape: a global perspective. *Humanit Soc Sci Commun*. 2024;11(1):1121. doi:10.1057/s41599-024-03560-x
91. Mennella C, Maniscalco U, De Pietro G, Esposito M. Ethical and regulatory challenges of AI technologies in healthcare: a narrative review. *Heliyon*. 2024;10(4):e26297. doi:10.1016/j.heliyon.2024.e26297
92. Perez-Sanpablo AI, Quinzanos-Fresnedo J, Gutierrez-Martinez J, Lozano-Rodriguez IG, Roldan-Valadez E. Transforming medical imaging: the role of artificial intelligence integration in PACS for enhanced diagnostic accuracy and workflow efficiency. *Curr Med Imaging*. 2025;21. doi:10.2174/0115734056370620250403030638
93. Niu S, Yin Q, Ma J, et al. Enhancing healthcare decision support through explainable AI models for risk prediction. *Decis Support Syst*. 2024;181:114228. doi:10.1016/j.dss.2024.114228
94. Wang H, Zhou Y, Xu H, et al. Therapeutic efficacy of FASN inhibition in preclinical models of HCC. *Hepatology*. 2022;76(4):951–966. doi:10.1002/hep.32359
95. Lee S, Chu Y, Ryu J, Park YJ, Yang S, Koh SB. Artificial intelligence for detection of cardiovascular-related diseases from wearable devices: a systematic review and meta-analysis. *Yonsei Med J*. 2022;63(Suppl):S93–S107. doi:10.3349/ymj.2022.63.S93
96. Williams DM, Bland P, Liu L, Farjo L, Francis IR, Meyer CR. Liver-tumor boundary detection: human observer vs computer edge detection. *Invest Radiol*. 1989;24(10):768–775. doi:10.1097/00004424-198910000-00008
97. Matsuo Y, LeCun Y, Sahani M, et al. Deep learning, reinforcement learning, and world models. *Neural Netw*. 2022;152:267–275. doi:10.1016/j.neunet.2022.03.037
98. Chen J, Wang X, Ma A, et al. Deep transfer learning of cancer drug responses by integrating bulk and single-cell RNA-seq data. *Nat Commun*. 2022;13(1):6494. doi:10.1038/s41467-022-34277-7
99. Bhatt AB, Bae J. Collaborative Intelligence to catalyze the digital transformation of healthcare. *NPJ Digit Med*. 2023;6(1):177. doi:10.1038/s41746-023-00920-w