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Application of artificial intelligence in hepatology: Minireview

Masuzaki R *et al*. AI in hepatology

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Abstract

With the rapid advancements in computer science, artificial intelligence (AI) has become an intrinsic part of our daily life and clinical practices. The concepts of AI, such as machine learning, deep learning, and big data, are extensively used in clinical and basic research. In this review, we searched for the articles in PubMed and summarized recent developments of AI concerning hepatology while focusing on the diagnosis and risk assessment of liver diseases. Ultrasound is widely conducted for the routine surveillance of hepatocellular carcinoma along with tumor markers. Computer-aided diagnosis is useful in the detection of tumors and characterization of space-occupying lesions. The prognosis of hepatocellular carcinoma can be estimated *via* AI using large-scale and high-quality training datasets. The prevalence of nonalcoholic fatty liver disease is increasing worldwide and pivotal concern in the field is who will progress and develop hepatocellular carcinoma. Most AI studies require a large dataset, including laboratory or radiological findings and outcome data. AI will be useful in reducing medical errors, supporting clinical decisions, and predicting clinical outcomes. Thus, cooperation between AI and humans is expected to improve healthcare.

**Key words:** Artificial intelligence; Deep learning; Machine learning; Hepatocellular carcinoma; Prognosis; Computer-aided diagnosis

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**Core tip:** Artificial intelligence (AI) plays a significant role in our daily life and the research field. In this review, we summarized the recent findings of AI concerning hepatology. AI will be useful in the detection and diagnosis of liver tumors and the discrimination of high-risk patients for hepatic decompensation and hepatocellular carcinoma development. Furthermore, AI can be utilized in basic research, such as in the interpretation of genomics, transcriptomics, and proteomics. We hope that this review will help in future management.

**INTRODUCTION**

Recent developments in artificial intelligence (AI)-related techniques have shown a remarkable improvement in the field of healthcare[1]. Among others, AI comprises search algorithms, expert systems, machine learning, and deep learning[2]. Machine learning requires feature characteristics input by a human; however, technical advances achieved by innovation in computer science leads to a more sophisticated deep learning method[3]. Deep learning provides new insight into existing diseases but not into why the chosen parameters cannot be interpreted or understood. The issue of ensuring the balance between white box and black box AI is widely debated among the research community[4]. Nevertheless, exploration and translation of black box AI could lead to a better understanding of the disease mechanism. Moreover, it could pave the way for novel discoveries in their treatment.

Such advances in hepatology can be useful for detecting tumors and screening high-risk populations for hepatocellular carcinoma (HCC) development. A curable treatment for HCC can be adopted when the tumors are found in early stages[5]. Routine ultrasonography is widely accepted as a screening method for HCC[6]. However, an ultrasound (US) is highly dependent on the sonographer’s skill. Thus, AI detection systems can be used for efficient detection.

Infections from the hepatitis B virus and hepatitis C virus are well-recognized risk factors for hepatic decompensation and HCC development[7-9]. In addition, nonalcoholic fatty liver disease (NAFLD) has been recently identified as a risk factor. The prevalence of NAFLD is increasing and has been estimated at 24% worldwide. Its incidence is observed to be highest in South America and the Middle East followed by Asia, United States, and Europe[10,11]. Chronic liver diseases cause liver fibrosis and progresses through mild fibrosis to cirrhosis. Liver fibrosis is also one of the well-known risk factors for hepatic decompensation and HCC development[12,13]. Any chronic liver disease could be worse without proper treatments. To determine who is at high-risk for HCC development and disease progression in such a population is a crucial clinical question. The deep learning methods are expected to be useful in identifying high-risk patients. In this review, we summarize the recent advances of AI in hepatology and discuss their clinical implications. In this review, we searched for the literature in PubMed and summarized recent developments of AI concerning hepatology.

**CURRENT AI METHODOLOGY**

AI systems can be roughly divided into four categories: search algorithm, expert system, machine learning, and deep learning. Machine learning generates a mathematical algorithm from the training dataset and utilizes it to predict outcomes or make decisions[14]. Moreover, machine learning is divided into supervised and unsupervised learning. In a supervised learning model, the algorithm learns from a labeled dataset (individual parameters and outcomes). Conversely, deep learning is based on the neural network structure inspired by the human brain. There are different types of neural networks in deep learning, and representative types are artificial neural network, convolutional neural network (CNN), and recurrent neural network.

Artificial neural network is a computational analysis tool inspired by the biological nervous system[15]. It consists of three layers: input, hidden, and output. Each layer comprises several “neurons,” and the hidden layer processes the input and the output layer produces the result. Through an appropriate training process, the weights among the neural connections are adjusted to optimize the result.

CNN is an image-based machine learning method that is directly inspired by the visual cortex of the brain[16]. A basic CNN consists of convolution layers, nonlinear layers, and pooling layers. CNNs are currently one of the most successful deep learning models because of their unique ability to process spatial information[17].

Recurrent neural network is a type of neural network with feedback connections[18,19]. It exhibits great performance in labeling and predicting sequential data. A prominent example of sequential data is natural language. Recurrent neural network maintains the history of input data within the network, and the output is produced from the past input. In the following sections, we discuss related studies from the literature. The content is summarized in Table 1.

**DIAGNOSIS OF LIVER DISEASES AND TUMOR DETECTION**

Currently, imaging examinations are displayed and stored as digital images. Furthermore, computer-aided diagnosis/detection (CAD) has already been applied for chest nodule detection[20] and cerebral aneurysm detection[21]. Recently, Mei *et al*[22] reported an AI system that used chest computed tomography along with clinical symptoms, exposure history, and laboratory testing to enable rapid diagnosis of coronavirus disease 19. The results of this AI system depicted an area under the receiver operating characteristics (AUROC) of 0.92[22].

However, the CAD system is costly, and regular maintenance is required for its use. Nevertheless, it can help healthcare workers in diagnosing and detecting tumors. The first CAD system was approved by the Food and Drug Administration for mammography in 1998[23]. Nowadays, the CAD system uses deep learning for the analysis and classification of medical images[16]. Big data availability and increased chip processing capability enable foreseeable advances in deep learning-based systems. The following section summarizes the recent AI research on focal and diffuse liver diseases.

***Detection of focal liver diseases***

Hassan *et al*[24] used the stacked sparse auto-encoder system to detect HCC, hemangioma, and liver cysts from US images. They used a four-step framework as follows. First, the processing images were enhanced while the background noises were reduced. Subsequently, liver segmentation was conducted using the level set method and fuzzy c-means clustering algorithm. Next, stacked sparse auto-encoder was employed to identify latent features from unlabeled input data in an unsupervised manner. Finally, a softmax layer was used to diagnose different focal liver diseases. The sensitivity and specificity of the proposed deep learning system were 98.0% and 95.7%, respectively[24]. Sato *et al*[25] developed a machine-learning model for predicting HCC in 539 HCC-positive and 1043 non-HCC patients at a tertiary referral center, and the AUROC of the model for HCC was 0.940 compared to 0.766, 0.644, and 0.683 for alpha-fetoprotein, des-gamma-carboxyprothrombin, and Lens culinaris agglutinin-reactive fraction of alpha-fetoprotein, respectively.

***Staging of diffuse liver diseases***

Biswas *et al*[26] reported that deep learning techniques were superior to conventional machine learning techniques for detecting fatty liver disease through US examinations. The study was based on 63 patients (27 healthy and 36 abnormal), and the AUROCs of the support vector machine, extreme learning machine, and deep learning were 0.79, 0.92, and 1.0, respectively. Byra *et al*[27] employed an Inception-ResNet-v2 CNN pre-trained on ImageNet for NAFLD diagnoses using US examinations in 55 obese patients admitted for bariatric surgery. They used a wedge biopsy liver sample as the reference standard. The AUROC of the approach was 0.9777, compared to 0.9590 for the conventional hepatorenal index. The detection of steatosis is beneficial in the field of hepatology. However, more data are needed for better AI applications, and resources, such as liver biopsy samples, are limited because of their invasiveness.

Recently, US elastography has been widely used in clinical practice for noninvasive diagnosis of liver fibrosis stages and as a surrogate marker for clinical outcomes such as HCC development, liver failure, and rupture of esophageal varices[28-31]. Wang *et al*[32] reported deep learning radiomics for shear wave elastography, and the AUROC of the model for diagnosis of cirrhosis was 0.97 (95% confidence interval: 0.94-0.99), which outperformed the biomarkers. Generally, the stiffness value of US elastography is considered to be affected by inflammation, obstructive jaundice, liver congestion, fasting, and steatosis[33,34]. Deep learning methods integrating stiffness values and elastograms with other clinicopathological factors will be powerful tools for the diagnosis of liver fibrosis.

**RISK ASSESSMENT OF LIVER DISEASE**

The risk assessment of HCC is crucial for the apt management of patients with chronic liver diseases. Saillard *et al*[35] implemented two deep learning algorithms based on whole digitized slides for predicting the survival of HCC patients after hepatic resection. They first created a composite score using clinical, biological, and pathological factors for survival prediction. However, both deep learning models reported higher performance than the composite score. An expert pathologist examined the high-risk and low-risk slides obtained from the models. Subsequently, the pathologist observed that the high-risk group had cellular atypia, vascular spaces, and macrotrabecular architectural pattern. In contrast, the low-risk group had tumoral fibrotic stroma, immune cells, and fibrosis in both tumor and nontumor areas[35]. These findings will lead to further research focusing on the inflammatory reaction against HCC.

The deep learning model proposed by Chaudhary *et al*[36] integrated RNA sequencing (15629 genes), miRNA sequencing (365 miRNA), and methylation data (19883 genes) from The Cancer Genome Atlas. The model detected a critical subgroup that was associated with frequent *TP53* inactivation mutations, higher levels of stemness markers (*KRT19* and *EPCAM*), tumor marker (*BIRC5*) expression, and activated Wnt and Akt signaling pathways[36]. Deep learning models regarding the prognosis of chronic liver disease patients have not yet been fully evaluated. Thus, machine models have been used to determine the prognostic model in several studies[37,38]. A deep learning model requires a considerable amount of data than a traditional machine learning algorithm. Therefore, machine learning sometimes fits in clinical settings with limited datasets. Singal *et al*[37] used a random forest model to predict HCC development in Child A or B cirrhotic patients. The model was validated through the Hepatitis C Antiviral Long-term Treatment Against Cirrhosis cohort and depicted better performance than the traditional regression analysis. Konerman *et al*[38] used the Hepatitis C Antiviral Long-term Treatment against Cirrhosis (HALT-C) Trial cohort to construct a random forest model to predict outcomes of patients with chronic hepatitis C and validated it with 1007 patients during a median of 4.9 years of the observation period. The AUROC for 1 year and 3 years risk of clinical outcomes was 0.78 (95% confidence interval: 0.73-0.83) and 0.76 (95% confidence interval: 0.69-0.81).

**LIMITATIONS OF AI TECHNOLOGY**

Although the algorithms mentioned above are promising, AI has several limitations[39]. First, it may not be possible to understand how and why the model is created. Second, AI does not conform to personal preferences and legal responsibility. If the AI makes a wrong decision, who will be held accountable for this result? Moreover, a biased AI could affect the outcome of several patients. Therefore, careful attention should be paid to the interpretation of AI’s decision. Third, to avoid the overfitting problem, multicenter studies with high-quality datasets to validate the models are required. Fourth, the protection of privacy and security of data is crucial. The personal medical history should be protected and hacking or manipulating the model should be strictly avoided.

**CONCLUSION**

Digitalization of image examinations and big data availability has resulted in advancements to the AI system represented by deep learning research, especially in the detection of liver diseases. There exists a robust gold standard, *i.e.* histological diagnosis obtained by either biopsy or resection for the detection of liver tumors. However, for the surveillance of NAFLD patients, the gold standard is not just the degree of fat accumulation but also the clinical outcomes of who will develop HCC and who will progress to liver failure. The quality of deep learning models highly depends on the training dataset. A large volume of high-quality data is required to build an accurate and useful AI system for identifying liver diseases.

The application of AI in medical imaging has a good prospect and value. It has been reported that successful applications of AI technologies in endoscopic images for esophageal cancer[40], gastric cancer[41-43], small intestinal cancer[40], colorectal cancer[44,45], analysis of computed tomography for pancreatic cancer[46,47], and others[48-50]. Hepatologists should learn from these other areas.

AI will also be an essential element in the management of liver diseases to reduce medical errors, select the best treatment, and predict outcomes. Nevertheless, even with further advances in computer science, decisions on real clinical practices are affected by the patient’s will, treatment availability, and financial issues. Moreover, social rapport plays a vital role in building a patient’s trust and satisfaction[51]. Thus, cooperation between humans and AI is expected to improve healthcare in the future.

**REFERENCES**

1 **Mahmud M**, Kaiser MS, Hussain A, Vassanelli S. Applications of Deep Learning and Reinforcement Learning to Biological Data. *IEEE Trans Neural Netw Learn Syst* 2018; **29**: 2063-2079 [PMID: 29771663 DOI: 10.1109/TNNLS.2018.2790388]

2 **LeCun Y**, Bengio Y, Hinton G. Deep learning. *Nature* 2015; **521**: 436-444 [PMID: 26017442 DOI: 10.1038/nature14539]

3 **Le Berre C**, Sandborn WJ, Aridhi S, Devignes MD, Fournier L, Smaïl-Tabbone M, Danese S, Peyrin-Biroulet L. Application of Artificial Intelligence to Gastroenterology and Hepatology. *Gastroenterology* 2020; **158**: 76-94.e2 [PMID: 31593701 DOI: 10.1053/j.gastro.2019.08.058]

4 **Camacho DM**, Collins KM, Powers RK, Costello JC, Collins JJ. Next-Generation Machine Learning for Biological Networks. *Cell* 2018; **173**: 1581-1592 [PMID: 29887378 DOI: 10.1016/j.cell.2018.05.015]

5 **Masuzaki R**, Yoshida H, Tateishi R, Shiina S, Omata M. Hepatocellular carcinoma in viral hepatitis: improving standard therapy. *Best Pract Res Clin Gastroenterol* 2008; **22**: 1137-1151 [PMID: 19187872 DOI: 10.1016/j.bpg.2008.11.005]

6 **Sato T**, Tateishi R, Yoshida H, Ohki T, Masuzaki R, Imamura J, Goto T, Kanai F, Obi S, Kato N, Shiina S, Kawabe T, Omata M. Ultrasound surveillance for early detection of hepatocellular carcinoma among patients with chronic hepatitis C. *Hepatol Int* 2009; **3**: 544-550 [PMID: 19669240 DOI: 10.1007/s12072-009-9145-y]

7 **Omata M**, Cheng AL, Kokudo N, Kudo M, Lee JM, Jia J, Tateishi R, Han KH, Chawla YK, Shiina S, Jafri W, Payawal DA, Ohki T, Ogasawara S, Chen PJ, Lesmana CRA, Lesmana LA, Gani RA, Obi S, Dokmeci AK, Sarin SK. Asia-Pacific clinical practice guidelines on the management of hepatocellular carcinoma: a 2017 update. *Hepatol Int* 2017; **11**: 317-370 [PMID: 28620797 DOI: 10.1007/s12072-017-9799-9]

8 **European Association for the Study of the Liver**. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. *J Hepatol* 2018; **69**: 182-236 [PMID: 29628281 DOI: 10.1016/j.jhep.2018.03.019]

9 **Heimbach JK**, Kulik LM, Finn RS, Sirlin CB, Abecassis MM, Roberts LR, Zhu AX, Murad MH, Marrero JA. AASLD guidelines for the treatment of hepatocellular carcinoma. *Hepatology* 2018; **67**: 358-380 [PMID: 28130846 DOI: 10.1002/hep.29086]

10 **Younossi Z**, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, George J, Bugianesi E. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. *Nat Rev Gastroenterol Hepatol* 2018; **15**: 11-20 [PMID: 28930295 DOI: 10.1038/nrgastro.2017.109]

11 **Eguchi Y**, Hyogo H, Ono M, Mizuta T, Ono N, Fujimoto K, Chayama K, Saibara T; JSG-NAFLD. Prevalence and associated metabolic factors of nonalcoholic fatty liver disease in the general population from 2009 to 2010 in Japan: a multicenter large retrospective study. *J Gastroenterol* 2012; **47**: 586-595 [PMID: 22328022 DOI: 10.1007/s00535-012-0533-z]

12 **Yoshida H**, Shiratori Y, Moriyama M, Arakawa Y, Ide T, Sata M, Inoue O, Yano M, Tanaka M, Fujiyama S, Nishiguchi S, Kuroki T, Imazeki F, Yokosuka O, Kinoyama S, Yamada G, Omata M. Interferon therapy reduces the risk for hepatocellular carcinoma: national surveillance program of cirrhotic and noncirrhotic patients with chronic hepatitis C in Japan. IHIT Study Group. Inhibition of Hepatocarcinogenesis by Interferon Therapy. *Ann Intern Med* 1999; **131**: 174-181 [PMID: 10428733 DOI: 10.7326/0003-4819-131-3-199908030-00003]

13 **Shiratori Y**, Imazeki F, Moriyama M, Yano M, Arakawa Y, Yokosuka O, Kuroki T, Nishiguchi S, Sata M, Yamada G, Fujiyama S, Yoshida H, Omata M. Histologic improvement of fibrosis in patients with hepatitis C who have sustained response to interferon therapy. *Ann Intern Med* 2000; **132**: 517-524 [PMID: 10744587 DOI: 10.7326/0003-4819-132-7-200004040-00002]

14 **Deo RC**. Machine Learning in Medicine. *Circulation* 2015; **132**: 1920-1930 [PMID: 26572668 DOI: 10.1161/CIRCULATIONAHA.115.001593]

15 **Ramesh AN**, Kambhampati C, Monson JR, Drew PJ. Artificial intelligence in medicine. *Ann R Coll Surg Engl* 2004; **86**: 334-338 [PMID: 15333167 DOI: 10.1308/147870804290]

16 **Suzuki K**. Overview of deep learning in medical imaging. *Radiol Phys Technol* 2017; **10**: 257-273 [PMID: 28689314 DOI: 10.1007/s12194-017-0406-5]

17 **Min S**, Lee B, Yoon S. Deep learning in bioinformatics. *Brief Bioinform* 2017; **18**: 851-869 [PMID: 27473064 DOI: 10.1093/bib/bbw068]

18 **Sussillo D**, Barak O. Opening the black box: low-dimensional dynamics in high-dimensional recurrent neural networks. *Neural Comput* 2013; **25**: 626-649 [PMID: 23272922 DOI: 10.1162/NECO\_a\_00409]

19 **Park K**, Kim J, Lee J. Visual Field Prediction using Recurrent Neural Network. *Sci Rep* 2019; **9**: 8385 [PMID: 31182763 DOI: 10.1038/s41598-019-44852-6]

20 **Lee SM**, Seo JB, Yun J, Cho YH, Vogel-Claussen J, Schiebler ML, Gefter WB, van Beek EJR, Goo JM, Lee KS, Hatabu H, Gee J, Kim N. Deep Learning Applications in Chest Radiography and Computed Tomography: Current State of the Art. *J Thorac Imaging* 2019; **34**: 75-85 [PMID: 30802231 DOI: 10.1097/RTI.0000000000000387]

21 **Ueda D**, Yamamoto A, Nishimori M, Shimono T, Doishita S, Shimazaki A, Katayama Y, Fukumoto S, Choppin A, Shimahara Y, Miki Y. Deep Learning for MR Angiography: Automated Detection of Cerebral Aneurysms. *Radiology* 2019; **290**: 187-194 [PMID: 30351253 DOI: 10.1148/radiol.2018180901]

22 **Mei X**, Lee HC, Diao KY, Huang M, Lin B, Liu C, Xie Z, Ma Y, Robson PM, Chung M, Bernheim A, Mani V, Calcagno C, Li K, Li S, Shan H, Lv J, Zhao T, Xia J, Long Q, Steinberger S, Jacobi A, Deyer T, Luksza M, Liu F, Little BP, Fayad ZA, Yang Y. Artificial intelligence-enabled rapid diagnosis of patients with COVID-19. *Nat Med* 2020 [PMID: 32427924 DOI: 10.1038/s41591-020-0931-3]

23 **Zhou LQ**, Wang JY, Yu SY, Wu GG, Wei Q, Deng YB, Wu XL, Cui XW, Dietrich CF. Artificial intelligence in medical imaging of the liver. *World J Gastroenterol* 2019; **25**: 672-682 [PMID: 30783371 DOI: 10.3748/wjg.v25.i6.672]

24 **Hassan TM,** Elmogy M, Sallam ES. Diagnosis of Focal Liver Diseases Based on Deep Learning Technique for Ultrasound Images. *Arab J Sci Eng* 2017; **42**: 3127-3140 [DOI: 10.1007/s13369-016-2387-9]

25 **Sato M**, Morimoto K, Kajihara S, Tateishi R, Shiina S, Koike K, Yatomi Y. Machine-learning Approach for the Development of a Novel Predictive Model for the Diagnosis of Hepatocellular Carcinoma. *Sci Rep* 2019; **9**: 7704 [PMID: 31147560 DOI: 10.1038/s41598-019-44022-8]

26 **Biswas M**, Kuppili V, Edla DR, Suri HS, Saba L, Marinhoe RT, Sanches JM, Suri JS. Symtosis: A liver ultrasound tissue characterization and risk stratification in optimized deep learning paradigm. *Comput Methods Programs Biomed* 2018; **155**: 165-177 [PMID: 29512496 DOI: 10.1016/j.cmpb.2017.12.016]

27 **Byra M**, Styczynski G, Szmigielski C, Kalinowski P, Michałowski Ł, Paluszkiewicz R, Ziarkiewicz-Wróblewska B, Zieniewicz K, Sobieraj P, Nowicki A. Transfer learning with deep convolutional neural network for liver steatosis assessment in ultrasound images. *Int J Comput Assist Radiol Surg* 2018; **13**: 1895-1903 [PMID: 30094778 DOI: 10.1007/s11548-018-1843-2]

28 **Masuzaki R**, Tateishi R, Yoshida H, Goto E, Sato T, Ohki T, Imamura J, Goto T, Kanai F, Kato N, Ikeda H, Shiina S, Kawabe T, Omata M. Prospective risk assessment for hepatocellular carcinoma development in patients with chronic hepatitis C by transient elastography. *Hepatology* 2009; **49**: 1954-1961 [PMID: 19434742 DOI: 10.1002/hep.22870]

29 **Fung J**, Lai CL, Seto WK, Wong DK, Yuen MF. Prognostic significance of liver stiffness for hepatocellular carcinoma and mortality in HBeAg-negative chronic hepatitis B. *J Viral Hepat* 2011; **18**: 738-744 [PMID: 20659306 DOI: 10.1111/j.1365-2893.2010.01355.x]

30 **Sandrin L**, Fourquet B, Hasquenoph JM, Yon S, Fournier C, Mal F, Christidis C, Ziol M, Poulet B, Kazemi F, Beaugrand M, Palau R. Transient elastography: a new noninvasive method for assessment of hepatic fibrosis. *Ultrasound Med Biol* 2003; **29**: 1705-1713 [PMID: 14698338 DOI: 10.1016/j.ultrasmedbio.2003.07.001]

31 **Castéra L**, Vergniol J, Foucher J, Le Bail B, Chanteloup E, Haaser M, Darriet M, Couzigou P, De Lédinghen V. Prospective comparison of transient elastography, Fibrotest, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C. *Gastroenterology* 2005; **128**: 343-350 [PMID: 15685546 DOI: 10.1053/j.gastro.2004.11.018]

32 **Wang K**, Lu X, Zhou H, Gao Y, Zheng J, Tong M, Wu C, Liu C, Huang L, Jiang T, Meng F, Lu Y, Ai H, Xie XY, Yin LP, Liang P, Tian J, Zheng R. Deep learning Radiomics of shear wave elastography significantly improved diagnostic performance for assessing liver fibrosis in chronic hepatitis B: a prospective multicentre study. *Gut* 2019; **68**: 729-741 [PMID: 29730602 DOI: 10.1136/gutjnl-2018-316204]

33 **Castéra L**, Foucher J, Bernard PH, Carvalho F, Allaix D, Merrouche W, Couzigou P, de Lédinghen V. Pitfalls of liver stiffness measurement: a 5-year prospective study of 13,369 examinations. *Hepatology* 2010; **51**: 828-835 [PMID: 20063276 DOI: 10.1002/hep.23425]

34 **Srinivasa Babu A**, Wells ML, Teytelboym OM, Mackey JE, Miller FH, Yeh BM, Ehman RL, Venkatesh SK. Elastography in Chronic Liver Disease: Modalities, Techniques, Limitations, and Future Directions. *Radiographics* 2016; **36**: 1987-2006 [PMID: 27689833 DOI: 10.1148/rg.2016160042]

35 **Saillard C**, Schmauch B, Laifa O, Moarii M, Toldo S, Zaslavskiy M, Pronier E, Laurent A, Amaddeo G, Regnault H, Sommacale D, Ziol M, Pawlotsky JM, Mulé S, Luciani A, Wainrib G, Clozel T, Courtiol P, Calderaro J. Predicting survival after hepatocellular carcinoma resection using deep-learning on histological slides. *Hepatology* 2020 [PMID: 32108950 DOI: 10.1002/hep.31207]

36 **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**: 1248-1259 [PMID: 28982688 DOI: 10.1158/1078-0432.CCR-17-0853]

37 **Singal AG**, Mukherjee A, Elmunzer BJ, Higgins PD, Lok AS, Zhu J, Marrero JA, Waljee AK. Machine learning algorithms outperform conventional regression models in predicting development of hepatocellular carcinoma. *Am J Gastroenterol* 2013; **108**: 1723-1730 [PMID: 24169273 DOI: 10.1038/ajg.2013.332]

38 **Konerman MA**, Lu D, Zhang Y, Thomson M, Zhu J, Verma A, Liu B, Talaat N, Balis U, Higgins PDR, Lok ASF, Waljee AK. Assessing risk of fibrosis progression and liver-related clinical outcomes among patients with both early stage and advanced chronic hepatitis C. *PLoS One* 2017; **12**: e0187344 [PMID: 29108017 DOI: 10.1371/journal.pone.0187344]

39 **Topol EJ**. High-performance medicine: the convergence of human and artificial intelligence. *Nat Med* 2019; **25**: 44-56 [PMID: 30617339 DOI: 10.1038/s41591-018-0300-7]

40 **Namikawa K**, Hirasawa T, Yoshio T, Fujisaki J, Ozawa T, Ishihara S, Aoki T, Yamada A, Koike K, Suzuki H, Tada T. Utilizing artificial intelligence in endoscopy: a clinician's guide. *Expert Rev Gastroenterol Hepatol* 2020: 1-18 [PMID: 32500760 DOI: 10.1080/17474124.2020.1779058]

41 **Hirasawa T**, Aoyama K, Tanimoto T, Ishihara S, Shichijo S, Ozawa T, Ohnishi T, Fujishiro M, Matsuo K, Fujisaki J, Tada T. Application of artificial intelligence using a convolutional neural network for detecting gastric cancer in endoscopic images. *Gastric Cancer* 2018; **21**: 653-660 [PMID: 29335825 DOI: 10.1007/s10120-018-0793-2]

42 **Namikawa K**, Hirasawa T, Nakano K, Ikenoyama Y, Ishioka M, Shiroma S, Tokai Y, Yoshimizu S, Horiuchi Y, Ishiyama A, Yoshio T, Tsuchida T, Fujisaki J, Tada T. Artificial intelligence-based diagnostic system classifying gastric cancer and ulcer: Comparison between the original and newly developed systems. *Endoscopy* 2020 [PMID: 32503056 DOI: 10.1055/a-1194-8771]

43 **Jin P**, Ji X, Kang W, Li Y, Liu H, Ma F, Ma S, Hu H, Li W, Tian Y. Artificial intelligence in gastric cancer: a systematic review. *J Cancer Res Clin Oncol* 2020 [PMID: 32613386 DOI: 10.1007/s00432-020-03304-9]

44 **Kudo SE**, Misawa M, Mori Y, Hotta K, Ohtsuka K, Ikematsu H, Saito Y, Takeda K, Nakamura H, Ichimasa K, Ishigaki T, Toyoshima N, Kudo T, Hayashi T, Wakamura K, Baba T, Ishida F, Inoue H, Itoh H, Oda M, Mori K. Artificial Intelligence-assisted System Improves Endoscopic Identification of Colorectal Neoplasms. *Clin Gastroenterol Hepatol* 2020; **18**: 1874-1881.e2 [PMID: 31525512 DOI: 10.1016/j.cgh.2019.09.009]

45 **Jin EH**, Lee D, Bae JH, Kang HY, Kwak MS, Seo JY, Yang JI, Yang SY, Lim SH, Yim JY, Lim JH, Chung GE, Chung SJ, Choi JM, Han YM, Kang SJ, Lee J, Chan Kim H, Kim JS. Improved Accuracy in Optical Diagnosis of Colorectal Polyps Using Convolutional Neural Networks with Visual Explanations. *Gastroenterology* 2020; **158**: 2169-2179.e8 [PMID: 32119927 DOI: 10.1053/j.gastro.2020.02.036]

46 **Dalal V**, Carmicheal J, Dhaliwal A, Jain M, Kaur S, Batra SK. Radiomics in stratification of pancreatic cystic lesions: Machine learning in action. *Cancer Lett* 2020; **469**: 228-237 [PMID: 31629933 DOI: 10.1016/j.canlet.2019.10.023]

47 **Park S**, Chu LC, Fishman EK, Yuille AL, Vogelstein B, Kinzler KW, Horton KM, Hruban RH, Zinreich ES, Fouladi DF, Shayesteh S, Graves J, Kawamoto S. Annotated normal CT data of the abdomen for deep learning: Challenges and strategies for implementation. *Diagn Interv Imaging* 2020; **101**: 35-44 [PMID: 31358460 DOI: 10.1016/j.diii.2019.05.008]

48 **Abajian A**, Murali N, Savic LJ, Laage-Gaupp FM, Nezami N, Duncan JS, Schlachter T, Lin M, Geschwind JF, Chapiro J. Predicting Treatment Response to Intra-arterial Therapies for Hepatocellular Carcinoma with the Use of Supervised Machine Learning-An Artificial Intelligence Concept. *J Vasc Interv Radiol* 2018; **29**: 850-857.e1 [PMID: 29548875 DOI: 10.1016/j.jvir.2018.01.769]

49 **Hujoel IA**, Murphree DH Jr, Van Dyke CT, Choung RS, Sharma A, Murray JA, Rubio-Tapia A. Machine Learning in Detection of Undiagnosed Celiac Disease. *Clin Gastroenterol Hepatol* 2018; **16**: 1354-1355.e1 [PMID: 29253540 DOI: 10.1016/j.cgh.2017.12.022]

50 **Qian T**, Zhu S, Hoshida Y. Use of big data in drug development for precision medicine: an update. *Expert Rev Precis Med Drug Dev* 2019; **4**: 189-200 [PMID: 31286058 DOI: 10.1080/23808993.2019.1617632]

51 **Mauksch LB**, Dugdale DC, Dodson S, Epstein R. Relationship, communication, and efficiency in the medical encounter: creating a clinical model from a literature review. *Arch Intern Med* 2008; **168**: 1387-1395 [PMID: 18625918 DOI: 10.1001/archinte.168.13.1387]

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**Table 1 Clinical applications of artificial intelligence**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Samples** | **Diagnosis** | **AI technique** | **Accuracy, %** | **AUROC** | **Ref.** |
| Focal liver disease detection | US | Benign tumors | DL | 97.2 | NA | [23] |
| Serum tests, clinical data | HCC | ML (gradient boosting)/DL | 87.34/83.54 | 0.940/0.884 | [25] |
| Diffuse liver disease staging | US | FLD | DL/SVM/ELM | 100/82/92 | 1.0/0.79/0.92 | [26] |
| US | NAFLD | DL | NA | 0.9777 | [27] |
| Elastography | Cirrhosis | DL | NA | 0.97 | [32] |
| Risk assessment | Clinical, pathohistological data | Poorer survival after HCC resection  | 2 DL models | NA | 0.78, 0.75 (c-index) | [35] |
| Sequence data | Poorer survival after HCC resection | DL | NA | 0.68 (c-index) | [36] |
| Clinical data | HCC development | ML | NA | 0.64 (c-index) | [37] |
| Clinical, histological data | 1-yr and 3-yr clinical outcomes | ML | NA | 0.78, 0.76 | [38] |

AUROC: Area under the receiver operating characteristics; c-index: Confidence interval; DL: Deep learning; ELM: Extreme learning machine; FLD: Fatty liver disease; HCC: Hepatocellular carcinoma; ML: Machine learning; NAFLD: Nonalcoholic fatty liver disease; SVM: Support vector machine; US: Ultrasonography; NA: Not available.