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ARTIFICIAL INTELLIGENCE IN HEPATOCELLULAR CARCINOMA SCREENING AND MEDICAL TREATMENT

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Abstract:

Hepatocellular carcinoma (HCC) is the third most prevalent cause of cancer-related death worldwide and the fifth most common cancer with an annual incidence of over 500,000 cases worldwide [1,2]. The cirrhosis that underlies the great majority of HCC tumors is most frequently caused by alcohol-related liver disease, hepatitis B or hepatitis C virus infection, or nonalcoholic fatty liver disease (NAFLD). HCC still has a dismal five-year survival rate of 15% despite recent therapy improvements, such as the use of Atezolizumab + Bevacizumab for unresectable HCC. These factors are mostly attributable to delayed diagnosis and the poor effectiveness of current therapies [3, 4].

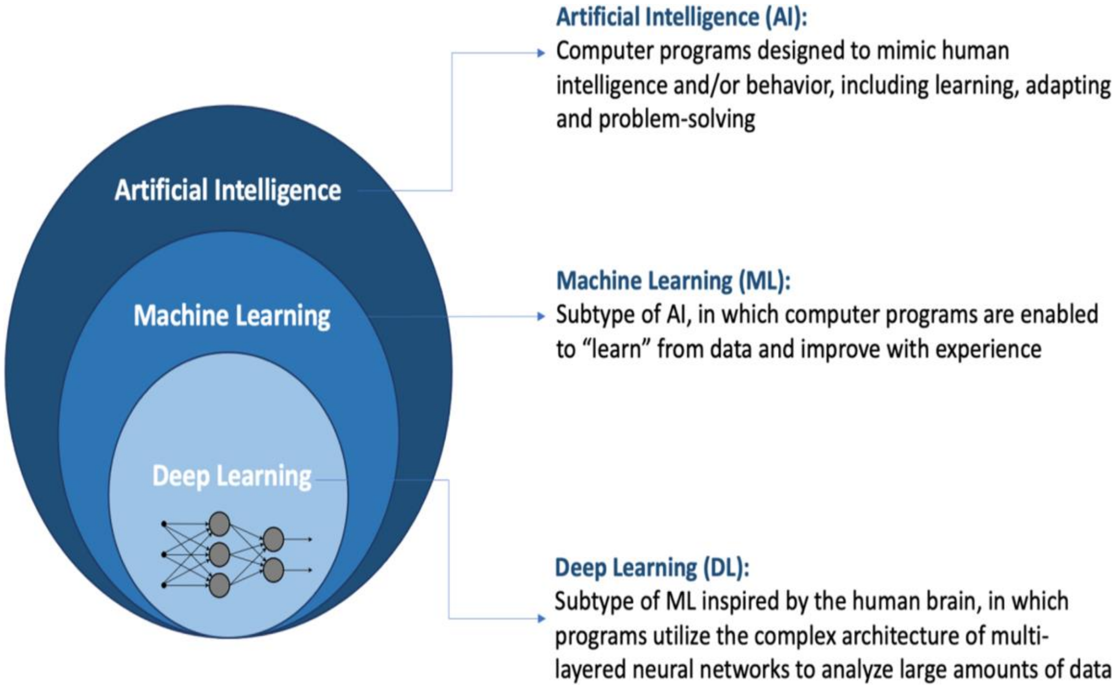
Keywords:
Artificial Intelligence, Machine Learning, Deep Learning, Liver Cancer

Introduction

The wide variation in HCC risk factors and etiology makes it difficult to forecast and prognosticate using current methods. Artificial intelligence (AI) has recently become a unique opportunity to improve the whole gamut of clinical care for hepatocellular carcinoma (HCC). This can be achieved in three ways: (1) by enhancing the prognostication of patients with established HCC; (2) by increasing the accuracy of HCC diagnosis in patients undergoing liver biopsies or surveillance imaging; and (3) by improving future HCC risk prediction in patients with liver disease.

The field of artificial intelligence includes computational search algorithms, machine learning （ML） and deep learning models. **Figure 1.**

In machine learning (ML), a computer runs iterative models to gradually improve performance on a given task, like outcome classification. By adding more training data over time, ML models are made to get better and better at optimizing algorithm parameters. The desired output gets more accurate over time with training. Deep learning (DL) is a subset of machine learning (ML) models that are built with neural networks (NN) that draw inspiration from human brain neuroanatomy.



Artificial Intelligence (AI):
Computer programs designed to mimic human intelligence and/or behavior, including learning, adapting and problem-solving

Machine Learning (ML):
Subtype of AI, in which computer programs are enabled to "learn" from data and improve with experience

Deep Learning (DL):
Subtype of ML inspired by the human brain, in which programs utilize the complex architecture of multi-layered neural networks to analyze large amounts of data

Figure 1. Definitions of Artificial Intelligence (AI), Machine Learning (ML) and Deep Learning (DL)

Due to DL models' inherent dependence on the volume and variety of their training dataset, current limitations of DL approaches include overfitting of data, limited explainability of data, and the potential for poor generalizability. We will discuss the rapidly changing role of AI in HCC diagnosis, prognosis, and prediction, as well as its associated challenges, in this review.

AI for hepatocellular carcinoma occurrence prediction.

The ability to use large-scale, longitudinal data elements for automatic feature selection over long-term follow-up has recently been made possible by the rapid expansion of available electronic health record (EHR) data. This has improved HCC risk prediction. Consequently, a number of recent studies have improved incident HCC prediction by utilizing AI techniques on longitudinal EHR data. It has been suggested that by enhancing risk stratification of patients with chronic liver disease, enhanced HCC risk prediction models utilizing AI techniques could be used to personalize HCC surveillance strategies.

Using radiomics in ultrasonography

Using a training dataset of 367 ultrasound images and the accompanying radiological reports, Schmauch and colleagues created a supervised deep learning model that could classify liver lesions as benign or malignant with a mean AUROC of 0.93 and 0.92, respectively [12]. Recently, a deep convolutional neural network (DCNN) was developed and externally validated by Yang and colleagues using a large multicenter ultrasound imaging database from 13 hospital systems. The final model showed an AUROC of 0.92 for differentiating benign from malignant liver lesions, and it performed similarly to clinical radiologists' judgment in terms of diagnostic accuracy (76.0%) and accuracy to contrast-enhanced CT (84.7%), which was only marginally less accurate than magnetic resonance imaging (MRI, 87.9%). [13].

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI)

A fast expanding field of study focuses on better characterizing liver lesions that are indeterminate. In clinical practice, a patient is usually referred for additional imaging, such as a contrast-enhanced CT scan or MRI, if an abdominal ultrasound reveals a new liver lesion. Certain liver lesions may be deemed to have pathognomonic features of HCC based on the satisfaction of particular radiologic criteria; therefore, a liver biopsy is not necessary for additional histological confirmation. However, liver nodules seen on CT or MRI frequently exhibit unclear features; therefore, the current guidelines suggest either a liver biopsy or serial imaging at close intervals.

It is challenging and time-consuming to manually segment liver radiographic features for radiomics-based assessments of HCC due to the wide variability of liver and liver lesion radiographic features. Researchers were asked to create AI-based algorithms for the Liver Tumor Segmentation (LiTS) Challenge in 2017, which used a global dataset of 200 CT scans (130 training scans and 70 validation scans) to automatically segment liver tumors.

Since manually creating MRI features can be costly and technically challenging, AI has not been used as much in MRI imaging of HCC tumors. As a result, most published studies have involved small numbers of patients. However, in order to differentiate HCC from liver adenomas, cysts, or hemangiomas as well as from metastases, a previous study integrated clinical data with MRI imaging-based classifiers. The results showed a sensitivity of 0.73 for detecting HCC, but a specificity of only 0.56.

AI for prognostication in established HCC

A number of deep learning algorithms have been developed to enhance the prediction of HCC recurrence/survival from CT scan, MRI, or pathological images because the morphological features of the disease have a significant impact on the prognosis of patients. Saillard et al. developed a model based on the processing of digital slides with HCC that was more accurate than scores incorporating all pertinent clinical, biological, and pathological features in predicting the survival of patients with HCC treated by surgical resection. The ability of MRI or CT scan images to be predictive is also being studied in an exponentially increasing number of studies. Ji et al. assessed the risk of HCC recurrence following surgical resection by combining a number of biological and clinical characteristics, such as tumor margin status and serum alpha-fetoprotein albumin-bilirubin (ALBI) grade, with radiomics signatures. In order to forecast microvascular invasion, cytokeratin 19 expression (a progenitor phenotype), or an early tumor recurrence, other authors also attempted to process CT scan or MRI images [18–21]. The predictive capacity of AI techniques for transarterial chemoembolization (TACE) in advanced HCC was examined in a number of studies.

Present obstacles preventing AI from being used for prognosticating and predicting HCC risk

While AI has great potential to improve patient stratification and HCC detection, machine learning algorithms are still rarely used in clinical settings. It is true that standardization and thorough assessment using metrics that ideally include patient outcomes and care quality, along with the right kind of stakeholder involvement and supervision, will be necessary for the safe translation of deep learning models.

The primary barrier is probably cultural, but there are still other problems, like patient anonymity and the possibility of re-identification, the expense of storing and providing data, and the requirement for explicit consent before sharing.

The racial, ethnic, and socioeconomic diversity of the cohorts utilized to create and train AI models aimed at HCC risk prediction, diagnosis, and prognostication has not been sufficiently present up to this point. This is a crucial problem because the quality and volume of input data determine how accurate AI-based algorithms are. Future research must therefore make sure that promising AI-based tools are carefully validated in diverse cohorts comprising patients from all socioeconomic backgrounds and members of racial and ethnic minorities.

Conclusion

It is envisaged that AI will significantly alter how we treat patients with HCC. Even though the last ten years have seen tremendous advancements, HCC risk prediction, diagnosis, and response prediction still require urgent improvement. To fully integrate such technologies in clinical practice, a number of obstacles still need to be overcome. These include the necessity of creating reliable methods for the gathering, sharing, and storing of structured data as well as the requirement to show the dependability and resilience of models. We now need to show that these methods are effective in a clinical setting by comparing model performance to that of currently available, conventional staging systems and by carefully designing large-scale prospective trials. We already know that AI can predict a very large set of clinically relevant features.

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