IJBC 2023; 15 (3):4-12

Iranian Journal of Blood & Cancer

Journal Home Page: www.ijbc.ir

Review

Beyond human capacity: How artificial intelligence (AI) is enhancing cancer diagnosis and treatment

Mehrnaz Sadat Ravari[1], Majid Momeny[2*]

[1]Research Center for Hydatid Disease in Iran, Kerman University of Medical Sciences, Kerman, Iran
[2]The Brown Foundation Institute of Molecular Medicine, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, TX 77030, USA

ARTICLE INFO

Article History:
Received: 24/06/2023
Accepted: 19/08/2023

Keywords:
Artificial intelligence (AI)
Deep learning
Prediction
Cancer
Diagnosis
Treatment

***Corresponding author:**
Majid Momeny, Ph.D.
The Brown Foundation Institute of Molecular Medicine, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, TX 77030, USA
Email: Majid.momeny@gmail.com

Abstract

In recent years, artificial intelligence (AI) has revolutionized several aspects of human life. The availability of high-dimensionality datasets with progression in high-performance computing, and innovative deep learning architectures which are the subdomains of AI, have led to promising functions of AI in the medical contexts, particularly in oncology. Regarding the capacity of AI models in recognition and learning patterns as well as associations, these systems can be utilized in various aspects of cancer research including cancer diagnosis and treatment. To be precise, AI models are able to analyze medical images such as stained histopathology slides and radiology images and consequently pave the way for cancer diagnosis, grading, classification, tumor characterization, and prognosis prediction. Moreover, AI algorithms can assess a myriad of medical data to recognize patterns and make predictions about patient treatment outcomes, enabling more personalized treatment plans. Accordingly, AI-assisted cancer treatment strategies have been shown to notably improve the quality of cancer treatment with chemotherapy, immunotherapy, and even radiotherapy while reducing the treatment toxicities.

Please cite this article as: Sadat Ravari M, Momeny M. Beyond human capacity: How artificial intelligence (AI) is enhancing cancer diagnosis and treatment. Iranian Journal of Blood and Cancer. 2023;15(3):4-12.

1. Introduction

The initial definition of artificial intelligence (AI) dates back to 1956. In compliance with its name, AI refers to machines with the capacity to learn and recognize associations and patterns and ultimately use these concepts to make decisions for unseen data (1). AI comprises a vast area in which machine learning and so on deep learning are two main subdomains. Regarding the powerful ability of deep learning in image and face recognition, it has drawn several attractions which can broaden its applicability to numerous aspects of science including medicine and cancer research (2). One of the considerable advantages of AI in cancer research is its capacity to process and analyze large amounts of data swiftly and accurately. This feature is especially crucial in the domain of cancer, where a vast amount of imaging, genetic, and clinical data must be analyzed (3). AI algorithms are able to detect correlations that may not be readily apparent to human experts, enabling more accurate diagnoses and more effective treatments. In this regard, AI has proven to be a powerful tool, aiding in various tasks such as image analysis, radiomics, pathology analysis, liquid biopsy analysis, and treatment response prediction and monitoring (4). Besides, deep learning is able to identify genome alterations and epigenetic changes and consequently predict and classify tissues into a cancer type or a healthy one (5). It has been demonstrated that AI systems are able to pave the way for personalized treatment plans that take into account each patient's unique genetic and clinical characteristics, thereby enhancing treatment outcomes and reducing side effects (6). Indeed, AI has also been used to develop predictive models that can help identify patients who are at higher risk of developing cancer or who are likely to respond to a particular treatment. Accordingly, AI algorithms can analyze data to identify alterations that can increase the risk of developing specific types of cancer and evaluate the expression of biomarkers to predict the responsiveness of patients to a particular chemotherapy, immunotherapy, and radiotherapy regimen (7). All in all, in the current study, a brief overview of AI and its roles in cancer research in two main domains including diagnosis and treatment were provided.

2. AI subdomains in cancer

Due to the ability of AI in recognizing and learning patterns and associations, this programmed machine could be used for decision-making on new input data like medicine and cancer. It was demonstrated that machine learning and deep learning are the prominent subdomains of AI able to actualize AI. In fact, deep learning could be per se a subset of machine learning (3).

2.1. Natural language processing

Natural language processing, a subdomain of AI, is a technique that involves the use of algorithms to analyze and comprehend human language. Indeed, they are able to produce structured data from unstructured free text. In cancer research, natural language processing algorithms have been implemented to analyze electronic health records (EHRs) and other clinical documents to extract information about cancer diagnoses, treatments, and outcomes (8). Natural language processing can pave the way for researchers and clinicians in identifying patterns and correlations in clinical data that may not be apparent, leading to more accurate diagnoses and more effective treatments. According to a systematic review, several natural language processing systems (not all of the analyzed ones) were able to process medical free text and generate structured output (9). As one of the greatest advents, ChatGPT is a developed natural language processing that uses AI algorithms to understand and generate human-like language responses to text-based inputs (10).

2.2. Reinforcement learning

Reinforcement learning is an AI technique that involves the use of algorithms to learn from experience by interacting with an environment. Reinforcement learning algorithms have been utilized in personalized medicine to apply treatment approaches for cancer patients based on their genetic and clinical characteristics. Indeed, in precision medicine, the most effective therapeutic approach is recommended to patients specific to their molecular and clinical features (11, 12). For instance, in a recent study, a deep reinforcement learning model was proposed called proximal policy optimization ranking (PPORank) which is able to rank drugs according to their predicted influences on cell lines or patients and recommend the most effective therapeutic medicine (13). Regarding oncology, reinforcement learning has been demonstrated to be an effective method in chemotherapy dosing and dynamic treatment of cancer patients (14).

2.3. Machine learning

Machine learning, as the greatest subdomain of AI, is an algorithm-based approach to analyzing complex data sets. To be precise, by far the most significant benefit of machine learning is its capacity to learn from data and improve its performance with time. Therefore, as machine learning algorithms are exposed to more data, they become more accurate and efficient. Regarding cancer studies, machine learning algorithms have been used to conduct numerous tasks, including image analysis, radiomics, pathology analysis, liquid biopsy analysis, and treatment response prediction and monitoring (15).

2.4. Deep learning

Deep learning is a subdomain of machine learning and is inspired by the architecture of brain neuronal structures. Therefore, deep learning utilizes deep neural networks (DNNs) to develop sophisticated models with vast and complex data sets in order to gain the ability to predict (16). Despite machine learning algorithms that need careful designing of raw data, deep learning has the ability to learn the ideal deep features that are the most suitable for the task at hand in an automatic manner through a training process (17). Indeed, by means of this ability, deep learning shows an improvement in several AI tasks related to cancer and oncology such as image analysis, radiomics, and pathology analysis, demonstrating considerable potential in improving the accuracy and efficiency of cancer diagnosis and treatment. With deep learning, algorithms can recognize patterns in medical images that are indicative of cancer, leading to more accurate diagnoses and efficient treatment (18).

Convolutional neural networks (CNNs) are the most common architectures of deep learning out of various DNNs. Generally, CNNs are able to conduct some non-linear transformations on the structured data like the raw pixels of an image in order to learn appropriate features automatically (4). Regarding their ability to analyze pictures, they have been applied to detect cancer lesions and classify malignancy images (19-21). In order to provide an overview of AI and its subdomains, **Figure 1** was depicted.

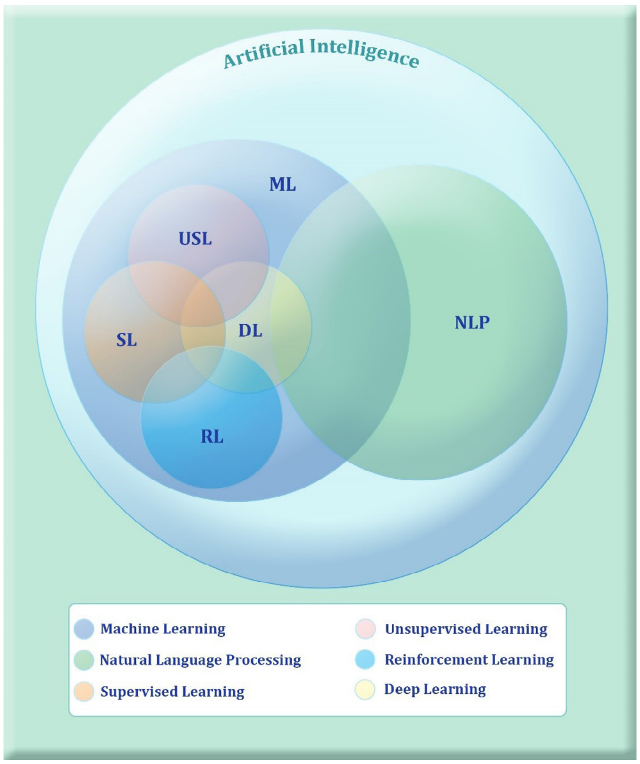

Figure 1. **AI and its major subdomains.** AI refers to machines capable of learning and identifying patterns and relationships. Therefore, it is a vast area that comprises several subdomains, the important of which is machine learning. In fact, machine learning is the greatest subdomain of AI which has several subdomains. In supervised learning, improvement and development require a sophisticated supervisor to minister a labeled dataset and provide it for the learning algorithm. By contrast, unsupervised learning systems can identify hidden patterns to extract data from an unlabeled dataset without any supervision. However, reinforcement learning could be developed by experience via exploring different actions to maximize long-term rewards. Deep learning models are the ultimate development of AI systems able to mimic the human brain. In other words, they could learn patterns and process data in order to make decisions. Natural language processing systems utilize machine learning and deep learning to analyze text and spoken words in a way humans are able to do. They actually provide a platform to give humans a chance to interact with machines in their own language and scales.

3. The application of AI in cancer diagnosis

The diagnosis of cancer is not only an important action to detect tumors accurately before cancer turns into an aggressive one but also it is essential in grading and further monitoring the cancer. The application of AI systems in the diagnosis of cancer has been elevated considerably in recent years due to their ability to deeply interpret images (18).

3.1. Diagnosis based on liquid biopsy data

The evaluation of liquid biopsies is a technique analyzing biological fluids for cancer-related biomarkers such as circulating tumor DNA and cell-free DNA. Accordingly, a system called CancerSEEK was developed and evaluated in 1005 patients with non-metastatic solid tumors. This system had the ability to assess genetic mutations as well as protein biomarker alterations with the aid of AI in the blood. They demonstrated that CancerSEEK was able to detect positive cancers in a median of 70% of the cancer types (22).

3.2. Diagnosis based on radiography data

Regarding medical images obtained during some non-invasive techniques like magnetic resonance imaging (MRI), computed tomography (CT) scans, and mammograms, DNNs showed promising outcomes (23-25). For instance, a proposed CNN was utilized to evaluate 14696 image patches obtained from 120 CT scans of patients with interstitial lung diseases. They demonstrated that the proposed CNN was able to detect lung patterns with 85.5% accuracy for classifying patients (26). Moreover, another study utilized a three-dimensional (3D) ResNet algorithm based on CT scan data and predicted occult peritoneal metastasis with an area under the receiver operator curve (AUROC or AUC) of 0.922 in colorectal cancer cases which was considerably higher than the conventional method (AUC of 0.791) (27). In a study of 172 patients with prostate cancer, a deep learning CNN system was able to detect cancer based on analyzing MRI images with 0.84 AUC which was more significant in comparison with a non-deep learning system (28). Radiomics is an analyzing method that involves extracting quantitative features from images to develop predictive models for cancer (or any condition) diagnosis and treatment (29). Indeed, AI algorithms analyze radiomics data, facilitating accurate and effective cancer diagnosis. In summary, any AI system should conduct radiomics approach in some steps.

First, systems should delineate the region of interest (ROI) in two-dimensional (2D) or the volume of interest (VOI) in 3D (segmenting images). Then, they should homogenize images by considering and analyzing several factors such as the spacing of pixels and grey-level intensities (processing images). In the following, they calculate the features (extracting features), and finally, the number of features should be decreased in order to build statistical and machine learning models (selecting features) (30).

3.3. Diagnosis based on histopathology data

The powerful algorithms utilized in DNNs give these systems the ability to analyze images derived from stained slides of surgically-removed tissues. In a study of cervical cancer, a deep learning AI system was developed to assess p16/Ki-67 dual-stained slides. They exhibited that the AI system had an equal sensitivity and higher specificity compared with conventional pop smears and manual staining. This system was able to diminish the referral to colposcopy by one-third (31). Similarly, in a study of patients with colorectal cancer, the effectiveness of an AI-aided colonoscopy to detect adenoma was evaluated. They showed that the AI system was able to elevate the adenoma detection rates and the mean number of adenomas per patient significantly compared with standard colonoscopy implying the effectiveness of AI to improve the quality of cancer diagnosis (32). The capacity of a deep learning algorithm to detect metastasis of breast cancer by analyzing hematoxylin and eosin (H&E)-stained tissue sections of lymph nodes has been evaluated. They exhibited that the CNN algorithm detected metastasis with 0.994 AUC while the best pathologic detection yielded an AUC of 0.884 which was also more time-consuming (33). A deep learning system that learned domain-agnostic features was utilized for the diagnosis and grading of prostate cancer. It was demonstrated that the AI system was able to detect prostate cancer based on whole slide images with an AUC of 0.93 (34). These results indicate that it could be possible for a developed AI system to analyze medical images with higher accuracy and extremely lower time. Besides, one of the possible roles of deep learning is its ability to predict the origin of unknown primary tumors which is still a challenging issue (35). Regarding myelodysplastic syndromes (MDS), the most accurate and reliable method of diagnosis is detecting cellular dysplasia in the bone marrow (BM) biopsy or aspirate (36). Indeed, deep learning models like CNN facilitated the way MDSs could be diagnosed by their ability to analyze images. In this regard, a study utilized Xception CNNs and VGG16 to analyze BM biopsies from 236 patients with MDS and myeloproliferative neoplasm (MPN) in order to predict the diseases. Interestingly, they found that the deep learning model was able to predict genetic and cytogenetic aberrations with the best performance for identifying mutations in TET2 (AUC of 0.94) and spliceosome (AUC of 0.89) genes as well as chromosome 7 monosomy (AUC of 0.89) (37). In another study, a deep learning model was developed to distinguish between follicular lymphoma and follicular hyperplasia based on whole slide images of lymph nodes. They demonstrated that the Bayesian neural network (BNN) was able to provide a diagnostic prediction accurately with an AUC of 0.99 (38).

3.4. Prediction based on gene mutations

AI systems and deep learning are able to identify genetic as well as epigenetic heterogenicity. It was demonstrated that a deep learning algorithm could be trained to predict myriad gene expression signatures, gene alterations, and molecular tumor subtypes by evaluating H&E-stained slides (39). Accordingly, a deep convolutional neural network (inception v3) showed promising ability to predict six various genetic mutations (AUC ranged from 0.733 to 0.856) of lung cancer by analyzing whole-slide H&E-stained images (40). In a study, a transfer learning model based on MobileNetV2 architecture was trained and developed (MSINet) to identify microsatellite instability. They assessed its capacity in colorectal cancer H&E-stained whole-slide images and showed that the MSINet model with an AUC of 0.931 exceeded the performance of experienced pathologists to predict microsatellite instability (41).

4. The application of AI in cancer therapy

AI systems are able to extract data from medical records in order to establish an efficient model with the ability to the rate of responses to treatments in patients and the risk of tumor relapse. Therefore, the healthcare providers are able to administer the appropriate and accurate therapeutic approach (18, 42, 43).

4.1. Immunotherapy and chemotherapy

Personalized treatment, also known as precision medicine, involves developing treatment plans tailored to each patient's unique characteristics, such as genetics, medical history, and lifestyle factors. Deep learning algorithms can analyze large amounts of patient data to identify patterns and make predictions about treatment outcomes, enabling more personalized treatment plans (44). By providing a personalized therapeutic method, not only the poor clinical outcomes can be improved but also the high costs of treatments could be diminished (4).

A chief domain is immunotherapy, in particular, immune checkpoint inhibitors (ICIs) which has been demonstrated to have generally low response rates; however, in some studies, they exhibited promising and long-term clinical advantages (4). With this regard, the situation of biomarker expression in the tumor microenvironment like PD-L1 is important to predict how patients could respond to ICIs. However, these data should be obtained by some invasive and costly methods like biopsies. In a study of melanoma, a deep learning model was applied to histology and clinical data in order to predict the responses of ICIs. They demonstrated that the AI system was able to categorize patients into responder and non-responder with an AUC of 0.8 (45). By integrating clinical, genomic, and transcriptomic data into a logistic regression-based model, the resistance to PD-1 inhibitors was demonstrated with AUC between 0.73 and 0.83 in patients with advanced melanoma (46). Regarding chemotherapy, several studies showed the capacity of AI systems in predicting the response to neoadjuvant chemotherapeutic regimens in patients with several malignancies including nasopharyngeal carcinoma (47, 48), breast cancer (49, 50), and rectal carcinoma (51). In a recent study, a deep learning network with the ability to analyze whole slide images was utilized to investigate the outcomes of chemotherapy-received patients with colorectal cancer. They demonstrated that the deep learning signature was able to predict disease-free survival and overall survival of patients. Besides, there was a relationship between deep learning signature data and worse disease-free survival after three months of treatment (52).

4.2. Radiotherapy

The data- and image-driven frameworks in radiotherapy provide an encouraging platform for the development of AI models. In particular, AI systems could pave the way for target volume and organs at risk (OAR) delineation which requires a lot of manual work and physical effort (53). It has been demonstrated that CNN-based semantic segmentation is a top-notch technology in the automated OAR delineation in some organ-related abnormalities such as polycystic kidneys (54), liver (55), rectal cancer (56), and head and neck carcinomas (57-59). By utilizing a 3D CNN model in MRI data to construct an automated contouring method for nasopharyngeal carcinoma, researchers revealed that AI model showed 79% accuracy. Besides, the CNN model outperformed 50% of radiation oncologists and exhibited equal performance in the left 50%. The AI system was able to reduce interobserver variation and contouring time by 54.5 and 39.4%, respectively (60). Another context in which AI could improve the efficacy is treatment radiotherapy planning which is an action that requires several trial-and-error attempts. An initial study showed that there weren't any significant differences between the automated treatment planning method and real clinical plans in prediction and dose optimization in patients with head and neck carcinoma (61). Moreover, other implications of AI in radiotherapy could be the prediction of radiation side effects (62, 63), generating synthetic CT (64, 65), and reconstruction of images (66, 67). **Figure 2** represented an overview of how AI systems could be developed and make decisions regarding cancer diagnosis and treatment.

5. Conclusion and future prospects

In conclusion, the role of AI, machine learning, and deep learning in cancer research is increasingly becoming more important and promising. The ability of AI systems to analyze vast amounts of data such as medical images like CT scans and histopathological images and medical records by understanding the relationships and patterns has improved the accuracy and speed of cancer diagnosis. DNNs have the capacity to understand the patterns of H&E-stained whole tissue sections of cancerous tissues and are able to predict the prognosis and classification of the disease. It was also demonstrated that AI is being used to predict cancer by analyzing genes and biomarkers, which can help tailor personalized treatment plans for patients.

Furthermore, AI can utilize medical records to build a model to predict the responsiveness to the treatments; thus, AI systems have been used to classify cancer patients into responders and non-responders to certain chemotherapy and immunotherapy like ICIs, which can greatly improve patient outcomes and reduce the risk of unnecessary treatments. The application of deep learning models in radiotherapy is also showing promising results, as it can facilitate target volume and OAR delineation and help optimize treatment plans and reduce side effects.

However, there are still several challenges that need to be addressed before AI can be fully integrated into cancer research. Ethical and legal considerations, including data privacy and security, bias, and discrimination, accountability and liability, and informed consent, all

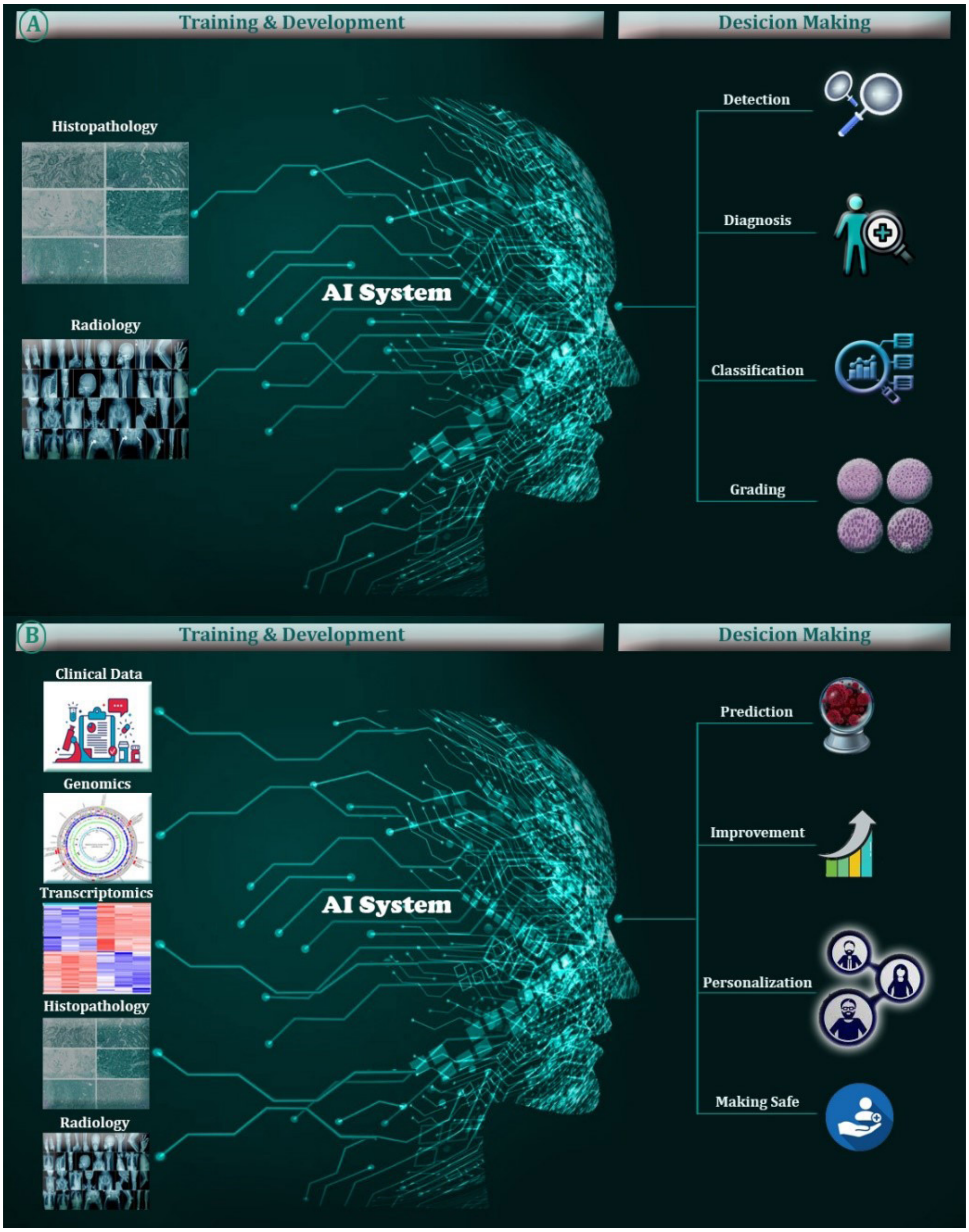

Figure 1. **The way how AI systems are trained and developed in order to make decisions. A.** AI algorithms are able to recognize patterns and associations in medical images. To be precise, these deep learning systems can be trained based on given data in order to identify alterations between a cancerous feature and a normal one by analyzing histopathologic whole tissue slides and radiologic records like CT scans and MRI data. With this ability, they serve as an efficient tool to improve the diagnosis of cancers in several areas such as detecting the first onset of disease, diagnosis of tumors and their origins, and classifying and grading the present cancer. **B.** The great capacity of AI and deep learning models give these systems a way to analyze medical records such as clinical data, genomic and transcriptomic information, and histopathology and radiology images by evaluating patterns and relationships. In this way, AI systems could be developed in order to predict the responsiveness of patients to certain therapeutic approaches such as chemotherapy, immunotherapy, and radiotherapy. Besides, AI models can improve the performance of cancer treatment by enhancing therapeutic responsiveness via biomarker evaluation and reducing treatment side effects via adjusting the dosage. Overall, they could increase the efficacy of therapeutic strategies by personalizing therapies based on the characteristics of each patient.

need to be carefully considered and addressed to realize the full potential of AI in cancer research and treatment.

The use of AI in cancer research provides significant opportunities for improving patient outcomes and advancing our understanding of cancer. However, addressing challenges related to data quality and quantity as well as ethical and legal considerations will be essential for realizing the full potential of AI in cancer studies. In the future, patient empowerment will be vital for encouraging patients to participate in their own care. This can help to address issues of informed consent and trust in AI-based cancer care. Moreover, collaboration between institutions and countries will also be essential to establish diverse datasets that could be used to train and develop AI algorithms. This will enable AI to generalize to various patients and cancer types, improving the effectiveness and equity of AI-based cancer care.

Conflicts of interest

The authors declare that they have no conflict of interest.

Acknowledgment

The authors would like to express their gratitude to the Kerman University of Medical Sciences (Kerman, Iran).

References

1. McCarthy J, Minsky ML, Rochester N, Shannon CE. A proposal for the dartmouth summer research project on artificial intelligence, august 31, 1955. AI magazine. 2006;27(4):12-.
2. LeCun Y, Bengio Y, Hinton G. Deep learning. Nature. 2015;521(7553):436-44.
3. Shitara K, Özgüroğlu M, Bang Y-J, Di Bartolomeo M, Mandalà M, Ryu M-H, Fornaro L, Olesiński T, Caglevic C, Chung HC. Pembrolizumab versus paclitaxel for previously treated, advanced gastric or gastro-oesophageal junction cancer (KEYNOTE-061): a randomised, open-label, controlled, phase 3 trial. The Lancet. 2018;392(10142):123-33.
4. Bhinder B, Gilvary C, Madhukar NS, Elemento O. Artificial Intelligence in Cancer Research and Precision Medicine. Cancer Discov. 2021;11(4):900-15.
5. Chen Z, Li X, Yang M, Zhang H, Xu XS. Optimization of deep learning models for the prediction of gene mutations using unsupervised clustering. J Pathol Clin Res. 2023;9(1):3-17.
6. Papadakis GZ, Karantanas AH, Tsiknakis M, Tsatsakis A, Spandidos DA, Marias K. Deep learning opens new horizons in personalized medicine. Biomed Rep. 2019;10(4):215-7.
7. Zhang S, Bamakan SMH, Qu Q, Li S. Learning for Personalized Medicine: A Comprehensive Review From a Deep Learning Perspective. IEEE Rev Biomed Eng. 2019;12:194-208.
8. Zeng J, Cruz-Pico CX, Saridogan T, Shufean MA, Kahle M, Yang D, Shaw K, Meric-Bernstam F. Natural Language Processing-Assisted Literature Retrieval and Analysis for Combination Therapy in Cancer. JCO Clin Cancer Inform. 2022;6:e2100109.
9.Kreimeyer K, Foster M, Pandey A, Arya N, Halford G, Jones SF, Forshee R, Walderhaug M, Botsis T. Natural language processing systems for capturing and standardizing unstructured clinical information: A systematic review. J Biomed Inform. 2017;73:14-29.
10. Vaishya R, Misra A, Vaish A. ChatGPT: Is this version good for healthcare and research? Diabetes Metab Syndr. 2023;17(4):102744.
11. Barretina J, Caponigro G, Stransky N, Venkatesan K, Margolin AA, Kim S, Wilson CJ, Lehár J, Kryukov GV, Sonkin D, Reddy A, Liu M, Murray L, Berger MF, Monahan JE, Morais P, Meltzer J, Korejwa A, Jané-Valbuena J, Mapa FA, Thibault J, Bric-Furlong E, Raman P, Shipway A, Engels IH, Cheng J, Yu GK, Yu J, Aspesi P, Jr., de Silva M, Jagtap K, Jones MD, Wang L, Hatton C, Palescandolo E, Gupta S, Mahan S, Sougnez C, Onofrio RC, Liefeld T, MacConaill L, Winckler W, Reich M, Li N, Mesirov JP, Gabriel SB, Getz G, Ardlie K, Chan V, Myer VE, Weber BL, Porter J, Warmuth M, Finan P, Harris JL, Meyerson M, Golub TR, Morrissey MP, Sellers WR, Schlegel R, Garraway LA. The Cancer Cell Line Encyclopedia enables predictive modelling of anticancer drug sensitivity. Nature. 2012;483(7391):603-7.
12. Menden MP, Iorio F, Garnett M, McDermott U, Benes CH, Ballester PJ, Saez-Rodriguez J. Machine learning prediction of cancer cell sensitivity to drugs based on genomic and chemical properties. PLoS One. 2013;8(4):e61318.
13. Liu M, Shen X, Pan W. Deep reinforcement learning for personalized treatment recommendation. Stat Med. 2022;41(20):4034-56.
14. Yang CY, Shiranthika C, Wang CY, Chen KW, Sumathipala S. Reinforcement learning strategies in cancer chemotherapy treatments: A review. Comput Methods Programs Biomed. 2023;229:107280.
15. Chiu YC, Zheng S, Wang LJ, Iskra BS, Rao MK, Houghton PJ, Huang Y, Chen Y. Predicting and characterizing a cancer dependency map of tumors with deep learning. Sci Adv. 2021;7(34).
16. Wainberg M, Merico D, Delong A, Frey BJ. Deep learning in biomedicine. Nat Biotechnol. 2018;36(9):829-38.
17. Meyer P, Noblet V, Mazzara C, Lallement A. Survey on deep learning for radiotherapy. Comput Biol Med. 2018;98:126-46.
18. Chen ZH, Lin L, Wu CF, Li CF, Xu RH, Sun Y. Artificial intelligence for assisting cancer diagnosis and treatment in the era of precision medicine. Cancer Commun (Lond). 2021;41(11):1100-15.
19. Bi WL, Hosny A, Schabath MB, Giger ML, Birkbak NJ, Mehrtash A, Allison T, Arnaout O, Abbosh C, Dunn IF, Mak RH, Tamimi RM, Tempany CM, Swanton C, Hoffmann U, Schwartz LH, Gillies RJ, Huang RY, Aerts H. Artificial intelligence in cancer imaging: Clinical challenges and applications. CA Cancer J Clin. 2019;69(2):127-57.
20. Krizhevsky A, Sutskever I, Hinton GE. ImageNet classification with deep convolutional neural networks. Communications of the ACM. 2017;60(6):84-90.
21. Esteva A, Kuprel B, Novoa RA, Ko J, Swetter SM, Blau HM, Thrun S. Dermatologist-level classification of skin cancer with deep neural networks. Nature. 2017;542(7639):115-8.
22. Cohen JD, Li L, Wang Y, Thoburn C, Afsari B, Danilova L, Douville C, Javed AA, Wong F, Mattox A, Hruban RH, Wolfgang CL, Goggins MG, Dal Molin M, Wang TL, Roden R, Klein AP, Ptak J, Dobbyn L, Schaefer J, Silliman N, Popoli M, Vogelstein JT, Browne JD, Schoen RE, Brand RE, Tie J, Gibbs P, Wong HL, Mansfield AS, Jen J, Hanash SM, Falconi M, Allen PJ, Zhou S, Bettegowda C, Diaz LA, Jr., Tomasetti C, Kinzler KW, Vogelstein B, Lennon AM, Papadopoulos N. Detection and localization of surgically resectable cancers with a multi-analyte blood test. Science. 2018;359(6378):926-30.
23. Ciompi F, Chung K, van Riel SJ, Setio AAA, Gerke PK, Jacobs C, Scholten ET, Schaefer-Prokop C, Wille MMW, Marchianò A, Pastorino U, Prokop M, van Ginneken B. Towards automatic pulmonary nodule management in lung cancer screening with deep learning. Sci Rep. 2017;7:46479.
24. Kang G, Liu K, Hou B, Zhang N. 3D multi-view convolutional neural networks for lung nodule classification. PLoS One. 2017;12(11):e0188290.
25. Zhao W, Yang J, Sun Y, Li C, Wu W, Jin L, Yang Z, Ni B, Gao P, Wang P, Hua Y, Li M. 3D Deep Learning from CT Scans Predicts Tumor Invasiveness of Subcentimeter Pulmonary Adenocarcinomas. Cancer Res. 2018;78(24):6881-9.

26. Anthimopoulos M, Christodoulidis S, Ebner L, Christe A, Mougiakakou S. Lung Pattern Classification for Interstitial Lung Diseases Using a Deep Convolutional Neural Network. IEEE Trans Med Imaging. 2016;35(5):1207-16.
27. Yuan Z, Xu T, Cai J, Zhao Y, Cao W, Fichera A, Liu X, Yao J, Wang H. Development and Validation of an Image-based Deep Learning Algorithm for Detection of Synchronous Peritoneal Carcinomatosis in Colorectal Cancer. Ann Surg. 2022;275(4):e645-e51.
28. Wang X, Yang W, Weinreb J, Han J, Li Q, Kong X, Yan Y, Ke Z, Luo B, Liu T, Wang L. Searching for prostate cancer by fully automated magnetic resonance imaging classification: deep learning versus non-deep learning. Sci Rep. 2017;7(1):15415.
29. Neisius U, El-Rewaidy H, Nakamori S, Rodriguez J, Manning WJ, Nezafat R. Radiomic Analysis of Myocardial Native T(1) Imaging Discriminates Between Hypertensive Heart Disease and Hypertrophic Cardiomyopathy. JACC Cardiovasc Imaging. 2019;12(10):1946-54.
30. van Timmeren JE, Cester D, Tanadini-Lang S, Alkadhi H, Baessler B. Radiomics in medical imaging—"how-to" guide and critical reflection. Insights into Imaging. 2020;11(1):91.
31. Wentzensen N, Lahrmann B, Clarke MA, Kinney W, Tokugawa D, Poitras N, Locke A, Bartels L, Krauthoff A, Walker J, Zuna R, Grewal KK, Goldhoff PE, Kingery JD, Castle PE, Schiffman M, Lorey TS, Grabe N. Accuracy and Efficiency of Deep-Learning-Based Automation of Dual Stain Cytology in Cervical Cancer Screening. J Natl Cancer Inst. 2021;113(1):72-9.
32. Wang P, Berzin TM, Glissen Brown JR, Bharadwaj S, Becq A, Xiao X, Liu P, Li L, Song Y, Zhang D, Li Y, Xu G, Tu M, Liu X. Real-time automatic detection system increases colonoscopic polyp and adenoma detection rates: a prospective randomised controlled study. Gut. 2019;68(10):1813-9.
33. Ehteshami Bejnordi B, Veta M, Johannes van Diest P, van Ginneken B, Karssemeijer N, Litjens G, van der Laak J, Hermsen M, Manson QF, Balkenhol M, Geessink O, Stathonikos N, van Dijk MC, Bult P, Beca F, Beck AH, Wang D, Khosla A, Gargeya R, Irshad H, Zhong A, Dou Q, Li Q, Chen H, Lin HJ, Heng PA, Haß C, Bruni E, Wong Q, Halici U, Öner M, Cetin-Atalay R, Berseth M, Khvatkov V, Vylegzhanin A, Kraus O, Shaban M, Rajpoot N, Awan R, Sirinukunwattana K, Qaiser T, Tsang YW, Tellez D, Annuscheit J, Hufnagl P, Valkonen M, Kartasalo K, Latonen L, Ruusuvuori P, Liimatainen K, Albarqouni S, Mungal B, George A, Demirci S, Navab N, Watanabe S, Seno S, Takenaka Y, Matsuda H, Ahmady Phoulady H, Kovalev V, Kalinovsky A, Liauchuk V, Bueno G, Fernandez-Carrobles MM, Serrano I, Deniz O, Racoceanu D, Venâncio R. Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer. Jama. 2017;318(22):2199-210.
34. Singhal N, Soni S, Bonthu S, Chattopadhyay N, Samanta P, Joshi U, Jojera A, Chharchhodawala T, Agarwal A, Desai M, Ganpule A. A deep learning system for prostate cancer diagnosis and grading in whole slide images of core needle biopsies. Sci Rep. 2022;12(1):3383.
35. Lu MY, Chen TY, Williamson DFK, Zhao M, Shady M, Lipkova J, Mahmood F. AI-based pathology predicts origins for cancers of unknown primary. Nature. 2021;594(7861):106-10.
36. Montalban-Bravo G, Garcia-Manero G. Myelodysplastic syndromes: 2018 update on diagnosis, risk-stratification and management. American journal of hematology. 2018;93(1):129-47.
37. Brück OE, Lallukka-Brück SE, Hohtari HR, Ianevski A, Ebeling FT, Kovanen PE, Kytölä SI, Aittokallio TA, Ramos PM, Porkka KV, Mustjoki SM. Machine Learning of Bone Marrow Histopathology Identifies Genetic and Clinical Determinants in Patients with MDS. Blood Cancer Discov. 2021;2(3):238-49.
38. Syrykh C, Abreu A, Amara N, Siegfried A, Maisongrosse V, Frenois FX, Martin L, Rossi C, Laurent C, Brousset P. Accurate diagnosis of lymphoma on whole-slide histopathology images using deep learning. NPJ Digit Med. 2020;3:63.
39. Kather JN, Heij LR, Grabsch HI, Loeffler C, Echle A, Muti HS, Krause J, Niehues JM, Sommer KAJ, Bankhead P, Kooreman LFS, Schulte JJ, Cipriani NA, Buelow RD, Boor P, Ortiz-Brüchle N, Hanby AM, Speirs V, Kochanny S, Patnaik A, Srisuwananukorn A, Brenner H, Hoffmeister M, van den Brandt PA, Jäger D, Trautwein C, Pearson AT, Luedde T. Author Correction: Pan-cancer image-based detection of clinically actionable genetic alterations. Nat Cancer. 2020;1(11):1129.
40. Coudray N, Ocampo PS, Sakellaropoulos T, Narula N, Snuderl M, Fenyö D, Moreira AL, Razavian N, Tsirigos A. Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning. Nat Med. 2018;24(10):1559-67.
41. Yamashita R, Long J, Longacre T, Peng L, Berry G, Martin B, Higgins J, Rubin DL, Shen J. Deep learning model for the prediction of microsatellite instability in colorectal cancer: a diagnostic study. Lancet Oncol. 2021;22(1):132-41.
42. Courtiol P, Maussion C, Moarii M, Pronier E, Pilcer S, Sefta M, Manceron P, Toldo S, Zaslavskiy M, Le Stang N, Girard N, Elemento O, Nicholson AG, Blay JY, Galateau-Sallé F, Wainrib G, Clozel T. Deep learning-based classification of mesothelioma improves prediction of patient outcome. Nat Med. 2019;25(10):1519-25.
43. Bychkov D, Linder N, Turkki R, Nordling S, Kovanen PE, Verrill C, Walliander M, Lundin M, Haglund C, Lundin J. Deep learning based tissue analysis predicts outcome in colorectal cancer. Sci Rep. 2018;8(1):3395.
44. Timmerman L. What's in a name? A lot, when it comes to'precision medicine'. Xconomy. 2013.
45. Johannet P, Coudray N, Donnelly DM, Jour G, Illa-Bochaca I, Xia Y, Johnson DB, Wheless L, Patrinely JR, Nomikou S, Rimm DL, Pavlick AC, Weber JS, Zhong J, Tsirigos A, Osman I. Using Machine Learning Algorithms to Predict Immunotherapy Response in Patients with Advanced Melanoma. Clin Cancer Res. 2021;27(1):131-40.
46. Liu D, Schilling B, Liu D, Sucker A, Livingstone E, Jerby-Arnon L, Zimmer L, Gutzmer R, Satzger I, Loquai C, Grabbe S, Vokes N, Margolis CA, Conway J, He MX, Elmarakeby H, Dietlein F, Miao D, Tracy A, Gogas H, Goldinger SM, Utikal J, Blank CU, Rauschenberg R, von Bubnoff D, Krackhardt A, Weide B, Haferkamp S, Kiecker F, Izar B, Garraway L, Regev A, Flaherty K, Paschen A, Van Allen EM, Schadendorf D. Author Correction: Integrative molecular and clinical modeling of clinical outcomes to PD1 blockade in patients with metastatic melanoma. Nat Med. 2020;26(7):1147.
47. Qiang M, Li C, Sun Y, Sun Y, Ke L, Xie C, Zhang T, Zou Y, Qiu W, Gao M, Li Y, Li X, Zhan Z, Liu K, Chen X, Liang C, Chen Q, Mai H, Xie G, Guo X, Lv X. A Prognostic Predictive System Based on Deep Learning for Locoregionally Advanced Nasopharyngeal Carcinoma. J Natl Cancer Inst. 2021;113(5):606-15.
48.Peng H, Dong D, Fang MJ, Li L, Tang LL, Chen L, Li WF, Mao YP, Fan W, Liu LZ, Tian L, Lin AH, Sun Y, Tian J, Ma J. Prognostic Value of Deep Learning PET/CT-Based Radiomics: Potential Role for Future Individual Induction Chemotherapy in Advanced Nasopharyngeal Carcinoma. Clin Cancer Res. 2019;25(14):4271-9.
49. Huynh BQ, Antropova N, Giger ML, editors. Comparison of breast DCE-MRI contrast time points for predicting response to neoadjuvant chemotherapy using deep convolutional neural network features with transfer learning. Medical imaging 2017: computer-aided diagnosis; 2017: SPIE.

50. Ha R, Chin C, Karcich J, Liu MZ, Chang P, Mutasa S, Pascual Van Sant E, Wynn RT, Connolly E, Jambawalikar S. Prior to Initiation of Chemotherapy, Can We Predict Breast Tumor Response? Deep Learning Convolutional Neural Networks Approach Using a Breast MRI Tumor Dataset. J Digit Imaging. 2019;32(5):693-701.
51. Shi L, Zhang Y, Nie K, Sun X, Niu T, Yue N, Kwong T, Chang P, Chow D, Chen JH, Su MY. Machine learning for prediction of chemoradiation therapy response in rectal cancer using pre-treatment and mid-radiation multi-parametric MRI. Magn Reson Imaging. 2019;61:33-40.
52. Sun C, Li B, Wei G, Qiu W, Li D, Li X, Liu X, Wei W, Wang S, Liu Z, Tian J, Liang L. Deep learning with whole slide images can improve the prognostic risk stratification with stage III colorectal cancer. Comput Methods Programs Biomed. 2022;221:106914.
53. Sahiner B, Pezeshk A, Hadjiiski LM, Wang X, Drukker K, Cha KH, Summers RM, Giger ML. Deep learning in medical imaging and radiation therapy. Med Phys. 2019;46(1):e1-e36.
54. Kline TL, Korfiatis P, Edwards ME, Blais JD, Czerwiec FS, Harris PC, King BF, Torres VE, Erickson BJ. Performance of an Artificial Multi-observer Deep Neural Network for Fully Automated Segmentation of Polycystic Kidneys. J Digit Imaging. 2017;30(4):442-8.
55. Hu P, Wu F, Peng J, Liang P, Kong D. Automatic 3D liver segmentation based on deep learning and globally optimized surface evolution. Phys Med Biol. 2016;61(24):8676-98.
56. Men K, Dai J, Li Y. Automatic segmentation of the clinical target volume and organs at risk in the planning CT for rectal cancer using deep dilated convolutional neural networks. Med Phys. 2017;44(12):6377-89.
57. van Rooij W, Dahele M, Ribeiro Brandao H, Delaney AR, Slotman BJ, Verbakel WF. Deep Learning-Based Delineation of Head and Neck Organs at Risk: Geometric and Dosimetric Evaluation. Int J Radiat Oncol Biol Phys. 2019;104(3):677-84.
58. Liang S, Tang F, Huang X, Yang K, Zhong T, Hu R, Liu S, Yuan X, Zhang Y. Deep-learning-based detection and segmentation of organs at risk in nasopharyngeal carcinoma computed tomographic images for radiotherapy planning. Eur Radiol. 2019;29(4):1961-7.
59. Ibragimov B, Xing L. Segmentation of organs-at-risks in head and neck CT images using convolutional neural networks. Med Phys. 2017;44(2):547-57.
60. Lin L, Dou Q, Jin YM, Zhou GQ, Tang YQ, Chen WL, Su BA, Liu F, Tao CJ, Jiang N, Li JY, Tang LL, Xie CM, Huang SM, Ma J, Heng PA, Wee JTS, Chua MLK, Chen H, Sun Y. Deep Learning for Automated Contouring of Primary Tumor Volumes by MRI for Nasopharyngeal Carcinoma. Radiology. 2019;291(3):677-86.
61. Fan J, Wang J, Chen Z, Hu C, Zhang Z, Hu W. Automatic treatment planning based on three-dimensional dose distribution predicted from deep learning technique. Med Phys. 2019;46(1):370-81.
62. Ibragimov B, Toesca D, Chang D, Yuan Y, Koong A, Xing L. Development of deep neural network for individualized hepatobiliary toxicity prediction after liver SBRT. Med Phys. 2018;45(10):4763-74.
63. Valdes G, Solberg TD, Heskel M, Ungar L, Simone CB, 2nd. Using machine learning to predict radiation pneumonitis in patients with stage I non-small cell lung cancer treated with stereotactic body radiation therapy. Phys Med Biol. 2016;61(16):6105-20.
64. Maspero M, Savenije MHF, Dinkla AM, Seevinck PR, Intven MPW, Jurgenliemk-Schulz IM, Kerkmeijer LGW, van den Berg CAT. Dose evaluation of fast synthetic-CT generation using a generative adversarial network for general pelvis MR-only radiotherapy. Phys Med Biol. 2018;63(18):185001.
65. Liu Y, Lei Y, Wang Y, Wang T, Ren L, Lin L, McDonald M, Curran WJ, Liu T, Zhou J, Yang X. MRI-based treatment planning for proton radiotherapy: dosimetric validation of a deep learning-based liver synthetic CT generation method. Phys Med Biol. 2019;64(14):145015.
66. Madesta F, Sentker T, Gauer T, Werner R. Self-contained deep learning-based boosting of 4D cone-beam CT reconstruction. Med Phys. 2020;47(11):5619-31.
67. Terpstra ML, Maspero M, d'Agata F, Stemkens B, Intven MPW, Lagendijk JJW, van den Berg CAT, Tijssen RHN. Deep learning-based image reconstruction and motion estimation from undersampled radial k-space for real-time MRI-guided radiotherapy. Phys Med Biol. 2020;65(15):155015.