https://doi.org/ 10.48047/AFJBS.6.5.2024. 9075-9090

African Journal of Biological Sciences

THE RISE OF AI IN ONCOLOGY – THE POWER OF AI IN DETECTING, TREATING AND CURING CANCER- NARRATIVE REVIEW

[1]Dr G.Nadeswari*, [2]Dr C. Pradeep , [3]Dr Parul Tikoo, [4]Dr Shabeena SultanaShaik, [5]Dr.Jennifer Christian ,[6] Dr. Swetha .T

1. MD Pathology, Consultant Pathologist,Aster Narayanadri Hospital,Tirupati, AndhraPradesh, India, Email-nadeswari.guntupalli@gmail.com
2. MDS Prosthodontist & Oral Implantologist , Clinical Director, Dentistrybytes,Tamil Nadu, India, Email- bkpradeep22@gmail.com
3. Senior Lecturer , MDS (oral medicine and radiology) ITS Dental College Muradnagar, India, Email- parultikko7@gmail.com
4. BDS, FMC Dental Surgeon, Hyderabad, India, Email- shabina3693@gmail.com
5. Medical Officer Dental,GMERS Medical College attached General Hospital,Gandhinagar,Gujarat, India, Email- Jen.333.christ@gmail.com
6. MDS (Oral and maxillofacial surgery), FAM (Medical cosmetologist), FCLCP (Fellow inCleft lip and cleft palate surgeries), Tamil Nadu, India, Email- drswetha25@gmail.com

Article History
Volume 6, Issue 5, 2024
Received: 15 May 2024
Accepted: 02 Jun 2024
doi: *10.48047/AFJBS.6.5.2024. 9075-9090*

ABSTRACT

Cancer remains a formidable foe, claiming millions of lives globally each year. However, a new wave of innovation is emerging on the horizon, wielding the power of artificial intelligence (AI). This narrative review delves into the burgeoning field of AI in oncology, exploring its transformative potential in detecting, treating, and even curing cancer.

Artificial intelligence is increasingly being used in oncology, particularly in cancer diagnostics and computer vision. Applications are being developed across the cancer continuum and multidisciplinary practice. However, ethical and legal considerations limit their widespread application and reproducibility, including inherent bias when trained with underrepresented data sets. Barriers to widespread adoption include ideological and workflow concerns, limited prospective validation studies, and ideological and workflow concerns. The future of precision oncology may see the use of living databases of multimodal data types improving clinical models.

Continuous or semicontinuous algorithm training is essential for achieving new degrees of medical personalization in the future. This technology may extend life and enable more cures in hyper individualized cancer screening and prevention strategies, systemic cancer therapeutics and radiation, restaging and surveillance testing, and diagnostic and treatment interventions.

KEYWORDS - Artificial intelligence (AI) ,Machine learning (ML) , Precision oncology Clinical decision support (CDS, Image analysis, Genomics, Generative A

INTRODUCTION AND BACKGROUND

Cancer, a relentless adversary, continues to cast a long shadow, with an estimated 19.3 million new cases and nearly 10 million deaths projected worldwide in 2020 according to the World Health Organization (WHO) [1]. However, a beacon of hope emerges from the realm of artificial intelligence (AI). Personalised clinical care and cancer research are rapidly changing due to artificial intelligence (AI). The availability of high-dimensionality datasets, improvements in high-performance computing, and novel deep learning architectures have all contributed to the rise in the application of AI in oncology research. Molecular characterization of tumours and their microenvironment, drug discovery and repurposing, cancer detection and classification, and patient treatment outcome prediction are just a few of these applications [2].

Recent advancements are fueling optimism. A 2023 report from McKinsey & Company estimates that AI has the potential to generate up to $3 trillion per year in value for the healthcare sector by 2 030, with a significant portion likely impacting oncology [3]. This economic impact reflects the potential for AI to improve efficiency and potentially save lives.

Moreover, a 2022 study published in Nature Reviews Cancer highlights the tangible benefits of AI in specific areas. Researchers report that AI algorithms can outperform traditional methods in identifying subtle tumor patterns on mammograms, potentially leading to earlier diagnoses and better patient outcomes for breast cancer [4].

Cancer early detection is still a major global challenge. Effective screening programmes do not include all at-risk groups and are constrained by public support, funding, etc [5]. Expanding screening programmes without an evidence-based recommendation, however, can result in a large financial burden and waste money in health systems with limited resources [6].

With increased therapeutic ratio and lower doses to normal tissue, high precision image-guided radiotherapy (RT) has improved patient outcomes. However, there is still a chance that some patients will experience severe side effects.The potential for tumour control and cure is often restricted in clinical settings due to the radiation tolerance of normal tissues in close proximity to the target volume. This limits the safe dose that can be administered [7].

Patients in developed countries receive a cytological or histological diagnosis of their disease, with the diagnosis ranging from benign to (pre)malignant. This accounts for an estimated 0.2% of global healthcare costs [8].

The type, grade, and other prognostic factors of (pre)malignant diseases are determined; these provide details about the cancer stage, whether the tumour has been completely removed, potential therapeutic targets, and whether the disease may run in the family. With the use of all this data, medical professionals can determine the best course of action for each patient, which may include surgery, radiation, systemic therapies such as endocrine and chemotherapy, targeted and immunotherapy, and more [4,6,7].

Even though pathology diagnoses are typically useful and trustworthy, reproducibility problems or misdiagnosis can occur when interpreting morphological patterns visually. For instance, there is a great deal of variation in the grading of breast and prostate cancer between and within laboratories, which has an impact on treatment [9].

AI systems are approved for clinical use in some tumor types, including liver cancer. Research shows AI can analyze histopathology, radiology, and natural language, replacing manual tasks and accessing hidden information. However, few applications have been large-scale clinical trials or approved products. The authors advocate for AI incorporation in all stages of liver cancer management, presenting a taxonomy of AI approaches and outlines a policy for AI-based management, including interdisciplinary training [10].

Recent developments have significantly improved AI's ability to automatically gather and record cancer data, including diagnosis dates, treatment responses, and tumor characteristics. This automation streamlines the creation of complex cancer databases, which can then be used to develop even more powerful AI models [11] .This review goes beyond basic definitions, exploring the diverse ways AI is being implemented in cancer care. This includes drug discovery, analyzing tumor profiles, and providing clinical decision support systems for doctors[12]. The future of AI in oncology even extends to patient-facing chatbots, augmented reality surgical visualization tools, and hospital scheduling systems. In essence, the review emphasizes the potential of AI to revolutionize cancer care by focusing on technologies and algorithms that have a direct impact on patients[13].

REVIEW

This review comprehensively analyzed published articles exploring the potential of artificial intelligence (AI) in various aspects of oncology. To ensure a thorough investigation, we conducted a meticulous search across reputable databases like PubMed and Google Scholar. Our search strategy incorporated a combination of keywords such as "artificial intelligence," "machine learning," "cancer diagnosis," "cancer treatment," and "oncology." This multifaceted approach aimed to capture all relevant research on AI applications within the field. Following the initial search, we meticulously selected 53 articles demonstrating significant relevance for in-depth review. By analyzing these articles, this review endeavors to illustrate the burgeoning field of AI in oncology, highlighting its potential to revolutionize cancer detection, treatment, and overall patient care.

AI Eyes on Cancer: How Machines are Revolutionizing Imaging Diagnosis

Radiology and pathology are two medical specialties that benefit greatly from the application of artificial intelligence [14]. AI is being used in radiology for a variety of purposes, particularly in the analysis of radiological data obtained during routine cancer care through the use of DL algorithms for disease classification, detection, segmentation, characterization, and monitoring[15,16].

In studies involving cancer screening, image classification is essential. AI can assist radiologists in classifying small lesions, improving results, and saving time. Better organisational workflow can also be created with its assistance (e.g., determining a high priority group of reports to be reviewed and reported)[17]. Research has demonstrated that the integration of artificial intelligence and human labour enhances mammography screening for breast cancer[18].

Using bounding boxes, AI can help identify malignant lesions, such as lung nodules or brain metastases. By helping doctors interpret medical images, this technology improves their ability to detect[19]. AI is also useful for segmentation, which is the process of grouping individual pixels based on organs or lesions (like brain gliomas) in order to improve prognostication, risk assessment, and management [20]. Through the extraction of undetectable features from medical images, deep learning techniques may be able to identify patterns and characteristics of disease. Combining these with clinicogenomic data is of increasing interest to the field of radiomics, which studies these features[21]. Radiomics can be used to treat a variety of cancers, including lung, brain, and liver tumours. Similar to skilled neuroradiologists, deep learning using radiomic features from brain MRI can distinguish between brain gliomas and brain metastases[22]. AI can significantly change cancer monitoring by detecting discriminative features in imaging unreadable by humans [23].

AI-based imaging algorithms are being used in clinical practice to identify and track cancerous lesions, guiding management[24]. A U.S. Food and Drug Administration-approved software program allows comprehensive detection of pulmonary nodules, lung malignancy prediction, and management guidelines incorporation[25]. Deep neural networks are also used to detect enlarged lymph nodes or colonic polyps in CT images and improve colon polyp detection during colonoscopy. Augmented interpretation of endoscopic images consistently improves esophageal cancer detection accuracy[26].

Image Analysis in Oral Squamous Cell Carcinoma

In digital pathology, automatic segmentation of digitized histological images plays a crucial role in developing tools for diagnosis, prognosis, and treatment. This technique involves computational analysis of the images, where pixels with similar color and intensity are grouped together. These groupings likely correspond to specific structures within the tissue, such as cells, blood vessels, and other components. By analyzing the shapes and sizes of these segmented regions, researchers can extract valuable qualitative and quantitative data about the underlying tissue characteristics [27,28].

StarDist utilizes a unique approach based on star-convex polygons to effectively represent the round shape of cell nuclei [29]. This innovative method allows it to process various image formats, including the standard H&E staining used in histology and fluorescence microscopy images specifically highlighting nuclei. By accurately defining nuclear regions, StarDist enables the extraction of several morphological parameters related to the shape of the nucleus. Additionally, it facilitates the analysis of nuclear density and condensation.

AI-based analysis of oral lesions using novel deep convolutional neural networks for early detection of oral cancer[30] shown in the **Figure 1**

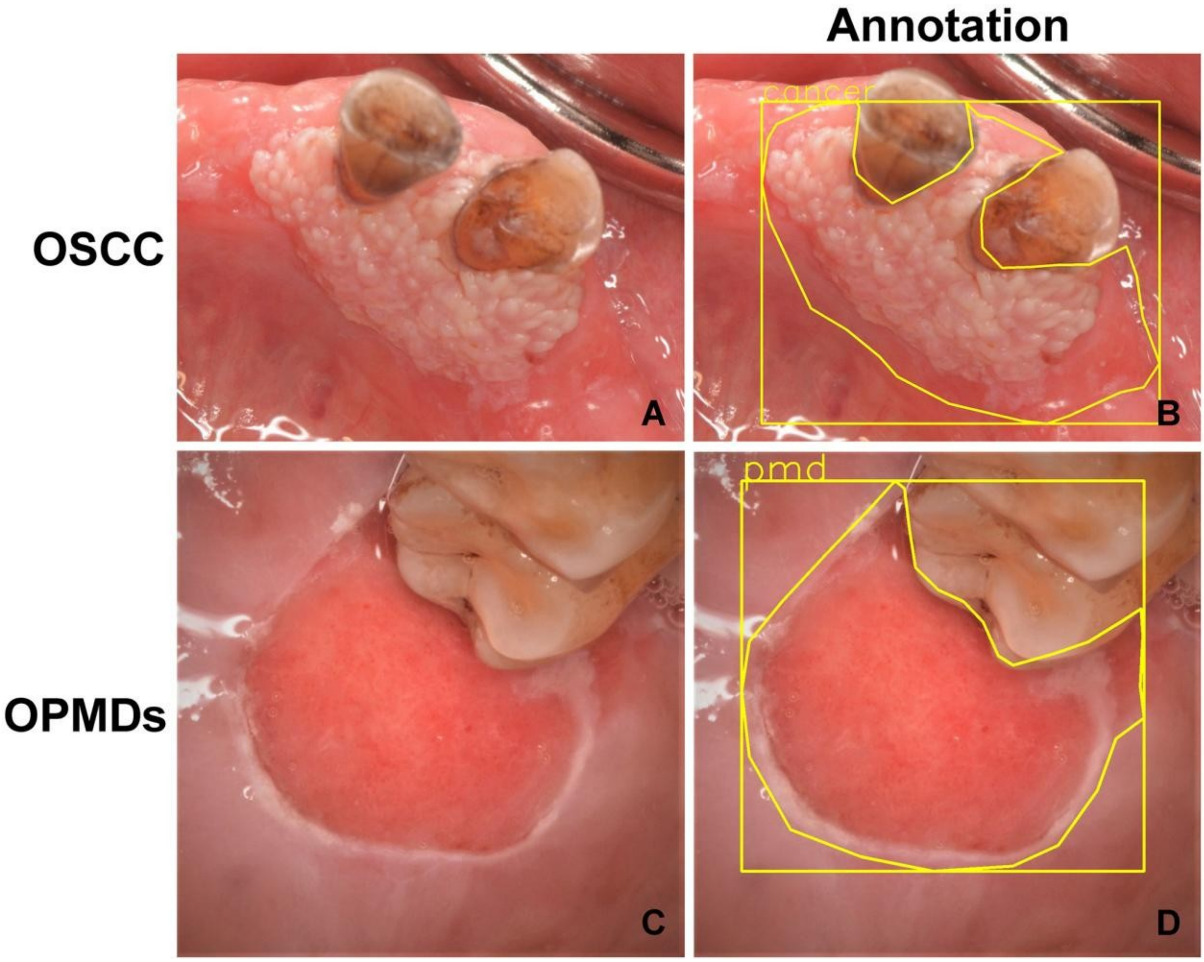

Figure 1 Examples of the oral squamous cell carcinoma (OSCC) and oral potentially malignant disorders (OPMDs) images from the dataset showing. (A) OSCC image; (B) annotation of OSCC image by surgeons; (C) OPMDs image; (D) annotation of OPMDs image by surgeons [30].

Permission has been obtained from the original publisher for the re-publication of this figure [30]

AI in oncology research

Open-source healthcare statistics have enabled researchers to develop tools for cancer identification and prognosis. Deep learning and machine learning models offer efficient solutions on distributed datasets, with advanced-federated learning models being deployed for data analysis. Oncology heavily relies on evidence-based systems for cancer-risk assessment, diagnosis, prognostic tracking, treatment, and surveillance monitoring [27].Algorithm-based AI is expected to shift towards radiological image interpretation, EHRs, and data mining for more precise cancer therapy. The cost-savings from intelligent AI applications in the US healthcare sector are estimated to reach $52 billion in 2021 [28]. The effectiveness of AI intervention in cancer research depends on proper data for developing ML and DL models. The future of digital healthcare and clinical practices is expected to shift towards algorithm-based AI for more precise cancer therapy[28-31]. **Figure2** depicts the AI in oncology research .

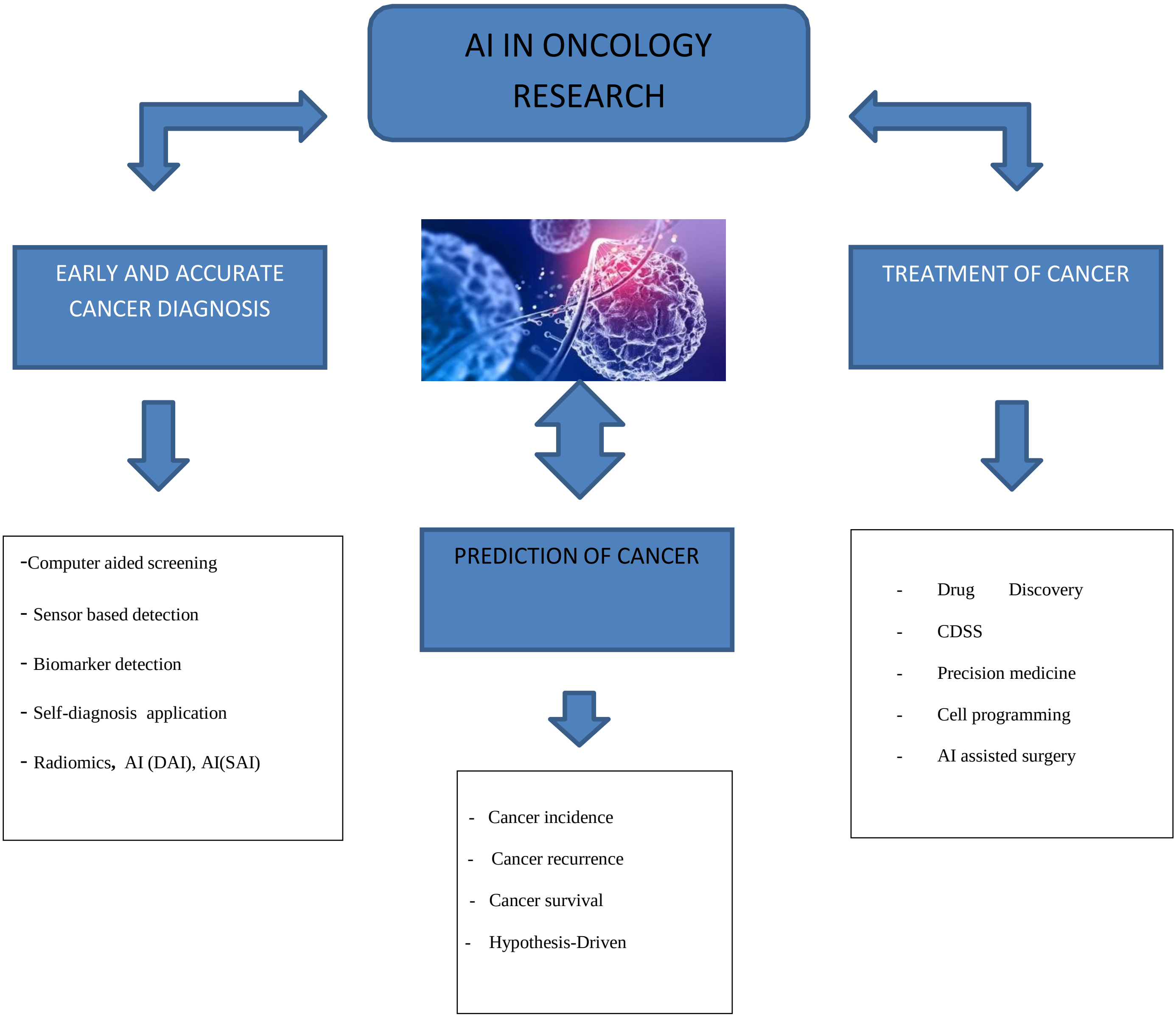

Figure 2 AI in oncology research [28-31]

Hypothesis-Driven Artificial Intelligence

Hypothesis-driven AI is a new class of AI algorithm that uses big omics data to understand the complex causes of cancer. It has applications in oncology, tumor classification, patient stratification, cancer gene discovery, drug response prediction, and tumor spatial organization [32] .This approach offers a targeted, informed approach, focusing on specific hypotheses and reducing computational resources. It encourages domain-specific knowledge integration and validates hypotheses through thought experiments. AI tools can improve patient outcomes by transforming complex data into early-stage cancer patterns, prioritizing actionable genomic alterations, and validating hypotheses about tumor heterogeneity and acquired resistance [33].

Tumor classification is crucial for clinicians to understand the type and stage of a tumor and treatment plans. One challenge is classifying cancers of unknown primary (CUP) origin, which account for 3-5% of all cancers worldwide. Pathology assessment is often lacking for these tumors, making it difficult to determine primary cancer types. Currently, targeted therapies for CUPs are lacking[34]. To address this, Moon et al. developed the Oncology NGS-based Primary Cancer-Type Classifier (OncoNPC, 2023), an XGBoost-based classifier. Their key hypothesis is that genomic signatures, age, and sex of patients encode the information needed for accurate classification. They trained OncoNPC on targeted next-generation sequencing (NGS) from 36,445 tumors across 22 cancers to identify specific cancer types and unknown primary tumor cancer types [35].

Generative AI (GAI) has the potential to revolutionize cancer research by incorporating hypothesis-driven AI models. GANs, a generative model, can simulate realistic biological data, such as genomic and imaging data, making them valuable when access to large datasets is limited. In cancer research, GANs can generate synthetic patient cohorts, increasing the robustness and generalizability of current predictive AI models. GANs can also simulate the evolution of cancer over time, providing insights into dynamic changes in tumor biology and aiding in the development of personalized treatment strategies. GAI can encapsulate gene-gene pairs that modulate drug response phenotypes, advancing our understanding of phenotypic behaviors in cancer cells [36].

Hypothesis-driven AI is a new class of AI algorithms that has the potential to overcome challenges in oncology research. Unlike conventional AI, this approach requires ingenuity, creativity, innovation, and careful selection of domain knowledge. It allows researchers to formulate hypothetical modes of gene-gene or gene-pathways associations underpinning cancer etiology and develop learning algorithms to validate these hypotheses[37]. This approach can lead to the discovery of novel gene-gene and gene-pathway associations, which are often overlooked by conventional AI. By aligning computational methodologies with well-informed hypotheses, hypothesis-driven AI offers a targeted and informed approach to issues ranging from tumor detection to drug targeting [38].

Automated total body mapping (ATBM)

A prospective study has validated the use of automated total body mapping (ATBM) with automated lesions detection in 2D total body imaging (TBP) for dermatologists to detect melanoma. The study found that most clinically relevant lesions were correctly identified and segmented by the detection software. The main reasons for undetected melanoma (CRML) were addressed by avoiding occlusion during imaging and improving lesion detection and segmentation algorithms. The findings are crucial for the application of deep learning-based algorithms for diagnosing lesions. The study highlights the feasibility of automated lesion detection in TBP images, which is relevant for developing AI-based skin cancer screenings [39].

AI , Virtual Reality(VR) and Radiomics

AI models have been successfully integrated into brain tumor diagnosis, prognosis, and treatment, but challenges persist, such as limited access to high-quality data, interpretability and explanationability concerns, and generalizability across diverse populations and tumor types. The reproducibility of radiomic-based features is also challenging due to variations in image acquisition parameters. The introduction of the radiomic quality score (RQS) has been pivotal in standardizing radiomics. Despite the importance of external validation, only 29.4% of original studies included external validation. Racial disparities in brain tumor management introduce complex dynamics shaped by race, socioeconomic variables, and geographical influences. Addressing these disparities in AI-based methods is crucial for advancing cancer care. Additionally, disparities in brain tumor rates and outcomes, particularly in glioblastoma, manifest differently between males and females, emphasizing the need for AI-based approaches to factor in sex-related influences across incidence, survival, tumor biology, genetics, treatment response, and prognosis [40].

The use of Virtual Reality (VR) for preoperative evaluation in lung cancer surgery is limited. However, studies have shown that VR can improve decision-making and surgical planning in challenging cases. Frajhof et al.[41] evaluated VR as a tool to improve surgical planning in a challenging video-assisted thoracoscopic surgery case. Perkins et al[42]. developed a mixed-reality tool that provided 3D visualization of lung structures and allowed for interaction with the model to simulate lung deflation and surgical instrument placement. Tokuno et al. [43]developed a dynamic simulation system for anatomic pulmonary resection, which can mimic the deformation of lung structures. Ujiie et al.[44] developed a VR navigation tool with head-mounted displays that generated virtual dynamic images based on patient-specific CT for lung segmentectomy. Sadeghi et al.[45] conducted a pilot study in 10 patients, assessing the clinical applicability of their AI-based 3D VR platform for lung segmentectomy. Backius et al[46] confirmed this trend in a cohort of 50 patients undergoing pulmonary segmentectomy, observing an adjustment in the surgical plan in 52% of patients after VR visualization compared to CT scan evaluation only.

A study[47] aimed to develop an automatic learning algorithm to predict survival in children with malignant disorders undergoing hematopoietic stem cell transplantation (HSCT). The researchers analyzed allogenic HSCTs performed on children between 1991 and 2021, analyzing survival using Kaplan-Meier, log-rank test, and Cox regression. They constructed a prognostic index and a predictive model using a random forest algorithm to forecast 1-year survival. The prognostic index was associated with 3-year overall survival, while the random forest model achieved 72% accuracy.

AI radiomics has shown promising potential in predicting the response to systemic therapies, particularly for sorafenib, the earliest tyrosine kinase inhibitor (TKI) approved as a first-line treatment for advanced HCC.[48] Recent studies [49]have shown that ML radiomic analysis based on CECT can predict somatic mutations related to sorafenib response, β-arrestin1 phosphorylation, and early response to combined sorafenib and NK cell therapy in HCC. Radiomic features extracted from skeletal muscle and adipose tissue also exhibited potential in predicting the 1-year survival of HCC patients receiving sorafenib monotherapy or selective internal radiation therapy (SIRT) combined with sorafenib.[50].

AI radiomics can also predict the expression of immunotherapy-related targets and the efficacy of immunotherapy. CT-based radiomic models, such as the contrastive learning network (CLNet), can predict the expression of PD-1 and PD-L1 and can help identify potential candidates for immunotherapy. CECT-based radiomics can also help predict the response to anti-PD-1 therapies in patients with advanced HCC and guide individualized treatment plans [51,52].

Limitation & Future Direction

Artificial intelligence (AI) in oncology has proven to be more effective than expert opinion-based scoring systems in cancer applications, leading to increased clinical implementation. As the field matures, AI-informed methods will continue to be explored and integrated into practice. Combining molecular data with whole-electronic health records (EHR) data elements can help explain observable biologic phenomena, leading to a more organic synthesis of health information. Cancer has the largest number of clinically relevant mutations and the most multimodality treatment options, making it the most need for individualized care.

A future AI tool could use multi-omics, medical imaging, liquid biopsy omics, physiological data, and patient self-reported outcomes to track patient outcomes and inform future treatment responses. This would improve accuracy in predicting tumor progression and identify novel drug repurposing opportunities for specific cancer types.

AI algorithms are expected to become integral to healthcare in the near future, with oncology applications focusing on data intelligence, better tumor understanding, and more precise treatment options. Risk assessment tools in smartphone applications will provide immediate cancer risk estimates, motivating patients to seek medical care and follow recommendations. In primary care settings, algorithms will help physicians decide when to refer patients to high-complexity health centers and allow better resource allocation based on cancer risk.

CONCLUSION

AI is revolutionizing healthcare by enhancing cancer research, screening, diagnosis, treatment, and monitoring. It can also reduce healthcare costs and disparities. AI tools have been developed using various medical data, including free-text, laboratory and imaging results, radiological images, and omics data. Hypothesis-driven AI, unlike conventional AI, requires creativity and domain knowledge selection to formulate hypotheses and validate them through thought experiments. This approach offers targeted solutions for cancer detection and drug targeting. As AI advances, it can improve cancer detection rates, offer more effective treatment options, and reduce cancer. However, current applications are most effective for oncologists. Further research is needed to ensure accuracy, fairness, and transparency in AI models.

References:

1. World Health Organization - Cancer: https://www.who.int/news/item/01-02-2024-global-cancer-burden-growing--amidst-mounting-need-for-services
2. Alirezaei et al. 2021. Artificial intelligence in cancer: a review: https://www.nature.com/bjc/
3. McKinsey & Company. 2023. The potential impact of AI in healthcare: On the verge of transformation: https://www.mckinsey.com/industries/healthcare/our-insights/transforming-healthcare-with-ai
4. Liu et al. 2022. Artificial intelligence for breast cancer detection and classification: a review: https://www.nature.com/articles/s41591-023-02625-9
5. Ahnen DJ, Wade SW, Jones WF et al. The increasing incidence of young-onset colorectal cancer: a call to action. Mayo Clin. Proc. 89(2),216–224 (2014).
6. Verma V, Sprave T, Haque W et al. A systematic review of the cost and cost-effectiveness studies of immune checkpoint inhibitors 11 Medical and Health Sciences 1112 Oncology and Carcinogenesis. J. Immunother. Cancer 6(1), 1–15 (2018).
7. Chaudary N, Hill RP, Milosevic M. Targeting the CXCL12/CXCR4 pathway to reduce radiation treatment side effects. Radiother Oncol. 2024 May;194:110194. doi: 10.1016/j.radonc.2024.110194.
8. van Diest PJ, Flach RN, van Dooijeweert C, Makineli S, Breimer GE, Stathonikos N, Pham P, Nguyen TQ, Veta M. Pros and cons of artificial intelligence implementation in diagnostic pathology. Histopathology. 2024 May;84(6):924-934.

9. van Dooijeweert C, van Diest PJ, Willems SM, Kuijpers CCHJ, Overbeek LIH, Deckers IAG. Significant inter- and intra-laboratory variation in grading of ductal carcinoma in situ of the breast: a nationwide study of 4901 patients in The Netherlands. *Breast Cancer Res. Treat.* 2019; **174**; 479–488.
10. Calderaro, J., Žigutytė, L., Truhn, D. *et al.* Artificial intelligence in liver cancer — new tools for research and patient management. *Nat Rev Gastroenterol Hepatol* (2024). https://doi.org/10.1038/s41575-024-00919-y
11. Haddad T, Helgeson JM, Pomerleau KE, et al. Accuracy of an artificial intelligence system for cancer clinical trial eligibility screening: retrospective pilot study.JMIR Med Inform. 2021;9:e27767.
12. Chen H, Engkvist O, Wang Y, et al. The rise of deep learning in drug discovery. Drug Discov Today. 2018;23:1241-1250.
13. Nadarzynski T, Miles O, Cowie A, et al. Acceptability of artificial intelligence (AI)-led chatbot services in healthcare: a mixed-methods study. Digit Health. 2019;5:2055207619871808
14. Jha S, Topol EJ. Adapting to artificial intelligence: radiologists and pathologists as information specialists. JAMA 316(22), 2353–2354 (2016).
15. Bi WL, Hosny A, Schabath MB et al. Artificial intelligence in cancer imaging: clinical challenges and applications. CA Cancer J. Clin.69(2), 127–157 (2019).
16. Hosny A, Parmar C, Quackenbush J, Schwartz LH, Aerts HJWL. Artificial intelligence in radiology. Nat. Rev. Cancer 18(8), 500–510(2018).
17. Ghosh A. Artificial intelligence using open source BI-RADS data exemplifying potential future use. J. Am. Coll. Radiol. 16(1), 64–72(2019).
18. Schaffter T, Buist DSM, Lee CI et al. Evaluation of combined artificial intelligence and radiologist assessment to interpret screening mammograms. JAMA Netw. Open 3(3), e200265 (2020).
19. Farina E, Nabhen JJ, Dacoregio MI, Batalini F, Moraes FY. An overview of artificial intelligence in oncology. Future Sci OA. 2022 Feb 10;8(4):FSO787. doi: 10.2144/fsoa-2021-0074
20. Shaver MM, Kohanteb PA, Chiou C *et al.* Optimizing neuro-oncology imaging: a review of deep learning approaches for glioma imaging. *Cancers (Basel)* 11(6), 829 (2019).
21. Kocher M, Ruge MI, Galldiks N, Lohmann P. Applications of radiomics and machine learning for radiotherapy of malignant braintumors. Strahlenther. Onkol. 196(10), 856–867 (2020).

22. Bae S, An C, Ahn SS et al. Robust performance of deep learning for distinguishing glioblastoma from single brain metastasis using radiomic features: model development and validation. Sci. Rep. 10(1), 12110 (2020).
23. Ardila D, Kiraly AP, Bharadwaj S, et al. End-to-end lung cancer screening with three-dimensional deep learning on low-dose chest computed tomography. NatMed. 2019;25:954-961.
24. Baldwin DR, Gustafson J, Pickup L, et al. External validation of a convolutional neural network artificial intelligence tool to predict malignancy in pulmonary nodules. Thorax. 2020;75:306-312.
25. SpadacciniM,Marco A, Franchellucci G, et al. Discovering the first US FDA-approved computer-aided polyp detection system. Future Oncol. 2022;18:1405-1412.
26. Roth HR, Lu L, Liu J, et al. Improving computer-aided detection using convolutional neural networks and random view aggregation. IEEE Trans Med Imaging. 2016;35:1170-1181.
27. Kistenev, Y.V.; Vrazhnov, D.A.; Nikolaev, V.V.; Sandykova, E.A.; Krivova, N.A. Analysis of Collagen Spatial Structure Using Multiphoton Microscopy and Machine Learning Methods. Biochemistry 2019, 84, 108–123.
28. Abdulhamit, S. Practical Machine Learning for Data Analysis Using Python. In Chapter 3—Machine Learning Techniques; Academic Press: Cambridge, MA, USA, 2020; pp. 91–202; ISBN 9780128213797
29. Schmidt, U.; Weigert, M.; Broaddus, C.; Myers, G. Cell detection with star-convex polygons. In Proceedings of the International Conference on Medical Image Computing and Computer-Assisted Intervention, Granada, Spain, 16–20 September 2018.
30. Warin K, Limprasert W, Suebnukarn S, Jinapornthamm S, Jantana P, Vicharueang S. AI-based analysis of oral lesions using novel deep convolutional neural networks for early detection of oral cancer. PLoS One. 2022 Aug 24;17(8):e0273508. doi: 10.1371/journal.pone.0273508
31. Shreve, J.; Khanani, S.; Haddad, T. Artificial Intelligence in Oncology: Current Capabilities, Future Opportunities, and Ethical Considerations. Am. Soc. Clin. Oncol. Educ. Book 2022, 42, 842–851. [CrossRef] [PubMed]
32. Available online: https://www.mckinsey.com/industries/life-sciences/our-insights/delivering-innovation-2020-oncologymarket-outlook (accessed on 14 October 2022).

33. Sebastian AM, Peter D. Artificial Intelligence in Cancer Research: Trends, Challenges and Future Directions. Life (Basel). 2022 Nov 28;12(12):1991.
34. Xianyu Z, Correia C, Ung CY, Zhu S, Billadeau DD, Li H. The Rise of Hypothesis-Driven Artificial Intelligence in Oncology. Cancers (Basel). 2024 Feb 18;16(4):822.
35. Varadhachary, G.R.; Raber, M.N. Cancer of unknown primary site. N. Engl. J. Med. **2014**, 371, 757–765.
36. Pavlidis, N.; Khaled, H.; Gaafar, R. A mini review on cancer of unknown primary site: A clinical puzzle for the oncologists. J. Adv.Res. **2015**, 6, 375–382.
37. Moon, I.; LoPiccolo, J.; Baca, S.C.; Sholl, L.M.; Kehl, K.L.; Hassett, M.J.; Liu, D.; Schrag, D.; Gusev, A. Machine learning for genetics-based classification and treatment response prediction in cancer of unknown primary. Nat. Med. 2023, 29, 2057–2067.
38. Ganguli, R.; Lad, R.; Lin, A.; Yu, X. Novel Generative Recurrent Neural Network Framework to Produce Accurate, Applicable, and Deidentified Synthetic Medical Data for Patients With Metastatic Cancer. JCO Clin. Cancer Inform. 2023, 7, e2200125.
39. Frazer, J.; Notin, P.; Dias, M.; Gomez, A.; Min, J.K.; Brock, K.; Gal, Y.; Marks, D.S. Disease variant prediction with deep generative models of evolutionary data. Nature 2021, 599, 91–95.
40. Winkler JK, Kommoss KS, Toberer F, Enk A, Maul LV, Navarini AA, Hudson J, Salerni G, Rosenberger A, Haenssle HA. Performance of an automated total body mapping algorithm to detect melanocytic lesions of clinical relevance. Eur J Cancer. 2024 May;202:114026. doi: 10.1016/j.ejca.2024.114026.
41. Cè, M. et al. Artificial intelligence in brain tumor imaging: a step toward personalized medicine. Curr. Oncol. 30, 2673–2701 (2023).
42. Frajhof L., Borges J., Hoffmann E., Lopes J., Haddad R. Virtual reality, mixed reality and augmented reality in surgical planning for video or robotically assisted thoracoscopic anatomic resections for treatment of lung cancer. *J. Vis. Surg.* 2018;4:143. doi: 10.21037/jovs.2018.06.02.
43. Perkins S.L., Krajancich B., Yang C.J., Hargreaves B.A., Daniel B.L., Berry M.F. A Patient-Specific Mixed-Reality Visualization Tool for Thoracic Surgical Planning. Ann. Thorac. Surg. 2020;110:290–295. doi: 10.1016/j.athoracsur.2020.01.060
44. Tokuno J., Chen-Yoshikawa T.F., Nakao M., Matsuda T., Date H. Resection Process Map: A novel dynamic simulation system for pulmonary resection. J. Thorac. Cardiovasc. Surg. 2020;159:1130–1138. doi: 10.1016/j.jtcvs.2019.07.136.

45. Ujiie H., Yamaguchi A., Gregor A., Chan H., Kato T., Hida Y., Kaga K., Wakasa S., Eitel C., Clapp T.R., et al. Developing a virtual reality simulation system for preoperative planning of thoracoscopic thoracic surgery. J. Thorac. Dis. 2021;13:778–783. doi: 10.21037/jtd-20-2197.
46. Sadeghi A.H., Maat A.P.M., Taverne Y.J.J., Cornelissen R., Dingemans A.-M.C., Bogers A.J.C., Mahtab E.A. Virtual reality and artificial intelligence for 3-dimensional planning of lung segmentectomies. JTCVS Tech. 2021;7:309–321. doi: 10.1016/j.xjtc.2021.03.016.
47. Bakhuis W., Sadeghi A.H., Moes I., Maat A.P., Siregar S., Bogers A.J., Mahtab E.A. Essential Surgical Plan Modifications After Virtual Reality Planning in 50 Consecutive Segmentectomies. Ann. Thorac. Surg. 2023;115:1247–1255. doi: 10.1016/j.athoracsur.2022.08.037
48. Echecopar C, Abad I, Galán-Gómez V, Mozo Del Castillo Y, Sisinni L, Bueno D, Ruz B, Pérez-Martínez A. An artificial intelligence-driven predictive model for pediatric allogeneic hematopoietic stem cell transplantation using clinical variables. Eur J Haematol. 2024 Jun;112(6):910-916.
49. Y.-Y. Tao, Y. Shi, X.-Q. Gong, L. Li, Z.-M. Li, L. Yang, X.-M. Zhang Radiomic analysis based on magnetic resonance imaging for predicting PD-L2 expression in hepatocellular carcinoma Cancers (2023), p. 15
50. J.H. Yoon, H. Kim CT radiomics in Oncology: Insights into the tumor microenvironment of hepatocellular carcinoma Radiology, 307 (2023), Article e222988
51. Bo Z, Song J, He Q, Chen B, Chen Z, Xie X, Shu D, Chen K, Wang Y, Chen G. Application of artificial intelligence radiomics in the diagnosis, treatment, and prognosis of hepatocellular carcinoma. Comput Biol Med. 2024 May;173:108337
52. T. Xie, Y. Wei, L. Xu, Q. Li, F. Che, Q. Xu, X. Cheng, M. Liu, M. Yang, X. Wang, F. Zhang, B. Song, M. Liu Self-supervised contrastive learning using CT images for PD-1/PD-L1 expression prediction in hepatocellular carcinoma Front. Oncol., 13 (2023), Article 1103521
53. M.R. Tomaszewski, R.J. Gillies The biological meaning of radiomic featuresRadiology, 298 (2021), pp. 505-516