Science Bulletin 68 (2023) 448–451

Contents lists available at ScienceDirect

Science Bulletin

journal homepage: www.elsevier.com/locate/scib

News & Views

Artificial intelligence for clinical oncology: current status and future outlook

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There has been an explosion of research activities and clinical investigations on the use of artificial intelligence (AI) in oncology during the past decade. This is driven primarily by technological advances in computing power and sophisticated AI algorithms, as well as the availability of a large amount of digitized data generated during routine cancer care. AI has the potential to transform clinical oncology by enabling more accurate and efficient diagnosis and providing clinicians with personalized treatment options for cancer patients. Here, we highlight some specific applications of AI in clinical oncology, which include improving cancer detection and diagnosis, aiding in prognostication and risk stratification, and predicting treatment responses and outcomes of cancer patients (Fig. 1). We will discuss the remaining challenges and future outlooks of translation and adoption of AI for clinical oncology.

AI is an umbrella term broadly used to describe various techniques of machine intelligence capable of performing human tasks. Machine learning is a sub-field of AI that refers to algorithms that can learn from data and perform tasks without explicit programming. These range from simple decision trees to more complex random forests and have been used in the medical literature for several decades. Deep learning, yet another sub-field of AI and machine learning, has recently emerged as a powerful technique that can automatically learn feature representations or patterns from unstructured data (such as images) and generate useful predictions through multiple layers of artificial neural networks [1,2]. This collection of sophisticated AI algorithms including machine learning and deep learning has found numerous and ever-expanding real-world applications ranging from robotics and computer vision to natural language processing. AI is poised to have a positive impact on human society for decades to come.

In clinical oncology, the most promising applications of AI have been focused on improving cancer screening, detection, and diagnosis using a variety of imaging modalities including clinical photographs, radiology scans, and pathology slides. In a pioneering study, Esteva et al. [3] trained a deep learning model, specifically a deep convolutional neural network, for the classification of skin lesions using clinical photographs. The model achieved a diagnostic performance on par with board-certified dermatologists for distinguishing skin cancer from benign lesions as well as for identifying melanoma, the deadliest skin cancer. AI has also been used for real-time detection of gastrointestinal malignancies on endoscopy images with a sensitivity similar to that of expert endoscopists [4]. Additionally, it has been demonstrated that AI tools can be used to detect and diagnose breast cancer in mammograms [5] and lung cancer in computed tomography scans with an accuracy comparable or superior to that of practicing radiologists [6]. In digital pathology, AI has been shown to improve the diagnostic accuracy and efficiency of time-consuming tasks such as the detection of cancer metastases in lymph nodes on whole slide images [7].

In addition to improving cancer detection and diagnosis, AI can also aid in prognostication and improving risk stratification of cancer patients beyond tumor-node-metastasis (TNM) staging. In a large international study, Skrede et al. [8] developed a deep learning model to predict survival outcomes after primary colorectal cancer resection from digitized hematoxylin and eosin-stained sections. The model was extensively evaluated in independent patient populations, outperformed established molecular and morphological prognostic markers, and gave consistent results across tumor and nodal stage. Electronic health records provide a rich resource for understanding the impact of treatment interventions for diverse patient populations. Recently, Morin et al. [9] developed an AI framework for continuous learning from health data while capturing and integrating longitudinal clinical records of cancer patients. They demonstrate that natural language processing of clinical notes could be used to continuously update estimates of an individual's prognosis throughout the disease course.

AI may enable molecular characterization of tumors such as predicting clinically actionable cancer-driver mutations from routine diagnostic images. For instance, it has been shown that AI models may predict the genomic mutations in non-small cell lung cancer from radiology images and hematoxylin and eosin-stained tissue slides [10,11]. Such technologies may be useful in practical situations when tumor tissue is insufficient or unavailable for genomic sequencing. Additionally, this can be deployed in a low-

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https://doi.org/10.1016/j.scib.2023.02.015

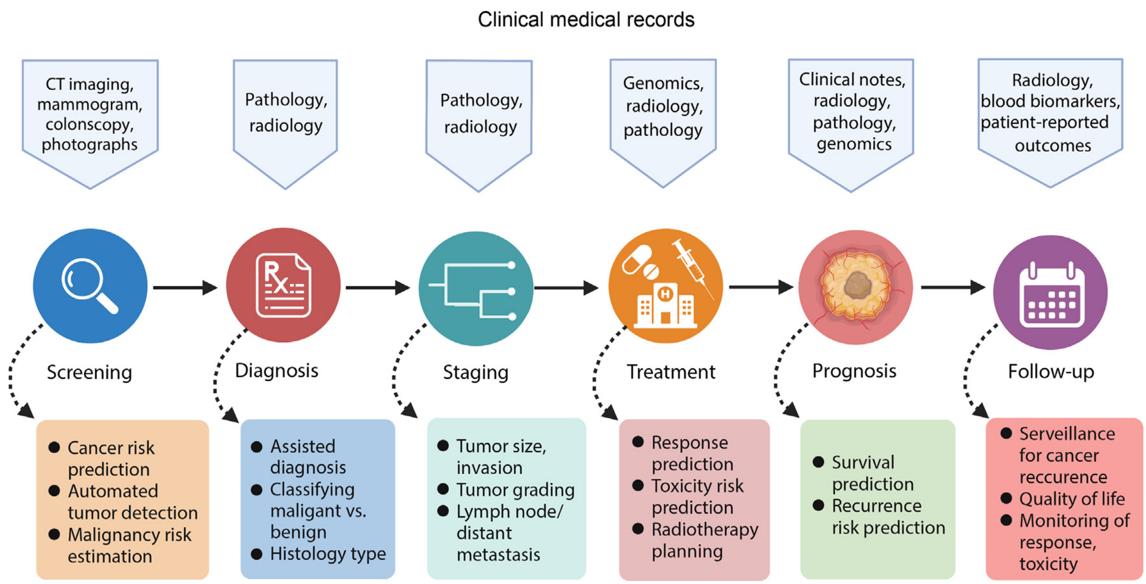

Fig. 1. Examples of potential applications of AI in clinical oncology. (Created with BioRender.com).

resource setting to triage patients for molecular profiling using routinely available clinical images.

One of the most tantalizing applications of AI is the ability to predict therapeutic response and benefit, which has important implications for personalized treatment strategies. Different from cancer screening applications whereby AI can be used as an adjunctive tool to assist expert diagnosticians, recommending treatment bears much more substantial consequences. Thanks to decades of basic and translational research, it has now been well established that the tumor microenvironment plays an important role in cancer initiation and progression and is a key determinant of treatment response and resistance. Built on this biological knowledge, Jiang et al. [12,13] developed an AI approach to non-invasively evaluate the immune and stromal tumor microenvironment status from radiological images and further showed that the model could predict benefits from chemotherapy in gastric cancer. This approach could not only overcome the practical limitations of insufficient tissue specimens but also address the fundamental issue of sampling bias due to intratumor spatial heterogeneity.

Although significant progress has been made in the development of AI for clinical oncology, there remains a huge gap in demonstrating the value of AI for improving patient outcomes. Many obstacles must be overcome before the impact of AI in clinical oncology can be realized. Below, we will discuss some of the key challenges and potential solutions to these problems, which include data availability, technical validity, interpretability, clinical validity, clinical utility, clinical adoption, and real-world application.

A prerequisite to building reliable AI models is the availability of large amounts of high-quality data. This is especially true for developing state-of-the-art deep learning models that are highly complex and flexible with many more parameters to fit than the number of data points. However, due to several reasons including privacy concerns as well as logistic and administrative issues, access to data has been challenging in healthcare. In addition to forming multi-institutional collaborations on an ad hoc basis, systematic efforts will be required for building large datasets with representative patient populations. There is slow but steady progress in data sharing with a number of publicly available data repositories such as The Cancer Imaging Archive that could facilitate the training and validation of AI models. From a technical perspective, new AI techniques may offer a viable solution by obviating privacy concerns. Federated learning allows for models to be trained from multi-institutional datasets without requiring access to data but instead by sharing model parameters.

In clinical practice, data are typically acquired and collected with varying protocols across different institutions and healthcare systems. Therefore, it is important to ensure that AI models are robust to these technical variations and reproducible across heterogeneous datasets. A prominent example is radiology AI, wherein many imaging-based features (and models capturing these features) are highly sensitive to variations in scan protocols and parameters. To address these issues, Wu et al. [14] proposed radiological features of tumor morphology and spatial heterogeneity that are specially designed to ensure comparability across diverse tissue contrast and imaging modalities. Using an international heterogeneous dataset of 1682 patients from 12 cohorts, they identified four radiological tumor subtypes that demonstrate distinct prognoses after conventional therapies and predict response to immunotherapy.

For high-stake decisions such as cancer diagnosis and treatment, clinicians would demand to know why the model makes a certain prediction, and the interpretability of AI becomes a critical issue. While it is entirely feasible to train AI models directly from input, this data-driven approach results in black-box models that lack intuitive understanding or clear reasoning behind their predictions. It will be crucial to incorporate pathobiology into the design of deep learning models to enhance interpretability.

To establish the evidence for clinical validity, AI models should be prospectively validated in clinical trials. The lack of rigorous validation represents one of the largest hurdles toward the clinical translation of AI. To date, the overwhelming majority of published studies on medical AI are performed using retrospective analysis of existing datasets. While this is the most convenient place to start, retrospective studies particularly on AI are subject to various forms of bias that may lead to overly optimistic results. There is an unmet need for prospective validation of AI models to ensure reproducibility and generalizability in diverse patient populations. One strategy to establish high-level evidence for clinical validity is by leveraging data from completed large multi-center phase III clinical trials conducted by national or international cooperative oncology groups. It is crucial that the AI models have already been fully developed and are locked down before performing validation.

Once clinical validity has been established, the next key milestone is to demonstrate clinical utility. Depending on the particular applications in oncology, this can include increasing cancer detection yield and diagnostic accuracy, improving patient survival or quality of life, and reducing healthcare costs and resource utilization. The gold standard for establishing clinical utility is randomized controlled trials (RCT) comparing outcomes in patients randomly assigned to AI-driven intervention vs. standard of care. There is a paucity of AI-based RCTs published to date and a few studies have shown improved detection of adenoma in endoscopy compared with standard clinical care [15]. For certain endpoints such as improved survival, these trials can be very expensive and time-consuming to conduct. Nevertheless, this will provide the highest level of evidence for clinical utility, which is often needed for regulatory approval and clinical adoption.

When AI models have been extensively validated, they may be finally adopted and deployed for real-world clinical use. A number of issues should be taken into consideration. How AI models interface with the end users can significantly impact clinical adoption. The optimal strategy should be designed to facilitate and encourage human-AI interaction and collaboration. The effect of AI on clinicians' performance will need to be carefully evaluated to avoid or mitigate potential automation bias. One unique aspect of AI is its evolving nature in that AI models are capable of adapting to new data and may change over time. Therefore, the performance of AI should be continuously monitored post-deployment. Finally, there are ethical and legal implications of deploying AI models in the real-world setting, which have been discussed elsewhere in detail.

Moving forward, the next-generation AI will be able to leverage the complementary power of multi-modal datasets to maximize the value of precision oncology. In proof of principle studies, AI models that integrate clinical data, radiological images, pathology slides, and genomics features have been shown to achieve superior performance than single-modal AI for predicting treatment response, e.g., neoadjuvant chemotherapy in breast cancer and immunotherapy in lung cancer [16,17]. Additional data modalities such as endoscopic or surgical images may also be incorporated into specific applications whenever available. Another promising avenue of future investigation is to design customized neural network architectures that are informed by biological principles, and these fully interpretable AI models may enable preclinical discovery and clinical prediction in cancer patients. It is important to recognize that the most effective use of AI is augmenting, rather than replacing clinician's capabilities. We envision that future applications of AI will need to shift from human vs AI to human-AI collaboration, and the optimal strategies to integrate AI into a clinician's workflow should be explored in order to improve cancer diagnosis and treatment while minimizing harm.

For any technological advance, clinical translation and adoption are a long winding road fraught with risks and challenges, and AI is no exception. However, we believe that these challenges are not insurmountable and can be effectively tackled with given sufficient resources and dedication from all stakeholders. We are hopeful that close multi-disciplinary collaboration between AI researchers and clinicians along with technological innovation in AI algorithms and the ever-growing availability of digitized data should bring AI's impact to fruition. The future of AI in clinical oncology is bright.

Conflict of interest

The authors declare that they have no conflict of interest.

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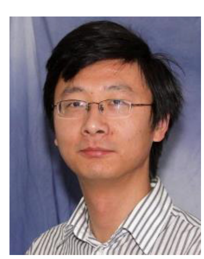
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