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Review Article

Artificial intelligence in radiation oncology: How far have we reached?

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ABSTRACT

Technological advances have revolutionized the field of radiation oncology (RO) as more and more departments are now equipped with modern linear accelerators and planning systems, resulting in the generation of a considerable amount of clinical, imaging, and dosimetric data. Artificial intelligence (AI) can utilize all these data points to create models which can expedite decision-making, treatment planning, and response assessment. However, various roadblocks impede the speed of development in this field. While data quality and security are the top priorities, legal and ethical issues are equally important. This scoping review provides an overview of the emerging possibilities resulting from an integration of modern RO workflow and AI-based technologies.

Keywords: Artificial intelligence, Radiomics, Deep learning, Machine learning, Radiotherapy planning

INTRODUCTION

Radiation oncology (RO) is a rapidly evolving branch of oncology, and up to half of all cancer patients will require radiotherapy (RT) intervention at some point in the course of their disease.[1] With immense technological development, radiation planning and delivery have become precise and accurate, and consequently, the processes involved have become complex. This complexity has added another dimension to the already existing problem of adequately trained staff, that is, time-consuming workflows. In addition, predictive analyses of RT plans and delivered doses will be required soon to improve the quality of RT plans.

Artificial intelligence (AI) has shown promising applications in healthcare. In contrast to simple automation [Figure 1], it involves learning complex rules and patterns from historical data, which are then used to predict outcomes or simplify complex tasks. In this scoping review, we will discuss the application of AI to increase the efficiency, accuracy, and quality of the RT workflow, which may improve value-based cancer care delivery in resource-constrained settings.

ARTIFICIAL INTELLIGENCE IN RADIATION ONCOLOGY

The RO cancer care continuum includes treatment decisions, planning, delivery, and follow-up. In addition, treatment planning comprises several sub-processes: target and normal tissue segmentation, inverse planning, dose optimization, decision support, quality assurance (QA), and outcome prediction. The efficiency of these procedures can be enhanced by integrating AI, and progress has been made in tasks like contouring and planning.

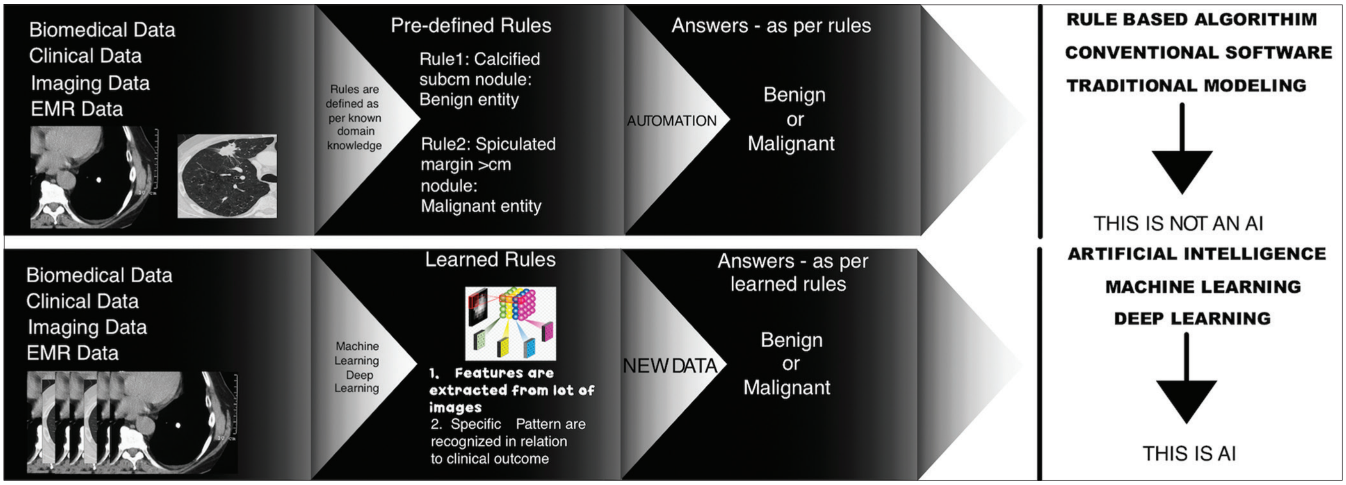

Figure 1: The difference between automation and artificial intelligence.

The broad application of AI in RO can be divided into two parts:

1. Process-driven AI
   a. Decision tools
   b. Segmentation
   c. RT planning
   d. Dose optimization
   e. QA
   f. Treatment delivery
2. Outcome-driven AI (Predictive Modeling)
   a. Prognostication
   b. Response assessment
   c. Toxicity prediction.

PROCESS-DRIVEN AI – DECISION TOOLS

The magnitude and rate of data accumulation have challenged our ability to analyze, interpret and apply multiple data points simultaneously. For example, in a study[2] among specialized thoracic radiation oncologists (ROs) (experience ranging from 3 to 20 years), the predicted treatment outcome of lung cancer patients was no better than a random guess (AUC ranging from 0.52 to 0.59), while AI based model performance was significantly better (AUC of 0.61 to 0.77). Another example is the prediction of complications and emergency visits before starting radiation treatment, which improves the existing clinical workflow.[3] Synthesizing accumulating evidence concerning patients' clinical/imaging data and objectively determining appropriate therapy is becoming more taxing. AI has the potential to speed up this process, presumably without introducing any subjective biases. Finally, while every RO applies their judgment to personalize RT plans based on their patient's unique clinical/imaging characteristics, AI can take this a step further by suggesting a specific treatment plan to achieve the optimal dose[4] based on predicted radiation sensitivity.[5]

PROCESS-DRIVEN AI – SEGMENTATION

Delineation of the gross disease (GTV) and associated regions of risk (CTV) are the cornerstones of modern RO, yet it is the most time-consuming step. It is well known that inter-observer variation in target delineation affects treatment outcomes,[6] and while auto-contouring solutions provided by commercial vendors of treatment planning systems have attempted to accelerate this process,[7,8] their acceptance remains low. Although based on a knowledge-based framework, the efficiency of auto-contouring algorithms remain variable and frequently generates incorrect contours due to inherent limitations[9] (especially near soft tissues[10]), which require manual corrections. This defeats the purpose of "auto-contouring" as it exists today.

Deep learning techniques such as convolutional neural networks or adversarial neural networks hold promise in this field as the performance of these algorithms reaches close to human levels both for tumors[11] and normal tissue segmentation.[12] Nevertheless, further research is required to generate high-quality prospective data with robust external validation and broader generalizability before these algorithms are widely adopted in the clinical workflow.

PROCESS-DRIVEN AI – RT PLANNING

RT planning involves patient positioning and immobilization before performing the simulation computed tomography (CT) scan. Depending on the disease site, this process can be very involved and requires coordination between ROs, physicists, and technologists. AI solutions can predict probable dose distributions based on diagnostic images;[4] Similarly, we can predict the optimal treatment position and immobilization so that the whole simulation process is streamlined.

Patients requiring specialized treatment techniques such as Deep Inspiration Breath Hold (DIBH) for left-sided breast cancer usually undergo 3 days of assessment to determine eligibility for this technique. Deep learning-based algorithms can be used on routine X-ray chest images[13] to identify their eligibility for DIBH and help in better resource utilization and patient care. In addition, generating synthetic CT scans from magnetic resonance imaging (MRI) using generative adversarial networks[14] can further smoothen the simulation workflow as the patient does not have to undergo RT planning CT scans if they have already undergone RT planning MRI.

Image co-registration (between simulation CT and MRI or PET-CT) plays a key role in determining the true extent of the tumor, as combining information from different imaging modalities overcomes the limitations of the simulation CT alone. However, commercially available registration methods lack generalizability, while deep learning-based approaches perform better, are more robust, and are generalizable across multiple imaging modalities.[15] These AI applications can enhance the modern RT simulation workflow.

PROCESS-DRIVEN AI – DOSE OPTIMIZATION

The generation of a high-quality deliverable RT plan is a multi-step process. Several studies[4] have shown that optimal dose distribution can be predicted (along with identifying machine parameters to achieve this dose distribution), and dose calculation can be accelerated using a knowledge-based approach.[16] Despite these advances, planning and dose optimization are not fully automated and frequently require human intervention, without which they can result in suboptimal dose distributions.[17]

Moreover, this approach is unsuitable for complex RT plans requiring photons and electrons. Recently, AI-based methods can generate RT plans comparable to or superior to humans.[18,19] The ideal solution would be to predict the best dose distribution followed by generating a treatment plan that matches closely to the predicted dose distribution, making the whole process fully automated.

PROCESS-DRIVEN AI – QA

QA involves patient-specific QA, aiming to detect human errors in treatment plans and anomalies in planning software. On the other hand, machine-related QA involves testing isolated parts of the treating machines. These processes involve many repetitive, time-consuming tasks. Patient-specific QA passing rates can be predicted using an AI algorithm that can flag the possible sources of errors, avoiding the need to measure physical doses.[20] In addition, the data acquired during the daily use of radiation machines can be used to predict future trends, and potential errors and improve machine-related QA efficiency.[21]

PROCESS-DRIVEN AI – TREATMENT DELIVERY

Patient scheduling for radiation treatment and on-treatment assessment can be made more efficient by utilizing AI approaches to identify the most important contributing factors to long waiting times.[22] Accurate treatment setup is one of the most crucial steps in overall radiation workflow and depends heavily on integrated cone beam CT (CBCT) devices. Although CBCT has revolutionized radiation treatment delivery by facilitating image-guided radiation therapy, poor image quality is a significant issue affecting the overall setup verification and treatment delivery time. AI has been used to improve the quality of these images by generating higher-resolution images, making it easier to match them with the simulation CT scan, thus speeding up the time for setup verification.[23] In addition, moving organs such as the lung and liver require real-time tumor tracking, and AI has shown great potential to accurately track tumor motion by predicting the anticipated trajectory of the tumor within milliseconds.[24]

OUTCOME-DRIVEN AI – PROGNOSIS, RESPONSE, AND FOLLOW-UP

Be it RO or any other field of medicine, understanding the prognosis of a particular condition and predicting response is of utmost importance. Also significant is the toxicity associated with the proposed treatment. There has been an enormous effort by researchers to model relevant clinical factors to predict treatment outcomes in terms of treatment response and toxicity. Many machine learning and deep learning AI techniques have recently been utilized to demonstrate their potential for better overall survival, response, and toxicity prediction.[25-29] These AI-based prediction models can provide precise point-of-care recommendations, thus enhancing clinical decision support.

Radiation planning dosimetric data can be integrated with orthogonal data like genomics, medical imaging, and electronic medical records to build robust Tumor Control Probability Models and Normal Tissue Complication Probability Models.[2,30] Radiomics is a field of medical imaging analytics where features are extracted from images based on complex interrelationships of pixels and voxels.[31] The amount of data extracted through the radiomics approach is enormous and needs AI-based techniques to make sense of this data. Initially, it was reported for the prognostication of lung cancer patients who underwent definitive RT,[32] following which many studies were initiated to study other outcomes like response prediction,[33] toxicity prediction,[34] determining the nature of lung nodules and exploring imaging genomics[35,36] to name just a few. Although much research is being done in these fields, we do not have any validated model for routine clinical use.

ISSUES AND CHALLENGES

The radiomics approach mentioned above has been studied extensively but often fails or lacks external validation[37] because of a bias toward tumor volume.[38,39] In addition, deep learning techniques have been criticized for their "black-box" nature (despite their excellent accuracy), as we are not fully aware of the reasons for their prediction. To tackle this, recently, there has been a focus on Explainable AI,[40] and if widely implemented, it will eventually drive adoption by AI skeptics.

Another significant challenge is the availability of high-quality datasets for AI-Model training and validation. Therefore, our primary emphasis must be on high-quality data collection and curation, as a lack of consistency in standardizing this medical data impedes progress in this field.[41-43]

Once medical data in institutional databases are standardized, the next challenge is to form multi-institutional collaborations across all possible geographic locations. At present, models are being trained on locally available limited-size datasets, thus creating better-performing models only on that localized geographic entity and lack generalizability. This is a consequence of the legal and ethical issues encompassing sharing medical data between different institutions, as the patient's right to privacy and data protection is an essential prerequisite that must be fulfilled at any cost.[44,45]

An important step toward overcoming this hurdle is federated model training, where medical data does not leave the institution's database. Instead, only model training is done in each institution, and the parameters learned from each model are combined, thus incorporating all geographic heterogeneities and resulting in a generalized model that may work globally.[46] In addition, this can overcome racial biases in AI algorithms and make them ethically sound.[47]

It is also anticipated that the dynamics of the patient-doctor relationship will change with the utilization of AI, and the focus will be on the patient-healthcare establishment relationship. However, we must also be forewarned that unethical AI practices pose a unique challenge,[48] and a strong technical and legal infrastructure needs to be created to protect patients and organizations.

CONCLUSION

AI and RO form a comfortable blend and can lead to a perfect example of integrated AI-guided workflow. AI-based approaches can be applied to every aspect of the RT workflow continuum. As the modern RO department adopts more and more of these approaches, the efficient utilization of resources will lead to all stakeholders (ROs, medical physicists, and radiation technologists) spending less time on technical processes and more time optimizing outcomes for our patients. The steady march of technological advancement leads to a fear of becoming redundant, yet with history as a witness, each significant step forward in our specialty has shifted our responsibilities. The approaching integration of AI is no different.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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