SPECIAL SERIES: RADIATION AND ADVANCED TECHNOLOGIES IN LMICS

Using Artificial Intelligence for Optimization of the Processes and Resource Utilization in Radiotherapy

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abstract

The radiotherapy (RT) process from planning to treatment delivery is a multistep, complex operation involving numerous levels of human-machine interaction and requiring high precision. These steps are labor-intensive and time-consuming and require meticulous coordination between professionals with diverse expertise. We reviewed and summarized the current status and prospects of artificial intelligence and machine learning relevant to the various steps in RT treatment planning and delivery workflow specifically in low- and middle-income countries (LMICs). We also searched the PubMed database using the search terms (Artificial Intelligence OR Machine Learning OR Deep Learning OR Automation OR knowledge-based planning AND Radiotherapy) AND (list of Low- and Middle-Income Countries as defined by the World Bank at the time of writing this review). The search yielded a total of 90 results, of which results with first authors from the LMICs were chosen. The reference lists of retrieved articles were also reviewed to search for more studies. No language restrictions were imposed. A total of 20 research items with unique study objectives conducted with the aim of enhancing RT processes were examined in detail. Artificial intelligence and machine learning can improve the overall efficiency of RT processes by reducing human intervention, aiding decision making, and efficiently executing lengthy, repetitive tasks. This improvement could permit the radiation oncologist to redistribute resources and focus on responsibilities such as patient counseling, education, and research, especially in resource-constrained LMICs.

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INTRODUCTION

The anticipated increase in cancer burden over the next few years could potentially overwhelm the oncology care system, especially in resource-constrained low- and middle-income countries (LMICs).[1,2] Although radiotherapy (RT) is an indispensable component of cancer care, access to it worldwide is very inequitable, with the current density of RT machines per million population ranging from 0 to 11.6, depending on the economic situation of a country.[3] The RT process starts with a series of visits to radiation oncology (RO) clinic, culminating in the final diagnosis, staging, and prognostication after which a radiation treatment protocol is assigned. Once a protocol is assigned, the subsequent RT treatment process can be categorized into imaging, target and organs-at-risk (OARs) segmentation, treatment plan generation, onboard imaging, treatment delivery, and quality assurance (QA) checks. These steps are labor-intensive and time-consuming, requiring multiple levels of human-machine interaction and a high degree of precision.[4] The patient continues to visit the clinic on conclusion of therapy for toxicity management and follow-up. This workflow is summarized in Figure 1.

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The RT workflow requires meticulous coordination between trained medical professionals with diverse expertise, i.e., radiation oncologists, medical physicists, dosimetrists, and radiation therapists.[5] Understaffing and workforce burnout is, unfortunately, a common problem plaguing RO in LMICs heightened by the ongoing COVID-19 pandemic.[6] Training the highly specialized RO workforce requires a high cost and time commitment. The role of artificial intelligence (AI) and machine learning (ML) in optimizing RT processes to achieve the best human, technological, and financial resource utilization is worth exploring.

ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING

Russell and Norvig[7] have defined AI as “the designing and building of intelligent agents that receive precepts from the environment and take actions that affect that environment.” A more perceptive definition given by Goel is “the science of building artificial minds by understanding how natural minds work and understanding how natural minds work by building artificial minds.” ML is a branch of AI that allows computer systems to progressively learn, train, and improve on the knowledge

CONTEXT

Key Objective

We review the role of artificial intelligence (AI) and machine learning (ML) in improving the efficiency of various radiotherapy processes and the challenges in their clinical integration.

Knowledge Generated

AI and ML can improve the accuracy, robustness, and speed of radiotherapy processes by reducing or eliminating human interference, aiding in decision making, and efficiently executing time-consuming, repetitive tasks. As its clinical utility remains yet to be proven, multi-institutional collaborative effort between various stakeholders is urgently needed, before the revolutionary impact of AI and ML bears fruition.

Relevance

The anticipated increase in cancer burden over the next few years coupled with cancer care becoming more personalized and tailored could potentially pressurize the oncology care system in the years to come, especially in low- and middle-income countries.

gained from a variety of input data without being overtly programed.[8] AI and ML can improve the accuracy, robustness, and speed of RT processes by reducing or eliminating human interference, aiding in decision making, and efficiently executing lengthy, repetitive tasks.[9] Using ML can free up time for more rewarding tasks such as education, research, patient counseling, and quality checks. The following review focuses on the potential use of ML and AI to transform the existing RT workflow and create a sustainable model that can be adopted in LMICs to supplement human efforts in labor-intensive tasks: segmentation, planning, and QA.

ROLE OF ML IN IMAGE SEGMENTATION

Manual segmentation (or contouring) of the target and OARs is a time-consuming and highly subjective task that lies at the core of RT planning. Historical solutions offered by technology to this conundrum include edge- and region-based methods and atlas-based methods of autosegmentation.[10]

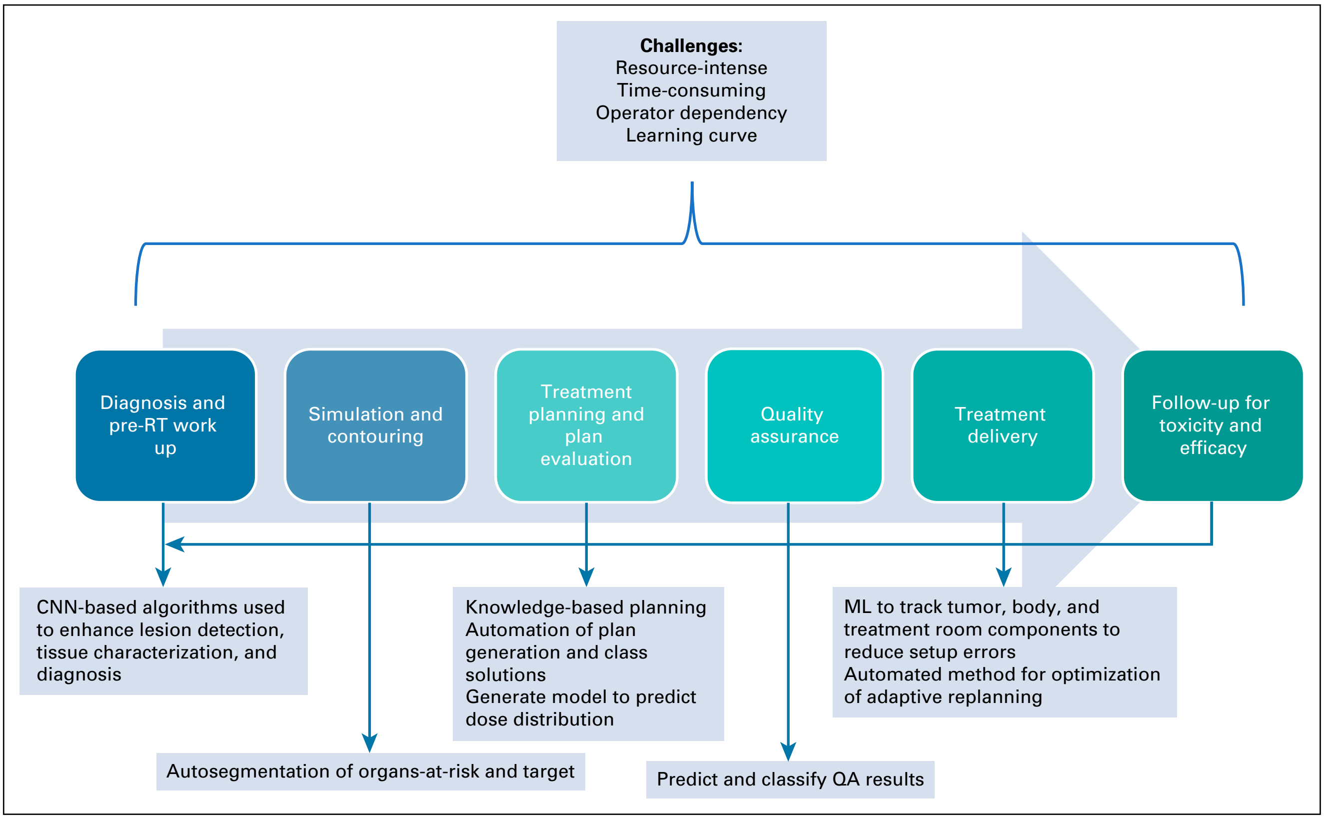

FIG 1. Utility of AI/ML in RT processes. AI, artificial intelligence; CNN, convolutional neural networks; ML, machine learning; QA, quality assurance; RT, radiotherapy.

Deep learning (DL), a subset of ML, is essentially a neural network with three or more layers. These can comprise simple feed-forward models such as artificial neural network or complex models such as convolutional neural networks (CNN) and recurrent neural networks. CNN has been increasingly used to learn complex nonlinear relationships within the imaging data to speed up and improve OARs delineation in mediastinum, pelvis, thorax, brain, and head/neck.[11] Image segmentation on the basis of DL uses either patches or regions of an image or the entire image as input to estimate the likelihood that a given image sample belongs to the object being segmented. The likelihood map can be further enhanced by methods combining DL and deformable models.[12] Multiple papers published using ML for auto-segmentation of OARs have demonstrated no clinically meaningful difference between segmentation by model and clinicians or radiographers with very high values of dice similarity coefficient, while recording a significant reduction in time needed for the segmentation.[13-17] For example, the average segmentation time for abdominal OARs liver, stomach, duodenum, and kidneys was 7.1 minutes with automation versus 22.6 minutes when done manually.[13] Lesion segmentation is more complex than OARs segmentation because of the heterogeneity in shape, size, and location of the target and, therefore, is still in nascent stages.[12] Computer-aided diagnosis methods, including conventional radiomics and CNN-based algorithms that enhance lesion detection in diagnostic radiology, can potentially be used in lesion segmentation during RT planning.[18]

ROLE OF ML IN RADIOTHERAPY TREATMENT PLAN GENERATION AND ADAPTIVE PLANNING

The advent of intensity-modulated RT and volumetric modulated arc therapy that offer exceptionally conformal RT delivery has increased manifold the intricacy and complexity of RT planning. High-precision treatment procedures such as stereotactic body ablative RT often consume hours or even days of human effort for planning.[19] Knowledge-based planning (KBP), which uses data from previous good cases to inform current patient planning parameters, has emerged as a powerful tool to accelerate the process of RT planning.[19] Efforts are ongoing to establish indigenous KBP models for cancers common in LMICs, such as cervical cancers, and validate them in various geoethnic populations to test efficacy in patients with different anatomies on the basis of geographical locations.[20,21] Supervised DL algorithms have been used for beam direction optimization, where the possible subsequent beam distribution is predicted on the basis of patient anatomy.[22] Use of DL in the prediction of spatial dose distribution has been extensively explored, with different architectures of CNN being used to predict the geometric and planning parameters of historical patients.[22] A significant gain in time has been reported with ML over non-ML methods such as column generation to select beam orientations, calculate the dose influence matrices, and finally solve the fluence map optimization with comparable dosimetry.[23] ML algorithms have also been used to enhance KBP further to generate treatment plans.[24] Recent studies have even attempted to emulate the decision-making strategy of human planners when solving a specific dosimetric trade-off problem, thereby potentially reducing the element of subjectivity.[25]

Another unique approach is the use of Pareto surface–based techniques for multicriteria optimization, where a database of plans is created for a single patient and the plan that achieves the best balance between different treatment planning goals is chosen by the planner and the physician.[26,27] The Erasmus i-cycle (created in an academic university) is a vendor-neutral algorithm using multicriteria optimization that is in clinical use for external beam therapy and is being developed for CyberKnife, proton therapy, and brachytherapy (BiCyle).[28-32]

ROLE OF ML IN RADIOTHERAPY ONBOARD IMAGING AND TREATMENT DELIVERY

ML techniques, including DL approaches, have dealt with intra- and interfraction patient and organ motion during RT treatment delivery to aid tumor gating and motion tracking.[33] Frameworks have been built using neural networks trained on collected patient breathing data to predict the breathing pattern while delivering RT.[34] ML has been used to aid motion tracking by assisting in the detection of the tumor (markerless tracking) or surrogate markers.[35] ML has been used to help avert setup errors and patient safety hazards by tracking the treatment room components and the patient's body in real time using 3D cameras to fine tune a CNN for object recognition.[36] A group of scientists have developed a computer vision–based pneumatic soft robot actuator to better estimate a patient's head pitch motion and to manipulate the patient head position on the basis of sensed head pitch motion, thereby potentially eliminating the need for immobilization with a thermoplastic mask.[37]

The role of ML in online adaptive RT planning has been extensively explored, mainly in deformable registration and dose warping, facilitating high registration accuracy and efficient execution even if graphical processing units are unavailable.[38] A proof-of-concept study investigates online multileaf collimator tracking to generate appropriate safety margins for online adaptation of the treatment plan on the basis of the patient's motion and the ability of the machine to follow these excursions.[39] Algorithms can assist physicians in supervising variations during treatment course by evaluating daily setup variations and anatomic changes, for early identification of adaptive replanning requirement.[40]

ROLE OF ML IN RADIOTHERAPY QUALITY ASSURANCE

Implementing regular and meticulous QA in RT is expected to lead to more accurate treatment delivery and better clinical outcomes. ML has excellent potential to enhance the efficacy and efficiency of RT QA processes as they are often repetitive and time-consuming. ML techniques have been used to predict gamma passing rates and the probability of the plan failing patient-specific intensity-modulated RT QA by analyzing plan complexity; multiple components of the delivery system such as multileaf collimator, imaging system, and mechanical and dosimetric parameters, and plan delivery log files over time.[41-43] Another approach has identified RT treatment delivery errors using radiomics-based feature extraction from patient-specific gamma images.[44] A study has applied artificial neural network–based time series prediction modeling to predict the performance of beam symmetry of linear accelerators over time.[45] Although these in silico approaches of various ML tools have augmented RT QA procedures, it is pertinent to establish its real utility in the clinical context before implementation.

OTHER APPLICATIONS OF AI IN RADIATION ONCOLOGY

Data Annotation, Radiomics, and Response Prediction

Radiomics is a method that extracts a large number of features from medical images using data characterization algorithms.[46] Many institutions and health networks, including from India, are working to create repositories of annotated medical data and medical images including outcomes of treatment for furthering radiomic research in large image data sets.[47,48] Distributed learning approaches with AI support have been used to conduct population-based studies on routine data and build decision support models.[49,50] Image banking combined with predictive/prescriptive AI is a cost-effective and efficient alternative to identify signatures for response, toxicity, and outcome prediction after cancer treatment.[51-53]

Natural Language Processing

Natural language processing (NLP) is a branch of AI that enables computers to interpret human language. NLP has already found application in the medical world to facilitate data extraction from free text in electronic medical records. The specific utility of NLP being explored in RO is standardization of contours and plans nomenclature to enable efficient data extraction.[54]

ORIGINAL RESEARCH FROM LMICS USING AUTOMATION AND ML TO OPTIMIZE RT PLANNING, TREATMENT DELIVERY, AND QA PROCESSES

We searched the PubMed database using the search term (Artificial Intelligence[tw] OR Machine Learning[tw] OR Deep Learning[tw] OR Automation[tw] automated[tw] OR knowledge-based planning[tw] AND Radiotherapy[tw]) AND (list of Low- and Middle-Income Countries as defined by the World Bank at the time of writing this review). The search yielded a total of 90 results, of which results with first authors from the LMICs were chosen. The reference lists of retrieved articles were also reviewed to search for more studies. No language restrictions were imposed. A total of 20 research items with unique study objectives conducted with the aim of enhancing RT processes were studied in detail and are presented in Table 1.

The majority of studies have focused on the utilization of CNN and other networks for autosegmentation.[55-62] The striking reduction in time burden seen with incorporating these algorithms while maintaining the accuracy of contours can prove to be pivotal in resource allocation in LMICs. The studies on autoplanning have mainly used KBP.[20,21,62,63] Developing indigenous models with local data rather than adopting western models to fit into the local workflow seems to be the standard approach, which is undoubtedly remarkable. Studies from LMICs using AI/ML to assist in online adaptive planning, treatment delivery, and QA are few and far between, and more work in this area must be encouraged.[64,66-68]

CHALLENGES OF INTEGRATING AUTOMATION AND ML INTO CLINICAL PROCESSES

Although AI has already become pervasive in our day-to-day activities and has the potential to influence how medicine is practiced, many challenges remain before its complete integration into RT processes, as listed below.[69]

1. Clinical utility yet to be determined: Most ML-based solutions are still in the stage of technological incubation, with the onus on the RO team to establish their clinical value.
2. Risk analysis of automation and AI: QA studies for automated treatment planning tools have been conducted, which stress the need for comprehensive manual review of the plans by physicians and physicists before implementation.[70]
3. Black-box nature of AI algorithms: In the case of failure of AI-based solutions, there is no straightforward framework to fix the outcome or predict errors. This lack of transparency and difficulty in understanding the outputs and predicting failures may make physicians hesitant and distrustful to rely on AI in patient-related decisions, further delaying the adoption of AI into clinical practice. It is essential to train the RO staff to correctly use the ML model and accurately interpret the intended utility, scope, and limitations.
4. Interpretation: It is necessary to remember that even if some algorithms can perform at near-human ability, the way they perceive and interpret the inputs differs from the human mind.
5. Training data: A machine learning algorithm's accuracy and generalizability are influenced heavily by the quality and quantity of the training data more than the mathematical parameters. Since individual institutional data sets are bound to be minor, data sharing across multiple institutions can make the ML/DL algorithms more robust. Distributed learning is an emerging approach to securely transferring data sets between institutions.[71]
6. Patient privacy and anonymity: The potential of distributed learning to provide evidence-based personalized care in LMICs is immense. However, care should be taken to uphold the rules of ethics, standardization, and stringent privacy regulations.[72]

In conclusion, integrating AI and ML in RT processes may allow radiation oncologists to spend more time on patient

TABLE 1. Original Research From LMICs Using Automation and ML to Optimize RT Planning, Delivery, and QA Processes

S. No.	Author(s), Country, and Year of Publication	RT Process Optimized	Purpose of the Study	Study Design	Automation Tool/AI Framework/ML Algorithm/Network Architecture Used	Significant Findings	Limitations of the Study
1	Liu et al, China 2021[55]	Segmentation	Automatic segmentation of CTV and OARs after breast conservation surgery	Processing time measured for AI tool and pre- and post-AI assistance	Network architecture: CNN	Contouring time 20 and 30 minutes for CTV and OAR, respectively, reduced to 10 and 5 minutes with AI assistance	Single center, ground truth approved by only two oncologists, subjective scoring system, CT images with pacemaker and contrast not used
2	Diniz et al, Brazil 2020[56]	Segmentation	Esophagus segmentation from planning CT images using an atlas-based DL approach	Training and testing of residual U-Net	Network: U-Net: a type of deep CNN	Efficiency and accuracy surpassing all earlier reports in the literature	Technical concerns as enumerated by authors, dissimilarity in training data
3	Men et al, China 2017[57]	Segmentation	Automatic segmentation of target and OARs in rectal cancer	Comparison of performances of two networks	Network: Deep dilated CNN *v* U-Net	45 seconds per patient for segmentation of CTV and all OARs with good accuracy	Segmentation of intestine and colon not as good as other organs
4	Xue et al, China 2020[58]	Segmentation	DL-based automatic detection and segmentation of brain metastases	Evaluation of a new DL model	Network: Cascaded 3D fully convolution network	Detection accuracy of 100% and strong correlation of segmentation with manual segmentations. Can simplify stereotactic RT planning and follow-up	Fixed size of the located nidus region used—more flexibility of method needed
5	Yang et al, China 2014[59]	Segmentation	ML algorithm for autosegmentation of parotids on MRI	Validation of the automated parotid segmentation algorithm	ML algorithm: Support vector machine training	Potential to perform longitudinal or large-scale clinical studies to understand toxicity of parotid gland and treat radiation-induced xerostomia	CT-based method might have been more practical than MRI in LMICs
6	Liu et al, China 2020[60]	Segmentation	Autosegmentation of CTV for post-MRM RT in breast cancer	Construction and validation model for autosegmentation of chest wall CTV	Network: CNN	It took 3.45 seconds to delineate chest wall CTV using the model	Single center, ground truth approved by only two oncologists, subjective scoring system
7	Pan et al, China 2021[61]	Segmentation	Autosegmentation of hippocampi on MRI	Validation of the new DL model	Network: CNN	Positive impact on improving delineation accuracy and reducing work load	Selection bias inherent to retrospective studies
8	Xia et al, China 2021[62]	Segmentation + plan generation	AI-based full-process solution for rectal cancer RT	Combination of knowledge-based and script-based planning	Network: CNN	Total time for full-process planning without contour modification = 7 minutes, physician accepted 80% of autoplans without further operation	Solution may not be suitable for sites with complex target segmentation and beam angle selection protocols
9	Sarkar et al, India 2019[63]	Plan generation	Non-DVH predictive method of KBP for VMAT SRS and SRT	Validation of the library plan-based model in new cases	ML algorithm: Not specified (commercial)	Model completes SRS/SRT plans in 1.5 runs	Plan quality dependent on quality of library plans

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TABLE 1. Original Research From LMICs Using Automation and ML to Optimize RT Planning, Delivery, and QA Processes (Continued)

S. No.	Author(s), Country, and Year of Publication	RT Process Optimized	Purpose of the Study	Study Design	Automation Tool/AI Framework/ML Algorithm/Network Architecture Used	Significant Findings	Limitations of the Study
10	Swamidas et al, India 2021[20]	Plan generation	KBP for VMAT of cervical cancer	KBP model configured from institutional database compared with CP	ML algorithm: DL-based autosegmentation algorithm (commercial)	Comparable and for some organs, superior performance than CP	Modifications to the model not possible: Would need reconfiguration and revalidation for a set of dose constraints
11	Huang et al, China 2020[73]	Plan generation	Develop an autoplanning platform to be interfaced with a commercial treatment planning system	Comparison of autoplans with manual VMAT plans for head and neck and prostate	ML algorithm: MCO	Autoplans clinically acceptable with better OAR sparing	Manual check needed to avoid system being trapped in a dead loop to achieve all dosimetric goals
12	Swamidas et al, India 2021[21]	Plan generation	Geoethnic validation of KBP models for image-guided VMAT in locally advanced cervical cancer	Compare and validate KBP models developed in two geoethnic patient populations	ML algorithm: DL-based autosegmentation algorithm (commercial)	Protocol compliance good in both clinical and KBP plans, across the institutions	Only abstract available
13	Li et al, China 2020[74]	Plan generation	Automated estimation of BED	Comparison of dose parameters between pre- and post-programed models	NestNet, a variant of U-Net used to predict the BED distribution	Model predicts biologic dose distributions accurately—may pave the way for completely automated BED-based planning	Only anatomic information used for optimization; beam data, and calculation parameters not used
14	Wang et al, China 2013[75]	Plan evaluation	Treatment plan quality evaluation	Semiautomated plan quality evaluation program compared with manual recording	Automation tool: JAVA and MATLAB-based	Evaluation time reduced from 10-20 to 2 minutes while maintaining accuracy	Difference of 0.2% in volume or 0.6 Gy in dose between the semiautomated program and manual recording
15	Jiang et al, China 2020[76]	Plan evaluation	CNN-based dosimetry evaluation of esophageal RT planning	Model predicting DVH from DTH	DL: 1D-CN	Average prediction error on the planned target volume, left lung, right lung, heart, and spinal cord is 2.94%	Model takes multiple steps to predict DVH instead of end-to-end prediction, beam orientation not taken into account
16	Osman and Tamam, Sudan 2022[64]	Dose distribution prediction	KBP for IMRT in head and neck cancer	KBP model used to generate model to predict dose distribution, which was compared with ground-truth plan	Attention-gated 3D U-Net architecture model	Attention-gated convolutions technique reduces network's redundancy and improves prediction performance compared with a baseline standard U-Net model	Model trained on a fixed beam configuration making it less generalizable to other sites and techniques
17	Nouri et al, Iran 2017[65]	Treatment delivery	Evaluates accuracy of the neural network estimating tumor positions in real-time RT	Comparison of neural network training methods	AI algorithms: Neural network, GA, and PSO	Neural network algorithm can precisely trace the location of tumor. Accuracies of 0.8%, 12%, and 14% in the neural network, GA, and PSO, respectively	Clinical implication not enumerated

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TABLE 1. Original Research From LMICs Using Automation and ML to Optimize RT Planning, Delivery, and QA Processes (Continued)

S. No.	Author(s), Country, and Year of Publication	RT Process Optimized	Purpose of the Study	Study Design	Automation Tool/AI Framework/ML Algorithm/Network Architecture Used	Significant Findings	Limitations of the Study
18	Liang et al, China 2020[66]	Onboard imaging	To evaluate and quantify intrafraction target motion in liver	A fully automated framework for analyzing intrafraction motion using orthogonal kV X-ray projections	U-Net to segment the fiducial markers	Precision and recall of the fiducial detection model were in excess of 95% demonstrating high model performance	Only select tumor locations were studied limiting generalizability
19	Li et al, China 2019[67]	QA	Assess accuracy of ML to predict and classify QA results for VMAT plans	GPR prediction accuracy of PL and classification performance of PL and RF were evaluated	ML algorithms: PL regression model to predict GPR, RF model to classify QA as pass or fail	ML can assist VMAT QA and reduce QA workload	Exploratory study: Only GYN and head and neck VMAT plans used to train the ML model
20	Abubakar et al, Nigeria 2021[68]	Offline image guidance protocols	Develop automated method for optimization and reduction of PTV margin using logged setup errors	Extract setup errors in three translational directions	Automated algorithm: MATLAB-based	Algorithm calculates weekly offline setup error correction values automatically: PTV margins can be accordingly reduced up to 48% for head and neck cancers	Does not consider rotational errors

Abbreviations: 1D-CN, one-dimensional convolutional network; AI, artificial intelligence; BED, biologically equivalent dose; CNN, convolutional neural networks; CP, clinical plans; CT, computed tomography; CTV, clinical target volume; DL, deep learning; DTH, distance to target histogram; DVH, dose volume histogram; GA, genetic algorithm; GPR, gamma passing rate; GYN, gynecological; IMRT, intensity-modulated RT; JAVA and MATLAB, computer programing languages; KBP, knowledge-based planning; LMICs, low- and middle-income countries; MCO, multicriteria optimization; ML, machine learning; MRI, magnetic resonance imaging; MRM, modified radical mastectomy; OARs, organs at risk; PL, poisson lasso; PSO, particle swarm optimization; PTV, planning target volume; QA, quality assurance; RF, random forest; RT, radiotherapy; S. No., serial number; SRS, stereotactic radiosurgery; SRT, stereotactic radiotherapy; VMAT, volumetric modulated arc therapy.

consultation, teaching, and research in resource-constrained setups with a heavy workload. Given the transformative impact that AI-based technology can bring to clinical processes and workflow, it is essential to integrate these concepts early in medical education and RO residency to facilitate a better understanding of the methods and encourage innovation. We have in front of us a means to revolutionize the practice of RT as we know it. It is our responsibility toward the future generation to understand, plan, prioritize, conduct meaningful research, integrate and constantly improve AI and ML in RT without bias or prejudice, and deliver it to settings where the impact would be maximum.

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