Addressing the Global Expertise Gap in Radiation Oncology: The Radiation Planning Assistant

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ABSTRACT

PURPOSE Automation, including the use of artificial intelligence, has been identified as a possible opportunity to help reduce the gap in access and quality for radiotherapy and other aspects of cancer care. The Radiation Planning Assistant (RPA) project was conceived in 2015 (and funded in 2016) to use automated contouring and treatment planning algorithms to support the efforts of oncologists in low- and middle-income countries, allowing them to scale their efforts and treat more patients safely and efficiently (to increase access).

DESIGN In this review, we discuss the development of the RPA, with a particular focus on clinical acceptability and safety/risk across jurisdictions as these are important indicators for the successful future deployment of the RPA to increase radiotherapy availability and ameliorate global disparities in access to radiation oncology.

RESULTS RPA tools will be offered through a webpage, where users can upload computed tomography data sets and download automatically generated contours and treatment plans. All interfaces have been designed to maximize ease of use and minimize risk. The current version of the RPA includes automated contouring and planning for head and neck cancer, cervical cancer, breast cancer, and metastases to the brain.

CONCLUSION The RPA has been designed to bring high-quality treatment planning to more patients across the world, and it may encourage greater investment in treatment devices and other aspects of cancer treatment.

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INTRODUCTION

Radiation therapy is an important part of comprehensive cancer treatments, with half of all patients requiring at least one treatment course during their disease. By 2040, 70% of the annual cancer cases are expected to be in low- and middle-income countries (LMICs), but <50% of patients in those countries have access to radiotherapy.[1] Roughly 80% of the world's patients with cancer have access to only 5% of global radiotherapy resources.[2] The Lancet Oncology Commission estimated that closing this gap could save nearly one million lives per year,[1] although estimates suggest an additional 50,000 radiation oncologists and medical physicists would be required to achieve this. In parallel with recruitment and training efforts, there is a need to improve workflow efficiency, helping clinical teams to scale their efforts to treat more patients while controlling overall costs and resource availability. Automation, including the use of artificial intelligence, has been identified as a possible opportunity to help reduce the gap in access and quality for radiotherapy and other aspects of cancer care; efficiency gains can also increase the return on investment for radiotherapy.[1,3]

With this background, the Radiation Planning Assistant (RPA) project was conceived in 2015 (and funded in 2016) to use automated contouring (to outline treatment targets and normal tissues on computed tomography [CT] scans) and treatment planning (to define the position, intensity, and shape of the radiation beams) to support the efforts of oncologists in LMICs, allowing them to scale their efforts and treat more patients safely and efficiently (to increase access). This initiative includes the development of a complete portfolio of automated planning tools across a range of tumor types and indications for treatments. To ensure that the RPA tools are suitable for LMIC clinics, these tools have

CONTEXT

Key Objective
To develop artificial intelligence-based tools to support high-quality radiotherapy treatment planning in clinics in low- and middle-income countries.

Knowledge Generated
Automated contouring and planning is possible with a simple user interface that maximizes ease of use and minimizes risk.

Relevance
The new tools may help support clinical teams provide high quality, consistent radiotherapy treatment plans for their patients.

been codeveloped through partnerships with clinical teams in South Africa, the Philippines, and Tanzania, as well as the United Kingdom and the United States.

We have significantly benefited from project-specific feedback about local patient populations, common presentations, and treatment paradigms, as well as detailed usability testing of the RPA itself. Over that time, and guided by these partnerships, we have improved our capabilities (including the introduction of and improvements in deep learning–based autocontouring[4,5]), culminating in a fully automated end-to-end web-based tool.[6] We hope to provide the RPA at minimal (most likely zero) cost to clinics in LMICs that would otherwise not have access to these tools or expertise, thus supporting universal health coverage by increasing the affordability of cancer treatment and reducing premature mortality (important United Nations Sustainable Development Goals). Here, we review the development of the RPA, with a particular focus on clinical acceptability and safety/risk as these are important indicators for the successful future deployment of the RPA to increase radiotherapy availability and ameliorate global disparities in access to high-quality radiation oncology.

USER WORKFLOWS

The RPA was designed following a software as a service approach to keep operating costs low (no local installation, no service, and easy upgrade with minimal customization) and to keep the system highly robust. The overall workflow for creating a radiotherapy plan using the RPA is demonstrated in Figure 1. The users must complete a service request (which includes the physician's radiation prescription and treatment technique) and upload a patient's CT scan. The RPA then automatically generates contours and a treatment plan. For complex plans (eg, volume-modulated arc therapy [VMAT] for head and neck cancer), the user may add and edit autocontours before automatic optimization of the final treatment plan. The treatment plan (Digital Imaging and Communications in Medicine [DICOM] format) is then downloaded from the RPA website and imported into the user's own treatment planning system (TPS), where the dose must be recalculated for their specific local treatment device. This reduces the need to customize the RPA to different local treatment devices. This is reasonable for some models of linear accelerator which have been shown to have very consistent beam characteristics,[7] but customization may be

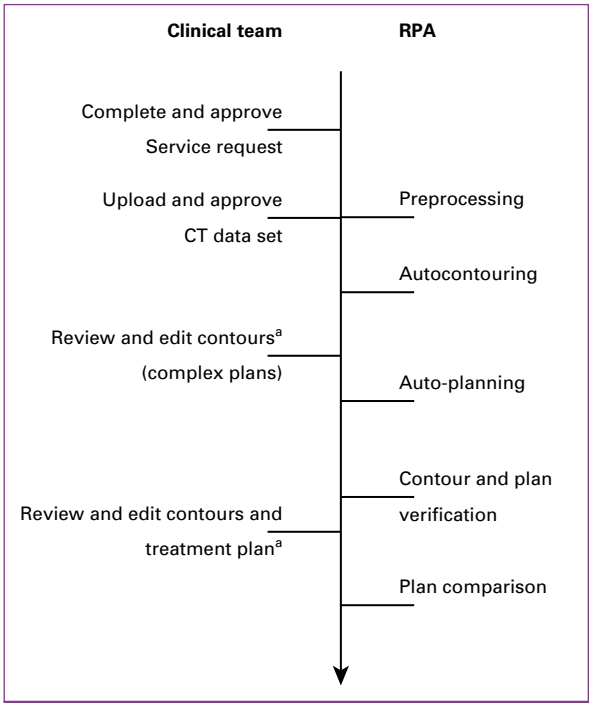

FIG 1. Workflow for creating radiation therapy treatment plans, showing tasks performed by the clinical team (left side) and tasks that are automatically performed by the RPA (right side). User tasks marked with [a] are performed in the users own treatment planning system. The review and edit contours step is only performed for complex planning (ie, VMAT). The RPA preprocessing step includes automatic detection of the marked isocenter (described in the CT upload section of this paper). CT, computed tomography; RPA, radiation planning assistant; VMAT, volume-modulated arc therapy.

needed for some machines. The users (treatment planner and oncologist) may make edits to the plan. The plan then enters the user's typical clinical workflow, including peer review and quality assurance checks.

Finally, the user can upload their final (recalculated and edited) plan to the RPA website, where an automated comparison between the final plan and the automated RPA plan is performed. This is a useful check of data integrity in the overall workflow and will provide the ability to monitor systems to identify changes or differences in patient populations, workflows, and so on.

AUTOMATED CONTOURING AND PLANNING

Contouring

At the start of the RPA project, all autocontouring was performed using an in-house multiatlas contouring tool. This gave largely acceptable results but has since been replaced by deep learning approaches, which the study team has found to be robust to variations in patient setup (which differ at different clinics), as well as having improved robustness to variations in CT image acquisition and reconstruction parameters.[8] Physician reviews of autocontours are positive, with one study on RPA autocontouring of patients with cervical cancer finding that 80% of the clinical target volumes (CTVs), 97% of the organs at risk, and 98% of the bony structure contours were clinically acceptable on the basis of physician review.[9] Similarly, high levels of acceptability and geometric agreement were reported for head and neck CTV contouring (lymph node contouring).[10]

Three-Dimensional Conformal Radiation Therapy Plans

Cervical Cancer

The RPA includes three approaches to treat cervical cancer—two versions of the traditional four-field box, which is recommended by ASCO and the International Atomic Energy Agency for use in low-resource settings[11,12] and VMAT. The user can then choose on the basis of their specific patient and available resources.[13]

The simplest approach to four-field box treatments of cervical cancer determines the field apertures using bony landmarks that are autocontoured and then projected into the beams eye view.[14] Beam weights are then optimized to minimize dose heterogeneity. We have consistently found that 90% of plans generated using this technique were deemed acceptable for treatment on physician review. The advantage of this technique is that it is simple, very easy to edit, and requires minimal review by the physician.

In the second approach, the RPA autocontours CTV structures and then applies prescribed margins for internal target volume and planning target volume before using these to determine the field apertures.[15] The advantage of this technique is that the target coverage will be more reliable because it is based on contoured targets (rather than surrogates). It does, however, require more time to review. When combined with subfields (field-in-field) to further minimize dose heterogeneity, physician acceptance is very high (≥99%).[15]

Postmastectomy Breast Cancer

For treatment of the chest wall, targets, normal tissues, and other planning structures are first automatically contoured.[14] The beams (tangential fields with matching supraclavicular field) are then positioned using a support vector machine approach. Finally, the dose distributions are optimized by adding field-in-field segments to minimize dose heterogeneity. Initial testing has shown that physicians accept around 50% of the plans as is and require minor changes for the remaining plans.[14] Edits to the autogenerated plans took around 12 minutes, compared with 120 minutes to manually create a plan from scratch.[16]

Whole Brain

The first version of whole-brain planning generated field apertures using a deep learning model that was trained using digitally reconstructed radiographs (DRRs) and field apertures.[17] This has been deployed clinically in the MD Anderson Cancer Center (MDACC) clinic. The study team has found, however, that the system would benefit from better customization to suit variations in clinical practice. For that reason, a second approach has been developed that mirrors the use for cervical cancer—autocontouring of the important landmark structures (eyes, etc), projection of these into the beams eye view, and determination of the field aperture on the basis of preset rules.[18] The rules can be customized if the tool is used at a clinic with different preferences for the field shapes.

VMAT

VMAT plans are generated using RapidPlan knowledge-based planning tool in the Eclipse treatment planning System (Varian Medical Systems), with optimization objectives derived through iterative testing and physician feedback. The goal is to achieve a high-quality treatment plan for the majority of patients without the need for a repeat optimization.[15,19,20] A review of the plans of 50 patients with head and neck cancer by 14 radiation oncologists at a multidisciplinary conference dedicated to head and neck cancer found that they had similar impressions of both the clinical plans and the autoplans.[19] Autoplans were considered acceptable for use for 88% of head and neck cases (compared with 78% for manual plans). Similar results were found for VMAT plans for cervical cancer, with 94% of plans found to be clinically acceptable.[15]

Contour and Plan Verification

After the final plan is generated, the RPA automatically performs internal quality assurance to help reduce risk. This

is a combination of comparing the RPA output with the results of independent models (eg, an independent auto-contouring model)[18,21–23] and comparison of the plan parameters (eg, monitor unit [MU]) with previous population ranges. Failure modes and effects analysis (FMEA) evaluation showed that the addition of these checks may reduce risk by increasing the probability of catching errors.[24]

Plan Comparison

Once the user has finalized the treatment plan in their own treatment planning system, including making any necessary edits and calculating the final dose, they have the option of uploading their final clinical plan to the RPA. The RPA then automatically compares the treatment machine settings (MU, jaw positions, etc) and dose distributions for final plan with the plan that the RPA had automatically generated. Differences are highlighted in a report. This process is intended to provide a visual check that data has correctly transferred between the RPA and the local TPS, as well as providing data on the frequency and extent to which the clinical team are editing the RPA plan. There are several potential safety benefits, including checking for automation bias (where the user tends to overly rely on the automated plans being correct) and differences in patient populations (requiring larger edits), but these are still under investigation.

USER INTERFACES

Complete and Approve the Service Request

The service request is how the oncologist communicates the treatment details to the RPA. An example for a simple case is shown in Figure 2 and a complex case in Figure 3.

The final service request must be approved by an oncologist. The study team has designed and evaluated the service request through unpublished usability testing, hazard testing, and FMEA.[24,25] The following are some examples of features to improve usability and reduce risk:

1. Only one active approved service request can exist for each patient.
2. Unnecessary questions are avoided as incorrect answers could unintentionally become part of the patient chart.[25]
3. Data entries (eg, prescribed dose) have specific limits to reduce the risk of accidental entry of incorrect data.
4. Verification check boxes to ensure that correct target coverage was selected (eg, for CTV selections for head and neck cancer treatments).
5. The approving user must be a radiation oncologist and must scroll through all parts of the service request before final approval.[24]

Upload and Approve the CT Data Set

The user uploads CT images to the RPA. The RPA then performs multiple basic checks on the image (eg, orientation and evenly spaced slices) and automatically identifies the marked isocenter (fiducial markers and three-point setup). The user must then review the CT image and isocenter information using a basic web-based CT viewer and confirm that this is the correct CT that should be used for planning (eg, correct positioning). The user interface for this step is shown in Figure 4.

The following are some examples of features to improve usability and reduce risk:

1. Only one active approved CT can exist for each patient.
2. Careful design of questions and quick hints that require the user to confirm certain aspects of the CT image set that could either reduce the reliability of the automatic algorithms or directly affect the treatment plan.
3. As part of this process, the user must confirm whether the RPA has correctly identified marked isocenter by reviewing the CT and positioning of radiopaque markers. The RPA never automatically identifies the marked isocenter for breast cases as the common use of wires and additional markers increases the risk of incorrectly placing the marked isocenter. In addition, when an isocenter is not found, this information is provided to the user in the plan report. Shift information is provided to the user in the RPA plan report but is not sent to the users TPS. The user is responsible for this step, and they should compare the shifts identified in their TPS with those in the RPA. This approach was considered to minimize risk associated with incorrect identification of marked isocenter (by the RPA), as well as giving a second check for this important step in preparing radiotherapy plans.

DEPLOYMENT

Many of these tools are already in routine use at MDACC, where they are used in the planning of around 350 patients every month. On the basis of this experience, as well as previous FMEA studies, user simulations, and hazard testing, the study team have identified the following key considerations for the safe and effective clinical deployment of the RPA:

1. Manual plan checks. Physician and physicist review of the final contours and plans, physics review, and other checks are essential components of automated treatment planning.[24] We also encourage the use of checklists, which can improve the rate of error detection by around 20%.[26]
2. Automated quality assurance. Automated verification steps may substantially reduce the risk of automated planning.[24] These are not replacements for the manual plan checks but can provide an additional layer of error detection.
3. Training and commissioning. Training (eg, face-to-face, videos) should educate the end users of automation planning about the potential sources of error, the impact of these errors on the patient, and that careful manual review of the plans is essential. This may also be important for managing automation bias.[25]

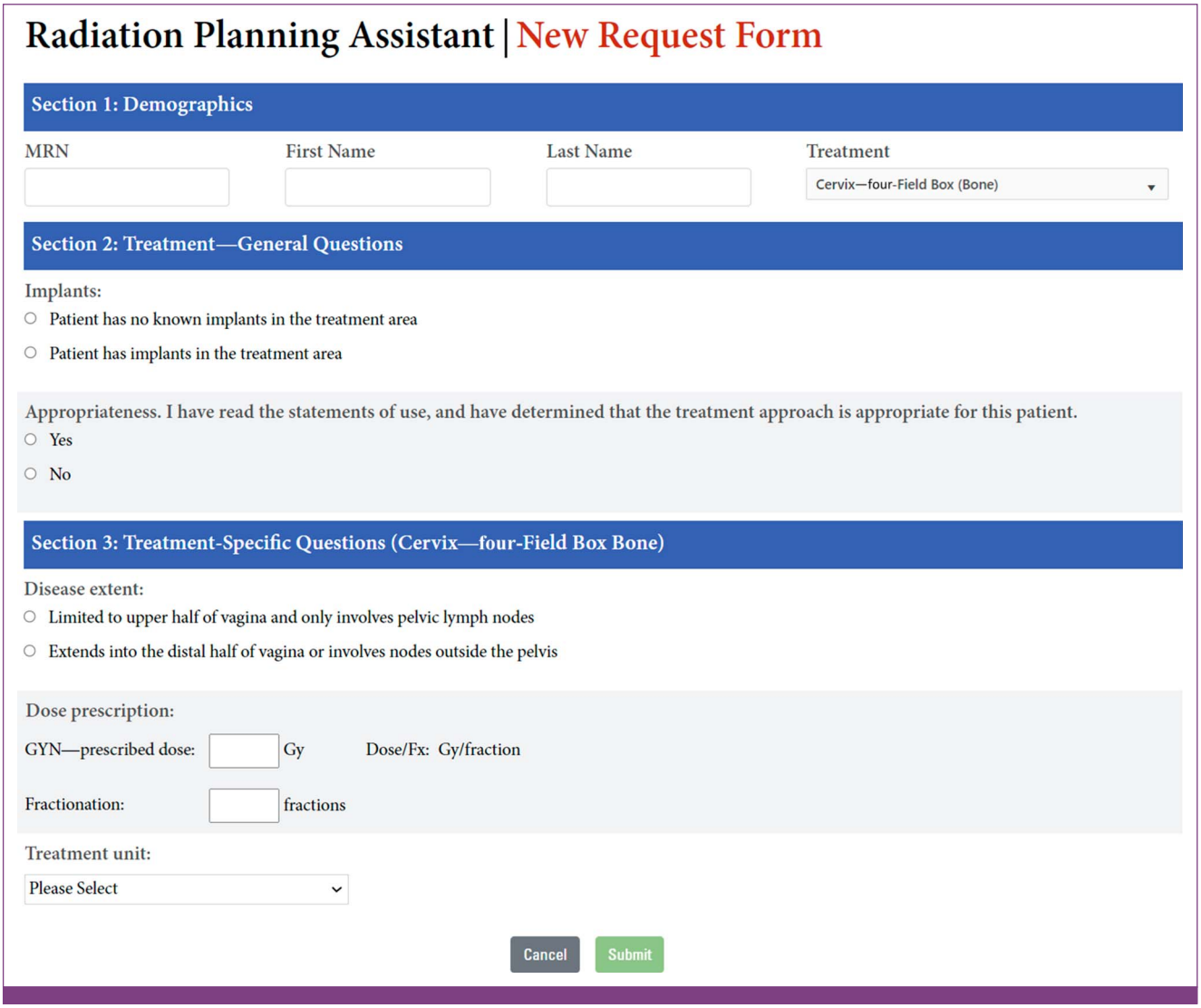

FIG 2. Screenshot of the service request user interface. GYN, gynecology; MRN, medical record number.

Additional considerations for future development and deployment that may improve efficiency and/or reduce risk include:

1. Respect local practice. Local oncology teams know what works best in their clinics, and seeking to change this could actually increase inconsistency and risk.[12,25] For example, changing how patients marked isocenter is identified just because the RPA expects a specific approach could, if communication and adoption are not perfect, result in inconsistencies in how this important task is performed. Future development should maintain flexibility to avoid needing changes in local practice.
2. Reduce data transfer. The current version of the RPA involves transferring data to and from the RPA and the user's local TPS. This has been identified as a risk point that we plan to remove in future versions (eg, with scripting to reduce the number of manual steps needed to transfer data).[27]

Hurdles to Use

McGinnis et al[27] surveyed potential RPA users in sub-Saharan Africa and central America and found that the main anticipated barriers to RPA use include lack of reliable internet, potential subscription fees, and the need for the RPA to work with additional disease sites. Connectivity will need to be addressed, possibly including the use of low earth orbit satellite systems which may bring internet service to remote areas, as well as reducing latency compared with terrestrial fiber.[28] Many clinics may require these improvements in internet connectivity if they are to take advantage of the automated tools that will be offered by the RPA. Cybersecurity will also need to be constantly reviewed to allow confidence in execution. Another consideration is the management of Protected Health Information (PHI). The RPA requires upload of some PHI (eg, patient name). We only require information that is necessary for correct

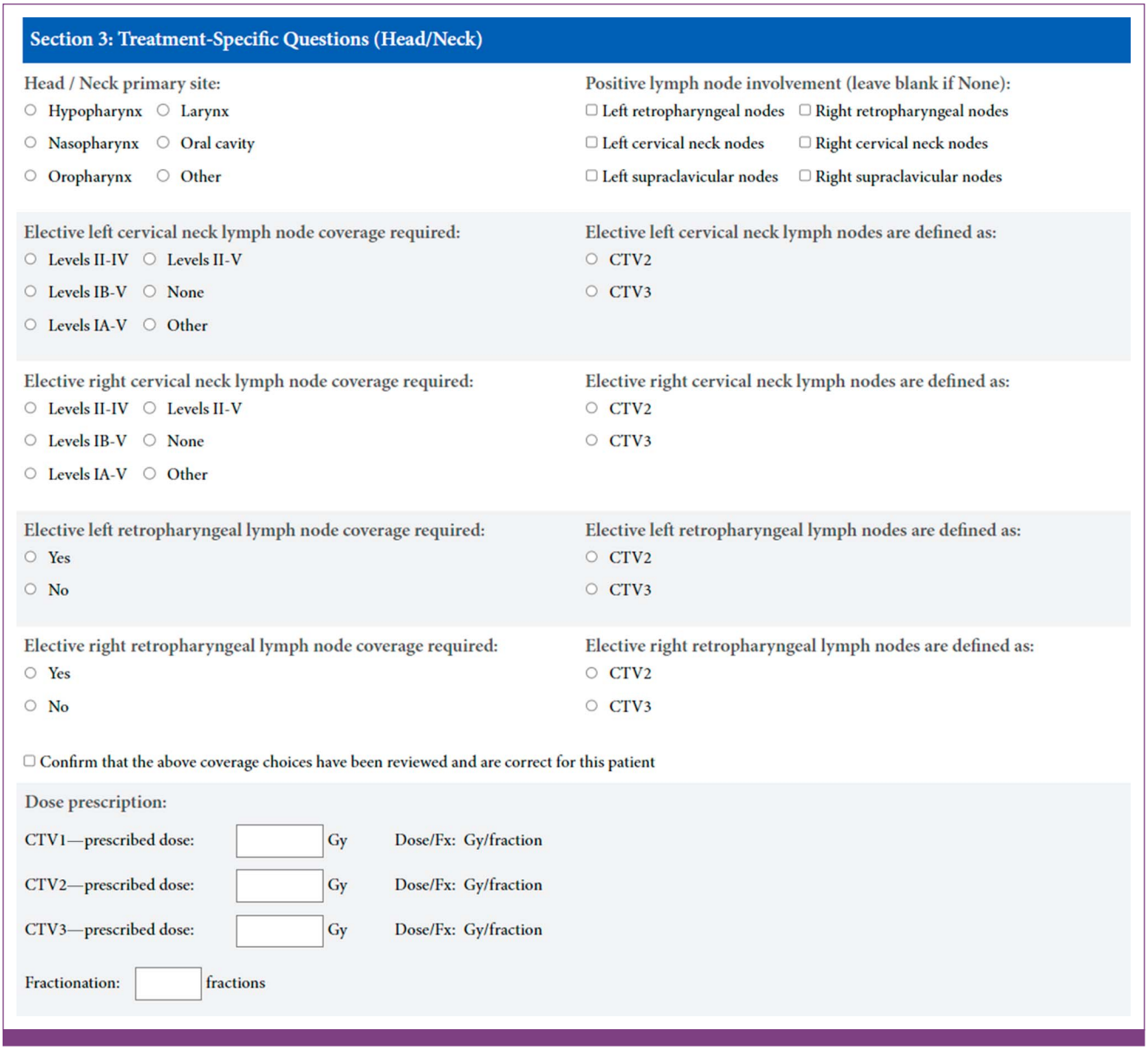

FIG 3. Screenshot of the treatment-specific questions for VMAT planning for head and neck cancer. Coverage selections are automatically populated after selection of the primary site and lymph node involvement, although the user can change these and must confirm their selections. CTV, clinical target volume; VMAT, volume-modulated arc therapy.

identification and matching of CT and service request. Most PHI (such as patient name) is removed before sending data to the calculation servers, and we expect to regularly clear PHI from the system, thus reducing long-term risk and cybersecurity risks. In the future, cloud-based solutions will be necessary to ensure that data are stored in the appropriate geographic regions.

The fully automated nature of the RPA means that running costs for the service can be kept very low, with high reliability and scalable capacity.[29] Other concerns of potential RPA users about the future use of the RPA included administrative red tape and the possibility of missed opportunities for contouring training at academic centers.[30] Specifically, if trainees use autocontouring tools then they may not learn important skills in interpreting and contouring cross-sectional anatomy.[31] This concern about the impact of automation on training is commonly expressed and will have to be carefully addressed as we move forward.

DISCUSSION

Overall, our experience indicates that the RPA is likely to be widely accepted by clinical teams when it is released clinically. This is supported by the experience in using some of these tools in the MDACC clinic. The RPA is, of course, under continual development. On the basis of the experience described above, the study team has additional advanced prototypes and expects to add features to the RPA, such as three-dimensional conformal radiation therapy and VMAT

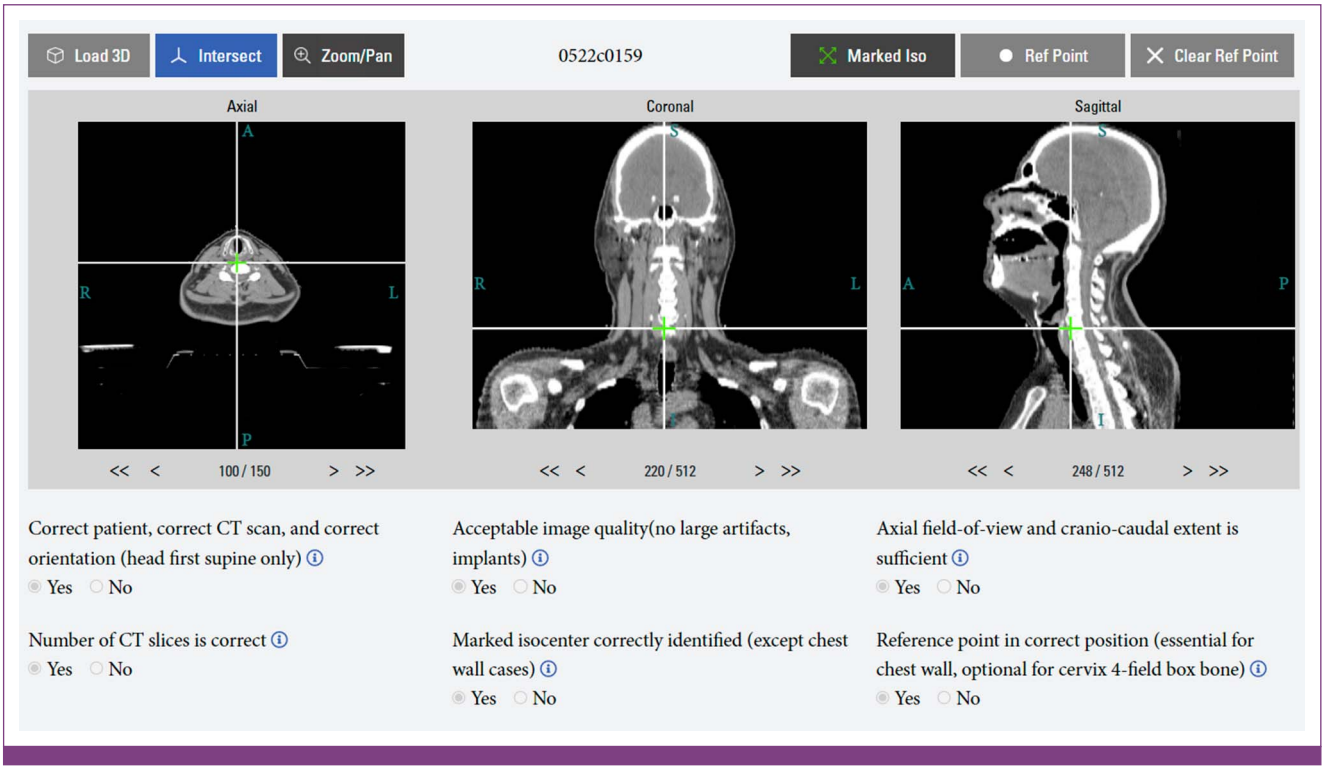

FIG 4. Screenshot of the user interface for CT approval. CT, computed tomography.

planning for prostate, lung, rectal,[32] and other GI cancers and pediatric craniospinal irradiation. In addition, future plans are to integrate RPA treatments for palliation of symptoms (eg, treatment of vertebral bodies,[33] bladder, hips) and also the ability to plan with cobalt-60 units, which can have advantages in low-resource environments.[34]

The RPA is being designed to offer high-quality, reliable tools to clinics with limited resources. The system development includes the software lifecycle, quality, and risk management processes needed for regulatory approval. This is important as, to our knowledge, there is currently no clear consensus on the validation and quality assurance of emerging machine learning tools in radiotherapy.[31] The system design considers robustness as well as overall cost and ease of deployment. The RPA has been designed in close collaboration with potential users in LMICs, and we intend to build on this to further optimize the system for these specific users, patient populations, and clinical practices in collaboration with local developers and users. This includes automation for simpler treatments, such as four-field box treatments and complex VMAT planning. There are, however, an increasing number of commercial (eg, DLC Expert, Mvision, Limbus.ai, and ART-Plan) and open-source (eg, Unet, Vnet, and nnUnet) autocontouring[35,36] and, to a lesser degree, autoplanning[37] solutions available. In addition, the availability of scripting in some commercial treatment planning systems has further increased the ability of clinical teams to develop tools to improve their workflows.[38,39] The role of the RPA in this environment is likely to constantly change, as we work to help clinics that are not benefitting from these other available tools, with the long-term goal of helping to improve equality and equity in the availability of cancer treatments across the world.

The next step is clinical deployment with our collaborators across the world. The RPA has been designed following industry standards (eg, the International Organization for Standardization, the International Electrotechnical Commission), and it has been submitted to the US Food and Drug Administration and will obtain other quality certifications. We are also undertaking prospective multicenter evaluation of the RPA in four countries (India, South Africa, Malaysia, and Jordan) recruiting an estimated 1,100 patients to assess the real-time implementation and cost-effectiveness of the RPA in different health care systems as part of the ARCHERY trial,[40] which may further support implementation and acceptance of tools such as the RPA. Our goal is to make these tools available to clinical teams who would not otherwise have access to similar tools, with the goal of increasing the quality and availability of radiotherapy worldwide by improving workflows and treatment planning.

The RPA focuses on one aspect of the many challenges in addressing the severe lack of access to radiotherapy in LMICs. That is, it is hoped that it will help clinical teams scale their efforts to create high-quality, consistent treatment plans for more patients. We still need more highly trained individuals to support safe, effective treatments for all aspects of radiotherapy treatment, including ensuring that the

outputs of the RPA are correct and appropriate for each patient. This means that deployment of tools such as the RPA should be accompanied by continued and enhanced efforts to improve investment in local human capital, training, and equipment that is appropriate to the local situation. The RPA is being developed to contribute to these efforts, potentially helping bring high-quality treatment planning to more patients across the world.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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