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Automated Radiation Treatment Planning for Cervical Cancer

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The radiation treatment-planning process includes contouring, planning, and reviewing the final plan, and each component requires substantial time and effort from multiple experts. Automation of treatment planning can save time and reduce the cost of radiation treatment, and potentially provides more consistent and better quality plans. With the recent breakthroughs in computer hardware and artificial intelligence technology, automation methods for radiation treatment planning have achieved a clinically acceptable level of performance in general. At the same time, the automation process should be developed and evaluated independently for different disease sites and treatment techniques as they are unique from each other. In this article, we will discuss the current status of automated radiation treatment planning for cervical cancer for simple and complex plans and corresponding automated quality assurance methods. Furthermore, we will introduce Radiation Planning Assistant, a web-based system designed to fully automate treatment planning for cervical cancer and other treatment sites.
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Introduction

Treatment planning for radiation therapy is an extremely complex process that involves many different tasks performed by a team of highly trained and experienced people (Fig. 1). Even simple tasks typically involve many button clicks by a radiation oncologist or treatment planner. As such, radiation therapy treatment planning is a time-consuming, inefficient, and expensive process. Furthermore, individual team members' preferences and skills can lead to much variability in the performance of individual tasks (eg, contouring, plan optimization).[1−5] Fortunately, automation, which is the use of technology to perform a process or procedure with minimal human assistance, may significantly enhance the uniformity, efficiency, and speed of the radiation therapy-planning process. In fact, almost all of the tasks listed in Figure 1 are candidates for automation except for taking a computed tomography (CT) scan and administering treatment.

The potential benefits of automating the radiation therapy treatment-planning process are:

- Improved efficiency. After patients receive their radiation therapy-planning CT scan, they often have to wait a week or more before starting treatment. Automation of the treatment-planning workflow could enable patients to start treatment shortly after their CT scan. This would bring many benefits, including significant cost savings for the patient.
- Improved quality and consistency of treatment plans. Researchers have shown that plans of poor quality can negatively impact patient outcomes.[3,6−8]
- Improved safety. Hand-offs between staff are known to be a risk point, with miscommunication between staff members potentially impacting the safety of radiation therapy.[9−13] Automation of multiple tasks (rather than individual tasks) can reduce the number of hand-offs between staff.

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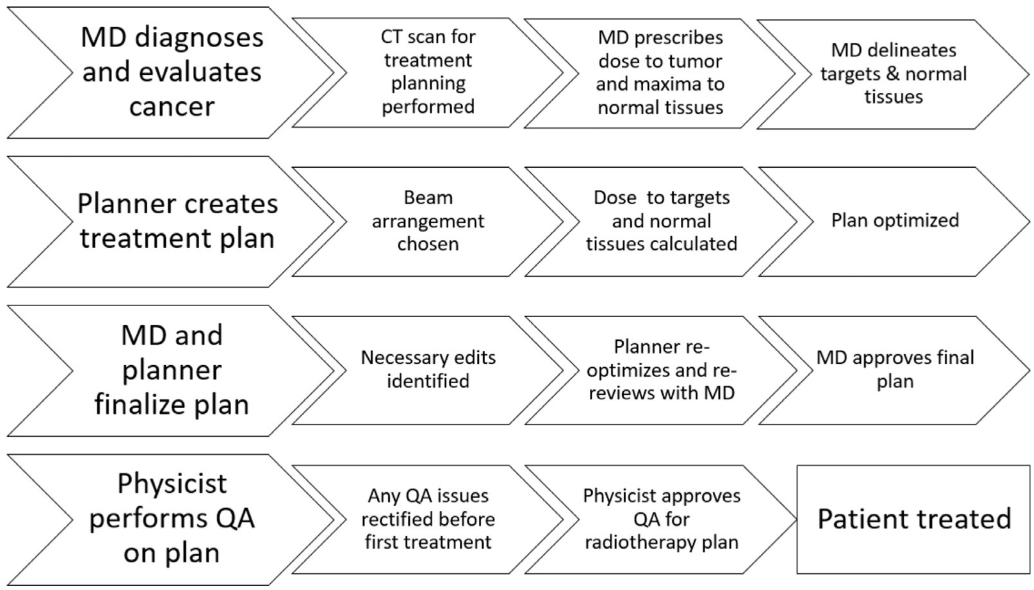

Figure 1 Flow chart of the radiation therapy-planning process. Abbreviations: CT, computed tomography; MD, doctor of medicine; QA, quality assurance.

- Increased access to high-quality radiation therapy across the world. Access to radiation therapy is severely lacking across the world, partially because of a lack of appropriate staff.[14] Automation can make planning easier, thus enabling existing staff to spend more time on other important tasks.

In this review, we describe how automation has been used to develop simple and complex external beam radiation treatment plans for cervical cancer.

Automation of Simple Plans (Four-Field Box Treatments)

Four-field box treatments use 4 orthogonal radiation fields. Each field shape is based on the location of bony landmarks or soft tissue structures. This treatment approach is simple and effective and is recommended for treatment of invasive cervical cancer in low-resource settings.[15,16] Kisling et al[17] developed an automated approach to determining beam apertures based on bony landmarks (Fig. 2). First, the bony pelvis, femoral heads, sacrum, and fourth and fifth lumbar vertebral bodies (L4 and L5, respectively) are automatically contoured. The bony structures are then projected into each beam's eye view; several landmarks, such as the widest extent of the pelvic inlet, are identified; and the beam apertures are determined according to a set of predefined rules. More recently, the same research group replaced the multi-atlas segmentation approach with a deep learning approach, which increased the success rate for auto-planning from 90% to above 95%.

Alternative approaches to the method developed by Kisling et al are proposed in the literature. For example, Cardenas et al[18] recently described the use of a convolutional neural network (CNN) approach to predicting field apertures. They used digitally reconstructed radiographs as inputs and physician-approved beam apertures as the ground truth. In this work, they found that using the projection images alone was prone to error in some uncommon situations, such as patients with metal hardware (eg, from spine reconstruction) or excessive contrast in the bowel.

The manual tasks involved in planning a simple four-field box are all straightforward. However, the challenge is that the tasks are many, and they are performed by various staff members, meaning that the entire process is subject to delays caused by hand-offs between staff. Thus, although the automation of the field shape has only modest potential for time savings (given the simplicity of the field shapes), the real benefit comes when this task is combined with other automated tasks such as dose calculation and the optimization of field weights to achieve homogeneous dose distributions. Kisling et al[17] described such an approach, which included optimizing beam weights to minimize dose heterogeneity. Full automation means that treatment plans can be ready for final physician review within a few minutes (rather than a few days, which is currently typical without automation), potentially enabling patients to start treatment the same day that they receive their CT scans.

Automation of Complex Plans

Volumetric modulated arc therapy (VMAT) is the most advanced beam-delivery technique for treating invasive cervical cancer. Unlike the optimization process for the simple plan described above, the optimization process for VMAT requires precisely defined soft tissue contours. Therefore, development of a fully automated contouring system is essential for an automated process. These contours can then be used as input to advanced automated inverse treatment-planning approaches.

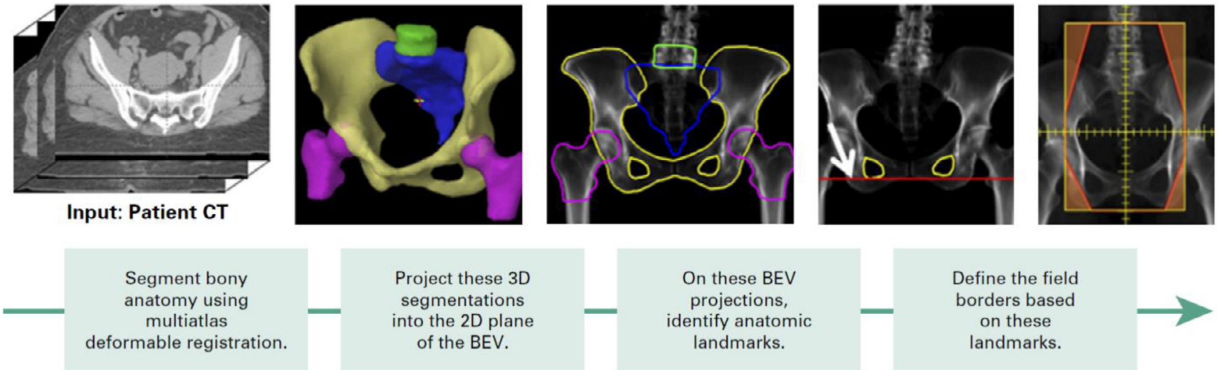

Figure 2 An automated approach to determining the field shapes for simple cervical cancer treatment. Abbreviations: 3D, three-dimensional; 2D, two-dimensional; BEV, beam's eye view (from Kisling et al[17]).

Automated Contouring

Over the past few decades, atlas-based auto-contouring methods have been among the most advanced such methods,[19–23] and researchers have successfully used them in the development of auto-contouring tools for some of the critical organs in the female pelvis. As described above, Kisling et al[17] developed a deformable, multi-atlas technique for automatic segmentation that can auto-contour the bony pelvis, femoral heads, sacrum, and fourth and fifth lumbar vertebral bodies. Young et al[24] used atlas-based segmentation to automatically generate endometrial cancer nodal clinical target volumes (CTVs); this led to a 26% time savings for the clinicians and increased the accuracy of the nodal CTV contours by 2% as per Dice similarity coefficient calculations. Furthermore, Bondar et al[25] automatically generated cervix-uterus contours on daily CT scans acquired with a CT-on-rails system. This involved deformable registration and manually drawing of contours on patients' pretreatment CT scans.

On the other hand, atlas-based auto-contouring methods may be suboptimal for contouring soft-tissue organs in the female pelvis because the shape and relative positions of the organs differ substantially among individuals and are therefore unpredictable. However, recent developments in deep learning techniques—specifically, CNN-based image segmentation techniques[26–29]—overcame this limitation of atlas-based auto-contouring methods. The performance of CNN-based models improves as the number of training data sets increases;[20] in contrast, atlas-based models are optimized with 10-20 training data sets.[23,24,30,31] Training the CNN-based models with various data sets enables the models to "understand" the general features of the soft-tissue organs in the female pelvis; thus, the models become more suitable for identifying patterns in patient-specific features.

Because of these advantages, researchers have investigated the possibility of auto-contouring organs using CNN-based segmentation models for multiple body sites. The auto-contouring studies of patients with prostate or rectal cancer that used CNN-based models showed that automatically generated bladder, rectal, and femur contours on CT images have an accuracy equivalent to the interobserver variabilities among different radiation oncologists.[32,33] Liu et al[34] developed the CNN-based auto-segmentation tool to segment 7 organs-at-risk (bladder, bone marrow, left and right femurs, small intestine, and spinal cord) in cervical cancer CT images and achieved clinically acceptable outcomes. Our group has been developing a CNN-based auto-contouring method for primary and nodal CTVs and 6 normal structures (bladder, bowel space, left and right femurs, rectum, and spinal cord) that will automate cervical VMAT planning as shown in Figure 3. Most of the contours were clinically acceptable on test data.

Automated Planning

Knowledge-based planning (KBP) can automate both IMRT and VMAT-planning processes. KBP software programs, such as RapidPlan (Varian Medical Systems, Palo Alto, CA) and Erasmus-iCycle (Elekta AB, Stockholm, Sweden), are commercially available, and the performance of KBP models created using the software has been validated in many research studies. In regard to cervical cancer KBP models, Ma et al[35] tested an IMRT RapidPlan model for postoperative cervical cancer patients and showed that planning target volume coverage was within 1% and critical organ dose metrics were within 4% of manual plan results. Also, Li et al[36] and Tinoco et al[37] showed that IMRT and VMAT RapidPlan models for cervical cancer patients are better than or equal to clinical plans. Sharfo et al[38] showed that, for patients with cervical cancer, their dual-arc VMAT Erasmus-iCycle model created plans that were equivalent to or better than manually generated dual-arc VMAT and 9-beam IMRT. Thus, an automatically generated IMRT or VMAT plan for cervical cancer made using KBP techniques will be clinically acceptable if the user can provide high-quality plans for model training.

Automated Quality Assurance

Once the treatment plan is complete, standard-of-care requires that it is carefully reviewed prior to treatment. This treatment plan review process is an important part of

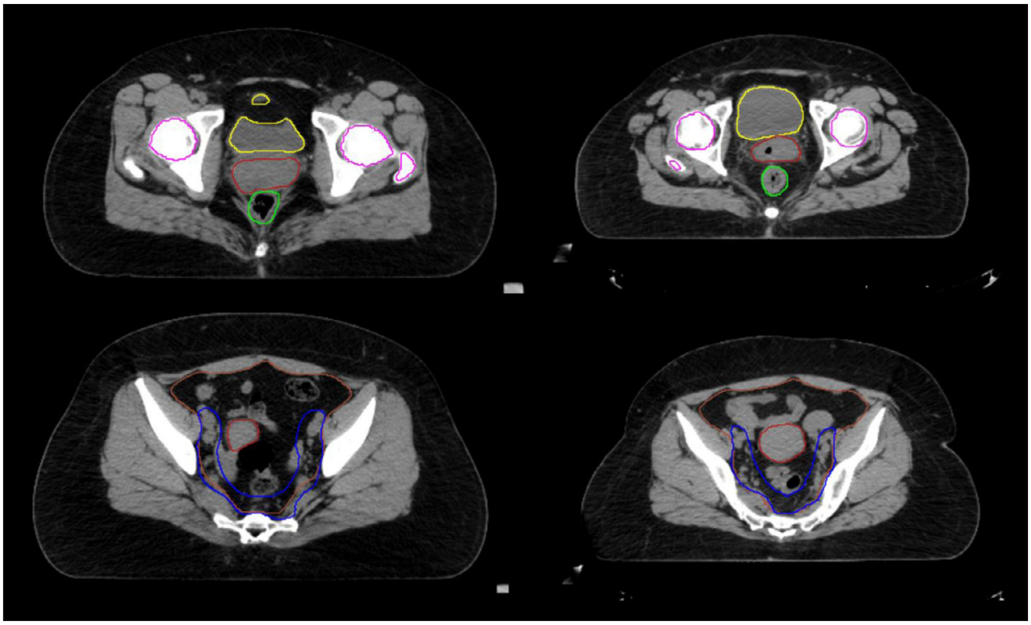

Figure 3 Unpublished recent results from our work on autocontouring. The images are of 2 patients. In the upper images, the primary CTV (red), bladder (yellow), rectum (green), and femurs (pink) are shown. In the lower images, the primary CTV (red), nodal CTV (blue), and bowel space (brown) are shown. (Color version of figure is available online.)

radiation therapy planning. It has several different components, all of which help maintain quality, consistency, and safety:

- Peer review. This is a review of the proposed treatment approach by radiation oncologists and other clinical staff. It includes a review of the treatment plan and may include a review of the contours used in the plan.
- Physics plan check. This is primarily a review of the technical aspects of the plan, such as the dose-calculation accuracy, but the check can also include a second review of the clinical aspects of the plan.
- Therapists' check. Therapists typically review the plan for completeness and "treatability."

Aspects of the physics plan check and therapists' check, such as recalculation of the radiation dose, detection of elements of the plans which cannot be carried through, and verification of correct data transfer from the planning system to the oncology information system, have been automated for many years. However, less attention has been paid to automation of the quality assurance process for simple and complex treatment plans for cervical cancer. In particular, automating tasks that are part of the peer-review process has received less attention than has automating other aspects of treatment planning.

Automated Quality Assurance for Simple Plans

For simple cervical cancer treatment plans, 2 quality assurance tasks determine the quality of a patient's treatment: confirmation of the shapes of the treatment apertures and verification of the radiation dose. Verifying the dose calculation in a treatment plan by recalculating the same plan using independent software is a routine clinical practice. Although older software required extensive manual entry, this is no longer the case, and many clinics have implemented automated dose-calculation verification.

As with dose verification, the automated beam aperture quality assurance is possible using 2 independent beam aperture-prediction algorithms. This was first demonstrated by Kisling et al,[39] who used the 2 methods summarized above—a deep learning approach and an automatic algorithm from automatically generated bone contours. The comparison of 2 algorithms can be used to verify the field apertures. For most patients, both algorithms agree (generally meaning that the aperture is clinically acceptable). On occasion, however, 1 algorithm fails. In such instances, the cases are flagged for the algorithm user to indicate that additional review by a physician is needed.

Figure 4 shows how 2 independent beam aperture-prediction algorithms can be compared to verify field apertures. The histogram in Figure 4 shows the mean surface distance between the 2 algorithms for a set of apertures that had been scored by a radiation oncologist as acceptable or unacceptable. This example illustrates that this approach can identify the majority of patients for whom the automatically generated apertures would have been inappropriate. The main advantage of these automated quality assurance techniques is that the radiation oncologist may not have to review the plan until the final plan is ready – rather than the more usual situation where they have to be involved to draw the initial field apertures, and then again to review the final plan.

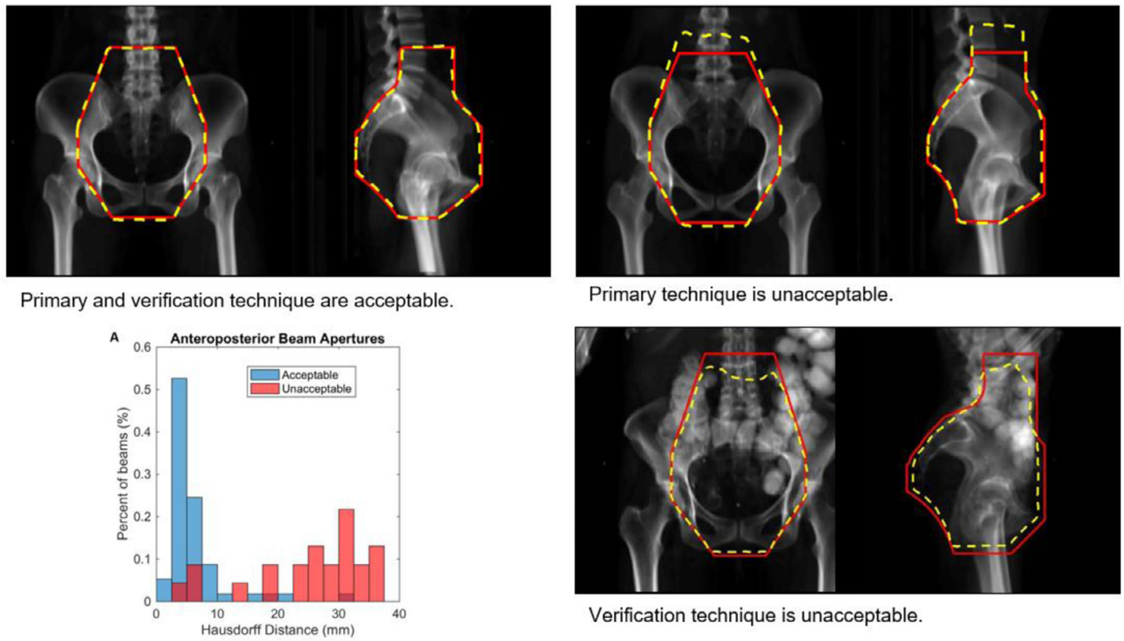

Figure 4 Automatic quality assurance process for simple plans using the 2 independent beam aperture-prediction algorithms. Red solid lines and yellow dashed lines indicate the primary and verification techniques, respectively. (Color version of figure is available online.)

Automated Quality Assurance for Complex Plans

Contour Quality Assurance

Although manual reviews of automatically generated contours should be conducted before the contours are used for clinical purposes, automated contouring quality assurance tools can still be beneficial as a means of avoiding potential mistakes. Most automatic contouring error-detection techniques use machine-learning algorithms to identify irregularities in extracted features and/or geometric locations of contours. McIntosh et al[40] identified errors in contours by extracting the geometric and intensity features of contours and analyzing the features with a conditional random forests model. Chen et al[41] developed a geometric attribute distribution model that uses relative geometric positions between organs to detect contouring errors. Most of these feature- and location-based algorithms assume that the tested organs always have similar features and relative geometries. These assumptions are valid for bony anatomies or for the organs in static region, such as the head and neck. However, because most of the critical organs in the female pelvis vary in size, shape, and position—even in the same patient at different time points—most feature- and location-based algorithms are not suitable for patients with cervical cancer. In contrast to this, Rhee et al's approach[42] involves calculating the volume overlap between 2 contours created from 2 independent auto-contouring algorithms to identify errors in the reference contours. Because no prior assumptions are made when identifying contouring errors, this approach would be the more appropriate means of detecting contouring errors for the organs in the female pelvis.

Plan Quality Assurance

Automatic verification of the accuracy, quality, and safety of planned dose distributions can be achieved in a variety of ways. First, the dose-calculation accuracy can be verified using independent software, as discussed above. The overall plan quality can be verified in a peer-review process in which each treatment plan is reviewed by other radiation oncologists and clinical staff. This is the verification procedure followed in many clinical practices and clinical trials. It involves not a review of the details of the dose calculation or other plan parameters, which are checked as part of physics checks, but rather a review of the overall suitability of the plan for a specific patient.

This peer-review process is extremely time-consuming, and therefore researchers have invested much work in the development of automated peer-review processes. These include the use of scorecards to assess whether the plan meets expected dose metrics and the prediction of dose distributions (or dose-volume histograms) by matching a patient's anatomy with anatomical data from a library of patients or with machine-learning data based on the geometry and dose prescriptions of previous patients.[43–48] More recently, groups of researchers have extended these ideas to predict the likely dose distribution for a patient using deep learning approaches.[49,50] Although not yet in widespread clinical use, these automated plan checks all have the potential to help clinical team members, especially dosimetrists, determine whether they have achieved the optimal plan for their patients. These automated plan quality assurance techniques are probably of particular use to clinical teams at centers that are transitioning to complex plans and have limited experience in assessing the quality of individual treatment plans.

Safe Clinical Use of Automated Treatment Planning

Automated contouring and treatment planning will likely bring increased consistency and improved efficiency to radiation therapy treatment planning. An important point to realize, however, is that even with automated techniques that appear to be very robust, errors will occasionally happen. These may be caused by algorithm errors (eg, incorrect automatic contouring) or by human error (eg, entering an inappropriate prescription). Also, errors that are less likely to be detected with automated processes than with manual planning may occur. One example of this is the use of an incorrect CT field of view, which gives a circular edge to the patient in the CT images. This circular edge is immediately obvious to a human planner but may not be identified in an automated process (unless the program is specifically trained to identify such scenarios). Thus, although automation has many potential advantages, the risks must be carefully considered and mitigated when introducing automation to clinical practice.

A failure mode and effects analysis of the deployment of fully automated treatment planning for cervical cancer identified 3 components required for patient safety[51]:

- User training. Carefully designed user training is essential, not only for the planners (to prevent error modes in automatically generated plans), but also for the staff involved in plan quality assurance (as new error modes that they are not used to checking for may appear).
- Manual plan checks by radiation oncologists, physicists, and other clinical team members. The active participation of experienced clinical staff is essential to the safe deployment of automated planning approaches.
- Automated plan verification (quality assurance). Wherever possible, automated solutions should be incorporated into plan verification.

The Radiation Planning Assistant Project

There are many examples of the development and clinical use of partially automated tasks in radiation therapy, but full automation has, until recently, been reasonably rare. The University of Texas MD Anderson Cancer Center's Radiation Planning Assistant (RPA) project is an early example of a system designed to fully automate the contouring and treatment-planning processes. The RPA, which is not yet in clinical use, was developed as a web-based service (http://rpa.mdanderson.org) and was started specifically to serve clinics in low- and middle-income countries where staffing is insufficient. The local user will upload a CT scan of a patient and a detailed plan order. Next, the RPA will automatically generate contours and/or a treatment plan that the user will then download to their own treatment-planning system. Finally, the user will recalculate the radiation dose (for their own local treatment linear accelerator) before making edits to and approving the final plan.

Initial efforts regarding the RPA have focused on treatment plans for cervical cancer (four-field box), breast cancer (postmastectomy, tangents, and supraclavicular fields), and head and neck cancer (VMAT), although further development for other anatomies is ongoing. The RPA is likely to be one of the first fully automated systems in clinical use, and additional fully automated tools soon will be available for use with common commercial treatment-planning systems or though other hospital-led development efforts.

Conclusions

Automation of radiotherapy treatment planning can provide improvements in efficiency, safety, and quality. The majority of tasks for external beam radiation therapy treatment planning for patients with cervical cancer, including the determination of field borders (four-field box), contouring, and complex planning (VMAT), have been automated. Although these tools are not all available clinically at this point, they likely will be available within the next year and widely available within 3-5 years.

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