

PreciseART® ADAPTIVE RADIATION THERAPY SOFTWARE: DOSE MONITORING, RE-PLANNING, AND DELIVERY VERIFICATION



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OVERVIEW OF ADAPTIVE RADIATION THERAPY

During the course of an individual patient’s radiation therapy regimen, adequate dose coverage of the prescribed target volume and dose avoidance for organs at risk (OAR) can be compromised due to interfraction variations in either the target volume or OARs. These variations are often specific to individual patients and include translational shifts (e.g., setup error), rotations, and anatomic changes (e.g., tumor shrinkage, organ deformation, weight loss). The current standard practice to address interfraction variations is to reposition the patient based on images acquired immediately prior to the radiation therapy (RT) delivery, i.e. image-guided RT (IGRT). This repositioning method, however, cannot adequately account for interfraction variations such as deformation. Adaptive radiation therapy (ART) is introduced to fully address any interfraction variations (Yan et al. 1997). ART is a state-of-the-art approach that uses a feedback process to account for patient-specific anatomic or biological changes during the treatment, thus delivering highly individualized radiation therapy for cancer patients (Li 2011).

Standard IGRT practice involves the acquisition of a volumetric image prior to each treatment fraction, which is then co-registered with the planning image to calculate a couch shift, if needed, to restore the relative location of the target volume within the treatment ports. Couch shifts however can only correct for translational errors and partially for rotational errors (Figure 1). If substantial non-translational interfraction anatomic changes arise, such as changes in the size or shape of the tumor volume or OARs, or overall patient weight gain or loss, they may be identified in the daily IGRT image, which in turn can serve as the basis for a revised radiotherapy plan. Further, using robust rigid and deformable image registration (DIR) tools, the cumulative dose distribution throughout the treatment course can be quantified.

Figure 1.

A diagram illustrating the limitations of relying on couch shifts alone for plan adaptation for various interfraction changes to the region of interest.

		Couch Shift	Plan Adaptation
TRANSLATIONAL ERRORS		✗ ✓	✓
ROTATIONAL ERRORS		✗ ✓	✓
DEFORMATIONAL ERRORS		✗	✓
TREATMENT RESPONSE VOLUME CHANGE		✗	✓
INDEPENDENT MOTION OF ORGANS		✗	✓

In the current practice, however, analyzing interfraction changes from daily IGRT images is subjective, qualitative, and labor intensive. An observer on the radiotherapy team (e.g., radiation therapist, medical physicist, or reviewing physician) determines a need for ART simply by visually inspecting the IGRT image and grossly identifying macroscopic anatomic changes relative to the original planning image, often without rigorously evaluating the dosimetric impact. Software tools that can analyze interfraction anatomic changes and evaluate the resulting dosimetric effects based on the IGRT image in an automatic manner are highly desirable. With such tools, determining a need for ART thus becomes objective and quantitative. The automated image registration includes no observer bias and the automated calculations of region of interest (ROI) volume and dose changes trigger predefined thresholds when clinically significant deviation occurs.

The TomoTherapy® System (Mackie et al. 1993) and Radixact® System, the next-generation TomoTherapy platform, combined with the newly-released Accuray Precision® Treatment Planning System and iDMS® Data Management System, incorporate these necessary tools required for offline ART. These fully integrated systems include: software to inversely plan conformal dose distributions to target volumes, on-board fan-beam megavoltage CT (MVCT) for daily IGRT, DIR software to map the daily IGRT images to the plan CT, and dose calculation and summation software to assess the dose distribution variations

during the treatment course due to interfraction anatomic changes. Furthermore, the platform’s unique design with common imaging and treatment isocenter reduces the sources of error, and the fan beam MVCT provides accurate, heterogeneous superposition dose calculation without additional modification or special quality assurance (QA) (Langen et al. 2005).

OFFLINE QUANTITATIVE ART WITH PreciseART® ADAPTIVE RADIATION THERAPY SOFTWARE

The Accuray Precision® Treatment Planning software (TPS) has optional applications to perform offline ART analyses (PreciseART® Adaptive Radiation Therapy option) and to create revised treatment plans (PreciseRTX® Retreatment option).

ACCURAY DIR ALGORITHM

The central part of PreciseART is its DIR algorithm. The proprietary Accuray DIR algorithm is a fast multi-modal method capable of accurate non-rigid image registration between a wide range of imaging modalities. Extensive tests have shown good registration accuracy across a wide range of imaging modalities and anatomical site applications. Good spatial registration accuracy can be achieved even in challenging clinical applications, such as interfraction abdominal DIR, involving large daily variations in organ position and shape (Gupta et al. 2014).

The algorithm is used for mono-modal multi-atlas DIR in three automatic anatomy segmentation tools in the Accuray Precision TPS: Brain AutoSegmentation™ (based on T1w MR), Head & Neck AutoSegmentation™ (based on CT), and Male Pelvis AutoSegmentation™ (based on CT). The algorithm is also used in three image registration applications: PreciseART (to register CT-MVCT), PreciseRTX® (to register CT-CT), and Deformable Image Registration (to register CT-MR and CT-CT and help with organ delineation).

The algorithm uses a nonparametric non-rigid transformation to represent the deformation field. It assumes no specific parameterization of the transformation; instead it explicitly estimates the deformation field subject to smoothness regularization. Such an approach allows estimating even complex organ deformations. The Accuray DIR optimizes the similarity criterion, local Normalized Correlation Coefficient (NCC),

$$NCC(I_{ref}, I_{mov}) = \frac{\sum_{x,y,z}(I_{ref}(x,y,z) - \bar{I}_{ref})(I_{mov}(x,y,z) - \bar{I}_{mov})}{\sqrt{\sum_{x,y,z}(I_{ref}(x,y,z) - \bar{I}_{ref})^2} \sqrt{\sum_{x,y,z}(I_{mov}(x,y,z) - \bar{I}_{mov})^2}}$$

where \bar{I}_{ref} is the reference image neighborhood patch and I_{mov} is the “moving” image neighborhood patch. \bar{I}_{ref} and \bar{I}_{mov} are the mean values of the volume patches. The similarity criterion is defined over small neighborhood patches, which allows for robust image matching even in the presence of intensity inhomogeneities and artifacts. The image similarity criterion is optimized iteratively over the entire image domain in a multi-resolution, coarse-to-fine scheme. The estimated deformation field is regularized using a smoothing operator at each iteration. A typical application uses 3 to 4 resolution levels and up to 500 iterations at each level. The algorithm is implemented using the nVidia CUDA GPU framework and is highly parallelized. A CT-MR DIR using a 300×300×300 voxel region of interest can be completed in 9 seconds on production GPU hardware (i.e., nVidia Quadro M5000). This makes the algorithm practical for real-time ART applications.

FULLY INTEGRATED AND AUTOMATED DOSE MONITORING

PreciseART takes as input the plan CT, the plan structure set, the plan delivery beam intensity pattern (sinogram), and all daily MVCT IGRT images and daily patient registrations to date. The single-fraction (daily) dose is calculated upon each MVCT using the sinogram and the CT-number-to-physical-density table associated with the MVCT scan at the time of treatment. A merged daily image is created using the plan CT to fill in the superior, inferior, and axial portions not included in the daily MVCT. Note that the daily MVCT should cover the anatomy to be monitored.

For the patients enrolled into the program, the dose monitoring process is initiated as soon as each fraction delivery is completed. The system automatically creates a merged daily image, deforms the plan ROI contours onto the daily image, calculates the dose on the daily image, accumulates the daily dose onto the plan CT, and generates a report with user-defined metrics, flags and trends. The entire process takes approximately 15–20 minutes per fraction, depending on the size and resolution of the MVCT, making the report available shortly after the fraction delivery. Aside from the initial enrollment into the program, no user intervention is required. Patients can be enrolled at any time during the treatment course, just after the approval of the treatment plan or after some fractions have been delivered. PreciseART® has access to all daily MVCTs, density models, and daily registrations recorded in iDMS, and runs the process for each fraction that has been delivered.

USER-DEFINED AUTOMATED REPORT

The PreciseART® dashboard is an integrated MIM viewer (MIM Software, Inc., Cleveland, Ohio) especially designed for offline ART analyses. It lists the enrolled patient plans, the delivered fractions for each plan, and displays a report for each fraction that summarizes the ROI volume and dose variations. The report includes tables, graphs, dose volume histograms (DVHs) and isodose displays predefined by the user. The ROIs and DVH metrics to tabulate are typically predefined based on the clinic’s treatment planning objectives for a given disease site (e.g., rectum V40Gy < 40% for a pelvis plan). For both the planned dose and dose recalculated upon the daily MVCTs, the table indicates whether a given ROI objective was fulfilled (with a green checkmark) or not fulfilled (with a red circle). The reviewer can thus identify at a glance if the predefined DVH metrics are no longer met (Figure 2). For a given fraction, tables can be generated comparing the planned dose with daily, accumulated and projected dose. The daily dose is a single fraction MVCT-recalculated dose. The accumulated dose is the accumulation of all prior fraction MVCT-recalculated doses. The daily dose and accumulated dose are scaled to the full treatment course to facilitate comparison with the planned dose. The projected dose is similar to the accumulated dose except it accumulates the dose up to the latest fraction and repeats the latest fraction for the remaining treatment course. This projected dose is an estimation of the dose that will be delivered if the treatment isn’t re-planned.

Figure 2. A portion of the report automatically generated for a female pelvis patient, which shows at a glance which DVH metrics were met (green checkmarks) or not met (red circles) by either the reference treatment plan (fourth column from the left) or the dose recalculated upon the daily MVCT (sixth column from the left).

Contour	Constraint Name	Total Planned Dose	Fulfilled	Projected Dose	Fulfilled	% Change	Change
PTV para-aortics(0.7cm)	D 95	47.94 Gy	✓	44.18 Gy	●	-7.84	-3.76
Sub PTV Pelvic nodes/ing jng nodes,para metria(0.7)	D 95	50.51 Gy	✓	48.69 Gy	✓	-3.60	-1.82
Sub PTV uterus/cervix/vagina(1.5)	D 95	50.68 Gy	✓	48.81 Gy	✓	-3.69	-1.87
Unified Pelvic PTV	D 95	50.52 Gy	✓	48.63 Gy	✓	-3.74	-1.89
PTV Pelvic LN Boost(0.5)	D 95	56.22 Gy	✓	53.11 Gy	✓	-5.53	-3.11
Unified pelvic eval PTV	D 95	50.61 Gy	✓	48.71 Gy	✓	-3.75	-1.90
Rectum	V 40 Gy < 40%	100.00 % Contour Vol	●	100.00 % Contour Vol	●	0.00	0.00
Bladder	V 40 Gy < 30%	81.84 % Contour Vol	●	80.01 % Contour Vol	●	-2.24	-1.83
SpinalCord	Max < 45 Gy	29.11 Gy	✓	28.06 Gy	✓	-3.61	-1.05
Vagina	V 40 Gy	100.00 % Contour Vol	✓	100.00 % Contour Vol	✓	0.00	0.00
Vulva	V 40 Gy	8.30 % Contour Vol	✓	5.69 % Contour Vol	✓	-31.45	-2.61

DVHs from the planned, accumulated and projected dose can also be added to the report for further analyses. Axial, sagittal, and coronal slices showing the differences between the planned dose and the daily MVCT-recalculated dose can also be displayed. The slices within which the dose differences are maximal are displayed by default.

The report can also include graphs of ROI volumes and DVH metrics as a function of the fraction number to monitor trends (Figure 3). The ROI volumes are obtained from deforming the ROIs from the plan CT to the daily MCVT. The ROI volumes from the reference plan are also included for comparison. The DVH metrics are obtained from the daily MVCT-recalculated dose. This enables the quantitative monitoring of anatomic changes and their dosimetric effects, which is otherwise not possible by visual inspection of the daily MVCT alone.

Note that the list of enrolled patients on the PreciseART dashboard is color-coded to identify at a glance which patients have had at least one daily fraction in which the recalculated dose did not satisfy the DVH metrics for at least one of the ROIs. This may expedite the Radixact® treatment review process in the clinic. In practice, approximately two minutes is required to review the report for one patient.

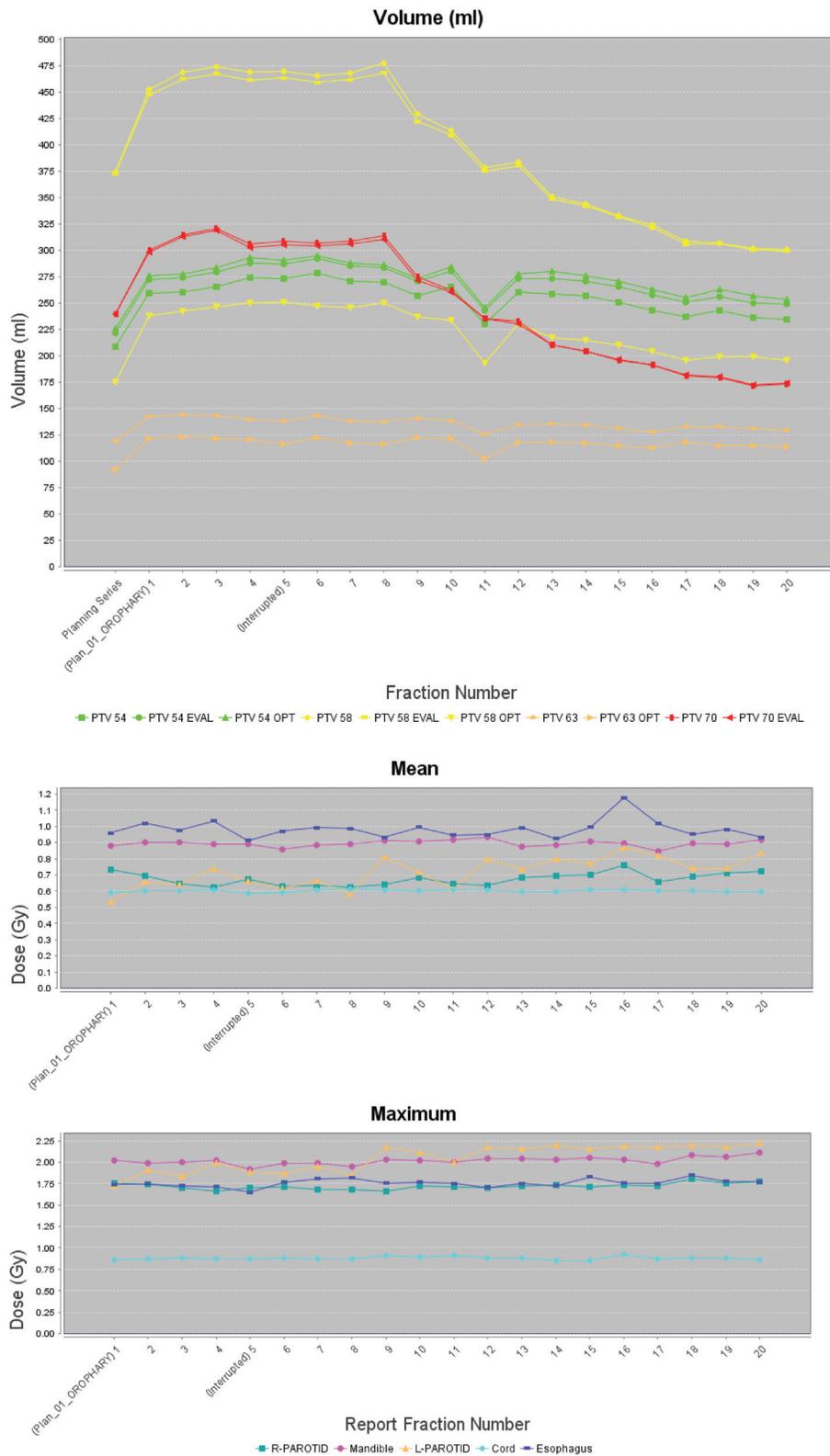


Figure 3. Graphs from the report automatically generated for a head and neck patient, showing the volume of selected target ROIs (top frame) and the maximum and mean dose of selected OARs (bottom frame) as a function of fraction number. In this example, we can observe significant tumor shrinkage resulting in a gradual increase in the left parotid maximum and mean dose.

NON-RIGID DEFORMATION QA TOOLS

The integrated MIM viewer includes, among other tools described later, tools to assess the quality of the DIR. Overlay of planned and deformed contours can be displayed for visual inspection, Dice similarity index and other statistics can be calculated for these contours, and the Reg Reveal™ tool, specifically designed for DIR QA, is also a standard feature (Figure 4).

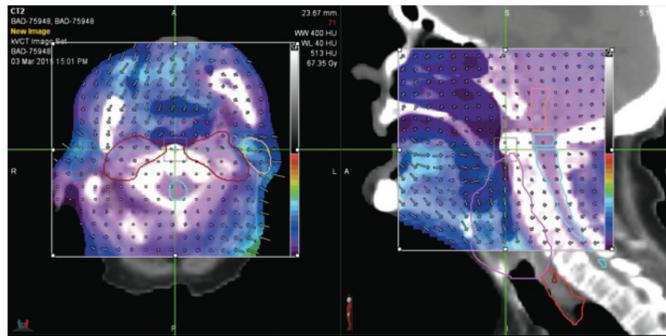


Figure 4. Reg Reveal™ DIR QA tool is available with the integrated MIM Software plug-in.

With appropriate licensing from MIM Software, a Jacobian determinant ($|J|$) map can be calculated within a user-defined projection of the fused image to identify regions of lower or higher local changes in volume, and thus can provide an independent assessment of the deformation algorithm's performance. Values of $|J|$ closer to 1 denote regions of minimal changes in local volume, whereas $|J| > 1$ corresponds to compression or expansion of tissue; if a volume change is not expected, $|J| > 1$ suggests an incorrect non-volume-preserving deformation. Example $|J|$ maps for DIR tests upon an anthropomorphic pelvis phantom are shown in Figure 5.

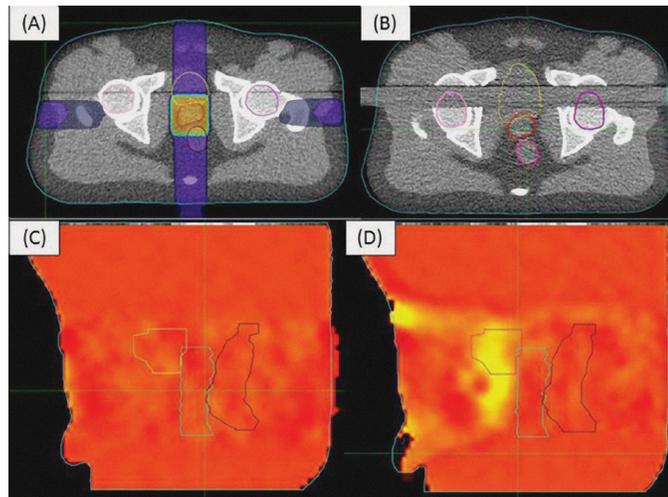


Figure 5. The top frames are axial images of MVCT scans of an anthropomorphic pelvis phantom, (A) without and (B) with 2.5 cm solid water inserted in the phantom. Jacobian determinant $|J|$ maps along a mid-sagittal projection are shown in the bottom frames, for a DIR of the phantom with itself (C) without the insert and (D) with the insert. Orange regions denote $|J| = 1$, while increasingly yellow regions indicate increasing values of $|J|$. In frame (D), a bright yellow region demonstrates increased deformation to accommodate the additional 2.5 cm of solid water, which is expected.

EVALUATION TOOLS AND REPORTS

The PreciseART® dashboard also provides several review workflows to evaluate the daily MVCT registration and the dose recalculation (Figure 6). These review workflows utilize the MIM Software plug-in. Three workflows are available to evaluate the MVCT-recalculated dose at a given fraction. The Daily Dose Review workflow compares the planned daily dose with the MVCT-recalculated daily dose for the selected fraction. The Accumulated Dose Review workflow is similar to the Daily Dose Review workflow, except that the expected planned dose up to the selected fraction is compared with the calculated, deformed, and summed doses from each daily MVCT acquired to date. The Projected Dose Review workflow is similar to the Accumulated Dose Review workflow except it accumulates the dose up to the selected fraction and repeats the selected fraction for the remaining treatment course.

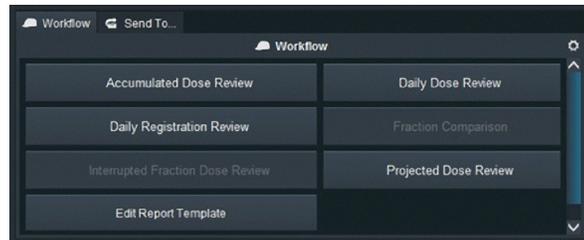


Figure 6. A screen capture of the review workflows available on the PreciseART dashboard. These review workflows utilize the MIM Software plug-in.

The Daily Registration Review workflow displays an overlay of a given fraction's daily MVCT with the CT image and structure sets from the reference plan; the translational and rotation IGRT-guided patient shifts for that fraction are accounted for in the overlay. This functionality is similar to the registration feature on the treatment delivery software console (Figure 7). Measurement and annotation tools are also available.

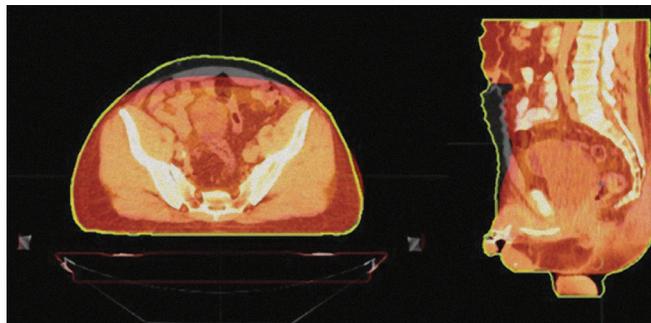


Figure 7. Screen captures from the Daily Registration Review workflow showing the daily CT (color wash), reference plan CT (gray scale), and patient external contour from the reference plan. Patient weight loss is noticeable in these images.

The format in which the tables, graphs, DVHs, and isodose displays are presented in the automated report can be customized using the Edit Report Template workflow. Report templates can be customized for specific disease sites or contingencies; for example, a report template specific to head and neck treatments can be defined to monitor ROIs and DVH metrics in the head and neck region, provided that the ROI names match the template format. DVH metrics tables such as that presented in Figure 2 can be defined to correspond to a clinic's usual planning criteria for a given disease site. Once a report template is created and saved, it becomes available for selection in a drop-down list during the initial enrollment of the patient into PreciseART.

**CLINICAL APPLICATIONS OF PreciseART®:
EXPERIENCES AT FROEDTERT & MEDICAL COLLEGE OF WISCONSIN CLINICAL CANCER CENTER**

CLINICAL WORKFLOW

At the Froedtert & Medical College of Wisconsin (F-MCW) Clinical Cancer Center, our routine clinical application of PreciseART® typically proceeds as follows:

- (1) As soon as the attending physician approves a Radixact® treatment plan, each patient is enrolled into PreciseART in the iDMS®.
- (2) Typically on a weekly basis, to coincide with general weekly chart reviews, an observer (typically a medical physicist) checks for inconsistencies in the following locations of the report:
 - (a) The graphs of ROI volumes or DVH metrics versus fraction number, looking for either sudden or sustained decreases or increases (trends).
 - (b) The display of axial, sagittal, and coronal slices within which the dose differences are maximal, looking for significant dose differences.
 - (c) The DVHs for the reference plan and MVCT-recalculated dose (both accumulated and projected dose), looking for significant variations.
- (3) Whenever the treating therapists observe differences between the daily MVCT and the reference plan CT, an overlay of the two image sets is done using the Daily Registration Review workflow. For example a reduction or increase in tissue at the anterior aspect is suggestive of weight loss or gain.

If any of the above appears inconsistent with the reference plan for more than one to two fractions, the review workflows are used to further investigate the quality of the daily rigid registration to confirm any anatomic changes and dose differences between the planned dose and the daily, accumulated, and projected dose to evaluate the dosimetric impacts. If the observed inconsistencies are indeed due to anatomical changes and significantly deteriorate the intended treatment plan, the physician would review the information and decide if re-planning is needed. If re-planning is needed, PreciseRTX® facilitates re-planning based on the original plan and the available information from the review workflows on the dose already delivered.

STATISTICS TO-DATE ON PATIENTS ENROLLED AND RE-PLANNED USING PreciseART

The Radixact Treatment Delivery System, Accuray Precision Treatment Planning System, and iDMS Data Management System were released for clinical use at F-MCW in October 2016. As of August 4, 2017, 100 patients have been planned and treated on this system. Among this cohort, 95 patients have been enrolled into PreciseART. Although, initially, only selected patients were enrolled, later we decided to enroll all patients as a part of routine Radixact treatment plan preparation after experiencing the ease of use of this fully automated software. Results from the PreciseART analyses have prompted re-planning in 15 patients (16%); this is an increase over our clinic's rate of re-planning prior to implementation of PreciseART. Observations for some of these patients are presented on following pages.

CLINICAL EXAMPLES

PROSTATE CASE: WEIGHT LOSS

Described in Figures 8, 9, and 10 is a prostate case prescribed 70 Gy in 28 fractions. At fraction 10, a Daily Dose Review analysis was performed, in response to reports of a reduced tissue thickness at the anterior aspect. As is shown in Figure 10, modest increases in dose to the PTV were indicated. Yet the prostate dose increase was considered to be clinically acceptable and the DVHs for the bladder and rectum were unchanged; thus the patient was not re-planned.

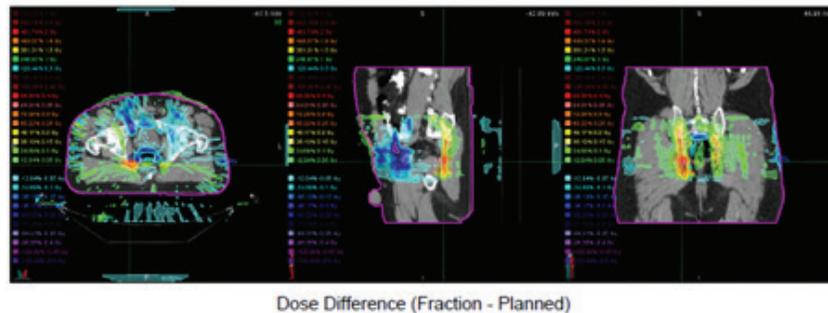


Figure 8. The isodose differences (daily MVCT-recalculated dose on fraction 10 relative to reference plan dose) as displayed in the report. Blue regions indicate reduced daily dose, present primarily at the patient's anterior aspect. Orange/red regions indicate increased daily dose, primarily lateral and posterior to the prostate. The isodose difference display prompted further reviews of the registration and dose differences using the review workflows.

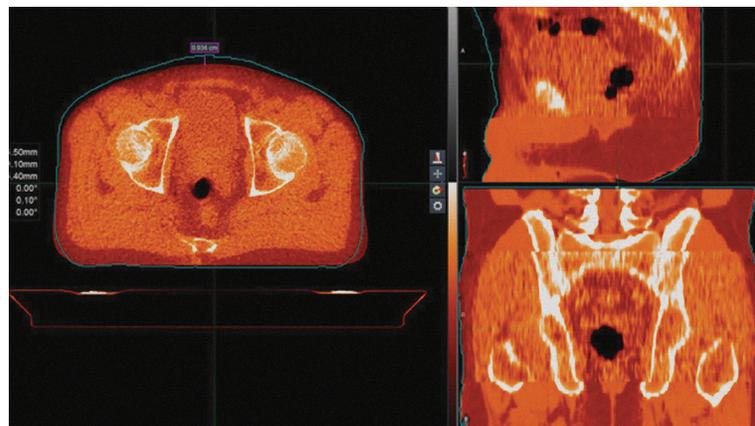


Figure 9. A comparison of the daily pre-fraction MVCT on fraction 10 relative to the patient external contour (cyan) from the reference plan, as generated within the Daily Registration Review workflow. The patient skin surface is recessed relative to the external contour from the reference plan; this difference peaks at approximately 0.9 cm at midline.

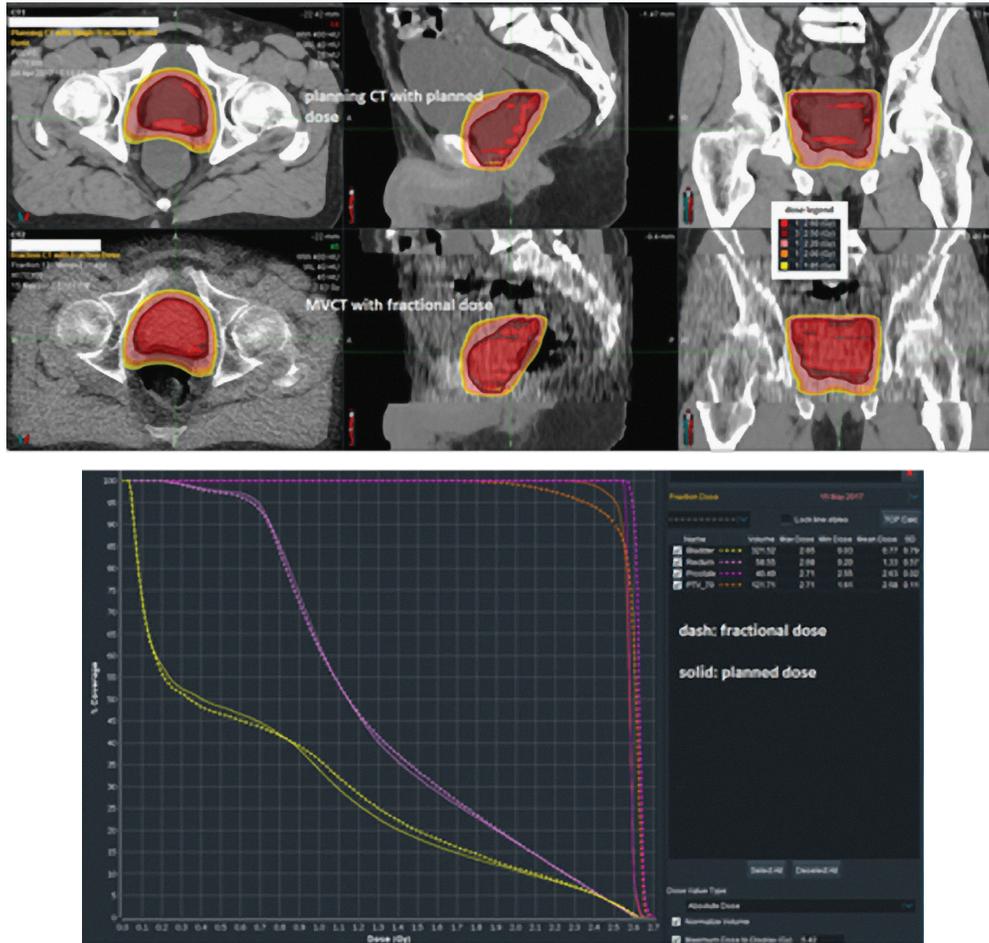


Figure 10. Isodose and DVHs as displayed using the Daily Dose Review workflow. In the vicinity of the prostate PTV, the dose as calculated upon the reference plan CT (top row in figure) is the prescribed 2.5 Gy per fraction (dark red color wash). The daily MVCT-recalculated dose (middle row in figure) indicates an increased PTV dose of 2.6 Gy for this fraction (bright red color wash). Note that, although the report's isodose difference display (Figure 8) indicated increased daily dose posterior to and lateral to the PTV, the increased daily dose within the PTV (relative to the single-fraction planned dose) is more evident in the Daily Dose Review workflow. In the DVH, the solid lines correspond to the plan and dashed lines to the daily MVCT-calculated dose on fraction 10. The increase in dose to the PTV (red lines) is apparent as well. Note that the daily MVCT-calculated doses to the bladder (yellow lines) and rectum (purple lines) agree well with the planned doses to these structures.

FEMALE PELVIS CASE: WEIGHT GAIN

Described in Figures 11, 12, and 13 is a female pelvis (cervix) case prescribed 50.4 Gy in 28 fractions to the primary cervical PTV and regional lymph nodes, while simultaneously administering 56 Gy in 28 fractions to a pelvic lymph node boost volume. At fraction 5, a Daily Dose Review analysis was performed in response to reports of increased tissue thickness at the anterior aspect. As shown in Figure 13, a reduction of the primary PTV dose of approximately 17% was observed; the patient was re-simulated, and a revised plan was implemented after fraction 6.

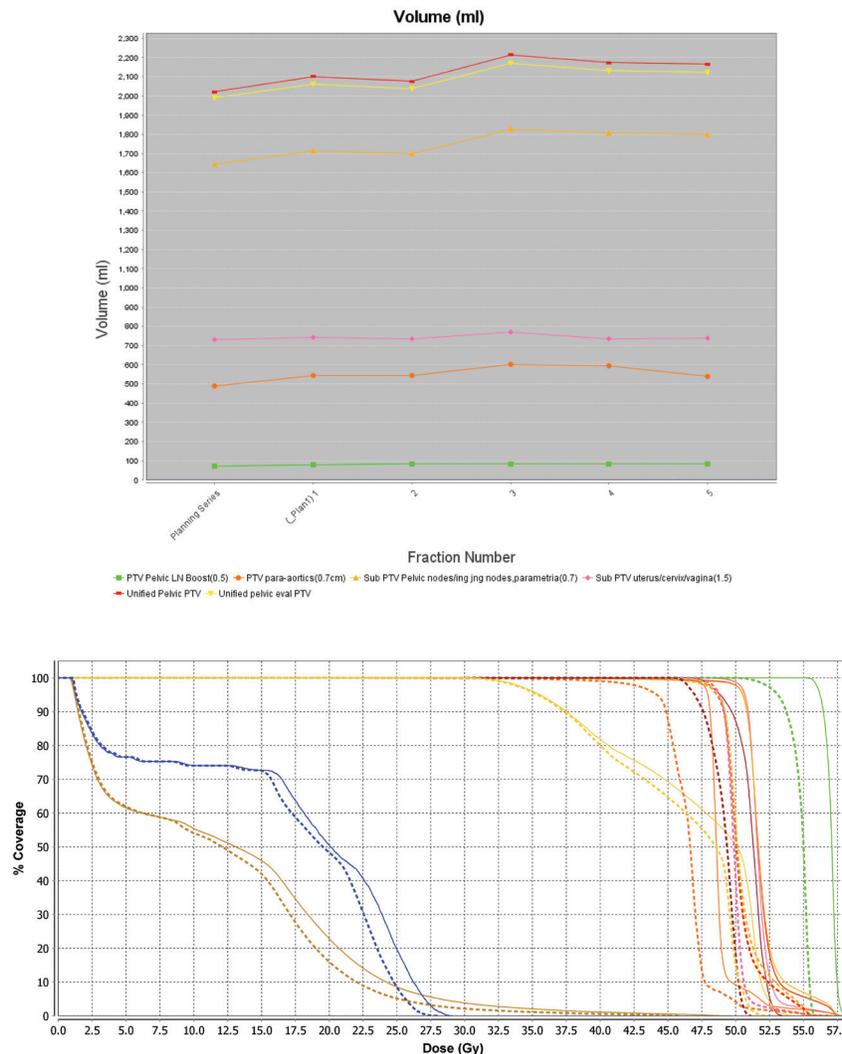


Figure 11. A graph from the report (top frame) illustrates a steady increase in the para-aortic PTV (orange line) and the unified pelvic PTV (red line). The apparent increase in the volumes of the unified pelvic PTV triggered a more detailed review of the case. For the projected dose DVH (bottom frame), the solid lines correspond to the reference plan and dotted lines to the daily MVCT recalculation at fraction 5. Decreased doses to each of the ROIs are apparent. In particular, the coverage to the pelvic boost PTV (green lines) would have been reduced by approximately 4 Gy, if the original plan had been carried on to the full treatment course.

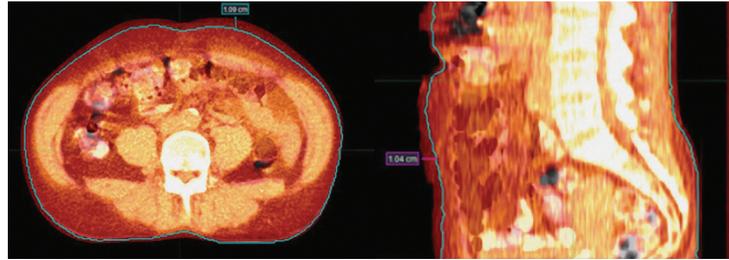


Figure 12. A comparison of the daily MVCT on fraction 5 relative to the patient external contour (cyan) from the reference plan, as generated within the Daily Registration Review workflow. The patient skin surface is extended relative to the external contour from the reference plan; this difference peaks at approximately 1 cm at midline.

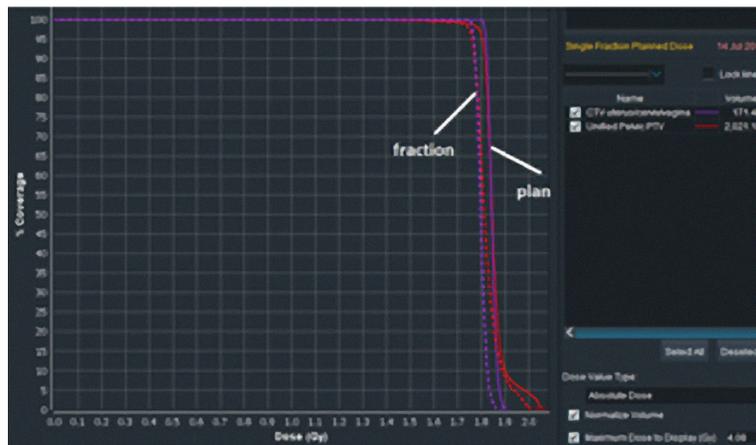
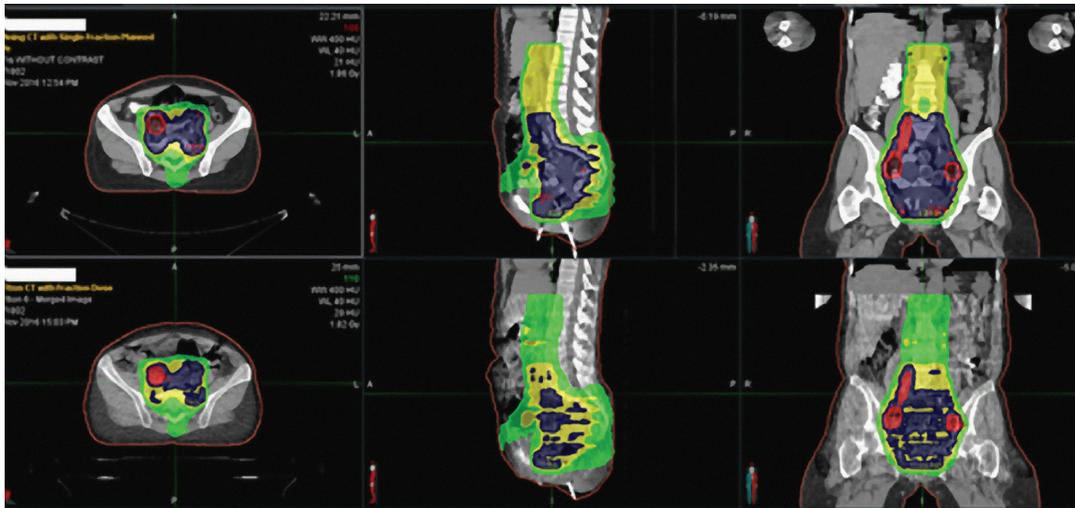


Figure 13. Isodose and DVHs as displayed using the Daily Dose Review workflow. In the vicinity of the pelvic PTV, the dose as calculated upon the reference plan CT (top row) is the prescribed 1.8 Gy per fraction (black color wash). The daily MVCT recalculation at fraction 5 (middle row) indicates a reduction of the 1.8-Gy isodose for this fraction. In the DVH, the decrease in dose to the pelvic PTV (red lines) is approximately 0.3 Gy per fraction (17% of the prescribed dose).

BILATERAL CHEST WALL CASE: SHIFT OF IMPLANTS

Described in Figures 14, 15 and 16 is a bilateral chest wall case prescribed 50.4 Gy in 28 fractions to both chest walls (with tissue expanders in place) and their regional lymph nodes. At fraction 11, a Daily Dose Review analysis was performed in response to reports of displacement of the tissue expanders relative to the original CT simulation. As shown in Figure 16, regions of increased dose and decreased dose were apparent, and a revised plan was implemented after fraction 13.

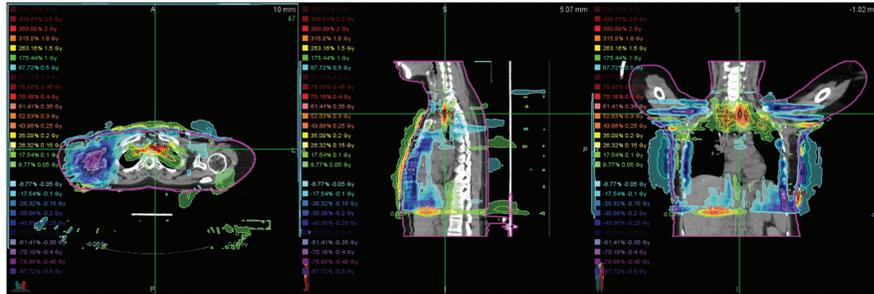


Figure 14. The isodose differences (daily MVCT recalculated dose at fraction 11 relative to reference plan dose) as displayed in the report. Blue regions indicate reduced daily dose, particularly apparent at the chest wall as seen in the sagittal and coronal projections. These dose differences prompted further reviews of the registration and the dose differences using the review workflows.

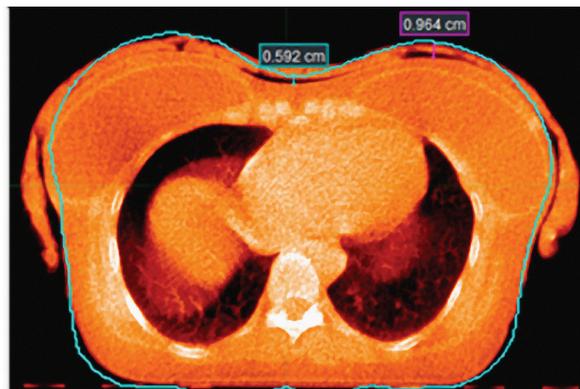


Figure 15. A comparison of the daily pre-fraction MVCT at fraction 11 relative to the patient skin surface (cyan) from the reference plan, as generated within the Daily Registration Review workflow. Considerable displacements of the implants within the chest wall are apparent.

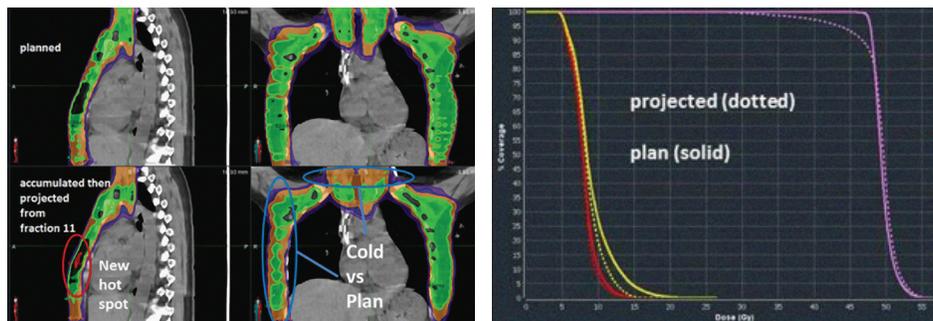


Figure 16. Isodose and DVHs as displayed using the Projected Dose Review workflow.

In the vicinity of the chest wall PTV, the dose as calculated upon the reference plan CT (top row) is the prescribed 1.8 Gy per fraction (green color wash). The MVCT recalculation projected from fraction 11 (middle row) indicates regions of increased dose (red isodose line in the chest wall on the sagittal view) and decreased dose (particularly in the right chest wall and supraclavicular regions, apparent on the coronal view). In the DVH, the decrease in dose to the PTV (purple lines) at the 95% coverage level is approximately 10% of the prescribed dose.

HEAD AND NECK CASE: WEIGHT LOSS

Described in Figure 17 is a head and neck case prescribed 70 Gy in 35 fractions to a left tonsil PTV, while simultaneously administering 56 Gy and 63 Gy to the regional lymph nodes. At fraction 14, a Daily Dose Review analysis was performed, in response to reports of overall patient weight loss during the treatment course. As shown, the dose to the left-sided PTV (originally prescribed 2 Gy per fraction) increased by approximately 5%. The patient was re-simulated, and a revised plan was implemented after fraction 22.

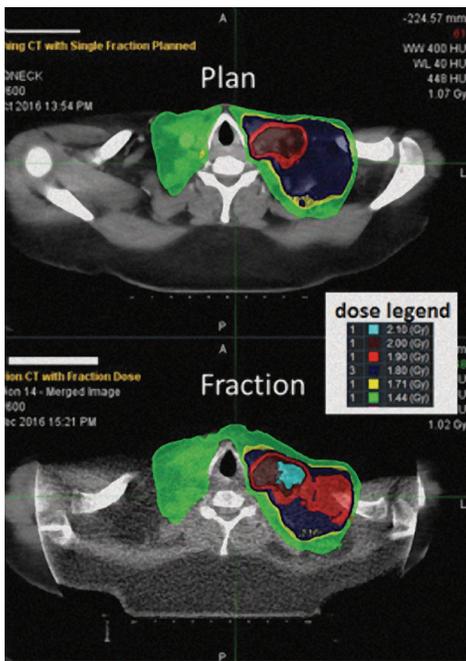


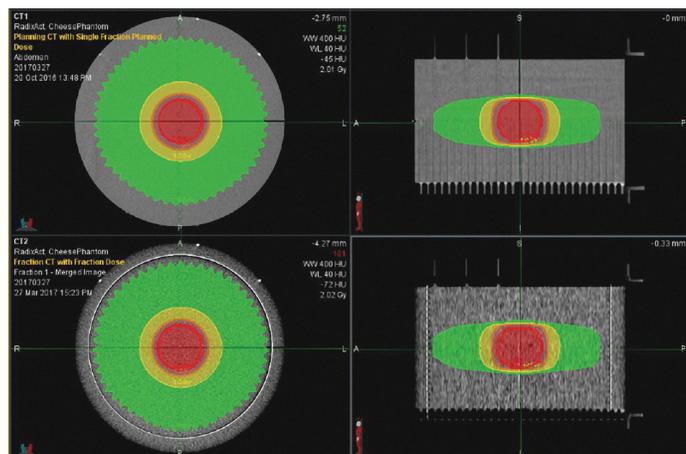
Figure 17. Isodose distribution as displayed using the Daily Dose Review workflow for the original head and neck plan (top frame) and for the MVCT recalculations (bottom frame) at fraction 14. Within the left-tonsil PTV, the maximum dose exceeds 2.1 Gy, a 5% increase over the prescribed dose per fraction of 2 Gy. Note also the spillage of the 2 Gy isodose region lateral to the left-tonsil PTV, which is attributed to the overall weight loss of the patient.

USE OF PreciseART® AS A CLINICAL QA TOOL

In addition to monitor interfraction changes that may develop in patients during the treatment course, PreciseART® can also identify errors in planning and linac simulation that might otherwise be missed during the conventional radiotherapy QA process. To demonstrate these capabilities, a series of phantom experiments were performed; these are summarized below. For each of these tests, a reference TomoHelical™ plan was generated upon a solid water cylindrical phantom with a diameter of 30 cm and length of 18 cm. A 6 cm diameter spherical PTV was drawn at the center of the phantom, and 2 Gy per fraction was prescribed to cover 95% of the spherical PTV.

CONTROL CONDITION:

Figure 18. To verify PreciseART® dose calculation accuracy on MVCT images, the phantom was aligned with the Radixact isocenter in the same manner as in the reference plan, an MVCT scan was acquired and a fraction delivered. This triggered PreciseART automated calculations and report. In this configuration, the MVCT-recalculated dose (bottom frame) agreed with the planned dose (top frame) to within 1%, which demonstrated that the MVCT recalculations were correct.



WEIGHT GAIN SIMULATION:

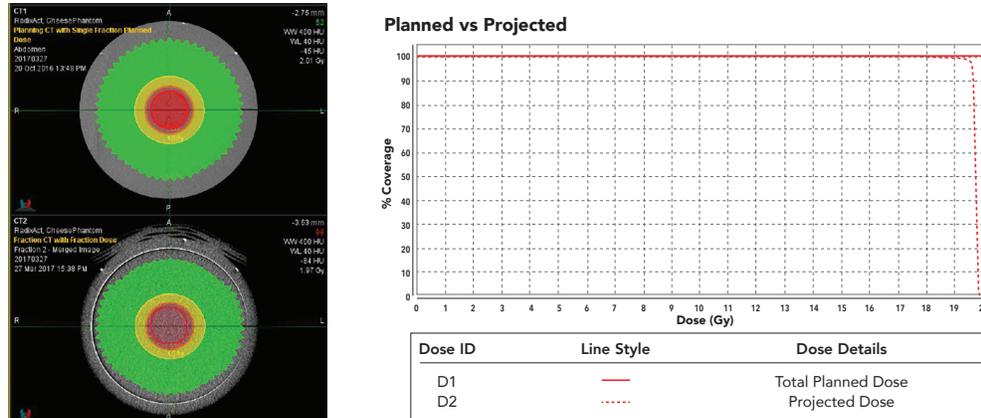
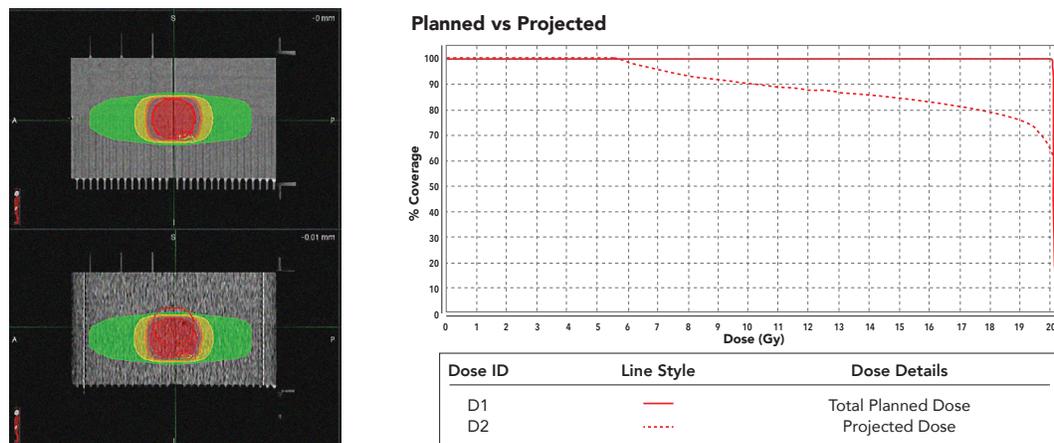


Figure 19. To simulate weight gain, 2 cm of superflab bolus was placed atop the phantom (lower left frame), and another MVCT scan and treatment delivery were performed. The DVH (right frame) was obtained from the report for this fraction. For the MVCT recalculation (dotted line), the dose covering 95% of the PTV was approximately 1.95 Gy per fraction, which corresponded to a 2.5% decrease in the dose relative to the reference plan (solid line).

SETUP ERROR SIMULATION



Contour	Constraint Name	Total Planned Dose	Fulfilled	Projected Dose	Fulfilled	% Change	Change
PTV	V 100% RX >95%	99.98% Contour Vol	✓	63.96 Contour Vol	●	-2.77	-1.95

Figure 20. To simulate a gross setup error, the phantom was positioned on the Radixact® Treatment Delivery System in a way that the phantom center was displaced 2 cm longitudinally relative to the machine isocenter. The MVCT recalculation shows reduced PTV coverage on the isodose distribution (top left) and the DVHs (top right). Note that gross fractional dose deviations to ROIs such as in the above case can also be identified in the DVH metrics table (bottom).

INCORRECT DENSITY ASSIGNMENT:

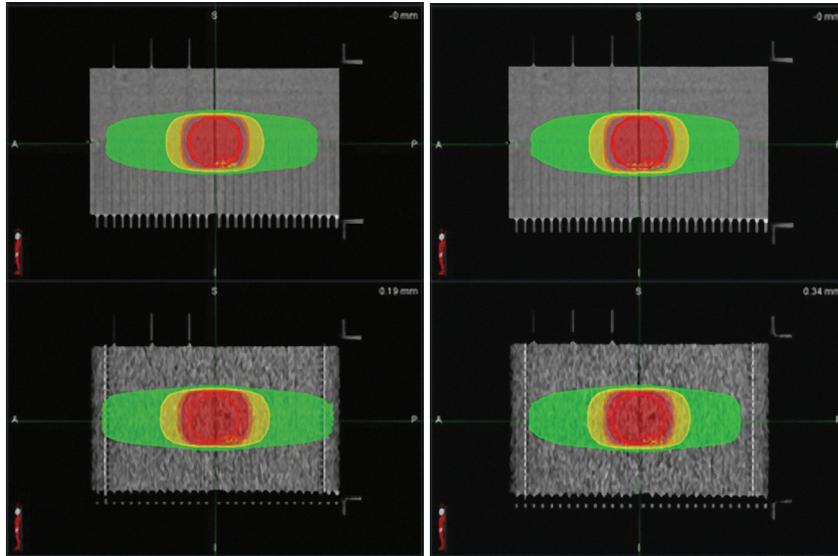


Figure 21. Errors in CT density assignments in the reference plan can be identified with the MVCT recalculation. The left frames show the reference plan calculation (top) and the MVCT recalculation (bottom) for an instance in which the phantom density (nominally 1 g/cm³) was forced to 1.25 g/cm³ in the reference plan CT. On MVCT recalculation, the mean dose to the PTV increased by 15%, and the 2-Gy isodose line (red) spilled outside the PTV. In the right frames, the phantom density in the reference plan CT was forced to 1.05 g/cm³; in the resulting MVCT recalculation, spillage of the 2-Gy isodose line is also seen, although the mean PTV dose increase was approximately 2.5%. It should be noted that a gross error in the reference CT density is not ordinarily investigated during conventional plan reviews; however, it is readily identifiable from the automated MVCT recalculations.

INCORRECT COUCH INSERTION:

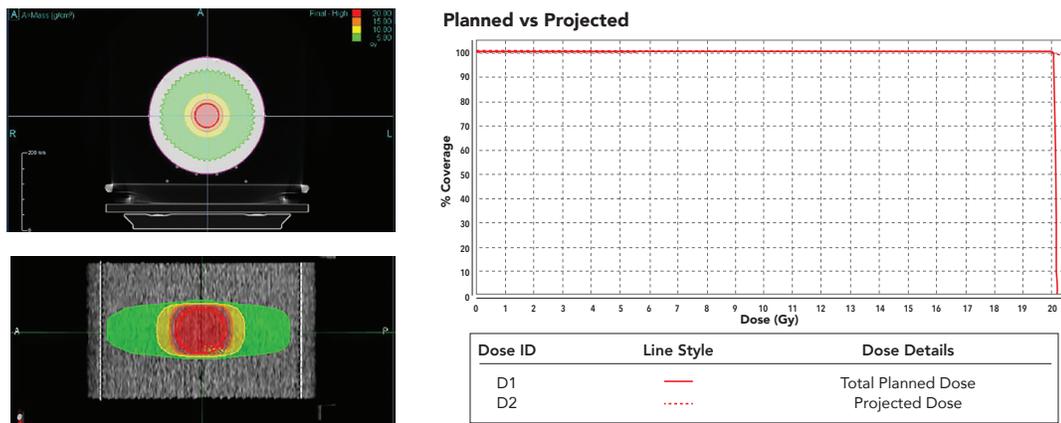


Figure 22. A treatment plan was created with an incorrect couch insertion (too far inferiorly), causing a portion of the simulation CT couch top to be included in the optimization, but not during treatment (upper left frame). The MVCT recalculation (upper right frame) demonstrates spillage of the 2-Gy isodose distribution (red) outside of the PTV. The DVH (bottom frame) shows a slight (approximately 2%) increase in the PTV dose from the MVCT recalculation, which did not include the portion of the CT couch that was present in the reference plan.

SUMMARY AND OBSERVATIONS FROM CLINICAL EXPERIENCE, CHANGES IN PRACTICE, AND BENEFITS TO PATIENTS AND CLINICIANS

The PreciseART® option within the Accuray Precision® TPS can objectively, quantitatively, and effectively identify interfraction changes for which re-planning might be indicated and clinically beneficial. It automatically performs DIR between the plan CT and daily MVCT IGRT image, deforms plan ROIs onto the daily MVCT, calculates dose on the daily MVCT, accumulates dose onto the plan CT, and summarizes ROI volume and dose changes in a user-defined report. Each of these steps is automated; user intervention is required only to enroll a patient plan into PreciseART and to review the report. In addition to the report, review workflows are available to facilitate a more in-depth analysis of the daily IGRT registration and daily, accumulated, and projected dose.

Isodose difference displays within the report can hint toward changes in patient size (e.g., weight loss or weight gain) on the order of 1 cm, which in turn can be confirmed via the review workflows. It should be noted that for conventional radiation therapy using periodic target-to-skin distance readings for the setup and the treatment beams, the action level for recalculation of monitor unit settings is typically 1 cm.

In addition to flagging interfraction anatomic changes, PreciseART can also identify errors (such as incorrect density assignments and couch insertion) within the planning CT image. Since such errors may not ordinarily be detected in the routine plan QA process, it is recommended as standard procedure to enroll each Radixact and TomoTherapy patient into PreciseART to automatically recalculate the dose upon the first fraction MVCT and look for inconsistency.

Initially, only selected Radixact® patients were enrolled into PreciseART, but after experiencing the ease of use of this fully automated software and its value as a quality assurance tool, we currently enroll all patients. To date, PreciseART has prompted re-planning for approximately 16% of the enrolled cases. This rate is an increase over the standard frequency for which the need for re-planning is identified using manual assessment. A review of patients planned and treated using VMAT with daily cone-beam CT indicated that approximately 6% of them required re-planning. The rate of re-planning for Radixact patients may increase as our clinic becomes more familiar with the tool. Further, using the reports and review workflows made available, our clinic is expected to initiate the re-planning process earlier in the treatment course. This demonstrates that radiation therapy is necessarily a patient-specific process, indicating a need for increased effort within the radiation therapy team to devote to ART. PreciseART software's seamless integration and automation made this practical in our clinic.

REFERENCES

- Gupta V, Wang Y, Romero A, Myronenko A, Jordan P, Heijmen B, and Hoogeman M, "Fast and Accurate Auto-Segmentation of Abdominal Organs at Risk for Online Adaptive Radiotherapy," *Med. Phys.* 41 (6) (2014) p. 205
- Langen K, Meeks S, and Poole D, "The Use of Megavoltage CT (MVCT) Images for Dose Recomputation," *Med. Phys.* 32 (6), (2005) p. 2025
- Li XA, editor, *Adaptive Radiation Therapy*, CRC Press Taylor & Francis Group, Boca Raton, Florida (2011)
- Mackie TR, Holmes T, Swerdloff S, Reckwerdt P, Deasy JO, Yang J, Paliwal B, and Kinsella T, "TomoTherapy: A new concept for the delivery of dynamic conformal therapy," *Med. Phys.* 20 (6) (1993) pp. 1709-1719
- Yan D, Vicini F, Wong J, and Martinez A, "Adaptive radiation therapy," *Phys. Med. Biol.* 42 (1) (1997) pp. 123-132
- Accuray Precision® Treatment Planning System (TPS) has optional applications to perform offline ART analyses (PreciseART® Adaptive Radiation Therapy option) and to create revised treatment plans (PreciseRTX® Retreatment option).



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