An on-line replanning scheme for interfractional variations

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Ability of online adaptive replanning is desirable to correct for interfraction anatomic changes. A full-scope replanning/reoptimization with the current planning techniques takes too long to be practical. A novel online replanning strategy to correct for interfraction anatomic changes in real time is presented. The scheme consists of three steps: (1) rapidly delineating targets and organs at risk on the computed tomography of the day by modifying original planning contours using robust tools in a semiautomatic manner, (2) online segment aperture morphing (SAM) (adjusting beam/segment apertures) by applying the spatial relationship between the planning target contour and the apertures to the new target contour, and (3) performing segment weight optimization (SWO) for the new apertures if necessary. The entire scheme was tested for direct-aperture-based IMRT on representative prostate and abdomen cases. Dose volume histograms obtained with the online scheme are practically equivalent to those obtained with full-scope reoptimization. For the days of small to moderate organ deformations, only the SAM is necessary, while for the large deformation days, both SAM and SWO are required to adequately account for the deformation. Both the SAM and SWO programs can be completed within 1 min, and the overall process can be completed within 10 min. The proposed SAM-SWO scheme is practically comparable to full-scope reoptimization, but is fast enough to be implemented for on-line adaptive replanning, enabling dose-guided RT. © 2008 American Association of Physicists in Medicine. [DOI: 10.1118/1.2952443]

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I. INTRODUCTION

The ability to image radiation therapy patients in the treatment room has made it possible to address the problems of interfraction variations in patient anatomy and setup uncertainties.1–14 There have been many schemes proposed for correcting interfraction variations. These include offline adaptive correction schemes15–18 and online correction techniques.19–26 Offline adaptive processes have been used to correct systematic positioning errors.15,18 Offline replanning after imaging feedback by taking into account what has been delivered has also been proposed.15,18 For online correction, both patient repositioning1,3–5,8,26 and plan adjustments19,20,22,23,25 have been proposed. Most online correction schemes rely on figuring out the translations needed to match the images of the day to those used for planning and adjusting patient position accordingly using couch motion.1,3,6,8,26 This scheme of shifting the patient while delivering the same plan is only a first order correction for the following reasons: (1) target rotations cannot be corrected with translations of the patient, (2) in general, not only the target location but also the target volume and shape can change, and (3) the geometric relationship of the target with its surrounding normal structures will also vary from day to day. As a result, the current online correction scheme cannot take full advantage of the imaging capability.

Knowing the changes in patient anatomy, the ideal technique for correcting the problem is to reoptimize the treatment plan based on the image taken immediately before the treatment. For a new treatment plan to be optimized, the target and surrounding structures must first be delineated on the images of the day. Pencil beam dose distributions must be recomputed since the anatomy has changed, which is compounded by the problem that the computed tomography (CT) numbers of the cone beam CTs (CBCTs) are different from the Hounsfield units of fan beam CT images.27 The intensity optimization and subsequent leaf sequencing also take significant time. With today’s technology, this process cannot be completed within a reasonable time when the patient is laying on the treatment couch. Therefore, a fast correction scheme that may or may not approach the ideal solution of replanning should be applied.

Here we propose an online scheme to address interfractional anatomy changes, including both dislocation and deformation. Major steps in the scheme includes: (1) morphing beam segment shapes to match the new location and shape of
the target, and (2) optimizing the new segment weight. Unlike most of the online correction methods proposed previously,22,28 our online correction method does not require complicated deformable registration, therefore, can be fast and practical. The online approach requires an offline dose accumulation based on deformable registration. This work presents the online scheme. The offline approach will be described in a separate study.

II. MATERIALS AND METHODS

II.A. Overall online correction scheme

The purpose of this study is to develop an effective and feasible correction method that can realistically be completed while the patient is still on the table. This technique is intended to avoid the lengthy reoptimization without sacrificing the plan quality. The online correction method takes place in the following work flow: (1) acquiring CT images of the day with in-room CT like CT-on-rails29 or cone beam CT30 right before the fractional dose is delivered to the patient, (2) rapidly delineating the target (e.g., planning target volume) (PTV) by modifying planning (previous) contours to fit the new locations and shapes of the targets and OARs from the CT of the day using a robust and semiautomatic tool, (3) adjusting (morphing) beam/segment apertures based on differences between planning (previous) contours and the new contours of the day using the segment aperture morphing (SAM) algorithm described below, (4) computing the dose distribution for each new aperture, (5) delineating other structures, (6) optimizing beam/segment weights of the new apertures, using the segment weight optimization (SWO) tool described below, and (7) transferring the new beams/segments for delivery.

Various measures were considered to ensure the entire procedure can be completed within a practically acceptable time frame (approximately 10 min). These measures include: (1) the use of robust software tools and hardware allowing contours to be modified rapidly, (2) computing dose distribution for new apertures, using a computer system with 8 CPUs, in two separate steps, TERMA and convolution-superposition computation. The TERMA calculation, not requiring exact shape of aperture, is performed during the period of the target delineation. The convolution superposition is carried out while OARs are being delineated. Software and hardware tools developed to speed up contour delineation include: (1) quickly drop and drag planning contours onto the CT of the day, (2) simultaneously delineate based on axial, sagittal, and coronal views, and (3) interpolate contours for skipped images. In addition, we used a user-friendly interactive pen (Cintiq 21UX, Wacom) display. This is a cordless, battery-free pen-on-screen device, allows user to draw by hand, providing significant time savings. These tools are implemented in a commercial planning system (Panther, Prowess, Inc., Chico CA). It was found that the time required to delineate a prostate case (e.g., prostate PTV, bladder, and rectum) was within 2 min.

II.B. Segment aperture morphing

The SAM algorithm is designed to calculate the MLC morphing (leaf shifts) based on the beam’s eye view (BEV) of the new target (new target projection) (NTP) and the BEV of the old target (old target projection) (OTP) for each beam angle and each segment. The SAM process starts with, first, dividing the old aperture shape (leaf positions) into a number of discrete points (boundary points) (BPs). For this study, we used ten BPs for each 1 cm thick MLC. Second, the coordinates of each BP is linearly transformed from OTP to NTP according to the formula

\[
\begin{align*}
  y' &= \frac{Y'}{Y}, \\
  x' &= \frac{X'}{X}.
\end{align*}
\]

The \((x, y)\) are the distances of the BP to the contour edge in OTP and \((x', y')\) are the distances to the contour edge in NTP. \((x_0, y_0)\) and \((x_0', y_0')\) are the coordinates of the edge of the NTP and OTP, respectively, at the BP. \((X, Y)\) and \((X', Y')\) are the total extent of the OTP and NTP, respectively, at the BP. Therefore, the coordinates of each BP in the OTP and NTP are \((x_0 + x, y_0 + y)\) and \((x_0' + x', y_0' + y')\), respectively. This equation is further illustrated in Fig. 1. For each BP in OTP, there is always a unique point in the NTP that has the same relative distances. For a BP that is outside the OTP, its distance from the edge of the NTP is kept the same as for the OTP. Last, the new leaf position is obtained by averaging all the new BPs that are within the width of the leaf. The jaw positions are also adjusted accordingly to conform to the outermost opening of the aperture. Note that, for the example shown in Fig. 1, OTP is centered but NTP is not, indicating that the SAM can handle both organ deformation and translational shift. Figure 2 further illustrates how SAM process transforms the MLC banks of an aperture.

The SAM algorithm was initially implemented using MATLAB (Mathworks, Natick, MA) software development environment, and then implemented in the Prowess planning sys-
objectives defined by the user. For a given set of segments, the total dose at voxel \( p \) is a function of segment weights \( \omega \) and can be expressed as

\[
D_p(\omega) = \sum_{i=1}^{M} \omega_id_{ip},
\]

where \( i \) is the segment number and runs over all segments \( (M) \) in question, \( d_{ip} \) is the dose at voxel \( p \) contributed by segment \( i \) for a unit weight of the segment. The optimization involves finding a set of segment weights \( \omega \) which minimizes an objective function. Objective function (cost function) is a weighted sum of user selected objectives (e.g., max dose, target dose uniformity, and dose volume constraints) for the target and OARs, which is minimized during the optimization. A smaller value of the objective function indicates a better plan and the relative weights that are assigned to each objective by user are based on the relative importance of each separate objective. For the cases studied, the objective functions contained (i) dose uniformity penalty for target (standard deviation of the dose in target), (ii) mean dose penalties for critical structures, (iii) max dose penalty at the unspecified tissue outside the target volume, and (iv) various dose volume histogram (DVH) penalties as needed at several (volume, dose) points.

To implement the algorithm, a software package was developed based on the MATLAB system and was designed to interface with a commercial treatment planning system (Panther, Prowess). The package accepts input of three-dimensional (3D) dose distributions of all possible beams and structure contours and determines a set of segment weights so that the objective function defined based on the prescription and dose-volume constraints can be minimized. The objective function as a function of segment weights, and the dose constraints can be either linear or nonlinear. A nonlinear optimization procedure developed within the MATLAB system, which uses a sequential quadratic programming (SQP) method, was employed to optimize the segment weights. In SQP, a quadratic programming (QP) subproblem is generated at each iteration. The QP subproblem is solved using an active set strategy (also known as a projection method) similar to that described by Gill et al.\cite{31} The solution to the QP subproblem is used to form a search direction for a line search procedure. The step length along the search direction is determined in order to produce a sufficient decrease in an objective function similar to that proposed by Han.\cite{32} The search direction along with the step length is then used to form a new iteration. The SQP methods represent the state of art in nonlinear programming methods and have been tested in terms of its efficiency, accuracy, and percentage of successful solutions, over a large number of test problems.\cite{33}

Because the SWO uses the precomputed segment dose distributions, it can be carried out rapidly. The SWO is inherently faster than the conventional IMRT optimization because the number of variables (search space dimension) for SWO (number of segments) is much smaller than that for the IMRT optimization (number of beamlets). In addition, for the IMRT optimization, the dose calculation is usually per-
formed twice: e.g., pencil-beam calculation for optimization and the convolution for final dose calculation. This two-step process, which not only increases computing time but also degrades plan quality, is not required for the SWO. The time required for SWO increases with the number of segments and the size of the calculation volume. For example, it took less than 1 min to compute a prostate case of 28 beam segments.

II.D. Test on sample patient cases

To prove in principle, the online correction (SAM/SWO) algorithms were tested on selected four CT data sets acquired in a total of four fractions from two prostate and one pancreas cases. These patients were treated using a linac with daily CT guidance based on a CT-on-rail (Primatom, Siemens). The patients were positioned based on three skin marks prior to CT acquisition. The original IMRT plans were generated based on their planning CT data using the commercial planning system (Panther, Prowess) which employs the direct aperture optimization (DAO) algorithm. It has been demonstrated that the DAO-IMRT uses a small number of segments, a significant advantage for the present SAM and SWO algorithms. For each of the cases, seven coplanar beams were used and the number of segments per each beam was set at 4 (except for one of the prostate patients it was 3). Uniformly distributed beam directions were selected.

The magnitude of interfractional variations (dislocation and deformation) for these four CT data sets is different. To quantify the magnitude of deformation, the percent volume overlapping (PVO) for the targets between the planning CT and the CT of the day was calculated. The reported PVO values are the maximum values that can be obtained by rigid-body registration. A small PVO indicates a large deformation between the target volumes based on the planning CT and the CT of the day.

For each CT data set, five different scenarios were considered: (1) original-no reposition, i.e., the original IMRT plan applied on the daily CT images with isocenter determined from skin marks (this represents the conventional treatment with no image guidance), (2) reposition, i.e., the original IMRT plan applied on the daily CT images with isocenter determined to achieve the maximum overlap between the new and the old (planning) target volumes (this represents the current common practice of IGRT), (3) SAM, i.e., the original IMRT segments modified by the SAM method based on the daily CT images, (4) SAM+SWO, i.e., the original IMRT segments modified by the SAM methods and the SWO applied based on the daily CT images, and (5) reoptimization, i.e., a new full-blown IMRT plan generated based on the daily CT using the same planning system (Panther, Prowess) with the same objectives used for the original plan. The DVHs of target and OARs for all these five scenarios were compared to demonstrate the effectiveness of the online correction schemes. The reoptimization plan (scenario 5) should be considered as the ideal situation, gold standard. Scenario 1 (original-no reposition), the historical way of treatment, represents the worst case scenario.

All IMRT optimizations were done with the Prowess dose engine (convolution/superposition algorithm). The SWO used the precomputed dose distribution for each segment, which was calculated in CMS XiO (St Louis, MO) (also convolution/superposition algorithm). All final doses were calculated in XiO. All doses were calculated with the same dose engine, and evaluated with same software tools to make sure that no bias was introduced into the comparisons. Re-optimization plans required 5 min to more than half an hour depending on the complicatedness of the case, not including the contouring process.

To study whether the present SAM/SWO approach with using the simple aperture morphing algorithms is equivalent to other methods with more complicated mechanisms for aperture morphing, we also generated plans using the B-splines35 and “demons”36 deformable registration algorithms implemented in C++ using the Insight Toolkit. Original apertures were adjusted by using these algorithms according to the relationship between new and old target projections (NTP and OTP) based on the CT of the day.

III. RESULTS

It can be observed in Fig. 3 that for the first prostate case (prostate_1) the prostate deformation from the planning CT for fraction A is moderate, while it is significant for fraction B. The enlarged deformation is mainly due to the enlarged rectum filling at fraction B as shown in Fig. 3(c). The PVOs were 85% and 74% for fractions A and B, respectively. Figure 4 presents the DVHs obtained under the five scenarios for the two fractions displayed in Fig. 3. It is seen, from Fig. 4, that the prostate (the target volume) would be significantly underdosed if it was treated conventionally (scenario 1). This underdosing is more pronounced for fraction B [Fig. 4(b)], where a larger deformation in the prostate shape is observed. As seen from Fig. 4(a), the coverages of the prostate volume by the prescription dose (70.2 Gy) are 77%, 91%, 94%, and 95% for scenarios 2–5, respectively. This implies that, for the situation with a moderate prostate deformation, the DVH obtained with the SAM method (scenario 3) is close to the gold standard (scenario 5), thus the SAM alone may be adequate from the practical point of view. For the large deformation seen in Fig. 3(c), the coverages of the prostate volume by the prescription dose are 64%, 80%, 95%, and 98% for scenarios 2–5, respectively, indicating both SAM and SWO processes (scenario 4) are required. It should be noted that the rectal DVHs obtained with the SAM/SWO methods are comparable or better than those of the original plan or the full-blown reoptimization (scenario 5, gold standard).

The results of the second prostate case (prostate_2) are depicted in Fig. 5. The prostate, rectum, and bladder contours in a sagittal plane drawn on the planning CT with empty bladder, and on the CT of a treatment day with full bladder, are shown in Fig. 5. The prostate deformation (PVO=84%) due to the different bladder filling is seen in Fig. 5(b). The DVHs for the prostate, rectum and bladder obtained based on the treatment CT for the five scenarios are shown in Fig. 5(c). It was noticed that, for scenario 1, the
isocenter as determined based on skin markers was moved from inside the prostate in the planning CT to outside the prostate in the treatment CT. This displacement results in geographic missing as indicated by the deficient DVH in Fig. 5. The SAM alone is sufficient to yield a good prostate coverage (98%), which is even higher than that (95%) from the reoptimized plan (scenario 5). However, the rectal DVH by the SAM is worse than that by the reoptimization. This gets improved with the use of the SWO. Overall, the combined SAM+SWO method generates a plan comparable to that from the reoptimization in terms of both tumor coverage and normal organ sparing. It should be noted that the SAM was done without shifting the isocenter position, eliminating the need of patient repositioning (via couch shifting).

The data for the pancreatic cancer case are depicted in Fig. 6. In Fig. 6(a), the contours of pancreas, stomach, kidney, and liver, obtained from both the planning CT and the CT of a treatment day, are overlaid in an axial slice of the plan CT. The PVO for the pancreas contours obtained between the planning CT and the treatment CT is 69%. The DVHs of pancreas, stomach, left kidney, and liver obtained based on the treatment CT for scenarios 2–4, are plotted in Fig. 6(b). The DVHs for scenario 1 were found to be almost identical to those for scenario 2, due to the negligible change in the center of the mass of pancreas between the planning CT and the treatment CT, therefore, are not shown in Fig. 6(b). It is seen that the SAM method (scenario 3) improves both target coverage and normal structure sparing, except a hot spot found inside the pancreas. By applying SWO, this hot spot is effectively removed and the DVHs for normal structures, especially the stomach, are further improved. This, again, indicates that the combined SAM and SWO technique can generate plans comparable to those from reoptimization.

Comparison between the SAM/SWO algorithm and the B-splines and the demons algorithms are presented in Fig. 7.
for the prostate_1, fraction B. The results indicate that SAM alone or SAM/SWO combined method is better than or equivalent to the two complicated algorithms. The time required by the SAM was significantly shorter than those required by the B-splines and the demons algorithms.

IV. DISCUSSION

A crucial issue for an online adaptive radiotherapy (ART) strategy is whether it can be implemented with a practically acceptable accuracy and time frame. Several previously proposed online ART methods, although can accurately correct for the anatomic changes observed from the treatment CT images, involve complicated algorithmic processes, such as online deformable registration, therefore, may not be practical. Mohan et al. suggested an online correction method that modifies each of the beam intensities by deformable registration of the intensity patterns based on the contour projection areas on the BEV. For deformable registration, they use the Thirion’s demons algorithm in a two-dimensional (2D) fashion. Their process requires a leaf sequencing process to convert the newly generated intensity patterns into deliverable MLC segments. Feng et al. proposed another method that directly modifies the aperture shapes of each segment based on the 2D vectors generated from a 3D deformable registration based on b-splines. The deformable registration determines the 3D dislocation vectors for a large number of voxels. These 3D vectors are averaged (collapsed) into 2D vectors in the BEV projection and then used for beam aperture modification. Deformable registration is generally time consuming and algorithmically com-
Deformable registration to transfer the original contours from the planning CT to the treatment CT has been suggested.\textsuperscript{24,22,28} This process is generally time consuming and complex. Also, the full deformable registration is overkill for the purpose of contour generation, since it provides the dislocation vector for each voxel from old to new anatomy, however, only the identification of which voxels to be included by the contour is needed. It has been a concern that the interobserver inconsistency and finite CT resolution can lead to errors in target delineation. Such errors would be carried “systematically” over to the daily CTs if an autosegmentation based on deformable registration is used. Whereas, when the contours are drawn each day, these errors would become random, resulting in reduced effects on dosimetry. Another issue is that the automatically generated contours always need to be evaluated by a human observer.

The present online scheme needs to be implemented with offline dose accumulation. Also, it is always feasible to generate an updated plan with full-blown optimization based on the latest CT data offline. The planning CT mentioned in this article can actually refer to the latest (previous) CT. The gradual anatomic variations such as tumor volume shrinkage or growth can be addressed by either the offline or the online approaches, while the random unpredictable anatomic variations can be corrected only by the online scheme.

The proposed method is applicable for both IMRT and 3DCRT. We used the DAO-based IMRT plans because DAO can generate IMRT plans with smaller number of segments and monitor units and with less irregular apertures.\textsuperscript{24} The time required by the proposed scheme, especially the dose calculation, is directly proportional to the total number of segments/beams. The number of segments of IMRT plans typically increases with the level of modulation requirement of the dosimetry.\textsuperscript{37,38} Robust image guidance methods like the one proposed in this article can help reduce the geometric margins, resulting in less demanding dosimetry which, in turn, reduces the number of segments.

The proposed scheme would be applicable to sites where large day-to-day variations in the shape of the tumor are common. Prostate gland and seminal vesicles are well known to show daily shape deformation and dislocation due to the different bladder and rectum filling.\textsuperscript{13,39–41} In particular, the hypofractionated treatments could benefit from this method due to the increased requirement for delivery precision with a less number of fractions and higher fractional doses. Also abdominal regions are prone to large daily shape deformations. Another possible site for the online ART scheme could be head and neck where many junctions between the C-vertebrae and the skull would lead to poor setup reproducibility and would cause large changes in shape and volume, especially if the volumes extend over large distances.

The proposed method requires the contours of important structures to be drawn online, which may be time consuming. Although methods of aperture adjustment without contour generation have been proposed\textsuperscript{8} for certain sites (prostate and seminal vesicles), the verification of dosimetry improvement before treatment is not possible without the contours. We plan to incorporate automated contour generation tools that will speed up the process.

Fig. 7. The prostate and rectal dose volume histograms for reposition (thick solid), SAM (thick dashed), reoptimization (dotted), B-spline (solid), and Demon’s (dashed) deformable registration methods for prostate_1.
clude the targets of the chest and draining nodes of the breast. The online scheme could effectively correct for the inter-fractional variations in a short time frame, as compared with the conventional repeating CT-repositioning process.

V. CONCLUSION

An online real-time ART approach that can correct for interfractional anatomy variations (dislocation and deformations) in a two-step (SAM and SWO) process is presented. It has been demonstrated that the present SAM/SWO approach can significantly improve dose distributions obtained with the current rigid-body shift. The approach, not requiring repositioning, is effective and practically accurate as compared to reoptimization (golden standard). For a small or moderate deformation, for example PVO $> 80\%$, the plan with SAM alone (without SWO) is adequate, resulting in the similar time required for this approach to that with repositioning. For a large deformation (PVO $< 80\%$), the SAM combined with the SWO can generate plans practically equivalent to the reoptimization plan within an acceptable time frame. Unlike the previously proposed online ART strategies, the current online approach does not require deformable registration, therefore, can be implemented in a practically acceptable time frame (e.g., within 10 min).

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