A case study for online plan adaptation using helical tomotherapy

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ABSTRACT

Helical tomotherapy’s ability to provide daily megavoltage (MV) computed tomography (CT) images for patient set-up verification allows for the creation of adapted plans. As plans become more complex by introducing sharper dose gradients in an effort to spare healthy tissue, inter-fraction changes of organ position with respect to plan become a limiting factor in the correct dose delivery to the target. Tomotherapy’s planned adaptive option provides the possibility to evaluate the dose distribution for each fraction and subsequently adapt the original plan to the current anatomy. In this study, 30 adapted plans were created using new contours based on the daily MVCT studies of a bladder cancer patient with considerable anatomical variations. Dose to the rectum and two planning target volumes (PTVs) were compared between the original plan, the dose that was actually delivered to the patient, and the theoretical dose from the 30 adapted plans. The adaptation simulation displayed a lower dose to 35% and 50% of the rectum compared to no adaptation at all, while maintaining an equivalent dose to the PTVs. Although online adaptation is currently too time-consuming, it has the potential to improve the effectiveness of radiotherapy.

Key words: Adaptive radiation therapy, bladder cancer, replanning

Introduction

Radiation therapy has proved to be an effective tool in the fight against cancer. Intensity modulated radiation therapy (IMRT) is a technique that delivers high levels of radiation to the tumor and provides sharp dose gradients to spare surrounding healthy tissues.¹ One factor that severely limits IMRT is target position uncertainty. The introduction of image-guided radiotherapy (IGRT) through various on-board imaging devices assists in correcting daily patient set-up and reduces a portion of the uncertainty.²

The most frequent usage of the term adaptive radiation therapy (ART) for cancer patients refers to changing the radiation delivery, taking into account “slow” or systematic variations of patient anatomy (e.g. weight loss, tumor growth or shrinkage, etc.). ART may be further complicated with functional imaging to assess tumor response as the driver for changes.³ In general, ART is a therapy where information gained during the course of treatment is used to alter treatment.

Typically, the irradiated area is larger than gross tumor volume (GTV). A clinical target volume (CTV) is created by adding a margin to account for microscopic extensions. To account for inter- and intra-fraction anatomy changes and organ motion, a planning target volume (PTV) is created that adds a margin to the CTV. One possible method to increase dose to the tumor while decreasing damage to surrounding tissue could be to reduce the PTV margin by creating “adapted” plans⁴⁻⁵ that take changes in organ position between fractions into consideration. Alternately, adapted plans can maintain the dose to the target while decreasing the dose to the surrounding healthy tissues.⁶

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Currently, such adaptation is performed “offline”: the delivery is modified for treatment fractions following the day when the necessity to adapt has been detected. There have been several interesting reviews published on
this topic, including those by Wu et al.\textsuperscript{[9]} and Kupelian et al.\textsuperscript{[10,11]}

Immediate “online” adaptation, when the patient’s delivery is modified after imaging but prior to delivery, has an advantage of accounting for both systematic and random anatomy changes. Clearly, it should be performed quickly, and to this end there have been advances in shortening the adaptation time.\textsuperscript{[12]}

Helical tomotherapy’s ability to generate megavoltage (MV) computed tomography (CT) images is mainly used to provide proper daily patient positioning.\textsuperscript{[13,14]} Past studies have shown that although their quality is surpassed by that of kilovoltage (kV) CT images, the MVCT images produced by a helical tomotherapy unit are adequate for image guidance in radiotherapy and can be used reliably for re-contouring.\textsuperscript{[15,16]} This property makes it possible to create adapted plans that account for changes in anatomy. In our clinic, lung cancer patients sometimes required re-planning due to considerable tumor shrinkage and important weight loss in the neck accompanied by changes in shape and position of organs at risk, which warranted creation of a new plan in the head and neck cancer patients.

There have been various studies done previously on adapting plans for shrinking tumor volume and patient weight loss.\textsuperscript{[4,5,17-19]} In this case study, we are optimizing the plan of a bladder cancer patient on a daily basis using pre-treatment MVCT studies in order to simulate online adaptive planning. This patient caused concern to our radiation therapists due to seemingly large inter-fraction variation in shapes and volumes of the bladder and rectum. While it is not yet feasible to efficiently provide online adaptation clinically, this simple study provides some insight into whether or not adaptation provides substantial benefits.

**Materials and Methods**

The patient reported in this study was treated on the Hi-Art helical tomotherapy (TomoTherapy Inc., Madison, WI, USA) unit at our center. This 84-year-old male was diagnosed with high-grade transitional cell carcinoma of the bladder. He received eight weekly cycles of carboplatin chemotherapy at 65 mg/m\textsuperscript{2} body surface area: two cycles were delivered prior to the start of radiation therapy and the remaining six cycles were concurrent with radiation treatment. The patient was set up in the supine position for his CT simulation 2 weeks before the start of radiation. The structures for initial treatment planning were contoured by a radiation oncologist using Pinnacle\textsuperscript{3} (version 9.0, Philips, Amsterdam, The Netherlands), and included the rectum, penile bulb, right and left femurs, the external contour, and four targets. Two CTVs were delineated: one to receive a total of 60 Gy (CTV 60) and another to receive at least 45 Gy over the course of 30 fractions (CTV 45) as shown in Figure 1. The CTV 45 encompassed the bladder with a variable margin, as well as the prostate. The CTV 60 was within the CTV 45, and encapsulated the GTV and possible microscopic extensions throughout the bladder and prostate. Each CTV was expanded by a three-dimensional margin of 10 mm to form the PTV 45 and PTV 60. Tomotherapy treatment planning was completed and verified by delivery quality assurance with the ArcCHECK (Sun Nuclear, Melbourne, FL, USA) 3 days in advance of treatment.

The patient used in this study was selected because considerable changes in the inter-fraction anatomy were observed early in the treatment by MVCT, as demonstrated in Figure 2. Much of this was a consequence of inconsistent bladder and rectal filling, as well as gas. Occasionally, the patient’s small bowel was found protruding into the CTV 60 at the time of imaging. To remedy this, the patient was instructed to drink water and release gas before being re-imaged 30 minutes later. There were three occurrences where the patient was imaged twice for set-up prior to treatment, and one occurrence where he was imaged three times.

The images for this retrospective study were acquired through the daily pre-treatment MVCT scans on our Hi-
Art unit. The TomoTherapy Planned Adaptive® software (version 4.0.4) was used to create merged images. As kVCT slices are separated by a distance of 3 mm, the merged images must interpolate between the 6-mm MVCT slices to create 3-mm slices. The merged images replace the segment of the kVCT planning study with the 40-cm field of view of the MVCT study. The original kVCT contours were overlaid on the merged images, and then manually altered to correspond to the daily anatomical changes. Although the boney structures remained the same, the rectum and CTV contours had to be redone for each fraction.

For each fraction, the merged studies and structure set were then exported to Pinnacle®, where the PTVs were created by introducing a three-dimensional 10-mm margin to the CTVs because in the current version of tomotherapy it is possible to create only two-dimensional margins to the structures. The finalized structure sets were then exported back to the tomotherapy planning system.

The Planned Adaptive software (TomoTherapy Inc.) was used to calculate the dose distribution that would be produced in the patient on each fraction by using radiation fluence from the original plan and the merged kVCT/MVCT study with its adapted structure contours. Such dose distribution is called verification dose. This procedure allows for the evaluation of the expected dose delivered to the patient with changing anatomy without plan adaptation. The sum of these daily verification doses over the course of 30 fractions gives the total dose to the regions of interest (ROIs).

At this point, new plans were created on TomoTherapy Planning Station (version 4.0.4) using the adapted structure sets and merged studies. The original optimization protocol was used; all constraint parameters were kept the same as those in the initial plan.

The cumulative dose as simulated for using daily adaptation procedure was determined by summing the planned dose for each ROI (divided by the total number of fractions in order to mimic a single fraction delivery with each plan) calculated by every adapted plan. Daily ROI volume variation was also recorded.

Results

The dose–volume histogram (DVH) data for both the adapted plans and the verification dose calculation procedure applied to plans are shown in Table 1. The dose delivered to the ROIs without any adaptation was evaluated through post-treatment verification dose calculation. The dose is higher than both the original planned dose and the predicted dose, with online adaptation in all aspects. The cumulative dose to the rectum produced with daily adaptation afforded a slightly higher D_{15} (2.8%) and D_{25} (0.9%) than the original plan. The increased D_{15} and D_{25} display linear relationships (R^2 = 0.76 and R^2 = 0.60, respectively) with the percentage of the rectal volume that overlapped with the PTV 60, as shown in Figure 3. The adapted plans displayed an equivalent D_{35} to the rectum and lowered the D_{50} from the original plan by 2.7%. The D_{95} to the PTV 45 and PTV 60 was equivalent in all approaches.

Random anatomy changes continued throughout the complete treatment. The volume of the CTV 45 varied

### Table 1: Cumulative doses (Gy) to the rectum and planning target volumes (PTVs) for the original plan, as evaluated for changed anatomy with no plan adaptation, and for the daily adapted plans

| Plan         | No adaptation | Daily adaptation |
|--------------|---------------|------------------|
| Rectum       | D_{15} 53.16  | 56.82            | 54.64            |
|              | D_{25} 48.3   | 51.2             | 48.72            |
|              | D_{35} 44.82  | 46.79            | 44.8             |
|              | D_{50} 40.17  | 41.62            | 39.1             |
| PTV 45       | D_{95} 45.23  | 46.39            | 46.09            |
| PTV 60       | D_{95} 59.63  | 60.01            | 59.73            |

D_{x}: Dose to x% of the region of interest, PTV x: Planning target volume to receive a minimum of x Gy

![Figure 3](image-url) Change in dose to 15% and 25% of the rectum (D_{15} and D_{25}) as a function of the percentage of the rectal volume that overlapped with the planning target volume receiving 60 Gy (PTV 60)

![Figure 4](image-url) Percent of the rectal volume that overlapped with the planning target volume receiving 60 Gy over the course of treatment
from 234 to 416 cm³, with an average of 326 ± 47 (SD) cm³.
The rectal volume ranged from 147 to 395 cm³, averaging
201 ± 55 cm³. There was no correlation between the CTV
45 and the volume of rectum on any given day. The volume
fluctuations did not improve throughout the duration of
treatment. The percentage of the rectum that overlapped
with the PTV 60 remained random throughout treatment,
as shown in Figure 4.

Daily contouring took approximately 30 minutes per
fraction, while the remainder of the re-planning process
took approximately 90 minutes. Over the course of 30
fractions, it would be expected to take an extra 60 hours
of resources to provide online adaptation with current
technology and processes.

Discussion

In this case study, we assessed the use of helical
tomotherapy’s MVCT imaging capacity to create daily
adaptive plans that would further tailor specific radiation
therapy treatments for one individual patient. With the
current technology, online adaptation is far too time-
consuming to be a realistic option. Often, a single adapted
plan can be effective if anatomy is changing at a consistent,
predictable rate.

However, daily adaptation to account for anatomy changes
may become feasible as technology advances. This study
suggests that online adaptation may be beneficial, but it
seems that adaptation need not be done at every fraction.

Our goal in the adaptation procedure was to maintain
the same dose to the PTV 45 and PTV 60, while sparing the
rectum. The evaluation with the Planned Adaptive software
used daily images with contours “of the day” and the
radiation fluence of the original plan. We have not found
any underdose [quantified by the D95 parameter in Table 1]
of either PTV 45 or PTV 60. This is the result of the volume
shrinkage of both targets by 3% for the PTV 60 and by 9%
for the PTV 45 on average per fraction, so that the planned
radiation fluence could provide the prescribed dose coverage
for the PTVs even if they change their positions with respect
to the original plan. However, rectal sparing was different
as the patient’s anatomy no longer matched the plan. This
resulted in higher doses to the rectum, as shown in the “No
adaptation” column of Table 1, due to large variations in
the rectum position with respect to the PTV 45 and PTV
60. The daily adaptations resulted in very close D95 values
of the PTV 45 for the initial plan and a summation of adapted
plans because the normalization at D95 for the prescription
dose was used both for the initial plan and each adapted
plan. Adaptation improved upon some aspects, displaying
a lower D95, and D2,5 from the rectum. The increases of D15,25
and D50, were unavoidable with the given anatomy changes. We found no correlation between the
CTV 45 and the volume of rectum on any given day. The
higher dose proved to be a direct result of a larger portion
of the rectum overlapping with the high dose region of the
PTV 60 as shown in Figure 3. The rectum overlap data with
the PTV 60 [Figure 4] have a large spread, but a distinct,
negatively sloped trend because usually, as the treatment
progresses, the patients have a mild diarrhea that effectively
decreases the rectal volume and its overlap with the PTV. A
large PTV margin (10 mm) combined with high mobility of
the rectum leads to increased irradiation of healthy organs
in radiotherapy for bladder cancer.

All organs at risk in our study were within generally
accepted tolerance levels. While there may not be a
considerable benefit to the patient in this case, the same
cannot be said for all circumstances. In the treatment
of this particular patient, DVH parameters in the initial
plan for the rectum were well below Radiation Therapy
Oncology Group (RTOG) tolerance levels, while in other
cases (where sparing of sensitive organs is very close to
tolerance levels) the adaptation procedure may be crucially
important. Daily adaptation may be more relevant for
patients with plans that include sharper dose gradients,
often seen with tumors located in the head and neck or
spinal areas. With these cases, a slight anatomy change left unaccounted for could prove critical to the
surrounding healthy tissue. Our group is continuing this
work on a larger patient base so that the study becomes
more comprehensive.

There are tangible benefits to online adaptation,
although such adaptation is currently too time-consuming
to be practical. Until the planning process is shortened to
a more reasonable time, a possible intermediate step could
be adapting plans for the first few fractions where the
patient’s anatomy is considerably different. As treatment
progresses, therapists could use whichever plan best fits the
patient for that day.

Conclusions

We explored the potential benefits of daily “online”
plan adaptation using the MVCT capability of helical
tomotherapy on a bladder patient. While the dose
to the rectum and targets was acceptable in all cases,
online adaptation managed to provide a lower dose to
healthy tissue than no adaptive planning at all, while
maintaining the correct dose to the targets. Further
study is required on a larger patient database in order to
develop recommendations on the type of patient-specific
parameters or some combinations of parameters that can
serve as a robust indication for plan adaptation. Currently,
online plan adaptation with IGRT is too time-consuming
to be done on a clinical basis. However, with the constant
increase in speed and processing power of technology, it is
likely that it will one day become a reality.
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