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Multiadaptive Plan (MAP) IMRT to Accommodate Independent Movement of the Prostate and Pelvic Lymph Nodes

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Introduction

It is estimated that 40% or more of patients with intermediate to high risk prostate cancer will relapse locally and systemically within five years after definitive radiotherapy. We hypothesize that this high rate of failure is partly due to under-irradiation of the pelvic lymph nodes. One of the challenges when using intensity modulated radiation (IMRT) in concurrent treatment of the prostate and the pelvic lymph nodes is the independent movement of the prostate relative to the lymph nodes, rendering the conventional iso-center shifting method of tracking prostate movement inadequate. The purpose of this research is to develop a novel method using multi-adaptive plan (MAP) IMRT to accommodate independent movement of the two targeted tumor volumes. In order to evaluate effectiveness of the MAP IMRT approach, we first established a baseline benchmark by creating a set of ideal IMRT plans for each patient based on the daily acquired mega-voltage (MV) or kilo-voltage (KV) cone beam computed tomography (CBCT), which represents the ideal case of daily online treatment planning. Based on this established benchmark, we can further evaluate two adaptive strategies: strategy A creates a set of IMRT plans individually optimizing on a series of possible prostate positions in the planning CT; and strategy B creates a set of multi-adaptive plans by dynamically adjusting the radiation apertures to accommodate the daily position of the prostate.

Body

Task 3- (5) Alignment Focus of Daily Imaging Guidance

The preliminary results of this task were reported in last year's report, but we conducted further analysis this year.

Briefly, we created a set of IMRT plans, which retrospectively simulated real-time adaptive planning based on the acquired daily verification KV-CBCT images. These plans were the benchmarks for three other adaptive methods (described in next paragraph). These sets of simulated real-time adaptive plans are referred to as ideal MAP plans. Because real-time planning is not yet clinically practical, we proposed an adaptive strategy by shifting multi-leaf collimator (MLC) leaves without requiring real-time planning or dose recalculations. The plans created with this method are referred to as MLC-shift plans.

Six patients, with a total 124 fractions of kV-CBCT images with concurrent prostate and lymph node treatments, consented to this retrospective study. For each KV-CBCT, the contours of prostate, bladder, and rectum were manually delineated. If the lymph nodes were fixed with respect to bony anatomy, the contours of lymph nodes were transferred from the planning CT after bone-based rigid image registration. The daily prostate displacements were obtained using dual image registrations: alignment to the bone and alignment to the prostate. For each fraction, four IMRT plans were created: (a) MLC-shifting plan; (b) iso-center shifting plan according to alignment to the bony structures; (c) iso-center shifting plan according alignment to the prostate contour of the day; (d) simulated real-time adaptive plan.

This year, using the clinical planning margins to the prostate and pelvic lymph nodes, we investigated if the MLC-shifting adaptive method is necessary. Our clinical planning margins were generous, 6 mm posterior and 8 mm elsewhere for the prostate and 5 mm uniform planning

margin for the pelvic lymph nodes. For these planning margins, if the MLC-shifting adaptive is not necessary, where should the daily verification images be aligned to: the prostate contour or the pelvic bones? Furthermore, we explored whether the focus of the daily imaging alignment depended on the magnitude of the prostate displacement.

Table 1: Lists percentage of the total fractions (124) that daily dose to 99% of the prostate organ (D99) received 100%, 97% of the prescription dose (RX), 97% of planned D99, and 97% of re-planned D99 for four types of verification plans.

Prostate	MLC-Shift (%)	Iso-Shift- Contour (%)	Iso-Shift- Bone (%)	*rART (%)
D99> Prescribed dose	65.4	83.9	47.6	96.0
D99> 97% of the prescribed dose	98.4	97.6	73.4	96.8
D99> 97% of the planned D99	96.8	94.4	70.2	96.8
D99> 97% of the re-planned D99	93.5	93.6	67.7	

*rART = real time adaptive plan

Table 2: Lists percentage of the total fractions (124) that daily dose to 99% of the pelvic lymph nodes (D99) received 100%, 97% of the prescription dose (RX), 97% of planned D99, and 97% of re-planned D99 for the four types of verification plans.

Pelvic Lymph nodes	MLC- Shift (%)	Iso-Shift- Contour (%)	Iso-Shift- Bone (%)	rART (%)
D99> Prescribed dose	56.4	62.9	79.9	92.7
D99> 97% of the prescribed dose	98.4	98.4	98.4	100.0
D99> 97% of the planned D99	98.4	98.4	97.6	99.2
D99> 97% of the re-planned D99	94.4	96.8	95.2	

Magnitude of prostate movement and adaptive strategies

We found that in 83% (103 /124 fractions), the prostate motion magnitude was ≤ 0.74 cm while in remaining 17% fractions the motion magnitude was ≥ 0.74 cm. The magnitude of 0.74 cm is the equivalent of 0.5 cm inter-fraction prostate movement in both superior-inferior and anterior-posterior directions with 0.2 cm movement in the lateral directions. In 83% of the fractions(103 fractions), 97%, 94.2%, and 76.7% achieved D99 of the prostate $\geq 97\%$ of the initial IMRT planned D99 of the prostate for the MLC-shift, iso-shift-contour, and iso-shift-bone methods,

respectively. For the prostate displacement > 0.74 cm, 95.2 % (20/21 fractions) of the fractions had D99 of the prostate $> 97\%$ of the prostate initial IMRT planned D99 for the MLC-shift and iso-shift-contour plans but only 38% of the fractions met the criterion for the iso-shift-bone plans.

We concluded that depending on the prostate displacement patterns, aligning daily images to the pelvic bones would require a planning margin of the prostate greater than 8 mm/6 mm posterior. Aligning to the prostate soft tissue, a planning margin of 5 mm to the PLN is adequate and the planning margins to the prostate can be further reduced. Despite anatomical changes in the rectum and bladder, dosimetrical changes in doses received by 5% volume of the organ at risk (D5) were less than 5% of the real- time planned dose. With smaller planning margins or greater magnitudes of the prostate displacement, MLC-shifting method may be considered.

Task 3-(4) Shifting the planned daily dose matrix

On task 3-4 of the statement of work, we planned to apply the shifted MLC portals to the corresponding KV-CBCT or MV-CBCT and calculate the final dose distribution using the commercial treatment planning system (Pinnacle, Philips Medical Systems). The calculated daily dose provided us dosimetric information for each fraction. To assess the impact of treatment outcomes, we would know the cumulative treatment effect – the total dose from all treatment days. Because of different reference frames from daily images, we could not obtain cumulative doses from the daily calculated dose without using deformable image registration. The uncertainty in deformable imaging registration might lead to erroneous cumulative dose. Alternatively, knowing the daily iso-center shift from aligning to the prostate contour, we could shift the planned dose matrix on the opposite directions of the iso-center shift. Because the shifted planned dose matrices were from the same reference frame, we could sum these dose matrices together to obtain a cumulative dose. For this purpose, we developed an in-house program written in MATLAB to shift the planned daily dose matrix according to the iso-center shifts by aligning to the prostate contours. The shifted matrices were input to the Computational Environment for Radiotherapy Research (CERR) software for display and other analysis.

The dose matrix was recorded in a 3-D array, with a fixed step size in each direction, δx , δy and δz . The volume of a voxel in the dose matrix was determined by $\delta x \times \delta y \times \delta z$. If the measured shifts of the prostate were dx , dy and dz , then the corresponding shifts of the dose matrix would be $-dx$, $-dy$ and $-dz$ as if the prostate were shifted back to its original location.

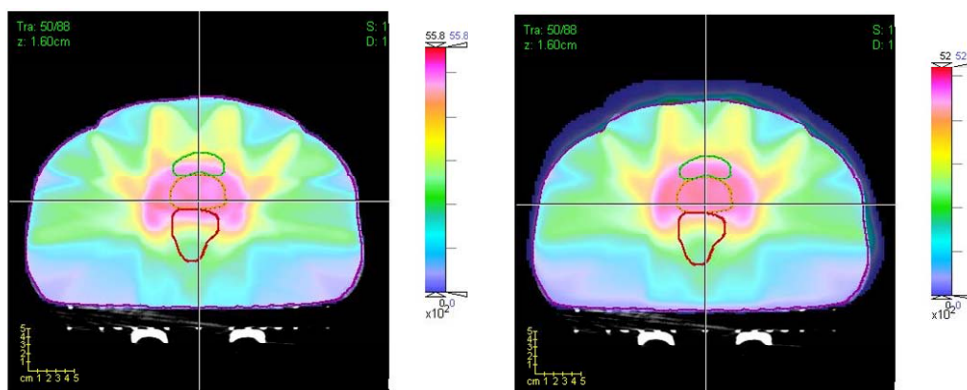


Figure 1: Color map images showing: a) the shifted dose distribution for the first fraction for a patient with 20 fractions. b) The composite dose distribution.

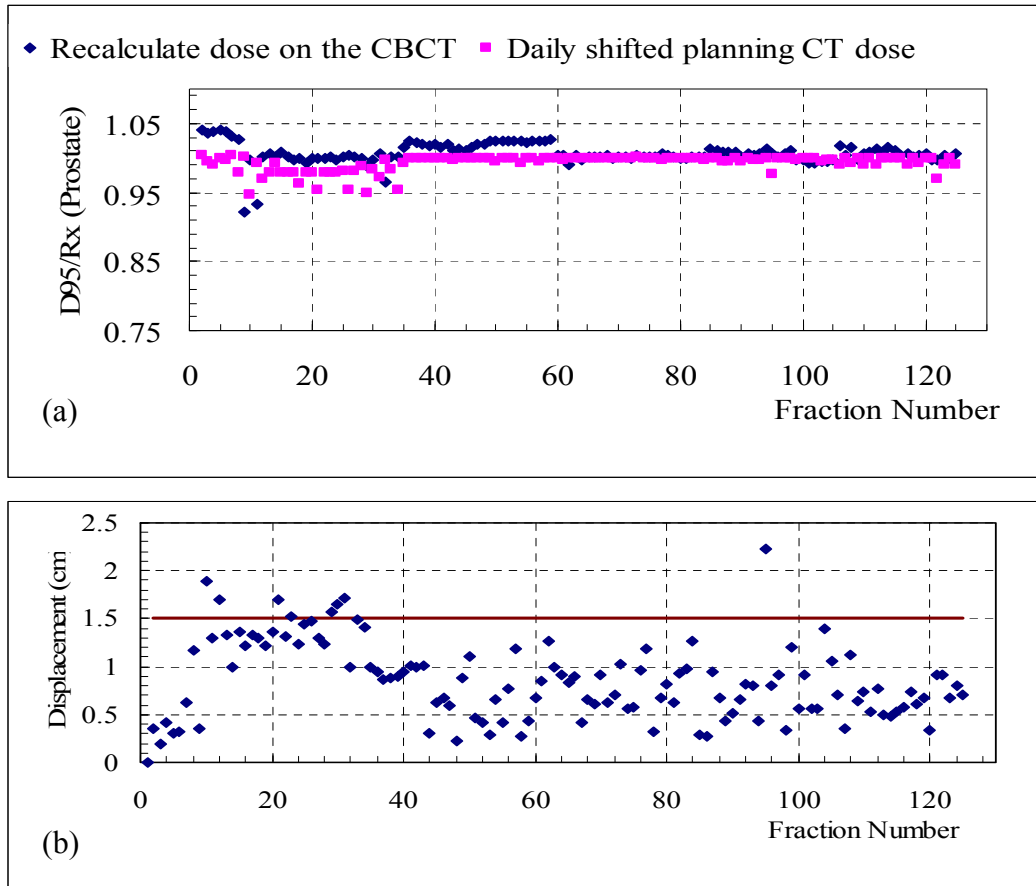


Figure 2: (a) *D95 for the daily shifted planning CT dose method and the recalculated dose on the CBCT for the prostate as a function of the fraction number.* (b) *The daily displacement was calculated based on the contour shift as a function of the fraction number.*

From Figure 1 to Figure 3, we concluded:

1. For prostate displacement less than 1.5 cm, the dose matrix shifting method resulted in 93% and 98% fractions within 5% differences from the recalculation method for D95 of prostate and pelvic lymph nodes, respectively. These numbers decreased to 58% and 71% when 2% dose difference criterion was used.
2. Allowing a daily dose difference of 5%, shifting of the planned dose matrix provided an effective means of evaluating daily dose changes for concurrent IMRT treatment for prostate and pelvic lymph nodes. The utility of this tool is to provide a common coordinate frame to obtain composite dose distributions.

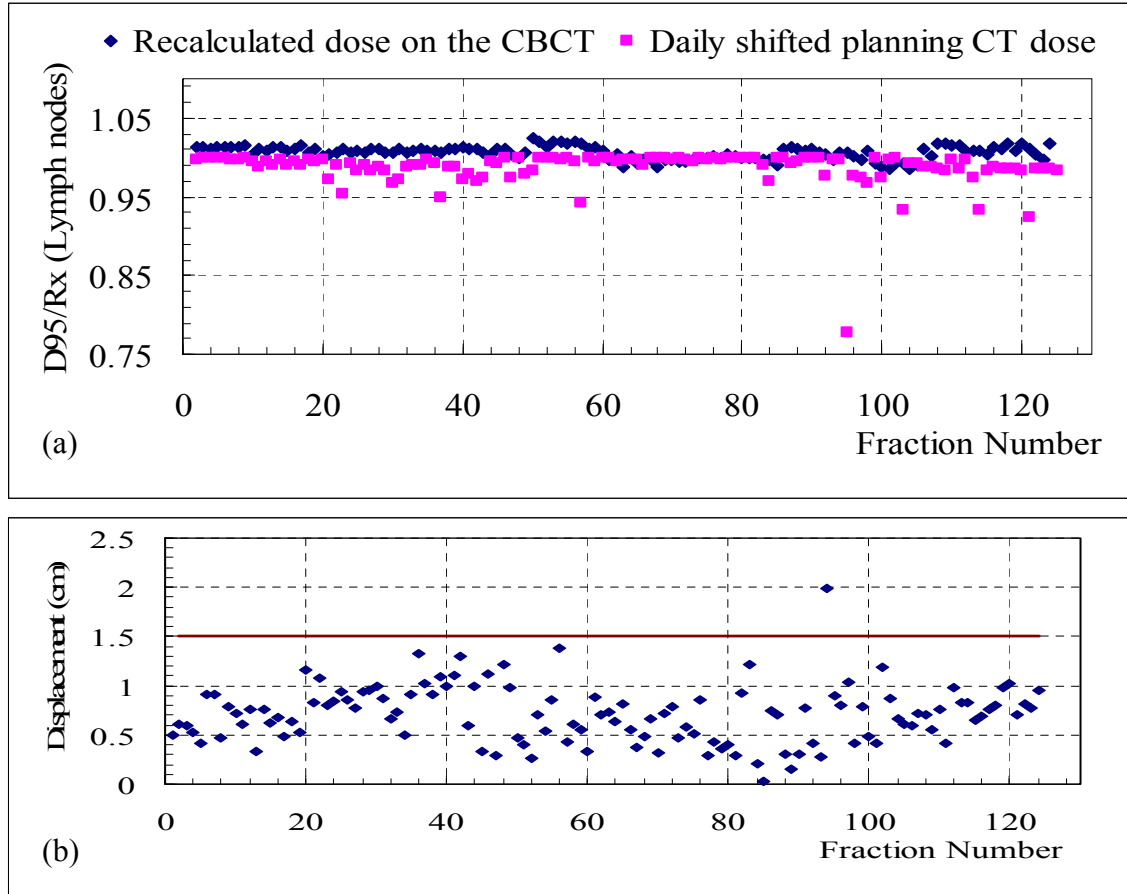


Figure 3: (a) *D95 for the daily shifted planning CT dose method and the recalculated dose on the CBCT for the lymph nodes as a function of the fraction number.* (b) *The daily displacement calculated based on the bony shift as a function of the fraction number.*

Task 4-1: Overcome MLC leaf width limitations

Our previous study showed that adjusting selected MLC leaf pairs to follow prostate movement is an effective strategy to account for daily prostate displacement during concurrent treatment with the pelvic lymph nodes. The MLC leaf width affects quality of MLC shifting plans for the longitudinal prostate motion compensation. This study is to investigate the effect of the MLC leaf width in compensation of the prostate movement.

Fifty-one daily CT on-rail scans from three patients were available for this study. On these CTs, the prostate, bladder and rectum were manually contoured, and the contours of the pelvic lymph nodes were transferred from the planning CT after rigid bony registration. Daily prostate shift was obtained from a dual image registration (one aligned to the bones, and the other aligned to the prostate contour). The prescription doses for all patients were 56 Gy to 98% of the prostate, and 50.4 Gy to 98% of the lymph nodes. The planning margin for prostate was 4 mm in posterior and 6 mm elsewhere. For each patient, three different IMRT plans were created based on a planning CT using three linear accelerator machines with a leaf width of 2.5, 5, and 10 mm, respectively. For each daily CT, a specific MLC shifted plan was created for each of the three machines (a total of 153 treatment plans). The positions of the MLC leaf pairs encompassing the prostate were shifted based on the magnitude and direction of the daily prostate movement by using an in-house computer program. The shifted MLC positions were then loaded back to the planning system for dose calculations.

Figure 4 shows the magnitudes of the prostate movements in three principal axes. We confirmed that the lateral prostate movement is minimal, less than 0.2 cm. The magnitudes of the prostate movement in two other directions were similar to those observed from a different group of patients, who underwent MV-CBCT based imaging guidance.

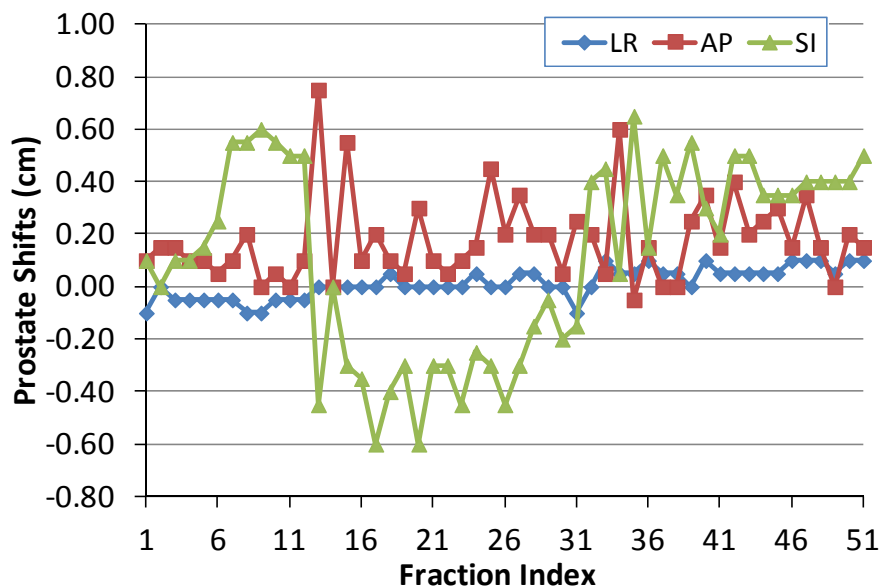


Figure 4. The prostate movements along the left-right (LR), anterior-posterior (AP), and superior-inferior (SI) axes.

Figure 5 shows an example of dose distribution differences when different MLC leaf widths were applied to the plan. Noticeably, the 1.0 cm leaf width may potentially under dose the inferior port of the prostate.

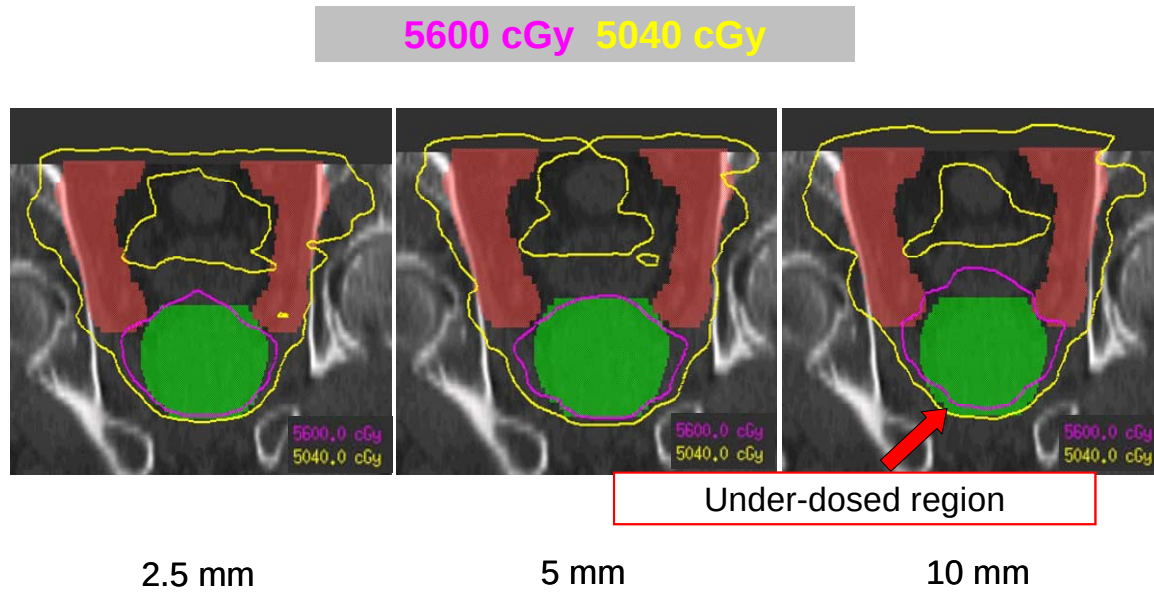


Figure 5. Isodose distributions of MLC-shifted plans with initial IMRT plan using a leaf width of 2.5 mm, 5 mm, and 10 mm, respectively. The prostate shift of the day was 1.0 mm to the left, 1.5 mm to the anterior, and 3.5 mm to the inferior.

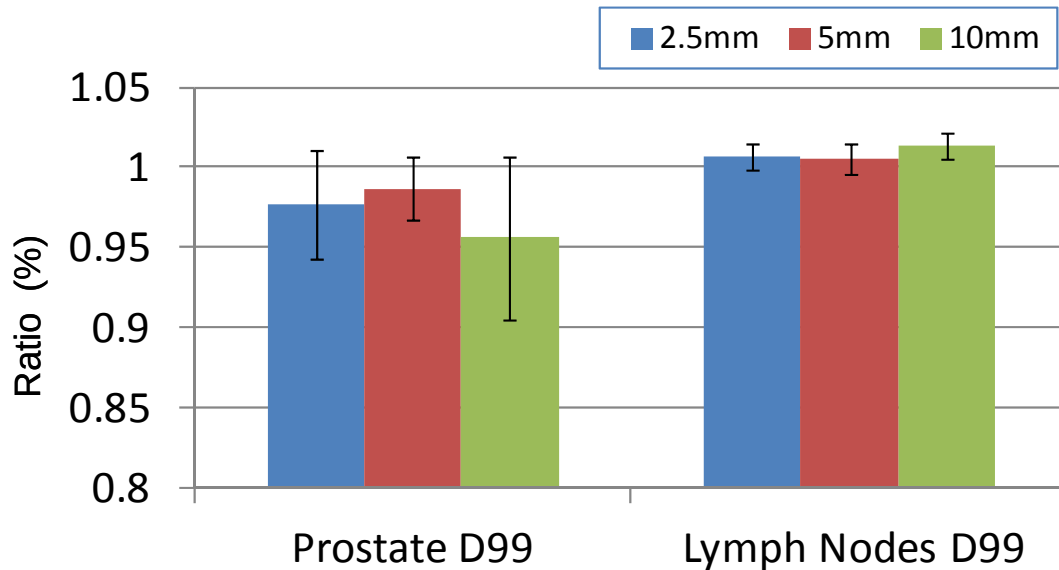


Figure 6. Average prostate D99 (dose received by 99% volume of the organ) and lymph nodes D99, expressed as a ratio of the daily dose to the planned daily dose. Error bar represents one standard deviation.

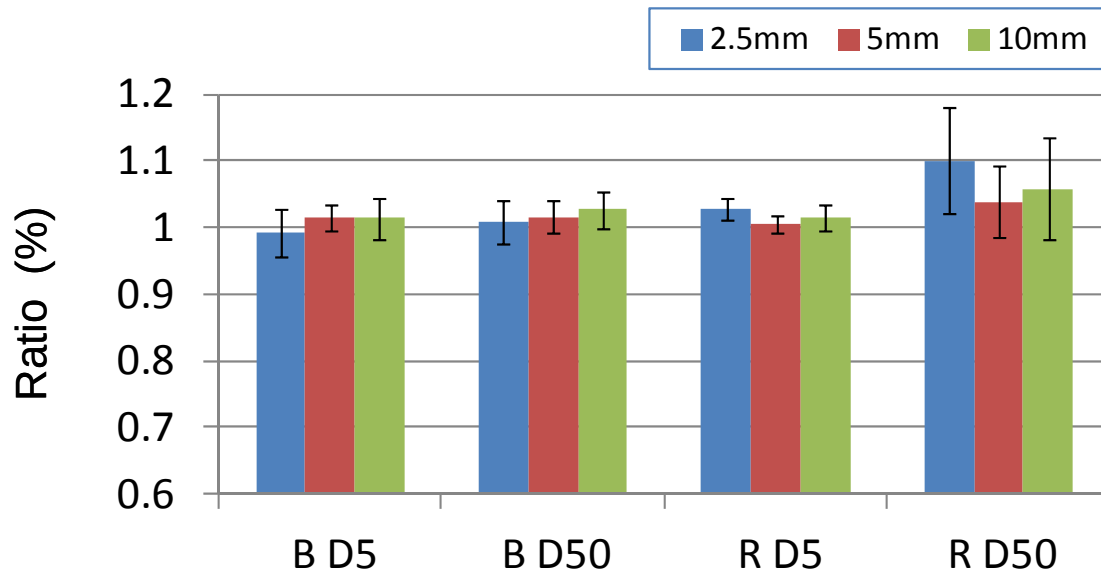


Figure 7. Average D5 (dose received by 5% volume of the organ) and D50 (dose received by 50% volume of the organ) of the bladder and rectum. Columns represent mean value (normalized to the planned dose) and the error bar corresponds to one standard deviation.

From Figure 4 to Figure 7, we found that

1. The average prostate movement (absolute value) along the longitudinal direction was 3.5 ± 1.7 mm (range: -6 to 6.5 mm).
2. The difference in D99 of the PTV-prostate between the daily dose and the planned dose was $2.3 \pm 3.3\%$, $1.3 \pm 2.0\%$, and $4.4 \pm 5.1\%$ for 2.5, 5, and 10 mm leaf width plans, respectively ($p \ll 0.05$).
3. Average dose coverage to the lymph nodes did not degrade from planned doses for all three different leaf widths. The corresponding differences in D99 of the planning lymph nodes between daily and planned doses were $0.7 \pm 0.9\%$, $0.6 \pm 0.9\%$, and $1.4 \pm 0.8\%$ for the three leaf widths.
4. The mean differences in D50 were 0.8%, 1.6%, and 2.7% for the bladder, and 10.0%, 3.9%, and 5.7% for the rectum, respectively.

In conclusion, using the MLC leaf shifting method to compensate for prostate movement in the longitudinal direction depends on the MLC leaf width and the magnitude of the prostate motion. Using a leaf width of 5 mm was adequate for the MLC-shifting method to compensate for prostate movement in the longitudinal direction.

Key Research Accomplishments

- (a) We concluded that depending on the prostate displacement patterns, aligning daily images to the pelvic bones would require a planning margin of the prostate greater than 8 mm/6 mm posterior. Aligning to the prostate soft tissue, a planning margin of 5 mm to the PLN is adequate and the planning margin to the prostate can be further reduced. With reduced planning margins or greater magnitudes of the prostate displacement, MLC-shifting method may be beneficial.
- (b) Allowing 5% daily dose difference, shifting planned dose matrix provided an effective means to obtain cumulative dose distributions under a common coordinate frame.
- (c) According to the studied prostate motion pattern, we found that using a leaf width of 5 mm is sufficient to accommodate MLC-shifting method in compensation of the prostate movement in the longitudinal direction.

Reportable Outcomes

- a. S. Ferjami, G Huang, Q. Shang, and P. Xia: “*Shifting MLC to Follow the Prostate Movements While Concurrently Treating Pelvic Lymph Nodes*”, abstract, Med. Phys. Vol 39, No.6, 3904 (2012).
- b. S. Ferjami, G Huang, Q. Shang, and P. Xia: “*Using Shifting Planned Dose Matrix to Evaluate Daily Dose Changes for IMRT Prostate Treatment*”, abstract, Med. Phys. Vol. 39, No.6, 3659 (2012).
- c. Q. Shang, P. Qi, A. Vassil, G. Huang, P. Xia: “*Effect of MLC Leaf Width on MLC Leaf Shifting Algorithm for Concurrent Treatment of Prostate and Pelvic Lymph Nodes*”, abstract, Med. Phys. Vol. 39, No.6, 3657 (2012).

Conclusion

In summary, in this period of research, we submitted three manuscripts. One of which is under revision for publication. The abstract and manuscript were reported in last year's report (in Appendix A & D). The other two manuscripts were also reported in last year's report (in Appendix B and C). We presented three new abstracts at the annual meeting of American Association of Physicists in Medicine (AAPM) in Charlotte, North Carolina on July 30, 2012.

Using our current planning margins to the prostate (6 mm posterior and 8 mm elsewhere) and pelvic lymph nodes (5 mm uniform), we found that aligning daily images to the pelvic bones would require a planning margin of the prostate greater what we used clinically. Aligning to the prostate soft tissue, a planning margin of 5 mm to the PLN is adequate while the planning margin to the prostate can be further reduced. With smaller planning margins or greater magnitudes of the prostate displacement, MLC-shifting method may be beneficial. Treatment outcomes can be better correlated with the total cumulative dose rather than the daily fractional dose. Therefore, we found that shifting the planned dose matrix can provide an effective means to obtain a cumulative dose under a common coordinate reference frame. This method, however, may cause up to a 5% dose difference when compared to the recalculation using daily KV-CBCT.

After comparing three commonly available MLC leaf widths of 2.5 mm, 5mm, and 10 mm, we found that the use of a leaf width of 5 mm was adequate for applying the MLC-shifting method to compensate for prostate movement in the longitudinal direction.

Appendices

Appendix A: Accepted as an oral presentation at the Annual Meeting of American Association of Physicists in Medicine at Charlotte, NC, July 29-Aug 2, 2012.

Shifting MLC to Follow the Prostate Movements while Concurrently Treating Pelvic Lymph Nodes

S. Ferjami, G Huang, Q. Shang, and P. Xia

Purpose: Concurrent irradiation of prostate and lymph nodes encountered the problem of prostate daily change in position and shape while the lymph nodes are relatively fixed to bony structure. In this paper we address this issue by evaluating the MLC tracking method and compare it to the conventional iso-center shift methods using daily kilo-voltage cone beam CT (KV-CBCT).

Methods and Materials: Six patients with a total 124 fractions of kV-CBCT images with concurrent prostate and lymph nodes treatment were studied. For each KV-CBCT, the contours of prostate, bladder, and rectum are manually delineated. Assuming that the lymph nodes are fixed with respect to bony anatomy, the contours of lymph nodes are transferred from the planning CT after bone-based rigid image registration. The daily prostate displacements are obtained using dual image registrations: alignment to the bone and alignment to the prostate. For each segment of an IMRT plan, an in-house program automatically identified MLC pairs that are collimated to the prostate and adjusted the positions of these leaf pairs according to measured prostate displacements. The shifts MLC positions are input back to the planning system and applied to the corresponding KV-CBCT for dose calculation. The dose to 95% (D95) of prostate and lymph nodes, and dose to 5% and 50% (D5 and D50) of the rectum and bladder, are

evaluated and compared to the dosemetric values obtained from the conventional iso-center shifting methods.

Results: MLC-shift and iso-center shift based on prostate contour methods give comparable dose distribution for the prostate. For more than 97% of the total 124 fractions, the 95% of the prostate volume would receive its daily dose of the prescribed dose within 3% difference for both methods.

The obtained results confirm what it was expected that MLC-shift method is comparable to the bony tracking method for the lymph nodes and has 10% higher coverage in daily received dose wise than the iso-center based on the prostate contour

The MLC-shift method can match the daily prostate location very well specially for displacements under 1 cm, good coverage to the lymph nodes and in the same time gives good dose avoidance for the bladder, 5% of the volume would receive a dose 14% lower than the dose receive in case of bony Iso-center method. For the rectum 5% of the volume would receive a daily dose within 3% higher than the ones receive in the case of the conventional isocenter methods.

Conclusions: The MLC-shift method is valuable tool for concurrent treatment of two independently moving targets, especially for patients with large organ motion. The process does not require re-planning and can be automated.

Using Shifting Planned Dose Matrix to Evaluate Daily Dose Changes For IMRT Prostate Treatment

S. Ferjami, G Huang, Q. Shang, and P. Xia

Purpose: Summation of the daily DVH from the KV-cone beam CT (KV-CBCT) to obtain a composite dose volume histogram (DVH) is challenge. Directly translating the planned dose matrix according to the measured daily prostate displacements provided a common reference frame for a composite DVH from daily DVHs. The purpose of this study is to evaluate the shifting planned dose matrix method when compared to the dose recalculation method using daily KV-CBCT.

Methods and Materials: Six patients, who received concurrent IMRT treatment for the prostate and pelvic lymph nodes with 124 daily CBCTs, were selected for this study. Contours for each CBCT were transferred from the planning CT after soft tissue registration for the prostate and after bony registration for the pelvic lymph nodes. Using the same planning beam configurations, we re-calculated doses for these CBCTs after shifting to the corrected treatment isocenters. The planned dose matrix translation was performed by an in house program written in MATLAB and incorporated with the Computational Environment for Radiotherapy Research (CERR) software. The corresponding daily DVH was obtained by shifting the planned dose matrix according to the shifts of the treatment iso-center. To compare these two methods, selected endpoint doses for the tumor targets and sensitive structures were extracted from these DVHs.

Results: For the prostate displacement less than 1.5 cm, the dose matrix shifting method resulted in 93% and 98% fractions within 5% differences from the recalculation method for D95 of the prostate and pelvic lymph nodes, respectively. These numbers, however, reduced to 58% and 71% when 2% dose difference criterion was used.

Conclusion: Allowing 5% daily dose difference, shifting planned dose matrix provides an effective means to evaluate daily dose changes for concurrent IMRT treatment for the prostate

and pelvic lymph nodes. The utility of this tool is to provide a common coordinate frame to obtain a composite dose distribution.

Effect of MLC Leaf Width on MLC Leaf shifting Algorithm For Concurrent Treatment of Prostate and Pelvic Lymph Nodes

Q. Shang, P. Qi, A. Vassil, G. Huang, P. Xia

Purpose: Our previous study showed that adjusting selected MLC leaf pairs to follow prostate movement is an effective strategy to account for daily prostate displacement during concurrent treatment with the pelvic lymph nodes. The MLC leaf width affects quality of MLC shifting plans for the longitudinal prostate motion compensation. This study is to investigate effect of the MLC leaf width in compensation of the prostate movement.

Methods: Fifty-one daily CT on-rail scans from three patients were available for this study. On these CTs, the prostate, bladder and rectum were manually contoured, and the lymph nodes contours were transferred from the planning CT after rigid bony registration. For each patient, three different IMRT treatment plans were created based on a planning CT using three leaf widths of 2.5 mm, 5 mm, and 10 mm. For each CT, the prostate displacement was determined by dual imaging registration and compensated by shifting MLC plans resulting a total of 153 MLC shifted plans.

Results: Among 51 daily CTs, the average prostate movement along the superior/inferior direction was 1.1 ± 3.7 mm (range: -6 mm to 6.5 mm). The differences in D99 of the prostate between the dose of the day and dose of the plan were $2.3 \pm 3.3\%$, $1.3 \pm 2.0\%$, and $4.4 \pm 5.1\%$ for 2.5 mm, 5 mm, and 10 mm leaf width plans, respectively ($p \ll 0.05$). The corresponding differences in D99 of the lymph nodes were $0.7 \pm 0.9\%$, $0.6 \pm 0.9\%$, and $1.4 \pm 0.8\%$. The mean

differences in D50 were 0.8%, 1.6, and 2.7% for the bladder, and 10.0%, 3.9%, and 5.7% for the rectum, respectively.

Conclusions: Using the MLC Shifting method to compensation for prostate movement in the longitudinal direction depends on the MLC leaf width and the magnitude of the prostate motion. Leaf width with 5 mm can provide sufficient tumor coverage without significantly affecting dose to the critical structures.