Published in final edited form as:

Phys Med Biol. 2013 April 7; 58(7): 2349–2361. doi:10.1088/0031-9155/58/7/2349.

Dosimetric benefit of DMLC tracking for conventional and sub-volume boosted prostate intensity-modulated arc radiotherapy

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Abstract

This study investigated the dosimetric impact of uncompensated motion and motion compensation with dynamic multileaf collimator (DMLC) tracking for prostate intensity modulated arc therapy. Two treatment approaches were investigated; a conventional approach with a uniform radiation dose to the target volume and an intraprostatic lesion (IPL) boosted approach with an increased dose to a subvolume of the prostate. The impact on plan quality of optimizations with a leaf position constraint, which limited the distance between neighbouring adjacent MLC leaves, was also investigated. Deliveries were done with and without DMLC tracking on a linear acceleration with a high-resolution MLC. A cylindrical phantom containing two orthogonal diode arrays was used for dosimetry. A motion platform reproduced six patient-derived prostate motion traces, with the average displacement ranging from 1.0 to 8.9 mm during the first 75 seconds. A research DMLC tracking system was used for real-time motion compensation with optical monitoring for position input. The gamma index was used for evaluation, with measurements with a static phantom or the planned dose as reference, using 2% and 2 mm gamma criteria. The average pass rate with DMLC tracking was 99.9% (range 98.7–100%, measurement as reference), whereas the pass rate for untracked deliveries decreased distinctly as the average displacement increased, with an average pass rate of 61.3% (range 32.7–99.3%). Dose-volume histograms showed that DMLC tracking maintained the planned dose distributions in the presence of motion whereas traces with > 3 mm average displacement caused clear plan degradation for untracked deliveries. The dose to the rectum and bladder had an evident dependence on the motion direction and amplitude for untracked deliveries, and the dose to the rectum was slightly increased for IPL boosted plans compared to conventional plans for anterior motion with large amplitude. In conclusion, optimization using a leaf position constraint had minimal dosimetric effect, DMLC tracking improved the target and normal tissue dose distributions compared to no tracking for target motion >3 mm, with the DMLC tracking distributions showing generally good agreement between the planned and delivered doses.

Keywords

motion management; intrafraction motion; integrated boost

1. Introduction

Dose escalation studies have shown improved biochemical control with increasing radiation doses to the prostate in patients with prostate cancer (Kuban et al 2008, Al-Mamgani et al 2008, Zelefsky et al 2008). Intraprostatic lesions (IPLs) can be identified by imaging modalities such as magnetic resonance imaging (MRI) (Cruz et al 2002, Puech et al 2009, Groenendaal et al 2010). Pathological studies have determined that IPLs are the sites of recurrences of prostate cancer. An increased dose to the IPLs may therefore increase disease control (Cellini et al 2002, Pucar et al 2007), an approach that has been investigated in planning and modelling studies (Pickett et al 1999, Kim and Tomé 2008, Ost et al 2011) as well as in small clinical studies (De Meerleer et al 2005, Singh et al 2007). Creating complex dose distributions in which small volumes within the prostate are boosted to a higher dose could therefore be beneficial to patients as compared to the conventional approach where the whole prostate is prescribed a uniform dose.

The impact of prostate motion on the delivered dose and required margins in radiotherapy has been investigated in several studies (Li et al 2008, Litzenberg et al 2006, Hossain et al 2008). Several methods can compensate for target motion during radiotherapy, including moving the source (Depuydt et al 2011, Nioutsikou et al 2008), gating the beam (Shirato et al 2000), moving the treatment couch (Wilbert et al 2008), and adjusting the beam using real-time dynamic multileaf collimator (DMLC) tracking (Zimmerman et al 2009, Falk et al 2010, Keall et al 2011, Sawant et al 2008, Poulsen et al 2010, Tacke et al 2010, McQuaid and Webb 2008). Restricting the complexity of the multileaf collimator (MLC) configuration can make treatment plans more robust to DMLC tracking (Falk et al 2010).

The aims of this study were: (1) to examine the possibility of boosting the IPL, while decreasing the complexity of the MLC configuration, without compromising the plan quality; (2) to investigate the potential benefit of DMLC tracking of IPL boosted and conventional prostate treatments for a range of target motion; and (3) to determine whether IPL boosted plans were more sensitive to uncompensated intrafraction motion than conventional treatment plans.

2. Materials and methods

2.1. Treatment planning

Four patients with prostate cancer were used in this study. For two patients, IPLs visible on T2W MRIs were delineated and for the two other patients, artificial spherical IPLs were drawn in the peripheral zone of the prostate with a volume of 2.1 cm^3 which was the median volume in 19 identified IPLs in Lips et al (2009). The patient data are shown in table 1.

For the plan optimization, the Delta4 dosimetric phantom (Scandidos, Uppsala, Sweden) was used instead of the patient CT data. This allowed for comparison between the delivered dose to the phantom and the optimized dose distribution. To account for the different beam attenuation, the dose per fraction was adjusted according to the ratio in isocenter dose for a full arc for the phantom and for the patient CTs. Thus, the plans optimized to the phantom volume had approximately the same number of monitor units as the plans would have had if optimized to the patient volume. The following contours were propagated from the patient CT to the phantom: the prostate, the seminal vesicles, the PTV, the IPL, the rectum and the bladder. The femoral heads were excluded as they were only partially localized within the phantom volume. The PTV was created by expanding the prostate and the seminal vesicles with 5 mm margin in the AP and LR directions and with 7 mm margin in the SI direction. The PTV was reduced in overlap regions between the PTV and the rectum. For optimization in the IPL boosted cases, a $\text{PTV}_{\text{minus IPL}}$ structure was created by subtracting the PTV by the

IPL volume with a 4 mm margin around the IPL. No planning margin was however used for the IPL, which allowed a high dose to the IPL without compromising the planning objectives for the maximum dose to the PTV_{minus IPL}.

IMAT treatment plans (RapidArc from Varian Medical Systems, Palo Alto, CA) were optimized in a research version of Eclipse version 10 either with or without an IPL boosted approach for delivery on a Novalis TX linear accelerator with a high-definition MLC (2.5 mm central leaf width). The conventional approach was planned for 2.3 Gy per fraction to the PTV, corresponding to 2 Gy per fraction to the patient volume. For the IPL boosted case, the dose to the IPL was increased to 2.79 Gy, or 121% of the PTV dose, corresponding to circa 94 Gy in a 39 fraction schedule. In order to make the plans robust to DMLC tracking, a leaf position constraint (LPC) was applied during the optimization (Falk *et al* 2012). The LPC limited the allowed distance between adjacent MLC to 0.83 cm, which was the maximum possible leaf travel between two MLC/gantry control points used in the IMAT delivery, and assured that the MLC aperture during tracking could be shifted by one leaf in case of target motion perpendicular to the MLC leaf direction. No LPC equated standard treatment planning, where no leaf position constraints were imposed. Optimizations with and without a LPC were compared to evaluate the impact of the LPC on the plan quality. Only plans with LPC were used during the experimental part of this study. To facilitate DMLC tracking, the jaws were set approximately 2 cm wider than the largest PTV projection. Each plan was optimized with a single 358° arc with a 45° collimator, used 6 MV and a maximum dose rate of 600 MU/min. No monitor unit objective was used in the optimizations.

2.2. Prostate motion traces

The motion traces used in this study were extracted from a dataset of prostate motion obtained during 548 radiotherapy fractions (Langen et al 2008). In this study, the first 75 seconds (the delivery time for a single arc) after patient set-up was used with the first position adjusted to origin. Of the 548 traces, within the first 75 s, 14 traces (2.6%) had a maximum 3D-displacement > 10 mm and 5 traces (0.9%) had an average 3D-displacement > 5 mm. Six of the motion traces were selected for use in the experimental part of this study, with average displacements ranging from 1.0 mm to 8.9 mm (figure 1). The used motion traces were selected to give a representation of the range of motion available in the dataset, including atypical but possible motion with large displacements.

2.3. Experimental setup

Target motion was performed with a motion platform (HexaMotion from Scandidos, Uppsala, Sweden), capable of accurately reproducing target motion in three dimensions (Falk *et al* 2011). The Delta4 dosimetric phantom was integrated with the motion platform, which allowed the dose to be measured with the phantom moving according to the prostate motion traces. The phantom consisted of two orthogonal diode array placed in a cylindrical PMMA phantom. The diodes were separated by 5 mm in the central 6 cm × 6 cm of the arrays, and by 10 mm in the rest of a 20 cm × 20 cm area.

A research DMLC tracking system, described by Sawant *et al* (2008), with a direct optimization leaf sequencing algorithm (Ruan *et al* 2009), was used to compensate for target motion. The phantom location was obtained with infrared reflective markers placed on the phantom and monitored with the optical part of the ExacTrac system (Brainlab, Germany). The location was then sent to the DMLC tracking software which in real-time calculated new MLC positions that compensated for the observed motion. As prostate motion generally lack the periodicity of lung motion, no prediction algorithm was used for the measurements.

To investigate the uncertainty of the measurements repeated measurements were performed for a single plan and motion trace.

When the DMLC tracking system controlled the MLC, the closed MLC leaves next to an open aperture were placed with their ends adjacent to the nearest leaf opening, ready to be used for compensation of motion perpendicular to the leaf direction. More peripheral closed leaves were placed beneath the jaws (Sawant *et al* 2008). To investigate the impact that connecting the DMLC tracking system had on the dosimetric faithfulness, measurements were made to a static phantom with the following configurations: (1) no tracking, *i.e.* conventional IMAT treatment with the tracking system disconnected; (2) standard tracking with the leaves adjusted as described above; and (3) the tracking system set to emulate the no tracking treatment, *i.e.* with all leaves placed according to the treatment plan. For these measurements, in order to eliminate uncertainty originating in monitoring system, a simulated input with zero displacement was used.

2.4. Evaluation

To evaluate the dosimetric effect of compensated and uncompensated motion, gamma evaluation and dose reconstruction were used. Gamma evaluation of the measured dose was performed in the Delta4 software and gamma evaluation of the reconstructed dose was done with in-house developed software. Either the dose to a static target (delivered with tracking for tracking measurements and without tracking otherwise) or the planned dose was used as reference. For the measured doses, gamma calculations were done in 2D along the diode array planes when measurements were used as reference and in 3D around the diodes when the planned dose was used as reference. Gamma calculation was done for diodes receiving >5% of the prescribed dose.

Dose reconstruction was done for each delivery (both tracking and non-tracking) by creating motion-encoded Dicom treatment plans that reflected the actual treatment delivery and modelled intra-treatment target motion by isocenter shifts (Poulsen *et al* 2012). The motion-encoded plans were generated by an in-house developed computer program based on the original treatment plan, log files of gantry and MLC motion during the treatment and the motion trace reproduced by the phantom. The method has been described previously (Poulsen *et al* 2012) but is briefly repeated here for completeness. The positions in the motion trace were assigned to bins with 1 mm³ size and the MLC and gantry positions were assigned to the bin that corresponded to the phantom position during the arc. Together with the dose data from the original plan, a treatment plan was then created with one isocenter for each bin. Each motion-encoded plan consisted of approximately 1500 control points, corresponding to 20 control points per second (20 Hz logging of the MLC positions) during approximately 75 seconds treatment delivery. The motion encoded treatment plans were imported into the treatment planning system where dose calculation resulted in reconstructed dose distributions that allowed 3D gamma analysis and DVH evaluation (Poulsen *et al* 2012). Gamma calculations were done once every 1.0 mm³ for the reconstructed doses, throughout the volume that received >5% dose. The structures included in the DVH evaluation were the target volumes: the prostate, the PTV, the PTV_{minus} IPL, the IPL, and the organs at risk (OARs): the rectum and the bladder. The same rigid motion was assumed for all structures. The difference in the D98% to IPL and prostate and V70Gy to the rectum and bladder between untracked delivery with motion and without motion was calculated for the IPL boosted and the conventional approaches, and tested for any significant difference with the Wilcoxon signed rank test.

3. Results

Comparison of planned DVHs showed that the decreased plan modulation caused by the LPC led to a small decrease in plan quality, and the additional planning challenge associated with the IPL boosted approach caused a slight further decrease in PTV homogeneity (figure 2). The planned number of monitor units was lower with LPC (mean 640 MU, range 579–703) than without LPC (mean 675 MU, range 643–741), but did not depend systematically on the addition of the IPL boost.

A visualisation of the effect that motion had for the IPL boosted and the conventional approach is shown in figure 3 using reconstructed doses for patient #1: for the static case, trace “C” and trace “F” (with an average displacement of 3.3 mm and 8.9 mm respectively). While the dose distribution for trace “C” without tracking resembled the static dose distribution reasonably, the larger motion for trace “F” resulted in large dose redistributions. As seen in the right side of the figure, tracking was able to restore the planned dose even for the large motion of trace “F”. The gamma pass rates for these examples (with 2% 2 mm criteria) are indicated in figure 3 while figure 4 shows the gamma pass rates for all experiments. With the planned dose as reference, the gamma pass rate for the tracked deliveries was higher than for non-tracked deliveries when the average displacement exceeded 3 mm, while similar pass rates were seen for both tracked and non-tracked deliveries for smaller average displacements (Figure 4, top, left). The lowest pass rate for a single tracked measurement was 93.4%, (98.0% with 3% 3 mm criteria), and the average pass rate was 96.7% (99.7% with 3% 3 mm criteria). Using the planned dose as reference resulted in some dose discrepancies for tracking due to the different positions of closed leaves in the experiments and in the plan (figure 4, left graph inserts). This discrepancy was absent when the static measurements were used as reference as the static measurements had the same closed leaves positions as the tracking experiments (figure 4, right inserts). When measurements with a static target were used as reference, higher pass rates were seen with tracking for all investigated motion traces (figure 4, top, right). The same trend in gamma results was observed for measured and for reconstructed doses, indicating that the dose reconstruction method worked adequately (compare top and bottom panels in Figure 4). The difference in number of points used for gamma calculation was the probable cause of the difference in pass rates between evaluations of measured and reconstructed doses; the gamma calculation for the measured doses were based on the readings from at least 500 diodes, whereas >2,000,000 calculation points were used for the reconstructed doses.

The DVHs showed that untracked motion had a large impact on both the target conformity and the doses to OARs, especially for the motion traces with an average displacement > 3 mm (figure 5). As seen in figure 5, the OAR doses depended considerably on the particular motion trace in the non-tracked deliveries. In general, traces leading to increased rectum doses resulted in decreased bladder doses, and vice versa (figure 5). This is a result of the typical prostate motion directionality where anterior prostate motion increases the rectum dose and inferior motion decreases the bladder dose. This is illustrated further in figure 6 which shows how the rectum and bladder volumes receiving 89.5% or more of the prescribed dose (corresponding to 70 Gy or more (V70Gy) for a prescribed dose of 39×2 Gy) depended systematically on the direction and magnitude of the traces. Larger inter-patient variability occurred for the larger displacements. A larger increase in rectum dose was seen for the motion in the anterior direction for the IPL boosted cases compared to the conventional cases. For the tracked deliveries, the V70Gy for the OARs varied only slightly for the different motion traces (figure 6). Statistical analysis with the Wilcoxon signed rank test showed that for the IPL boosted approach, untracked motion had a significantly larger impact on the D98 to the IPL and the V70Gy to the rectum ($p < 0.001$) than for the conventional approach (including all traces). When the analysis was limited to trace “A” to

trace “C”, the p-value was slightly increased but still < 0.01 . No significant difference was found for the prostate D98 and the bladder V70Gy.

Five repeated tracking measurements for a single plan and motion trace (trace “E” in figure 1) showed excellent repeatability; with a static measurement as reference the gamma pass rate was 97.5 – 97.8% using 1% and 1 mm criteria and 100% using 2% and 2 mm criteria. With the planned dose as reference, the pass rate was 76.9 – 79.6% (1%, 1 mm) and 97.5 – 98.1% (2%, 2 mm). Measurements with the tracking software emulating a standard delivery showed an increased agreement with the no tracking delivery compared to the standard tracking. The effect was absent when the planned dose was used as reference (table 2). This indicated that some dose discrepancy was caused by connecting the tracking system.

4. Discussion

This study investigated the possibility of optimizing prostate IMAT treatment plans with a boost to a subvolume of the prostate with the added constraint on the distance to adjacent MLC leaves, the dosimetric effect of uncompensated motion and motion compensation with DMLC tracking and whether boosted plans were more sensitive to uncompensated motion. Treatment planning with increased dose to intraprostatic lesions has previously been studied for different approaches of rotational therapy (Ost *et al* 2011, Jolly *et al* 2011). This study added the aspect of planning constraints to make the plans robust for DMLC tracking, as suggested in (Keall *et al* 2011). In Falk *et al* (2012) the effect of the position constraint was studied for lung treatments, finding no significant difference in plan quality but significant improvement of DMLC tracking accuracy with more stringent leaf distance constraints. The improved DMLC tracking performance and thus the need of leaf constraints was expected to be lower for prostate motion when compared to lung motion. This study was limited to either no or a very stringent constraint and any trade-off between plan quality and DMLC tracking accuracy is subject to further study. This study used no additional planning margins around the intraprostatic lesions. This could be motivated by the fact that the area surrounding the lesion is already a high dose area, *i.e.* the standard PTV, and the impact of setup errors and small motion would therefore, arguably, be limited. Obviously, adding a margin around the IPL would tend to increase the overall PTV dose and in particular the dose to the urethra.

For the deliveries with motion, DMLC tracking was superior to no tracking for all investigated prostate motion traces when the effect of motion was isolated, *i.e.* when measurements with a static target were used as reference in the gamma evaluation, and stringent (2% and 2 mm) gamma criteria were used. However, when the evaluations were performed versus the planned dose, a benefit of tracking was seen only for motion traces with average displacements larger than 3 mm. Comparison of the tracked deliveries with the planned dose was associated with certain challenges; the DMLC tracking software moved unused leaves from their planned position (to avoid leakage irradiation and keep the leaves ready for tracking). This made deliveries with tracking and no motion to deviate slightly from the planned dose. Optimizing treatments with this taken into account would likely improve the agreement with the planned dose. Measurements with the tracking software emulating a standard delivery showed increased agreement with the static delivery but no difference on the agreement with the planned dose.

The measurement and the dose reconstruction strategy used in this study assumed that the target moved rigidly along with the OARs and used external markers as substitute for actual target localization. There are several methods that could be used for real-time target localization of either the tumour or markers during treatments, including kV imaging (Poulsen *et al* 2010), electromagnetic localization (Keall *et al* 2011), MV-imaging with the

treatment beam, MRI and ultrasound. However, as the purpose of this study was to investigate the planning and dosimetric aspect of DMLC tracking, the use of external markers was warranted. Although limited to translational motion in this study, DMLC tracking also has the potential to correct for rotation (Wu *et al*/2011) and deformation. It should finally be noted that the DMLC tracking software is a research system that is under development and its performance can be expected to be improved in future versions.

5. Conclusions

For the investigated cases, dose escalation to a subvolume of the prostate was achieved without any clear increase in risk organ doses. An added constraint on the distance between adjacent MLC leaves in the treatment plan introduced only a very minor reduction of the plan quality. The delivered dose with DMLC tracking was for the first time compared directly to the planned dose calculated with the treatment planning system for patient cases. The evaluation showed that DMLC tracking could accurately deliver the planned dose with or without dose escalation and regardless of target motion extent. For the patient-derived motion traces used in this study, the use of DMLC tracking improved the dose fidelity for traces with average motion larger than 3 mm when compared to the planned dose. Without tracking, and assuming that the OARs move with the target (*i.e.* no deformation), the risk of increasing the dose to the rectum was higher for the IPL boosted approach than the conventional approach, while it was unaffected for the bladder. Similarly, without tracking, the coverage of the prescribed dose to the intra-prostatic lesions was significantly more sensitive to motion for the IPL boosted plans.

Acknowledgments

The authors wish to thank the Katja Langen and Patrick Kupelian (MD Anderson Orlando) for use of the prostate motion database, Pekka Uusitalo, Janne Nord and Jarkko Peltola (Varian Medical Systems, Helsinki, Finland) for supplying the research version of the treatment planning system used in this study, Stephan Erbel and Cornel Schlossbauer (Brainlab, Germany) for support in using ExacTrac for position monitoring, Dan Ruan (University of California, Los Angeles) and Byung Chul Cho (University of Ulsan College of Medicine, Korea) for development of the DMLC tracking software, Herbert Cattell (Varian Medical Systems, Palo Alto) for contributions to the DMLC tracking programme. The authors also like to thank Thomas Carlslund and Mikael Olsen (Rigshospitalet, Copenhagen) for technical support during installation of the DMLC tracking system and Jonas Bengtsson Scherman (Rigshospitalet, Copenhagen) for assistance with gamma calculations. Per Munck af Rosenschöld have research and educational collaboration agreements with Varian Medical Systems, Palo Alto, US. Paul Keall acknowledges the grant support of US NIH/NCI R01-93626 and an NHMRC Australia Fellowship. Research support from Varian Medical Systems, the Niels Bohr Institute (University of Copenhagen) and Snedkermester Sophus Jacobsen og hustru Astrid Jacobsens Fond and The Danish Cancer Society is gratefully acknowledged. The manuscript was reviewed by but not commented on by Varian Medical Systems.

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Figure 1.

The six prostate motion traces used in this study. The average 3D displacements relative to isocenter during 75 seconds are shown in brackets.

Figure 2.

Impact on plan quality of a leaf position constraint (LPC) on plans with and without intraprostatic lesion (IPL) boost. Compiled planned DVHs based on four plans for each planning strategy, showing the impact on plan quality caused by applying LPC and IPL boosting.

Figure 3.

Example of reconstructed dose distributions in the axial plane at isocenter for patient #1, with and without IPL boost, without tracking (middle and left) and with tracking (right), for the static delivery, trace "C" and trace "F" (average displacements 3.3 mm and 8.9 mm, respectively). The delineated structures are the PTV (cyan), the prostate (dark red), the IPL (orange) and the rectum (brown). The patient CT is shown here for visual guide as the plans were optimized for a phantom volume.

Figure 4.

The gamma index pass rate (using 2% and 2 mm criteria) for a static target and six prostate motion traces with and without DMLC tracking, with either planned dose (left) or static measurement as reference (right), for the measured doses (top) and reconstructed doses (bottom). Each value is an average of four plans, the error bars show standard deviation. The inserts highlight the area with similar pass rates.

Figure 5.

Reconstructed DVHs with and without DMLC tracking for the investigated prostate motion traces and two treatment approaches; with IPL boost (top), no IPL boost (bottom). The DVHs are averaged for four treatment plans.

Figure 6.

The change in risk organ volume receiving more than 70 Gy (89.5%) for untracked and tracked plans, plotted versus average motion amplitude in AP for rectum and SI for bladder (positive values indicate phantom motion anteriorly and superiorly, respectively). The change was calculated for each patient relative to the value for the static delivery with no tracking and no IPL boost. The error bars show range.

Table 1

Patient data. For patients 1 and 2, IPLs were contoured based on MRI images, for patient 3 and 4, fictitious spherical IPLs were drawn in the peripheral zone.

Patient number	PTV volume (cm ³)	Prostate volume (cm ³)	IPL volume (cm ³)
1	61.3	13.8	2.3
2	137.0	44.5	5.7
3	117.4	47.6	2.1
4	83.9	27.9	2.1

Table 2

Gamma index pass rate for repeated static measurements with either a measurement with no tracking or the planned dose as reference. The average for three deliveries is shown with range in brackets, except for “no tracking vs. no tracking”, for which two deliveries were compared with a third.

	Gamma pass rate 0.5% 0.5 mm	Gamma pass rate 1% 1 mm
tracking standard vs. no tracking	94.2 [93.8–94.6]	97.8 [97.8–97.8]
tracking emulate vs. no tracking	97.9 [97.3–98.7]	100 [100.0–100.0]
no tracking vs. no tracking	100 [100.0–100.0]	100 [100.0–100.0]
tracking standard vs. planned dose	88.4 [86.5–90.1]	98.9 [98.9–99.0]
tracking emulate vs. planned dose	88.9 [88.3–89.9]	98.8 [98.6–99.0]
no tracking vs. planned dose	93.1 [92.2–94.4]	99.6 [99.4–99.7]