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The dosimetric effect of intrafraction prostate motion on step-and-shoot IMRT plans – magnitude, correlation with motion parameters, and comparison with helical tomotherapy plans

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Abstract

Purpose—1) To determine daily and cumulative dosimetric effects of intrafraction prostate motion on step-and-shoot IMRT plans. 2) To evaluate the correlation of dosimetric effect with motion-based metrics. 3) To compare on a fraction-by-fraction basis the dosimetric effect induced in step-and-shoot and helical tomotherapy plans.

Methods and Materials—Intra-fraction prostate motion data from 486 fractions and 15 patients were available. A motion-encoded dose calculation technique was used to determine the variation of the CTV D_{95%} values with respect to the static plan for step-and-shoot (SNS) plans. The motion data were analyzed separately and the correlation coefficients between various motion-based metrics and the dosimetric effect were determined. The dosimetric impact was compared with that incurred during another intensity modulated radiation therapy technique to assess correlation across different delivery techniques.

Results—The mean (± 1 SD) change in D_{95%} in the CTV over all 486 fractions was $-0.2 \pm 0.5\%$. After the delivery of 5 and 12 fractions the mean (± 1 SD) changes over the 15 patients in CTV D_{95%} were $0.0 \pm 0.2\%$ and $0.1 \pm 0.2\%$, respectively. The correlation coefficients between the CTV D_{95%} changes and the evaluated motion metrics were, in general, poor and ranged from $r = -0.2$ to $r = -0.39$. Dosimetric effects introduced by identical motion in SNS and helical tomotherapy (HT) IMRT techniques were poorly correlated with correlation coefficient of $r = 0.32$ for the CTV.

Conclusions—The dosimetric impact of intra-fraction prostate motion on the CTV is, in general, small. In only 4 % of all fractions did the dosimetric consequence exceed 1% in the CTV. As expected, the cumulative effect was further reduced with fractionation. The poor correlations

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between the calculated motion parameters and the subsequent dosimetric effect implies that motion based thresholds are of limited value in predicting the dosimetric impact of intra-fraction motion. The dosimetric effects between the two evaluated delivery techniques were poorly correlated.

Keywords

IMRT; Intra-fraction motion; Dosimetry

1. Introduction

The emergence of intra-fraction prostate motion data has prompted concern about possible detrimental dosimetric effects of this motion, particularly for intensity modulated radiation therapy (IMRT) treatments. Using measured intra-fractional data several investigators have assessed this dosimetric uncertainty for step-and-shoot (SNS) deliveries (1-3). Using two patient plans, a 2 mm prostate-to-PTV margin, and motion data from 35 patients Li *et al.* reported a reduction in minimum dose to the prostate of up to 15% for single treatment fractions (2). However, the cumulative effect of motion after a typical treatment course was less than 2%. Similarly, Noel *et al.* analyzed the course of treatment for a prostate patient using measured intra-fraction motion data (3). For a 3 mm prostate to PTV margin a mean reduction in $D_{\min}$ and a mean increase in $D_{95\%}$ of $10.3 \pm 12.2\%$ and $0.9 \pm 0.1\%$ was reported, respectively (3). The cumulative effect after 40 fractions was reduced to 8.3 and 0.1% for $D_{\min}$ and $D_{95\%}$. The $D_{95\%}$ is the minimum dose that covers 95% of the target volume (4).

Both of the above studies used a static dose distribution and motion data to generate dosimetric results. However, this method does not account for the inter-play effect of the MLC motion with the target dynamics. This inter-play has the potential to cause dose perturbations within the central region of the target volume that are not ameliorated with margins since these only reduce the dosimetric effect in the target periphery.

The dosimetric importance of the MLC inter-play effect is not well understood for random motion such as prostate inter-fraction motion. To assess the importance of modeling the MLC interplay effect, Li *et al.* compared their static dose convolution approach with a segment based dose convolution approach, where the latter accounts for intra-fraction motion data (5). For individual fractions the two methods resulted in reported $D_{\min}$ reductions that differed by up to 4.4%. However, the reported cumulative results agreed within 1% after as few as five fractions. In this current work a technique that accounts for all treatment dynamics, including the MLC motion, is used to calculate daily and running cumulative variations from the planned target $D_{95\%}$ for intra-fractional motion data collected from 15 patients. The intra-fraction prostate motion data are analyzed separately to score the amount of motion that was present during each fraction. These scores are correlated with the calculated $D_{95\%}$ variations to evaluate if, and which motion-based metrics are useful predictors of the dosimetric perturbations. Lastly, the dosimetric effect of motion on step-and-shoot plans are compared to another intensity modulated delivery technique (helical tomotherapy) in terms of magnitude. The correlation between the respective dosimetric effects is investigated since the two IMRT techniques differ fundamentally in treatment dynamics.

2. Methods and Material

Prostate plans were generated retrospectively for 15 patients. The retrospective SNS plans were designed to deliver a minimum dose of 2 Gy to 95% of the planning target volume (PTV $D_{95\%}=2$ Gy) per fraction. A research version of the Pinnacle treatment planning

system (TPS) (Version 8.1.x, Phillips Healthcare, Andover, MA) was used to generate the treatment plans. The retrospective plans were planned for delivery with a Varian 23IX linear accelerator with a 120 leaf multileaf collimator (MLC) (Varian Medical Systems, Palo Alto, CA). The clinical target volume (CTV) was drawn by the attending physician. A 3 mm CTV-to-PTV posterior margin was used while a 5 mm margin was used elsewhere. Seven fields and a maximum of 100 segments per plan were used. The smallest allowed segment size was 3 cm³ and each segment delivered at least 3 MU.

To calculate the dose distribution in the presence of intra-fraction motion the fluence maps were exported from the TPS for each segment. Using an in-house developed code, the fluence maps were shifted in position for each monitor unit to account for intra-fraction motion. The modified fluence maps were re-imported to the TPS and used for dose calculations. This model assumes that the patient moves as a rigid body. Details of the motion encoded dose calculations have been presented elsewhere (6). Since the fluence is exported for each individual segment, this motion-encoding technique accounts for all treatment dynamics including the MLC inter-play effect. The change in D_{95%} for the CTV and PTV were calculated from the ratio of the motion encoded values to the respective planned values.

The PTV dosimetry was monitored since this volume, in the motion-encoded algorithm, effectively represents a zero-margin target that moves with the same trajectory as the CTV. For each patient the running cumulative change in D_{95%} was calculated by adding the dose distributions successively. Since the model is based on the assumption that the patient moves as a rigid body, no deformable image registration is needed to accumulate the daily dose distributions.

Motion data were measured using an electro-magnetic tracking device that monitors the position of the center-of-mass of three implanted markers (Calypso Medical, Seattle, WA). 486 tracks from 15 patients were available for analysis. Prior to using the tracking device to monitor the center-of-mass motion, the device was used for the initial patient alignment. Tracking was started immediately after patient alignment. Several motion-based metrics were calculated. These included the percentage of treatment time that the target was displaced beyond a certain displacement threshold and the mean displacement. In an effort to take the dosimetric gradients into account a dose gradient weighted effective displacement was calculated. For example, CTV displacements smaller than the margins were not weighted while displacements beyond the margins were weighted by the inverse of the dose fall off beyond the margin in the particular direction. For example, displacements into a region of 70% target dose were weighted by a factor of 0.3. For the PTV all displacements were weighted by the inverse of the dose fall off. Correlations between daily D_{95%} degradations and these parameters were evaluated by calculating Pearson's product-moment correlation coefficient *r*.

To facilitate comparison of the SNS plan degradations with HT-plan degradations previously reported results were used (7). The patient data sets and motion tracks were identical for both delivery techniques as were the CTV-to-PTV margins. To ensure that identical motion data was used in both plans, the SNS plans were adjusted in time to match the HT treatment time. This was achieved by adjusting the assumed dose rate during the SNS motion encoded calculations. In addition, a continuous delivery was assumed, that is, the time between segments and gantry angles was set to zero. This resulted in treatment times that ranged from 316 to 445 seconds with assumed dose rates that ranged from 70 to 135 MU/minute. This adjustment in treatment time may affect the SNS results since it alters the motion data that is used for calculation. However, this effect is of little practical

consequence since the respective treatment times are similar to the actual SNS treatment times.

3. Results

The mean (± 1 SD) change in $D_{95\%}$ in the CTV was $-0.2 \pm 0.5\%$ and $-0.5 \pm 1.1\%$ in the PTV. The largest degradations for a single fraction were -6.4 and -12.7% for the CTV and PTV, respectively and these did not occur in the same fraction. For each fraction changes in $D_{95\%}$ are plotted in Figure 1. For the CTV the percentage of fractions that varied more than 5, 3, and 1% in $D_{95\%}$ were 0.2, 0.2, and 4%. The respective percentages for the PTV are 0.8, 2.5, and 12%. The dosimetric effect in the CTV was poorly correlated with the effect in the PTV with an r -value of 0.53. In three of the four fractions that suffered excessive PTV $D_{95\%}$ degradations, the degradation was peripheral and did not affect the CTV coverage.

The development of the cumulative $D_{95\%}$ is of interest since any detrimental effects in individual fractions may average out if the location of the dose perturbation varies from fraction to fraction as is likely the case with random prostate motion. Figure 2 shows the running cumulative variation in $D_{95\%}$ for the CTV and PTV as a function of accumulated fractions. Table 1 lists the mean ($\pm$ SD) variation in both target volumes after the delivery of 3, 5, 12, and 25 fractions.

The correlation between motion data and the dosimetric variations was explored. Figure 3 shows scatter plots of all dosimetric variations in the CTV and PTV plotted against the fraction of treatment time that the prostate was displaced by more than 10 and 5 mm. The displacement vector is the length of the three-dimensional displacement vector and is calculated from the displacement in three directions. In addition, the dosimetric data are plotted against the mean displacement vector and the dose gradient weighted effective displacement. The correlation coefficient is shown in each subplot. Table 2 lists the correlation coefficients for all calculated motion metrics. For the CTV and PTV the correlation coefficients r ranged from -0.20 to -0.39 and -0.61 to -0.75 , respectively. The corresponding r^2 -value, i.e. the coefficient of determination, was largest at 0.56 for the correlations between the change in PTV $D_{95\%}$ and the dose gradient weighted effective displacement. The r^2 -values indicate what fraction of the dosimetric effect can be attributed to the particular motion score.

Lastly, the fraction-by-fraction correlation between the dosimetric effect in the CTV and PTV introduced by identical motion in helical tomotherapy and step-and-shoot plans have been investigated. For the CTV the correlation was poor with an r -value of 0.32. For the PTV the correlation coefficient degraded further to an r -value of 0.12. In Figure 4 the CTV and PTV $D_{95\%}$ degradations in the HT treatment are plotted against the $D_{95\%}$ degradations that are introduced by identical motion in SNS plans for each of the 486 fractions. The distribution for the HT data is wider than the SNS distribution with a mean ($\pm$ SD) of $0.6 \pm 3.3\%$ and $-0.2 \pm 2.9\%$ for the CTV and PTV, respectively. While few fractions result in an increase $D_{95\%}$ for SNS treatments, increases of up to 5% in $D_{95\%}$ are observed for the HT treatments.

4. Discussion

The variations in $D_{95\%}$ values that are introduced in the CTV and PTV by motion were, in general, small with means of less than 1% and respective standard deviations of 0.5 and 1.1%. For the CTV, only 4% of all fractions experienced a $D_{95\%}$ degradation of more than 1%. The respective value for the PTV was 12% while only 2.5% of all fractions experienced PTV $D_{95\%}$ degradations larger than 3%. The finding that the CTV is less affected by motion

shows that in this delivery technique margins offer some degree of protection from intra-fraction motion. Any residual dosimetric effects in the CTV may be due to the MLC inter-play effect or due to CTV displacements beyond the CTV-to-PTV margin. While different margins were not explored the difference in dosimetric impact on the PTV and CTV attests to the effectiveness of the employed margins to provide protection to the CTV that moves during treatment delivery. Targets with smaller margins would suffer dosimetric degradations that would be expected to range from those reported for the CTV to those reported for the zero-margin PTV.

Consistent with the finding by others, the current findings show that the cumulative effect of intrafraction prostate motion is reduced significantly with minimal fractionation. After the delivery of 5 fractions only 2 of the 15 patients had a degradation of the cumulative PTV $D_{95\%}$ of about 1% while the mean cumulative PTV degradation was -0.3 % with a standard deviation of 0.4%. After 5 fractions none of the patients experienced a degradation of more than 0.5% in the CTV $D_{95\%}$. This data confirms that the effect of random motion, such as prostate intra-fraction motion, averages out with fractionation.

The $D_{95\%}$ was selected for scoring the dosimetric variations since it is the dose-volume metric used for dose prescription. Studies that monitored both $D_{95\%}$ and $D_{\min}$ sensitivities to intrafraction motion found that the latter is more sensitive than the former. However, the minimum dose is very sensitive to calculation uncertainties since it is typically located in a high dose gradient region (4). A more robust metric, i.e. $D_{95\%}$, was chosen as an indicator of plan degradation.

The algorithm treats the moving CTV as a rigid body and hence intrafraction deformation and rotation are unaccounted for. Data on these two effects are sparse. Interfraction (day-to-day) deformation has been investigated for prostate patients and is found to be small for prostate (<1 mm) and seminal vesicles (< 3mm) (8). Since the time period of interest for intrafraction effects is much shorter it is reasonable to assume that intrafraction deformation, if present, is even smaller and that its dosimetric consequence is negligible. While intrafraction rotations of up to 27° have been reported, reported mean rotations are smaller at of $2.5 \pm 2.3^\circ$ (9). These rotations were measured between the pretreatment radiograph and a portal image taken about 8 minutes later. Voxels that are peripheral will experience a displacement of about 1-2 mm due to this rotation while voxels that are in the center of rotation experience no displacement. The dosimetric consequence of not accounting for these rotational displacements is not obvious. However, given the relatively small mean displacement of the peripheral voxels the inclusion of rotational effects it is not likely to change the general findings of the reported results.

Dosimetric effects in the CTV are poorly correlated with the actual motion data. Taking the dose gradient into account increases the correlation coefficient marginally to -0.39 for the CTV. From this low correlation value it can be concluded that, for the CTV, only about 15% ($r^2=0.152$) of the dosimetric effect can be directly attributed to the calculated motion metric. While the calculation of dose gradient weighted effective displacement is an approximation in itself, the low coefficient of determination indicates that effects that are not well correlated with the calculated motion metrics contribute significantly to the dosimetric effects that were observed in the CTV. MLC interplay effects have the potential to perturb the delivered dose distribution in the CTV independently of CTV-to-PTV margins and this interaction may have intricate dependencies that are not well characterized by any of the extracted motion metrics. While intra-fraction motion is the source of this dosimetric uncertainty it appears that none of the extracted motion-based metrics can be used to predict the dosimetric effect in the CTV with sufficient accuracy. If any of the extracted motion metrics were used to define intervention thresholds during treatment, false negative and false

positive events would result. Hence, no motion metric was found that could be used with confidence to predict dosimetric degradations in the CTV. While intra-fraction motion monitoring may be of limited use to establish intervention thresholds for the prevention of dosimetric effects, the data are essential to facilitate the calculation of dosimetric effects using motion-encoded dose calculation techniques. While the employed technique accounts for the MLC-interplay effect, the importance of including this effect was, however, not tested in this work. No motion convolution with the static dose was performed for comparison. Work performed by others indicates that the MLC-interplay effect plays a minor role for SNS plans particular if the cumulative effect is of interest (5).

For the PTV, the correlation coefficient with the motion-based metrics were better with r -values of about 0.75, meaning that about half of the dosimetric effect observed in the PTV can be attributed to the motion data. Since the PTV is, in clinical practice, a geometrical concept designed to protect the CTV, any dosimetric effect to this volume is of lesser interest than the effect in the CTV. Alternatively, the PTV can also be thought of as a no-margin target that is hence more susceptible to the effects of intra-fraction motion for SNS plans.

The particulars of a different delivery technique are paramount since identical motion data can have very different dosimetric effects as is evident from the poor correlation of the SNS and HT data. Because of different treatment dynamics, the dosimetric effect can vary with delivery technique as shown in Figure 4. The dosimetric effect for HT plans has a larger standard deviation, but motion can result in either higher or lower doses being delivered to the target. The dosimetric effect of motion on SNS plans is, in general, smaller, but typically results in a lower dose being delivered to the target. In addition, the geometric location of the dosimetric effect may be different. In this current paper evidence is presented that the CTV-to-PTV margins offer some protection to the CTV from intra-fraction motion for SNS plans. In a previous manuscript data were presented that showed a fairly strong correlation between the $D_{95\%}$ effect in the CTV and PTV for helical tomotherapy treatments (r -value of 0.9) (10). This data allowed the conclusion that for helical tomotherapy treatment CTV-to-PTV margins do not offer the intended protection from intra-fraction motion. If the dosimetric effect of motion is to be compared between different delivery techniques, it is important that the treatment dynamics of both delivery techniques are taken into account. The assumption of a moving target within a static dose cloud will not reveal technique dependent intricate dependencies.

5. Conclusion

In agreement with previous publications, this study finds that the dosimetric effect of intra-fraction prostate motion is typically small for step-and shoot intensity modulated radiation therapy treatments. The cumulative effect is reduced with fractionation. Since the correlation between the extracted intra-fraction motion metrics and the introduced dosimetric effect in the CTV is poor, it is not obvious yet how motion monitoring can be used to prevent dosimetric degradations in this target volume.

An accurate determination of the dosimetric consequence of intra-fraction motion can be achieved with motion-encoded dose calculation techniques. Two motion-encoded techniques that take all machine related dynamics into account were used to show that identical motion can result in dosimetric effects that differ in magnitude and geographical location between different delivery techniques.

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Figure 1.
The percent change in $D_{95\%}$ for the PTV and CTV for each daily fraction.

Figure 2.
Running cumulative $D_{95\%}$ variations from the plan for the CTV and PTV.

Figure 3.

Dosimetric variations plotted against the fraction of treatment time for which the prostate was displaced by more than 5, and 10 mm (row 1 and 2). In row 3 and 4 the correlation with the mean displacement and the dose gradient weighted effective displacement are plotted. The Pearson's correlation coefficient r is shown for each dependency.

Figure 4.

For each daily fraction the changes introduced by motion in helical tomotherapy (HT) plans in the CTV and PTV are plotted against the degradations introduced in the SNS plans. HT and SNS data are projected and plotted in histogram format to the right and inferior to the scatter plot.

Table 1

Mean cumulative dosimetric variation after the delivery of 3, 5, 12, and 25 fractions.

Cumulative number of fractions	Mean ($\pm$ SD) variation in CTV D _{95%}	Mean ($\pm$ SD) variation in PTV D _{95%}
3	-0.1 $\pm$ 0.2 %	-0.3 $\pm$ 0.5 %
5	0.0 $\pm$ 0.2%	-0.3 $\pm$ 0.4 %
12	0.1 $\pm$ 0.2 %	-0.2 $\pm$ 0.3 %
25	0.1 $\pm$ 0.2 %	-0.2 $\pm$ 0.2 %

Table 2

Pearson's product-moment correlation coefficients r between motion-based metrics and the $D_{95\%}$ change induced by the motion in the CTV and PTV.

Motion-based metric	Correlation with CTV $D_{95\%}$ variation	Correlation with PTV $D_{95\%}$ variation
% of time that prostate was displaced > 10 mm	-0.29	-0.72
% of time that prostate was displaced > 7 mm	-0.26	-0.69
% of time that prostate was displaced > 5 mm	-0.25	-0.72
% of time that prostate was displaced > 3 mm	-0.20	-0.61
Mean displacement	-0.26	-0.70
Dose gradient weighted effective displacement	-0.39	-0.75