The Impact of Tissue Inhomogeneity Corrections in the Treatment of Prostate Cancer with Intensity-Modulated Radiation Therapy

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Purpose: To investigate the effects of tissue inhomogeneity corrections on the dose delivered to prostate cancer patients treated with Intensity-Modulated Radiation Therapy (IMRT).

Methods and Materials: For five prostate cancer patients, IMRT treatment plans were generated using 6 MV or 10 MV X-rays. In each plan, seven equally spaced ports of photon beams were directed to the isocenter, neglecting the tissue heterogeneity in the body. The dose at the isocenter, mean dose, maximum dose, minimum dose and volume that received more than 95% of the isocenter dose in the planning target volume ($V_{p>95\%}$) were measured. The maximum doses to the rectum and the bladder, and the volumes that received more than 50, 75 and 90% of the prescribed dose were measured. Treatment plans were then recomputed using tissue inhomogeneity correction maintaining the intensity profiles and monitor units of each port. The prescription point dose and other dosimetric parameters were remeasured.

Results: The inhomogeneity correction reduced the prescription point dose by an average 4.9 and 4.0% with 6 and 10 MV X-rays, respectively. The average reductions of the $V_{p>95\%}$ were 0.8 and 0.9% with the 6 and 10 MV X-rays, respectively. The mean doses in the PTV were reduced by an average of 4.2 and 3.4% with the 6 and 10 MV X-rays, respectively. The irradiated volume parameters in the rectum and bladder were less decreased; less than 2.1% (1.2%) of the reduction in the rectum (bladder). The average reductions in the mean dose were 1.0 and 0.5% in the rectum and bladder, respectively.

Conclusions: Neglect of tissue inhomogeneity in the IMRT treatment of prostate cancer gives rise to a notable overestimation of the dose delivered to the target, whereas the impact of tissue inhomogeneity correction to the surrounding critical organs is less significant.

Key Words: Inhomogeneity corrections, IMRT, Density correction, Prostate

INTRODUCTION

Radiotherapy is an established standard treatment modality for localized prostate cancer.

In recent years, dose escalation has been a subject of extensive study in the treatment of prostate cancer, since the dose to the tumor has been thought of as a key factor increasing tumor control probability.[1-4] Many dose escalation studies were performed by using an intensity-modulated radiation therapy (IMRT) because of its feasibility to deliver higher doses to the treatment target volumes while sparing the surrounding normal structures.[5-9]

Meanwhile, the toxicity of critical normal organs such as the bladder and rectum, which are associated with high dose radiation, has been an accompanying issue. In order to prevent radiation induced toxicity, several analyses found correlations between the acute/late toxicity of critical organs and predictable dosimetric quantities, such as dose volume histograms (DVH) and dose statistics.[5-6,11-16]

The dosimetric quantities predicted in the treatment plans could have deviations from institution to institution, however, depending on the procedure of dose calculation. One of the known sources for deviation in dose calculation has been

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tissue inhomogeneity in the treatment volume. The presence of different electron density materials such as bony structure and gas in the rectum influences the International Commission on Radiation Units and Measurements (ICRU) point dose, as well as the dose distribution in the treated volume.[17] Tissue inhomogeneity has not been actively considered in many clinical trials because of the uncertain effects of various inhomogeneity correction algorithms.

Review of the extensive literature regarding tissue inhomogeneity correction effects on lung cancer treatment[17-26] revealed few investigations for tissue inhomogeneity effects on the three-dimensional (3-D) treatment of prostate cancer.[17,27] Among others, Ginestet et al[27] reported that inhomogeneity induced errors were critically dependent on the beam direction, which is diverse in 3-D conformal plans. This result implies tissue inhomogeneity-induced deviation is dependent on the treatment technique. The impact could also be larger in the IMRT treatment than 3-D conformal treatment because of the beam intensity-modulation. To our knowledge, however, no data has been provided which addresses the impact of inhomogeneity correction on the target as well as on the critical organs with IMRT treatment for prostate cancer. Therefore, we performed the analysis of inhomogeneity correction effects on the absolute dose and relative dose distribution of the target and critical organs in the IMRT treatment of prostate cancer by using a convolution/superposition algorithm.[28-30] Our results show tissue inhomogeneity correction has more significant effects on the target than the critical organs in the treatment volume. Our results have relevance to the dose-escalation trials and the toxicity analysis of critical organs for IMRT.

METHOD AND MATERIALS

In this study, we considered five patients treated for localized prostate cancer. The treatment planning study consisted of two parts: the first involved planning without inhomogeneity corrections, and the second involved planning with inhomogeneity corrections. The treatment planning study was carried out using the Pinnacle 6.0 m software, using convolution/superposition algorithms for dose calculation. In the first part of the study, two IMRT plans using 6 or 10 MV X-rays were generated for each patient. Both plans employed seven equally spaced and weighted coplanar ports of photon beams (gantry angles: 0, 51, 102, 204, 255, and 306) directed to isocenter.

The clinical target volume (CTV) was the prostate or prostate plus seminal vesicle. The planning target volume (PTV) was the CTV plus a safety margin of 8~10 mm except for the front of the rectal wall, where the margin was 5 mm. PTV1 was defined as the prostate plus the margin, and PTV2 was the prostate with seminal vesicles plus the margin.

In the computations, the tissue inhomogeneity in the patient body was turned off, assuming that all tissue densities are in unity (1 g/cm^3). The homogeneous dose, daily 2 Gy to the ICRU point in the PTV, was assigned; constraints to the rectum wall and bladder were assigned to 1.5 Gy to 10% of rectum and bladder volumes. The intensity-modulated beam profiles were then computed with a 4 mm dose grid in all directions, using the iterative optimization process module in the Pinnacle. In the process of optimization, a pencil beam algorithm was employed. After completion of optimization, the dose distribution was recomputed by using the convolution/superposition algorithm.

For the comparison of plans, several dosimetric quantities describing the absolute dose and relative dose distribution in the target and in the critical organs were collected. In the target, the absolute dose was measured at the ICRU reference point (D_{iso}) which is located at the isocenter. Other quantities such as mean dose (D_{pmean}), maximum dose (D_{pmax}), and minimum dose (D_{pmin}) were also measured. In order to compare the dose conformity of the target, the volume, which received a dose of more than 95% of the isocenter dose ($V_{p>95\%}$), was measured. It is important to note that the isocenter dose associated with this definition was the dose actually delivered to the isocenter.

In the critical organs, the mean dose (D_{rmean}; rectum, D_{bmean}; bladder), maximum dose (D_{rmax}; rectum, D_{bmax}; bladder) and minimum dose (D_{rmin}; rectum, D_{bmin}; bladder) were measured. The accumulated DVH was quantified by measuring the following quantities: volumes receiving more than 50, 7 and 90% of the prescribed dose in the rectum ($V_{r>50\%}$, $V_{r>75\%}$, and $V_{r>90\%}$, respectively) and bladder ($V_{b>50\%}$, $V_{b>75\%}$, and $V_{b>90\%}$, respectively).

In the second part of the planning study, the computed tomography number-based inhomogeneity corrections were initi-

ated and the dose distribution was recomputed in each of the treatment plans. In the computation process, all beam parameters such as beam energy, beam number, gantry angle, field size, intensity profiles and monitor units of each portal entrance of the beam were maintained so as to make the conditions identical to those of the plans without tissue inhomogeneity corrections. Prescription point dose and other dosimetric quantities accessing the dose distribution in the target, the rectum, and the bladders were re-measured.

RESULTS

Table 1 shows the dosimetric parameters relevant to the target. Prescription point dose, minimal, maximal, and mean doses are presented in the table. The representative dose-volume histograms of PTV in homogeneous or heterogeneous media are presented in Fig. 1. As shown in Table 1, the inhomogeneity correction reduced the prescription point dose (D_{iso}) by 5 (4.9) and 4% (3.9%) with 6 and 10 MV X-rays repectively on average in the PTV1 (PTV2). The reduction rates were similar regardless of the PTV1 or PTV2. The minimal, mean, and maximal doses were all reduced by similar rates, about 1~2% less than the decrease of the prescription point dose (D_{iso}). In order to check the dose conformity of the target, $V_{p>95\%}$ in the inhomogeneity uncorrected plan was compared to that of the inhomonogeneity corrected plan. As shown in Table 2, the decrease of $V_{p>95\%}$ was about 1% (0.35~1.24%). The variation of dose conformity was slightly larger in PTV2, where the original dose conformity was poorer than PTV1. Also, the DVH of the inhomogeneity corrected plan was intentionally shifted to a higher dose until the volume received more than 50% of the prescription, matching the DVH line of the inhomogeneity uncorrected plan. The inset of Fig. 1 shows that the differences between the two overlaid lines were very small and the dose conformity of the target was not changed much. Hence, the dose in the target tended to reduce uniformly.

The dosimetric parameters relevant to the critical organs are presented in Tables 3 and 4, and the representative dose-volume histograms of the rectum and bladder are depicted in Fig. 2 and 3, respectively. The maximum point dose in the rectum was reduced by on 4.7 average of with 6 MV X-rays

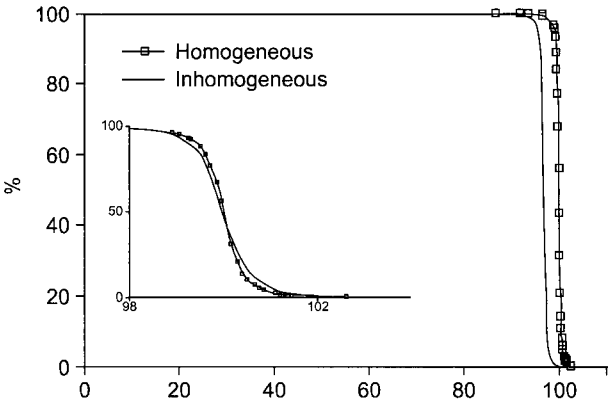

Fig. 1. DVHs of the PTV: X-ray energy=10 MV, PTV=prostate plus margin.

Table 1. Dose statistics in the PTV.

	PTV1						PTV2					
	6 MV			10 MV			6 MV			10 MV		
	H (%)	I (%)	Δ (%)	H (%)	I (%)	Δ (%)	H (%)	I (%)	Δ (%)	H (%)	I (%)	Δ (%)
D_{iso}*	100.5	95.5	−5.0	100.8	96.8	−4.0	99.5	94.6	−4.9	100.6	96.7	−3.9
D_{pmean}*	99.6	95.2	−4.4	99.8	96.2	−3.6	99.1	95.2	−3.9	99.2	96.1	−3.1
D_{pmax}*	107.3	103.1	−3.9	102.9	99.4	−3.5	106.1	102.5	−3.6	106.5	103.7	−2.8
Dpmin*	90.4	86.8	−3.6	90.7	87.9	−2.8	86.5	83.5	−3.0	86.5	84.2	−2.3

*normalized to the prescription dose

D_{iso}, D_{pmeam}, D_{pmax} and D_{pmin} are the isocenter dose, the mean dose, the maximum dose, and the minimum dose in the PTV, respectively, PTV1: the prostate plus margin, PTV2: the prostate with seminal vesicles plus margin, H: the plannings without inhomogeneity correction, I: indicates the plannings with inhomogenetiy corrections, Δ: the data differences between H and I

and 3.8% with 6 and 10 MV X-rays, respectively. The average reduction in the bladder was 3.6% and 3 at 6 and 10 MV X-rays, respectively. These reduction rates were similar to the decrease rate of the target maximum dose.

The mean dose and DVHs of the critical organs which could be relevant to radiation toxicity were only slightly affected by the inhomogeneity corrections. The mean dose decreases were only 0.6~1.1% in the rectum and 0.4~0.8% in the bladder.

Table 2. Change of target conformity.

	PTV1						PTV2					
	6 MV			10 MV			6 MV			10 MV		
	H (%)	I (%)	Δ (%)	H (%)	I (%)	Δ (%)	H (%)	I (%)	Δ (%)	H (%)	I (%)	Δ (%)
$V_{p>95\%}$*	97.3	97.6	0.3	97.1	97.6	0.5	93.4	94.6	1.2	93.1	94.2	1.2

* normalized to the Planning Target Volume
$V_{p>95\%}$: the volume receiving more than 95% of the isocenter dose, $V_{p>95\%}$ is defined relevant to the actual isocenter dose rather than the prescription dose.

Table 3. Mean dose and DVH parameters in the rectum.

	Rectum (PTV=PTV1)						Rectum (PTV=PTV2)					
	6 MV			10 MV			6 MV			10 MV		
	H (%)	I (%)	Δ (%)	H (%)	I (%)	Δ (%)	H (%)	I (%)	Δ (%)	H (%)	I (%)	Δ (%)
D_{rmean}*	26.8	26.0	−0.8	26.4	25.7	−0.7	33.5	32.3	−1.2	34.8	33.9	−0.9
D_{rmax}*	99.3	94.7	−4.6	99.6	95.9	−3.7	100.2	95.4	−4.8	99.6	95.8	−3.8
$V_{r>50\%}$†	26.3	25.4	−0.9	26.3	25.5	−0.8	28.9	27.6	−1.4	33.1	32.0	−1.0
$V_{r>75\%}$†	11.1	9.9	−1.2	10.9	9.9	−1.0	12.6	11.1	−1.5	13.3	11.9	−1.4
$V_{r>90\%}$†	5.4	3.7	−1.7	5.1	3.8	−1.3	6.2	4.1	−2.1	5.8	4.1	−1.7

*normalized to the prescription dose, †normalized to the rectal volume
D_{rmean} and D_{rmax} are the mean dose and the maximum dose in the rectum, repectively.
$V_{r>50\%}$, $V_{r>75\%}$, and $V_{r>90\%}$ are rectal volumes receiving more than 50%, 75% and 90% of the prescription dose

Table 4. Mean dose and DVH parameters in the bladder.

	Bladder (PTV=PTV1)						Bladder (PTV=PTV2)					
	6 MV			10 MV			6 MV			10 MV		
	H (%)	I (%)	Δ (%)	H (%)	I (%)	Δ (%)	H (%)	I (%)	Δ (%)	H (%)	I (%)	Δ (%)
D_{bmean}*	21.9	21.5	−0.4	21.9	21.6	−0.3	37.9	37.1	−0.8	38.4	37.8	−0.6
D_{bmax}*	101.3	97.8	−3.5	101.2	98.4	−2.8	102.5	98.8	−3.7	102.1	99.0	−3.1
$V_{b>50\%}$†	18.8	18.5	−0.3	18.0	17.8	−0.2	37.8	37.1	−0.7	38.3	37.7	−0.6
$V_{b>75\%}$†	10.0	9.6	−0.4	11.0	10.0	−1.0	14.7	13.6	−1.1	15.0	14.0	−1.0
$V_{b>90\%}$†	6.8	6.0	−0.8	7.2	6.7	−0.4	8.0	7.1	−0.9	8.0	7.1	−0.9

*normalized to the prescription dose, †normalized to the bladder volume
D_{bmean} and D_{bmax} are the mean and maximum doses in the bladder, respectively.
$V_{b>50\%}$, $V_{b>75\%}$, and $V_{b>90\%}$ are bladder volumes receiving more than 50%, 75% and 90% of the prescription dose

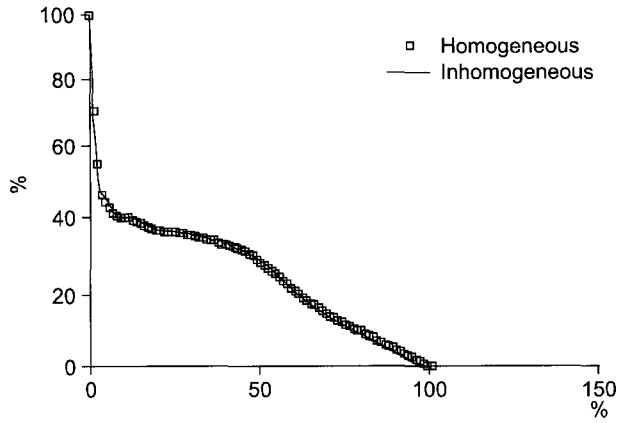

Fig. 2. DVHs of the rectum: X-ray energy=10 MV, PTV= prostate plus margin

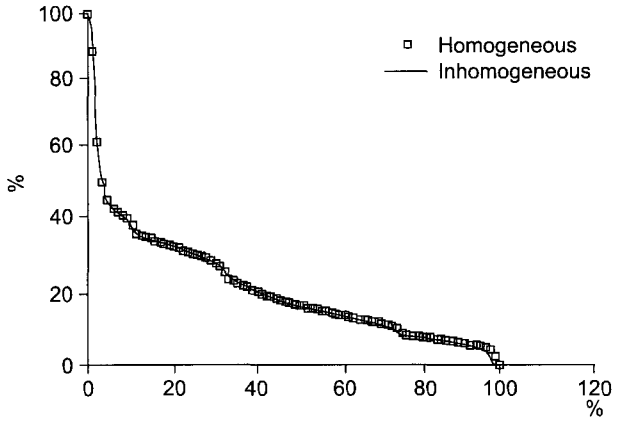

Fig. 3. DVHs of the Bladder: X-ray energy=10 MV, PTV= prostate plus marginFigure Legends.

In the rectum, $V_{r>50\%}$, $V_{r>75\%}$, and $V_{r>90\%}$ decreased by 1.1～1.3%, 1.1～1.5% and 1.3～2.1%, respectively. In the bladder, the volume reductions of $V_{b>50\%}$, $V_{b>75\%}$, and $V_{b>90\%}$ were also small, which were 0.2～0.8%, 0.5～1.2%, and 0.4～1.2%, respectively.

DISCUSSIONS AND CONCLUSIONS

In our results, the inhomogeneity corrections appeared to play different roles in the target and in critical organs for the IMRT treatment plan. In the target, the prescription dose, and the dose statistics, all decreased by notable amounts with inhomogeneity corrections, whereas the effects of the correction on the mean dose and DVHs of the rectum and the bladder were not that significant.

The Photon Treatment Planning Collaborative Working Group reported that in the 3-D treatment the mean dose of the prostate treated by 15 MV X-rays could have a 6% reduction in dose by inhomogeneity correction, while the mean dose of the rectum and bladder was not reduced.[17] Ginestet et al[27] performed a systematic analysis on the inhomogeneity correction effects of 3-D conformal prostate treatment, showing that inhomogeneity correction effects were dependent on beam direction and that deviation at the ICRU point reached up to 4.5% at 18 MV X-rays. Although 6 and 10 MV X-ray energies were investigated in this study at higher energies (15～18 MV X-rays), the reduction rates of IMRT treatment will not differ much from the previously reported values of 3-D treatments because of the increased contribution of pair production of those energy regions.

These observed dose reductions are mainly due to the presence of high atomic number tissues and bony structures around the prostate, increasing the attenuation of the primary radiation. The distribution of these bony structures is not isotropic. This anisotropic distribution does not appear to be important to the relative dose distribution. The variation of intensity profiles due to high density tissue also appear to have little effect on the relative dose distribution, since the target dose conformity changed little.

In comparison to the 3-D conformal treatment, IMRT uses more consistent beam directions between institutions. As long as equally spaced isocentric beams are employed, we believe that the use of different number of beams (five or nine beams) will not change the dose reduction rate markedly.

For the critical organs, the mean dose and all DVH parameters were not strongly affected by the inhomogeneity corrections. These observations are possibly due to the fact that among seven ports of incident photon beams, only a small portion of beams is responsible for the dose in the rectum or the bladder. The dosimetric quantities considered to be correlated to rectal toxicity are the volumes that receive more than 50～70 Gy as mean dose.[5,11] In our observations, neither percentage parameters ($V_{r>50\%}$, $V_{r>75\%}$, $V_{r>90\%}$, $V_{b>50\%}$, $V_{b>75\%}$, and $V_{b>90\%}$) nor the mean dose were affected by inhomogeneity correction. Hence, any results driven by the DVH analyses and mean dose of the rectum or the bladder would be

irrelevant to the inhomogeneity correction.

In summary, we compared the dose statistics and dose distributions of five prostate cancer patients for IMRT treatment calculated by convolution /superposition algorithm, with and without inhomogeneity corrections. We assessed the difference between the two calculation results, caused mainly by the presence of high-density bony structures. For all patients studied, the inhomgeneity correction reduced the isocenter dose by an average 4~5% and the mean dose by an average 3~4% in the target. The deviation of the target conformity was not that significant. The effects of the critical organ data such as the mean dose and volume parameter in the DVH were not affected significantly by the inhomogeneity correction. Our results indicate that the prescribed dose difference between the inhomogeneity corrected and uncorrected studies needs to be taken into account in the intercomparison of delivered dose. However, the results of complication studies on the critical organs, which were induced by the DVH and mean dose analysis of the critical organ, will be consistent independent of the inhomogeneity correction.

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전립선암의 세기조절 방사선 치료시 밀도보정의 효과

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한영이 · 박 원 · 허승재

목적: 전립선암의 세기조절 방사선 치료 시, 조직의 밀도보정 여부가 선량분포에 끼치는 영향을 연구한다.
재료 및 방법: 5명의 전립선 암 환자에 대하여 6 MV와 10 MV의 광자선에 대하여 각각 치료계획을 수립하였다. 각각의 계획에서 7개의 조사선이 설정되었고, 선량계산 시에는 체조직의 밀도의 불균일성을 무시하였다. 선량 처방점인 회전중심점에서의 흡수선량과 계획표적용적(PTV)의 최대선량, 최소선량, 평균선량과 처방점선량의 95% 이상의 받는 부피($V>_{p95\%}$) 등을 측정하였다. 직장과 방광 내에서의 최대선량, 최소선량, 최방선량의 50%, 75%, 90% 이상을 받는 부피를 측정하였다. 동일한 조건에서 조직의 밀도 불균일성을 포함하여 선량분포를 재계산하고, 측정한 모든 물리량을 재측정하였다.
결과: 밀도보정을 함으로써, 처방점에서의 흡수 선량은 6 MV에서 평균 4.9% 10 MV에서는 평균 4% 감소하였다. $V>_{p95\%}$는 6 MV와 10 MV에서 각각 0.8%와 0.9% 감소하였다. PTV의 평균 흡수 선량은 6 MV와 10 MV에서 각각 4.2%와 3.4% 감소하였다. 직장과 방광에서의 흡수선량은 약 1~2%의 차이를 보였다.
결론: 전립선암의 세기변조 방사선치료시에 밀도보정을 무시하는 것은 표적에는 고려할 만한 선량의 차이를 유발하며, 주위의 위험장기에 미치는 영향은 미미하다.

중심단어: 밀도보정, 세기조절방사선치료, 전립선암