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Comparison of dose volume histograms for supine and prone position in patients irradiated for prostate cancer—A preliminary study

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ABSTRACT

Aim: To compare DVHs for OARs in two different positions – prone and supine – for prostate cancer patients irradiated with a Tomotherapy unit.

Background: In the era of dose escalation, the choice of optimal patient immobilization plays an essential role in radiotherapy of prostate cancer.

Materials and methods: The study included 24 patients who were allocated to 3 risk groups based on D'Amico criteria; 12 patients represented a low or intermediate and 12 a high risk group.

For each patient two treatment plans were performed: one in the supine and one in the prone position. PTV included the prostate, seminal vesicles and lymph nodes for the high risk group and the prostate and seminal vesicles for the intermediate or low risk groups. DVHs for the two positions were compared according to parameters: Dmean, D70, D50 and D20 for the bladder and rectum and Dmean, D10 for the intestine. The position accuracy was verified using daily MVCT.

Results: Prone position was associated with lower doses in OARs, especially in the rectum. Despite the fact that in the entire group the differences between tested parameters were not large, the Dmean and D10 for the intestine were statistically significant. In the case of irradiation only to the prostate and seminal vesicles, the prone position allowed for substantial reduction of all tested DVH parameters in the bladder and rectum, except D20 for bladder. Moreover, the Dmean and D50 parameter differences for the bladder were statistically significant.

No significant differences between positions reproducibility were demonstrated.

Conclusion: In patients irradiated to prostate and seminal vesicles, the prone position may support sparing of the rectum and bladder.

The reproducibility of position arrangement in both positions is comparable.

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1. Background

Radiotherapy is one of the main radical treatment methods for patients with locally advanced prostate cancer, contributing to the prolongation of overall survival (OS) and disease-free survival (DFS). In case of early stage prostate cancer, irradiation is an alternative treatment method to surgery and the outcome following both treatments are similar.¹⁻³ Such a high therapeutic efficiency is achievable through dose escalation, which would not be possible without strong development of irradiation techniques.⁴ It has been shown in a number of randomized trials that doses above 66 Gy contribute to a longer duration of DFS and biochemical control.⁵⁻⁸ Through intensity modulated radiation therapy (IMRT), it has become possible to provide a relatively safe treatment with doses to prostate above 70 Gy and comparable doses for adjacent organs at risk (OAR) (bladder and rectum) as for 3D technique.⁹ In recent years, the high conformal techniques like Tomotherapy or CyberKnife has become available. With these techniques, it is possible to obtain a larger dose-decrease gradient outside the target, so dose escalation has become even safer.¹⁰

Simultaneously with the introduction of new techniques, attempts are also being made to reduce the doses in the organs at risk through appropriate patient preparation for each fraction of treatment. The use of rectal balloon and bladder filling reduces unexpected changes in volume of the rectum or bladder and decreases prostate motion.^{11,12} Searching for new ways to escalate the dose, immobilization methods were brought to focus. In the literature there are various papers exploring differences in dose distribution relative to a treatment position – supine or prone.¹³⁻¹⁷ However, previously published works focused on the 3D planning technique. Techniques currently used, such as IMRT or Tomotherapy, are much more conformal, thus the planning dose distribution between both positions can be more significant.

2. Aim

The aim of this study is to compare two different stabilisation techniques of patients irradiated for localised or locally advanced prostate cancer. For this purpose a comparison of dose volume histograms (DVHs) in the supine and prone treatment positions will be carried out. Through daily megavoltage computed tomography (MVCT) positioning accuracy in the supine and prone position will also be evaluated.

3. Materials and methods

The study included 24 patients with locally advanced prostate cancer radically treated with Tomotherapy at the Radiotherapy Department II at the Greater Poland Cancer Centre between July 2009 and May 2010. No exclusion criteria were applied during recruitment to this study. Patients were between 55 and 86 years of age (average 65.90, median 64.00, standard deviation (SD) 7.53), with body weight from 65 to 105 kg (average 84.18, median 83.00, SD 11.90) and height in the range of 159 to 180 cm (average 170, median 170, SD 0.06). For all patients, the body mass index (BMI) was calculated and

Table 1 – The single factor risk group models described by D'Amico et al.¹⁴

Risk group	Risk factor
Low risk	PSA ≤ 10
	Gleason 2-6
	T1-T2a
Intermediate risk	Presence of 1 or more
	PSA 11-20
	Gleason 7
High risk	T2b-T2c
	Presence of 1 or more
	PSA > 20
	Gleason 8-10
	≥T3

its value ranged from 22.10 to 33.30 (average 28.40, median 28.90, SD 3.30).

Histopathology examination revealed a low degree of malignancy (G1) in 2 patients, intermediate degree (G2) in 8 and high degree (G3) in 10 patients. In 4 cases, the degree of biological malignancy was determined. The Gleason score in biopsy material varied in this group of patients from 6 to 9 (median 6, SD 1.35). The level of prostatic specific antigen (PSA) at the time of diagnosis ranged from 4.20 to 96.54 ng/ml (average 20.82, median 11.90, SD 22.47). Based on the transrectal ultrasound (staging), Gleason score and initial PSA (iPSA) value, patients were allocated to one of the three risk groups according to the criteria described by D'Amico (Table 1).¹⁸ There were 12 patients in the high risk group, 7 in the intermediate and 5 in the low risk group.

For each patient, two different immobilization methods – supine and prone – were used for radiotherapy planning. In the first case patient's legs and pelvis were stabilized with the knee-fix stand (Sinmed Combifix SYS/2P), the patient holding his hands clasped on the chest. For the prone position, a belly-board stand (Sinmed Bellyboard BB-CF/2P) was used. Computed tomography (CT) was performed in both positions for each patient at an interval of not more than 5 min. 30 min before this examination patients were asked to empty their bladder and then to drink 500 ml of water. No pharmacological or mechanical preparations like Enema or endorectal balloon were used.

In all cases, patient radiotherapy was planned with Hi-Art Tomotherapy Treatment Planning System. The delineated clinical target volumes (CTVs) were differentiated according to D'Amico risk groups. For patients in the low and intermediate risk groups, CTV included the prostate gland with seminal vesicles. For patients in the high risk group, the CTV included the prostate gland, seminal vesicles and external iliac, internal iliac, presacral and distal common iliac lymph nodes. The margins for planning target volume (PTV) ranged from 10 mm around designed CTV to 7 mm from the rectum side. The following OARs were also determined in all patients: the bladder, the rectum, bowels, left and right femoral heads. The rectum was delineated from the level of anal sphincter muscle to the sigmoid colon and the bladder from its apex to the bottom. Both OARs were determined as the whole volume of organs, not only the rectum or bladder wall. The contours of the bowels covered the entire peritoneal cavity below the upper edge of the 5th lumbar vertebra. Target volumes and OARs were

Table 2 – Dose volume histograms comparison of organ at risk for entire group.

Organ at risk	DVH parameter	% of prescribed dose in supine position	% of prescribed dose in prone position	p value
Bladder	Dmean	56.05	54.93	0.366
	D70	32.85	31.18	0.241
	D50	50.41	47.74	0.156
	D20	87.01	86.60	0.076
Rectum	Dmean	56.38	55.62	0.607
	D70	33.89	34.55	0.724
	D50	52.69	50.18	0.380
	D20	90.27	86.90	0.303
Intestine	D5	100.98	100.46	0.030
	Dmean	17.58	14.28	0.009
	D10	39.74	33.93	0.007

determined for each patient and in the supine as prone positions.

Radiotherapy was planned in a helical technique (helical tomotherapy) using modulated photon beam of 6 MV. For each position, the planned dose distribution and optimization of the treatment plan were calculated based on the aforementioned Hi – Art Tomotherapy Planning System. During the plan preparation, the doses for OARs were reduced to a minimum – maintaining the dose homogeneity in PTV between 95 and 107%, according to the protocol ICRU 50 and 62.^{19,20}

Patients were irradiated according to the treatment plan that was selected by comparison of the planned dose distribution in OARs in both immobilization methods. The following DVHs parameters were compared: Dmean (average dose in whole volume of OAR), D70 (dose given to 70% of OAR volume), D50 (dose given to 50% of OAR volume) and D20 (dose given to 20% of OAR volume). The accuracy of the treatment was verified by daily MVCT on the Tomotherapy unit. The resulting images were compared with the reference Images – CT slices performed for treatment planning.

For the sake of statistical analysis, the tested group was divided into two subgroups according to structures present in the target volume. The first subgroup consisted of patients solely irradiated for the prostate and the seminal vesicles, while the second group consisted of patients in whom the target volume included the prostate, the seminal vesicles and the pelvic lymph nodes.

The material was statistically analyzed using StatSoft Statistica v.8 software. The relationships between parameters

Dmean, D70, D50 and D20 for the bladder and rectum were tested using t-Student Test or Wilcoxon Test for dependent variables.

4. Results

The analysis of DVHs for the entire group of patients is presented in Table 2. The value of DVH parameters is expressed as a percentage of total prescribed dose. The average values of Dmean, D70, D50 and D20 for the bladder were lower in the prone position and the differences between these parameters in both treatment positions amounted 1.12%, 1.67%, 2.67% and 0.41%, respectively. There were no statistically significant differences observed between these parameters (t-Student Test, Wilcoxon Test). The analysis of DVHs for the rectum showed that the differences between the supine and prone position were not significant. Only the D5 difference for the rectum was statistically significant ($p=0.03$) in favor of stabilisation on belly-board, but its value amounted to 0.52% of prescribed dose. More significant differences were observed for the bowels. The average Dmean and D10 parameters were lower by 3.3% and 5.81%, respectively, in the prone position ($p=0.009$ and $p=0.007$).

A comparison of dose volume histogram parameters for the subgroup irradiated to the prostate gland and seminal vesicles showed more significant differences. The whole analysis is presented in Table 3. The detailed analysis of DVHs for the bladder demonstrated the superiority of the prone position

Table 3 – Dose volume histograms comparison of organs at risk for subgroup irradiated on prostate gland and seminal vesicles.

Organ at risk	DVH parameter	% of prescribed dose in supine position	% of prescribed dose in prone position	p value
Bladder	Dmean	48.16	44.80	0.070
	D70	25.47	21.75	0.092
	D50	41.94	36.81	0.829
	D20	76.73	77.51	0.782
Rectum	Dmean	48.67	44.18	0.050
	D70	23.80	21.09	0.116
	D50	40.44	31.98	0.032
	D20	87.17	79.28	0.053
Intestine	D5	100.80	99.85	0.016
	Dmean	2.86	2.46	0.109
	D10	7.53	5.07	0.260

Table 4 – Dose volume histograms comparison of organs at risk for subgroup irradiated on prostate gland, seminal vesicles and pelvic lymph nodes.

Organ at risk	DVH parameter	% of prescribed dose in supine position	% of prescribed dose in prone position	p value
Bladder	Dmean	63.94	65.05	0.497
	D70	40.23	40.61	0.837
	D50	58.87	58.66	0.929
	D20	97.28	95.68	0.059
Rectum	Dmean	64.10	67.05	0.116
	D70	43.98	48.01	0.222
	D50	64.94	68.38	0.383
	D20	93.37	94.52	0.637
Intestine	D5	101.17	101.08	0.732
	Dmean	32.30	27.18	0.028
	D10	69.03	65.40	0.620

– the Dmean, D70 and D50 were lower by 3.36%, 3.72% and 5.13%, respectively. Only the D20 parameter was 0.78% higher in case of the prone stabilisation. These differences were not statistically significant. Comparison of rectal dose distribution for this subgroup showed greater differences – Dmean was an average of 4.49% lower, while the D70, D50 and D20 were lower by 2.71%, 8.46% and 7.89%, respectively, in the case of the prone immobilization. The Dmean and D50 differences were statistically significant ($p=0.050$ and $p=0.032$, respectively).

The analysis of the second subgroup is presented in Table 4. It showed that the Dmean in the bladder and rectum were lower by 1.11% and 2.95%, respectively, in the supine position. However, the detailed analysis of bladder doses showed that D70 and D50 parameter differences were lower than 0.5% of prescribed dose while D20 was 1.6% higher in the supine position. Comparison of D70, D50 and D20 parameters confirmed the favourable distribution of rectal doses for supine immobilisation – the values of parameter differences were 4.03%, 3.44% and 1.15%, respectively. All of these differences were not significant, although the p value of D20 parameter for the bladder amounted to 0.059. More significant differences were observed for the bowels. The average Dmean and D10 parameters were lower by 5.12% and 3.65%, respectively, in the prone position. Moreover, the Dmean differences were statistically significant ($p=0.028$).

There were 654 daily MVCT matching analyzed – 336 for supine and 318 for prone immobilization. The average value of shifts in the X-, Y- and Z- axes were -0.35 (SD=3.83), -0.18 (SD=3.36) and 0.37 (SD=2.62) mm, respectively, in the supine position and 0.44 (SD=3.54), -0.52 (SD=3.43) and 0.09 (SD=2.78) mm for stabilization on belly-board. The average rotation value for both positions amounted to 0.7° . Therefore, the differences in the arrangement of reproducibility were comparable. Taking into account the margins for PTV (0.7–10 mm) both treatment immobilization methods were safe in terms of reproducibility of the position.

5. Discussion

In the present study, the prone position during radiotherapy in patients with prostate cancer was associated with lower doses in OARs, especially in the rectum. Despite the fact that in the entire group of patients the differences between tested

parameters were not large, the Dmean and D10 for the bowels were statistically significant. In cases of irradiation of only the prostate gland and the seminal vesicles, immobilization using belly-board allowed for substantial reduction of all tested dose volume parameters in the bladder and rectum, except for D20 for the bladder. The decrease of D50 parameter for the bladder by 5.13% and for the rectum by 8.46% of prescribed dose translates into reduction by 4.0 Gy and 6.6 Gy, respectively, for 78 Gy PTV. For the subgroup of patients irradiated to the prostate, seminal vesicles and pelvic lymph nodes, the prone position was associated with significant bowel sparing.

In the past decade, several studies have been published about immobilization for radiotherapy of prostate cancer. Most of them showed a beneficial dose distribution in the prone position. One of the first studies comparing the supine and prone positions was reported already in 1997. Zelefsky et al.¹³ proved significantly lower doses in the rectum for plans of irradiation in the prone position. Patients were immobilized using an aquaplast. The night before CT they were given enema and during the test a rectal catheter was inserted. Radiotherapy was planned using the 6-field 3D technique. The dose comparison was focused only on the Dmean parameter (mean dose in the volume of rectal wall) and V95 (rectal wall volume received 95% of prescribed dose). The authors did not observe significant differences for doses in the bladder, which could be due to the planning with an empty bladder. Filling of the bladder would increase the volume and move part of the bladder's volume away from the target area. Zelefsky drew attention to the fact that even a small increase in the distance between the prostate and the anterior rectal wall in prone position contributes to a substantial decrease in dose for the rectal wall.

In turn, McLaughlin et al.¹⁴ compared the effect of the position and irradiation technique (4-field vs. 6-field 3D technique) on the dose distribution in OARs. The study included 10 patients in whom only the prostate or the prostate with seminal vesicles was irradiated. CT was performed with an empty bladder. Authors showed that in the whole group of patients planned dose distribution in the front wall of the rectum was lower in the prone position, regardless of the technique used. However, the comparison focused on volumes that received 80% and 90% of prescribed dose. No differences in DVHs for the bladder were shown. Like Zelefsky,¹³ McLaughlin¹⁴ showed that in the prone position the rectum is located fur-

ther away from the target and hence the doses are lower. The authors also observed that the increase in this distance is the result of both the anterior displacement of the prostate from the rectum and the retraction of the rectum against the sacrum; the anatomical mechanism of this phenomenon is unknown. Based on these results, McLaughlin suggested that the patient's immobilisation is more important for DVHs than the number of fields in the 3D technique.

The above-mentioned results were confirmed in a phase II study published by O'Neil et al.¹⁵ The analysis included patients in whom only the prostate with seminal vesicles was irradiated. CT for treatment planning was performed without any special stabilization and rectum preparation. Patients were asked to maintain a filled bladder during the test and the subsequent radiation. Despite the use of only the 3-field 3D technique, the authors obtained a statistically significant reduction of V70 ($p < 0.001$) and V50 ($p = 0.011$) parameter for the rectum in prone position.

Different results were obtained by Baylay et al.¹⁶ in their randomised study of 28 patients. However, different patterns were used to prepare patients for each treatment position – supine with a full and prone with an empty bladder. Moreover, the PTV covered only the prostate gland without seminal vesicles. Treatment plans were performed using the 6-field 3D technique. Baylay et al. demonstrated statistically significant lower dose in the rectum and bladder for the supine position. These results were significant only if the margins for PTV in the prone position were larger due to the greater motion of the gland in the sagittal axis, based on the analysis of portal image alignment and verification to bones structures and fiducial markers. These observations were not confirmed by other studies.^{14,17,21} In the case of the same margins for PTV in both positions, the dose differences were not statistically significant.

Favorable dose distribution in the rectum for the supine position was also shown by Kato et al.²² But this comparison referred to the IMRT technique for the supine position and the 3D technique for the prone position. They also observed an increase in the mean distance between the rectum and prostate by about 5 mm (in some cases more than 20 mm) in the prone treatment position. The application of such a highly conformal technique as IMRT or Tomotherapy for the prone position could significantly change the presented results.

The choice of appropriate position is one of the basic and most important aspects of treatment planning. A number of available accessories enable a faithful reproducibility on the basis of skin markers, bone and soft-tissue structures in both the supine and prone positions. Traditionally accepted standard for irradiation of patients with prostate cancer is the supine position. However, there are not available clear and reliable research data on large groups of patients confirming the superiority of this position in terms of reproducibility, displacement of internal organs and, above all, the planned dose distribution in organs at risk. Additionally, previously published studies related to irradiation in the 3D technique which in the era of dose escalation has given way to more conformal techniques such as IMRT or Tomotherapy. The presented data confirm the need to carry out study on large group of patients to determine an optimal position during prostate cancer irradiation in the era of highly conformal radiotherapy.

6. Conclusion

In patients irradiated to the prostate and seminal vesicles, the prone position may support sparing of the rectum and bladder.

The prone position on the belly-board stand is associated with significant bowel sparing in all patients irradiated to prostate cancer, especially those from the high risk group.

The reproducibility of position arrangement in both treatment positions is comparable on the basis of daily MVCT verification.

The study on a large group of patients is needed to finally determine an optimal position during prostate cancer irradiation.

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