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Original article

Evaluation of combining bony anatomy and soft tissue position correction strategies for IMRT prostate cancer patients

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ABSTRACT

Background: Radiotherapy treatment requires delivering high homogenous dose to target volume while sparing organs at risk. That is why accurate patient positioning is one of the most important steps during the treatment process. It reduces set-up errors which have a strong influence on the doses given to the target and surrounding tissues.
Aim: The aim of this study was to investigate the efficiency of combining bony anatomy and soft tissue imaging position correction strategies for patients with prostate cancer.
Materials and methods: The study based on pre-treatment position verification results determined for 10 patients using kV images and CBCT match. At the same patients' position, two orthogonal kV images and set of CT scans were acquired. Both verification methods gave the information about patients' position changes in vertical, longitudinal and lateral directions.
Results: For 93 verifications, the mean values of kV shifts in vertical, longitudinal and lateral directions equaled: -0.11 ± 0.54 cm, 0.26 ± 0.38 cm and -0.06 ± 0.47 cm, respectively. The same values achieved for CBCT matching equaled: 0.07 ± 0.62 cm, 0.22 ± 0.36 cm and -0.02 ± 0.45 cm. Statistically significant changes between the values of shifts received during the first week of treatment and the rest time of the irradiation process were found for 2 patients in the lateral direction and 2 patients in vertical direction among kV results and for 3 patients in the longitudinal direction among CBCT results. A significant difference between kV and CBCT match results was found in the vertical direction.
Conclusions: In clinical practice, CBCT combined with kV or even portal imaging improves precision and effectiveness of prostate cancer treatment accuracy.

1. Background

The number of prostate cancer patients who have been treated using advanced external beam radiotherapy (EBRT) techniques like intensity modulated radiotherapy (IMRT) is increasing rapidly.[1–3] This irradiation technique gives the opportunity to increase tumor dose while decreasing doses delivered to normal tissues, which results in improving survival and reducing treatment-related complications.[4–9] To

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avoid undesirable target underdosing or normal tissue overdosing, caused by PTV margin reduction, internal target motion and problems with setup accuracy, it is necessary to monitor and verify patient's daily position according to the special verification procedures day by day.[5,10–13] The most widely practiced ones are based on imaging using electronic portal devices (EPIDs) or kV imaging devices. In both cases bony anatomy is used to verify patient position changes.[12,14–16] These checking procedures represent rather off-line correction strategies[17] and are based on two commonly used protocols: shrinking-action level (SAL) and no-action-level (NAL).[1,18–20] For both of them, during the first fractions, systematic patient positioning changes are estimated and then used for corrections. In the SAL-protocol, additionally the possible time trends are controlled. Unfortunately, several studies have showed that for many target localizations this kind of correction, which uses bony anatomy matching, is partly satisfactory. As it was proven for prostate radiotherapy, its motion in relation to bony anatomy can be considerable, especially in anterior–posterior direction.[1,12,21,22] With the technology improvement, a precise detection of prostate position has become possible using more advanced image-guided strategies based on computed tomography (CT), like cone beam computed tomography (CBCT, Varian Medical Systems, Palo Alto, USA). It gives the ability to visualize soft tissues and internal organs.[1,23] That is why, comparing to portal imaging or kV imaging, CBCT match results are more reliable but the verification procedure is more time-consuming, especially when it is performed and verified on-line before a daily treatment session.

2. Aim

The aim of this study was to investigate the efficiency of combining bony anatomy and soft tissue position correction strategies for patients receiving external beam radiotherapy for prostate cancer.

3. Materials and methods

The study involved 10 consecutive patients with prostate cancer treated in the Greater Poland Cancer Centre. As a part of bladder preparation, all patients were instructed to drink 500 ml of water before planning CT and then before all treatment sessions. To obtain rectum's volume reproduction, this organ at risk (OAR) was prepared pharmaceutically. For each patient, slices were acquired in the supine position with 3 mm slice thickness and no contrast medium.[24–26]

Clinical target volumes (CTVs) were represented by prostatic gland (CTV1), seminal vesicles (CTV2) and lymph nodes (CTV3). Corresponded planning target volumes (PTVs) were created by adding 1 cm margin in all directions, except for posterior margin where 0.5 cm was added.[2,8,17] For each patient, a seven-field IMRT plan was created. The treatment planning was done using Eclipse v.8.2.24 Treatment Planning System (Varian Medical Systems, Palo Alto, USA). All fields were coplanar with 20 MV photon beam quality. The total dose of 50 Gy was delivered in 25 fractions of 2 Gy per fraction, 5 days per week. After this part of the external beam treatment, all patients received a boost dose. In most cases, the prostate was boosted using the real-time high dose rate (HDR) brachytherapy technique.

All patients were treated on Varian Clinac 2300C-D (Medical Systems, Palo Alto, USA) linear accelerator equipped with a multi-leaf collimator (MLC), which consisted of 80 leaves with 1 cm width in isocentre. Before first fraction, the isocentre location was marked with three tattoos (anterior–posterior, lateral left and lateral right) on patient's skin in the simulation suite.[24] Based on these tattoos, before each treatment session, a system of wall-mounted alignment lasers was used for daily patient positioning.[27] Then, on-line kV alignment was verified to adjust patient's daily position to pre-treatment imaging. Two orthogonal (0° and 270°) kV images were registered to digitally reconstructed radiographs (DRRs) generated in the treatment planning system.[12] Based on anteroposterior (0°) image, the lateral (lat) and longitudinal (lng) displacements were determined. From the second projection (270°), the information about position changes in vertical (vrt) and longitudinal (lng) directions was set.[17] This first part of patient position verification was based on the matching of daily bony anatomy with reference images.[17,20] After that, in the same patient position as for kV verification, CT scans were acquired. On-line prostate position correction was done according to the results obtained by comparing CBCT scans to the reference set of planning CT scans[28] in vertical, longitudinal and lateral directions. The CBCT match was based on the results of automatic match, which was manually corrected according to the daily prostate position. The results of both kV and CBCT verifications in relation to the reference images were evaluated by a physician. As an additional parameter, the rotation was analyzed and checked for being below the limit value of 3°, as set in our clinical protocol. After making a CBCT-based shift, no additional re-imaging was done. This scheme of verification between images acquired prior to the treatment with images acquired before single treatment fraction (both kV and CBCT) was carried out every third day, on average. Before every fraction with no kV vs. CBCT alignment, patients were positioned based on the on-line kV verification results. All patients started irradiation procedure on Monday.

4. Results

The study based on the total number of 93 sets of kV/CBCT verifications available for comparison. The reference images and structures were taken from the treatment planning system – DRRs for 93 sets of kV images and planning CT scans for 93 pre-treatment CBCT series. For the group of patients analyzed, the minimum number of verifications was 8 and the maximum was 11. The median number of kV/CBCT procedures per patient was 9.

Analyzing all match results, the mean values in each direction for both verification procedures were determined. The mean values of shifts for kV match results in vertical, longitudinal and lateral directions with SD (both in cm) equaled: -0.11 ± 0.54, 0.26 ± 0.38 and -0.06 ± 0.47, respectively. The same values achieved based on CBCT matching equaled: 0.07 ± 0.62 cm, 0.22 ± 0.36 cm and -0.02 ± 0.45 cm, respectively. The longitudinal and lateral mean values represented similar

Table 1 – The percentage kV and CBCT match results detected in −0.3 cm to 0.3 cm and −0.5 cm to 0.5 cm ranges from the isocentre.

	vrt	lng	lat
<−0.3 cm; 0.3 cm>			
kV	55.91	58.06	50.54
CBCT	50.54	60.22	51.61
<−0.5 cm; 0.5 cm>			
kV	70.97	79.57	78.49
CBCT	65.59	81.72	80.65

tendency (CBCT lng: 0.22 ± 0.36 cm, kV lng: 0.26 ± 0.38 cm, CBCT lat: −0.02 ± 0.45 cm, kV lat: −0.06 ± 0.47 cm), unlike the vertical results. The percentages of kV and CBCT match results which were detected in two ranges (−0.3 cm to 0.3 cm and −0.5 cm to 0.5 cm) are presented in Table 1. The calculation shows that for longitudinal and lateral axes the amount of kV and CBCT results detected in a specific range are similar, but values analyzed in the vertical direction differed more than 5% both for 0.3 cm and 0.5 cm ranges. The number of observations with more than 1.0 cm and 1.5 cm movements from the isocentre is presented in Table 2. The highest registered shift was found for the vertical CBCT and was −1.80 cm. In two other directions: longitudinal and lateral, the maximum values were tracked among kV data and equaled 1.40 cm and 1.10 cm. Detailed results are shown in Table 3, where the signs of individual values were introduced according to the signs of the Cartesian system. More specifically, the beginning of this system is set in each treatment plan isocentre and the positive directions of vertical, longitudinal and lateral axes correspond to the posterior, superior and left side of the patient, respectively.

Table 2 – The number of observations which exceeded 1.0 cm and 1.5 cm movements from the isocentre.

	vrt	lng	lat
Number of observations ≥1.0 cm			
kV	9	3	5
CBCT	13	2	5
Number of observations ≥1.5 cm			
kV	3	0	0
CBCT	3	0	0

Table 3 – The mean values (mean) with standard deviation (SD), minimum (MIN), maximum (MAX) and median (MED) of kV and CBCT match results in three directions: vertical (vrt), longitudinal (lng) and lateral (lat).

	kV			CBCT		
	vrt	lng	lat	vrt	lng	lat
Mean [cm]	−0.11	0.26	−0.06	0.07	0.22	−0.02
SD [cm]	0.54	0.38	0.47	0.62	0.36	0.45
MIN [cm]	−1.50	−0.80	−1.10	−1.80	−0.80	−1.00
MAX [cm]	1.60	1.40	1.10	1.40	1.30	1.00
MED [cm]	−0.20	0.30	−0.10	0.10	0.20	0.00

All values mentioned above were analyzed statistically. The values of shifts from the first week of treatment were compared with match results received during the rest time of the irradiation process. This was done independently for both kV and CBCT to identify the influence of stress factors at the beginning of the treatment. Taking into account the number of verifications done during the first week of treatment, all patients were divided into 2 groups: 6 patients vs. 4 patients with two or three verifications, respectively. Differences between the groups were verified using *t*-test and Mann–Whitney's test and considered significant if the *p*-value was under 0.05. Among kV data, statistically significant changes in the lateral and vertical directions were found. Together, these differences were tracked for four patients from the whole group – vertical significant changes for two patients and lateral significant changes for two patients. A different tendency was found in CBCT data. In this case, statistically significant changes between values received during the first week and the rest time of the treatment were tracked for three patients in the longitudinal direction.

kV and CBCT match results collected during the treatment process were analyzed to track the possible dependence on the position verification technique. To do that, all these related values were verified using *t*-test. A significant change between kV and CBCT match results was found only in the vertical direction. As position correction changes in this direction are often reported in literature,[1,12,21,22] additionally vertical values (separately kV and CBCT) were compared with values of changes in the other directions. *t*-Test analysis showed statistically significant differences between vertical and longitudinal data both for kV and CBCT match results.

5. Discussion

The quality of radiotherapy treatment process is evaluated by controlling doses delivered to target volumes and normal tissues.[6] One of these treatment controlling procedures concern verification of patient position.[16] In this study, two different verification methods of patient position accuracy were used. In the group of 10 prostate patients, the values of position changes were tracked using kV imaging and CBCT scans. The analysis of all procedures showed that in most cases longitudinal kV and CBCT match results were moved towards the head. Mean lateral kV and CBCT displacements were set around the isocentre point with the tendency to be situated towards the right side of the patient. The values of standard deviations for the longitudinal and lateral axis and these two analyzed verification procedures were similar. Only in the vertical direction did the mean values represent a different tendency and were burdened with the highest SD values.

Shifts detected with the OBI system but, as opposed to our study, based on verification of gold markers' position were analyzed by Logadóttir et al.[11] In their study, the accuracy value calculated as the mean from average shifts estimated for all fractions for each patient equaled: −0.36 mm for kV and 0.18 mm for CBCT (the mean lateral accuracy), 0.07 mm for kV and −0.16 mm for CBCT (the mean longitudinal accuracy) and −0.52 mm for kV and −0.15 mm for CBCT (the mean vertical accuracy). Except lateral uncertainties, all these values are smaller than our results. Different tendencies were also found for the signs of analyzed movement values obtained in Logadóttir and our study. This is probably the effect of different reference points or structures used for verifications, as well as patients' preparation before and, consequently, during treatment. Unfortunately, diet restrictions or other rectum and bladder filling procedures were not mentioned in the article. In that study,[11] the best agreement between shifts measured based on soft-tissue vs. internal markers position was found in the lateral direction. The values estimated in the longitudinal axis represented the same tendency. As in our analysis results, the difference determined in the vertical direction was the highest with different signs of translation values obtained for localization of prostate using the prostate or internal markers. In Boda-Heggemann et al.[4] study, CBCT matching was done on the basis of implanted iodine-125 seeds. The interfraction shifts of prostate relative to the bony structures were also minimal in the lateral direction (-0.3 ± 1.5 mm). Compared to Logadóttir et al.[11] results, anterior–posterior shifts (corresponding to the vertical axis) were smaller than shifts detected in the cranio-caudal direction (corresponding to longitudinal axis): 0.9 ± 3.6 mm vs. 3.2 ± 2.6 mm.[4] The same tendencies as both in our study and that of Logadóttir et al.[11] analysis was found in Foster et al.[29] comparison of transabdominal ultrasound system (BAT) vs. electromagnetic transponders (the Calypso system). Although, that analysis compared completely different techniques than our study, the largest initial localization errors were also detected in the vertical direction with mean anterior–posterior offsets observed in the opposite directions: -4.3 ± 6.4 mm for Calypso and 1.3 ± 11.6 mm for BAT. In both techniques standard deviation values measured for mean couch shifts are relatively high: between 3.8 and 6.4 mm for Calypso and 11.4 and 12.8 mm for BAT.

In another position verification study done by Sandhu et al.[2] the setup error determined by measuring the inaccuracy in patient alignment using skin tattoos compared to bony anatomy verification, the average values with standard deviations equaled 5.2 ± 7.1 mm in the vertical direction, 4.9 ± 7.5 mm in the longitudinal direction and 3.6 ± 5.6 mm in the lateral direction.

Such comparisons between our data and published data can be done endlessly, but as mentioned by Logadóttir et al.,[11] in a majority of studies there is one important limitation – the comparison is only based on a single point (usually the isocentre) or points (corresponding to fiducial markers' position). In our study, to avoid this effect, we used a more precise evaluation in which we took the whole prostate's volume into consideration during the CBCT verification procedure.

The other aspect of comparing position verification techniques is connected with discussing the advantages and disadvantages of different IGRT strategies. In routine clinical practice, EPID is the most popular position verification tool,[17] as it is easy and fast to use even in on-line scheme. This widely available instrument gives the possibility to verify treatment field outlines or MLC positions with respect to patient bony anatomy using high-energy treatment beam (MV). To improve the quality of 2D setup images, instead of MV-based position correction, diagnostic X-rays (kV) are used.[30] Unfortunately, all planar verification images distinguish only bony structures. Both EPID and kV-based alignments require surrogate to localize the target. The position of implanted gold markers or other fiducials like iodine-125 seeds can be easily (even automatically) detected,[1] but this implantation makes the procedure invasive and still, except bones, there is no information about spatial relationship between the target and adjacent organs at risk.[30] The other on-board solution, CBCT, overcomes this technical aspect. Generally, all CT scanners used in treatment rooms do not require surrogate to visualize soft tissue targets and organs. Volumetric data can be used for dose calculation and adaptive radiotherapy, but the verification procedure is more time-consuming than for EPID/kV imaging. To minimize the dose from pre-treatment imaging, non-ionizing methods can be applied. Using ultrasound devices, one can obtain information about the localization of prostate. The method is non-invasive, low cost, easy to implement and not so time-consuming, but, on the other hand, it is susceptible to inter-observer variations, can be applied for selected (rather slim) patients and can cause a displacement owing to the pressure of the imaging probe on the patient's lower abdomen.[30] Radiofrequency transponder coils allow to overcome these problems. The non-ionizing method of localizing the target in 3D, based on implantation of radiofrequency transponder coils, which are tracked electromagnetically in real time during external radiotherapy treatment.[30] This verification tool works very well but the experience in a reliable and safe technique for implantation of transponders and demonstration of its stability within implanted tissue is needed.[21]

Throughout further analysis, all kV and CBCT mean values of shifts were converted into percentage values. While between -0.5 cm and 0.5 cm distance away from the isocentre about 80% of match results from the longitudinal and lateral axes were detected both for kV and CBCT, in the vertical direction for kV data it was about 70% and for CBCT data it was about 66%. On the other hand, it should be underlined that analyzing results obtained for a single set of kV and CBCT, considerable differences were found. Those differences showed the superiority of soft tissue position correction strategies over bony anatomy verification procedures, as in extreme cases they equaled 2.4 cm in the vertical direction (0.6 cm for kV and -1.8 cm for CBCT), 1.2 cm in the lateral direction (-0.6 cm for kV and 0.6 cm for CBCT) and 1.4 cm in the longitudinal direction (1.4 cm for kV and 0.0 cm for CBCT).

Similar percentage analysis was done in Kupelian et al.[27] multi-institutional clinical study. Comparing Calypso position verification results with kV X-ray based systems, the majority of displacements in the longitudinal and lateral directions were found to be within 0.5 cm. Among lateral shifts, about 8% exceed 1 cm with largest offsets (about 2.5 cm) observed for large patients. Compared to the results received in the other axes, displacements detected in the vertical direction were prominent with 45% of values within 0.5 and 1.5 cm, which leads to the conclusion that rectum emptier than during initial simulation results in mostly posterior displacements. In Sandhu et al.[2] study also the proportion of patients with shifts exceeded 0.5 cm was higher in anteroposterior axis than in the other directions.

Our results of motion study demonstrated some tendencies. The additional information was collected using statistical tools. *t*-Test verification showed significant differences between kV and CBCT match results in the vertical direction. This was confirmed by an additional statistical comparative analysis which revealed the difference between vertical and longitudinal values of kV match results and the same vertical and longitudinal difference in CBCT data.

All these data, divided into different groups, were analyzed to find a possible correlation between stress factors at the beginning of the treatment with values of position changes. Depending on the position correction technique, results represented no obvious tendency. Based on the results of statistical comparative analysis, more differences were found for the bony anatomy alignment technique (four patients in vertical or lateral directions). In three cases, CBCT match results demonstrated statistically significant differences in the longitudinal axis. This could inform the lack of tendencies connected with stress factors during the first week of treatment in relation with rest time of the irradiation process or with a little tendency which resulted from pelvis tension. The tension effect is mainly related to bony anatomy alignment variations. These variations will be widely checked in the next step of this combining study.

During the study, patients' position changes were estimated not only in three directions, the rotation was also tracked. This parameter was only checked for being under the limit value of 3°. According to CBCT match results, in the case of one patient from analyzed group this value was over the limit which was connected with the patient's anatomy changes and strongly contributed to difficulties in adequate positioning and correctness of dose delivery. That is why, after the eighteenth fraction, the second treatment plan for this patient was prepared based on a new set of CT scans. This demonstrates the qualitative superiority of soft tissue imaging verification techniques over bony anatomy alignment. The effect of prostate tilt was quantitatively analyzed by Boda-Heggemann et al.,[4] who also used CBCT verification tool. As a result, they reported that prostate tilting motion should be considered with regard to choosing the PTV margins and adaptive radiation therapy technique.

As this evaluation of combining bony anatomy and soft tissue position correction strategies was only the start point, our assumption was to track match results initially within the group of 10 consecutive prostate patients, which can be regarded as a small group. On the other hand, however, the analysis was based on 93 sets of verification procedures, that is on 186 kV images and 93 series of CBCT scans, 6 values per single verification per one patient and 558 values analyzed during the study, which is not so little. In previously mentioned studies, results were obtained for a minimum of 7 patients (with 61 CBCTs) in Boda-Heggemann et al.[4] and a maximum of 41 patients in Kupelian et al.[27] and Foster et al.[29] As both of them were multi-institutional clinical studies done in the same five participating centres, this gives approximately 8 patients per one cancer centre.

Further analysis of prostate motion data with OARs volume change comparison will be provided for a bigger group of patients controlled with the same position correction strategy in a follow-on article. With those initial results, we think that our scheme of verification enables analysis of more than interfraction patient movement, without any loss of information due to setup imaging being to rare.

6. Conclusions

Both verification techniques, based on kV imaging or CBCT scans, are crucial to maintain a proper patient's position during the irradiation process and, consequently, improve reproducibility of field placement. Compared to kV or even portal verification, in terms of treatment delivery precision and accuracy improvement, CBCT could be named a set-up error minimization method. On the other hand, it is a more time-consuming position verification tool. That is why, in clinical practice combining it with a bony anatomy matching procedure by doing CBCT once or twice a week seems to improve precision and effectiveness of prostate cancer treatment accuracy with no geographical miss and excessive workload.

Conflict of interest

None declared.

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