NUKLEONIKA 2008;53(4):167–171

ORIGINAL PAPER

Evaluation of set-up verification with the analysis of systematic and random errors in radiotherapy – a study of the Great Poland Cancer Centre

Łukasz Szczurek,
Agnieszka Skrobała,
Tomasz Piotrowski,
Agata Jodda

Abstract. The aim of this study was the examination of influence of location tumors and methods of immobilizing on values of geometrical errors during treatment, and the analysis of set-up errors in reference to the method of irradiation in three groups of patients before and after corrections. This study included three groups of patients with prostate cancer (59 patients, 277 portal images), head and neck (60 patients, 285 portal images) and brain tumor (45 patients, 175 portal images). Ratios of IMRT vs. 3D-CRT were respectively: in I group 76% vs. 24%, in II group 95% vs. 5% and III group 83% vs. 17%. Set-up errors were compared in reference to the technique of irradiation and stage of treatment. The displacements were significantly higher in the first group compared with head, neck and brain tumors; 5.66, 4.05, 3.93 mm, respectively. The values of the vector lengths were significantly dependent on the type of irradiation technique (3D-CRT vs. IMRT) only in the first group ($p < 0.001$). The average of vector length in I, II and III group were significantly reduced from; 5.67, 4.02, 3.91 mm to 5.13, 3.63, 3.57 mm after correction, respectively. The Spearman test is indicating a low negative correlation between set-up errors and the following fractions. The applied methods of patients positioning with prostate cancer produce a worse repeatability than the ones used for patients with head, neck and brain cancers. Portal verification reduces values of set-up errors. Significant differences in the magnitude of displacements before and after correction were observed. No significant differences between value of displacement and number of fraction were revealed.

Key words: electronic portal devices • positioning patient • three-dimensional-conformal radiation therapy (3D-CRT) • intensity-modulated radiation therapy (IMRT) • oncology

Ł. Szczurek✉, A. Skrobała, A. Jodda
Department of Medical Physics,
Great Poland Cancer Centre,
15 Garbary Str., 61-866 Poznań, Poland,
Tel.: +48 61 854 05 53, Fax: +48 61 854 05 50,
E-mail: szczureklukasz@gmail.com

T. Piotrowski
Department of Electroradiology,
Karol Marcinkowski University of Medical Sciences,
15 Garbary Str., 61-866 Poznań, Poland

Received: 26 February 2008
Accepted: 24 June 2008

Introduction

Set-up verification is one of the most important parts of radiotherapy. The evaluation of geometric errors is very useful to assurance of accurate and repeatable patient set-up in a modern technique of irradiation. In our Institution set-up error can be measured using portal imaging with special films or an electronic portal imaging device (EPID). In this study the second method of verification was used.

The main purpose of this paper was the assessment of the influence of location of tumors and the methods of immobilizing on values of the geometrical errors, evaluation of displacements during radiotherapy process, a comparison of displacements before and after correction and examination of set-up errors in reference to the method of irradiation (IMRT – intensity modulated radiation therapy and 3D-CRT – three-dimensional-conformal radiation therapy).

Materials and methods

The retrospective study population consisted of 3 groups of patients, with prostate cancer (59 patients; 277 portal images), head and neck (60 patients; 285 portal images) and brain cancer (45 patients; 175 portal images) treated at our Institution between May 2006 and January 2007. Ratios of IMRT vs. 3D-CRT were respectively: in I group 76% vs. 24%, in II group 95% vs. 5% and III group 83% vs. 17%. On average, portal images were obtained for 5 fractions per patient. For every patient, we acquired two portal images in 0 and 90 angle gantry position (AP and LAT) during verification, using a typical exposure time 3 MU at a dose rate of 300 MU/min and 6 MV energy. Displacements between digitally reconstructed images (DRR) and portal images (EPID) were estimated along the three axes: R-L (right-left), A-P (anterior-posterior) and C-C (cranial-caudal). In this study we were not interested in rotations. The physicists who made verification were instructed to use only rigid bone structures (e.g. mandible, skull base, femoral head) as matching structures in order to avoid registration errors due to different leg positions in group with prostate cancer. The evaluation of disagreement was made using the line based method where the lines corresponding to the bone structures were marked on the DRR and EPID images, then the pictures were manually fixed (Fig. 1). DRRs were obtained from the treatment planning software (Eclipse 6.5) [6].

The images were acquired using a Varian Clinac 2300 CD and 600 and a Varian EPID (an Amorphous Silicon® AS500) with a resolution of 512 × 384. During CT and treatment, all patients were positioned supine, this position in the first group revealed a substantially lower prostate movement compared to the prone position [4]. In the first group, the patient's ankles were immobilized using a commercially available holding device (Combifix, Sinmed, Reeuwijk, The Netherlands) in other groups there were used thermoplastic masks (5 – point head and shoulders mask and 3 – point head mask with larynx extension Sinmed). In groups with prostate cancer and head and neck cancer for each patient, a CT scan (Siemens Somaton Sensation Open) was obtained with a slice thickness of 5 mm, in the third group a slice thickness of 0.3 cm.

In our Institution a special verification protocol is used. In the first stage we obtained the values of displacement, the magnitude of the set-up error used in this study 5 mm – action level for IMRT and 0.7 mm for 3D-CRT were defined to be a maximum of tolerance (the possible maximum) dropping after reposition or resimulation in the second stage [8, 13]. A correction is performed when the set-up uncertainties exceed the action level.

The averages of displacements, vector of displacements and geometrical errors were obtained for every group of patients [1, 3, 5, 9, 10, 11]. Nonparametric tests were used to statistical study. The vector of displacement was defined as follows:

(1) $$V = \sqrt{x^2 + y^2 + z^2}$$

where: x – displacements left-right L-R; y – displacements cranial-caudal C-C; z – displacements anterior-posterior A-P.

A group of total of P patients, and a number of F_p measured fractions for each patient "p". The total number of measured fractions, N, is defined by

(2) $$N = \sum_{p=1}^{P} F_p$$

A measurement of displacements of patent p during fraction f along the principal axes is defined by x_{pf}, therefore, the overall mean of all measurements, M, can be given by:

(3) $$M = \frac{1}{N} \sum_{p=1}^{P} \sum_{f=1}^{F_p} x_{pf}$$

The variation around this mean has two components. The first is the random error. Standard deviation of the random errors is defined as:

(4) $$\sigma = \sqrt{\frac{1}{N-P} \sum_{p=1}^{P} \sum_{f=1}^{F_p} (x_{pf} - m_p)^2}$$

where m_p denotes the patient average

(5) $$m_p = \sum_{f=1}^{F_p} \frac{x_{pf}}{F_p}$$

The second component is given by systematic error

(6) $$\Sigma = \sqrt{\frac{P}{N(P-1)} \sum_{p=1}^{P} F_p (m_p - M)^2}$$

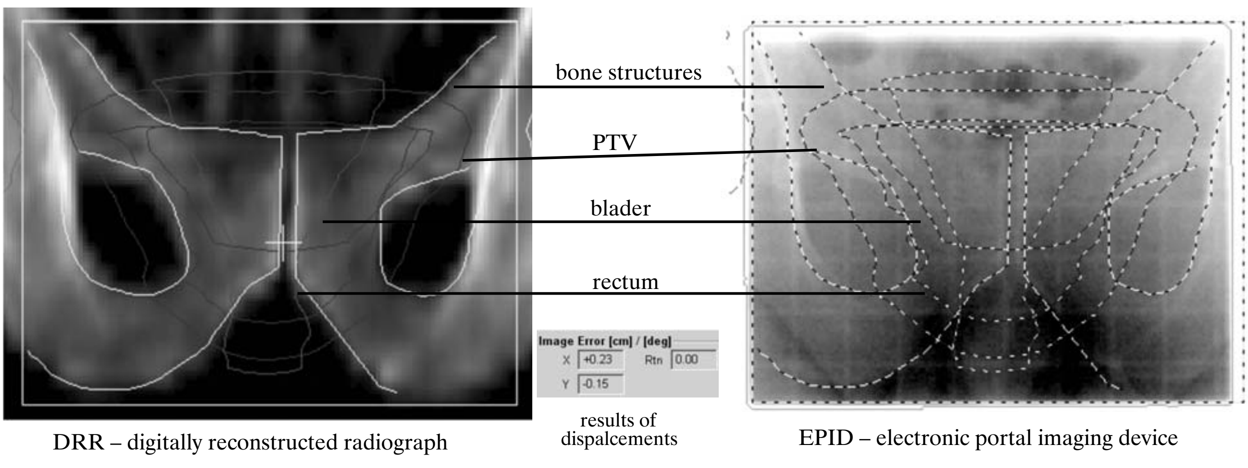

Fig. 1. An example of manual methods, delineated bony structures are marked on the DRR and EPID image, then the pictures were manually fixed.

Table 1. Analysis of set-up errors using 3D methods for prostate cancer

Prostate cancer	3D translations* (mm)		
	L-R	C-C	A-P
Overall mean (mm)	0.29	–2.34	1.32
Systematic error (mm)	1.89	2.16	2.46
Random error (mm)	2.84	3.27	2.87

* three principal axes (L-R – left–right; C-C – cranial-caudal; A-P – anterior-posterior).

Table 2. Analysis of set-up errors using 3D methods for head and neck cancer

H&N cancer	3D translations* (mm)		
	L-R	C-C	A-P
Overall mean (mm)	–0.19	–0.22	0.18
Systematic error (mm)	2.10	1.73	1.59
Random error (mm)	2.52	2.24	2.08

* three principal axes (L-R – left–right; C-C – cranial-caudal; A-P – anterior-posterior).

Table 3. Analysis of set-up errors using 3D methods for brain cancer

Brain cancer	3D translations* (mm)		
	L-R	C-C	A-P
Overall mean (mm)	–0.24	–0.46	0.41
Systematic error (mm)	2.28	1.72	1.62
Random error (mm)	2.41	1.85	2.09

* three principal axes (L-R – left-right; C-C – cranial-caudal; A-P – anterior-posterior).

Table 4. Comparison of the mean displacements for all images

Group	I	II	III
R-L	0.29	–0.19	0.41
A-P	1.32	0.18	0.24
C-C	–2.34	–0.22	–0.46
p ($\alpha < 0.05$)*	< 0.001	0.036	< 0.001

* p – value is obtained from Kruskal-Wallis test.

Results

Comparison of set-up errors for all images

The values of displacements and geometrical errors in the group with prostate cancer, head and neck, brain cancer for all images (before and after correction) were given in Tables 1, 2, 3, respectively. The overall mean displacements in all the three principal axes were significantly higher in the group with prostate cancer compared with the other groups. A comparison of overall means for all groups is given in Table 4.

In addition, the vector lengths were compared using a Kruskal-Wallis test analysis with the threshold $\alpha = 0.05$ (which corresponds to 95% confidence). Comparisons showed significant differences inside this groups (Fig. 2).

The highest value of the vector length, was observed in the first group, 5.66 mm, and the lowest value obtained for the third group. In this study we did not refer to patient's obesity. This issue is important in patients in the first group (increased pelvic movement of obese patient). Some institutions calculated a special index: BMI (body mass index) which are calculated according to the formula:

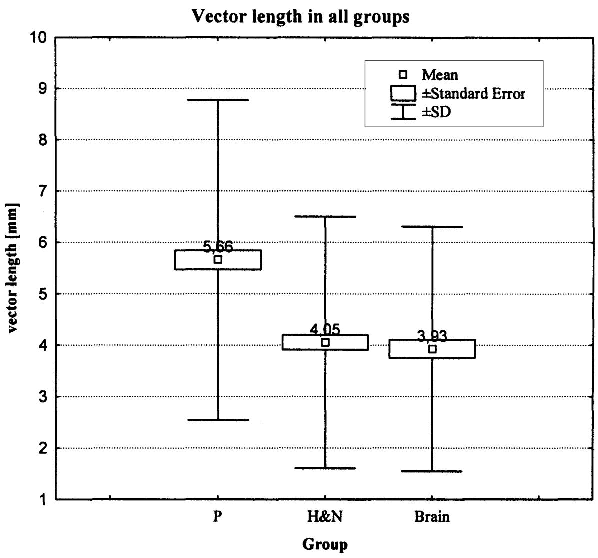

Fig. 2. Comparison value of vector length in groups.

$$\text{BMI} = \frac{\text{body weight (kg)}}{\text{body height}^2\ \text{(m)}} \quad (7)$$

Unpublished data showed that patients with BMI of more than 30 tend to show larger interfractional set-up deviations than those below 30 [12]. Future studies are currently under way to evaluate this index.

Vector length comparison in reference to 3D-CRT and IMRT

We compared the vector of displacements in reference to the studied group and method of irradiation using a Mann-Whitney U-test (Table 5).

Comparing Table 5, it appeared that the patients with prostate cancer treated with IMRT vs. 3D-CRT had a significant difference of vector length; 4.86 mm and 6.65 mm, respectively. Our scores have a guidance for physicians and treatment planners in calculating the appropriate margins for tumors. Comparing of columns 3 and 4 shows similar values of displacements in head and neck and brain tumors.

Comparison of set-up errors before and after correction

In addition, the patients in all groups were divided into subgroups with acceptable displacements and where the

Table 5. Vector length in groups for 3D-CRT and IMRT

Patient group	I	II	II
	Vector length (mm)		
IMRT	4.86	3.61	3.43
3D-CRT	6.65	4.37	2.99
p ($\alpha < 0.05$)*	< 0.001	0.27	0.26

* p – value is obtained from the Mann-Whitney U-test.

Table 6. Summary of clinical routine of portal verification for all cases

Group	Number of images	Within boundaries	Outside boundaries*
I	277 (100%)	241 (87%)	36 (13%)
II	285 (100%)	255 (89%)	30 (11%)
III	175 (100%)	161 (92%)	14 (8%)

* Displacements accepted after fine-tuning.

measurements exceeded the action level (Table 6).

Among all patient about 90% cases had tolerance uncertainties (< 5 mm). Column 4 shows the number of cases that fall inside of the acceptable level of displacements after reposition or resimulation. Then, the calculated mean displacements and geometrical errors are shown for images where set-up errors exceeds the action level (Tables 7–9).

The analysis revealed significant differences between the value of vector length for each group (Wilcoxon test), (Table 10).

The average of vector length in I, II and III groups were significantly reduced from: 5.67, 4.02, 3.91 mm before correction to 5.13, 3.63, 3.57 mm after correction, respectively (Fig. 3).

Correlation between displacements and number of fractions

Moreover, correlation coefficients between the vector length and the number of fractions were calculated using the Spearman test. In this part of our study we try to check the influence of the following fraction during the whole process of the treatment. For the second group, the correlation coefficient is approximately $r = -0.41$, indicating a low negative correlation between these parameters. Similar values of coefficients were calculated in other groups (Table 11).

Discussion

Through this study a special protocol was established to perform the analysis of set-up errors and correction using, the measurements of bone landmark displacements [7]. This revealed to be very practical and was accepted by physicians, physicists and radiographers instantly in our Institution. The patients with prostate cancer gave higher displacements than the patients where we used thermoplastic masks (head and neck cancer and brain cancer). Therefore, this group of patients required a special care and should be monitored more often using

Table 7. Comparison of set-up errors in groups of patients with prostate cancer before and after correction

Prostate cancer	Pre-action		3D translations* (mm)		Post-action	
	L-R	C-C	A-P	L-R	C-C	A-P
Overall mean (mm)	0.35	–2.28	1.41	0.33	–1.79	1.38
Systematic error (mm)	1.81	2.20	2.56	1.75	2.06	2.41
Random error (mm)	2.83	3.25	2.92	2.70	2.67	2.71

* three principal axes (L-R – left-right; C-C – cranial-caudal; A-P – anterior-posterior).

Table 8. Comparison of set-up errors in groups of patients with H&N cancer before and after correction

Head and neck cancer	Pre-action		3D translations* (mm)		Post-action	
	L-R	C-C	A-P	L-R	C-C	A-P
Overall mean (mm)	–0.25	–0.28	0.16	–0.33	–0.24	0.09
Systematic error (mm)	2.07	1.77	1.65	1.57	1.67	1.57
Random error (mm)	2.51	2.24	2.08	1.81	1.84	1.88

* three principal axes (L-R – left-right; C-C – cranial-caudal; A-P – anterior-posterior).

Table 9. Comparison of set-up errors in groups of patients with brain cancer before and after correction

Brain cancer	Pre-action		3D translations* (mm)		Post-action	
	L-R	C-C	A-P	L-R	C-C	A-P
Overall mean (mm)	–0.26	–0.45	0.34	–0.44	–0.41	0.32
Systematic error (mm)	2.27	1.76	1.64	2.01	1.49	1.67
Random error (mm)	2.40	1.88	2.12	1.88	1.72	2.01

* three principal axes (L-R – left-right; C-C – cranial-caudal; A-P – anterior-posterior).

Table 10. Comparison of vector length before and after correction in all groups of patients

Group	I	II	III
	Vector length (mm)		
Before action	5.67	4.02	3.91
After action	5.13	3.63	3.57
p ($\alpha < 0.05$)*	< 0.001	< 0.001	< 0.001

* p – value is obtained from Wilcoxon test.

Table 11. Correlation between the number of fractions and the vector length before correction

Region	Prostate	Head and neck	Brain
	Correlation coefficient*		
Vector length (mm)	–0.18	–0.41	–0.20

* Spearman correlation coefficient, expressed as r value, measures strength of linear relations between variables (r value; 0.0–0.2 indicates very weak to negligible correlation; 0.2–0.4, indicates weak, low correlation; 0.4–0.7, moderate correlation; 0.7–0.9, strong, high correlation; 0.9–1.0, very strong correlation).

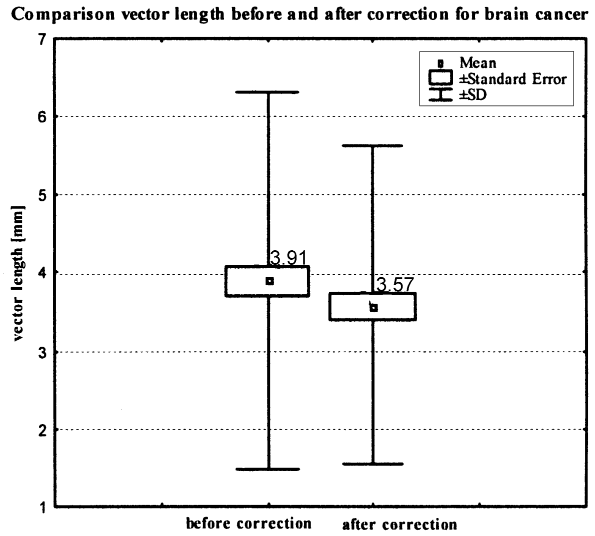

Fig. 3. The example of reduction vector length after correction in group with brain cancer.

EPID. This approach leads to an improved quality of treatment in patients with pelvic malignances.

Evaluation of vector of displacements in reference to technique of treatment (3D-CRT vs. IMRT) allowed to calculate and validate the appropriate planning margins for tumors, which include uncertainties in patient set-up, particularly in intensively modulated radiation therapy treatments which are more sensitive to patient positioning than the conventional type of irradiation [2, 8, 9, 13]. The patients with prostate cancer treated with 3D-CRT had significant differences of vector length in reference to the patients treated with IMRT. Moreover, the values of displacement applying 3D-CRT and IMRT were acceptable because the planning margin used in this group was higher; 1 cm and 0.5 cm, respectively. Comparisons in other groups of patients with head and neck cancer and brain cancer, have shown similar values of displacements lower than 0.5 cm for both techniques, therefore, planning margin were reduced to this value for these patients.

Verification by electronic portal imaging with high resolution amorphous silicon EPID improved treatment reproducibility through reduction of random set-up errors, systematic errors remained unchanged in all group of patients. Comparison values of the displacements before correction where the set-up errors exceed the action level and after correction showed significant differences for all patients and thus the value of portal verification were validated.

Evaluation of displacement in reference to the following fractions did not show significant differences in all groups of patients. The values of vector length were similar at the beginning and during the course of treatment. This indicated the necessity of regular portal verification during the whole process of radiotherapy.

Conclusions

In this paper, we have presented work on the application of a method we have developed in our Department to verify set-up errors during the process of radiotherapy. We have demonstrated that electronic portal imaging is a useful tool for a fast and reliable assessment and correction of various geometrical errors before and during the whole process of radiotherapy. Careful treatment planning, exact patient set-up, regular electronic portal imaging and simulator verification guarantee acceptable patient positioning and thus treatment delivery. The monitoring and verification of radiotherapy using EPID should be applied in radiation departments where three-dimensional-conformal radiation therapy and intensity-modulated radiation therapy are introduced.

References

1. Alasti H, Petric PN, Catton C *et al.* (2001) Portal imaging for evaluation of daily on-line setup errors and off-line organ motion during conformal irradiation of carcinoma of the prostate. Int J Radiat Oncol Biol Phys 49:869–884
2. Boehmer D, Bohsung J, Eichwurzel I *et al.* (2004) Clinical and physical quality assurance for intensity modulated radiotherapy of prostate cancer. Radiother Oncol 71:319–325
3. Coen W, Hurkmans, Remeijer P *et al.* (2001) Set-up verification using portal imaging; review of current clinical practice. Radiother Oncol 58:105–120
4. Dawson LA, Litzenberg DW, Brock KK *et al.* (2000) A comparison of ventilatory prostate movement in four treatment positions. Int J Radiat Oncol Biol Phys 48:319–323
5. Di Yan, Wong J, Michalski J *et al.* (1997) Adaptive modification of treatment planning to minimize the deleterious effects of treatment setup errors. Int J Radiat Oncol Biol Phys 38:197–206
6. Hashimoto S, Shirato H, Nishioka T *et al.* (2001) Remote verification in radiotherapy using digitally reconstructed radiography (DRR) and portal images: a pilot study. Int J Radiat Oncol Biol Phys 50:579–585
7. Malicki J, Milecki P, Nawrocki S *et al.* (2001) Evaluation of an electronic portal imaging device (Target view, GE) as a quality assurance tool. Reports of Practical Oncology and Radiotherapy 6;4:169–172
8. Manning MA, Wu Q, Cardinale RM *et al.* (2001) The effect of setup uncertainty on normal tissue sparing with IMRT for head-and-neck cancer. Int J Radiat Oncol Biol Phys 51:1400–1409
9. Remeuer P, Geerlof E, Ploger L *et al.* (2000) 3-D portal image analysis in clinical practice: an evaluation of 2-D and 3-D analysis techniques as applied to 30 prostate cancer patients. Int J Radiat Oncol Biol Phys 46:1281–1290
10. Samuelsson A, Mercke C, Johansson K *et al.* (2003) Systematic set-up errors for IMRT in the head and neck region: effect on dose distribution. Radiother Oncol 66:303–311
11. Smitsmans M, Wolthaus J, Artigan X *et al.* (2001) Automatic localization of the prostate for on-line or off-line image-guided radiotherapy. Int J Radiat Oncol Biol Phys 60:623–635
12. Song PY, Washington M, Vaida F *et al.* (1996) A comparison of four patient immobilization devices in the treatment of prostate cancer patients with three dimensional conformal therapy. Int J Radiat Oncol Biol Phys 34:213–219
13. Suzuki M, Nishimura Y, Nakamatsu K *et al.* (2006) Analysis of interfractional set-up errors and intrafractional organ motions during IMRT for head and neck tumors to define an appropriate planning target volume (PTV) – and planning organs at risk volume (PRV) – margins. Radiother Oncol 78:283–290