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Benefits of Six Degrees of Freedom for Optically Driven Patient Set-up Correction in SBRT

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To quantify the advantages of a 6 degrees of freedom (dof) versus the conventional 3- or 4-dof correction modality for stereotactic body radiation therapy (SBRT) treatments. Eighty-five patients were fitted with 5-7 infra-red passive markers for optical localization. Data, acquired during the treatment, were analyzed retrospectively to simulate and evaluate the best approach for correcting patient misalignments. After the implementation of each correction, the new position of the target (tumor's center of mass) was estimated by means of a dedicated stereotactic algorithm. The Euclidean distance between the corrected and the planned location of target point was calculated and compared to the initial mismatching. Initial and after correction median±quartile displacements affecting external control points were 3.74±2.55 mm (initial), 2.45±0.91 mm (3-dof), 2.37±0.95 mm (4-dof), and 2.03±1.47 mm (6-dof). The benefit of a six-parameter adjustment was particularly evident when evaluating the results relative to the target position before and after the re-alignment. In this context, the Euclidean distance between the planned and the current target point turned to 0.82±1.12mm (median±quartile values) after the roto-translation versus the initial displacement of 2.98±2.32mm. No statistical improvements were found after 3- and 4-dof correction (2.73±1.22 mm and 2.60±1.31 mm, respectively). Angular errors were 0.09±0.93° (mean±std). Pitch rotation in abdomen site showed the most relevant deviation, being -0.46±1.27° with a peak value of 5.46°. Translational misalignments were -0.68±2.60 mm (mean±std) with the maximum value of 12 mm along the cranio-caudal direction. We conclude that positioning system platforms featuring 6-dof are preferred for high precision radiation therapy. Data are in line with previous results relative to other sites and represent a relevant record in the framework of SBRT.

Key words: Lung cancer; Abdominal cancer; Set-up errors; Treatment couch; and SBRT.

Introduction

Over the last few years, several efforts have been made towards the development of computerized, image guided procedures for patient set-up and target localization. Related commercial systems have been made available on the market (1-4). Infra-red optical tracking of skin fiducials, surface detection and in-room MV or kV imaging currently represent the most used techniques (5-9). In optical point-based techniques, correction parameters are estimated by matching the real-time detected 3-D position of the external fiducials with respect to their reference position coming from the treatment plan (10-12). Alternatively, the body surface undergoing the irradiation is detected by means of optical body surface

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Abbreviations: dof, Degree of freedom; SBRT, Stereotactic Body Radiation Therapy; LL, Latero-lateral; AP, Antero-posterior; CC, Cranio-caudal; H&N, Head and Neck; IMRT, Intensity Modulated Radiation Therapy; MVCT, Mega Voltage Computed Tomography; KVCT, Kilo Voltage Computed Tomography; CTV, Clinical Target Volume; OAR, Organ at Risk; IR, Infra-red.

sensing technologies, and set-up correction is estimated by registering the current surface dataset with the corresponding CT body surface data (9, 13, 14). When in-room 2D (anterio-posterior, AP, latero-lateral, LL, oblique projections) or 3-D (cone-beam CT) imaging techniques are used, the size of the corrective shifts is obtained by registering bone and soft-tissue anatomy with the treatment plan, with or without the contribution of implanted radiopaque markers (5, 15-17).

Whatever method that is used, most registration algorithms are designed for estimating the 6 translational and rotational parameters, defining the isocentric rigid motion of the treatment couch, which best compensates the detected patient misalignment. However, full 6-dof patient set-up correction has been traditionally hindered by the fact that the majority of commercial radiotherapy couches feature a lower number of degrees of freedom, namely the three linear translations along the orthogonal axes and the rotation about the vertical axis (yaw). In order to overcome this limitation, Hornick *et al*. (18) described an auxiliary system to be mounted on the traditional treatment couch, in order to correct rotational misalignments. The device was computer-controlled and featured pitch and roll adjustments up to ±3° (19). More recently, commercial 6 degrees of freedom 'robotic' treatment tables have been made available. The device proposed by Medical Intelligence (Schwabmüchen, Germany) is based on parallel kinematics (*i.e*., six linear actuators allow the top couch to translate and rotate around its isocenter) and is directly coupled with an optical tracking system, which estimates the corrective parameters (20). BrainLAB A.G. (Heimstetten, Germany), in cooperation with Varian (Palo Alto, CA, USA), advertises the direct interfacing between the ExacTrac® X-ray optical and X-ray imaging localizer with a 6-dof top couch for the real-time and automatic table corrective motion. An alternative concept, proposed by Siemens (Erlangen, Germany) in the frame of their particle beam therapy integrated system, is based on serial kinematics manipulators derived from industrial robots. In addition, despite the related remarkable financial effort, custom-made 6-dof treatment couches/chairs are usually found in the currently operating particle beam therapy centers and are advertised for those under construction (21).

Regardless the specific method used for set-up error detection and corrective motion estimation, the current trend towards 6-dof patient set-up verification and automatic correction is conceptually justified by considering that a 6-dof correction potentially provides more accurate compensation of set-up geometrical deviations than a 3-dof or 4-dof correction. However, the actual improvement in patient-set-up accuracy, as a function of the number of degrees of freedom of the correction deserves an analysis based on quantitative data. Hong *et al*. (22) clinically evaluated the impact of 6-dof systems in patient set-up accuracy on head-neck (H&N) sites, in the framework of intensity modulated radiotherapy (IMRT). By implementing a protocol in which an optical localizer and a set of fiducials placed on a conventional H&N thermoplastic mask were employed for patient set-up, they demonstrated that angular deviations could not be ignored for fully taking advantage of IMRT precision in dose distribution. Similar conclusions, supporting the advantages of a 6-dof robotic couch, were more recently reported by Kaiser *et al*. (23). They measured the intra- and inter-fraction rotational variations on two populations of patients (H&N and prostate treatment) by registering pre-treatment megavoltage computed tomography (MVCT) images with planning kilovoltage CT (KVCT) images. Linthout *et al*. (24) performed an off-line analysis on 13 H&N patients to evaluate the feasibility of 6-dof based image fusion for correcting intra-fraction motion. They found rotations being not negligible with a maximum value of 4.9°.

We report a specific analysis focused on the quality of patient set-up error compensation, as a function of the number of dof currently available for patient set-up adjustment. Similarly to other recent works (9, 25), a rigid body approach was adopted to measure and correct external misalignments of surface surrogates relative to their planned position. Optical tracking techniques were applied for set-up error detection and estimation of corrective motion and an algorithm for stereotactic target position estimation (26) was run before and after correction, in order to investigate the benefit of increasing the dof of the corrective procedure in the quality of the alignment of the target of the irradiation and of all the critical structures, in which the radiation dose needs to be minimized. The study included also the quantification on a large patient population of the required range of motion of treatment table servo-controlled movements for automatic patient position correction procedure, following an initial, computer assisted manual alignment. Results demonstrated the significant improvement of the 6-dof correction, vs. 3- 4-dof ones, especially on target registration and pointed out the danger of patient set-up correction procedures based on a subset of the full dof corrective parameters (typically only the 3 translation), which are usually provided by commercial systems.

Table I
General overview of patients and treatment modalities included in the study.

Primary district	Number of fractions per patient	Number of involved patients	Number of fractions analyzed
	1	20	20
Lung	2	18	36
	3	7	21
	1	20	20
Abdomen	2	12	24
	3	8	25
Total			146

Material and Methods

A group of 85 informed and consenting patients, undergoing hypofractioned stereotactic body radiation therapy (SBRT) in supine position, were involved in the study. Patients were divided into two groups as a function of the irradiated district (Table I). Set-up data were collected at each irradiation session and a total number of 146 fractions were analyzed off-line.

Irradiation Technique

Treatment planning was based on CT scans acquired in free breathing condition. Scans were collected by means of a helical scanner (120 kV and 140 mA, Model: Prospeed, GE Medical Systems, Milwaukee, USA) with 3 mm slice thickness. BrainSCAN™ version 5.3 (BrainLAB A.G., Heimstetten, Germany) was used for the manual contouring of clinical target volume (CTV) and organs at risk (OAR) and for dosimetric evaluations. Safety margins around the CTV were established on a patient-specific case, taking into account prescribed guidelines (27) as well as set-up accuracy and errors and respiratory motion.

SBRT treatments were performed with single or multiple non-coplanar arcs of 6 MV photon beams and the total dose ranged between 8 and 45 Gy delivered in one, two, or three fractions. At every irradiation session, patient set-up was executed with the aid of the real-time feedback coming from an infra-red (IR) optical tracking system installed in the bunker (see *Set-up Data Acquisition*) and AP and LL portal images were acquired systematically for final set-up verification

Set-up Data Acquisition

Before CT scan acquisition for treatment planning, patients were immobilized in a personal whole-body vacuum cushion. A number ranging from 5 to 7 radiopaque and light reflecting markers were accurately placed on the subject's skin, in correspondence of visible natural skin landmarks or of dots marked with semi-permanent ink, within the irradiated body area. The position of the centroid of each marker was identified on CT slices through the same software used to design the treatment plan. According to the settings of this commercial software, the resulting co-ordinates of the fiducials were expressed with respect to an isocentric reference frame with the origin in correspondence of center of the contoured CTV and X, Y, and Z axes coinciding with LL, CC (cranio-caudal), and AP directions, respectively. This CT derived markers configuration was considered as the *reference dataset*.

At each therapy fraction, patients were fitted with the set of markers and were manually positioned on the treatment couch; during the manual alignment procedure, operators were provided with a real-time graphical feedback coming from the optical tracking system (EL.I.TE.™ , BTS Spa, Milano, Italy) installed in the therapy bunker in a two-TV camera configuration; system interface was implemented in order to provide the operators with the size of three-dimensional displacements of the current control point configuration with respect to the reference dataset.

According to Baroni *et al*. (10), the optical tracking system was calibrated by means of 7×7 marker grid, giving rise to a resulting working volume measuring 480×480×160 mm^3, which was centered at the LINAC isocenter and within which marker 3-D localization errors were found to be less than 0.5 mm. During the irradiation, markers co-ordinates were continuously recorded by the optical system for about 15 seconds at 100 Hz sample rate.

Implementation of the Corrective Procedures

Specific software tools developed in Matlab® environment (version 7, The MathWorks, Natick, MA) were used for data investigation. The 3-D coordinates of the marker configuration, at each therapy session, were averaged over the total irradiation time and were compared to the corresponding reference dataset for the assessment of fiducials displacements. A non-linear least-squares *point-based registration* procedure was applied to compute the corrective parameters [Φ Ω Ψ T_{LL}, T_{CC}, T_{AP}] for displacements minimization, being Φ (pitch), Ω (roll), Ψ (yaw), the rotations around LL, CC, and AP axes and T_{LL}, T_{CC}, T_{AP} the corresponding translations. In order to take into account different number of degrees of freedom for the set-up correction, the minimization procedure was applied under the following constraint conditions:

I. Φ, Ω ,Ψ=0 to consider 3-dof (translations only);
II. Φ, Ω=0 to consider 4-dof (translations and Ψ rotation, yaw);
III. no constraints, [Φ Ω Ψ T_{LL}, T_{CC}, T_{AP}], 6-dof.

Each current marker configuration was translated or roto-translated according to the outcomes of the minimization procedure under the specific constraint conditions and residual displacements after correction were used to assess the success of the simulated correction. Known angular shifts were applied to an anthropomorphic phantom to evaluate the accuracy in estimating rotational deviations. The difference between the measured and the desired rotational shift was 0.01±0.15° (mean±std) with a peak value of 0.3°.

Finally, we evaluate the quality of patient set-up when three (only translations) out of six computed corrective parameters (translations and rotations) are implemented.

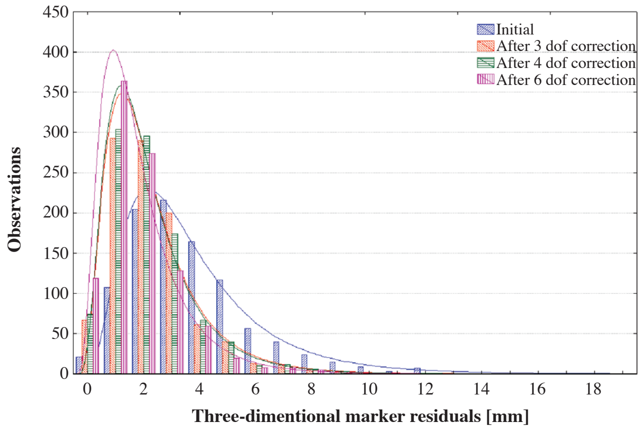

Figure 1: Distribution histograms of external control point initial and residual displacements after 3-dof, 4-dof, and 6-dof correction. To enhance the visibility of results the best fitting curve distribution was super-imposed (log-normal fitting).

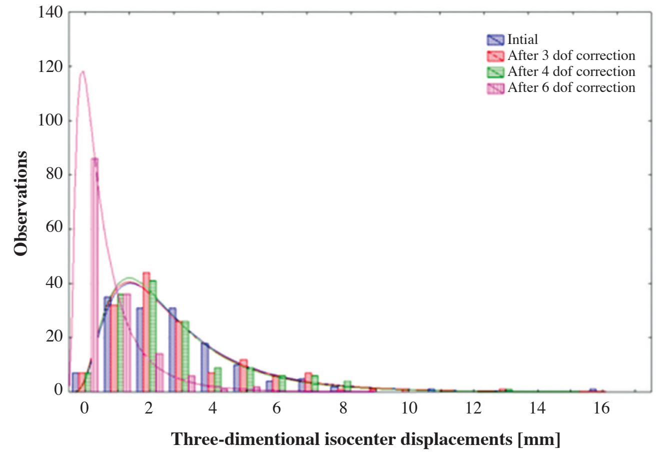

Figure 2: Distribution histograms of estimated target initial and residual displacements after 3-dof, 4-dof, and 6-dof corrections.

Estimation of Target Position

The configurations of control points before and after simulated correction were used for target current position estimation according to the weighted strategy algorithm proposed by Riboldi *et al*. (26). This method is based on the definition of a set of local reference frames from each possible configuration consisting of at least four fiducials (subset, *S*). For each subset, rules for local reference system definition were the following:

- origin in the centroid of the control points subset
- axes (X_s, Y_s, Z_s) aligned with the orthogonal principal directions of the control point distribution (26).

The *S*-related reference local coordinates of the target $[x_i\ y_i\ z_i]_s$ were obtained from the treatment plan, mapped in the absolute (LINAC) reference system $[X_i\ Y_i\ Z_i]_s$ and averaged for final target position estimation $[X_i\ Y_i\ Z_i]$ through the following weighted mean:

$$[X_i\ Y_i\ Z_i] = \frac{\Sigma_{\forall s} w_s \cdot [X_i\ Y_i\ Z_i]_s}{\Sigma_{\forall s} w_s} \qquad [1]$$

where the weight w_s is a function of the number of markers included in the subset S and of the fiducial localization errors [see Riboldi *et al*. (26) for more details].

Statistical Analysis

Non-parametric statistical tests were applied on the fiducials 3-D displacement population measured before the application of the simulated correction procedure. The first aim was to determine, through the Kolmogorov-Smirnov test, if the two patient populations (see Table I) differed significantly. The Kruskall-Wallis test and its post-hoc (Dunn-Sidak) were also run to investigate the existence of statistical differences among the different correction procedures on the external marker configuration. The software Statistica 6.0 (StatSoft Inc, Tulsa OK, USA) and the Statistics Toolbox of Matlab were used to perform the analysis.

Results

When considering the initial, pre-correction 3-D displacements affecting surface fiducials in SBRT treatments, similar values were found in lung and abdominal irradiation (*median*

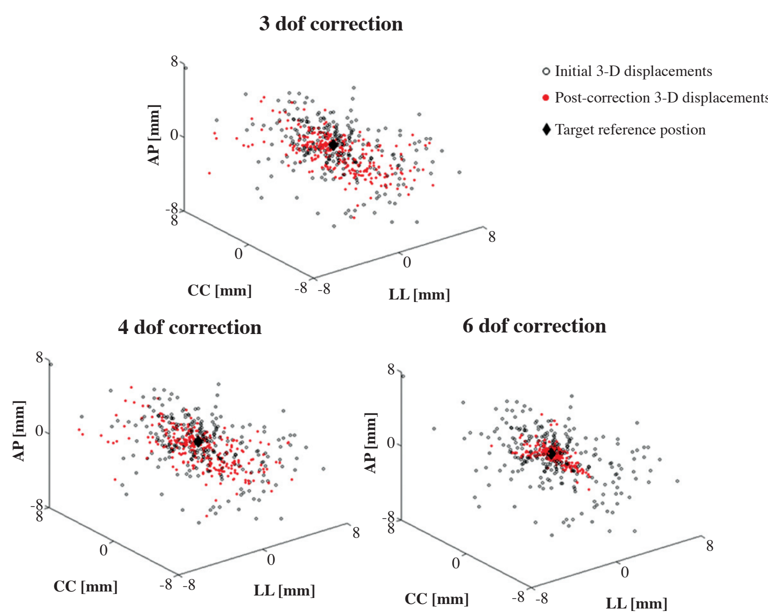

Figure 3: Scatter-plots of estimated target position before (empty circles) and after (solid circles) the simulated application of the three correction modalities. The symbol ♦ represents the planned target position on CT-image data.

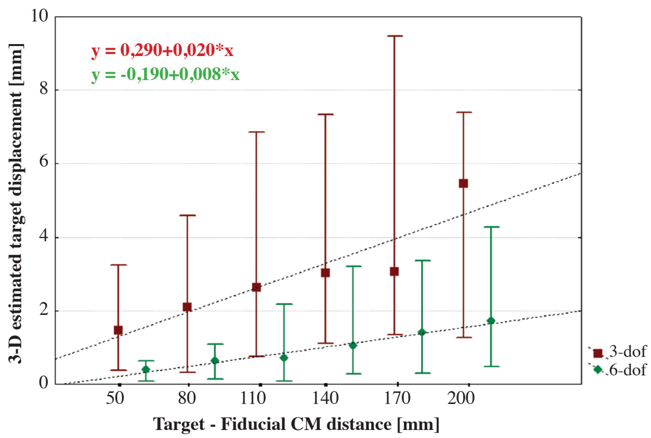

Figure 4: Estimated residual displacements on target (median ± quartile) after 3-dof and 6-dof correction, as a function of the distance between the reference target location and the centroid of marker configuration. Displacements data were grouped as a function of target-fiducials centroid distance with a 30-millimetre clustering. To enhance visibility, 6-dof data are arbitrarily shifted on the x-axis.

± *quartile*: 3.74 ± 2.55 mm and 3.92 ± 2.82 mm) with no statistically significant differences (non parametric between-group t-test equivalent Kolmogorov-Smirnov test, p=0.07). This allowed us to group data in a unique population.

Localization Errors on External Control Points

The effects of the simulated correction procedure in compensating the localization errors affecting surface fiducials are reported in Figure 1. Frequency histograms of pre-correction and residual displacements after 3-dof, 4-dof, and 6-dof correction procedures are reported. The best fitting curve distribution was super-imposed (log-normal fitting).

Pre-correction 3-D displacements (*median* ± *quartile*: 3.74 ± 2.55 mm, *95th percentile*: 8.48 mm) dropped to 2.45 ± 0.91 mm (95th percentile 5.60 mm), 2.37 ± 0.95 mm (95th percentile 5.51 mm), 2.03 ± 1.47 mm (95th percentile 4.87 mm) after the simulated application of 3-dof, 4-dof, and 6-dof correction, respectively. The non-parametric between-group ANOVA alternative, Kruskal-Wallis test, revealed statistically significant differences between initial and 3-dof, 4-dof, and 6-dof corrections (p=0.001). Specific post-hoc comparisons (Dunn-Sidak test) revealed that differences between pre-correction and post-correction displacements were always significant, regardless the number of degrees of freedom featured by the correction procedure, as reported in Table IIa.

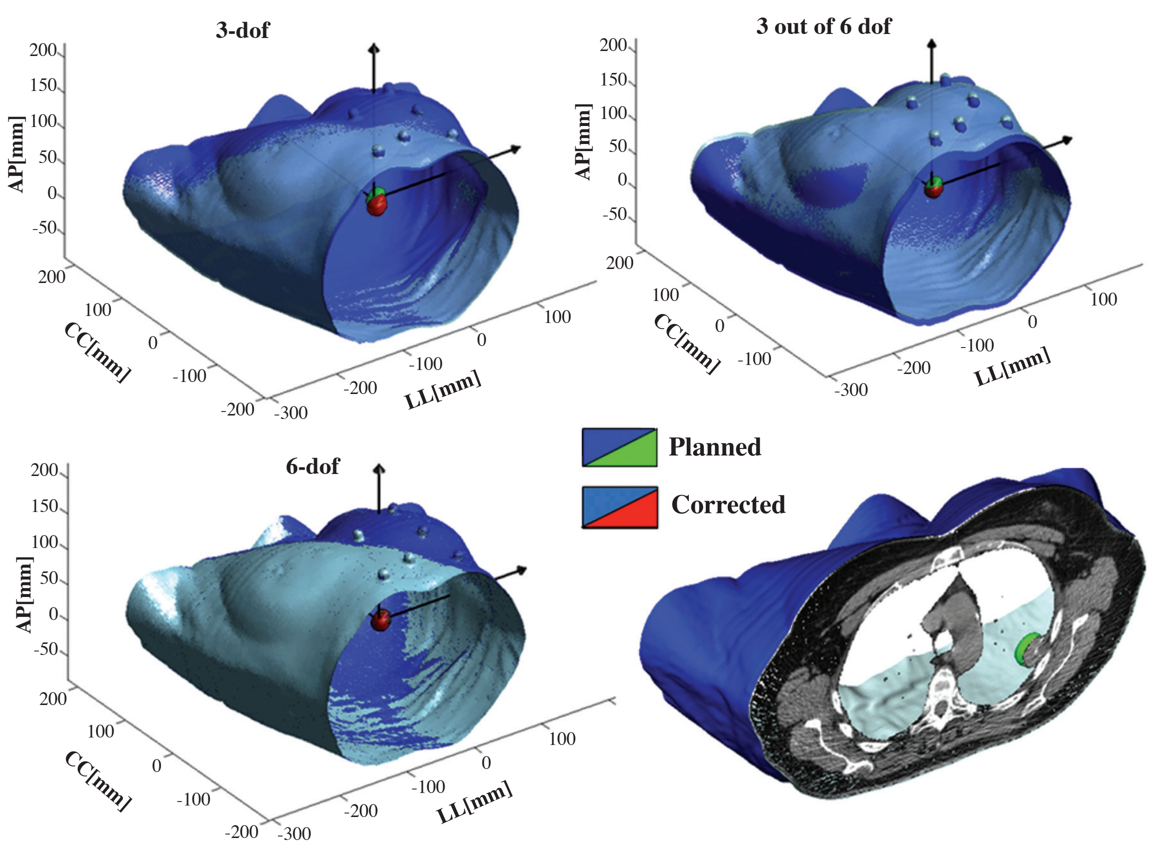

Figure 5: Surface rendering of patient skin with external markers and tumor mass (demonstrative case). 3-D models were obtained from DICOM images imported and segmented through Amira 4.1® software (example is showed in the lower-right panel) and were shifted according corrective parameters. The planned position is represented in blue (patient skin) and in green (tumor). The result of each correction is showed in light blue (patient skin) and red (tumor).

Table II
Results of non-parametric post-hoc comparison Dunn-Sidak test between each corrective procedure relative to external fiducials (Table IIa, top) and target position (Table IIb, bottom). The symbol * indicates statistical difference (p<10-6).

IIa	Initial	3 dof	4 dof	6 dof
Initial		*	*	*
3 dof	*			
4 dof	*			
6 dof	*			

IIb	Initial	3 dof	4 dof	6 dof
Initial				*
3 dof				*
4 dof				*
6 dof	*	*	*	

Localization Errors on Estimated Target Position

In Figure 2, results of the simulated correction procedure in compensating target registration error are reported. Pre-correction 3-D target displacements with respect to reference position (*median* ± *quartile*) were 2.98 ± 2.32 mm (95th percentile 7.16 m); post-correction values (*median* ± *quartile*) were 2.73 ± 1.22 mm (95th percentile 7.39 mm), 2.60 ± 1.31 mm (95th percentile 7.34 mm), 0.82 ± 1.12 mm (95th percentile 3.17 mm), for 3-dof, 4-dof, and 6-dof correction, respectively.

The Kruskal-Wallis test with post hoc comparison (Dunn-Sidak test) highlighted significant difference only between initial and residual displacements after 6-dof correction ($p<10^{-6}$), being statistically not significant (p=0.73) the improvement in estimated target position correction provided by 3-dof and 4-dof corrective procedures (Table IIb).

The higher performance of the 6-dof procedure in target position correction is depicted in Figure 3, which shows the distribution of the estimated target position (initial and corrected), as a function of the correction modality. The reduction of dispersion around the reference position is clearly visible when full 6-dof correction was applied.

We put forward the hypothesis that the higher sensitivity of target position registration to 6-dof based procedures is due to effects of geometrical error propagation (see ***Discussion*** section). This is supported by data reported in Figure 4, which shows the 3-D estimated residual errors on target after 3-dof and 6-dof correction, as a function of the distance (evaluated on CT-based treatment planning and sampled with a 30-mm spacing) between target and the centroid of the surface fiducials. The linear fitting gives evidence to the increasing trend of errors size due to target-fiducials center of mass distance, especially for 3-dof correction. The off-set between the two lines ranges from 0.75 mm (in correspondence of 40 mm distance) to 3 mm (in correspondence of 220 mm distance).

Range of Motion of Treatment Table

The range of variation (mean and standard deviation) and outliers (minimum-maximum) of the six corrective parameters estimated on all the evaluated irradiation sessions are reported in Table III. Rotations were up to ~5° in pitch direction.

Discussion

In this work, we reported the analysis of the effect that the number of degrees of freedom of the correction procedure has on the level of accuracy of automatic patient set-up. With respect to previous works (22, 23, 24), our analysis focused on the linear and rotational errors and included an estimation of dof number influence on the compensation of target registration error.

Experimental dataset consisted of 3-D positional data of external surrogates, captured by means of an infra-red optical localizer with high intrinsic accuracy (< 0.5 mm). The parameters of the patient set-up correction procedure were estimated by a point-based registration algorithm.

Concerning the potential inaccuracies due to remarking errors, the problem was faced on three different levels:

- skilled operators were instructed to reposition the control points by paying specific attention to superimpose the markers pedestal hole (2 mm in diameter) in correspondence of natural or artificial skin dots (about 2-3 mm in size); thus, credibly reducing the size of potential markers mispositioning (in absence of macroscopic errors) to the order of fraction of millimeter;
- as suggested by West *et al*. (27), marker number

Table III
Size of estimated required range of motion for patient set-up 6-dof correction.

		Translations [mm]			Rotations°		
		LL	CC	AP	Pitch	Roll	Yaw
Thorax	Mean	- 0.67	-0.55	0.69	-0.54	0.32	-0.05
	Stand. Dev	1.58	1.78	1.34	0.88	0.65	0.53
	Minimum	-4.49	-5.57	-2.97	-2.90	-1.29	-0.84
	Maximum	2.54	3.20	3.79	1.38	1.81	2.87
Abdomen	Mean	-0.25	-0.82	0.59	-0.38	0.27	-0.16
	Stand. Dev	1.39	3.30	1.74	1.60	0.72	0.48
	Minimum	-4.60	-11.65	-2.67	-5.46	-1.24	-1.30
	Maximum	3.37	6.13	8.56	4.94	1.61	1.17

redundancy was explicitly considered an issue in our experimental protocol, pushing us to use the highest number of markers allowed by the necessary swiftness of the clinical procedures; it is important to stress that the higher the marker number is, the lower is the influence of a badly repositioned marker on the overall estimation of the corrective parameters;

- the numerical estimation of target position before and after any correction was based on the weighted strategy proposed by Riboldi *et al*. (26), which was appositely designed to minimize errors of markers relocation and/or detection.

According to previous works dealing with patient set-up error, corrective point-based registration procedures were designed to estimate a variable number of the parameters of a rigid spatial transformation. A 'rigid body' approach (even if corrected by weight assigned to the external surrogates) was also underneath the method used for stereotactic estimation of target position (26). This strategy was justified by the required compliance with feasible and programmable motion of a 'robotic' treatment couch, and is put forward to represent the first stage of the question of target localization in extra-cranial radiotherapy, particularly when the target is involved in well-known processes of organ motion (due to respiration, tumor shrinkage, etc.). It steered the way in which the experimental data were collected: in thoracic and abdominal treatments for example, the duration of optical data acquisition was established in order to extend on at least two breathing cycles, thus averaging respiration movements in data elaboration. In an approach similar to slow CT, this allowed us to cancel the dynamic effects of respiration and to focus the analysis on the effects of the specific features of the correction procedure on the quality of the result.

Any kind of correction led to a reduction of the displacements on the external control point configuration, with a maximum in the case of six degrees of freedom (46% of reduction in the case of 6-dof versus 34% and 37% for 3- and 4-dof correction, respectively). However, a strong statistical difference between translations and rototranslations was not proved. On the contrary, the importance of a 6-dof adjustment was strongly supported by results relative to the target position before and after the re-alignment. In this case, the Euclidean distance between the planned and the current target location after the rototranslation was below 1 mm (median value), opposed to an initial displacement of 3 mm. No considerable improvements were found after 3- and 4-dof correction. This is due to the fact that point-based registration is designed to minimize the point-to-point distance only on external fiducials. Therefore, translations, that on average can compensate rotational errors on external markers, are not able to adjust the position of a point (target) not included in the registration procedure. In this context, we demonstrated that the error on the target location propagates as a function of the distance of the target itself from the center of mass of marker configuration (or any other surrogate, *i.e*., bone anatomy matching, surface registration, etc.). Referring to Figure 4, when the distance of the lesion from fiducials' CM is around 200 mm, 3-D isocenter displacement is 5.45 ± 4.07 mm and 1.82 ± 1.55 mm for 3-dof and 6-dof, respectively (median ± quartile values). It is important to underline that the method used for target position estimation allows one to reconstruct the position and therefore quantify the residual error after correction of any other point of interest belonging to the target and/or healthy tissue/OAR whose spatial reference coordinates are localized on CT planning images. Also in this case the size of geometrical inaccuracies will be proportional to their distance from fiducial points. The propagation of the error is valid even when the corrective procedure is designed to straightly compensate the misalignment on the target point. In this case, 3-dof are sufficient to align the tumor's CM but they are not able to register the surrounding healthy tissues and OAR volume.

A practical question might be "what is the effect of a 3-dof correction when 6-dof corrective are computed?" This is particularly relevant for those centers that have the use of the most recent automatic softwares for set-up errors detection but do not have adequate hardware (*i.e*., 6-dof treatment table) to perform a full correction. In Table IV and Figure 5, an exemplifying case is reported. The tumor, set in the left lung and with maximum size ~3 cm, was 177 mm dis-

Table IV
Comparison of residual errors [mm] on external control points (Mk) for a typical case.

	Initial				3-dof				6-dof				3 out of 6 dof			
	X	Y	Z	3D	X	Y	Z	3D	X	Y	Z	3D	X	Y	Z	3D
Mk1	3.41	6.67	3.98	8.48	-0.27	-1.27	-2.22	2.57	-0.64	-0.27	1.50	1.65	-3.48	-7.90	-6.95	11.08
Mk2	1.24	3.15	2.83	4.41	1.90	2.26	-1.06	3.13	1.17	1.55	-0.28	1.96	-1.31	-4.37	-5.80	7.38
Mk3	3.10	5.36	4.23	7.50	0.04	0.04	-2.47	2.47	-0.29	0.31	-0.74	0.86	-3.17	-6.59	-7.21	10.27
Mk4	4.01	6.31	0.77	7.51	-0.87	-0.90	0.99	1.60	-0.83	-1.22	-0.12	1.48	-4.08	-7.53	-3.74	9.35
Mk5	4.38	5.95	0.71	7.42	-1.23	-0.55	1.05	1.71	-0.87	-0.47	-0.28	1.03	-4.44	-7.18	-3.69	9.21
Mk6	2.70	4.98	-1.93	5.99	0.44	0.42	3.70	3.75	0.99	-0.28	-0.27	1.06	-2.77	-6.21	-1.04	6.88
Median	3.26	5.66	1.8	7.46	-0.12	-0.26	-0.04	2.52	-0.47	-0.28	-0.28	1.27	-3.33	-6.86	-4.77	9.28

tant from the marker set centroid. When a 3-dof correction was estimated, translations were T_{LL} = 3.14 mm, T_{CC} = 5.40 mm, and T_{AP} = 1.77 mm. In a 6-dof correction, translations were T_{LL} = -0.07 mm, T_{CC} = -1.23 mm, T_{AP} = -2.98 and were coupled with the three rotations being $\Phi = -2.03^{o}$, $\Omega = 1.34^{o}$, and $\Psi = -0.57^{o}$. The example clearly shows that by computing six corrective parameters and by ignoring rotational shifts it could be more dangerous than computing and performing a 3-dof correction. In fact, the sad side of the story is that in terms of target repositioning, the application of a 6-dof correction or of only translational component does not cause any difference, since isocentric correction algorithm are normally implemented. In case feedback to the operator is focused on target repositioning error, the above reported residual misalignments affecting control points (and, therefore, the whole volume between surface surrogates and target) would be totally transparent to the operator. Although the position of target is relatively correct, the configuration of surrounding healthy tissues and OARs changes leading to systematic errors. These are particularly dangerous in terms of dose delivery when dose escalation (like in SBRT) or non-conventional radiation (particle beams) are utilized. As regards this latter, particle range is very dependent on the tissues in its path (29) and systematic set-up errors can affect the cumulative dose in CTV (30). Further future investigation is needed to quantify the dosimetric impact of rotational deviations on target and OARs irradiation.

With regards to servo-mechanism technical requirements, specifications of pitch range of motion (see Table IV) could appear critical in terms of patient immobilization and effects on internal organ displacements. However, it must be underlined that those figures are peak values of collected data and that they agree with other results come out from previous works (22, 23) focused on different sites. The mean±2SD of pitch rotational error for the abdominal district (the worst case) was 0.38 ± 3.20^{o}. We believe that a pitch and roll range of corrective motion within $\pm 5^{o}$ is recommended to avoid problems in patient immobilization and inner organs displacements. A range of motion of ± 20 mm could satisfy the requirement in term of translational movements.

It is important to stress that these values represent corrective parameters for a fully automatic in-room adjustments of patient position by means treatment table servo-controlled movements, after an initial manual patient repositioning procedure based on optical laser alignment.

Conclusions

In conclusion, this work demonstrated the benefits of six degrees freedom correction in the framework of SBRT thus justifying the current commercial trend to equip therapy units with computerized treatment tables featuring full translational and rotational dof. Results of this study significantly support this option, as a way to increase the possibility of a fully automatic in-room adjustment of patient position, without requiring additional manual intervention.

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Conflict of Interest Statement

The authors declare that no conflict of interest exists for this study.

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