



# Surface-guided radiotherapy improves rotational accuracy in gynecological cancer patients

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## ABSTRACT

**Background:** The aim of this study was to determine if rotational uncertainties in gynecological cancer patients can be reduced using surface imaging (SI) compared to aligning three markers on the patient's skin with in-room lasers (marker-laser).

**Materials and methods:** Fifty gynecological cancer patients treated with external-beam radiotherapy were retrospectively analyzed; 25 patients were positioned with marker-laser and 25 patients were positioned with SI. The values of rotational (pitch and roll) deviations of the patient positions between the treatment-planning computed tomography (CT) and online cone-beam computed tomography (CBCT) were collected for both subcohorts and all treatment fractions after performing automatic registration between the two image sets. Statistical analysis of the difference between the two set-up methods was performed using the Mann-Whitney U-test.

**Results:** The median pitch deviation were 1.5° [interquartile range (IQR): 0.6°–2.6°] and 1.1° (IQR: 0.5°–1.9°) for the marker-laser and SI methods, respectively ( $p < 0.01$ ). The median roll deviation was 0.5° (IQR: 0.2°–0.9°), and 0.7° (IQR: 0.3°–1.2°) for the marker-laser and SI methods, respectively ( $p < 0.01$ ). Given the shape of the target, pitch deviations had a greater impact on the uncertainty at the periphery of the target and were considered more relevant.

**Conclusion:** By introducing SI as a set-up method in gynecological cancer patients, higher positioning accuracy could be achieved compared with the marker-laser set-up method. This was demonstrated based on residual deviations rather than deviations corrected for by image-guided radiotherapy (IGRT).

**Key words:** set-up uncertainties; IGRT; SGRT; pitch and roll; cervical cancer

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## Introduction

Traditionally, the set-up method in gynecological cancer patients consists of aligning three external skin markers on the patient's body with in-room lasers (marker-laser). The main drawback of positioning with marker-laser is the difficulty in detecting rotations based on three markers alone, particularly in patients with targets extending far

from the isocenter. In recent years, surface imaging (SI) has emerged as an accurate and effective alternative [1–5]. SI is most commonly used to position breast cancer patients [6–11]. SI has also been explored for other treatment sites, such as the lungs and prostate, with regard to set-up time and translational precision of patient positioning [12–15].

The SI system creates a 3D representation of the patient's surface through light reflected from

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the skin, which is referred to as the live image. The SI-based set-up is performed by positioning the live image (namely, the patient) in accordance with the reference image typically derived from the body contours generated from treatment-planning computed tomography (CT). SI potentially offers better control over rotational set-up errors given that agreement with the reference position is assessed over an extended area of the skin. The functionality, hardware, and limitations of the SI system have been described previously [9, 16, 17].

In image-guided radiotherapy (IGRT), kV or MV imaging is used to verify the position of relevant internal landmarks before starting treatment, regardless of which initial positioning method is used [18–21]. The set-up image is registered to the reference CT, and treatment couch shifts are applied accordingly to account for remaining deviations. The use of 4-degrees-of-freedom registration allows for corrections in the translational directions and in rotation around the vertical axis (yaw), whereas the use of 6-degrees-of-freedom couch and registration additionally considers rotations around the lateral and longitudinal axes (pitch and roll, respectively). There is evidence to suggest that rotational corrections would improve prostate cancer treatments, especially with regard to errors in pitch [22]. However, conventional 4-degrees-of-freedom registration is expected to remain the standard in the studied patient group [23].

When corrections are applied only to the translational directions and yaw, deviations in pitch and roll remain during the treatment fraction, and small rotations around the isocenter can lead to large errors at the periphery of the target. In some cases, such deviations require repositioning followed by additional set-up images before the treatment fraction can be delivered. However, initial set-up deviations in pitch and roll are often not corrected for, and thus affect the precision and/or reproducibility of the treatment. Rotational deviations from the planned treatment position can have a particularly severe impact on the accuracy in gynecological cancer patients when para-aortic (PA) lymph nodes are included in the external-beam radiotherapy target [24], which then extends from the pelvic region to the upper abdomen [25, 26].

Several studies have shown that SI results in more accurate initial patient positioning, measured by

the corrections applied using IGRT, as compared with marker-laser [5, 9, 15]; and Gonzalez-Sanchis et al. [10] showed that SI decreases the corrections needed for breast cancer patients, considering both translational and rotational deviations. However, while investigations using deformable phantoms indicate that the SI system effectively handles rotational deviations for superficial targets, the benefit seems smaller for targets at a certain depth [4, 8, 27]; more specifically, the location of the isocenter in the phantom has been shown to have a significant impact on SI registration accuracy.

In our study, we hypothesized that a more accurate initial patient positioning can be achieved using SI compared to marker-laser, reducing residual pitch and roll set-up uncertainties in gynecological cancer patients. Rather than evaluating IGRT-related couch shifts, we assessed the more clinically meaningful pitch and roll deviations between each treatment fraction CBCT and reference CT, based on retrospective image registration.

## Materials and methods

### Patient cohort and set-up methods

Fifty cervical cancer patients (with or without PA lymph nodes), treated with external-beam radiotherapy using a Varian Truebeam linear accelerator (Varian Medical Systems, USA) at Karolinska University Hospital, were retrospectively included in this study. According to local protocols, the large target including the pelvic lymph nodes is treated to 45 Gy in 25 fractions, with a 9-mm planning target volume (PTV) margin. The cervix clinical target volume (CTV) is treated to 50 Gy (one patient did not receive a boost to the cervix CTV), using simultaneous integrated boost technique, and is always included within the lower dose level. A 0-mm PTV margin is applied to limit the risk of side effects. Any lymph node targets receiving an additional boost are applied a 6-mm PTV margin.

The cohort consisted of two subgroups of 25 patients each, consecutively treated. The first subgroup was positioned with marker-laser in 2019, while the other subgroup, treated in 2021, was positioned with the SI system Catalyst HD (C-Rad, Sweden). The only difference in the treatment protocol between the two patient subgroups was the initial set-up method. All patients were positioned with

**Table 1.** Cone-beam computed tomography (CBCT) scanning protocol used for all included patients

kV-CBCT acquisition mode	Pelvis
X-ray voltage [kV]	125
X-ray current [mA]	60
X-ray millisecond [ms]	18
Scan fan type	Half fan
Bow-tie filter	Half
Gantry rotation [°]	360
Image length [cm]	17.5

their hands on their chests, and their legs and feet were immobilized using ProSTEP (Oncology Imaging Systems, UK). All patients were treated in 25 fractions, and positioned with either marker-laser or SI, but never a combination of the two set-up methods. Before each treatment delivery, a CBCT image was acquired following the initial patient set-up to fine-tune the patient's position with regard to translation and yaw (that is, no pitch or roll corrections were applied). For technical details of the CBCT acquisition see Table 1. Repositioning of the patient was performed if the residual deviations exceeded the PTV margins. In addition, if the suggested couch shift exceeded 5 cm in any direction and/or 5° in yaw, the patient was repositioned. New CBCT image(s) were always acquired after repositioning to verify the final set-up before treatment was delivered.

### Analysis of uncorrected set-up errors

To quantify the residual rotational errors when using the different patient positioning methods, retrospective registration was performed between the relevant CBCT images (i.e. the image acquired immediately before treatment) and the corresponding treatment-planning CT images. An automatic tool for registration in the Offline Review application in Aria 16 (Varian Medical Systems, USA) was used, allowing full translational and rotational adjustments, unlike the procedure for CBCT-based patient positioning, where pitch and roll were ignored. Default parameter settings with an intensity range of -290 HU to 294 HU were used, without manual corrections. The automatic registration was limited to the area around the symphysis and sacrum for all patients irrespectively of the length of the CTV, in order to be able to apply the same procedure for all patients, even where

the CTV extended outside the field of view. At treatment, the online registration was performed in the same way, although extended CBCT (to double the image length) are acquired for the first five fractions for PA targets. These extended images are then evaluated to confirm that the cranial part of the CTV remains within the PTV despite the focus on the symphysis and sacrum of the image registration. Then, no further extended CBCTs are acquired.

The resulting pitch and roll deviations between the planned and treatment positions were recorded for patients positioned using each set-up. A total of 625 treatment fractions were analyzed for each procedure. The number of acquired CBCT images for each fraction was recorded to indicate the need for repositioning and/or re-imaging after the first CBCT verification. Furthermore, for each patient, the spatial extent of the CTV was measured in the cranial-caudal (CC), anterior-posterior (AP), and lateral-medial (LM) directions from the isocenter to the most distant point of the target to estimate the potential impact of pitch and roll errors on target misalignment. Propagation of the rotational error to translational errors at the periphery of the target was performed by assuming rigid patient rotation. The error propagation was estimated separately for patients with and without PA lymph nodes included in the CTV.

The values of the residual pitch and roll for both positioning methods were tested for normality using the Shapiro-Wilk test. None of the variables were normally distributed. Thus, the Mann-Whitney U-test was used to test the hypothesis that the two set-up methods result in equal set-up accuracy for pitch and roll. Cross-table comparisons were performed with Fisher's one-sided exact test. Statistical significance was set at  $p < 0.05$ .

## Results

Target and imaging statistics are presented in Table 2. There was no difference in the fraction of patients with PA lymph nodes in the two subgroups and also the CTV length did not differ between the groups. The CTV volume, however, was greater in the marker-laser group. The values obtained for residual pitch and roll for the two positioning methods are shown in Fig. 1. A visual comparison between the range of pitch values for mark-

**Table 2.** Target and patient imaging characteristics, median (inter-quartile range)

	Total	Marker-laser	SI	p value	Without PA	With PA	p-value
Patients with PA	16 (32%)	9 (36%)	7 (28%)	0.38	–	–	
Patients with re-imaging	27 (54%)	17 (68%)	10 (40%)	0.04	14 (41%)	13 (81%)	< 0.01
CTV Volume [cm <sup>3</sup> ]	1021 (872–1178)	1101 (979–1228)	917 (794–1060)	0.03	978 (828–1060)	1150 (1041–1272)	0.02
CTV length [cm]	18.3 (17.1–25.1)	18.7 (17.1–25.7)	18.2 (16.9–22.2)	0.87	17.4 (16.3–18.4)	28.4 (25.4–31.2)	< 0.01

CTV — clinical target volume; SI — surface imaging; PA — para-aortic lymph nodes

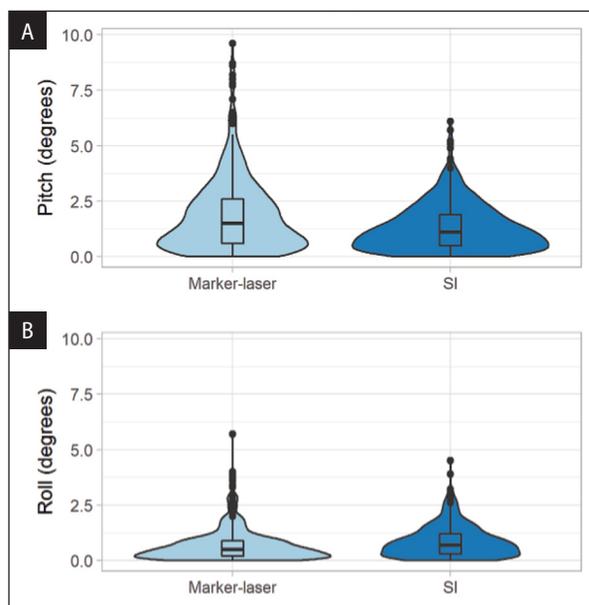
er-laser (Fig. 1A) and SI (Fig. 1B) indicates that the patients positioned with SI were somewhat less rotated than those positioned with marker-laser. This is confirmed by the standard deviation which was 1.6° and 2.3° for SI and marker-laser, respectively. In terms of roll, for which the deviation was smaller for both techniques ( $p < 0.01$ ), a corresponding improvement with SI-based positioning was not apparent in the visual comparison (Fig. 1C) and (Fig. 1D). Here, the standard deviation was 1.1° and 1.0° for SI and marker-laser, respectively. Fig. 1 also indicates that the overall rotational deviation is greater than the patient-level deviation, similar to Graf et al. [22]. This is confirmed by comparing the standard deviations above with the mean of each patient's standard deviation, which was 1.2° and 1.5° in pitch, for SI and marker-laser, and 0.8°

and 0.6° in roll, for SI and marker-laser, respectively.

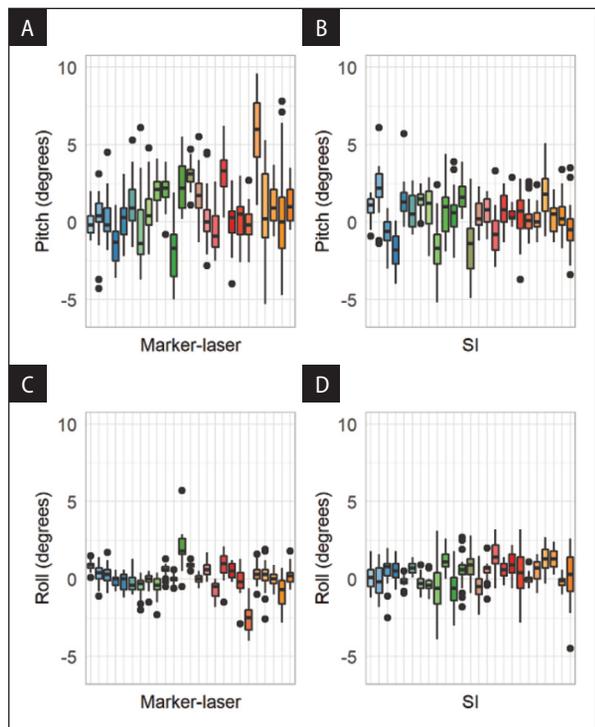
Although rotational deviations repeatedly occurred in the same direction in some patients, the population means were close to zero. Since set-up uncertainties are usually managed at the population level using symmetric PTV margins, the absolute values of the two techniques were compared. The median pitch deviation was 1.5° [inter-quartile range (IQR): 0.6°–2.6°] for the marker-laser method, while for the SI-based method, the median pitch deviation was 1.1° (IQR: 0.5°–1.9°) (Fig. 2A); the difference was statistically significant ( $p < 0.01$ ). In contrast, the median roll deviation was smaller for the marker-laser method than for the SI-based method ( $p < 0.01$ ): 0.5° (IQR: 0.2°–0.9°), and 0.7° (IQR: 0.3°–1.2°), respectively (Fig. 2B).

Using the marker-laser method, 17 patients were reimaged at least once, resulting in 50 additional CBCT images in this subgroup. In contrast, with the SI-based method, only 10 patients required re-imaging to confirm an adequate set-up before treatment delivery, resulting in 32 additional CBCT images. Reimaging was significantly decreased with SI (Tab. 2).

The CTV lengths were similar for both subgroups, but differed between patients with and without PA lymph nodes included in the CTV (Tab. 2). More specifically, we focused on the extent from the isocenter, in CC, AP and LM, respectively, since these are the relevant measures for rotational uncertainty. In the total cohort, the median extents for CC were 15.1 cm and 9.4 cm, 7.2 cm and 7.3 cm for AP, and 6.8 cm and 7.2 cm for LM, for patients with and without PA lymph nodes, respectively. Assuming that the rotational misalignment is constant from the isocenter to the most distant point



**Figure 2.** Violin plot of absolute pitch (A) and roll (B) deviations for each set-up method



**Figure 1.** Distributions of pitch- and roll deviations over the course of treatment, presented for each patient in the two positioning-method cohorts. **A.** Pitch deviations for marker-laser; **B.** Pitch deviations for surface imaging (SI); **C.** Roll deviations for marker-laser; **D.** Roll deviations for SI

of the CTV, and given the greater CC extents (especially for those with PA lymph nodes), the uncertainty at the CTV contour was affected more by the median *pitch* deviation than by the median *roll* deviation (see propagation calculations in Tab. 3).

### Discussion

Unlike previous studies, the current analysis evaluated the set-up-related deviations that the IGRT protocol did not correct for, rather than the corrections applied with IGRT after the initial set-up. These residual deviations persisted

during the delivery of the treatment fraction, with potential clinical impact. For prostate cancer patients, pitch errors have been shown to be greater than roll and yaw errors [22, 28]. Similarly, our analysis of gynecological cancer patients showed greater pitch deviations compared to roll deviations. Moreover, the dosimetric impact of rotational errors has been found to be dominated by pitch for prostate treatments, both in terms of target coverage [24, 28, 29] and bowel dose [28]. In contrast, Katayama et al. found no significant impact of roll errors on dose volume histogram (DVH) parameters [28].

The current study compared the rotational uncertainties associated with two different initial set-up methods. The results showed smaller pitch deviations for patients positioned with SI compared with those positioned with marker-laser, in line with the hypothesis. In contrast, roll deviations were larger with the SI-based method, although smaller in magnitude than the pitch deviations. Since rotational errors predominantly affect the dose at the periphery of the target [24, 30], the clinical impact of pitch and roll errors of equal magnitude is expected to differ. The clinical impact of deviations in pitch and roll was thus estimated by considering the maximum extent of the CTV from the isocenter, where the pitch deviation had an impact on the CC and AP directions, and the roll had an impact on the AP and LM directions. The larger extent of the target in the CC direction emphasizes the importance of pitch over roll accuracy. On average, the SI-based method offers a reduction of pitch-related misalignment of 1.0 mm at the cost of only 0.3 mm greater roll-related deviation. Further, when considering the consequence of larger deviations, such as a rotational misalignment corresponding to the upper quartile value in our cohort, the pitch-related deviation is reduced by 1.8 mm for the median length of the CTV including PA lymph

**Table 3.** Spatial deviation at the most distant point on the clinical target volume (CTV) contour from the isocenter, resulting from the median pitch- and roll deviations in each set-up method subgroup, as represented by the median extent of the CTV for patients with and without para-aortic (PA) lymph nodes, respectively

Median CTV extent	Pitch		Roll	
	With PA	Without PA	With PA	Without PA
Marker-laser method [mm]	3.9	2.5	0.6	0.6
SI-based method [mm]	2.9	1.8	0.9	0.9

SI — surface imaging

nodes (from 6.8 mm with marker-laser to 5.0 mm with SI). Meanwhile, roll-related deviation, with the same assumptions, only increased by 0.4 mm (from 1.1 mm with marker-laser to 1.5 mm with SI). Thus, SI results in an overall lower rotational uncertainty than marker-laser and offers the potential to reduce the PTV margin.

However, this error propagation likely overestimates the resulting translational uncertainties for both techniques, considering the assumption of rigid patient rotations. For example, a rotation in pitch is naturally followed by flexion of the vertebrae because the thorax of the patient must remain on the treatment couch, resulting in a smaller error than that implied by the rigid patient rotation scenario. Thus, the estimation of the resulting reduction in translational uncertainties should not be relied upon in absolute terms but rather interpreted in relative terms for the two techniques. Still, the conclusion regarding the greater importance of pitch based on this error propagation is well supported by simulations and dose accumulation analyses, as described above [24, 28, 29].

A limitation of our study is a potential bias between the subgroups with regard to age, BMI and, as seen in Table 2, CTV volume. Patient characteristics were not available in this data set. However, we expect any such bias to be limited given the consecutive recruitment of patients and CTV length is of greater relevance than CTV volume to rotational uncertainties. Many gynecological cancer patients experience abdominal swelling during radiotherapy because of concomitant chemotherapy. To limit the effect of swelling on positioning accuracy, mainly in the vertical direction, alignment of the live and reference images of the SI was prioritized in the upper abdomen and lower pelvic regions, while accepting a greater mismatch on the belly. Our smaller residual pitch deviations with the SI-based set-up indicate that this method reduces the effect of abdominal swelling on uncertainty.

In the current study, rotational uncertainties were evaluated predominantly in relation to the bony anatomy, since the image quality was not sufficient to allow image registration based on the position of the soft tissue target. Thus, only the set-up-related uncertainty could be studied, ignoring any variations in the internal soft tissue anatomy in relation to the bony anatomy, which are predominantly

caused by variations in bladder and rectal filling. However, this is mitigated by asking the patients to empty their bladder and recta when the treatment planning scan is acquired and prior to each treatment session.

In this study, absolute deviation values were analyzed because the magnitude, and not the direction, of rotational deviations is relevant for the (symmetric) PTV margin, which relates to uncertainties in the population rather than in the individual. The impact of rotational deviations on target dose coverage was beyond the scope of this analysis. However, clinical consequences of residual set-up errors, resulting from the delivered dose deviating from the planned dose, have been demonstrated in previous studies [31, 32].

The higher target-positioning accuracy resulting from SI in the current study confirms the general conclusions of previous studies that focused on translational deviations [5, 9, 15] for several treatment sites. We showed that, especially in patients undergoing PA lymph node treatments, for whom small rotational deviations at the isocenter can have a large impact on positioning accuracy at the periphery of the target, SI offers advantages over the marker-laser method. Previous phantom studies were unable to predict this advantage for nonsuperficial targets [4, 8, 27].

The less frequent use of extra imaging without compromising accurate patient positioning is potentially associated with faster treatment, improved patient comfort, and a lower IGRT patient dose. The better initial patient positioning with SI showed a reduced need for repeat CBCT imaging, which is in line with other studies, suggesting that IGRT can be replaced by surface-guided radiotherapy in some cases [9, 10].

## Conclusion

For gynecological cancer patients, rotational uncertainties were reduced during radiotherapy when SI is used as the initial set-up method, compared to the marker-laser set-up method. The main advantage of positioning with SI instead of marker-laser is the smaller pitch deviation, which may result in important improvements in accuracy in the periphery of the target, especially when the inclusion of PA lymph nodes results in an extended target.

### Ethical statement

This study was approved by the Swedish Ethical Review Authority. This was a retrospective study. The requirement for patient consent was waived by the ethics committee. This publication was prepared without any external source of funding. The authors declare that they have no competing financial interests or personal relationships that could have influenced the work reported in this paper.

### Conflicts of interest

Authors declare no conflict of interests.

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