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Original paper

Cone-beam CT-based inter-fraction localization errors for tumors in the pelvic region

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ABSTRACT

Purpose: To evaluate inter-fraction tumor localization errors (TE) in the RapidArc® treatment of pelvic cancers based on CBCT. Appropriate CTV-to PTV margins in a non-IGRT scenario have been proposed.

Methods: Data of 928 patients with prostate, gynecological, and rectum/anal canal cancers were retrospectively analyzed to determine systematic and random localization errors. Two protocols were used: daily online IGRT (d-IGRT) and weekly IGRT. The latter consisted in acquiring a CBCT for the first 3 fractions and subsequently once a week. TE for patients who underwent d-IGRT protocol were calculated using either all CBCTs or the first 3.

Results: The systematic (and random) TE in the AP, LL, and SI direction were: for prostate bed 2.7(3.2), 2.3(2.8) and 1.9(2.2) mm; for prostate 4.2(3.1), 2.9(2.8) and 2.3(2.2) mm; for gynecological 3.0(3.6), 2.4(2.7) and 2.3(2.5) mm; for rectum 2.8(2.8), 2.4(2.8) and 2.3(2.5) mm; for anal canal 3.1(3.3), 2.1(2.5) and 2.2(2.7) mm. CTV-to-PTV margins determined from all CBCTs were 14 mm in the AP, 10 mm in the LL and 9–9.5 mm in the SI directions for the prostate and the gynecological groups and 9.5–10.5 mm in AP, 9 mm in LL and 8–10 mm in the SI direction for the prostate bed and the rectum/anal canal groups. If assessed on the basis of the first 3 CBCTs, the calculated CTV-to-PTV margins were slightly larger.

Conclusions: without IGRT, large CTV-to-PTV margins up to 15 mm are required to account for inter-fraction tumor localization errors. Daily IGRT should be used for all hypo-fractionated treatments to reduce margins and avoid increased toxicity to critical organs.

1. Introduction

Image-guided radiotherapy (IGRT) has become the standard of care for intensity modulated radiotherapy (IMRT) for many tumors including prostate, gynecological and rectum/anal canal. The benefits of IGRT have been shown in retrospective patient series [1–4]. A clinically meaningful reduction in dose to organs at risk and in acute-toxicity levels was observed in patients treated with IGRT and IMRT for prostate cancer, as a result of improved techniques and tighter margins, which improve biochemical control [2] and reduce urinary and gastrointestinal toxicity [5]. There are various techniques for IGRT in the pelvic region such as the use of planar kV images to visualize implanted fiducial markers or surgical clips, cone-beam computed tomography (CBCT), ultrasound, and electromagnetic-based tracking [6–13]. CBCT makes possible the non-invasive verification of treatment delivery via on-board volumetric imaging and matching. Soft tissue matching using CBCT has been found to be comparable to fiducial matching with MV or kV imaging [11,14,15] in terms of correlation of shifts. Several authors investigated the inter-fraction localization data for pelvic cancers with soft-tissue based IGRT modalities. Most of them reported data for prostate cancer treated either with post-prostatectomy radiotherapy (RT) [16–18] or RT alone [11,18–23], while few data are available for

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gynecological [18,24–26] and rectal/anal canal cancers [18,27]. However, the optimal use of CBCT verification for different tumor sites is still being clarified and there is a wide variety of imaging protocols [11,26].

The aim of this study was to evaluate the inter-fraction tumor localization error in the pelvic region by means of a kilovoltage CBCT (kV-CBCT) in a large series of patients. It also proposed appropriate population-based clinical target volume (CTV) to planning target volume (PTV) margins in non-IGRT scenarios. The efficacy of 2 IGRT protocols (daily IGRT and weekly IGRT) was evaluated.

2. Materials and methods

2.1. Study protocol

The inclusion criteria for this retrospective study were as follows: 1) patients treated between January 2010 and March 2015 with RapidArc® on a Trilogy linac (Varian Medical System, Palo Alto, US) for prostate, gynecological, rectum/anal canal cancers; 2) informed consent for the use of anonymous data for research and educational aims; 3) availability of localization data of IGRT. Inter-fraction tumor localization error was assessed by means of CBCT images of the treatment volume after the initial setup to skin tattoos. The study was part of the research regarding clinical and dosimetric aspects of image-guided radiotherapy for prostate, gynecological and gastrointestinal cancers, notified to the Ethical Committee of our Institute (N79, N86/11, N87/11, respectively).

The data of 928 patients fulfilling the inclusion criteria were retrospectively analyzed. Table 1 shows the number of patients and CBCTs for each image guidance protocol.

2.2. CT simulation and treatment planning

All patients were instructed to empty the rectum and bladder and drink 500 ml of water about 1 h before the CT acquisition and the treatment sessions to achieve greater sparing of the small bowel and protection of the bladder. An anal marker or wire was placed around the gross tumor in the case of anal cancer and around the anus for rectal cancer, prior to simulation. A sterile PVC flexible rectal tube-24F with a radiopaque tip (Rusch, TeleflexMedical srl, Turin, Italy) (vaginal probe) was inserted into the vagina of patients with gynecological cancer and receiving RT alone, to facilitate the contouring of the gross tumor volume (GTV).

The planning CT scan (CT_{plan}) (High Speed, Ge Healthcare, UK) was performed with contiguous 2.5 mm slices. The patients were supine with a leg immobilization system (CombifixTH – CIVCO Medical Solutions, US) with both arms raised above the head (in the case of paraaortic lymph nodes irradiation) or positioned on the chest. In a few cases, rectum/anal canal patients were positioned prone using a carbon fiber Belly board (CIVCO Medical Solutions, US). Definitive skin tattoos were created at the time of CT virtual simulation. For patients who underwent radical RT for gynecological cancers, the tumor volume was delineated using information from magnetic resonance imaging (MRI), registered to the CT_{plan}. MRI was acquired on the same day as the CT_{plan} or within the same week.

Treatment plans, performed on Eclipse (Varian Medical System, Palo Alto, US), consisted of one or two 6 MV full arcs. Prescription doses, fractionation schemes and margins between the CTV and the PTV are reported in Table 2. In the case of re-irradiation or the presence of comorbidities, personalized doses and fractionation schemes were adopted.

Table 1
Number of patients and CBCTs per treatment site and IGRT protocol.

Treatment site	N° of pts	Total CBCTs	w-IGRT protocol		d-IGRT protocol	
			N° of pts	N°of CBCTs/ pt mean (range)	N° of pts	N°of CBCTs/ pt mean (range)
Prostate bed	334	4039	293	9.8 (7–19)	41	28.6 (19–33)
Prostate	190	4195	39	9.0 (5–13)	151	25.5 (5–38)
Gynecological	231	3164	175	9.9 (3–17)	56	25.0 (5–31)
Rectum	139	1382	113	9.4 (3–17)	26	12.4 (5–26)
Anal canal	34	444	30	11.4 (7–19)	4	25.3 (24–26)
Total	928	13,224	650		278	

Abbreviations: CBCT = cone-beam computed tomography; IGRT = image guided radiotherapy; d-IGRT = daily IGRT; w-IGRT = weekly IGRT; pts = patients.

2.3. IGRT protocols

Patients were first positioned by aligning the lasers with the skin tattoo and then a CBCT was acquired. Usually, a technique of 120 kVp and 200 mAs per scan was used, but imaging parameters were changed according to the patient's anatomy to optimize the image quality. The imaging acquisition protocol consisted of a full gantry rotation of 360° with half-fan bowtie filter and 660 frames per rotation. The thickness of the reconstructed CBCT slices was 2.5 mm.

For a few patients (7%) treated with RT alone for cervix cancer, the vaginal probe was inserted before the CBCT acquisition, to help the radiation oncologist localize the GTV and removed after treatment (see Fig. 1 patient B). Since the position of the vaginal probe was not reproducible from day to day, it just helped localize the tumor but anatomical structures alone were then used for image co-registration.

The CBCT was matched with the CT_{plan} by means of a rigid co-registration using automatic bone matching to determine the positioning error. The tumor localization error (TE) was determined by a manual adjustment of the rigid CBCT- CT_{plan} co-registration to match the tumor.

The radiation oncologist or trained radiographer used CTV and PTV, hip joints, sacral and lumbar vertebrae to correctly localize the tumor localization inside the pelvis. In the case of prostate bed irradiation, the position of the anterior rectal wall was verified. The radiographer checked visually that the fullness of bladder and rectum on CBCT was consistent with the CT_{plan}. When necessary, in agreement with the radiation oncologist, patients were asked to repeat the bladder-filling/rectum emptying procedure and a new CBCT was acquired, as any variation can modify the tumor position or cause the small bowel to fall into the PTV.

In patients who had undergone surgery, surgical clips were often used to help localizing the tumor bed. However anatomical structures were always used as well, because surgical clips are not stable over time, so cannot be considered as a surrogate of the tumor bed.

Two IGRT protocols were used: 1) daily online IGRT (d-IGRT); 2) weekly IGRT (w-IGRT), consisting of the acquisition of a CBCT for the first 3 fractions and subsequently once a week. Online corrections were applied prior to treatment for every fraction for which CBCT was carried out. Following the first 3 fractions, the systematic error was calculated and a correction applied for errors larger or equal to 4 mm. If, during the following 2 weeks, the error was > 4 mm in the same direction, 3 more checks were performed and correction for the systematic error applied again. Daily-IGRT was applied to hypo-fractionated treatments of prostate (26 fractions), radical RT treatment of cervical cancer (25–28 fractions), re-irradiations or in the presence of comorbidity. A total of 21 patients were treated with short-course RT for re-irradiation (5–10 fractions) (5 cervix and 16 rectal cancers). Weekly-IGRT was applied in all other cases.

For prostate bed treatments, the first IGRT procedure was performed by a radiation oncologist and subsequently ones by a trained radiographer, under doctor supervision in the case of a deviation greater than 4 mm. For all other tumor sites, the IGRT procedure was performed by a radiation oncologist expert in the specific pathology.

Total treatment time, including set-up, CBCT acquisition, image analysis and automatic patient repositioning, was on average 10 min.