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Ultrasound versus Cone-beam CT image-guided radiotherapy for prostate and post-prostatectomy pretreatment localization

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ABSTRACT

Purpose: To evaluate the accuracy of an intra-modality trans-abdominal ultrasound (TA-US) device against soft-tissue based Cone-Beam Computed tomography (CBCT) registration for prostate and post-prostatectomy pre-treatment positioning.
Methods: The differences between CBCT and US shifts were calculated on 25 prostate cancer patients (cohort A) and 11 post-prostatectomy patients (cohort B), resulting in 284 and 106 paired shifts for cohorts A and B, respectively. As a second step, a corrective method was applied to the US registration results to decrease the systematic shifts observed between TA-US and CBCT results. This method consisted of subtracting the mean difference obtained between US and CBCT registration results during the first 3 sessions from the US registration results of the subsequent sessions. Inter-operator registration variability (IOV) was also investigated for both modalities.
Results: After initial review, about 20% of the US images were excluded because of insufficient quality. The average differences between US and CBCT were: 2.8 ± 4.1 mm, –0.9 ± 4.2 mm, 0.4 ± 3.4 mm for cohort A and 1.3 ± 5.0 mm, –2.3 ± 4.6 mm, 0.5 ± 2.9 mm for cohort B, in the anterior-posterior (AP), superior-inferior (SI) and lateral (LR) directions, respectively. After applying the corrective method, only the differences in the AP direction remained significant ($p < 0.05$). The IOV values were between 0.6–2.0 mm and 2.1–3.5 mm for the CBCT and TA-US modalities, respectively.
Conclusions: Based on the obtained results and on the image quality, the TA-US imaging modality is not safely interchangeable with CBCT for pre-treatment repositioning. Treatment margins adaptation based on the correction of the systematic shifts should be considered.

Introduction

For accurate dose delivery in prostate cancer radiotherapy, a robust image-guided radiotherapy (IGRT) strategy based on soft tissue registration is required since some studies have shown that movements of prostate and bones are not correlated [1]. Indeed it has been shown that patient positioning with soft-tissue CBCT significantly reduced acute genitourinary toxicity compared to positioning with EPID without fiducial markers (FM) [2]. Two main categories of soft tissue IGRT modalities can be defined. The first category uses implanted surrogates for target localization, such as FM or implanted electromagnetic transponders [3,4]. Even though these techniques are relevant for prostate positioning, the associated risks with the surgical implantation of surrogates cannot be neglected, as well as the possibility for them to migrate during the treatment course [5]. Furthermore, the use of FM requires an X-ray imaging modality, such as megavolt electronic portal imaging (MV-EPI) or kilovolt projection imaging. The second category encompasses imaging modalities enabling a 3D acquisition such as CT-on-rails, cone beam computed tomography (CBCT), cine magnetic resonance imaging and ultrasound (US) imaging [6–13]. Among these modalities, CBCT is the most used. It allows a 3D visualization of both target volume

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and organs at risk, but involves a non-negligible additional dose to the patient [14]. Therefore, US imaging appears to be an interesting alternative since it is non-invasive and non-irradiating and thus does not imply any associated risk for the patient.

Three transabdominal US systems (TA-US) were commercialized over the past 15 years. The BAT® [12] (Nomos, Pittsburg, USA) and SonArray® [13] (Varian, Palo Alto, USA) devices are based on an inter-modality registration that consists of projecting the CT contours on the US treatment image to determine target misalignments. In contrast, the Clarity device (Elekta, Stockholm, Sweden) is an intra-modality system that compares a daily TA-US image acquired at the beginning of the treatment session to a reference TA-US image acquired during the planning CT acquisition [6–11]. Three studies have reported results on the accuracy of the Clarity TA-US system in clinical conditions. These studies were only performed on prostate patients and not on post-prostatectomy patients [7,9,10]. The system was compared with either MV-EPI associated with FM implants [7,10], or with 2D-kV bony registration and CBCT registration with FM or transponder implants [9]. All studies reported large discrepancies between the different modalities, with percentage of shifts agreement at 5 mm between 67.4% and 85.1%, and larger systematic errors found with the US device. Post-prostatectomy patients positioning comparisons between US imaging and another IGRT modality were investigated in one particular study [15]. They compared the registration results obtained with the inter-modality BAT system and the CT-on-rails device. The use of the US imaging was reported to be beneficial, but only if initial displacements of the prostate bed were larger than 4 mm. For displacements smaller than 4 mm the technique neither improved nor worsened target localization.

The Clarity TA-US device was installed 3 years ago in our department with the objective to replace soft-tissue based CBCT registration for both prostate and post-prostatectomy patients. To our knowledge, this is the first study reporting on the use of the Clarity system for post-prostatectomy positioning. Likewise, prostate positioning comparison between TA-US and a non-invasive volumetric imaging technique, i.e. without implanted markers, has never been performed in clinical conditions.

Therefore, the first objective of this study was to perform a comparison between TA-US registration and soft-tissue based CBCT registration on both prostate and post-prostatectomy patients. The inter-operator variability for the registration process was evaluated for each configuration. Finally, the potential gain of using the TA-US system routinely for patient positioning was studied by calculating the treatment margins adapted to the US modality.

Materials and methods

The US IGRT system

The 3D US–IGRT system (Clarity®) was described in detail elsewhere [10]. Briefly, it is based on a TA-US probe tracked by an infrared camera. For each acquisition, several hundreds of 2D US slices are acquired during a probe sweep and merged into a 3D image. During the planning CT session, a reference US image (US_{ref}) is acquired with the same patient set-up as during the CT acquisition. The US_{ref} image is superimposed directly on the CT image through a room calibration process, allowing visualization of the US_{ref} and CT images in the same coordinate system. Note that images are not registered but only superimposed. Thus the patient is supposed to be immobile between the 2 acquisitions. A reference positioning volume (RPV) is then delineated on the US_{ref} image. Over the treatment course, a daily US image (US_{daily}) is acquired at the beginning of each session, and manually registered on the US_{ref} image by projecting the RPV volume on the US_{daily} image. The accuracy of the system is checked daily by performing US acquisitions on an ultrasound phantom aligned on the room lasers, ensuring an uncertainty below 1 mm and 2 mm for the reference and the daily US systems, respectively [16].

Patients

This prospective study was approved by the hospital ethics committee. All included patients signed a letter of consent. 38 patients undergoing a prostate irradiation and 15 patients irradiated after prostatectomy were imaged using the TA-US device between July 2012 and November 2013. Planning target volumes (PTVs) were automatically generated by adding a 3D 7 mm uniform margin around the clinical target volumes for both localizations. The total prescription dose was 66 Gy for post-prostatectomy patients and 74 Gy to the PTV for prostate patients using a standard fractionation (2 Gy per fraction, 5 days a week). For each patient a VMAT plan was generated. The irradiation was delivered using 6-MV photons with an Elekta Synergy machine equipped with a Cone-Beam Computed Tomography (CBCT) device (XVI, Elekta, Stockholm, Sweden). A bladder filling protocol was given to all patients: one hour before the CT acquisition and each treatment session, patients had to empty their bladder and drink 500 mL of water. Special low-fiber diet instructions were also given before the treatment for the rectum preparation.

10 patients treated from July to October 2012 were excluded from this study to allow the radiation therapists (RT) to acquire some experience with the TA-US device. Likewise, 6 other patients were also excluded due to difficulty maintaining an adequate bladder filling during the treatment. Therefore, results were analyzed on 25 prostate patients (cohort A) and 11 post-prostatectomy patients (cohort B).

All patients were scanned in supine position, with 3 mm slice thickness and standard prostate protocol on a Brilliance CT Big Bore scanner (Philips Medical Systems, Best, The Netherlands). They were immobilized using a cushion under the knees. The same position was kept after the CT acquisition to acquire the US_{ref} image. The approximate time between US_{ref} and CT acquisitions was estimated to 3 minutes. For cohort A, the RPV was the whole or easily visible part of the prostate. The delineation was done semi-automatically by firstly contouring 2 or 3 axial and sagittal slices and using an automatic interpolation. If needed, a manual correction was applied. For cohort B, the RPV corresponded to the bladder neck since it was included in the clinical target volume according to the EORTC guidelines [17] (Fig. 1). To delineate this volume, the entire bladder was contoured on the US_{ref} image, then the volume was truncated superiorly, leaving only the bladder neck [18]. This was a fully manual process.

Image and data processing

In this study, US acquisitions were performed for data collection only. The patient repositioning was always carried out based on CBCT/CT registration results.

US acquisitions were performed at the beginning of each treatment session after laser-guided patient alignment. CBCT images were acquired directly after US_{daily} imaging in order to minimize the patient motion. Some patients were included in daily IGRT protocols, and others were imaged according to the "extended No Action Level" (eNAL) protocol [19], which consists of acquiring one CBCT/US_{daily} image during the first 3 irradiation sessions, and one CBCT/US_{daily} image per week until the end of the treatment.

Registration of CBCT images on the reference CT was done semi-automatically. First, an automatic bony alignment was performed using a clip box including pubic bones, using the XVI software. Then, a manual adjustment was done on the soft tissue target volume, i.e. the prostate for prostate patients and the prostatic bed for

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