TJ
ISSN 0300-8916
Tumori 2015; 00(00): 000-000
DOI: 10.5301/tj.5000305
SHORT COMMUNICATION

# Three-dimensional ultrasound-based target volume delineation and consequent dose calculation in prostate cancer patients with bilateral hip replacement: a report of 4 cases

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**ABSTRACT**

**Aim:** To investigate the role of 3D ultrasound (3D-US) in target volume delineation in prostate cancer radiotherapy.
**Methods:** Four patients with intermediate risk prostate cancer and metal artifacts on planning computed tomography (CT) due to previous bilateral hip replacement underwent 3D-US with the Clarity platform (Clarity System, Elekta, Stockholm, Sweden) to allow for image-guided procedures. Ultrasound and CT images were coregistered to allow for better delineation of the prostate gland and organs at risk (OAR). Electron density override (EDO) and standard electron density (EDS) methods were compared for appropriate dose calculation.
**Results:** 3D-US and planning CT minimized image artifacts, providing better evidence of patient anatomy, particularly regarding soft tissue visualization. Prostate gland and seminal vesicles were better delineated, particularly in the posterior aspect. Anterior rectal wall and bladder neck were more visible. No difference was found in terms of average planning target volume dose, $D_{15\%}$, or $D_{25\%}$ for rectum or $D_{15\%}$, $D_{25\%}$, or $D_{35\%}$ of bladder between EDO and EDS.
**Conclusions:** 3D-US proved to be a viable tool for target volume and OAR visualization in patients with prostate cancer with hip prostheses.

**Keywords:** 3-Dimensional ultrasound, Hip replacement, Image-guided radiotherapy, Prostate cancer, Prostheses

## Introduction

Treatment planning for 3D conformal external beam radiation therapy (EBRT) is based on the acquisition of a computed tomography (CT) scan in order to acquire patient anatomy for treatment volume selection and delineation and electron density mapping for proper dose calculation (1). Hip prosthesis is a frequent finding in the subset of patients undergoing EBRT, since this type of population is aging. Consequent imaging artifacts may represent a challenge in terms of both target delineation and dose calculation, especially for patients needing pelvic radiotherapy such as in the case of prostate cancer (2). Prostheses should be better taken into account at the time of treatment planning and geometrically avoided during radiation delivery (3). Several different approaches have been proposed to reduce metal artifacts impact during the planning process (4). Magnetic resonance imaging (MRI) might be a potential useful tool in this context, facilitating target definition and normal structure visualization through CT-MRI coregistration (5). However, several drawbacks remain, such as different patient positioning due to diverse couching systems, eventual image distortions, and heterogeneous dose calculation due to inaccurate electron density information because of metallic implants (5). Cone-beam CT (both kilovoltage CT and megavoltage CT) is generally available in modern linear accelerators as an on-board imaging system to perform image-guided radiotherapy (IGRT) (6). Images acquired at these energies are less prone to artifacts, as the primary modality of interaction is the Compton rather than the photoelectric effect (2). The Clarity platform (Clarity System, Elekta, Stockholm, Sweden) allows for the acquisition of 3D ultrasound scans (3D-US) of the pelvic region (Fig. 1), using a 2D transabdominal probe equipped with positional sensors that needs to be swept across the patient's sovrapubic region (7). The system uses an infrared camera to

**Accepted:** March 9, 2015
**Published online:** May 13, 2015

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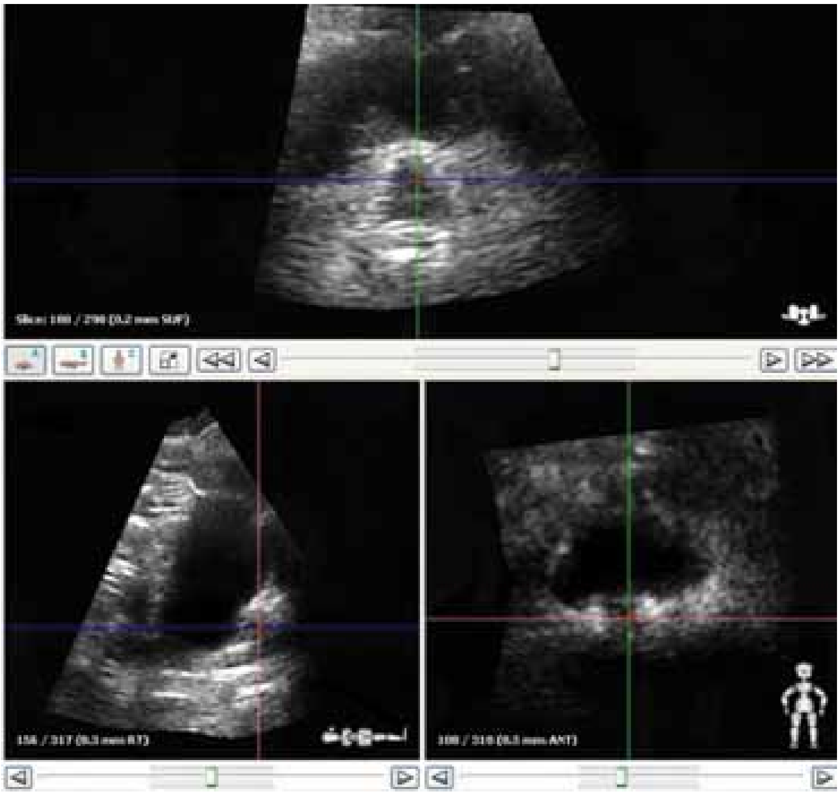

**Fig. 1 -** Axial, sagittal, and coronal view of 3D ultrasound imaging.

track sensors' positional changes, generating spatial information subsequently employed to reconstruct a 3D dataset, then utilized for target verification and patient alignment during IGRT procedures (8). We report on the use of the Clarity system for target volume delineation in a consecutive series of patients with prostate cancer with bilateral hip replacement undergoing definitive EBRT.

## Materials and methods

### *Inclusion criteria*

Patients diagnosed with organ-confined prostate cancer were accrued whenever stratified as intermediate risk according to the National Comprehensive Cancer Network classification: clinical stage cT2b-cT2c, Gleason sum = 7, and prostate-specific antigen (PSA) range 10-20 ng/mL (9). All patients previously had bilateral hip replacement. They underwent histologic confirmation and pretreatment evaluation (complete medical history, physical examination with digital rectal examination, PSA level, multiparametric pelvic MRI). Androgen deprivation therapy was allowed in a neoadjuvant, concomitant, and adjuvant setting for a total of 4-6 months. All patients should have a reliable US visualization of the prostate gland within the Clarity platform and metal artifacts observed during planning CT.

### *Setup, target volumes, and organs at risk definition*

Each patient underwent a planning CT scan of the pelvic region for treatment planning. Supine position was used with an indexed-shaped knee rest and ankle support (CIVCO Medical Solutions, Kalona, IA, USA). Three-millimeter axial images were acquired from the L5 vertebral body to the ischiatic region. An isocenter was found in virtual simulation and its projections were marked on the patient's skin under laser guidance. To increase daily reproducibility of setup in terms of bladder and rectal filling, all patients were instructed to drink 500 mL of water 1 hour before planning CT (as in every treatment fraction) and to perform a daily enema in addition to a low-residue diet from 3 days prior to simulation. Clinical target volume (CTV) included the entire prostate gland and the proximal aspect of the seminal vesicles. Since the enrolled patients had important image artifacts due to the presence of hip prostheses, a contouring process based only on simulation CT images was considered not reliable. Thus, a coregistration between planning CT scan and 3D-US images was performed and used at the time of treatment volume selection and delineation. The consistent soft tissue resolution of US in adjunct to the independence from metal artifacts strongly improved the delineation process. Given that US-driven visualization and delineation of the prostate gland is a highly operator-dependent process, the contouring process was performed only by well-trained physicians. A 10-mm margin expansion was added to generate the corresponding planning target volumes (PTVs) except in the posterior direction (7 mm), as established in our institutional protocol. Outlined organs at risk (OAR) were bladder and rectum (from the anal canal to the recto-sigmoid flexure), defined as solid organs, bilateral femoral heads, penile bulb, and peritoneal cavity, including small bowel. Organs at risk delineation was helped with 3D-US coregistration.

### *Dose prescription, planning, and delivery*

All patients received 61.1 Gy/26 fractions (2.35 Gy daily) to the seminal vesicles and a total nominal dose of 70.2 Gy/26 fractions to the prostate gland with a simultaneous integrated boost approach. The dose was prescribed following the International Commission of Radiation Units (ICRU 83) recommendations so that dose distribution was optimized to achieve 98% of all PTV receiving at least 95% of the prescription dose, with concurrent hot spot minimization ($D_{2\%}$<107% of prescribed dose). Dose constraints for OAR were set as follows: $V_{50}$<35%, $V_{60}$<25%, $V_{65}$<15%, and $V_{68}$<5% (rectum), $V_{60}$<35% and $V_{40}$<50% (bladder), $D_{mean}$<50 Gy (penile bulb), $D_{50}$<40 Gy, $D_{10}$<50 Gy, and $D_5$<60 Gy (peritoneal cavity), $D_{max}$<50 Gy (femoral heads). Radiation was delivered with a static intensity-modulated radiation technique employing a 5-field beam arrangement using 10-MV photons. The electron density (ED) for dose calculation was set to a value of 1 in order to avoid metallic artifacts perturbation of dose estimate. A specific 5-field beam arrangement was selected with the aim of avoiding hip prostheses laterally to the PTV (gantry angles: 0°, 30°, 160°, 200°, and 330°) (Fig. 3). In order to test whether this planning approach was appropriate, 10 patients with no hip replacement were selected to generate corresponding conformal plans with the same beam arrangement, comparing the use of ED override (EDO) with a fixed density value of 1 to a standard electron density (EDS) approach derived from CT to ED calibration curves. Doses to PTV, rectum, and bladder were compared by means of specific dose volume histogram values. The Clarity 3D-US system (Elekta, Crawley, UK) includes 2 separate platforms, located in the CT and treatment room, respectively, and a special dedicated workstation for image coregistration and storage. An optical tracking system (OTS) is employed to determine the position and orientation of the 3D-US probe, registered to the external laser system in both rooms, where the paired US data are referenced to the same spatial coordinates (7). This mutual referencing robustly correlated the simulation and treatment room coordinate systems. After simulation CT scan, a free-hand axial sweep is acquired, reconstructed, and employed to create 3D-US images using the detection performed by the OTS of an array of infrared reflectors connected to the probe handle. The acquisition of US images within the CT room coordinate system, driven by laser coordinates, allows for automatic registration between the different acquisitions at the Clarity workstation. However, the final registration is manually adjustable by the operator. A guidance structure is created, called positioning reference volume (PRV), within the Clarity workstation to be used as reference in the treatment room. During each treatment fraction, a free-hand axial sweep is acquired and then segmented into axial and sagittal planes (Fig. 1). Thereafter, the treatment PRV is automatically aligned with the reference PRV using an optimization algorithm based on gray values and thereafter manually by the operator. When the alignment is considered appropriate, the system automatically takes into account final target displacements with a couch translation alongside the 3 spatial vectors (8).

## Results

3D-US coregistration with simulation CT scan was able to minimize image artifacts due to high-density metal hip implants in all 4 patients, providing better evidence of patient anatomy, particularly in terms of soft tissue visualization (Fig. 2 and Fig. 3). Both prostate gland and the proximal portion of seminal vesicles were successfully delineated using the hybrid image. Interestingly, the imaging artifacts on the CT scan due to hip prostheses hid the posterior aspect of the prostate as the anterior rectal wall, potentially rendering difficult the visualization of the interface between these 2 structures. The same issue happened for the base of the prostate and the bladder neck. 3D-US was useful in the delineation of these specific regions. Also, the contouring process of the lateral extensions of the prostate gland and the seminal vesicles was enhanced by the use of 3D-US. The OAR such as rectum and bladder were delineated with higher accuracy. No difference was found in terms of average PTV dose, $D_{15\%}$, or $D_{25\%}$ for rectum or $D_{15\%}$, $D_{25\%}$, or $D_{35\%}$ for bladder (see Tab. I and Fig. 4 for details) between the 2 approaches (EDO vs EDS).

## Discussion

Radiation dose escalation has been proved to provide clinical benefit to patients with prostate cancer (10). In this context, correct and precise identification of both target volumes and critical structures are mandatory for accuracy and reliability of dose calculation (11). Several methods have been shown to provide a potential tool to deal with the issue of a poorly visualized anatomical region, with a tight dependence on the type of equipment available (12). Megavoltage CT used for planning purposes is able to consistently reduce image streaks, but requires intraprostatic fiducial marker implantation to enhance organ delineation (2). Magnetic resonance imaging has been demonstrated to improve delineation precision, but carries a tendency for geometric distortions, particularly prone to biases due to prostheses heterogeneity (5). Cone-beam CT (kilovoltage CT) has effective metal artifact-suppressing algorithms, even if the impact of metal artifacts may be magnified within the soft tissue region, given that the contrast of soft tissue is generally lower in cone-beam CT images. The Clarity platform, employing 3D-US, provides reliable imaging of patient anatomy even in the presence of hip replacement, as shown in our report. This information may be used to compensate for that missing in the CT scan and due to artifacts to drive target volume and OAR selection and delineation. Also, segmentation for planning purposes may be facilitated, increasing ballistic precision and reliability of the treatment process. All these methods have pros and cons as applied for prostate gland visualization in the presence of hip prostheses. Kilovoltage cone-beam CT may have the drawback of a higher impact of artifact presence on images because of the aforementioned lower soft tissue contrast (13). Megavoltage cone-beam CT may not necessarily guarantee a consistent spatial resolution due to high noise-to-signal ratio and low soft tissue contrast. Magnetic resonance imaging may have significant image distortion due to artifacts. On the contrary, 3D-US is less conditioned by these issues if employed in the contouring process. Perturbations of the dose distribution by hip prostheses during radiotherapy treatment of pelvic malignancies may result in unacceptable dose inhomogeneity within the target volume. Such an inhomogeneous dose distribution may compromise local control and, therefore, specific beam arrangements

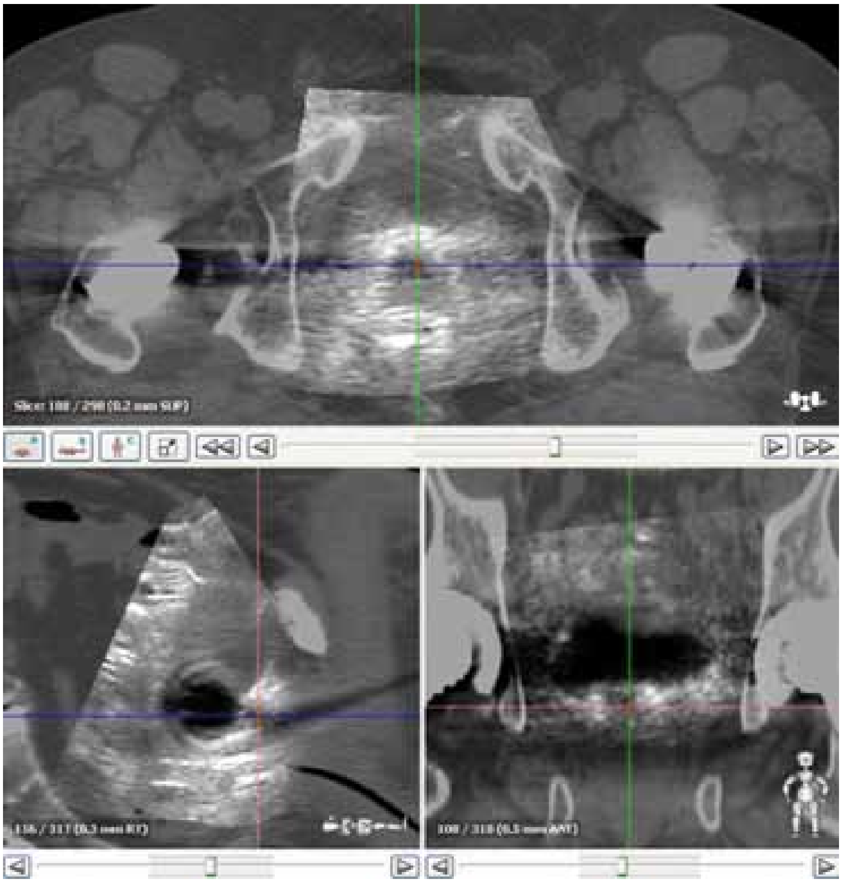

**Fig. 2 -** Coregistration between 3D ultrasounds and planning computed tomography.

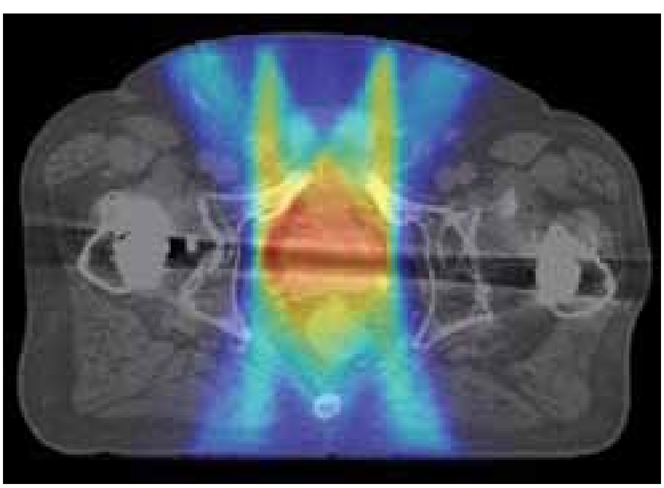

**Fig. 3 -** Dose distribution after treatment planning.

**TABLE I -** Difference in dose calculation between electron density override and standard electron density

| | PTV | Rectum | | Bladder | | |
|---|---|---|---|---|---|---|
| Patient | average | $D_{15\%}$ | $D_{25\%}$ | $D_{15\%}$ | $D_{25\%}$ | $D_{35\%}$ |
| 1 | -1.3 | -0.8 | -1.1 | -2.2 | -1.9 | 1.2 |
| 2 | 0.1 | 0.3 | 0.5 | 0.2 | 0.0 | 0.0 |
| 3 | -0.3 | -0.3 | -0.2 | -0.5 | 0.0 | 0.0 |
| 4 | -0.2 | 0.1 | 0.0 | -0.7 | -0.6 | -0.8 |
| 5 | -1.0 | -0.9 | -0.9 | -1.2 | -1.3 | -1.7 |
| 6 | -0.1 | -0.2 | 2.8 | -0.4 | -0.5 | -0.5 |
| 7 | 0.3 | 0.4 | 0.5 | -0.2 | 0.1 | 0.0 |
| 8 | -1.3 | 0.3 | 0.4 | 0.0 | 0.1 | 0.0 |
| 9 | 1.4 | 0.2 | 0.1 | -0.6 | -0.7 | -0.3 |
| 10 | -1.2 | -0.9 | -0.9 | -1.7 | -1.6 | -0.2 |

PTV = planning target volume.
p = NS.

aiming at avoiding those medical devices have been proposed (14). It is possible that this need may lead to a selection of less-than-ideal geometry with unintended excessive dose to OAR. Intensity-modulated radiotherapy (IMRT), with the possibility to generate abrupt dose falloffs, may be a viable tool to compensate for this issue. The differences shown by calculations without using heterogeneity correction (EDO) or using the CT to ED correction (EDS) for a standard conformal plan was not statistically significant for PTV and OAR, showing a negligible impact of heterogeneity calculation within the abdominal region. Thus, we selected static IMRT avoiding prostheses and using no heterogeneity correction for dose calculation within the metal artifact regions. 3D-US-driven IGRT requires an initial mandatory learning curve and strongly depends on the

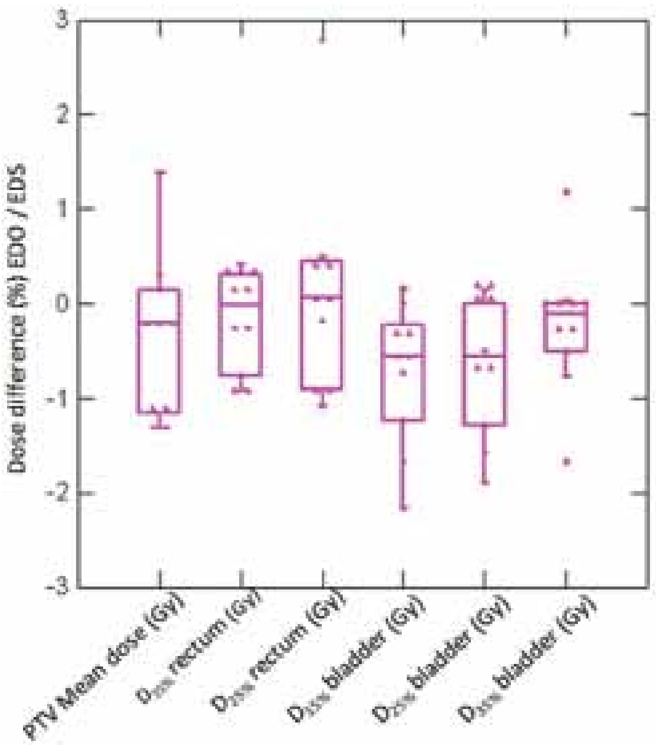


**Fig. 4** - Box plot shows dose difference to planning target volume (PTV) and organs at risk (OARs) between electron density override (EDO) and standard electron density (EDS).

operator's experience in terms of US image acquisition, visualization, and coregistration. Also, certain patients should be excluded from this technique because of low visibility of the prostate gland due to obesity. Finally, it has been demonstrated that the US probe may impact in terms of prostate localization due to operator pressure even within an intramodality repositioning device (15). The consequent uncertainties should be taken into account during CTV to PTV margin generation. Despite these limitations, 3D-US has shown to be a useful and reliable tool to enhance target volume and OAR visualization in patients with prostate cancer undergoing EBRT and having bilateral hip replacement.

## Disclosures

Financial support: None.
Conflict of interest: None.

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