Towards image-guided radiotherapy of prostate cancer

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ONLINE ULTRASOUND IMAGE-GUIDANCE FOR RADIOTHERAPY OF PROSTATE CANCER: IMPACT OF IMAGE ACQUISITION ON PROSTATE DISPLACEMENT

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ABSTRACT

PURPOSE Numerous studies reported the use of ultrasound image-guidance systems to assess and correct patient setup during radiotherapy of prostate cancer. We conducted a study to demonstrate and quantify prostate displacement resulting from pressure of the probe on the abdomen during transabdominal ultrasound image acquisition for prostate localization.

PATIENTS AND METHODS Ten healthy volunteers were asked to undergo one imaging procedure. The procedure was performed in a condition that simulates the localization of prostate during online ultrasound-guidance. A three-dimensional (3D) ultrasound machine was used. The procedure started with the placement of the probe on the abdomen above the pubis symphysis. The probe was tilted in a caudal and posterior direction until the prostate and seminal vesicles were visualized. The probe was then fixed with a rigid arm, which maintained the probe in a static position during image acquisition. The probe was then moved, in a short time, stepwise towards the prostate, acquiring images at each step. The prostate and seminal vesicles were identified and selected in all planes. The first 3D volume was used as reference 1, to which all other scans were matched using a grey-value matching algorithm.

RESULTS Prostate motion was quantified as a 3D translation relative to the patient coordinate system. The resulting translations represented the amount of prostate movement as a function of probe displacement. Between 7 and 11 images were obtained per volunteer, with a maximal probe displacement ranging between 3 and 6 cm. Prostate displacement was measured in all volunteers for all the probe steps and in all directions. The largest displacements occurred in the posterior direction in all volunteers. The absolute prostate motion was less than 5 mm in 100% of the volunteers after 1 cm of probe displacement, in 80% after 1.5 cm, in 40% after 2 cm, in 10% after 2.5 cm, and 0% after 3 cm. To achieve good-quality ultrasound images, the probe requires an average displacement of 1.2 cm, and this results in an average prostate displacement of 3.1 mm. No correlations were observed between prostate motion and prostate-probe distance or bladder size.

CONCLUSIONS Probe pressure during ultrasound image acquisition causes prostate displacement, which is correlated to the amount of probe displacement from initial contact. The induced uncertainty associated with this process needs to be carefully evaluated to determine a safe margin to be employed during online ultrasound image-guided radiotherapy of the prostate.
INTRODUCTION

High-dose conformal radiotherapy treatment improves clinical and biochemical outcome of patients with prostate cancer\(^\text{(1-3)}\), but can result in an increased risk of side effects\(^\text{(3)}\) because of the margins needed to compensate treatment uncertainties\(^\text{(4-8)}\). To understand and compensate geometrical errors, numerous studies have developed offline\(^\text{(9-12)}\) and online\(^\text{(9,13-16)}\) positioning systems to accurately reproduce the treatment planning on the treatment machine. Troccaz et al.\(^\text{(17)}\) were the first to report the use of transabdominal ultrasound (US) imaging to assess and correct patient setup according to the planning target volume. Recently, a transabdominal US-based targeting system has been commercialized (BAT, Nomos, Sewickley, PA), used\(^\text{(18-19)}\), and evaluated\(^\text{(20-22)}\). Recent reports show large inaccuracies and systematic errors between BAT and marker measurements: some of the error might be due to pressure of the probe on the abdomen\(^\text{(23-24)}\). The aim of this study was to quantify prostate displacement resulting from pressure of the probe on the abdomen during transabdominal US imaging for prostate localization.

PATIENT AND METHODS

Ten healthy volunteers were each asked to undergo one US-imaging procedure. The ages and weights of the healthy volunteers were not similar to the average patient with prostate cancer. The median age of the volunteers was young (approximatively 38 years old) and none of the volunteers had an excess weight. Each procedure was performed simulating the prostate localization during online image guidance for prostate cancer treatment. To increase prostate visualization on US images, each volunteer was asked to fill his bladder before the procedure, and was then installed in supine position with his arms by his side. No immobilization device was employed. A US machine with an attached transabdominal three-dimensional (3D) probe (Voluson 730, Kretz technik AG, Zipf, Austria) was used. The probe was attached to a rigid arm, which maintained the probe in a static position during image acquisition. Between the probe and the rigid
arm device, a stepper was mounted, which permitted a displacement of the probe in several accurate steps of 5 mm. Identical US probe settings were used for all volunteers. The procedure commenced with the placement of the probe on the middle of the abdomen in a sagittal midplane above the pubis symphysis tilted in a caudal and posterior direction with respect to the volunteers. The probe was tilted between 20° and 25° with respect to the vertical plane, to be oriented in the prostate direction and to decrease the amount of prostate gland that was hidden by the symphysis, such that the entire prostate could be imaged (Figure 1).

![Diagram of the experimental setup. The probe was tilted in caudal and posterior direction on the abdomen until the prostate and seminal vesicles were seen. The probe position was then fixed in this position. The first image was done and used as the reference. The probe was then gradually moved step by step in this direction.](image)

When the prostate and seminal vesicles were identified, with as small as possible pressure of the probe on the abdomen (weak), the probe start position and direction were fixed. The probe was then moved stepwise, towards the prostate. At each step, a 3D US image was obtained (Figure 2).
Figure 2. Effects of probe pressure on ultrasound images of one volunteer. The first image in the upper left corner was done with the smaller probe pressure, and then from the left to the right and from the top to the bottom, the probe pressure increased at each step of 5 mm. The bladder deforms and the prostate moves with increasing probe pressure.

The US machine acquires the 3D image set within 5 s. Including storage and DICOM transmission of the images, the entire imaging procedure took a very short time, less than 3 min. A short study time decreases the probability of prostate motion resulting from motion of intestinal gas in the rectum. It was therefore assumed that any observed prostate displacement was only due to the pressure of the probe on the abdomen. All the images were transferred to an in-house developed matching software package (van Herk, ICCR, 1997). The prostate and the seminal vesicles were not contoured but identified in all planes and selected using a clipping box on an image taken at intermediate pressure (Figure 3).

This 3D volume was then used as reference 1, to which the other scans were matched using a grey-value matching algorithm. For matching, only the region of interest defined by the clipping box was taken into account. Care was taken to exclude the bladder, which changed significantly in shape because of the probe pressure. Prostate motion was quantified as a 3D translation relative to the probe position. Rotations were not taken into account. All the matches were visually verified. The stepwise motion of the probe was next subtracted to quantify the motion in a patient related coordinate system. Because probe pressure was not measured with a pressure sensor, the resulting translations represent the amount of prostate movement as a function of probe displacement from the initial position.
required to get good-quality images. For each volunteer, one physician (X.A.) examined all images.

**Figure 3.** Effects of probe pressure on ultrasound images of one volunteer. On the left picture, the prostate and seminal vesicle volume have been selected using a clipping box (white square box in the upper left corner). The left principal window shows two half transverse views of two prostate image acquisitions after different probe pressure on the same volunteer (before matching). On the right principal window, the two half ultrasound transverse views have been matched and prostate motion can be deducted.

Finally, for all volunteers, the correlation coefficient between prostate motion and bladder size (defined by the largest diameter of the bladder on each image) and the correlation coefficient between prostate motion and prostate-probe distance (from the skin in contact with the probe above the pubis symphysis to the center of the prostate) was evaluated.

**RESULTS**

For all volunteers, the initial pressure on the abdomen was very small, resulting in poor image quality, but also in a small probability of prostate motion before starting the experiment. On each image, the prostate, seminal vesicles, bladder, and, to a lesser degree, rectum could be identified. Between 7 and 11 images were obtained per volunteer (average of 8), with a probe displacement ranging between 3 and 6 cm (6 to 12 steps). After visual
verification, the match results were considered accurate in all volunteers (Figure 3).

Prostate displacement was observed in all volunteers for all the probe steps, even for the first one. The largest prostate displacements occurred in the posterior direction, in the same direction in all volunteers (Figure 4A). Motion in the caudal direction is significant and occurred in all volunteers but one (Figure 4B), but the movement to right or left occurs at random (Figure 4C).

The amount of prostate motion was strongly correlated with the amount of probe displacement. According to the absolute prostate motion (vector length), the prostate motion was less than 5 mm in 100% of the volunteers after 1 cm of probe displacement, in 80% after 1.5 cm, in 40% after 2 cm, in 10% after 2.5 cm and 0% after 3 cm of probe displacement (Table 1).

The image quality was satisfactory to perform all matches. The images were considered as good-quality when the entire prostate and seminal vesicles could be visualized and drawn.

The prostate and seminal vesicles can be accurately visualized and drawn on the first image (5 mm probe displacement) in two volunteers, on the second image (1 cm probe displacement) in four volunteers, on the third (1.5 cm probe displacement) image in two volunteers, and on the fourth image (2 cm probe displacement) in two volunteers. Consequently, the average required probe displacement was 1.2 cm to obtain good-quality images resulting in an average absolute prostate displacement of 3.1 mm.

No correlations were found between prostate motion and prostate-probe distance or bladder size.
**Figure 4.** Effects of probe pressure on ultrasound images of 10 volunteers (each line represents one volunteer). A) Anteroposterior prostate displacement, B) craniocaudal prostate displacement, and C) lateral prostate displacement. With increasing probe displacement the prostate moves to the posterior (A) and caudal direction (B) and at random to the right or left direction (C).
Impact of US-IGRT on prostate displacement

Table 1. Effects of probe pressure/displacement on ultrasound images of 10 volunteers. Average and standard deviation of the absolute prostate displacement as a function of probe displacement. The amount of prostate motion is strongly correlated with the amount of probe displacement.

<table>
<thead>
<tr>
<th>Probe displacement (cm)</th>
<th>Absolute prostate motion Average (cm)</th>
<th>SD (cm)</th>
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<tbody>
<tr>
<td>0</td>
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<td>0.5</td>
<td>0.17</td>
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<td>1.0</td>
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<td>0.90</td>
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<td>3.0</td>
<td>1.14</td>
<td>0.71</td>
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<td>3.5</td>
<td>1.62</td>
<td>0.88</td>
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</table>

Abbreviation. SD = standard deviation.

Discussion

Since the introduction of an US system for prostate localization and patient positioning in radiotherapy, only a few articles or abstracts report on the reliability of this technique. Among these, two studies reported the impact of probe abdominal pressure on prostate motion in patients treated for prostate cancer. In our experiment, based on healthy volunteers, at least seven images were acquired per volunteer, resulting in a large range of abdominal probe displacement.

Prostate motion was observed even at small abdominal pressures. The absolute prostate motion was on average 3 mm for each centimeter of
abdominal probe displacement. Furthermore, prostate displacement occurred in all volunteers and in all directions. The major prostate displacement was into the posterior direction, much less in the caudal or right-left direction.

Using a Styrofoam dummy shaped as the distal end of the US probe (assuming that the physical dimensions of the BAT US probe was similar to the probe used in this study) during computed tomography scans, Serago et al.\(^\text{(21)}\) reported prostate motion with and without the pressure on the abdomen that would be exerted during an US scan. They reported displacements in posterior and caudal direction in 7 of 16 patients, with a range of 2.3 mm to 5 mm. No displacement was observed in lateral direction. However, the pressure applied was an approximation and varied from day to day and from one patient to another. It was probable that the displacement applied was between 1 and 1.5 cm of probe displacement, which was smaller than the maximum pressure we applied. If we select from our study the results for 1 cm of probe displacement, the ranges of prostate motion we obtain are very similar, except in lateral direction; from 0 to 3.4 mm, 0 to 3.1 mm, and 0 to 2.2 mm in posterior, caudal, and lateral directions, respectively. The absolute average prostate displacement after 1 cm probe displacement was 3.1 mm (2.4 mm, 1 SD) and was concordant with Serago’s observation (average prostate motion of 3.1 mm). The displacement we observed in lateral direction was the smallest displacement and was less than 5 mm in 50% of the volunteers after 3 cm probe displacement. No lateral displacements were observed by Serago. In these two studies, the size of the US probe was slightly different between the 3D probe we used, which was 3.5-cm width, and the two-dimensional BAT-system probe, which was 2.5-cm width.

McNeeley et al.\(^\text{(26)}\) performed a similar study using magnetic resonance imaging on six patients and observed smaller displacement, which were on average 1.6 mm (0.9 mm, 1 SD), 0.3 mm (0.6 mm, 1 SD), 1 mm (0.6 mm, 1 SD) in anterior, lateral, and cranial direction, respectively. The pressure on the abdomen was the same for each patient, but no indication of the applied amount of pressure was reported.

Powel et al.\(^\text{(27)}\) studied prostate movement during external beam radiotherapy by localizing the prostate at the same time by the BAT US system and with an electronic portal imaging system. The BAT system purports to accurately localize prostate position in 3D using a 5 minutes procedure that may be performed daily by the treating radiation therapists.
They noticed larger and more frequent prostate movements using the BAT system than those reported in literature, measured by other systems. This suggests that a systematic error can occur during image acquisition, even if other sources of errors might be possible (system calibration, intrafraction prostate motion, interobserver variability, image interpretation, or computed tomography–drawn contours). Two recent reports emphasized this last point and pointed out the inaccuracy of US guidance, especially in craniocaudal (CC) and lateral directions. Both studies evaluated the accuracy of BAT repositioning system compared with implanted markers. Van den Heuvel et al.\(^{(24)}\) found a significant correlation in CC direction between the residual errors and the shift performed by the BAT system, suggesting that induced errors can occur. Furthermore, Langen et al.\(^{(23)}\) observed that the number of larger errors (>5 mm) could be reduced in anteroposterior direction after BAT repositioning (from 40% before to 15% after), but not in the craniocaudal direction, where this number increased (14 on 40 experiments).

The total displacement we applied in our study was certainly higher than the displacement that would be exerted during a real US scan, which is probably between 1 and 2 cm, which was the average required-probe displacement that we found to result in good-quality images. This pressure may change from one operator to another and from one volunteer or one patient to another. In addition, the applied probe may influence to some extent the image quality (we used a high-quality 3D probe, whereas other studies used a two-dimensional probe). Using the BAT system, Serago et al. reported poor-quality images in 27% of their patients. They studied characteristics affecting US image quality and found that the amount of prostate gland superior to the pubis symphysis in an anteroposterior projection was statistically significantly correlated with good-quality two-dimensional images. To compensate the poor image quality with the two-dimensional probe, an increased tilted pressure above the pubic symphysis might be necessary, resulting in an increased prostate displacement.

Even though an US imaging system for localization and positioning of the patient for radiotherapy seems to be an attractive and a promising technique, alternative techniques have been described: megavoltage radiography of implanted markers\(^{(28)}\), the computed tomography scan\(^{(29)}\) or a cone-beam computed tomography scan\(^{(30)}\), or an intrarectal balloon to immobilized the prostate\(^{(31)}\). All these techniques have their own advantages and disadvantages. Further studies are needed to evaluate and compare all these methods with each other.
CONCLUSIONS

Probe displacement resulting from the applied pressure during US image acquisition causes prostate displacement. The only predictive factor found in this study (other possible factors were not studied) of motion is the amount of probe pressure (i.e., probe displacement), which needs to be as small as possible. Between 1.0 and 2.0 cm of probe displacement was needed to get good-quality images using a 3D probe. Even though an US imaging system for localization and positioning of the patient for radiotherapy seems to be an attractive and a promising technique, the uncertainties associated with this process need to be carefully evaluated to determine a safe margin to be employed during online US image–guided radiotherapy of the prostate.
REFERENCES


