Measurement and compensation for prostate movement in patients receiving daily IMRT treatment using BAT system compared with EPID

Chen Chen
Medical College of Ohio

Follow this and additional works at: http://utdr.utoledo.edu/graduate-projects
Graduate School

FINAL APPROVAL OF SCHOLARLY PROJECT
Master of Science in Biomedical Sciences
Concentration in
Medical Physics - Radiation Oncology

Measurement and Compensation for Prostate Movement in Patients Receiving Daily IMRT Treatment Using BAT System Compared with EPID

Submitted by
Chen Chen

In partial fulfillment of the requirements for the degree of Master of Science in Biomedical Sciences

Academic Advisory Committee
E. Ishmael Parsai, Ph.D. (Major Advisor)
Michael J. Dennis, Ph.D.

Signature

Dean, Graduate School
Keith K. Schlender, Ph.D.

Date of Presentation: 8-18-04
Date of Approval: 9-13-04
Measurement and Compensation for Prostate Movement in Patients Receiving Daily IMRT Treatment Using BAT System Compared With EPID

Chen Chen
Medical College of Ohio
# CONTENTS

**OBJECTIVES OF STUDY** ................................................................. 4  
**INTRODUCTION** ............................................................................. 5  
**LITERATURE STUDY** ................................................................. 7  
  1. Prostate anatomy, physiology and pathology review .................. 7  
  2. Brief review of EPID ............................................................... 8  
  3. Brief review of BAT ultrasound system ................................. 11  
**MATERIAL AND METHOD** .......................................................... 15  
  A. Materials used in this study .................................................. 15  
  B. EPID procedure ..................................................................... 15  
  C. BAT ultrasound alignments ................................................. 20  
  D. The volumetric study by CT and TRUS in PSI patients .......... 24  
    1. The prostate volumetric study from intra-operative planning. .... 24  
    2. Volumetric study from post-operative evaluation .................. 26  
    3. Image fusion ....................................................................... 28  
  E. Statistical analysis ............................................................... 30  
**RESULTS** .................................................................................. 31  
**DISCUSSION** ........................................................................... 35  
  1. EPID and BAT ultrasound ................................................... 35  
  2. Function of targeting in CT and BAT ultrasound ................... 36  
  3. Volumetric study in CT and TRUS ....................................... 38  
**CONCLUSION** ........................................................................ 41  
**REFERENCE** ........................................................................... 43
ABSTRACT

With the advent of Intensity Modulation Radiation Therapy (IMRT) in delivery of radiation dose for treatment of cancer, patient position reproducibility has become even more significant in the success of treatment than ever before. With much smaller field sizes and larger quantities of dose delivered through segmented fields that deliver dose with modulated intensity during the treatment, small movements result in large errors and potentially misadministration of dose. One of the sites we typically treat using this IMRT technique is the prostate. Comparing the anatomical position of target to the time of CT and original setup with when radiation is delivered is typically achieved through electronic portal imaging where films from original simulation are compared with digital films taken prior to treatment on the accelerator. This technique, however, allows anatomical landmark matching and does not allow visualization of the prostate gland on the day of treatment. A new device is implemented at the Medical College of Ohio known as the BAT system (B-mode Acquisition targeting system) that uses ultrasound to image the patient’s anatomy and allows comparison of the target volume with the original position of the gland at the time of CT treatment planning. This accounts for the position of the bladder and rectum on treatment day with respect to the target volume as well. In this study, we have evaluated 18 prostate cases using the BAT ultrasound system in comparison to EPID and will report on findings. Results of this comparative analysis and conclusions are presented on the state of the art technology for patient positioning and internal organ motion matching with planned treatment in radiation delivery.
OBJECTIVES OF STUDY

- To have basic knowledge about Electronic Portal Imaging Device (EPID) and B-mode acquisition and targeting (BAT) ultrasound systems.
- To compare the applications of EPID and BAT ultrasound systems for alignments of patients with prostate cancer receiving IMRT treatments.
- To quantify the difference between EPID and BAT in alignment of the prostate.
- To evaluate volumetrically, the variations between CT and Ultrasound images, specifically in imaging the prostate gland.
I. INTRODUCTION

Prostate cancer is the most commonly diagnosed and steeply increasing cancer and is the second leading cause of cancer death for men in the United States\(^1\),\(^2\). Radiation therapy remains one of the primary treatment modalities for patients with prostate cancer. The effectiveness of radiation therapy depends on the accuracy of dose delivery. The intensity-modulated radiation therapy (IMRT) is the most recent advance in the conformal radiation treatment by modifying the intensity of the radiation beam to conform the high dose region to a target volume while sparing normal tissues and organs (figure1). Higher doses to the prostate tend to increase chances for a cure, while lower doses to normal tissues and organs mean fewer side effects.

However, with escalated doses beyond 70 Gy the probability of normal tissue morbidity increases\(^3\). Therefore, the main challenge in IMRT has been uncertainty about the tumor's precise location. In order to minimize the normal tissue margins, quality assurance especially in the acquisition of portal image is very important to ensure accurate patient positioning related to treatment isocenter. In recent years, a number of electronic portal imaging devices (EPIDs) have been developed for beam verification and patient positioning. This technique allows anatomical landmark matching rather than visualization of the prostate gland. A new device is being used at the Medical College of Ohio known as the BAT system (B-mode Acquisition targeting system), which uses ultrasound to image the patient’s anatomy and allows comparison of the target volume.
with the original position of the gland at the time of planning. This system accounts for the condition of the bladder and rectum on treatment day with respect to the target volume as well. Some studies about the capabilities of this system have already been performed by comparing it with a CT-based method \(^{4-6}\). The purpose of this study is to evaluate the accuracy of the electronic portal imaging device (EPID) alignments utilizing BAT ultrasound system as a standard in prostate IMRT treatments. A quantitative volumetric evaluation between two different imaging modalities (ultrasound and CT) is also presented. Figure 1 shows an overlay of an isodose distribution from a typical 7-field IMRT plan over multiple views of CT slices.

Fig.1. Graphical illustration of a 7–field IMRT treatment plan for prostrate carcinoma; Isodose distribution lines are shown on CT transverse, sagittal, and coronal sections. 98 % isodose distribution line covers the target (prostate).
II. LITERATURE STUDY

1. Prostate anatomy, physiology and pathology review

The prostate gland is a single, doughnut-shaped gland about the size of a chestnut that lies inferior to the urinary bladder, anterior to the rectum and behind the base of penis. It surrounds the prostatic urethra (figure 2). The prostate secretes a milky, slightly acidic fluid (pH about 6.5) that contains: citric acid, which can be used by sperm for Adenosine triphosphate (ATP) production; acid phosphatase (the function of which is unknown); and several proteolytic enzymes, such as prostate-specific antigen (PSA), pepsinogen, lysozyme, amylase, and hyaluronidase. Secretions of the prostate gland enter the prostatic urethra through many prostatic ducts. Prostatic secretions make up about 25% of the volume of semen and contribute to sperm motility and viability. The prostate gland slowly increases in size from birth to puberty, and then expands rapidly. The size attained by age 30 remains stable until about age 45, when further enlargement may occur.

Prostate cancer develops from cells of the prostate gland. Almost all prostate cancers are adenocarcinomas, meaning that they develop from glandular cells. Prostate cancer generally grows slowly within the gland, but once it penetrates the outer rim of the gland, it may spread directly to tissues and organs near the prostate gland. Cancer cells may enter lymphatic vessels and spread out along these vessels toward the lymph nodes, where they can continue to grow. The cancer cells may metastasize to other parts of the body, particularly to the bone.
Fig 2. Illustration of prostate on lateral and posterior views (from Principles of anatomy & physiology; Tortora).

2. Brief review of EPID

The EPID is a convenient real-time, on-line imaging device. There is no need for film processing, and it is gradually replacing the radiographic film for geometric verification in radiation therapy. In early generation devices, the liquid ion-chamber and camera-based fluoroscopic EPIDs produced images of inferior contrast and spatial resolution. The recent generation of EPIDs uses flat panel photodiode arrays to detect the optical photons produced as a result of x-ray dose deposition in a scintillating screen. It has higher detective quantum efficiencies (DQE)\(^5\).

The portal imager used in this study is an Elekta iView GT imaging system (Elekta Oncology Systems, Ltd., Crawley, West Sussex, United Kingdom). This imaging system was developed by adopting Perkin Elmer amorphous silicon technique. The effective area of the EPID is 41 x 41 cm\(^2\), and a single image consists of 1024 pixel rows and 1024 pixel columns. The time required to read a frame is 320 mS, and a dose of 2 to 4 cGy is
sufficient to produce an image. From figure 3-(1), photons incident on the detector first interact with a copper plate, which removes low energy photons and electrons produced in the patient, and also acts as build-up\(^4\). The rest of the photons interact with a high atomic number scintillation screen made of gadolinium oxysulfide phosphor (Gd\(_2\)O\(_2\)S: Tb) under the copper plate, and deposit energy into the screen. Gd\(_2\)O\(_2\)S: Tb is very dense and has a K edge of 51 keV that enhances absorption at high energy\(^7\). The fraction of energy deposited in the screen is converted to optical photons. In each pixel, there is a photodiode that absorbs light from the scintillator and generates an electrical charge, as well as a thin film transistor switch (TFT) that serves to isolate each pixel element and acts as a switch to convey electrical charges to external electronics for read-out and image processing.

In a read-out procedure (figure 3-(2)), a negative voltage is first applied to the gate lines (R1, R2, R3) during exposure, causing all transistor switches to be turned off. The electrical charge remains at the capacitor of each pixel. Then during readout, positive voltage is sequentially applied to each gate line, one gate line at a time, and the switches are turned on. The switch of the multiplexer is opened at a time and sequentially connects each vertical wire via switches to the digitizer, allowing each pixel along each row to be read out. The sequential readout approach forms a digital image.

The iView GT Portal Imaging detector is mounted on a two-stage mechanical arm controlled by second hand-held controller. When opened (figure 3-(3)), the detector stage moves the detector clear of the middle-arm assembly first. Then the middle-arm stage
moves the detector into position longitudinally. The detector is allowed to move in the lateral direction. After capturing images, the detector is kept in the closed position (figure 3-(4)).


3. Brief reviews of the BAT system

Ultrasound refers to all sound waves of frequency higher than the upper limit of human hearing (> 20 kHz). The frequency of medical ultrasound usually is between 1 MHz and 30 MHz. The theory of ultrasound technique is similar to the echolocation used by bats,
whales and dolphins, as well as SONAR having been used by submarines since World War II.

The probe, also called a transducer, is the main part of the ultrasound machine. The transducer generates and receives sound waves using a principle called the piezoelectric (pressure electricity) effect, which was discovered by Pierre and Jacques Curie in 1880. There are natural and synthetic piezoelectric materials. Ultrasound transducers for medical imaging applications employ a synthetic piezoelectric ceramic, most often lead-zirconate-titanate (PZT). In its natural state, PZT has no piezoelectric properties until it is heated over the “Curie temperature” (328–365 °C). Afterwards, dipole molecules in the PZT can move freely. An external voltage is applied to PZT while the material is cooled to below its Curie temperature. The dipole molecules then retain their alignments (figure 4). At equilibrium, there is no net charge on PZT surface. When compressed, an imbalance of charge produces a voltage between the surfaces. Similarly, when a voltage is applied to both surfaces, the expanding or contracting crystal generates sound waves. Conversely, when sound or pressure waves hit the crystals, they emit electrical currents. Therefore, the same crystals can be used to send and receive sound waves. The probe also has a sound absorbing substance to eliminate back reflections from the probe itself (damping block), and an acoustic lens to help focus the emitted sound waves.

A highly compressible medium such as air has a low speed of sound. In a less compressible medium, such as water, the speed of sound is greater. The difference in the speed of sound at tissue boundaries is the fundamental cause of contrast in an ultrasound
image. The ultrasound frequency is not affected by changes of media. A high-frequency ultrasound wave provides superior resolution and image detail than a low-frequency ultrasound wave, but the depth of ultrasound penetration is reduced at higher frequencies.

Depending on the purposes of the application, transducer probes come in many shapes and sizes. Some probes are designed for various openings of the body (vagina, rectum, esophagus) so that they can get closer to the organ being examined (uterus, prostate gland, stomach); getting closer to the organ can allow for more detailed views.

When ultrasound energy propagates through a medium, interactions that occur include reflection, refraction, scattering, and absorption. Reflections of ultrasound waves are also called echoes. Some reflections occur at tissue boundaries where there are differences in the acoustic impedance of adjacent materials. The reflected ultrasound waves are received by the probe and relayed to the machine. Only a fraction are reflected and some ultrasound waves travel on further until they reach another boundary and get reflected. Scattering that occurs by reflection causes the ultrasound wave to diverge in different directions, and give rise to the characteristic texture and gray scale in the acoustic image. Absorption results in converting part of ultrasound energy into heat energy. The machine calculates the distance from the probe to the tissue or organ’s boundaries using the speed of sound in tissue (5,005 ft/s or 1,540 m/s) and the time of each echo's return (usually on the order of millionths of a second).
A large difference in acoustic impedance results in a large reflection. The acoustic impedance of air and muscle are $0.0004 \times 10^6$ kg/(m$^2$s) and $1.71 \times 10^6$ kg/(m$^2$s), respectively. So, the intensity reflection coefficient, $R_i$, is almost 100%. All ultrasound gets reflected and no observable images exit beyond an air-filled cavity. Therefore, Gel must be placed between the transducer and patient surface. Otherwise, sound will not be transmitted across the air-filled gap.

Fig.4. The piezoelectric element is composed of aligned molecular dipoles. An external voltage source applied to the element surfaces causes compression or expansion from equilibrium by realignment of the dipoles in response to the electrical attraction or repulsion force.

In B-mode ultrasound, the amplitude or the strength of the signal is designated by the brightness of the dot. The A-mode spike on display is converted into a dot. The position of the dot represents the depth of the interface from the transducer. Constructing a two-dimensional image of the interface is accomplished by compound B-scanning, whereby multiple sets of dots are combined to delineate the echo pattern from internal organs. The object is scanned in many different directions. The superimposition of multiple scan lines creates a composite two-dimensional image. In real-time scanning the displayed image is continuously and rapidly updated with new scan data as the beam is swept repeatedly.
throughout the field of view. The rate at which new information is displayed can be 30 or more frames per second.
III. MATERIAL AND METHOD

A. Materials used in this study

EPID (Elekta Oncology Systems Ltd.) used on SL15 and SL25 linear accelerators shown on figure 4; BAT ultrasound system (NOMOS Corporation; Sewickley, PA) shown on figure 11; ADAC pinnacle treatment planning computer system; The high speed General Electric CT scanner; Variseed 7.1 brachytherapy treatment planning system for volumetric study and image fusion; and the CIRS Model 053 Ultrasound prostate training phantom.

Furthermore, eleven prostate seed-implanted patients and 18 patients receiving external beam IMRT and treated in MCO radiation oncology department between April 2003 to March 2004 were used in this research project.

B. EPID procedure

Each patient was simulated in the simulation room. The radiation oncologist identified the isocenter relative to anatomical structures from the fluoroscopic images. With the laser alignment, the tattoos were marked on patient skin (figure 14, left), so that prior to each treatment the therapist would be able to easily identify the iso-center position and align the patient relative to external skin marks. However, the laser alignment for positioning is not sufficiently accurate because the physical position of internal organs will change at each treatment session. EPID can quickly match bone anatomies in real-
time with the simulation films to greatly improve the patient’s positioning in the clinical practice but will not be able to depict the position of internal organs and target volume such as the prostate. The following procedure is followed prior to initiating a radiation treatment for each patient:

1. First, simulation CT images are acquired and transferred to ADAC Treatment Planning System (RTPS) shown on the left in figure 5. On a digitally reconstructed radiograph (DRR) image, the dosimetrist creates an identical isocenter based on simulation X-ray film radiographs. As a reference, DRR images are then sent to iViewGT station (figure 5, right). Prior to each treatment, the patient is externally immobilized using vac-locks and the laser is initially aligned to marks on patient skin. The graticule is attached to the gantry (figure 6). With the gantry, we can easily see the isocenter and scales on the EPID image. The Orthogonal pair of EPID images is captured by the megavoltage beam. Images are visualized on the monitor of the iViewGT station (figure 7).

Fig.5. Left: ADAC pinnacle treatment planning system. The isocenter is created on DRR image based on simulation films. DRR images are sent to iView station over a local network. Right: iView station and program interface.
Measurement and Compensation for Prostate Movement in Patients Receiving Daily IMRT Treatment Using BAT System Compared With EPID

Fig. 6. An Elekta graticule attached to the accelerator gantry. They are displayed as a cross-wire and a series of dots equally spaced on one centimeter apart. A center of graticule would be identically displaced on isocenter of EPID image.


2. In iViewGT, the program of **template matching** is able to measure the isocenter displacement between EPID image and DRR image. For accomplishing measurements,
both images are rescaled. On an EPID image (right of figure 8), two points (A and B) on the image are identified within a certain distance of each other. Line C is drawn by dragging the cursor from A point to B point. On pop-up dialog box, the value of the distance is entered. The aspect ratio, which is the ratio of the length and width of one pixel, is set to one. Second, the relevant information such as the position of isocenter, the 10x10 field edges and anatomical structures is outlined as shown on the right of figure 8.

![Fig.8. Setting two AP images at same scale. Line C was drawn by dragging the cursor from A point to B point. On popping up dialog box, the value of distance between two points was entered. The aspect ratio was set to one; Creating template on DRR image. A 10 x 10 cm field and a crosshair of isocenter were drawn in DRR image. Anatomical structures were outlined.](image)

3. In template matching (figure 9), two isocenters are overlaid. The 10 x 10 cm field of the EPID image is carefully matched to the 10 x 10 cm field of DRR image (template). After clicking next step, the DRR template can be continuously moved over the EPID image until the two sets of anatomical structures are matched. The displacement in the superior-inferior direction (Y coordinate) and lateral direction (X coordinate) are
calculated respectively. A lateral image is shown in figure 10 of the displacements in anterior-posterior direction (Z coordinate).
C. BAT ultrasound alignments

The BAT uses orthogonal (axial and sagittal) ultrasound images to visualize the prostate and position the patient such that the prostate is at the same location relative to isocenter as the CT planning. The procedure used to determine the position of the prostate with respect to the day of simulation and to calculate the required re-positioning is as follows:

1. The CT images obtained from the patient on the day of simulation are transferred over to the ADAC treatment-planning computer. The radiation oncologist contours the prostate, seminal vesicle, bladder and rectum volumes in treatment planning system (figure12). In RTOG format, the information of contours and the location of isocenter are sent to the BAT system over local network (figure13, left). The medical physicist creates a patient study from the imported data at BAT workstation (Figure13, right).

Fig.11. BAT ultrasound system (left) and a close view (right).
2. The therapist sets up the patient on the treatment couch at the same position as in EPID (figure 14, left). The BAT cart is locked nearby the treatment couch. The ultrasound probe, which can recognize its position in 3D space and can be maneuvered in all directions, is oriented to the treatment machine’s isocenter through a docking system mounted on the Gantry (figure 14, right). This docking system is an easily removable
block tray holder. From the BAT system registration, it correlates the center of the treatment gantry with the position of the isocenter in CT images.

3. Once the gantry registration is completed, the live ultrasound panel is displayed. The therapist applies an amount of gel to the patient’s skin. Two suprapubic images are acquired along the axial and sagittal planes, respectively (figure 15). CT based contours of the prostate, bladder, and rectum are superimposed on the ultrasound images (figure 16). On the touch-screen menu, the medical physicist or radiation oncologist adjust the transverse and sagittal CT contours until a satisfactory match is obtained. The system subsequently calculates the respective shifts in 3D space necessary to obtain this particular match.

4. Then the probe is put on the couch cradle attached firmly to the couch rail so that the respectively achieved alignments can be recorded accurately. The patient on couch is shifted to within 0.7 mm of the desired position (the 0.7 mm is a predefined limit suggested by the manufacturer). The shifts from initial skin marks are recorded in the three directions: lateral right/left (X coordinate), anterior/posterior (Z coordinate), and superior/inferior (Y coordinate).
Fig. 14. On left: before treatment, patient was immobilized on the couch. The laser was aligned to marks on patient skin. On right: the BAT cart was locked nearby the treatment couch and was registered to the machine gantry. The docking system (A): an easily removable block tray holder also called gantry cradle (B). From this position, the BAT could learn the position of treatment gantry and position of the isocenter.

Fig. 15. Two suprapubic images were acquired along axial plane and sagittal plane, respectively.
Fig. 16. On the touch-screen menu, the transverse and sagittal CT contours were shifted in 3D by the medical physicist or radiation oncologist until a satisfactory match was obtained.

D. The volumetric study by CT and TRUS in PSI patients

Our aim in developing a correlation by image fusion between the volume of prostate obtained from CT images and the same volume computed from transverse images from ultrasound was to gain the ability to do a 3D volumetric match between images of CT and BAT system instead of the current 2D transverse superimposition. This image fusion technique could provide information in Prostate seed implantation (PSI) cases where the seed implantation into the prostate is carried out using the transverse ultrasound images, where the post implant evaluation is performed using transverse images obtained from CT. The volumes computed from contours drawn on transverse ultrasound slices vs. those of CT almost never match and the volume computed from CT is typically larger by 10-15%. This is a significant discrepancy and causes errors in the assumed radiation coverage and follow-up evaluations. Even though the current BAT technique does not allow multiple transverse image acquisition for this evaluation, but the possibility exists to more accurately match the central axis CT contours with the largest axial slice from the ultrasound.
The PSI is one of the most promising treatment options for patients with carcinoma of the prostate. Patients who present with clinical T1-T3 (A to C) adenocarcinoma of the prostate may be considered for PSI. Patients who are at significant risk of having micro-metastatic disease to the pelvic lymph nodes are not appropriate candidates. The field of radiation is generally confined to the prostate. The real-time 3D interactive prostate seed implantation technique improved treatment outcomes and decreased treatment-related morbidity.

Blasko and Wallner have reported excellent, early PSA and biopsy control employing PSI\(^1\). The VariSeed™ application is a brachytherapy treatment-planning package for transperineal ultrasound–guided implants. The software package can carry out pre–operative planning, intra-operative planning, and post–operative evaluation of prostate cancer treatment courses.

1. **The prostate volumetric study based on Ultrasound images from intra-operative planning.**

   1) Transrectal ultrasound (TRUS) is used as the imaging modality. Patient is in the lithotomy position. After registration and creating a new study in Variseed 7.1, we select the type of ultrasound import, type of source and activity. Transverse mode is selected for determining prostate volume.

   2) In the Ultrasound acquisition, the ultrasound probe, attached to a tracked stepper unit, is advanced to the base of the bladder to identify the most proximal part of the prostate. It is best to keep the ultrasound frequency at 5 MHz so as not to miss any anterior tissue. The prostate volume study starts at the base of the prostate or superior to the base of the prostate. The probe is then moved caudally at 5 mm intervals, and
the process is continued until the apex is reached. A series of axial images are obtained (figure 17, left).

3) The probe is then switched to longitudinal imaging, and the prostate length is determined. The probe is rotated to the mid-line and the urethra is identified.

4) In the template registration process, the markers on the VariSeed template are aligned and overlaid with the markers displayed on the underlying image so that the image resolution and starting needle positions are determined. The same urologist outlines the anatomical structure contours such as prostate, urethra, and rectum (figure 17).

5) The volume of prostate can be identified from the 3D view or DVH (figure 18).

Fig. 17. Left: the template registration process. The markers on the VariSeed template was aligned and was overlaid with the markers displayed on the underlying image. Right: In 2D view, the urologist outlined anatomical structure contours such as prostate, urethra, and rectum.
2. Volumetric study based on CT images from post-implant evaluation.

1) CT images are taken after 2 - 4 weeks of implant procedure. Under the same patient name, a post-operative study is created. Then DICOM CT images are imported to the Variseed7.1 treatment-planning system through the Image Import (figure19). When CT image files are imported, the system extracts the scale, orientation, and spacing information directly from these files. The inter–image distance must be the same between each two consecutive images.

2) The procedure for outlining anatomical structures on CT images is the same as on intra-operative planning. For the most part, the oncologist finishes contouring instead of the urologist (figure19).

3) From the 3D view, the volume of prostate is determined on CT images (figure20).
Fig. 19. Creating a new study under the same patient, DICOM CT files were imported through the Image Import.

Fig. 20. Left: 2D view of CT images. Right: 3D view of CT images including Prostate (yellow), Bladder (white) and Rectum (blue).

3. Image fusion.
1) The image fusion feature enables importing image data from an existing VariSeed study (ultrasound Data). This is created as a new secondary image volume and is specified by a name. The original volume (CT images) is called “Primary”.

2) After a secondary image volume is imported, in Register Source Volume to Destination Volume, the Source (ultrasound) and the Destination (CT images) are designated. Using the registration tool to determine a transformation that aligned the secondary volume with the primary volume, the Source Volume (ultrasound) is merged with the Destination Volume (CT).

3) In the Least Squares, there are three views of each image volume (figure 21). The volume on top is the Destination Volume (CT images), and the one on the bottom is the Source Volume (Ultrasound images). From left to right, the displays are Sagittal, Transverse, and Coronal. In the Least Squares, three or more points that correspond to the Source and Destination volumes are identified. Then VariSeed calculates the transformation.

4) In the Import Secondary Structures (figure 22), the structures of interest from the secondary volume are selected. Each structure name, display color, and print color should be unique. Using the blending feature, the display of the fused images can be adjusted by changing the opacity of one volume in relation to the other. 2D images and 3D images are reviewed (figure 23)
Fig. 21. In the Least Squares, the volume on top was the Destination Volume (CT images), and the one on the bottom is the Source Volume (Ultrasound images). From left to right, the displays were Sagittal, Transverse, and Coronal. At least three points that corresponded between the Source and Destination volumes were identified.

Fig. 22. In the Import Secondary Structures, the structures interested from the secondary volume was selected. Each anatomical structure has a unique color.
Fig. 23. The fused images in 2D view (left) and in 3D view.

E. Statistical analysis

The data gathered in this study are represented by descriptive statistics. For all distributions, mean and standard deviations and thus the variances were calculated. Paired sample t test was used in comparison studies by SPSS program.
IV. RESULTS

Among the 18 pairs of studies, the mean X, Y, and Z displacements from the isocenter are plotted on figure 24. Nearly 95% of the data falls to within 1.96 (or approximately 2) standard deviations on each side of the mean. This result nearly matches Frank Van den Heuvel’s study. On table 1, based on the isocenter of DRR, the mean displacement from isocenter in the lateral, superior-inferior, and anterior-posterior direction are -1.463 ± 2.319 mm, -0.356 ± 1.170 mm, and -1.748 ± 1.811 respectively with 95% confident interval, the mean of total displacement is 6.630 ± 1.135 mm in 3D. For BAT images mean shifts are 0.872 ± 1.435 mm, 1.118 ± 0.929 mm and 0.432 ± 1.737 mm respectively; the mean of total displacement is 4.881 ± 1.025 mm in 3D. In the Paired-Samples t test (table 2), 95% confidence interval of the difference are -4.734 ~ 0.064, -2.807 ~ -0.141, and -5.244 ~ 0.885 respectively. In two group’s comparison study, the calculated P values are 0.056, 0.032, 0.152 and 0.009 in X, Y, Z coordinate and 3D respectively. We adopted a P= 0.05 significance and found that there are no significant differences in the X and Z directions, but significant differences in the Y direction and total displacement in two group studies do exist.

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Modality</th>
<th>N</th>
<th>Range (mm)</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral (X)</td>
<td>EPID</td>
<td>18</td>
<td>-8.3 to 6.1</td>
<td>-1.46</td>
<td>5.02</td>
<td>1.18</td>
</tr>
<tr>
<td></td>
<td>BAT</td>
<td>18</td>
<td>-5.42 to 6.48</td>
<td>0.87</td>
<td>3.1</td>
<td>0.73</td>
</tr>
<tr>
<td>Superior/Inferior (Y)</td>
<td>EPID</td>
<td>18</td>
<td>-5.25 to 4.75</td>
<td>-0.36</td>
<td>2.53</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>BAT</td>
<td>18</td>
<td>-2.32 to 4.45</td>
<td>1.12</td>
<td>2.01</td>
<td>0.47</td>
</tr>
<tr>
<td>Anterior/posterior (Z)</td>
<td>EPID</td>
<td>18</td>
<td>-8.72 to 4.88</td>
<td>-1.75</td>
<td>3.92</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>BAT</td>
<td>18</td>
<td>-8.06 to 6.33</td>
<td>0.43</td>
<td>3.76</td>
<td>0.89</td>
</tr>
<tr>
<td>Total shift in 3 D</td>
<td>EPID</td>
<td>18</td>
<td>1.92 to 10.29</td>
<td>6.63</td>
<td>2.46</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>BAT</td>
<td>18</td>
<td>1.14 to 9.29</td>
<td>4.88</td>
<td>2.22</td>
<td>0.52</td>
</tr>
</tbody>
</table>
Table 2. Paired-samples t test in SPSS if $\alpha<0.05$, significant difference

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>95% confidence Interval of the Difference</th>
<th>t value</th>
<th>df</th>
<th>Sig. (2tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pair 1</td>
<td>X</td>
<td>-2.34</td>
<td>4.82</td>
<td>-0.65</td>
<td>-4.73</td>
<td>0.06</td>
<td>0.06</td>
</tr>
<tr>
<td>Pair 2</td>
<td>Y</td>
<td>-1.47</td>
<td>2.68</td>
<td>-0.32</td>
<td>-2.81</td>
<td>-0.14</td>
<td>0.03</td>
</tr>
<tr>
<td>Pair 3</td>
<td>Z</td>
<td>-2.18</td>
<td>6.16</td>
<td>-0.49</td>
<td>-5.24</td>
<td>0.89</td>
<td>0.15</td>
</tr>
<tr>
<td>Pair 4</td>
<td>3 D</td>
<td>1.75</td>
<td>2.53</td>
<td>0.49</td>
<td>0.49</td>
<td>3.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Fig. 24. Plot of sample means and 95% confidence intervals.

The boxplot (figure 25) visualizes the distribution of parameters. It displays the median, the interquartile range, and the smallest and largest values in each study group. The box extends from 25th to 75th percentile. The line represents the median. The lower boundary of the box represents the 25th percentile, while the upper boundary represents the 75th percentile. The vertical length of the box represents the interquartile range. Fifty percent of all cases have values within the shadow box. Figures 26 and 27 show three-
dimensional views of patient shifts determined by EPID and BAT, with the various shifts starting at the initial setup point (0,0,0).

![Boxplot visualizing the distribution of a variable. It displays the median, the interquartile range, and the smallest and largest values for a group. Fifty percent of all cases have values within the shadow box.](image)

Fig.25. The boxplot visualizing the distribution of a variable. It displays the median, the interquartile range, and the smallest and largest values for a group. Fifty percent of all cases have values within the shadow box.
Fig.26. In three-dimension view, EPID shift variation between different patients included in this study. The center point (0,0,0) is an initially defined isocenter in CT image.

Fig.27. In three-dimension view, BAT shift variation between different patients included in this study. The center point (0,0,0) is an initially defined isocenter in CT image.
Table 3. Statistical data analysis in TRUS and CT

<table>
<thead>
<tr>
<th>Modalities</th>
<th>N</th>
<th>Mean</th>
<th>Std. Error of Mean</th>
<th>Median</th>
<th>Std. Deviation</th>
<th>Range cm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRUS</td>
<td>11.00</td>
<td>35.56</td>
<td>4.58</td>
<td>31.03</td>
<td>15.20</td>
<td>17.09-61.06</td>
</tr>
<tr>
<td>CT</td>
<td>11.00</td>
<td>38.20</td>
<td>4.04</td>
<td>32.48</td>
<td>13.41</td>
<td>21.13-65.24</td>
</tr>
</tbody>
</table>

Table 4. Paired-samples t test in TRUS/US volumetric study if α=<0.05, significant difference

<table>
<thead>
<tr>
<th>Different Volume (cm³)</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error of Mean</th>
<th>95% confidence Interval of the Difference</th>
<th>t value</th>
<th>df</th>
<th>Sig. (2tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRUS/US</td>
<td>-2.64</td>
<td>5.55</td>
<td>1.67</td>
<td>-6.37</td>
<td>-1.58</td>
<td>10</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Fig. 28. Plot and Pearson correlation of CT and TRUS measurements.

Prostate volume estimates from TRUS and CT (figure 28) correlates strongly with each other (Pearson’s correlation coefficient = 0.932, p < .0001). The CT volumes are consistently larger than TRUS volumes (table 3). The mean TRUS volume is 35.56 cm³ (median 31.03) and the mean CT volume is 38.20 cm³ (median 32.48). On average, CT overestimates the prostate volume by 14.96% compared with the TRUS volume.
In comparison of TRUS/ US volumetric study, we used paired-samples t test in SPSS statistical software. A significance $\alpha=0.05$ was adopted and the calculated P value was 0.15. Since the value of calculation was larger than 0.05, the hypothesis of no significant differences between two image modalities was accepted.
V. DISCUSSION

Numerous studies have characterized the magnitude and nature of setup errors for a variety of clinical conditions. Random and systematic errors of up to 6 mm have been reported in previous studies. Variation of patient’s position and internal organ motions limit the efficiency of the delivery of IMRT in daily treatment.

1. EPID and BAT ultrasound

Since the late 1980, the rapid development of EPID adapted to linear accelerators has provided a new imaging modality. EPID techniques have improved and facilitated treatment verification compared with the conventionally used port film. With EPID, image acquisition is more rapid than portal films. Multiple images per fraction and their dynamic therapy are possible. Images are saved on optical disks without film manipulation, development, and storage. However, the efficiency of megavoltage x-ray detection still poses a major limit to the image quality. Although the quantum efficiency (QE) of the detector has been increased from 2% to 3% to about 18%, several monitor units (MUs) may have to be delivered to obtain an image of sufficient quality. Consequently, such image acquisitions could not be done on a daily basis. The limited times of EPID acquisition (once a week) could affect the accuracy of localization and the efficiency of dose delivery. Another limitation of the EPID is non-flexible fields required by the some types of treatments. Furthermore, the most significant limitation is that EPID can only compare anatomical structures presented on orthogonal images with DRR.
images or simulation X-film. Usually the isocenter is defined as the center of the target. Although in DRR images, the position of prostate or isocenter is related to the bony anatomies in the pelvis, EPID matching bone anatomies with DRR images does not account for the volume changes and internal organ motions. In fact, the day-to-day prostate mobility due to organ motions is about 4 mm (SD) in the AP and superior-inferior (SI) directions and 2 mm (SD) in the lateral direction. Prostate motions relative to the bony pelvis have been related to physiologic changes of rectum and to a lesser degree the bladder, or a response to the state of rectal and/or bladder filling. Daily motion is comparatively less in the lateral than in the anterior/posterior and superior/inferior dimensions. Our study partially agrees with those previous studies. From the pair sample t test (table 4), there is a significant difference in superior/inferior between both modalities. It is interpreted that when the BAT ultrasound is used, the superior/inferior motion of prostate could be detected predominantly than using EPID.

2. Function of targeting in CT and BAT ultrasound

Computed tomography has been regarded as a reliable and accurate radiographic tool to discern soft tissue structures and precisely correct field placement error. In Joseph Lattanzi’s study, using daily CT localization to improve daily target localization in prostate carcinoma comparing with the BAT ultrasound system, they found that BAT imaging was comparable to CT imaging for targeting purposes, and the absolute magnitude differences between CT and ultrasound measured shifts were small. However, CT is relatively static. The volume of prostate based on CT images in treatment planning system may not be the same as the volume acquired by the ultrasound at the moment of
treatment due to organ motions. BAT ultrasound images matching with CT contours may not be accurate relatively in this situation. In Lattanzi’s previous study, the discrepancies were attributed to organ movements between the acquisition of the CT data and the ultrasound measurement. In their follow-up study, the ultrasound measurements were taken in the CT suite and the discrepancies apparently disappeared\(^4\). Because of this limitation, the patient must remain immobilized during transport from the simulation room to the treatment room. The volume of prostate has to be determined not only for planning but also during treatment. Also, CT is inaccurate and highly observer-dependent for the localization of the prostatic apex\(^8\). As another limitation, serial CT examinations are costly both in terms of technical and personnel resources.

In contrast, BAT technique actually acquires a pair of orthogonal images that the maximal sectional anatomies, such as prostate, rectum and bladder, will be required and can be compared with the contours of CT images. As long as anatomical contours in both images are matched, the same isocenter is located in the BAT system. The BAT ultrasound system produces good quality images with minimal operator training required. In average, the time for the completed localization process is about 5 minutes. The BAT ultrasound is noninvasive and satisfies the ALARA (As Low As Reasonably Achievable) principle, which is important to optimize the equipment and methods to give as little radiation as possible. In the disadvantage, the inability to maintain a full bladder may cause uncertainties in the volume of prostate. Operator dependency has been investigated by a number of groups. The operator dependency is most likely a combination of the following causes: Error propagation of the CT delineation both systematic and stochastic.
errors, depending on the slice chosen by the operator; User error in identification of structures by ultrasound; and User error in alignment of structures.

3. Consistency between two modalities by volumetric study

Based on volume locations determined from CT images, we are able to adjust ultrasound images to achieve the patient’s positioning and localization. In order to have a precise match on both images, the evaluation of the volumetric consistency between these two imaging modalities is significant. The transrectal ultrasound (TRUS) can reconstruct a series of axial images and determine the volume of the prostate. The volume of prostate based upon TRUS images from intra-operative planning was used to compare with those based on CT images from post-operative evaluation in PSI patients. Previously two small studies suggested that TRUS underestimates the pathologic volume by 10-16%.19,20 This result is in agreement with our study (14.96%). In other studies, Narayana and Hoffelt found CT prostate volume were 47% and 50% respectively larger than the US21,22. The overestimation (7 out of 11 cases) of the prostate volume by CT exists in our study. This indicates that more normal tissues might receive the prescription dose if CT is used to determine the volume. In a contradictory study, Badiozamani et al found that there was close agreement between those two-image modalities, and the large volume on CT image was attributed to the puborectalis muscle and anterior venous plexus included in the target prostate volume25.

Also, some studies have mentioned that the delineation of the prostate using CT is highly dependent on the user’s subjective judgement17. Particularly, it is difficult in
distinguishing the prostate base from the bladder wall and the prostate apex from the penile bulb on CT images\textsuperscript{22}; the posterior edge of the prostate from the anterior wall of the rectum; and the superior edge of the prostate from the bladder\textsuperscript{26}. Since most post-implant CT images were captured in 2 – 4 weeks after implant procedure, the prostate swelling could be ruled out. Clinically the prostate is visible to the trained eye in both modalities. In the test phantoms, we can easily assess and identify the contained structures because of its uniformity and symmetry (figure 29). However, the phantoms used to study the efficacy and quality control are not subject to organ motion between measurements.

Fig.29. In the CIRS Model 053 Ultrasound prostate training phantom, the images were captured by ultrasound (A and B images from CIRS website) and CT (C: 2D view and D: 3D view).

In our further statistical study, paired sample t test was used to analyze the hypothesis of no significant difference between the two modalities. It indicates that there is no
significant difference between those two modalities, based in volumetric study. In figure 23, from 2D and 3D views it visualizes that two volumes of prostate were fused very well. This is from another point of view to prove the similarity between two image modalities. However, for CT based images, the tight contouring should be suggested in order to get a more accurate dosimetry evaluation and get a more precise matching with BAT images in patient positioning.

In this study, some drawbacks will be considered by neglects of systematic errors, random errors, delineation contours in EPID, CT and ultrasound images and a limited sample size. The quality of ultrasound images may not be reliable because of differences in training and techniques of the therapists who captured those images. In future work, more cases should be studied and included in order to get a more accurate statistical analysis with restricted methodology. In addition, we may prove BAT ultrasound to be useful and practical in other anatomical sites where daily localization and correction of target movement is critical for treatment, such as in the treatment of breast cancer.
VI. CONCLUSION

Ultrasound targeting is not only a fast and effective method to detect organ motion and setup inaccuracies, but also it is simple to operate, relatively inexpensive, and harmless to the patient. The application of this technology allows treatment margins and the amount of normal tissue in the radiation field to be reduced while ensuring that the prostate target is covered each day. Since a strong correlation is found between CT and TRUS and there is no significant difference in volumetric study, considering the benefits and lack of significant risks, BAT ultrasound is recommended as a standard tool in radiotherapy, especially for the conformal therapy. In addition, with some accessory software such as VariSeed 7.1, image fusion becomes visible and helps in the easy evaluation of the volume in image volumetric study.

ACKNOWLEDGMENT

I would like to thank Dr. E. Ishmael Parsai, Dan Schifter, Dr. Abhinit Priyadershi and Dr. William Mccoll in department of radiation oncology, Dr. Dennis in department of radiology in Medical College of Ohio. Also I really appreciate my wife who has been supporting me through these years.
REFERENCE


