



## Transabdominal Ultrasonography-Based Image Guidance during External Beam Radiotherapy for Cervical Cancer - An Initial Experience

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### Abstract

**Introduction:** Utero-cervical organ motion during External Beam Radiotherapy (EBRT) of cervical cancers poses a major challenge in treatment delivery. Accurate assessment of such organ motion is essential to derive appropriate internal target volume. We evaluated Trans-Abdominal Ultrasonography (TAUS) based image-guided radiotherapy system - 'Clarity<sup>®</sup> (Elekta)' for cervical cancer to estimate the magnitude and directions of the utero-cervical organ motion.

**Methods:** Fifteen patients of locally advanced cervical cancers planned for radical radio (chemo) therapy consented to this observational study. All underwent TAUS to determine the position of utero-cervical complex using the Clarity system during radiotherapy simulation. At the time of radiotherapy treatment delivery, the set-up errors were corrected using Cone-Beam Computed Tomography (CBCT), and then the position of utero-cervical complex was compared to that of simulation again using the Clarity TAUS system. The shifts of utero-cervical complex were documented in various directions and compiled for analysis.

**Results:** A total of 72 (73%) of 98 image sets were evaluable. The mean shifts for utero-cervical motion ranged from 3.2 ( $\pm$  7.6) mm to 10.7 ( $\pm$  10.5) mm. The organ motion was higher in anterior and superior directions [10.7 ( $\pm$  10.5) mm and 9.7 ( $\pm$  17.9) mm respectively] and also was higher during the latter part of the radiation treatment course.

**Conclusion:** TAUS combined with CBCT appears to be a feasible tool for image guidance and to assess uterocervical organ motion during EBRT for cervical cancers. In our initial results, organ motion appears to be variable depending on the direction of motion and timeline during the course of treatment.

### Introduction

Radio (Chemo) therapy is the treatment of choice for locally advanced cervical cancers. Precision radiotherapy has potential to improve therapeutic ratio and optimal image guidance is essential component of precision radiotherapy. Various methods for image guidance during External Beam Radiation Therapy (EBRT) including on-board radiographs, Computed Tomography (CT), Magnetic Resonance Imaging (MRI) etc. have been currently implemented in the routine clinical practice [1]. Precise delivery of EBRT for cervical cancers is challenging and the internal organ motion resulting from utero-cervical movements, tumor regression and variation in bladder/rectal filling lead to uncertainties in accurate treatment delivery. Daily variation in utero-cervical position can be substantial and is a major concern during conformal external radiation for cervical cancers. A number of image guidance methods including on-board radiographs, CT and MRI have been used to assess utero-cervical organ motion [2-4]. Ultrasonography (US) has been a viable imaging modality that has been widely applied in Gynecology practice for visualization of utero-cervical complex [5,6]. US are associated with better soft tissue visualization and comparable to MRI for cervical cancer [5,6]. US can be a valid option for image guidance during EBRT for cervical cancers and it has also been successfully implemented in prostate radiotherapy [7]. On similar principles, we evaluated commercially available US based Image-Guided Radiotherapy (IGRT) system i.e., Clarity<sup>®</sup> (Elekta) for cervical cancer.

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## Materials and Methods

After obtaining approval from institutional ethics committee, patients with histologically proven cervical cancers with stages IIB and IIIB (FIGO 2009) planned for radio (chemo) therapy were accrued between January-2014 to April-2014.

All patients underwent routine CT based radiotherapy planning and treatment. In addition, Transabdominal US (TAUS) was performed during simulation as well as during treatment delivery using US based IGRT system–Clarity® (Elekta). Using this system, utero-cervical position at the time of planning was matched with that of treatment delivery. The details of simulation and acquisition of images are as follows.

### Radiotherapy simulation

All patients underwent radiotherapy planning CT scan in supine position with knee rest. Bladder protocol consisted of emptying of bladder 45 min prior to scan and intake of 750 ml to 1000 ml of water after bladder emptying. Patients were also asked to empty the bowels before simulation.

### TAUS image acquisition using Clarity® system

Clarity® (Elekta) IGRT system consists of

- Ultrasound image acquisition station with curvilinear probe with infrared reflectors on probe
- Clarity® supported Non-Destructive Inspection (NDI) - A ceiling mounted infrared camera
- Ultrasound image calibration phantom

This system is designed for calibration and synchronization of isocenter of both CT simulator and Clarity®. After calibration of isocenter, planning CT was performed followed by acquisition of TAUS images in both axial and sagittal plane. The TAUS images were then transferred to Clarity® Automatic Fusion and Contouring (AFC) workstation and outline of cervix and uterus was delineated and termed as Reference Positioning Volume (RPV). RPV acts as reference position of utero-cervical organ at the time of radiotherapy planning which can be used to compare and document shifts that occur during treatment delivery session (Figure 1).

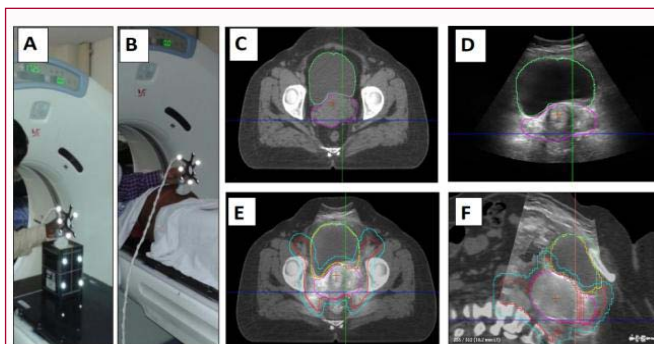
### Documentation of utero-cervical organ motion during treatment delivery

The isocenters were calibrated again at treatment delivery couch. Patient was positioned after ensuring same bladder and rectal filling protocols that were used while radiotherapy planning. First, a CBCT was performed and matched for pelvic bones/vessels to rectify the setup errors. Then, TAUS images were acquired in a similar fashion as that during CT planning. The outline of utero-cervix obtained at treatment delivery was matched with RPV and the shifts were documented in six directions: right-left (+X, -X), antero-posterior (+Y, -Y) and superior-inferior (+Z, -Z) (Figure 2). TAUS was performed 2 to 3 times a week during EBRT and these shifts were compiled and analyzed. We report our initial experience on feasibility and preliminary data on utero-cervical positional uncertainties in this article.

## Results

### Demographic details

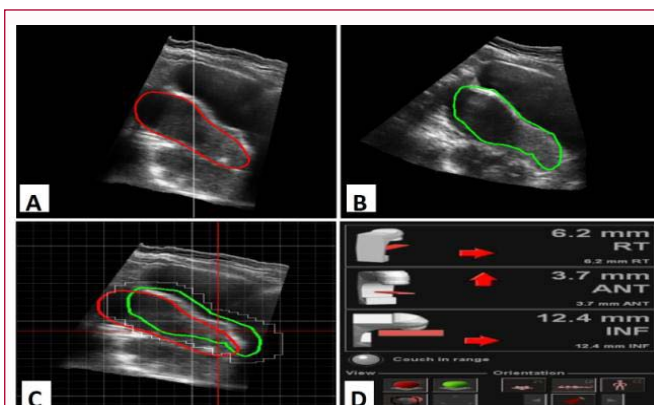
A total of 15 women with the International Federation of Gynecology and Obstetrics (FIGO, 2009) stage II (53%) and stage III



**Figure 1:** Trans-Abdominal Ultrasonography (TAUS) image acquisition and fusion. [A, B: Calibration of TAUS with iso-center of simulator; C-F: Co-registration of TAUS and Computed Tomography (CT) images and contours acquired at the time of planning.

**Table 1:** Shifts obtained after matching using Cone-Beam Computed Tomography (CBCT) and Trans-Abdominal Ultrasonography (TAUS).

Directions	Mean CBCT shifts in mm (SD) after bony match (Setup errors)	Mean TAUS shifts in mm (SD) after utero-cervical match (Organ motion)
+X (Right)	3.0 (3.2)	4.3 (6.7)
-X (Left)	6.3 (3.4)	3.5 (5.5)
+Y (Anterior)	3.8 (3.0)	10.7 (10.5)
-Y (Posterior)	3.5 (3.8)	3.2 (7.6)
+Z (Superior)	2.2 (2.0)	9.7 (17.9)
-Z (Inferior)	4.1 (2.4)	6.6 (8.5)



**Figure 2:** Matching of on-board Trans-abdominal ultrasonography images with reference (planning) volumes and derivation of shifts. Position of utero-cervical complex at the time of treatment delivery (red contours: A) are matched with position at the time of simulation which are termed reference positioning volume (green contours: B). Shifts between the positions are derived in various directions (C-D).

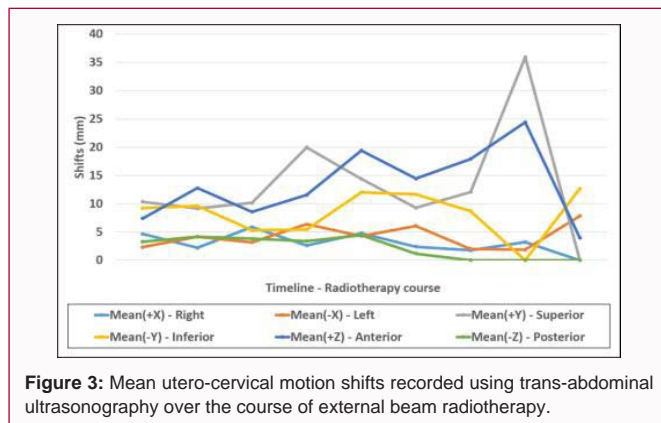
(47%) were accrued in the study. The median age was 55 years.

### Feasibility of the TAUS based IGRT process

A total of 98 image-sets (CBCT/TAUS) were available for matching. Twenty-six (26.5%) TAUS image sets were not evaluable in view of image quality concerns as a result of bowel gas or poor bladder filling. Hence, only 72 Image sets were included for the final analysis to derive organ motion. Median number of image sets (CBCT and TAUS pairs) acquired per patient was 7 (range 3 to 10). Mean number of evaluable image data sets per patient were 4.8 (3 to 10).

### Uterocervical motion

The setup errors were in the range of 2.2 mm to 6.3 mm for



the pelvic bony match and blood vessels (Table 1). The mean shifts for utero-cervical motion as detected by TAUS was in the range of 3.2 mm to 10.7 mm. Table 1 shows in detail the mean  $\pm$  Standard Deviation (SD) for CBCT and TAUS matching in each direction. Overall, the mean ( $\pm$  SD) shifts were higher in anterior and superior directions [10.7 ( $\pm$  10.5) and 9.7 ( $\pm$  17.9) respectively].

#### Temporal variation of uterocervical motion during radiotherapy course

The uterocervical organ motion was also variable over the course of radiotherapy course. Organ motion was as high as 36 mm and 24 mm in superior and anterior directions respectively during the latter half of the radiotherapy treatment course. Shifts in right and left directions seem to be stable throughout the course of treatment (Figure 3).

### Discussion

Our initial experience suggests the feasibility of utilization of TAUS based IGRT system to evaluate uterocervical organ position uncertainties during the course of external beam radiation for cervical cancers.

#### The highlights of our study include

Feasibility of integration of TAUS based image guidance in the existing IGRT systems; Documentation of shifts in various directions along the course of radiation therapy.

One of the limitations of use of TAUS for image guidance is an image quality issue which was seen in a proportion of our image sets. This is related to poor bladder filling or bowel gas affecting the quality of sonography images leading to poor quality images. There is a need to address this issue to consider implementation of TAUS as an image guidance tool in routine clinical practice. One also needs to account for inter-observer variations in interpretation of TAUS images. Uses of Auto-scan probe may improve inter observer variation as shown by Baker et al. [8]. The probe pressure on abdomen during TAUS may also influence organ motion and possible could have influenced the results of our study [9]. Despite the limitations of using TAUS, it can be a valuable tool for uterocervical motion assessment and image guidance [10,11]. Also, the integration of CBCT and TAUS based image guidance during EBRT for cervical cancer has a potential as an optimal image guidance protocol [12].

In our preliminary results, we demonstrated the extent of uterocervical organ motion. We aimed at evaluating the inter-fraction utero-cervical motions after correction of setup errors using CBCTs to address the Internal Target Volume margins using TAUS. The

shifts were systematically more in anterior-superior directions and the variations were more pronounced in the latter half of treatment course. This may be related to variable bladder and rectal fillings during course of EBRT which has been reported earlier [4]. It is also highly likely that tumor regression influences uterocervical positional uncertainties during latter part of radiotherapy course. Detailed analysis of uncertainties, factors influencing the organ motion and assessment of internal margins were not a part of this feasibility study. This can be done once the robustness of ultrasonography in image guidance for cervical cancer radiotherapy is established.

### Conclusion

The use of TAUS based image-guidance in radio-therapeutic management of cervical cancer appears feasible. Our study provides the proof of principle for the use of TAUS in combination with CBCT in image guidance during EBRT for cervical cancers. Considerable organ motion can potentially influence precise delivery of radiation particularly during the latter part of treatment course. Further clinical studies using TAUS to generate robust data and validation is warranted before incorporation in routine IGRT practice.

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