Inter-operator Variability in Defining Uterine Position Using Three-dimensional Ultrasound Imaging

Mariwan Baker*†‡, Jørgen Arendt Jensen† and Claus F. Behrens*

*Herlev Hospital, Department of Oncology(R) Herlev Ringvej 75, DK-2730 Herlev, Denmark
†Center for Fast Ultrasound Imaging, Dept. of Elec. Eng., Technical University of Denmark, DK-2800 Lyngby, Denmark
‡Center for Nuclear Technologies, Technical University of Denmark, DTU Risø Campus, DK-4000 Roskilde, Denmark.

***Abstract*—In radiotherapy the treatment outcome of gynecological (GYN) cancer patients is crucially related to reproducibility of the actual uterine position. This study is to evaluate the inter-operator variability in addressing uterine position using a novel 3-D ultrasound (US) system. The study is initiated by US-scanning of a uterine phantom (CIRS 404, Universal Medical, Norwood, USA) by seven experienced US operators. The phantom represents a female pelvic region, containing a uterus, bladder and rectal landmarks readily definable in the acquired US-scans. The organs are subjected to displacement by applied operator-pressure that mimics an actual GYN patient. The transabdominal scanning was performed using a 3D-US system (Clarity® Model 310C00, Elekta, Montreal, Canada). It consists of a US acquisition-station, workstation, and a 128-element 1D array curved probe. The iterated US-scans were performed in four subsequent sessions (totally 21 US-scans) in a period of four weeks to investigate the randomness of the inter-operator variability. An additionally US-scan was performed as a reference target volume to the consecutive scans. At first, the phantom was marked with ball bearings for daily laser alignment. In each session the US-scans were acquired by the seven operators. The uterus was outlined in each of the US image-sets using Clarity autosegmentation in the workstation. Further, the shifts in the uterine centre of mass relative to the reference were measured for the three orthogonal directions; left (+)-right (LR), anterior (+)-posterior (AP), and inferior (+)-superior (IS), respectively. The same operator delineated the target volumes. The average inter-operator deviation $\pm$1SD of the daily US scans was (in mm); LR: day 1 (-0.4$\pm$0.9), day 2 (-0.3$\pm$0.6), day 3 (-1.0$\pm$1.2), day 4 (1.3$\pm$0.5); AP: day 1 (0.0$\pm$1.7), day 2 (0.1$\pm$0.7), day 3 (-1.0$\pm$0.9), day 4 (0.2$\pm$1.2); IS: day 1 (-1.5$\pm$2.6), day 2 (0.1$\pm$1.8), day 3 (0.1$\pm$1.1), day 4 (0.5$\pm$3.1), respectively. The largest inter-operator discordance was observed to be 4.7 mm in the IS-direction in day 4. Published studies report significantly larger inter-fractional uterine positional displacement, in some cases up to 20 mm, which outweighs the magnitude of current inter-operator variations. Thus, the current US-phantom-study suggests that the inter-operator variability in addressing uterine position is clinically irrelevant.**

I. Introduction

In modern adaptive conformal radiotherapy with tight margins and steep dose gradients, such as intensity-modulated radiotherapy (IMRT), it is essential that the position of the clinical target volume (CTV) is precisely defined prior to each treatment fraction throughout the entire course of treatment. Recent technical innovations have enabled the direct integration of various image verification methods into the linear accelerator (LINAC). This allows patient and tumour positioning to be addressed and corrected. Nowadays, kilovoltage (kV) and megavoltage (MV) planar radiographic imaging, and kV volumetric cone beam CT imaging are standard image verification systems in many radiotherapy centres. Generally, these systems are implemented as Image Guided Radiation Therapy (IGRT) for daily target alignment, which enables correction of position misalignment, thereby improving the precision of radiation treatment [1]. However, the challenge of using these ionizing systems is insufficient soft tissue visualization, for instance of the uterus of GYN cancer patients. In some cases these systems require invasive methods, such as implanted fiducial markers in prostate radiotherapy [2]. Therefore, different non-ionizing 3-D ultrasound (3D-US) systems, such as the Elekta 3D Clarity® Soft Tissue Visualization system and the NOMOS B-mode Acquisition and Targeting (BAT) ultrasound system have been developed and introduced into radiotherapy for different cancer sites [3]–[5]. However, these US-systems have been found to be only applicable for cancer sites in soft tissue environments such as in GYN, prostate and postoperative lumpectomy cavity cancer patients. The uterus, where internal position variations are dependent on rectal and bladder filling, is an ideal site for US-scans. Some uncertainty factors such as inter-operator variability due to probe handling are present when using the US-system. Variations in the transducer probe pressure applied have previously been documented during 3D-US scan on prostate patients [6], [7].

The aim of the present study was to quantify the inter-operator variability using the Clarity US-system on a commercial GYN-phantom.

II. Materials and Methods

A phantom was scanned by seven operators in the course of four sessions over a period of four weeks (one session per week), a total of 21 scans (All the operators were not presented for each session). Each radiation therapist (RTT) participated in two weeks of intensive training provided by the manufacturer of Clarity as well as several practice sessions before the start of the study.

A. Phantom

The ultrasound training phantom (CIRS 404, Universal Medical, Norwood, USA) mimics the female pelvic region and

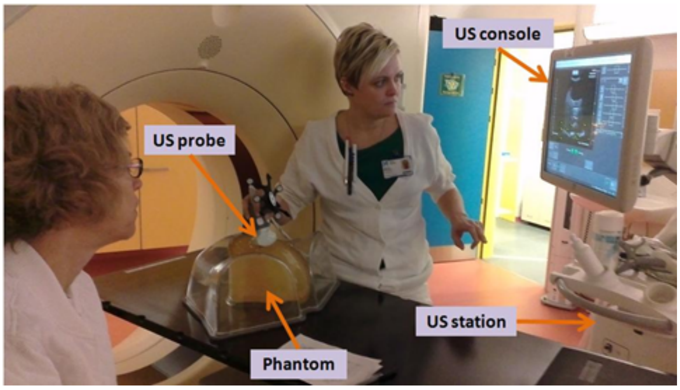

Figure 1. Phantom scanning is performed by means of a convex array probe in the CT-room. Real-time images can be visualized on the US console mounted on the US station.

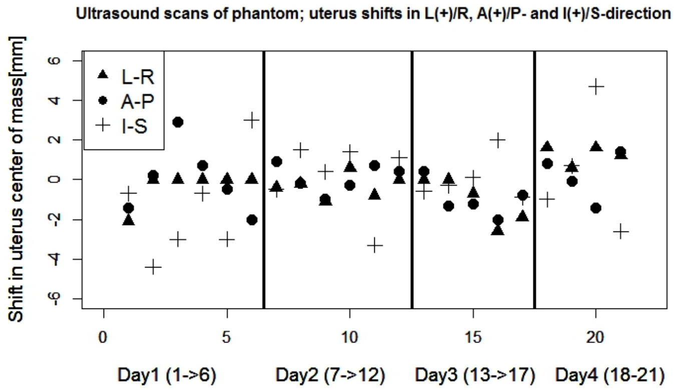

Figure 2. Daily US scans (day 1: 6 operators, day 2: 6 operators, day 3: 5operators, and day 4 only 4 operators). The plot shows uterine COM shifts in the L/R, A/P and I/S directions.

contains a uterus, bladder and rectum representing the standard female pelvic organs (Fig. 1). The organs are subjected to displacement of the exerted probe pressure. The phantom does not contain any skeletal structure such as femur head or pelvic bone. The phantom is constructed of material that is intended for ultrasound scans, thus all organs are easily defined in the acquired US-images. Initially, the phantom was marked with small spherical ball bearings (laser alignment markers), used to aid reproducibility of daily set-up prior to each US-scan session. Use of this technique requires acquisition of a reference US image data-set, and therefore during an initial session the best possible US-scan was selected as position reference to the following four consecutive sessions.

B. Clarity Ultrasound System

The Clarity ultrasound system (Clarity® Model 310C00, Elekta, Montreal, Canada)consists of two US-units: one located in the Computed Tomography (CT) simulation room and one in the treatment room. The two units are connected through a workstation/server. In this study all US-scans were performed in the CT room. Since the objective of the ongoing project at Herlev hospital is to implement the Clarity 3D-US system for both GYN and prostate patients throughout the course of their treatment, the treatment room unit will be utilized for daily IGRT. Each US-unit is equipped with a convex array probe for trans-abdominal 3D US-scanning. Every station consists of a ceiling-mounted infrared (IR) camera that can track the US-probe by monitoring the IR-reflectors/emitters mounted on it. The transducer probe consists of a 128-element 1-D array. To enable superimposition of the acquired 3D-US images to the reference US-image sets, the 3D-US system is calibrated to the same coordinate system as the CT and treatment rooms, respectively. The calibration procedure is accomplished by means of an alignment phantom. Quality assurance checks confirm the system calibration on each day of use. The daily check is passed only when the calibration precision is less than 1 mm.

C. Image Acquisition

The ultrasound image of the phantom (trans-abdominal US-scan) was acquired by all the seven experienced RTTs using the convex array probe. In each phantom scan the US-probe was placed on the first occasion with moderate pressure in the region corresponding to the pubic symphysis and rotated, after which it was swept cranially. Afterwards, the acquired image-sets were reconstructed, and the uterus, bladder and rectum were identified.

D. Organ Delineation and Data Analysis

The uterus, bladder and rectum were delineated in the reconstructed 3D US-image data sets using the Clarity work-station supplied by the manufacturer. In the workstation the delineation can be performed either manually or with aid of auto-segmentation. In this study the assisted segmentation was utilized for all outlined organs. A single operator (MB) conducted a retrospective analysis of the acquired US-image sets and delineated the organs. Descriptive statistics and a single-sample t-test was conducted for the phantom scans. Background variables such as alpha, null and alternative hypothesis, standard deviation (SD) and variance are described using descriptive statistics.

III. Results

A total of 21 US-scans were acquired by the same seven operators over the four sessions.The daily US scans is plotted during the four days and for all presented operators (Fig. 2).

Positional uterine Center of Mass (COM) shifts, in three orthogonal directions and of four days are plotted (Fig. 3). Positive shifts are left, anterior, and inferior. Qualitatively, these plots demonstrate that there are not significant differences in the shifts comparing mean of COM shifts, i.e. mean of the session scans for each day. One can observe that, in each direction (L/R, A/P, and I/S), the results are roughly centred about zero. The mean $\pm$SD of the daily phantom COM-shifts (average inter-operator deviation) was (mm): LR: day 1 (-0.4$\pm$0.9), day 2 (-0.3$\pm$0.6), day 3 (-1.0$\pm$1.2), day 4 (1.3$\pm$0.5); AP: day 1 (0.0$\pm$1.7), day 2 (0.1$\pm$0.7), day 3 (-1.0$\pm$0.9), day 4 (0.2$\pm$1.2); IS: day 1 (-1.5$\pm$2.6), day 2 (0.1$\pm$1.8), day 3 (0.1$\pm$1.1), day 4 (0.5$\pm$3.1), respectively. The largest inter-operator discordance was observed to be 4.7 mm in the IS-direction in day 4. None of the p-values for the three directions is smaller than 0.05. The largest lower/upper range of 95% CI is in I/S-direction in day 4 (-4.54–+5.44) (Fig. 4).

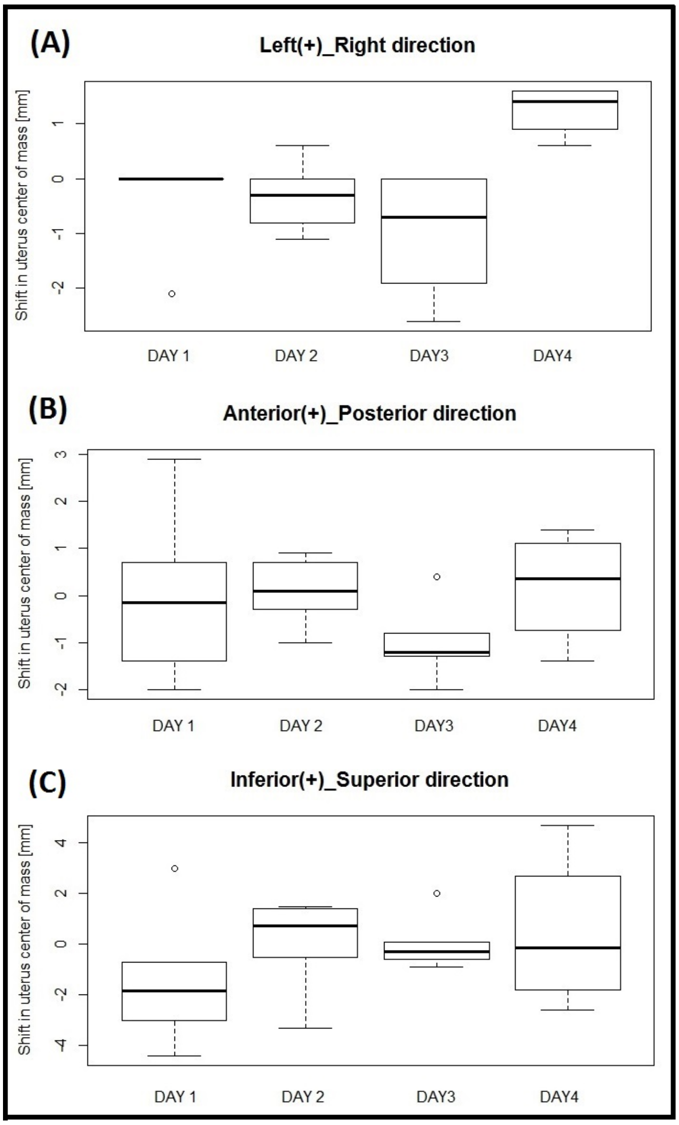

Figure 3. (A), (B) and (C): box-plots of uterine COM-shifts for the phantom on four days in the three cardinal directions; L/R, A/P, and I/S.

IV. Discussion

Inter-fractional positional uncertainty of the uterus, rectum and bladder of GYN patients has been a challenge in radiotherapy, and leads to larger applied set-up margins to account for the target displacement. Recently developed highly conformal (IMRT) treatment enables better dose conformity, thus steeper dose gradients. This means that the delineated CTV and organ at risks (OAR) are more susceptible to the uterine positional displacement. Uterine positional changes have been confirmed in previous reports to be strongly correlated to the daily variations in rectal-bladder filling [8], [9].

Recently, 3D-US is more frequently applied as IGRT-method. It has been used mostly in prostate alignment prior to the treatment fraction. Only few published papers are reporting the application of 3D-US on GYN-patients [10]–[12], but the focus is on quantifying inter-fractional bladder motion and variation in bladder volume rather than uterine positional change. Herlev Hospital is a pioneer in the application of a

		N	SD	Mean	df	t	95%CI (Lower/Upper)	P-value
	Direction of shifts							
Day1	Left-Right	6	0.86	-0.35	5	-1.00	-1.25/0.55	0.36
	Anterior-Posterior	6	1.74	-0.02	5	-0.02	-1.84/1.81	0.98
	Inferior-Superior	6	2.62	-1.47	5	-1.37	-4.22/1.28	0.23
Day2	Left-Right	6	0.60	-0.32	5	-1.29	-0.95/0.31	0.25
	Anterior-Posterior	6	0.71	0.08	5	0.29	-0.67/0.83	0.79
	Inferior-Superior	6	1.83	0.10	5	0.13	-1.82/2.02	0.90
Day3	Left-Right	5	1.17	-1.04	4	-1.99	-2.49/0.41	0.12
	Anterior-Posterior	5	0.88	-0.98	4	-2.48	-2.08/0.12	0.07
	Inferior-Superior	5	1.15	0.06	4	0.12	-1.36/1.48	0.91
Day4	Left-Right	4	0.47	1.25	3	5.29	050/2.00	0.01
	Anterior-Posterior	4	1.22	0.18	3	0.29	-1.76/2.11	0.79
	Inferior-Superior	4	3.14	0.45	3	0.29	-4.54/5.44	0.79

Figure 4. Tabulates values of one sample t.test of obtained uterine shifts using ultrasound scans of a phantom.

novel Clarity 3D-US system with focus on GYN diagnoses. The present study started by applying Clarity on a phantom and it will subsequently be used for GYN patients at Herlev. Different studies on the prostate have concluded that one of the drawbacks of using 3D-US as the IGRT method is probe pressure induced uncertainty of the target and OAR, and the variation in the probe handling by the observers. The challenge experienced by most of our operators during 3D US acquisition was to find an appropriate probe handling technique that captured the entire uterus from the cervical os to the fundus, as the image quality was poor in some cases. Obviously, poor image quality has an adverse influence on uterus delineation, thus leading to uncertainty about COM shifts.
In the present phantom study, we found no statistically significant differences in uterine COM shifts in the term of inter-observer variability (sample t-test with a 95% CI). All the acquired US-scans indicated that uterine COM displacements are in the vicinity of zero, with a daily mean value of less than 2 mm in all three cardinal directions (L/R, A/P and I/S). The recent study paper by Jurgenliemk-Schultz et al., [13], which investigated vaginal positional change and the correlation between vaginal shift and bladder-rectal filling, reported a daily vaginal CTV positional change of up to 2.3 cm in the A/P direction. In another study Chan et al., [14], report that the uterine head (fundus) can vary from day to day by over 24 mm. This large inter-fractional vaginal and uterine positional displacement outweighs the magnitude of our inter-operator variability.

V. Conclusions

Published studies report significantly larger inter-fractional uterine positional displacement, over 20 mm in some directions, which outweighs the magnitude of the current inter-operator variations. Thus, the current US-phantom-study suggests that the inter-operator variability in determining uterine position is clinically irrelevant.

ACKNOWLEDGEMENT

Sincere thanks to our hard-working colleagues who helped to conduct this study; Gullander L. (RTT), Pedersen S. K (RTT),

Zarp T (RTT), Jacobsson S (RTT), Pazhang S (radiographer), and Lynnerup V. K (radiographer).

CONFLICT OF INTEREST

The current study is a part of three years PhD research project at Herlev that is supported by Elekta, Inc.

REFERENCES

[1] T. R. Mackie, J. Kapatoes, K. Ruchala, W. Lu, C. Wu, G. Olivera, L. Forrest, W. Tome, J. Welsh, R. Jeraj, P. Harari, P. Reckwerdt, B. Paliwal, and M. Ritter, "Image guidance for precise conformal radiotherapy," *International journal of radiation oncology, biology, physics*, vol. 56, no. 1, pp. 89–105, May 2003. [Online]. Available: http://linkinghub.elsevier.com/retrieve/pii/S0360301603000907

[2] D. Litzenberg, L. a. Dawson, H. Sandler, M. G. Sanda, D. L. McShan, R. K. Ten Haken, K. L. Lam, K. K. Brock, and J. M. Balter, "Daily prostate targeting using implanted radiopaque markers," *International journal of radiation oncology, biology, physics*, vol. 52, no. 3, pp. 699–703, March 2002. [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/11849792

[3] J. Boda-Heggemann, F. M. Köhler, B. Küpper, D. Wolff, H. Wertz, S. Mai, J. Hesser, F. Lohr, and F. Wenz, "Accuracy of ultrasound-based (BAT) prostate-repositioning: a three-dimensional on-line fiducial-based assessment with cone-beam computed tomography," *IJROBP*, vol. 70, no. 4, pp. 1247–1255, March 2008.

[4] M. Pinkawa, M. Pursch-Lee, B. Asadpour, B. Gagel, M. D. Piroth, J. Klotz, S. Nussen, and M. J. Eble, "Image-guided radiotherapy for prostate cancer. Implementation of ultrasound-based prostate localization for the analysis of inter- and intrafraction organ motion." *Strahlentherapie und Onkologie*, vol. 184, no. 12, pp. 679–685, December 2008.

[5] F. L. B. Cury, G. Shenouda, L. Souhami, M. Duclos, S. L. Faria, M. David, F. Verhaegen, R. Corns, and T. Falco, "Ultrasound-based image guided radiotherapy for prostate cancer: comparison of cross-modality and intramodality methods for daily localization during external beam radiotherapy." *IJROBP*, vol. 66, no. 5, pp. 1562–1567, December 2006.

[6] J. P. McGahan, J. Ryu, and M. Fogata, "Ultrasound probe pressure as a source of error in prostate localization for external beam radiotherapy." *IJTOBP*, vol. 60, no. 3, pp. 788–793, November 2004. [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/15465195

[7] C. F. Serago, S. J. Chungbin, S. J. Buskirk, G. a. Ezzell, a. C. Collie, and S. a. Vora, "Initial experience with ultrasound localization for positioning prostate cancer patients for external beam radiotherapy." *IJTOBP*, vol. 53, no. 5, pp. 1130–1138, August 2002. [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/12128112

[8] A. Taylor and M. E. B. Powell, "An assessment of interfractional uterine and cervical motion: implications for radiotherapy target volume definition in gynaecological cancer." *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*, vol. 88, no. 2, pp. 250–257, August 2008. [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/18538873

[9] R. Ahmad, M. S. Hoogeman, M. Bondar, V. Dhawtal, S. Quint, I. De Pree, J. W. Mens, and B. J. M. Heijmen, "Increasing treatment accuracy for cervical cancer patients using correlations between bladder-filling change and cervix-uterus displacements: proof of principle." *Radiotherapy and oncology*, vol. 98, no. 3, pp. 340–346, March 2011. [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/21295877

[10] R. Ahmad, M. S. Hoogeman, S. Quint, J. W. Mens, I. de Pree, and B. J. M. Heijmen, "Inter-fraction bladder filling variations and time trends for cervical cancer patients assessed with a portable 3-dimensional ultrasound bladder scanner." *Radiotherapy and oncology*, vol. 89, no. 2, pp. 172–179, November 2008. [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/18703248

[11] A. Jhingran, M. Salehpour, M. Sam, L. Levy, and P. Eifel, "Vaginal motion and bladder and rectal volumes during pelvic intensity modulated radiation therapy after hysterectomy," *International journal of radiation oncology, biology, physics*, vol. 82, no. 1, pp. 256–262, January 2012.

[12] D. Yee, M. Parliament, S. Rathee, S. Ghosh, L. Ko, and B. Murray, "Cone beam CT imaging analysis of interfractional variations in bladder volume and position during radiotherapy for bladder cancer," *International journal of radiation oncology, biology, physics*, vol. 76, no. 4, pp. 1045–1053, March 2010. [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/19540057

[13] I. M. Jurgenliemk-Schulz, M. Z. Toet-Bosma, G. a. P. de Kort, H. W. R. Schreuder, J. M. Roesink, R. J. H. a. Tersteeg, and U. a. van der Heide, "Internal motion of the vagina after hysterectomy for gynaecological cancer." *Radiotherapy and oncology*, vol. 98, no. 2, pp. 244–248, February 2011. [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/21159394

[14] P. Chan, R. Dinniwell, M. a. Haider, Y.-B. Cho, D. Jaffray, G. Lockwood, W. Levin, L. Manchul, A. Fyles, and M. Milosevic, "Inter- and intrafractional tumor and organ movement in patients with cervical cancer undergoing radiotherapy: a cinematic-mri point-of-interest study," *International journal of radiation oncology, biology, physics*, vol. 70, no. 5, pp. 1507–1515, April 2008. [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/18164850