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ORIGINAL ARTICLE

Quantification and Correlational analysis of Uterine Movement Assessed by Daily Cone Beam CT During Radiotherapy for Cervical Cancer

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ABSTRACT

Background: Cervical cancer treatment with external beam radiotherapy (EBRT) is challenged by uterine motion, which may compromise target coverage. Daily cone-beam computed tomography (CBCT) allows quantification of inter-fraction displacement and may facilitate adaptive treatment strategies.
Objective: To quantify inter-fraction uterine displacement in cervical cancer patients undergoing EBRT using daily CBCT and evaluate its relationship with bladder volume and patient-specific factors.
Method: This prospective observational study was conducted at a tertiary oncology center in Karachi, Pakistan, after ethical approval. Six patients with intact cervical cancer receiving definitive chemoradiation were recruited through consecutive sampling. Daily pre-treatment CBCT scans were registered with planning CT images to measure uterine displacement in the anterior–posterior (AP), superior–inferior (SI), and right–left (RL) directions. Descriptive statistics were reported as mean ± standard deviation. Pearson correlation was used to assess relationships between variables, with $p < 0.05$ considered statistically significant. Analysis was performed using SPSS version 22.
Results: A total of 150 CBCT scans were analyzed. Mean uterine displacement was greatest in the AP direction (0.96 ± 0.22 cm), followed by SI (0.92 ± 0.17 cm) and RL (0.90 ± 0.13 cm). Maximum recorded displacements were 1.27 cm, 1.30 cm, and 1.19 cm in the AP, SI, and RL directions, respectively. Mean bladder volume during treatment was 330.75 $\pm$ 52.95 cm^3 . AP displacement demonstrated a moderate positive correlation with bladder volume that did not reach statistical significance ($r = 0.357$, $p \approx 0.08$). Greater uterine motion was observed among younger, higher-BMI, and multiparous patients. Motion variability was highest during treatment fractions 10–20.
Conclusion: Uterine motion during EBRT is direction-dependent and influenced by organ filling and patient-specific factors. Daily CBCT supports accurate motion assessment and may facilitate individualized margin design and adaptive radiotherapy approaches.
Keywords: Uterine Cervical Neoplasms; Cone-Beam Computed Tomography; Radiotherapy, Image-Guided; Radiotherapy, Intensity-Modulated.

INTRODUCTION:

Cervical cancer remains a significant global health concern and is the fourth most common cancer among women worldwide, with an estimated 604,000 new cases and 341,000 deaths reported in 2020, the vast majority occurring in low- and middle-income countries (LMICs) [1-3]. Recent GLOBOCAN 2022 data indicate that without intensified prevention and screening programs, LMICs will continue to bear a disproportionate share of this burden in the coming decades [3] . Persistent infection with high-risk human papillomavirus (HPV) types, primarily HPV-16 and HPV-18, accounts for over 70% of cervical cancer cases globally [1,4].

In Pakistan, cervical cancer is the third most common malignancy among women and a major cause of cancer-related mortality [5,6]. Estimates suggest an age-standardized incidence rate (ASIR) ranging from 5.2 to 8.4 per 100,000 women, translating to approximately 6,166 new cases annually – figures that surpass the WHO

elimination target threshold of 4 per 100,000 [6]. Data scarcity, absence of a national screening program, and low public awareness compound the challenge; less than 1% of Pakistani women have undergone cervical cancer screening in the past five years [2]. Moreover, HPV vaccination coverage remains negligible despite the vaccine's proven effectiveness and inclusion in many national immunization schedules worldwide [2,6].

In resource-limited settings, the lack of screening leads most women to present with advanced-stage disease, resulting in poorer outcomes [7,8]. Globally, approximately 84% of cervical cancer cases occur in such settings, where stage at diagnosis is a critical prognostic factor [7,9]. Women with locally advanced cervical cancer (LACC) – defined as FIGO 2018 stages IB3–IVA – experience substantially lower cure rates and higher recurrence compared to those diagnosed at earlier stages [7,10,11]. For invasive disease, treatment is stratified by staging systems, namely the International Federation of Gynecology and Obstetrics (FIGO) and the American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) TNM classification, last updated in 2018 and 2021, respectively [12].

For most patients with LACC, concurrent chemoradiotherapy (CCRT) with cisplatin remains the gold-standard treatment, followed by brachytherapy [9, 10, 14]. Evidence from meta-analyses and large phase III trials demonstrates superior survival outcomes for CCRT compared to radiotherapy alone [10,12], while advances such as intensity-modulated radiation therapy (IMRT) and image-guided adaptive brachytherapy have improved tumor targeting and reduced toxicity [7,11]. IMRT has been shown to significantly lower rates of grade ≥3 gastrointestinal and hematological toxicities compared to conventional radiotherapy, while maintaining comparable oncologic outcomes [7]. Nevertheless, treatment precision is challenged by pelvic organ motion, tumor regression, and variations in bladder or rectal filling, which can lead to under-dosing of the target volume or over-exposure of adjacent organs at risk [7,11].

Given these challenges, adaptive radiotherapy approaches using daily CBCT are increasingly employed to monitor and correct for inter-fraction motion, ensuring adequate clinical target volume (CTV) coverage [11,12]. This study aims to quantify inter-fraction uterine motion in patients with intact cervical cancer using daily CBCT and identify clinical and anatomical predictors influencing this displacement. As a pilot effort from a tertiary care center in a low- and middle-income country (LMIC), it shares practical experience with motion-adaptive radiotherapy in a resource-constrained setting.

Despite advances in radiotherapy techniques such as intensity-modulated and image-guided radiotherapy, inter-fraction uterine motion remains a major challenge in achieving accurate target coverage during external beam radiotherapy for cervical cancer. Although daily cone-beam computed tomography (CBCT) enables monitoring and adaptation to anatomical changes, limited data exist on motion patterns and their predictors, particularly in low- and middle-income settings.

We hypothesize that uterine motion is direction-dependent and influenced by bladder filling and patient-specific factors. Therefore, this study aims to quantify inter-fraction uterine motion using daily CBCT and evaluate its association with clinical and anatomical variables to support adaptive radiotherapy and margin optimization.

METHOD: This prospective observational pilot study was conducted at the Section of Radiation Oncology, Department of Oncology, at a tertiary care hospital in Karachi, Pakistan, over a six-month period following approval from the Ethical Review Committee (approval number 2024-9202-28195 dated 21-02-2024). Radiotherapy contouring and treatment planning were adapted from the EMBRACE II protocol for definitive radiotherapy of cervical cancer [13]. As this was a pilot exploratory study designed to evaluate the feasibility of daily CBCT-based assessment of uterine motion, no formal sample size calculation was performed. A convenience sample of six patients was enrolled, generating 150 CBCT scans (25 fractions per patient). These scans represented repeated intra-patient measurements and were interpreted accordingly. A non-probability consecutive sampling technique was employed. Adult patients (≥18 years) with histologically confirmed cervical cancer undergoing definitive external beam radiotherapy (EBRT) with concurrent weekly cisplatin were included. Patients receiving postoperative radiotherapy were excluded. All eligible patients underwent EBRT with concurrent weekly cisplatin followed by brachytherapy according to institutional protocol and EMBRACE II principles. Simulation was followed by a planning CT scan with a comfortably filled bladder and an emptied rectum according to the departmental bladder and bowel preparation protocol. Patients were instructed to void one hour before planning CT and before each treatment fraction, consume 500 mL of water or clear fluid, and refrain from voiding until imaging and treatment. Efforts were made to minimize rectal and sigmoid filling.

Patients were instructed to evacuate stool before both planning and treatment. If the rectal diameter was ≥4 cm, patients were asked to evacuate stool again or treatment was deferred for that day. Radiotherapy planning included registration of the planning CT with the diagnostic MRI. Gross Tumor Volume (GTV), Clinical Target Volume (CTV), and Planning Target Volume (PTV) were delineated according to the EMBRACE II consensus contouring guidelines, including elective nodal regions, cervix, uterus, bilateral parametria, and relevant vaginal segments. Daily pre-treatment CBCT scans were acquired for each fraction of EBRT. Images were registered to the planning CT using bony anatomy and subsequently evaluated for soft-tissue alignment of the cervix, uterus, and upper vagina. Target coverage and bladder and rectal filling patterns were assessed before treatment approval by the treating radiation oncologist. For each treatment fraction, the PTV from the planning CT was transferred to the daily CBCT dataset to evaluate maintenance of target coverage. The uterus and bladder were contoured on each CBCT scan, and maximal uterine displacement was measured in the superior–inferior (SI), anterior–posterior (AP), and right–left (RL) directions relative to the planning position. Bladder volume was calculated in cubic centimeters (cm^3) using the Aria 15 contouring tools, while rectal diameter was measured at the level of the uterine cervix in the axial plane. All measurements were recorded using a standardized data collection proforma. To minimize measurement bias, contouring and displacement measurements were independently reviewed by a second radiation oncologist, and any discrepancies were resolved by consensus. At the end of treatment, the mean maximal uterine displacement in each direction was calculated for each patient (Figure 1).

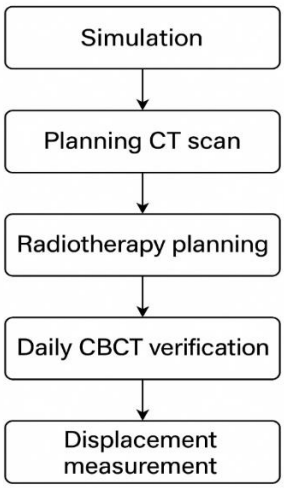

Figure 1. Schematic patient workflow diagram showing the link between simulation, CBCT verification, displacement measurement, and ITV calculation.

These values were explored in relation to clinical and anatomical variables, including age, body mass index (BMI), FIGO stage, bladder volume, rectal diameter, and parity, to identify potential motion-related trends that may inform future studies evaluating individualized internal target volume (ITV) margins. Treatment and imaging data were obtained from the hospital's electronic medical records and the Aria 15 planning system. Quantitative variables were summarized as mean ± standard deviation, while categorical variables were reported as frequencies and percentages. Associations between uterine displacement and continuous clinical or anatomical variables were explored using Pearson correlation coefficients. Given the pilot nature of the study, small sample size, and repeated intra-patient measurements, no multivariable regression or formal predictor analysis was performed, and the findings are presented as exploratory. Statistical analyses were performed using SPSS version 22 (IBM Corp., Armonk, NY), with a two-sided p-value <0.05 considered statistically significant.

RESULTS: The study included six patients with a mean age of 54.50 ± 15.00 years. A total of 150 CBCT scans, representing 25 fractions per patient, were acquired and analyzed as repeated intra-patient measurements to assess uterine motion.

FIGO staging was distributed as follows: IB3 (16.7%), IIA2 (16.7%), IIB (33.3%), IIC1 (16.7%), and IIIB (16.7%). External beam radiotherapy (EBRT) doses varied, with 33.3% of patients receiving 45 Gy in 25 fractions, 50% receiving 50 Gy in 25 fractions, and 16.7% receiving 50.4 Gy in 28 fractions.

All patients subsequently underwent brachytherapy one week following completion of concurrent chemoradiotherapy, receiving a total dose of 24 Gy delivered in three weekly fractions of 8 Gy each. The mean planning CT bladder volume was 331.71 ± 96.19 cm^3, with a median of 333.45 cm^3 (IQR: 174.0) (Table 1).

Table 1: Clinical characteristics of the patients.

Variable	Frequency (%)
Age (years), mean ± SD	54.50 ± 15.00
≤50 years (Premenopausal)	3 (50.0)
51–65 years (Peri-/Postmenopausal)	1 (16.7)
>65 years (Elderly)	2 (33.3)
Pathology	
Squamous Cell Cancer	6 (100.0)
ERBT Technique	
IMRT	6 (100.0)
Concurrent Chemotherapy	
Cisplatin 40 mg/m^2 weekly	6 (100.0)
ERBT Dose	
45 Gy/25 Fractions	2 (33.3)
50 Gy/25 Fractions	3 (50)
50.4 Gy/28 Fractions	1 (16.7)
FIGO Stage	
IB3	1 (16.7)
IIA2	1 (16.7)
IIB	2 (33.3)
IIC1	1 (16.7)
IIIB	1 (16.7)
Brachytherapy	
24 Gy in 3 fractions weekly, 1 week after EBRT	6 (100.0)
Brachytherapy Instrument	
Tandem and Ovoid	6 (100.0%)
Planning CT Bladder Volume (cm^3)	
Mean ± SD	331.71 ± 96.19
Median (IQR)	333.45 (174.0)

Daily cone-beam computed tomography (CBCT) demonstrated variability in uterine motion, bladder volume, and rectal diameter across treatment fractions. Mean uterine displacement in the anterior–posterior (AP) direction ranged from 0.51 ± 0.29 cm to 1.27 ± 0.76 cm. In the superior–inferior (SI) direction, displacement ranged from 0.60 ± 0.12 cm to 1.30 ± 0.57 cm, while right–left (RL) motion ranged from 0.63 ± 0.32 cm to 1.19 ± 0.39 cm. Bladder volume ranged from 249.30 ± 100.01 cm^3 to 477.46 ± 247.45 cm^3 across treatment fractions (Table 2).

Table 2. Mean ± SD uterine displacement and bladder volume measured on daily CBCT during radiotherapy

CBCT Number	ANT-POST (cm)	SUP-INF (cm)	RIGHT-LEFT (cm)	Bladder Volume (cm^3)
1	0.59±0.48	0.60±0.12	0.94±0.43	341.33±122.75
2	0.70±0.33	0.76±0.57	0.81±0.33	297.31±143.51
3	0.51±0.29	0.76±0.42	0.81±0.31	292.00±203.90
4	0.84±0.60	0.73±0.65	0.68±0.23	342.88±141.98
5	1.14±0.88	0.80±0.45	1.05±0.47	401.68±205.09
6	1.27±0.76	0.80±0.57	0.99±0.29	477.46±247.45
7	1.17±0.52	1.00±0.60	0.63±0.32	434.63±136.71
8	1.21±0.88	0.76±0.44	0.94±0.39	330.81±136.55
9	1.17±0.54	1.00±0.65	0.86±0.38	345.15±188.58
10	0.75±0.36	0.93±0.65	0.85±0.31	358.35±162.78
11	0.72±0.42	0.96±0.32	1.06±0.33	351.93±145.21
12	0.91±0.55	0.90±0.46	0.93±0.34	287.86±183.89
13	0.99±0.36	1.10±0.64	0.71±0.40	307.55±179.08
14	0.85±0.43	1.03±0.36	0.83±0.34	312.46±137.70
15	0.99±0.23	0.80±0.55	0.91±0.28	332.33±109.91
16	0.98±0.46	0.96±0.65	1.19±0.39	407.85±140.92
17	0.96±0.60	1.30±0.57	1.04±0.21	297.78±146.18
18	1.10±0.55	1.03±0.36	0.89±0.33	316.70±151.04
19	1.13±0.36	0.90±0.46	0.77±0.32	286.68±106.23
20	1.27±0.53	1.30±0.41	1.11±0.19	324.86±238.54
21	1.09±0.69	0.91±0.24	0.92±0.45	271.86±62.47
22	1.22±0.53	0.76±0.69	0.94±0.26	321.66±180.29
23	0.99±0.0.68	1.07±0.58	0.85±0.30	295.21±132.62
24	0.85±0.59	1.00±0.44	1.00±0.44	249.30±100.01
25	0.64±0.37	0.92±0.49	0.81±0.27	283.15±127.77

Mean	0.96±0.22	0.92±0.17	0.90±0.13	330.75±52.95

Uterine motion was analyzed across different age groups. Patients were stratified into three categories: ≤50 years (n=3), 51–65 years (n=1), and >65 years (n=2) to reflect premenopausal, peri-/postmenopausal, and elderly patient populations. In the superior–inferior (SI) direction, mean displacement was 1.26 ± 0.52 cm in the ≤50 years group, 1.02 ± 0.48 cm in the 51–65 years group, and 0.84 ± 0.39 cm in the >65 years group. In the anterior–posterior (AP) direction, mean displacement was 1.18 ± 0.41 cm, 1.05 ± 0.36 cm, and 0.91 ± 0.44 cm in the respective age groups. Right–left (RL) motion was 1.02 ± 0.31 cm, 0.94 ±0.29 cm, and 0.89 ± 0.33 cm across the three age groups (Figure 2).

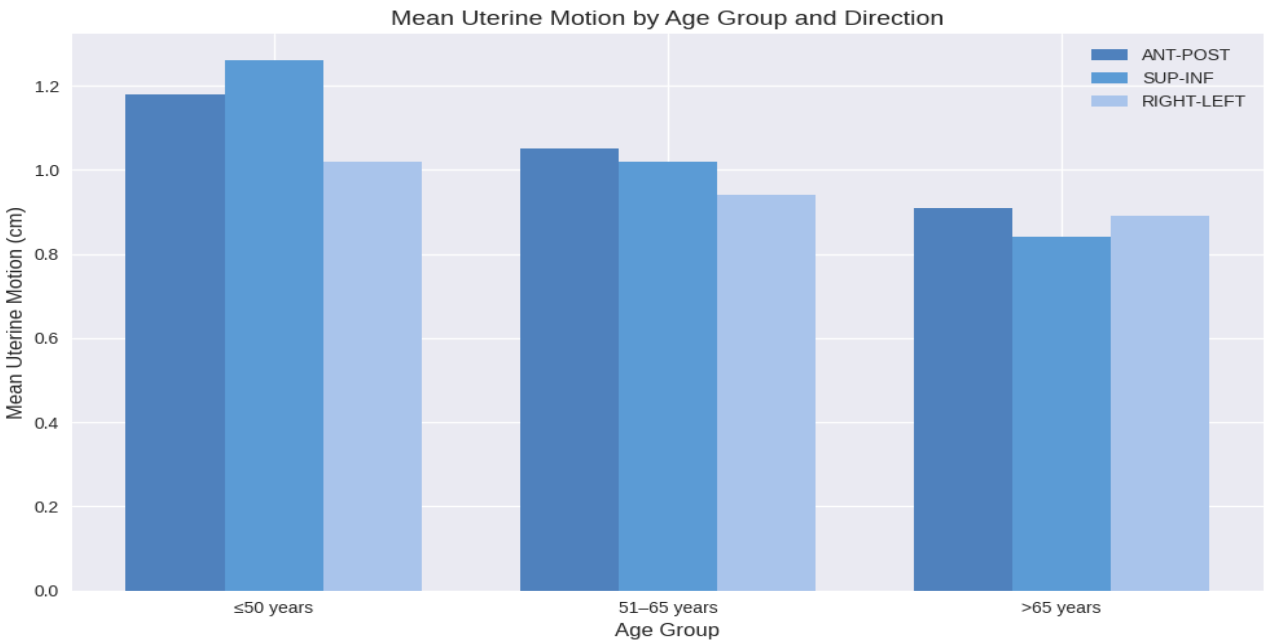

Figure 2. Grouped bar chart showing the relationship between patient age and uterine motion in three directions.

Uterine motion was evaluated in relation to body mass index (BMI). Patients with BMI ≥26 demonstrated greater mean uterine displacement across all directions compared to those with BMI ≤20. Patient 5 (BMI = 28) showed the highest overall displacement, while lower displacement values were observed in patients with lower BMI.

Uterine displacement was also analyzed according to FIGO stage. Patients with stage IIB and IIIC1 disease (n=3) demonstrated mean superior–inferior (SI) displacement of 1.21 ± 0.47 cm, compared to 0.94 ± 0.38 cm in patients with earlier stages (IB3 and IIA2, n=2). In the anterior–posterior (AP) direction, mean displacement was 1.15 ± 0.42 cm in advanced stages and 0.98 ± 0.33 cm in earlier stages. Right–left (RL) motion was 1.03 ± 0.36 cm in advanced stages and 0.89 ± 0.29 cm in earlier stages. These differences were not statistically significant ($p > 0.05$).

Pearson correlation analysis showed a moderate positive correlation between bladder volume and AP motion ($r = 0.357$, $p \approx 0.08$). SI and RL motions demonstrated weak correlations with bladder volume, which were not statistically significant (Figure 3, Table 3).

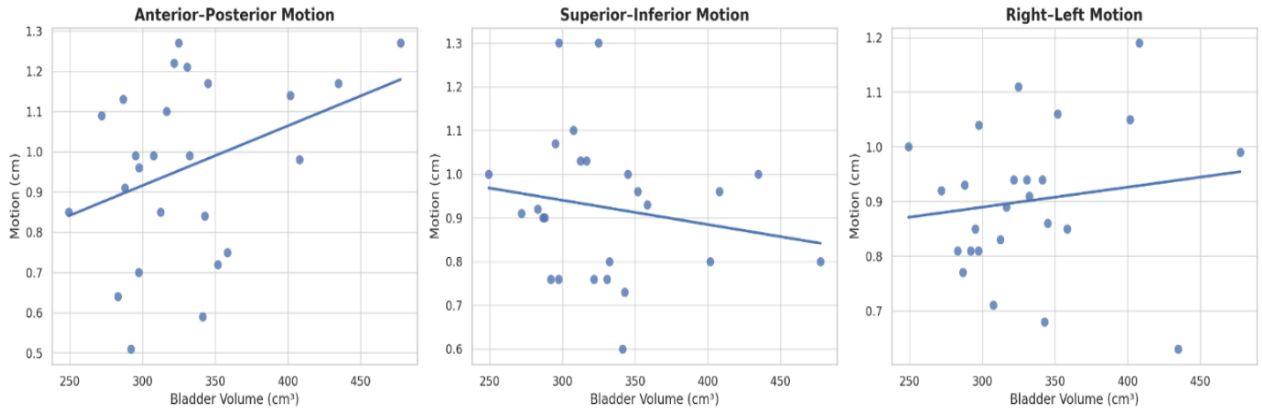

Figure 3: Scatter plots with regression lines showing the relationship between bladder volume and uterine motion (anterior–posterior, superior–inferior, and right–left) during EBRT for intact cervical cancer:

Table 3: Pearson correlation between bladder volume and uterine motion in three orthogonal directions during EBRT for intact cervical cancer

Direction	Pearson r	p-value
ANT–POST	0.357	0.0799
SUP–INF	-0.175	0.4021
RIGHT–LEFT	0.145	0.4896

Uterine motion was analyzed according to planning CT bladder volume categories. For patients with a planning CT bladder volume of 226–300 cm³ (n=2), mean displacement was 0.85 ± 0.03 cm in the anterior–posterior (AP) direction, 0.73 ± 0.09 cm in the superior–inferior (SI) direction, and 0.90 ± 0.24 cm in the right–left (RL) direction. The corresponding mean bladder volume during treatment was 347.64 ± 184.11 cm³. For patients with a planning CT bladder volume of 301–400 cm³ (n=3), mean displacement was 1.09 ± 0.08 cm (AP), 0.91 ± 0.32 cm (SI), and 0.95 ± 0.10 cm (RL), with a mean bladder volume of 303.16 ± 91.30 cm³ during treatment. For patients with a planning CT bladder volume >400 cm³ (n=1), displacement was 0.80 cm (AP), 1.32 cm (SI), and 0.74 cm (RL), with a mean bladder volume of 379.74 cm³ (Table 4).

Table 4: Mean ± standard deviation of uterine motion measured on CBCT according to planning CT bladder volume.

Planning CT Bladder Volume	ANT-POST (cm)	SUP-INF (cm)	RIGHT-LEFT (cm)	Bladder volume (cm^3)
226 – 300 (n=2)	0.85±0.03	0.73±0.09	0.90±0.24	347.64±184.11
301 – 400 (n=3)	1.09±0.08	0.91±0.32	0.95±0.10	303.16±91.30
>400 (n=1)	0.80±0.00	1.32±0.00	0.74±0.00	379.74±0.00

Uterine motion was analyzed in relation to rectal diameter. Patients with mean rectal diameters >3.5 cm demonstrated anterior–posterior (AP) displacement of 1.22 ± 0.38 cm, compared to 0.94 ± 0.29 cm in those with rectal diameters ≤3.5 cm. Superior–inferior (SI) and right–left (RL) displacements were also higher in patients with larger rectal diameters. Pearson correlation analysis showed a moderate positive correlation between rectal diameter and AP motion ($r \approx 0.42$, $p \approx 0.07$), while correlations for SI and RL directions were weaker and not statistically significant.

Uterine displacement was also analyzed according to patient parity, which ranged from 0 to 5. Higher parity values were associated with greater mean uterine displacement across all directions. Patients with parity of 4–

5 demonstrated higher displacement values, while the nulliparous patient (parity = 0) demonstrated lower displacement (SI: 0.84 cm, AP: 0.91 cm, RL: 0.89 cm).

Across the 25 fractions analyzed per patient, uterine motion varied over the course of treatment. Lower displacement values were observed in early fractions (1–5), while greater variability was observed during mid-treatment fractions (10–20), particularly in the SI and AP directions. Motion patterns in later fractions appeared more consistent (Figure 4).

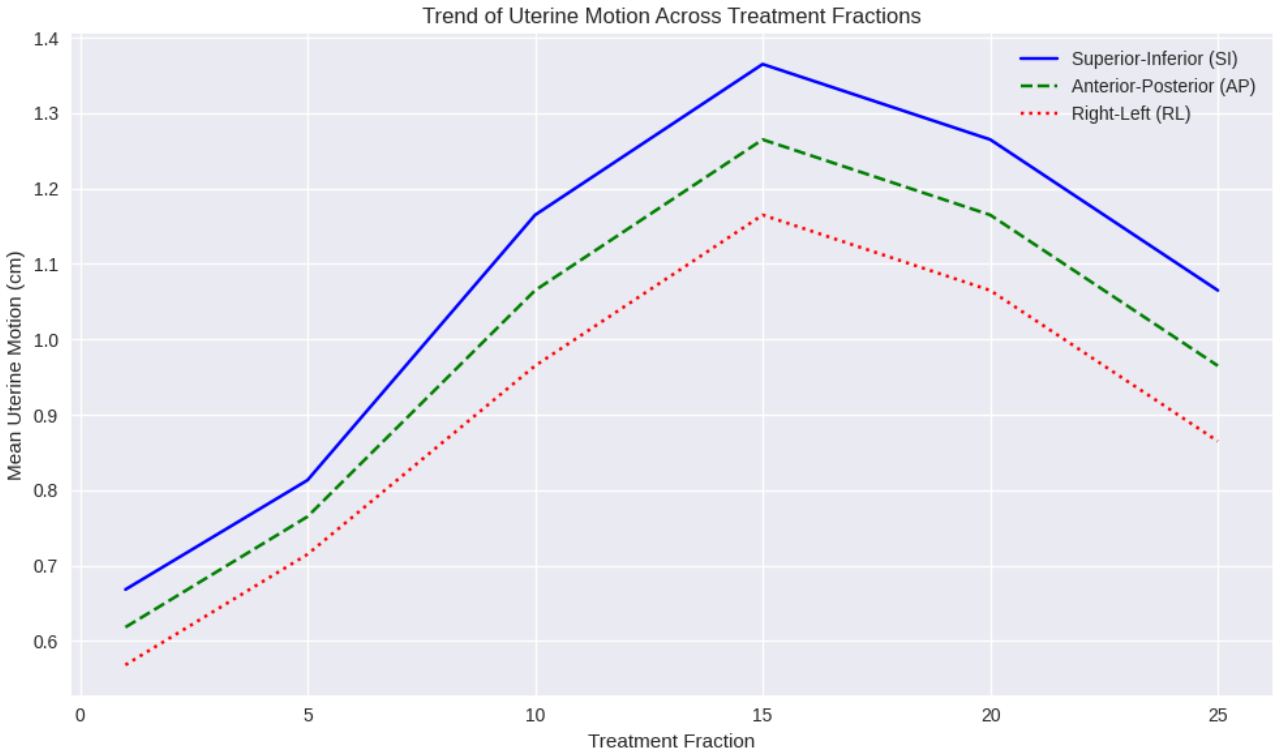

Figure 4 .Combined line plot illustrating mean uterine motion across 25 fractions of EBRT in six patients

DISCUSSION: Our results are consistent with previous reports demonstrating that the cervix–uterus complex exhibits direction-dependent motion influenced by bladder filling. Heijkoop et al. quantified intra-fraction cervix–uterus motion using pre- and post-fraction CBCT in 16 patients, reporting mean displacements of 0.1 ± 1.4 mm (LR), 1.8 ± 1.5 mm (CC/SI), and −2.8 ± 1.8 mm (AP) with a significant correlation between bladder inflow rate and motion ($r = 0.6$, $p < 0.01$) [14]. Similarly, Xu Li et al. demonstrated that larger bladder volumes resulted in greater AP and SI displacement, recommending bladder-filling protocols to minimize motion variability [15]. Our correlation analysis supports these observations, suggesting that individualized bladder management could improve motion predictability. Beyond bladder volume, uterine motion demonstrated trends with patient-specific variables. Younger patients (≤50 years) showed greater displacement, particularly in the SI and AP directions, possibly due to increased pelvic tissue elasticity. Higher BMI (≥25) was associated with increased motion, likely reflecting soft tissue variability and reduced positional reproducibility. Patients with advanced FIGO stages (IIB–IIIC1) and higher parity (≥3) also exhibited greater uterine mobility. Although these correlations did not reach statistical significance, they highlight the importance of individualized margin design and adaptive planning based on anatomical and clinical factors. Our findings are consistent with previous studies reporting substantial inter-patient variability in uterine motion during cervical cancer radiotherapy. Maemoto et al. demonstrated that uterine displacement is influenced by patient-specific anatomical and clinical factors, with considerable variability among individuals [16].

Adaptive radiotherapy (ART) strategies, such as the plan-of-the-day (POTD) approach described by Buschmann et al., have been shown to mitigate the impact of anatomical variations by selecting daily treatment plans matched to the day's anatomy [17]. In their study, ART achieved equivalent target coverage while reducing high-dose volumes to the bladder and rectum, particularly in patients with large daily anatomical

changes. The motion patterns in our cohort suggest that similar adaptive strategies could be beneficial, particularly for those exhibiting substantial AP motion.

Potter et al. and the EMBRACE II protocol emphasize the integration of image-guided ART with MRI-guided brachytherapy to optimize local control and minimize toxicity [13]. These protocols recommend PTV margins tailored to observed motion patterns, with anisotropic expansions in cases where motion is predominantly directional. Our findings of greater AP displacement suggest that an AP-weighted margin may be more appropriate than an isotropic expansion, thereby reducing unnecessary dose to organs at risk (OARs).

Wang et al. reported that motion uncertainties can be further compounded by rectal filling, pelvic floor relaxation, and patient positioning [18], literature suggests that simultaneous control of bladder and rectal status may be necessary to achieve optimal reproducibility.

From a clinical standpoint, the magnitude of motion observed in our study reinforces the need for daily image guidance. Stevens et al. highlighted that without daily CBCT, inter-fraction motion could result in target under-coverage in up to 30% of fractions for patients with highly mobile uteri [19]. Incorporating our motion data into margin recipes, such as the van Herk formula, would allow derivation of patient-specific ITV–PTV expansions that maintain ≥95% CTV coverage for ≥90% of patients

From a radiobiological perspective, interfractional uterine motion can lead to subtle but clinically relevant alterations in dose distribution across the HR-CTV and adjacent organs. Even small geometric uncertainties may cause underdosage of the tumor and increased exposure of surrounding tissues. Given the steep dose–response relationship for cervical carcinoma ($\alpha/\beta \approx 10$ Gy), a 5% reduction in delivered dose could theoretically lower tumor control probability (TCP) by up to 10% [20, 21]. Conversely, late-responding organs such as the bladder and rectum ($\alpha/\beta \approx 3$ Gy) exhibit greater sensitivity to fractionation effects, meaning that uncorrected motion may compromise the therapeutic ratio without offering proportional normal-tissue sparing [22].

By incorporating the observed uterine motion into the planning target volume (PTV) through an internal target volume (ITV) approach, our protocol mitigated most of this uncertainty, maintaining stable coverage across fractions. These findings reinforce that anisotropic, image-guided margin design effectively preserves both dosimetric and radiobiological robustness of cervical cancer radiotherapy.

Future work integrating deformable dose accumulation and voxel-level radiobiological modeling could provide a more comprehensive understanding of how geometric motion translates into biological outcome metrics such as TCP and NTCP, ultimately informing personalized adaptive strategies.

This study has several limitations. First, the small sample size and single-center design limit the generalizability of the findings. Although 150 CBCT scans were analyzed, these represented repeated observations from only six patients and should therefore be interpreted as exploratory rather than confirmatory. Second, the repeated-measures nature of the dataset precluded robust inference using conventional statistical methods, and no multivariable or longitudinal modeling was performed. Consequently, the observed relationships between uterine motion and patient-specific or anatomical factors should be regarded as descriptive trends rather than definitive predictors. Third, although contouring and displacement measurements were reviewed by two radiation oncologists using a standardized departmental protocol, formal assessment of inter- or intra-observer agreement was not performed. Finally, this study evaluated geometric motion only and did not incorporate deformable image registration, cumulative dose accumulation, or dosimetric analyses to quantify the impact of uterine motion on target coverage and organs at risk.

Future studies should include larger, multicenter cohorts with adequate statistical power and apply longitudinal analytical approaches, such as mixed-effects models, to appropriately account for repeated intra-patient measurements. Incorporation of deformable image registration, cumulative dose accumulation, and voxel-based radiobiological modeling would further clarify the relationship between geometric motion, delivered dose, tumor control probability (TCP), and normal tissue complication probability (NTCP). Such studies may facilitate the development of personalized adaptive radiotherapy protocols and individualized anisotropic margin strategies for patients with cervical cancer.

CONCLUSION: Our findings demonstrate that displacement is most pronounced in the anterior–posterior direction, with variability influenced by bladder filling, rectal diameter, BMI, age, FIGO stage, and parity, highlighting the clinical significance of daily CBCT in managing uterine motion during EBRT for intact cervical cancer. Without daily image guidance, these shifts could result in target under-coverage and unnecessary

irradiation of adjacent organs at risk. By capturing daily anatomical changes, CBCT enables precise verification, supports anisotropic planning margin determination, and facilitates adaptive radiotherapy approaches such as the plan-of-the-day strategy.

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