Ultrasound-Based Bladder Volume Assessment in Gynecological Radiotherapy: Agreement with CT/CBCT and Longitudinal Variation

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Abstract: *Background*: Consistent bladder filling is important in postoperative pelvic radiotherapy because changes in volume can alter the relationship between pelvic targets and adjacent organs at risk. CBCT provides three-dimensional verification but adds treatment-room time and imaging dose. Ultrasound offers a rapid, portable, non-ionizing method for checking bladder volume before treatment-room imaging.

Objective: To evaluate agreement between investigator-performed ultrasound (US) and reference planning CT/cone-beam CT (CBCT) bladder-volume measurements in postoperative gynecological radiotherapy, and to characterize longitudinal bladder-volume change during treatment.

Methods: This prospective, single-institution method-comparison study included 29 postoperative patients receiving adjuvant pelvic radiotherapy (14 with cervical and 15 with endometrial cancer). A total of 406 paired US-reference measurements were obtained at 14 scheduled time points from simulation to treatment day 25. Patients followed a standardized protocol of bladder emptying followed by 500 mL of water 40 minutes before imaging. US was performed with a GE LOGIQ F8 Expert system and curvilinear/convex transducer; the automated volume function used three orthogonal bladder dimensions. Three consecutive scans were obtained and the median was analyzed. Planning CT was the baseline reference and CBCT was the treatment reference. Agreement was assessed using a two-way mixed-effects, absolute-agreement, single-measure ICC and Bland-Altman methods adapted for repeated observations within patients, with patient-level bootstrap confidence intervals. Longitudinal change was evaluated with a linear mixed model.

Results: Mean bladder volume was 195.5 ± 71.6 mL by US and 199.2 ± 71.6 mL by reference CT/CBCT. The overall correlation was strong ($r = 0.951$, $p < 0.001$), and the single-measure absolute-agreement ICC was 0.950 (95% CI, 0.927-0.965). Repeated-measures Bland-Altman analysis showed a mean bias of -3.69 mL (95% CI, -6.48 to -1.27 mL), with limits of agreement of -47.52 mL (95% CI, -54.29 to -41.03) and 40.14 mL (95% CI, 36.47 to 44.26). Baseline US-planning CT bias was -2.28 mL, while treatment US-CBCT bias was -3.80 mL. In exploratory agreement-threshold analyses, 364/406 pairs (89.7%) were within 20%, 396/406 (97.5%) within 30%, 400/406 (98.5%) within 50 mL, and 405/406 (99.8%) within 100 mL. Mean reference volume declined from 249.6 ± 86.6 mL at baseline to 164.4 ± 49.3 mL on day 25; the mean participant-level percentage decline was 28.0% ± 25.5%.

Conclusion: Investigator-performed US showed close average agreement with planning CT/CBCT for bladder-volume estimation, but individual differences approaching approximately 50 mL remained within the repeated-measures limits of agreement. US may therefore be useful as a rapid preparation-screening adjunct, but it cannot verify postoperative target position or the full pelvic anatomy and should not replace clinically indicated image guidance. Patient-specific or plan-specific implementation thresholds require prospective validation against anatomy, dosimetry, workflow outcomes, and clinical endpoints.

Keywords: Ultrasound, bladder volume, cone-beam computed tomography, image-guided radiotherapy, postoperative radiotherapy, cervical cancer, endometrial cancer, method agreement, longitudinal variation.

1. INTRODUCTION

Postoperative external beam radiotherapy for cervical and endometrial cancer requires accurate and reproducible relationships among postoperative pelvic target volumes, the urinary bladder, rectum, bowel, and bony pelvis. Bladder preparation is particularly important because filling changes both the size and position of the bladder, can displace small-bowel loops superiorly away from high-dose pelvic regions, and can alter the spatial relationship between the bladder, rectum, and postoperative target. A fuller bladder may also reduce the proportion of bladder wall receiving higher doses. However, the theoretical dosimetric advantages of a maximally full bladder must be balanced against patient discomfort and poor day-to-day reproducibility. For this reason, many contemporary intensity-modulated radiotherapy (IMRT) and volumetric-modulated arc therapy (VMAT) workflows use a comfortably full rather than maximally full bladder protocol [1,2].

Image-guided radiotherapy (IGRT), most commonly using on-board cone-beam computed tomography (CBCT), enables three-dimensional assessment of

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patient setup and internal pelvic anatomy immediately before treatment. This information supports online position correction, tighter planning target volume margins, and more conformal treatment delivery [3-5]. Professional guidance emphasizes that image-guidance frequency should reflect treatment site, motion risk, available technology, and local quality assurance [6]. Although CBCT is clinically valuable, daily acquisition can increase treatment time, add low-dose radiation exposure, and consume linear-accelerator capacity. These burdens are especially relevant in high-volume centers, where failed bladder preparation may only become apparent after the patient has been positioned and imaged.

The need for bladder monitoring is not limited to dose-volume considerations. In postoperative patients after hysterectomy, the vaginal cuff and adjacent pelvic target structures may change position and shape between fractions, and these changes can be influenced by variations in bladder and rectal filling [7,8,10,11]. Serial imaging studies have also demonstrated marked interfraction bladder-volume variability and progressive reductions in achievable filling during a course of radiotherapy [9]. Consequently, bladder volume is clinically useful as a preparation indicator, but it cannot serve as a stand-alone surrogate for postoperative target position.

Ultrasound provides a practical method for measuring bladder volume before the patient enters the treatment room. It is portable, rapid, repeatable, and does not use ionizing radiation. In postoperative cervical-cancer radiotherapy, portable bladder scanning has been assessed alongside CBCT and shown potential for supporting bladder preparation while characterizing vaginal-cuff positional uncertainty [8]. Clinical implementation studies in cervical and endometrial radiotherapy have also shown that bladder scanning can support active volume-correction protocols [12]. More recently, a prospective comparison in a broader pelvic-radiotherapy population reported strong correlation between portable ultrasound and CT-derived bladder volumes, while also showing that measurement error may vary at larger bladder volumes [13].

The clinically desirable bladder volume is not necessarily the largest achievable volume. Recent cervical-cancer studies, including postoperative cohorts, have suggested that moderate filling, frequently in the range of 300-500 mL, may offer a favorable balance between small-bowel displacement and bladder or rectal dose [14,15]. In parallel, comparisons of conventional three-dimensional conformal radiotherapy with IMRT continue to demonstrate the importance of controlling dose to pelvic organs at risk [16]. These findings reinforce the need for a preparation protocol that is not only dosimetrically rational, but also reproducible over several weeks of treatment.

The primary aim of this study was therefore to determine the agreement between ultrasound measurements obtained by a trained study investigator and reference planning CT/CBCT bladder volumes in postoperative patients receiving adjuvant pelvic radiotherapy for cervical or endometrial cancer. Secondary aims were to describe the proportion of measurements meeting exploratory relative and absolute agreement thresholds, characterize bladder-volume change across the treatment course, compare agreement separately for planning CT and treatment CBCT, and examine the relationship between baseline and day-25 bladder volume without using a mathematically coupled baseline-change correlation.

2. METHODS

2.1. Study Design and Setting

This was a prospective, single-institution, observational method-comparison study conducted at Awat Radiation Oncology Center during 2025-2026. The revised report follows the reporting principles of the Strengthening the Reporting of Observational Studies in Epidemiology statement and the Guidelines for Reporting Reliability and Agreement Studies [17,18]. The study used a pragmatic consecutive sample of all eligible patients treated during the study period; no formal a priori sample-size calculation was documented in the source study materials.

2.2. Participants

Patients were eligible if they had undergone surgery for cervical or endometrial cancer and were scheduled to receive adjuvant external beam radiotherapy to the pelvis using a defined bladder-filling protocol. Patients receiving palliative treatment without a bladder-preparation requirement were excluded. Patients were also excluded if a medical condition prevented them from retaining urine for the required preparation and imaging interval. The analyzed cohort comprised 29 postoperative patients: 14 with cervical cancer and 15 with endometrial cancer. Age, body mass index (BMI), pathological stage, concurrent systemic treatment,

urinary symptoms/comorbidity, and renal or hydration variables were not included in the supplied analytic dataset and were therefore not reconstructed retrospectively.

2.3. Radiotherapy and Bladder-Preparation Protocol

All participants received postoperative adjuvant pelvic external beam radiotherapy to a prescribed dose of 45-50.4 Gy in 25-28 fractions. Before simulation and each scheduled treatment measurement, patients were instructed to empty the bladder 40 minutes before imaging, drink 500 mL of water, and avoid further voiding until imaging and treatment were completed. The intent was to produce a comfortably full bladder using a protocol that could be repeated throughout treatment. Measurements were obtained with the patient supine, matching the treatment position, to minimize positional differences between ultrasound and reference imaging.

2.4. Ultrasound Bladder-Volume Measurement

Immediately before reference imaging, bladder volume was measured using a GE LOGIQ F8 Expert ultrasound system (GE HealthCare) with a curvilinear/convex transducer. Patients were examined supine, consistent with the treatment position. The urinary bladder was identified sonographically and the system's automated volume-measurement function estimated volume from three orthogonal bladder dimensions. Three consecutive measurements were obtained during the same bladder-preparation episode, and the median of the three measurements was recorded as the US bladder volume for analysis. Each assessment required approximately 1 minute. All US examinations were performed by the same study investigator, a third-year radiation oncology board trainee who had received practical training in bladder-volume assessment under the supervision of an Assistant Professor of Radiology, using the same acquisition procedure throughout the study. The individual triplicate readings were not retained in the supplied analytic dataset, so within-operator repeatability of the three acquisitions could not be estimated retrospectively.

2.5. Reference CT/CBCT Measurement and Segmentation

At baseline, the reference bladder volume was obtained from the radiotherapy planning CT. During treatment, a standard pelvic CBCT was acquired on an Elekta Infinity linear accelerator approximately 2-3 minutes after the ultrasound examination. Images were exported from the clinical database and imported into 3D Slicer [19]. A single radiation oncologist delineated the urinary bladder using the same segmentation workflow across datasets, and the software-generated three-dimensional bladder volume was recorded in milliliters. Repeat segmentation by the same or an independent observer was not performed, so intraobserver and interobserver segmentation variability could not be quantified. The short US-to-CT/CBCT interval was intended to minimize, but cannot eliminate, volume change caused by continued urine production.

2.6. Measurement Schedule and Outcomes

Paired measurements were scheduled at 14 time points: baseline simulation, followed by treatment days 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, and 25. The final analyzed dataset contained 406 paired observations, which corresponds to 14 paired measurements for each of the 29 participants.

The primary outcome was agreement between US and reference CT/CBCT bladder volume. Measurement difference was defined as US minus reference volume; therefore, a negative value indicated US underestimation. Agreement was evaluated overall and separately for baseline US versus planning CT and treatment US versus CBCT. Exploratory threshold analyses used absolute relative differences of no more than 20% or 30% and absolute volume differences of no more than 50 or 100 mL. Relative difference was calculated as the absolute US-reference difference divided by the reference volume and multiplied by 100. These thresholds were used only to describe the magnitude of method agreement and were not interpreted as validated treatment-preparation, target-coverage, or CBCT-omission criteria.

Longitudinal outcomes were reference bladder volume at each scheduled time point, change from baseline to day 25, and participant-level percentage change. To summarize the maintainability of different starting volumes descriptively, patients were grouped by baseline reference volume as less than 200 mL, 200-300 mL, or more than 300 mL. Because a change score contains the baseline value and is therefore mathematically coupled to it, the revised inferential analysis used day-25 reference volume as the outcome and baseline reference volume as the predictor rather than correlating baseline directly with baseline-to-day-25 change.

2.7. Statistical Analysis

Statistical reanalysis for the revision was performed from the supplied source spreadsheet using Python 3.13.5 with NumPy 2.3.5, SciPy 1.17.0, and statsmodels 0.14.6. The dataset contained 29 participants with 14 complete paired measurements each (406 pairs) and no missing scheduled observations. Continuous variables were summarized using mean, standard deviation (SD), minimum, and maximum. All tests were two-sided and $p < 0.05$ was considered statistically significant, with multiplicity adjustment where specified.

Pearson correlation was reported descriptively to quantify linear association, but method agreement was evaluated separately. The intraclass correlation coefficient was recalculated as a two-way mixed-effects, absolute-agreement, single-measure ICC [ICC(A,1)], with each paired measurement occasion as the unit of analysis; 95% confidence intervals were obtained by 10,000 patient-level bootstrap resamples that preserved all repeated observations within a sampled participant [22]. Bland-Altman agreement was reanalyzed using the repeated-observations approach described by Bland and Altman [20,21]. For the combined dataset and the 377 treatment US-CBCT pairs, variance in the paired difference was decomposed into between-participant and within-participant components, and repeated-measures limits of agreement were calculated as mean bias ± 1.96 times the square root of the sum of those variance components. Patient-level cluster bootstrap resampling (10,000 resamples) provided 95% confidence intervals for the bias and limits of agreement. Baseline US-planning CT agreement used the conventional Bland-Altman calculation because each participant contributed one baseline pair. Proportional bias was assessed by a random-intercept mixed-effects regression of the method difference on the mean of the two methods.

Counts and proportions meeting each exploratory agreement threshold were recalculated directly from the 406 source-data pairs. A random-intercept linear mixed model assessed reference bladder-volume change over time while accounting for repeated observations within participants; planned comparisons of each treatment time point with baseline were Bonferroni-adjusted [23]. To avoid mathematical coupling in the baseline-volume analysis, day-25 reference volume was regressed on baseline reference volume. The slope and its 95% confidence interval were reported together with R2; baseline-volume categories were retained for descriptive presentation only, without an inferential claim that higher baseline volume causes poorer reproducibility.

2.8. Ethics

All participants provided written informed consent for the use of anonymized clinical and imaging data for research. The research protocol was approved by the Medical Research Scientific & Ethics Committee of the Kurdistan Higher Council of Medical Specialties, Kurdistan Region, Iraq (Meeting Code 558; 5 May 2025). Administrative authorization was also obtained from Awat Radiation Oncology Center.

3. RESULTS

3.1. Cohort and Measurement Characteristics

Twenty-nine postoperative patients receiving adjuvant pelvic radiotherapy were included: 14 with

Table 1: Cohort, Treatment, and Measurement Characteristics

Characteristic	Value
Patients, n	29
Cervical cancer, n (%)	14 (48.3)
Endometrial cancer, n (%)	15 (51.7)
Postoperative adjuvant pelvic radiotherapy prescription	45-50.4 Gy in 25-28 fractions
Bladder preparation	Void, drink 500 mL water, wait 40 minutes
Scheduled paired assessments per patient	14
Total paired observations	406
Ultrasound volume, mean ± SD (range), mL	195.5 ± 71.6 (50-397)
Reference CT/CBCT volume, mean ± SD (range), mL	199.2 ± 71.6 (35-408)
Unadjusted difference (US - reference), mL	-3.7

CBCT = cone-beam computed tomography; CT = computed tomography; SD = standard deviation; US = ultrasound. Age, BMI, stage, concurrent systemic treatment, and urinary-factor variables were not available in the supplied analytic dataset and are therefore not summarized.

cervical cancer (48.3%) and 15 with endometrial cancer (51.7%). Across 14 scheduled assessments per patient, all 406 paired US-reference measurements were available. Overall mean bladder volume was 195.5 ± 71.6 mL by US and 199.2 ± 71.6 mL by reference imaging. US volumes ranged from 50 to 397 mL and reference volumes from 35 to 408 mL. The unadjusted mean difference was -3.7 mL, indicating modest average underestimation by US (Table **1**).

3.2. Association and Absolute-Agreement ICC

US and reference CT/CBCT volumes were strongly linearly associated overall (Pearson r = 0.951, p < 0.001). The recalculated two-way mixed-effects, absolute-agreement, single-measure ICC was 0.950 (95% CI, 0.927-0.965). The corresponding ICCs were 0.959 (95% CI, 0.918-0.978) for the 29 baseline US-planning CT pairs and 0.947 (95% CI, 0.922-0.962) for the 377 treatment US-CBCT pairs. The previously reported value of 0.975 reflected an average-measures formulation; the single-measure ICC is reported here because clinical use concerns one US measurement compared with one reference measurement (Table **2**).

3.3. Repeated-Measures Bland-Altman Agreement

Repeated-measures Bland-Altman analysis of all 406 pairs showed a mean US-reference bias of -3.69 mL (95% CI, -6.48 to -1.27 mL). The between-participant variance component of the difference was 19.16 mL2 and the within-participant variance component was 480.85 mL2, giving repeated-measures limits of agreement of -47.52 mL (95% CI, -54.29 to -41.03) and 40.14 mL (95% CI, 36.47 to 44.26). Separate analyses were similar: baseline US versus planning CT had a bias of -2.28 mL with conventional limits of agreement from -50.29 to 45.74 mL, while treatment US versus CBCT had a repeated-measures bias of -3.80 mL with limits from -47.36 to 39.76 mL (Table **3** and Figure **1**). A mixed-effects proportional-bias analysis found no evidence that the US-reference difference changed systematically across the measured volume range (slope -0.009 mL per 1-mL increase in paired-method mean; 95% CI, -0.045 to 0.026; p = 0.605).

3.4. Exploratory Agreement-Threshold Analysis

Using an absolute relative difference of no more than 20%, 364 of 406 paired measurements (89.7%) met the threshold. At 30%, 396 pairs (97.5%) met the threshold. For absolute differences, 400 pairs (98.5%) were within 50 mL and 405 (99.8%) were within 100 mL (Table **4**). These percentages quantify measurement agreement only. They do not establish whether bladder preparation was acceptable for treatment, because the study did not compare US values with a patient-specific acceptable range derived from the planning condition and did not evaluate target coverage, registration, rectal filling, or other pelvic anatomy.

3.5. Longitudinal Bladder-Volume Change during Treatment

Reference bladder volume declined over the treatment course. Mean baseline volume was 249.6 ± 86.6 mL and mean volume on day 25 was 164.4 ± 49.3 mL, corresponding to an 85.1 mL reduction in the

Table 2: Association and Single-Measure Absolute-Agreement ICC for Ultrasound Versus Reference Imaging

Statistic	Overall (n=406)	Planning CT baseline (n=29)	Treatment CBCT (n=377)
Pearson correlation	r = 0.951; p < 0.001	r = 0.959; p < 0.001	r = 0.948; p < 0.001
ICC(A,1), 95% CI	0.950 (0.927-0.965)	0.959 (0.918-0.978)	0.947 (0.922-0.962)

CI = confidence interval; ICC(A,1) = two-way mixed-effects, absolute-agreement, single-measure intraclass correlation coefficient. Overall and CBCT ICC confidence intervals used patient-level cluster bootstrap resampling; the baseline analysis used one pair per participant.

Table 3: Bland-Altman Agreement Overall and by Reference Imaging Modality

Analysis	Mean bias (95% CI), mL	95% limits of agreement, mL
Overall CT/CBCT, repeated measures (n=406)	-3.69 (-6.48 to -1.27)	-47.52 (-54.29 to -41.03) to 40.14 (36.47 to 44.26)
Planning CT baseline (n=29)	-2.28 (-11.34 to 6.41)	-50.29 (-64.25 to -33.93) to 45.74 (31.97 to 56.76)
Treatment CBCT, repeated measures (n=377)	-3.80 (-6.93 to -1.20)	-47.36 (-54.40 to -40.64) to 39.76 (36.01 to 44.29)

CI = confidence interval; LoA = limits of agreement; US = ultrasound. Overall and treatment CBCT analyses used repeated-measures variance components and 10,000 patient-level bootstrap resamples. The baseline planning-CT analysis used conventional Bland-Altman calculations with bootstrap confidence intervals because each participant contributed one baseline pair.

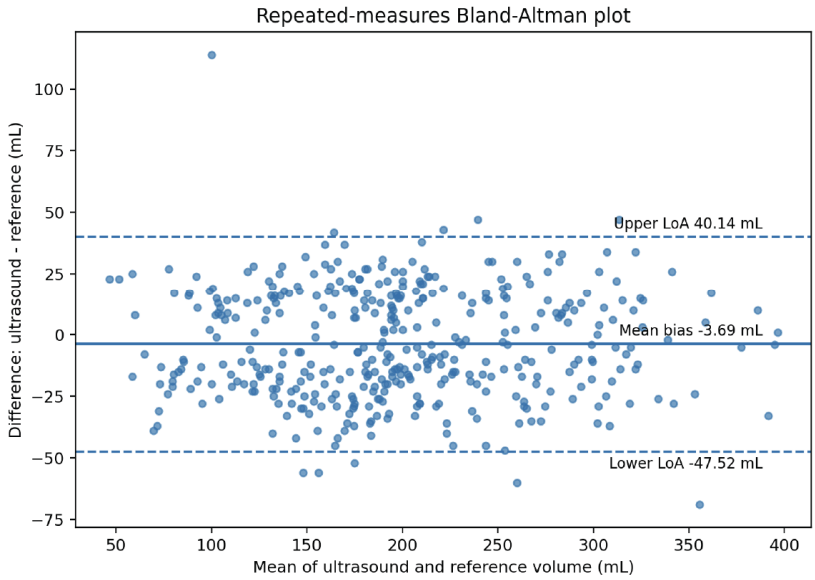


Figure 1: Bland-Altman plot of the difference between ultrasound and reference CT/CBCT bladder volumes against their mean for 406 paired observations. The solid horizontal line represents the repeated-measures mean bias (-3.69 mL), and the dashed lines represent the repeated-measures 95% limits of agreement (-47.52 and 40.14 mL). Difference was calculated as ultrasound minus reference volume. Repeated observations from the same participant were accounted for in estimation of the limits and confidence intervals.

Table 4: Exploratory Agreement Thresholds for Ultrasound Versus Reference CT/CBCT

Agreement threshold	Within threshold, n/406 (%)
Absolute relative difference ≤20%	364 (89.7)
Absolute relative difference ≤30%	396 (97.5)
Absolute difference ≤50 mL	400 (98.5)
Absolute difference ≤100 mL	405 (99.8)

Thresholds are descriptive method-agreement criteria, not validated clinical pass/fail criteria and not evidence for reducing CBCT frequency.

group mean (34.1%). The mean participant-level percentage decline was 28.0% ± 25.5%. In the random-intercept mixed model, mean reference volume was lower than baseline by day 7 (mean difference, -38.7 mL; Bonferroni-adjusted p = 0.011) and remained lower at all subsequent scheduled time points (all Bonferroni-adjusted p < 0.001).

The earlier analysis correlating baseline volume directly with baseline-to-day-25 change was removed because it is mathematically coupled. In the revised regression, day-25 reference bladder volume remained positively associated with baseline reference volume (slope = 0.268 mL per 1 mL at baseline; 95% CI, 0.069-0.466; p = 0.010; R2 = 0.221). Because the slope was well below 1, the data show convergence toward lower volumes over treatment; however, baseline measurement error and regression to the mean cannot be excluded. The baseline-volume

Table 5: Descriptive Change from Baseline to Treatment Day 25 by Baseline-Volume Category

Baseline category (n)	Baseline volume, mL	Day-25 volume, mL	Absolute decline, mL	Percentage decline, %
Small <200 mL (8)	144.5 ± 43.8	144.8 ± 50.5	-0.3 ± 30.8	-1.5 ± 20.0
Medium 200-300 mL (12)	247.7 ± 35.9	165.6 ± 41.7	82.1 ± 45.6	32.6 ± 16.2
Large >300 mL (9)	345.6 ± 37.2	180.4 ± 56.7	165.1 ± 50.2	48.0 ± 14.6
Overall (29)	249.6 ± 86.6	164.4 ± 49.3	85.1 ± 76.9	28.0 ± 25.5

Values are mean ± SD. Decline was calculated as baseline minus day-25 volume; therefore, a negative value indicates a small mean increase. Baseline categories are descriptive only; no inferential comparison of baseline category with a change score is used because of mathematical coupling and regression-to-the-mean concerns.

groups are therefore presented descriptively rather than as evidence that larger starting volumes are inherently less reproducible (Table **5**).

4. DISCUSSION

4.1. Principal Findings

In this prospective method-comparison study, investigator-performed US showed strong association and high single-measure absolute agreement with reference imaging across 406 paired observations. After accounting for repeated measurements within 29 participants, the mean bias was small (-3.69 mL) and the repeated-measures limits of agreement were approximately -48 to 40 mL. Agreement was similar when baseline planning CT and treatment CBCT were analyzed separately. The corrected threshold analysis showed that 89.7% of pairs differed by no more than 20%, 97.5% by no more than 30%, 98.5% by no more than 50 mL, and 99.8% by no more than 100 mL. These are method-agreement results, not validated treatment-preparation pass rates. The longitudinal analysis also confirmed a substantial decline in achievable bladder volume during treatment.

4.2. Comparison with Previous Ultrasound Studies

The present findings are consistent with earlier work showing that portable ultrasound can provide useful bladder-volume estimates in pelvic radiotherapy. Ahmad and colleagues reported a strong correlation between ultrasound and planning CT in cervical cancer [9]. Okamoto and colleagues evaluated portable bladder scanning against CBCT in postoperative cervical-cancer patients and found good agreement while also assessing vaginal-cuff uncertainty [8]. Claxton and Appleyard prospectively implemented daily ultrasound in cervical and endometrial radiotherapy and reported a mean US-CBCT difference of approximately -10 mL during an active volume-correction pathway [12]. Bai and colleagues prospectively studied a broader pelvic-tumor population and reported strong US-CT correlation, with performance varying at larger volumes [13]. Relevant prostate-radiotherapy literature provides complementary method-comparison and workflow evidence: Mullaney *et al*. compared three ultrasound readings with planning CT in 190 patients [24]; Ung *et al*. compared portable bladder-scanner volumes with planning CT/CBCT in post-prostatectomy radiotherapy [25]; Haworth *et al*. evaluated patient-specific ultrasound volume limits in a prostate-bed workflow linked to CBCT-based targeting surrogates [26]; and a more recent prospective prostate study compared daily ultrasound directly with CBCT [27].

Against this literature, the current average bias is small, but the clinically important result is the width of the individual limits of agreement rather than the correlation coefficient alone. Differences among studies should be interpreted in light of scanner technology, operator training, body habitus, disease site, reference-image acquisition, contouring practice, bladder-volume distribution, and whether active correction was applied. The present study used the median of three consecutive US measurements, which may reduce the effect of an isolated acquisition error, but the raw triplicate readings were not retained and therefore formal intraoperator repeatability could not be quantified.

4.3. Why Correlation and ICC are Not Sufficient

The high Pearson correlation and ICC do not by themselves establish interchangeability. Correlation describes linear association, while an ICC depends on the specified model, agreement definition, and unit of analysis. For this revision, the ICC was explicitly defined as a two-way mixed-effects, absolute-agreement, single-measure ICC, and its confidence interval was obtained with patient-level resampling. More importantly, the repeated-measures Bland-Altman analysis accounts for the fact that 406 pairs arose from only 29 participants. Even with a small mean bias, an individual US reading can differ from the reference by roughly 40-50 mL within the estimated limits of agreement, and occasional larger discrepancies occur. Ultrasound should therefore not be treated as numerically interchangeable with CT/CBCT for every fraction.

The relative and absolute threshold analyses are complementary descriptions of measurement difference rather than clinical pass/fail rules. A 50 mL discrepancy may be modest at a reference volume of 350 mL but proportionally large at 100 mL, whereas a 20% threshold permits a larger absolute discrepancy at higher volumes. Published prostate-bed workflows have used patient-specific limits and, in one implementation study, a 100 mL tolerance [26], while other method-comparison studies report relative differences in a similar general range [25,27]. Nevertheless, the 20%, 30%, 50 mL, and 100 mL cutoffs used here were exploratory analytical bands; they were not validated against postoperative target coverage or dosimetry in this cohort.

4.4. Potential Clinical Role as a Preparation-Screening Adjunct

A plausible future clinical role for ultrasound is as an upstream bladder-preparation screen before transfer to the treatment couch. Such a pathway should compare the US result with a patient-specific or plan-specific acceptable bladder-volume range derived from the planning condition, rather than with the CT/CBCT value acquired a few minutes later. A reading below range could prompt additional hydration and waiting, whereas an above-range reading could prompt partial voiding. This may reduce occasions when inadequate bladder preparation is discovered only after immobilization and imaging, but the present study did not prospectively test this workflow.

The 89.7% proportion within 20% agreement must therefore not be interpreted as evidence that 89.7% of treatment fractions were anatomically acceptable or that a similar proportion of CBCT scans could be omitted. CBCT evaluates overall pelvic anatomy and registration; bladder volume alone does not show rotational setup error, vaginal-cuff position, nodal target position, rectal filling, bowel distribution, or other anatomical changes that may require intervention. The study also did not measure target coverage, organ-at-risk dose, treatment-room time, imaging-dose savings, patient discomfort, or toxicity. Ultrasound should be considered a preparation-screening adjunct, not a substitute for protocol-defined image guidance.

4.5. Progressive Loss of Bladder Filling during Treatment

Mean reference bladder volume fell from 249.6 mL at baseline to 164.4 mL at day 25. The group-mean reduction was 34.1%, while the mean participant-level reduction was 28.0%; these estimates differ because one is a ratio of group means and the other averages individual percentages. The mixed model showed a statistically detectable reduction by day 7 after multiplicity adjustment, supporting continued monitoring rather than assuming that the simulation volume remains achievable throughout treatment.

The magnitude of bladder-volume change varies across published radiotherapy studies. Ahmad and colleagues reported marked reduction over treatment under a full-bladder protocol [9], whereas Claxton and Appleyard reported a smaller cohort-level decrease when daily ultrasound was embedded in an active correction pathway [12]. More recent postoperative imaging work also demonstrates variation in bladder and rectal filling together with vaginal-cuff displacement despite preparation protocols [28]. Differences in planned volume, hydration, treatment-related symptoms, active correction procedures, and treatment setting may contribute to these patterns.

The revised analysis avoids correlating baseline directly with a change score. Baseline volume predicted day-25 volume, but the regression slope was substantially below 1, indicating convergence of volumes over time. This pattern is compatible with difficulty maintaining larger initial volumes, but it can also be influenced by measurement error and regression to the mean. We therefore removed the earlier statement that larger baseline volumes are inherently less reproducible. The category summaries in Table **5** are descriptive and should be interpreted as hypothesis-generating rather than causal evidence.

4.6. Implications for Postoperative Target Geometry and Image Guidance

Bladder monitoring is clinically important because bladder-volume change may accompany displacement of the vaginal cuff and other postoperative pelvic target structures [7,8,10,11]. Nevertheless, the relationship is patient specific, and identical bladder volumes do not guarantee identical vaginal-cuff, nodal-target, rectal, or bowel anatomy. Daily or periodic volumetric imaging remains necessary whenever target visualization or adaptation is required. Postoperative imaging studies therefore support using bladder volume as one component of preparation assessment rather than as a stand-alone surrogate for target position [23-25].

The 2-3 minute interval between US and CT/CBCT was intentionally short and is a methodological strength, but the reference scan occurred after US. Continued urine production during that interval could therefore contribute to the small negative bias, meaning that part of the apparent US underestimation may reflect real bladder filling rather than measurement error alone. A second source of heterogeneity is that baseline reference volume came from planning CT whereas treatment reference volumes came from CBCT. The separate analyses showed similar mean bias and limits of agreement, which is reassuring, but CT and CBCT remain different acquisition and segmentation environments. Interfraction changes in vaginal cuff, bladder, rectal, and bowel anatomy have been documented in postoperative imaging studies [28-30], reinforcing that bladder volume is only one component of preparation assessment.

4.7. Strengths and Limitations

This study has several strengths. It was prospective, obtained paired measurements in the treatment position with only a 2-3 minute interval, sampled the full treatment course, and had complete data at all 14 scheduled time points for 29 participants. A single trained operator used a consistent US acquisition procedure and recorded the median of three consecutive readings. The revision also verified every numerical result directly against the supplied source dataset, specified the ICC model and unit, separated planning-CT and CBCT comparisons, and used repeated-measures Bland-Altman analysis with patient-level bootstrap confidence intervals.

Several limitations remain. First, this was a single-center study with 29 participants, so the number of independent patient clusters is modest even though 406 paired measurements were available. Second, the supplied analytic dataset did not contain age, BMI, stage, concurrent systemic treatment, urinary symptoms/comorbidity, or renal/hydration variables, preventing subgroup assessment of these potential modifiers. Third, all US examinations were performed by one trained investigator and all reference contours by one radiation oncologist. The individual triplicate US readings and repeat contour sets were not retained, so intraoperator US repeatability, interoperator reproducibility, intraobserver contour repeatability, and interobserver segmentation variability could not be estimated. Fourth, planning CT was the baseline reference whereas CBCT was used during treatment, although separate agreement analyses yielded similar results.

Finally, the study evaluated volume agreement rather than clinical effectiveness. It did not prospectively use US to determine whether treatment should proceed, define a patient-specific acceptable planning-volume range, reduce imaging frequency, quantify workflow time or imaging dose, assess postoperative target coverage or organ-at-risk dosimetry, or link bladder-volume discrepancies to toxicity. The 20%, 30%, 50 mL, and 100 mL bands were exploratory agreement thresholds rather than validated safety margins. Consequently, the data cannot establish that US-guided screening improves patient outcomes or permits CBCT reduction.

4.8. Future Research and Implementation

A future implementation trial should evaluate a predefined patient-specific or plan-specific bladder-volume range derived from the planning CT, with explicit correction steps for low and high US readings and mandatory image guidance at clinically appropriate intervals. Outcomes should include agreement and calibration by volume range, age/BMI and urinary factors, operator repeatability, segmentation reproducibility, preparation time, treatment-room time, repeat imaging, patient discomfort, imaging dose, target coverage, organ-at-risk dosimetry, and toxicity. Agreement analyses should continue to account for repeated observations within patients and should predefine clinically meaningful decision thresholds rather than deriving them from method agreement alone.

5. CONCLUSION

Investigator-performed ultrasound provided bladder-volume estimates with close average agreement and a high single-measure absolute-agreement ICC relative to planning CT/CBCT in postoperative gynecological radiotherapy. Repeated-measures analysis showed a small mean bias but individual differences of approximately 40-50 mL within the 95% limits of agreement. Ultrasound may therefore be useful as a rapid, non-ionizing preparation-screening adjunct, but volume agreement does not confirm postoperative target position or full pelvic anatomy and does not justify reducing CBCT frequency. Prospective validation against patient-specific planning ranges, anatomy, dosimetry, workflow outcomes, and clinical endpoints is required before an ultrasound-guided triage pathway is implemented.

ABBREVIATIONS

CBCT = cone-beam computed tomography

CI = confidence interval

CT = computed tomography

ICC = intraclass correlation coefficient

IGRT = image-guided radiotherapy

IMRT = intensity-modulated radiotherapy

LoA = limits of agreement

OAR = organ at risk

PTV = planning target volume

SD = standard deviation

US = ultrasound

VMAT = volumetric-modulated arc therapy.

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