

Scientific Article

Initial Clinical Experience Treating Patients With Gynecologic Cancers on a 6MV Flattening Filter Free O-Ring Linear Accelerator



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Abstract

Purpose: Radiation therapy (RT) is commonly used in the treatment of gynecologic cancers. Intensity-modulated RT (IMRT) has been shown to reduce gastrointestinal toxicity compared with 2-dimensional and 3-dimensional RT modalities. We report the initial clinical experience using IMRT for gynecologic cancers with a novel 6MV flattening filter free O-ring linear accelerator (6X-FFF ORL).

Methods and Materials: We retrospectively identified consecutive women with uterine or cervical cancer who received pelvic RT on Halcyon (Varian Medical Systems, Palo Alto, CA), a novel 6X-FFF ORL. We report their clinicopathologic data, RT details, early disease-control outcomes, acute toxicities, dose-volume histogram data, couch corrections, and treatment times.

Results: Seventeen women received RT on a 6X-FFF ORL for uterine cancer (76%) or cervical cancer (24%) between January 2017 and September 2019. RT was delivered postoperatively (82%) or to intact disease (18%), to a median dose of 50.4 Gy (range, 19.8-55.0 Gy) in 25 fractions (range, 11-28), with 12% receiving extended-field RT and 65% receiving chemotherapy. Target and organ-at-risk constraints were met in all plans. The 3-dimensional vector couch correction average was 0.90 ± 0.37 cm. The mean beam-on time was 2.9 ± 0.4 min and mean treatment time, from imaging start to beam-off, was 3.6 ± 0.4 min. Grade 2 fatigue, anorexia, diarrhea, bloating, and nausea occurred in 41%, 12%, 12%, 6%, and 6% of patients, respectively. There were no grade ≥ 3 toxicities.

Conclusions: In the initial clinical report of pelvic RT for gynecologic cancers using a 6X-FFF ORL, the linac showed versatility in treatment; comparability to flattening-filtered IMRT for early disease-control, toxicity, and dosimetry; and treatment speed that compared favorably to IMRT on a C-arm gantry. Accordingly, a 6X-FFF ORL may increase throughput or reduce day length in departments with high gynecologic cancer volumes, without compromising clinical outcomes.

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Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

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Introduction

Gynecologic cancers relevant to radiation therapy (RT) are largely composed of uterine and cervical cancers. These cancers are managed via a multidisciplinary approach involving surgery, external-beam RT (EBRT), brachytherapy (BT), or chemotherapy.¹⁻⁶

Pelvic RT in gynecologic cancers has improved from 2-dimensional, bony landmark-based RT,^{7,8} to 3-dimensional conformal RT (3D-CRT), wherein anatomic targets and organs-at-risk (OARs) are delineated in computed tomography (CT)-based treatment planning systems.³ This allows optimal RT dose shaping and calculation to OARs. More recently, intensity modulated RT (IMRT) has been used to further shape dose around OARs while still achieving maximal target coverage, with the goal of reducing toxicity.^{9,10} Volumetric-modulated arc therapy (VMAT), whereby RT is delivered in continuous, dynamic arcs, has also been used to deliver pelvic RT, with improvements in doses to OARs, comparable target coverage, and shorter delivery times than those of fixed-beam IMRT.¹¹ IMRT, whether by fixed-beam or VMAT, has been shown to reduce acute and late gastrointestinal (GI) toxicity during pelvic RT compared with 3D-CRT.^{9,10}

A novel 6MV-flattening-filter-free (6X-FFF) O-ring gantry linear accelerator (linac), Halcyon (Varian Medical Systems, Palo Alto, CA), was designed with the goal of delivering treatment more quickly and with greater throughput than a C-arm linac (CAL).¹² Flattening-filter-free (FFF) RT has demonstrated higher dose rate, less head scatter, and less penumbra in comparison to flattening-filtered (FF) RT.¹³ Plan comparison studies between 6X-FFF O-ring linacs (ORL) and CALs have been performed in head and neck cancer,^{12,14,15} breast cancer,¹⁵⁻¹⁷ prostate cancer,¹⁵ spine stereotactic-body RT (SBRT),¹⁸ brain metastasis stereotactic radiosurgery,¹⁹ and pediatric cancers.²⁰ Plans typically showed comparable plan quality and quicker estimated treatment delivery times for 6X-FFF ORLs. Clinical reports of a 6X-FFF ORL to treat patients have generally showed quick treatment times for a variety of complex breast setups and techniques, with reasonable toxicity and OAR doses compared with CALs.²¹

In this study, we report our initial clinical experience treating patients with gynecologic cancers on a 6X-FFF ORL. We hypothesized that pelvic RT on a 6X-FFF ORL would have early disease-control, acute toxicities, target and OAR doses, and treatment times that compare favorably to pelvic RT delivered by CALs.

Methods and Materials

We performed an institutional review board-approved retrospective review of women who underwent pelvic RT

on a 6X-FFF ORL for uterine or cervical cancer at our institution between January 2017 and September 2019. If patients met the inclusion criteria, there were no relevant exclusion criteria. Clinical RT planning, treatment timing, and image guided RT (IGRT) data were abstracted from patients' electronic medical records.

Prescriptions and constraints

Patients underwent CT simulation in supine position, with a knee-foot lock, and both full and empty bladder scans (treated with full bladders). Target volumes were contoured as per Radiation Therapy Oncology Group (RTOG) consensus guidelines for postoperative or intact cases, respectively.^{22,23} Women were treated with whole-pelvic RT in 1.8 Gy fractions to a total dose of 45 to 50.4 Gy. When clinically indicated, extended-field pelvic RT (EFRT), simultaneous integrated boost (SIB) to gross disease to a total dose of 55 Gy in 2.2 Gy fractions, or a high-dose-rate brachytherapy boost was used.

Treatment planning was performed in Eclipse (Varian Medical Systems, Palo Alto, CA; version 15.1 for Halcyon 1.0 and 15.6 for Halcyon 2.0) and used 6X-FFF photon VMAT. When EFRT was delivered, a dual-isocenter gradient match was performed if a single-isocenter plan was not possible owing to the maximum field size of the 6X-FFF ORL (28 cm superior to inferior). Coverage specifications were such that the prescription dose must cover 97% of the planning target volume (PTV), with a secondary target goal that 98% of the PTV must be covered by at least 95% of the prescription dose. PTV minimum dose was 93% and maximum dose 110% of prescription to either OAR or targets. OAR constraints were adapted from RTOG 1203 and included rectum V40 <80% (max <100%), bowel V40 <30% (max <70%), bladder V45 <35% (max <70%), pelvic bones V10 <90% (or V25 <90%), duodenum V55 <15 mL, kidneys V18 <50%, and spinal cord max <45 Gy.^{9,24}

Treatment planning

All treatment plans were generated with 2 to 4 arcs per isocenter in Eclipse version 15.1 or version 15.6. Standard VMAT planning techniques were applied with rotated collimators. Depending on initial optimization and sparing of OARs, additional arcs were added for further modulation. Modulation was performed with 1.0-cm width dual-layer stacked and staggered multileaf collimators.

Two patients were treated with EFRT, requiring 2 isocenters with 3 arcs each. The isocenters were separated by 8 cm in only the superior/inferior direction, to allow for auto-feathering and creation of a gradient region.

Image guidance

Daily IGRT was performed for all patients using cone beam CT (CBCT), given that the 6X-FFF ORL (1) cannot perform port films and (2) does not have a light field for skin marker or source-to-surface-distance confirmation. The initial version (version 1.0) of the 6X-FFF ORL contained only MV CBCT functionality, with CBCT dose included in the dose calculation within the treatment planning system. The subsequent version (version 2.0) of the 6X-FFF ORL was updated to contain KV CBCT functionality. Representative images from CT simulation, MV CBCT, and KV CBCT, showing improved IGRT resolution with KV CBCT are depicted in Fig 1.

Data analysis

The primary objectives of this report are to provide the initial clinical assessment of the versatility, early disease-control, toxicity, dose-volume histogram (DVH) data, couch corrections, and speed of RT on a 6X-FFF ORL for gynecologic cancers. Versatility was evaluated via the clinico-pathologic features, simulation techniques, and field designs of the uterine and cervical cancer patients treated on the 6X-FFF ORL. Disease control was assessed by reporting local, regional, and distant failure rates, as well as mortality. Acute toxicity was assessed using common terminology criteria for adverse events version 4.0 to 5.0 grading from provider-reported outcomes at weekly on-treatment and standard follow-up appointments. DVH data for targets and OARs were collected to evaluate plan dosimetry. Average treatment couch corrections applied based on daily online CBCT matching to

bony anatomy from CT simulation were collected to assess setup consistency and the potential additional value of daily CBCT on a 6X-FFF ORL. Speed was evaluated by beam-on time delivered to an electronic portal imaging device (EPID), average patient treatment time (daily CBCT and beam-on time), and average patient total room usage time.

Statistics

Data were reported using descriptive statistics (means, medians, ranges, and standard deviations when appropriate for continuous variables, and percentages for categorical variables). Time and couch correction values were compared with reference values qualitatively. Data were analyzed using the MATLAB R2018a Statistics Toolbox software package (The MathWorks Inc, Natick, MA).

Results

Types of patients treated on a 6X-FFF ORL

Our report included 17 consecutive patients with a median age at RT of 64 years (range, 38-88 years), evaluated at a median follow-up interval of 10.2 months (range, 1.1-21.2 months).

Patients were treated for uterine cancer (76%, $n = 13$) and cervical cancer (24%, $n = 4$). Two of the uterine patients (15%) received salvage treatment for vaginal cuff recurrences. Uterine and cervical cancer histologies were most commonly endometrioid adenocarcinoma (62%, $n = 8$) and squamous cell carcinoma (75%, $n = 3$), respectively. Patients with uterine cancer and cervical

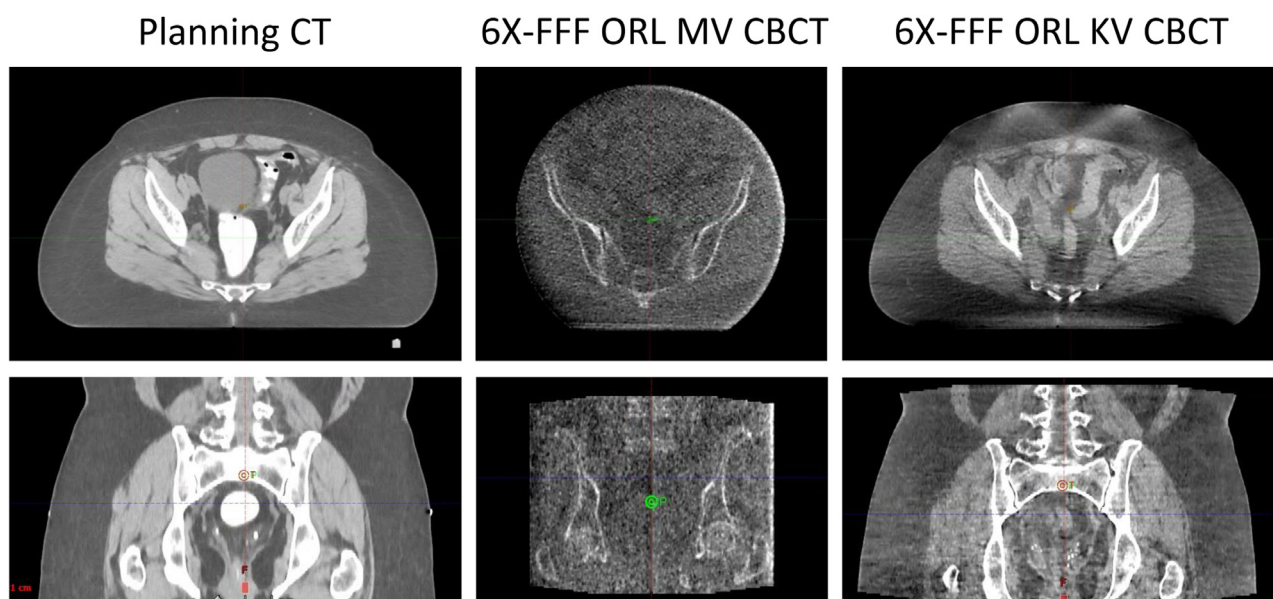


Figure 1 Imaging modality comparison. Representative images from planning computed tomography (CT), 6MV flattening filter free O-ring linear accelerator (6X-FFF ORL) MV cone beam CT (CBCT), and 6X-FFF ORL KV CBCT.

cancer most commonly had stage 3 (54%, $n = 7$) and stage 1 disease (75%, $n = 3$), respectively. Surgery was performed in 82% ($n = 14$) of patients. Chemotherapy was administered both concurrently with RT and sequentially in 12% ($n = 2$), concurrently in 18% ($n = 3$), and sequentially in 35% ($n = 6$). Concurrent chemotherapy consisted of cisplatin (100%, $n = 5$), and sequential systemic therapy consisted of carboplatin and paclitaxel (100%, $n = 8$).

RT details are presented in Table 1. All patients (100%, $n = 17$) were treated supine using VMAT. Most patients (94%, $n = 16$) were simulated with both full and empty bladders and treated with attempted full bladders. One patient (6%) was unable to tolerate bladder filling and was simulated and treated with a comfortably full bladder. Most patients received standard whole-pelvic RT (88%, $n = 15$). Two patients (12%) received EFRT using the dual-isocenter gradient match plan. Patients received a median RT dose of 45 to 50.4 Gy (range, 19.8-55.0 Gy) in 25 to 28 fractions (range, 11-28). The patient that received 19.8 Gy (concurrently with cisplatin) terminated planned treatment to 50.4 Gy early owing to nonmedical externalities. For IGRT, 6 patients (35%) received daily MV CBCT and 11 (65%) received daily KV CBCT. Six patients (35%) received a high-dose-rate BT boost after external-beam RT to a median dose of 18.5 Gy (range, 10-27.5 Gy) in 3 fractions (range, 2-5).

Dosimetric parameters are summarized in Table 2. All plans (100%, $n = 17$) met predetermined target coverage, rectal, bowel, bladder, pelvic bone, duodenal, kidney, and spinal cord constraints.

Early disease-control outcomes

There were 16 patients evaluable for early disease-control outcomes (1 patient terminated treatment early and was lost to follow-up). There were 4 (25%) failures: 1 (25%) local (distal vagina in FIGO IIC1 endometrioid uterine cancer), 1 (25%) regional (isolated para-aortic lymph node in FIGO IIC1 endometrioid uterine cancer), and 2 (50%) distant (1 omental in FIGO IB uterine carcinosarcoma, and 1 liver in a patient treated for vaginal cuff recurrence of initial FIGO IIIA serous uterine cancer), at 12.4, 2.7, 5.9, and 7.9 months from start of RT, respectively. All failures were outside of the RT fields. There was 1 (6%) death, noncancer-related, at 7.1 months from start of RT.

Acute toxicity summary

Of the 17 patients evaluable for toxicity outcomes, there were no grade ≥ 3 acute toxicities. Grade 1 toxicities that occurred in at least 10% of patients included diarrhea (59%, $n = 10$), nausea (53%, $n = 9$), fatigue (47%, $n = 1$), abdominal pain (29%, $n = 5$), bloating (29%, $n = 5$),

Table 1 Details of radiation therapy course

Variable	Value (%)
RT position	
Supine	17 (100)
RT field	
Whole pelvis	15 (88)
Extended field	2 (12)
Delivered dose (Gy)	
Median	50.4
Range*	19.8-2555.0
No. of fractions	
Median	25
Range	11-28
Bladder filling†	
Full and empty	16 (94)
Comfortable	1 (6)
IGRT	
MV CBCT	6 (35)
kV CBCT	11 (65)
Brachytherapy boost‡	
Yes	6 (35)
No	11 (65)
Boost modality	
High dose rate	6 (100)
Boost dose (Gy)	
Median	18.5
Range	10-27.5
Boost no. of fractions	
Median	3
Range	2-5
Systemic therapy	
Concurrent only	3 (18)
Sequential only	6 (35)
Concurrent and sequential	2 (12)
None	6 (35)

Abbreviations: CBCT = cone beam computed tomography; IGRT = image guided radiation therapy; RT = radiation therapy.

* One patient was planned to receive 50.4 Gy in 28 fractions but did not complete her course owing to social difficulties. She received 19.8 Gy in 11 fractions, with concurrent cisplatin.

† Patients were simulated with both full and empty bladders and treated with attempted full bladders. One patient was unable to tolerate bladder filling and was simulated and treated with a comfortably full bladder.

‡ Brachytherapy boosts are not delivered on the 6MV flattening filter free O-ring linear accelerator (6X-FFF ORL).

urinary tract pain (29%, $n = 5$), constipation (24%, $n = 4$), urinary frequency (24%, $n = 4$), RT dermatitis (18%, $n = 3$), urinary urgency (12%, $n = 2$), and vaginal dryness (12%, $n = 2$). Grade 2 toxicities that occurred included fatigue (41%, $n = 7$), anorexia (12%, $n = 2$), diarrhea (12%, $n = 2$), bloating (6%, $n = 1$), and nausea (6%, $n = 1$).

Patient setup uncertainty and IGRT experience

The average 3D vector couch corrections between skin-marker alignment and online CBCT-assisted

Table 2 Dosimetric parameters of targets and OARs

Variable	Value (%)
PTV	
V97 (median, range)	98.9 (95.8-100)
V 110	0 (0-0.3)
Rectum	
V40	59.2 (16.2-98.9)
Bowel bag	
V40	14.4 (1.7-35.3)
Large bowel	
Maximum (Gy)	53.2 (44.9-56.7)
Bladder	
V45	27.1 (0.2-52.3)
Pelvic bones	
V10	96.7 (90-99.5)
V25	71.5 (45.5-84.3)
Left pelvic bones	
V10	95.5 (85.4-99.2)
V25	66.5 (44.6-81.8)
Right pelvic bones	
V10	95.9 (87.1-99.5)
V25	64.4 (40.7-78.2)
Sacrum	
V10	100 (93-100)
V25	96.7 (47.9-100)
Duodenum*	
D0.03 mL (Gy)	47.8 (44-51.7)
V55 (mL)	0 (0-0)
Kidneys*	
V18	17.9 (13.2-22.5)
Spinal cord*	
Maximum (Gy)	23 (18.4-27.7)

Abbreviations: OAR = organs-at-risk; PTV = planning target volume.

* Only extended-field radiation therapy patients were evaluated.

positioning for all patients in this study, for all fractions of 6X-FFF ORL treatment, was 0.90 ± 0.37 cm (Fig 2).

Treatment time and throughput analysis

Figures 3 and 4 portray the treatment and in-room times, respectively, for standard fractions, initial fractions (including setup time), and outlier fractions (due to nonmachine-related issues). Outlier fractions included bladder filling variability requiring patients to leave the treatment table to drink and repeat their CBCT, physician and ancillary staff availability for IGRT checks and transport, or interlock issues requiring physics override. Such outlier times were shown in the figures but omitted from average calculations. Outlier treatments were recorded with explanations, to verify that delays were not related to the linac, and therefore not appropriate for mean calculation analysis of usual treatment. No times were omitted owing to quantitative criteria. Treatment times were recorded by the therapists proceeding treatment for 8

of the 17 patients in this report, as treatment times were not routinely recorded with the initial experience treating patients on this linac. Beam-on times without IGRT time incorporated were not routinely recorded and therefore were obtained from delivered plans for these 8 patients on an EPID. The average beam-on and treatment times for all patients were 2.9 ± 0.4 min and 3.6 ± 0.4 min, respectively. The average beam-on and treatment times for patients treated with 2-arc plans ($n = 1$) were 1.9 ± 0.0 min and 4.0 ± 0.4 min, 3-arc plans ($n = 3$) were 1.8 ± 0.3 min and 3.2 ± 0.5 min, and 4-arc plans ($n = 4$) were 2.9 ± 0.4 min and 3.7 ± 0.3 min, respectively. The average total linac room usage time (from changing room to treatment room back to changing room) for all patients was 10.8 ± 1.4 min (Fig 4). The average in-room time for the patient treated with a 2-arc plan was 11.21 ± 1.5 min, and for patients treated with 3-arc and 4-arc plans was 10.0 ± 0.5 min and 11.4 ± 1.8 min, respectively. A total of 42 values out of 127 values across 8 patients were excluded as outliers from the mean treatment time and total room time calculations, most commonly for inadequate or excessive bladder filling, delays in patient transport, and staff availability for checking IGRT or submitting overrides.

Discussion

In this study, we report the initial clinical experience treating patients with gynecologic cancers with RT on a 6X-FFF ORL and showed its versatility, early disease-control outcomes, acute toxicity, DVH data, couch corrections, and speed. Its versatility was shown through its ability to treat patients with multiple different diagnoses, stages, histologies, boost regimens (eg, SIB), image guidance methods, and pelvic nodal treatment \pm para-aortic treatment. We demonstrated that even for EFRT, which necessitates larger RT volumes, a dual-isocenter gradient match can ensure adequate target coverage when the target cannot be fully covered with a single-isocenter technique, despite field size limitations on a 6X-FFF ORL. Thus, a 6X-FFF ORL can treat patients with gynecologic cancers in most clinical situations in which IMRT is used.

Early disease-control outcomes for patients treated on the 6X-FFF ORL are comparable to published reports with no recurrences in the radiation field, albeit with relatively short median follow-up. In our study, there was 1 local (distal vagina), 1 regional (para-aortic node), and 2 distant recurrences. The 1 death was due to competing cardiovascular comorbidity in a patient with medically inoperable uterine cancer. In Post Operative Radiation Therapy in Endometrial Carcinoma-3, a randomized trial comparing postoperative whole-pelvis RT with chemoradiotherapy in patients with high-risk uterine cancer, there were 2.1% local, 4.9% to 9.2% regional, and 23.1% to 29.7% distant recurrence rates in the cohorts at 5

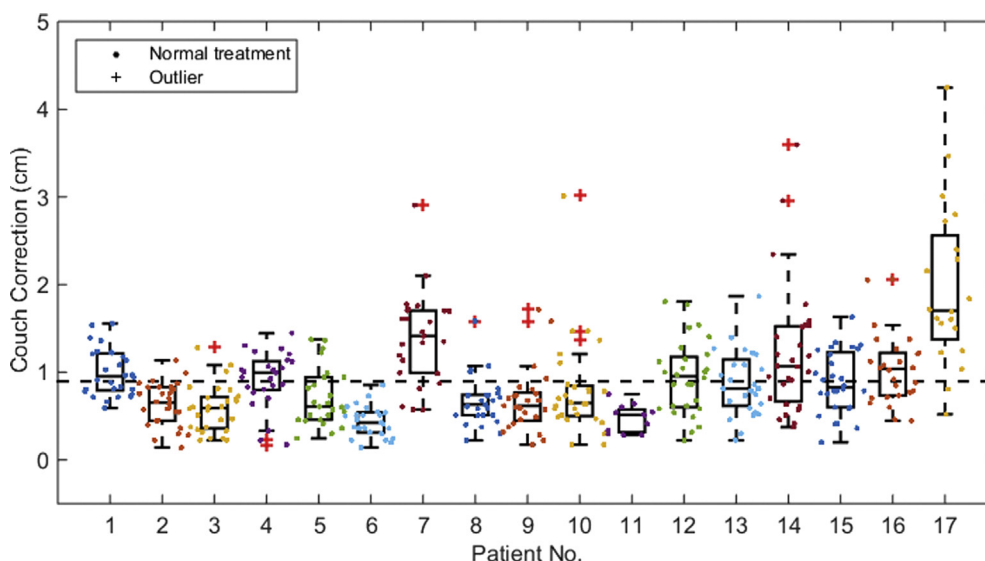


Figure 2 Couch corrections after initial setup based on image-guided radiation therapy (IGRT). Average 3-dimensional vector couch correction between skin-marker alignment and IGRT for all patients, for all fractions of 6MV flattening filter free O-ring linear accelerator treatment.

years.²⁵ In cervical cancer, GOG 109 compared post-operative whole-pelvis RT with or without concurrent chemotherapy and found 15% local and 13% distant recurrence rates in the entire cohort.⁵ When considering the differences between our small, heterogeneous cohort, which contained some patients with medically inoperable and metastatic disease before RT, and the large, highly selected cohorts in the previously mentioned studies, early disease-control on a 6X-FFF ORL is comparable.

Acute toxicity on the 6X-FFF ORL compared favorably with that of published toxicity data for pelvic IMRT on a CAL. In our study, no patients experienced grade ≥ 3

toxicities, and grade 2 toxicities were limited to fatigue (41%, $n = 7$), anorexia (12%, $n = 2$), diarrhea (12%, $n = 2$), bloating (6%, $n = 1$), and nausea (6%, $n = 1$). In RTOG 1203, a randomized trial comparing postoperative whole-pelvis RT (45-50.4 Gy in 1.8 Gy fractions with or without concurrent chemotherapy) delivered using IMRT versus 3D-CRT for uterine or cervical cancer, patients in the IMRT arm experienced 16.4% acute grade 3 to 4 toxicity, 26.2% grade ≥ 2 GI toxicity, and 33.7% experienced diarrhea frequently or almost constantly.⁹ Even with multiple patients receiving EFRT and concurrent chemotherapy, RT for gynecologic cancers on a 6X-FFF

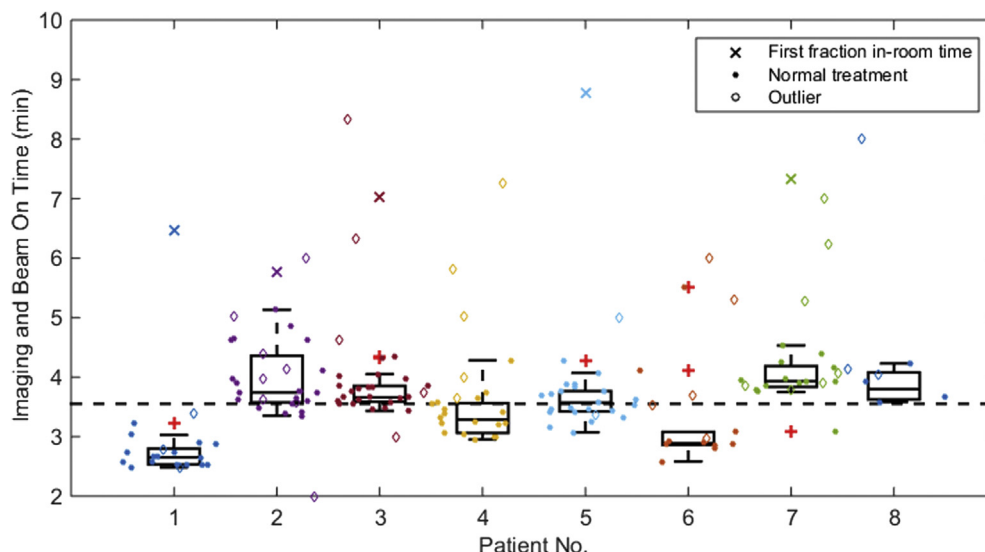


Figure 3 Treatment time. Average treatment time (from start of imaging to beam off), for 8 patients, for all standard fractions of 6MV flattening filter free O-ring linear accelerator treatment. The average treatment times for nonstandard fractions are separately displayed.

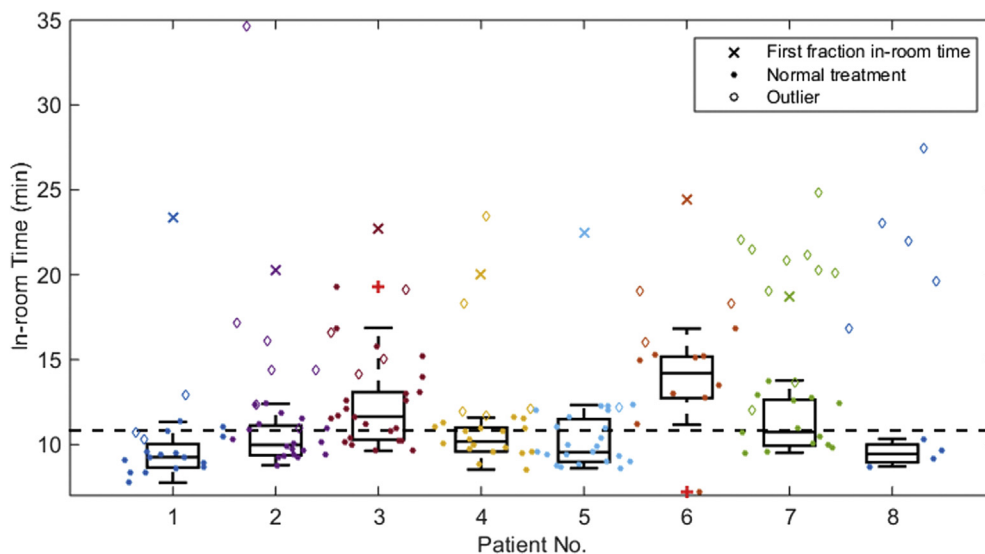


Figure 4 Total room time. Average total room time (time from leaving gowned waiting area to return), for 8 patients, for all standard fractions of 6MV flattening filter free O-ring linear accelerator treatment. The average total room times for nonstandard fractions are separately displayed.

ORL was well tolerated. It is possible that reduced transmission through the 6X-FFF ORL's dual-layer multileaf collimators, which has been shown in head and neck cancer to improve OAR sparing compared with a C-arm linac, may contribute to the favorable toxicity profile observed.¹⁴

Our study showed that pelvic RT plans, including EFRT plans, for gynecologic cancers on a 6X-FFF ORL were able to meet institutional or RTOG DVH constraints for targets and OARs for all patients, even with 6 (35%) patients receiving an average of approximately 0.04 Gy per fraction of additional dose from MV CBCT.²⁶

IGRT on a 6X-FFF ORL for pelvic RT using daily CBCT matching from skin marker alignment provided acceptable average 3D vector couch correction for all patients (0.90 ± 0.37 cm), despite not having a light field, crosshair, or skin-to-surface distance confirmation available. This value compares favorably with those of multiple published experiences of daily CBCT during pelvic IMRT/VMAT for gynecologic cancers, whose calculated average 3D vector couch corrections ranged from 0.45 to 0.91 cm.^{27,28} The average 3D vector couch correction value in Yao et al was 0.45 cm.²⁷ This was calculated using data from daily KV CBCT for pelvic VMAT for gynecologic malignancies, in which a 6-degrees-of-freedom couch was used. To optimize comparability to the 6X-FFF ORL, which contains a 3-degrees-of-freedom couch, we calculated Yao et al's average 3D vector couch correction using only medial/lateral, anterior/posterior, and superior/inferior corrections, which may underestimate those values in the absence of pitch, roll, and yaw. Monroe et al determined a 3D vector couch correction value of 0.91 cm.²⁸ This value comes from daily CBCT with match to gold fiducial vaginal cuff markers in

patients receiving pelvic RT for endometrial cancer, although it is not specified whether patients underwent MV or KV CBCT or what specific RT modalities were used. Direct statistical comparison between our data and the published values was not performed given the differences between our studies and the inherent limitations of comparing data across studies. Qualitatively, the couch corrections observed compare well.

The mean beam-on, treatment, and in-room times for a typical fraction were 2.9 ± 0.4 min, 3.6 ± 0.4 min, and 10.8 ± 1.4 min, respectively. These times remain short, even with multiple beam arrangements, using as many as 4 arcs. Although there are published data containing a reference value for calculated beam-on time for pelvic VMAT for cervical cancer on a 6X CAL (1.2 min),¹¹ to our knowledge, no analogous treatment time or in-room time data have previously been published to our knowledge, establishing our data as benchmark values. Direct comparison of our 6X-FFF ORL beam-on time delivered to an EPID with the published 6X CAL value would be inappropriate, as the CAL value was calculated, rather than delivered, which does not account for the added time associated with gantry movement and beam modulation and therefore underestimates the actual treatment delivery time. In addition, the CAL study did not specify how many patients received EFRT or 3- or 4-arc plans, which many of our patients received. Thus, pelvic RT on a 6X-FFF ORL is quick and compares favorably with published calculated beam-on time data.

Given the fast treatment times and high throughput for pelvic RT on a 6X-FFF ORL, this adds to the sparse body of published clinical experiences demonstrating quick treatments on this type of linac.²¹ Short treatment times may improve the tolerability of uncomfortable treatment

positions, prevent patients from waiting until late to receive treatments, decrease staffing needs improving resource allocation, and increase the number of patients able to receive treatment per day potentially reducing treatment delays due to resource limitations.

Our study has several limitations. Given the short follow-up interval, it is possible that additional recurrences, including in-field recurrences, have not yet been discovered. With longer follow-up, we will further assess disease-control. We will need to assess late toxicity, particularly in patients who received SIBs or BT boosts. Given that 6 (35%) patients received MV CBCT IGRT, which delivers higher imaging doses than KV CBCT, our DVH data may overestimate OAR doses, as newer 6X-FFF ORLs use KV CBCT. The heterogeneity of patients treated also may limit the generalizability of results. In addition, a small proportion of treatment times were excluded as outliers due to software malfunctions and interlock issues requiring physicist override, which were deemed nonlinac-related issues. Given the novelty of the 6X-FFF ORL, it is possible that such issues may be more common in new technology and therefore machine-related. If so, treatment times may be slightly longer than reported.

With this report, we share the first published clinical experience of 6X-FFF ORL RT for gynecologic cancers. We demonstrated that the linac was versatile in terms of the clinico-pathologic variety of patients treated, comparable to FF IMRT in terms of early disease-control outcomes and acute toxicity, acceptable in terms of dosimetric parameters and setup corrections, and at least as fast as RT on a CAL. RT on a 6X-FFF ORL may increase throughput or reduce length of day in departments with high gynecologic cancer volumes, without compromising disease-control, acute toxicity, or dosimetric outcomes.

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