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ORIGINAL RESEARCH

Helical tomotherapy provides efficacy similar to that of intensity-modulated radiation therapy with dosimetric benefits for endometrial carcinoma

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Background: The purpose of this study was to compare the efficacy of intensity-modulated radiotherapy (IMRT) and helical tomotherapy for endometrial cancer.

Methods: Between November 1, 2006 and November 31, 2010, 31 patients with histologically confirmed endometrial cancer were enrolled. All enrolled patients received total abdominal hysterectomy and bilateral salpingo-oophorectomy with adjuvant whole pelvic IMRT or helical tomotherapy.

Results: The actuarial 3-year overall survival, disease-free survival, locoregional control, and distant metastasis-free rates for the IMRT and helical tomotherapy groups were 87.5% versus 100%, 91.7% versus 51.7%, 91.7% versus 83.3%, and 91.7% versus 51.7%, respectively. The conformal index and uniformity index for IMRT versus helical tomotherapy was 1.25 versus 1.17 ($P = 0.04$) and 1.08 versus 1.05 ($P < 0.01$), respectively. Two of 31 patients with cervical stump failure were noted, one in the IMRT group and the other in the helical tomotherapy group. No acute or late grade 3 or 4 toxicities were noted, including proctitis, or genitourinary or gastrointestinal disturbances.

Conclusion: Helical tomotherapy is as effective as IMRT and has better uniformity and conformal indices, and critical organ-sparing properties. Prospective clinical trials are needed to evaluate the comparative efficacy of IMRT versus helical tomotherapy.

Keywords: endometrial cancer, helical tomotherapy, intensity-modulated radiotherapy

Introduction

Postoperative adjuvant radiotherapy is usually considered for women with intermediate-risk or high-risk early-stage endometrial cancer or with advanced disease to reduce the risk of vaginal and pelvic relapse. For high-risk and intermediate-risk groups, pelvic radiation has been reported to reduce the 4-year cumulative incidence of local recurrence from 13% to 5%.[1]

With advances in radiotherapy modalities, whole pelvic intensity-modulated radiotherapy (IMRT) is used in gynecologic malignancies with excellent planning target volume coverage and is associated with fewer acute gastrointestinal sequelae than conventional whole pelvic radiotherapy.[2] A number of groups have explored IMRT in the gynecologic setting as a method to minimize the gastrointestinal, genitourinary, and bone marrow toxicity commonly found with conventional whole pelvic radiotherapy.[3,4]

Helical tomotherapy is an image-guided rotational form of IMRT. Yang et al[5] reported that IMRT and helical tomotherapy yielded better conformity and delivered a lower integral dose to organs at risk compared with three-dimensional conformal

radiotherapy in postoperative whole pelvic irradiation of endometrial cancer. Similar results were also reported by Lian et al.[6] However, these reports did not include the clinical outcomes for endometrial cancer treated postoperatively by whole pelvic IMRT and helical tomotherapy. We report here our initial 4-year clinical experience of patients with endometrial cancer treated by IMRT or helical tomotherapy, focusing on clinical outcomes and toxicities.

Materials and methods

Patient characteristics

Between November 1, 2006 and November 31, 2010, 31 patients undergoing whole pelvic radiotherapy postoperatively for endometrial cancer at Far Eastern Memorial Hospital (FEMH) were enrolled. Retrospective patient data were collected with approval of the institutional review board of Far Eastern Memorial Hospital (FEMH-IRB-100059-E). Eligible patients had undergone total abdominal hysterectomy and bilateral salpingo-oophorectomy with or without additional surgical staging procedures for endometrial cancer no more than 8 weeks prior to the start of radiation therapy. Patients had no known metastatic disease outside of the pelvis. All patients had histologic grade 2 or 3 endometrial adenocarcinoma with more than 50% myometrial invasion, stromal invasion of the cervix, or extrauterine disease confined to the pelvis and/or positive peritoneal cytology. Patients with papillary serous or clear cell histology were excluded.

Staging investigations included a complete history and physical examination, fiberoptic endoscopic evaluation, complete blood counts, liver and renal function tests, chest x-ray, magnetic resonance imaging scans, and computed tomography (CT) scans of the pelvic region. The disease was staged according to the International Federation of Gynecology and Obstetrics (FIGO) criteria.

Delineation of target volumes

Radiotherapy was administered to the whole pelvic region in 25–28 fractions with 7-field IMRT or with helical tomotherapy, an image-guided IMRT (Tomotherapy Inc, Madison, WI), five times a week, totaling 45–50.4 Gy with vaginal intracavity brachytherapy (microSelectron® high dose remote afterloading machine treatment planning system, Genie, Nucletron, Veenendahl, The Netherlands). For vaginal intracavity brachytherapy, 2–6 fractions of 4.5–5.0 Gy at 0.5 cm at a high dose rate were delivered to the upper third of the vagina. Delineation and constraints were defined according to the consensus recommendations published by Small et al.[7] The clinical target volume included the internal, external, and common iliac nodes and the proximal vagina. The internal target volume was defined as the volume of the vagina and paravaginal soft tissues in both the empty and full bladder CT scans that were done at the time of simulation and fused together. In patients with disease involving the cervical stromal or pelvic lymph nodes, the presacral region to S3 was also included in the clinical target volume. A margin of 0.7 cm around the lymph node groups was used. The vaginal clinical target volume included the proximal 3–4 cm of the vagina and paravaginal tissues. A margin of 0.7 cm was added to the "vessel" contour in all dimensions and modified by anatomic boundaries (as clinically indicated for individual patients) to create the nodal clinical target volume, from which the pelvic bones, femoral heads, and vertebral bodies were excluded. Approximately 1.5 cm of tissue anterior to the S1, S2, and S3 sacral segments was usually added to the clinical target volume in order to include the presacral lymph nodes and uterosacral ligaments. The clinical vaginal and parametrial target volume should actually be an internal target volume to account for internal organ motion. The clinical target volume was expanded by 0.7 cm to create the planning target volume. The 90% isodose surface covered between 95% and 98% of the planning target volume, or volumes of overdose exceeding 115% <5% of the planning target volume could be considered acceptable. The field width, pitch, and modulation factor usually used for optimization of whole pelvic helical tomotherapy planning was 2.5 cm, 0.32, and 3.0, respectively.

Normal structures were contoured using a full-bladder CT scan. The organs at risk (ie, bladder, rectum, sigmoid, small bowel, and femoral heads) were contoured as solid organs. Dose-volume constraints for normal tissues were as follows: small bowel (2 cm above the most superior vessel contour) <30% to receive ≥ 40 Gy; rectum < 60% to receive ≥ 30 Gy; bladder < 35% to receive ≥ 45 Gy; and femoral head ≤ 15% to receive ≥ 30 Gy; pelvic bone marrow, and V10 < 95% and V20 < 76%.[8]

Conversion of hypofractionated dose to normalized total dose

To calculate the total dose of whole pelvic IMRT or helical tomotherapy and vaginal intracavity brachytherapy, the physical doses were converted into normalized total doses.[9–12] The normalized total dose gives the dose in 2 Gy fractions that would result in equivalent biological effect in the fractionation of interest. Normalized total doses were calculated according to the linear quadratic model with

normalization for acute effects ($\alpha/\beta = 10$). The normalized total dose was the sum of two components, ie, the normalized total dose of vaginal intracavity brachytherapy at 0.5 cm from the applicator surface and the normalized total dose of whole pelvic IMRT or helical tomotherapy in the planning target volume. The normalized total dose is given by NTD = D $\{[1 + d/(\alpha/\beta)]/[1 + 2\ Gy/(\alpha/\beta)]\}$, where D is the total dose in the hypofractionation regimen and d is the dose per fraction.

Follow-up

Upon completion of treatment, patients were evaluated every 3 months for the first year, every 4 months during the second year, every 6 months during the third year, and annually thereafter. At each visit, a physical and pelvic examination, blood counts, clinical chemistry, and chest x-rays were performed. CT scan, ultrasound, and other imaging studies were conducted when appropriate. Suspected cases of persistent or recurrent disease were confirmed by biopsy whenever possible. Acute and late toxicities (occurring > 90 days after the start of radiotherapy) were defined and graded according to the Common Terminology Criteria for Adverse Events version 3.0.

Statistical methods

Descriptive statistics (mean, median, proportions) were calculated to characterize the patient, disease, and treatment features as well as toxicities after treatment. Overall survival, disease-free survival, locoregional control, and distant metastasis-free rates were estimated using the Kaplan-Meier product-limit method. All analyses were performed using the Statistical Package for the Social Sciences, version 12.0 (SPSS Inc, Chicago, IL).

Results

Patient characteristics

All enrolled patients were treated following hysterectomy with whole pelvic IMRT or helical tomotherapy according to patient preference, followed by either brachytherapy (seven IMRT-treated and 10 for the helical tomotherapy-treated group) or not. Two patients (one for IMRT and one for helical tomotherapy, both stage IIIA) received concurrent postoperative chemoradiation with an intravenous infusion of cisplatin 40 mg/m^2 weekly for six cycles. The distribution of stage IIB–IIIC disease was 33% and 63% for the IMRT and helical tomotherapy groups, respectively. As seen in Table 1, patient characteristics were similar in the IMRT and helical tomotherapy groups.

Table 1 Patient characteristics

Groups/ variable	IMRT	HT	All
	Patients, n (%)		
Age (years)			
Mean	52.8	53.2	53.1
Range	42–69	40–66	40–69
Karnofsky performance status			
<60	0	0	0
≥70	12 (100%)	19 (100%)	31 (100%)
Pathology			
Adenocarcinoma	12 (100%)	19 (100%)	31 (100%)
FIGO stage			
Stage IB	3 (25.0%)	3 (15.8%)	6 (19.4%)
Stage IC	3 (25.0%)	3 (15.8%)	6 (19.4%)
Stage IIA	2 (16.7%)	1 (5.3%)	3 (9.7%)
Stage IIB	1 (8.3%)	5 (26.3%)	6 (19.4%)
Stage IIIA	2 (16.7%)	2 (10.5%)	4 (12.9%)
Stage IIIC	1 (8.3%)	5 (26.3%)	6 (19.4%)
Median dose for RT completion (range, Gy)	50.4 (45–60)	45 (44–50.4)	45 (44–60)
Mean time for RT completion (range, weeks)	6.6 (5–14)	5.6 (4–9)	6.0 (4–14)

Abbreviations: All, all patients in the study; FIGO, International Federation of Gynecology and Obstetrics; HT, helical tomotherapy; IMRT, intensity-modulated radiation therapy; RT, radiation therapy.

Treatment outcome

Median survival was 21 (range 6–45) months. Actuarial 3-year overall survival, disease-free survival, locoregional control, and metastasis-free survival rates were 94.1%, 71.4%, 88.0%, and 71.4%, respectively. Actuarial 3-year overall survival, disease-free survival, locoregional control, and metastasis-free survival rates for the IMRT versus helical tomotherapy group were 87.5% versus 100%, 91.7% versus 51.7%, 91.7% versus 83.3% and 91.7% versus 51.7%, respectively (Figures 1–3).

Locoregional failure and distant metastasis

Of the 31 eligible patients, 29 patients (93.5%) with no local recurrence and two with cervical stump failure were noted. One 55-year-old patient had stage IC, grade II endometrial cancer with focal vascular permeation and stump failure at month 5 after 54 Gy IMRT without vaginal intracavity brachytherapy. The other patient, also aged 55 years, had stage IIB, grade III endometrial cancer with perilymphovascular permeation and stump failure at month 27 after 45 Gy helical tomotherapy with 9 Gy vaginal intracavity brachytherapy.

Four patients had distant metastases. One 55-year-old patient with stage IC, grade II endometrial cancer had vascular

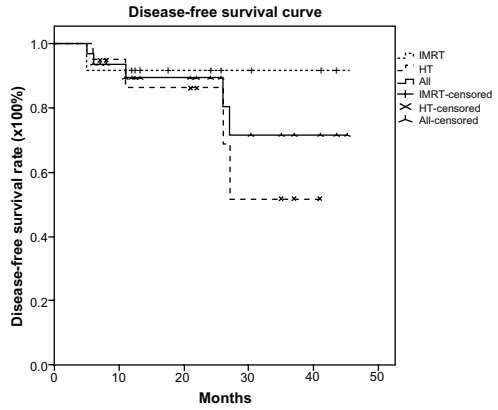

Figure 1 Actuarial disease-free survival rates at 3 years for 31 patients with endometrial cancer treated using whole pelvic intensity-modulated radiation therapy (n = 12) or helical tomotherapy (n = 19).

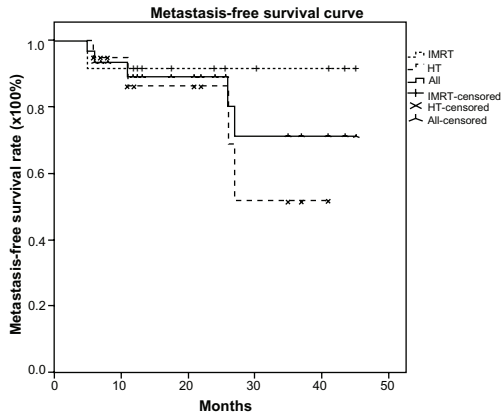

Figure 3 Actuarial metastasis-free survival rates at 3 years for 31 patients with endometrial cancer treated using whole pelvic intensity-modulated radiation therapy (n = 12) or helical tomotherapy (n = 19).

permeation and liver metastasis at month 11, a 40-year-old patient had stage IIA, grade II endometrial cancer with vascular permeation and liver metastasis at month 26, and a 51-year-old patient treated with helical tomotherapy had metastatic nodes in the left supraclavicular fossa at month 6. All of these patients received 45 Gy whole pelvic helical tomotherapy with 15 Gy vaginal intracavity brachytherapy. One 55-year-old patient had stage IC, grade II endometrial cancer with focal vascular permeation and lung metastasis at month 5 after 54 Gy IMRT without vaginal intracavity brachytherapy.

Dose-volume analysis and comparison of IMRT and helical tomotherapy

Compared with the IMRT group, the helical tomotherapy group had significantly better conformal and uniformity indices. Dose-volume histogram statistics for organs at risk are described in Table 2. Helical tomotherapy provided significantly better critical organ sparing than IMRT for the rectum, bladder, both femoral heads, and intestines. The planning target volume was 874 mL in the IMRT group and 975 mL in the helical tomotherapy group ($P = 0.44$, Table 2A). The normalized total dose of planning target volume in patients treated with whole pelvic irradiation followed by brachytherapy was 63 Gy in the IMRT group and 62 Gy in the helical tomotherapy group ($P = 0.93$). In this subgroup, helical tomotherapy provided better bladder, left-sided femoral head, and intestine sparing than IMRT (Table 2B).

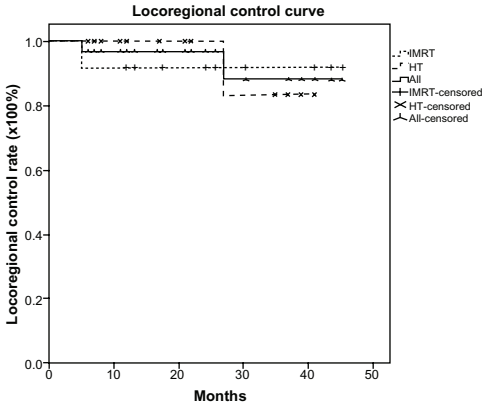

Figure 2 Actuarial locoregional control rates at 3 years for 31 patients with endometrial cancer treated using whole pelvic intensity-modulated radiation therapy (n = 12) or helical tomotherapy (n = 19).

Acute and late toxicity

No grade 3 or 4 acute or late toxicities with proctitis, genitourinary or gastrointestinal disturbances, or fistulae were noted. Of the 31 patients, two suffered from pain at their first sexual intercourse post-treatment. Rates of acute grade 1 and 2 diarrhea for the whole pelvic IMRT versus helical tomotherapy groups were 83.3% versus 16.7% and 89.5% versus 10.5%, respectively. Grade 2 diarrhea as a side effect of whole pelvic irradiation followed by brachytherapy occurred in 1/7 (14%) and 1/10 (10%) patients in the whole pelvic IMRT and helical tomotherapy groups, respectively. Only one patient (5.2%) suffered grade 3 leucopenia during concurrent chemoradiation therapy. There were no late grade 3 or 4 hematologic toxicities.

Discussion

IMRT has been used recently for gynecologic malignancies due to its superiority over conventional techniques with regard to sparing of normal tissue and dose delivery to an irregular target volume.[2,13] However, there have been very few reports on tumor control using IMRT as adjuvant treatment for endometrial cancer. Beriwal et al[14] reported encouraging results for 3-year overall survival and disease-free survival in women with endometrial cancer treated postoperatively by

Table 2A Comparison of dosimetric parameters and normal organs at risk for irradiation of endometrial cancer with IMRT and HT for all patients

All patients	IMRT (n = 12)	HT (n = 19)	*P* value
PTV			
Volume	874.4 ± 377.8	975.2 ± 320.5	0.44
UI	1.08 ± 0.02	1.05 ± 0.02	0.003
CI	1.25 ± 0.15	1.17 ± 0.06	0.04
Right femoral head			
Mean (%)	21.2 ± 5.1	17.3 ± 3.3	0.015
Left femoral head			
Mean (%)	21.8 ± 4.6	17.2 ± 3.3	0.002
Rectum			
Mean (Gy)	39.7 ± 8.3	33.5 ± 4.6	0.013
Intestine			
Mean (Gy)	27.9 ± 2.7	21.9 ± 3.4	<0.001
Bladder			
Mean (Gy)	40.2 ± 3.9	34.0 ± 4.0	<0.001
Right-sided iliac bone			
V10 (%)	92.8 ± 4.5	92.3 ± 8.3	0.64
V20 (%)	77.3 ± 6.9	69.4 ± 9.8	0.14
Left-sided iliac bone			
V10 (%)	93.7 ± 4.3	94.7 ± 6.1	0.71
V20 (%)	74.6 ± 7.7	69.7 ± 8.1	0.21

Note: Vx is the percentage of volume that receives ≥x Gy.
Abbreviations: CI, conformal index; HT, helical tomotherapy; IMRT, intensity-modulated radiation therapy; PTV, planned total volume; UI, uniformity index.

Table 2B Comparison of dosimetric parameters and normal organs at risk for irradiation of endometrial cancer with IMRT and HT for patients treated with whole pelvic irradiation followed by brachytherapy

Patient treated with whole pelvic irradiation followed by brachytherapy	IMRT (n = 7)	HT (n = 10)	*P* value
PTV			
Volume	891.5 ± 400.2	950.7 ± 362.4	0.75
NTD (Gy)	62.9 ± 12.4	62.4 ± 10.9	0.93
UI	1.06 ± 0.02	1.06 ± 0.02	0.59
CI	1.23 ± 0.09	1.17 ± 0.06	0.13
Right femoral head			
Mean (%)	20.2 ± 3.7	16.9 ± 3.1	0.07
Left femoral head			
Mean (%)	21.1 ± 4.0	16.9 ± 3.1	0.03
Rectum			
Mean (Gy)	37.5 ± 8.7	34.1 ± 4.6	0.30
Intestine			
Mean (Gy)	27.1 ± 1.8	22.8 ± 3.0	0.004
Bladder			
Mean (Gy)	39.3 ± 4.0	34.4 ± 3.2	0.017
Right side iliac bone			
V10 (%)	85.8 ± 13.0	93.6 ± 5.9	0.21
V20 (%)	65.8 ± 15.2	67.5 ± 8.5	0.81
Left side iliac bone			
V10 (%)	85.1 ± 16.0	94.7 ± 6.1	0.19
V20 (%)	65.0 ± 16.8	67.9 ± 6.0	0.75

Note: Vx is the percentage of volume that receives ≥x Gy.
Abbreviations: CI, conformal index; HT, helical tomotherapy; IMRT, intensity-modulated radiation therapy; NTD, normalized total dose; PTV, planned total volume; UI, uniformity index.

IMRT, with rates of 90% and 84%, respectively. Bouchard et al[15] also reported encouraging results for postoperative aperture-based IMRT in patients with endometrial cancer (Table 3). In the current study, the 3-year overall survival and locoregional control rates were 94% and 88%, respectively. Like previous studies, our data confirm the efficacy of post-operative IMRT for endometrial carcinoma.

Mundt et al[16] reported that patients with endometrial cancer and cervical involvement had a higher 3-year actuarial pelvic recurrence rate than those without cervical involvement (67.0% versus 33.1%, $P = 0.01$). In addition, patients with deep myometrial invasion had a higher pelvic recurrence rate (59.9% versus 26.4%) compared with those without deep myometrial invasion. Creutzberg et al[17] stated that the majority of locoregional relapses occurred in the vagina, mainly in the vaginal vault. In the current study, the total local failure rate was 6.5%. No pelvic relapses occurred, and only two patients had cervical stump failures (one from each treatment group), confirming previous reports and also highlighting the feasibility of postoperative IMRT and helical tomotherapy for patients with endometrial cancer. There was no statistically significant difference in 3-year local control rate between the IMRT and helical tomotherapy groups at similar doses (Figure 2). For stage III endometrial carcinoma, the 5-year local failure rate was 40%, even for patients who underwent resection with adjunctive radiotherapy.[18] However, in our study, the frequency of stage III disease was higher in the group receiving helical tomotherapy (37%) than that receiving IMRT (25%). Comparing both groups, the local control rate was similar but the percentage of stage III diseases was higher in HT treated group. This suggests HT could be as effective as IMRT, or potentially better.

There were no statistically significant differences in actuarial 3-year overall survival and locoregional control between the two radiation techniques used in our study. However, 3-year disease-free survival and distant metastasis-free survival rates for the IMRT group versus the helical tomotherapy group were 92% versus 52%, respectively. The higher rate of metastases after adjuvant radiotherapy for high-risk endometrial carcinoma is a thorny problem, although adjuvant radiotherapy could reduce the rate of pelvic relapse.[19–21] In the PORTEC (Postoperative Radiation

Table 3 Three-year estimated overall survival, disease-free survival, locoregional progression-free survival, and distant metastasis-free rates for postoperative intensity-modulated radiation therapy and helical tomotherapy ± chemotherapy for patients with endometrial cancer compared with selected published series treated by intensity-modulated radiation therapy

Selected published series	Postoperative patients	C/T	FIGO stage IC	FIGO stage IIA	FIGO stage IIB	FIGO stage IIIA	FIGO stage IIIC	Postoperative modality	Follow-up time	OS	DFS	LR PF	DMF
Beriwal et al[14]	47	7/47	29.8%	4.3%	17.0%	12.8%	17.0%	IMRT	3-year	90%	84%	100%	NA
Bouchard et al[15]	15	NA	80%			20%		AB-IMRT	3-year	NA	100%	NA	NA
Current study in	12	1/12	25.0%	16.7%	8.3%	16.7%	8.3%	IMRT	3-year	88%	92%	92%	92%
FEMH	19	1/19	15.8%	5.3%	26.3%	10.5%	26.3%	HT		100%	52%	83%	52%

Abbreviations: AB-IMRT, aperture-based IMRT; C/T, chemotherapy; OS, overall survival; DFS, disease-free survival; LRPF, locoregional progression-free survival; DMF, distant metastasis-free; IMRT, intensity-modulated radiation therapy; HT, helical tomotherapy; FEMH, Far Eastern Memorial Hospital; FIGO, International Federation of Gynecology and Obstetrics.

Therapy in Endometrial Carcinoma) trial, high-risk stage IC grade 3 tumors, had more than 20% of 5-year distant metastases rates than grade 1 and 2 tumors.[20] In a series of high-risk patients undergoing adjuvant chemotherapy without locoregional radiotherapy after surgery, recurrence rates were 16% for stage IIIA with one peritoneal site, and 48% for stage IIIA with multiple peritoneal sites, stage IIIB, or stage IIIC disease.[22] For advanced-stage endometrial carcinoma, Greven et al[23] reported that concurrent adjuvant chemoradiation therapy achieved an encouraging 4-year overall survival rate of 85%. In addition, their 4-year survival rate for stage III patients was 77%, suggesting additive effects of chemotherapy and radiation. Moreover, Hogberg et al confirmed that postoperative addition of adjuvant chemotherapy to radiation improves progression-free survival in patients with endometrial cancer.[24] In the current study, 63% of women in the helical tomotherapy group and 33% of women in the IMRT group had FIGO stage IIB–IIIC disease. However, only two stage IIIA patients received concurrent adjuvant chemoradiation therapy (one in each group). This could explain in part the lower disease-free and distant metastasis-free survival rates for the helical tomotherapy group.

Although adjuvant radiotherapy in patients with endometrial cancer can provide better local disease control, a clear concern about the addition of conventional locoregional radiotherapy is increased toxicity. In the Gynecological Oncology Group trial 99 report, two of 190 women receiving whole pelvic radiotherapy died from complications arising from intestinal injury, and six women had grade 3 or 4 bowel obstruction. In addition, 13% had grade 3 or 4 genitourinary, cutaneous, hematologic, or gastrointestinal toxicity.[1] In the PORTEC trial, severe late complications occurred in 3% of patients treated with whole pelvic radiotherapy.[25] In other retrospective studies, the reported frequency of late severe radiotherapy-related complications was 8%–11%.[26,27]

There have been several retrospective studies comparing the toxicity of IMRT with that of conventional techniques in patients with gynecologic cancers, and they indicate that IMRT has potentially significant advantages. Roeske et al noted that the percent volume of the small bowel region receiving 45 Gy was 13% in a whole pelvic IMRT group and 25% in a whole pelvic radiotherapy group, and that the rectal and bladder volumes were reduced by 23%.[13] Mundt et al[2] also reported that whole pelvic IMRT could reduce grade 2 acute gastrointestinal toxicity by 30% and the need for antidiarrheal medications by 40% compared with whole pelvic radiotherapy. Moreover, a 10% decrease in grade 2 genitourinary toxicity was seen for whole pelvic

IMRT in comparison with whole pelvic radiotherapy. In a further study, they found that the rate of chronic gastrointestinal toxicity was reduced by almost 40% with whole pelvic IMRT in comparison with whole pelvic radiotherapy. Further, the percentages of patients with grade 1, 2, and 3 toxicity following whole pelvic IMRT and whole pelvic radiotherapy was 8% versus 30%, 3% versus 17%, and 0% versus 3%, respectively.[28]

Patients with gynecologic cancer treated by IMRT may have lower rates of acute leukopenia and neutropenia than those treated with whole pelvic radiotherapy. In particular, patients with a volume of pelvic bone marrow receiving ≥ 10 (V_{10}) $\geq$95% were found to be more likely to experience grade ≥ 3 leukopenia (69% versus 25%, $P < 0.001$) than patients receiving $V_{20} > 76\%$ (58% versus 22%, $P = 0.001$).[8] At the 30-Gy level, the average volume of bone marrow irradiated was 38% using bone marrow-sparing whole pelvic IMRT, compared with 55% and 53% for conventional whole pelvic radiotherapy and whole pelvic IMRT, respectively.[4] Mell et al[29] also provided evidence that patients with a bone marrow (BM)-$V_{10} \geq 90\%$ had higher rates of grade 2 or worse leukopenia than did patients with BM-$V_{10} < 90\%$ (11% versus 74%, $P < 0.01$). These data highlight the potential of IMRT to spare bone marrow, which could diminish the chronic bone marrow suppression occurring after radiotherapy, thereby improving tolerance of chemotherapy.

Yang et al directly compared IMRT and helical tomotherapy with three-dimensional conformal radiotherapy for endometrial cancer.[5] They found the mean planned dose to organs at risk could be decreased with IMRT and helical tomotherapy compared with three-dimensional conformal radiotherapy. Further, when analyzing helical tomotherapy plans, using IMRT plans as the baseline, helical tomotherapy further decreased the rectal and bladder volumes receiving doses above 30 Gy. Our previous study showed that whole pelvic helical tomotherapy can decrease the mean dose successfully to 10 Gy for the rectum, 10 Gy for the bladder, and 9 Gy for the intestines when compared with whole pelvic radiotherapy for patients with cervical cancer, with 10% and 20% of patients developing grade 3 and grade 2 diarrhea, respectively.[3] However, without pelvic bone marrow sparing, even using helical tomotherapy to treat cervical cancer, 30% and 10% of patients still developed grade 3 leukopenia and grade 3 thrombocytopenia, respectively.

The reported incidence of intestinal and urinary bladder complications after postoperative radiotherapy with brachytherapy in endometrial cancer varies in the literature from 4% to 41% and from 0% to 21%, respectively.[26,27,30,31] In the series reported by Jereczek-Fossa et al it was noted that a vaginal intracavity brachytherapy and two-field radiotherapy technique was correlated with a higher normalized total dose and an increased risk of bowel and/or bladder complications.[26] In the current study, whole pelvic helical tomotherapy provided better conformal and uniformity indices than IMRT. With a similar planning target volume in both groups, whole pelvic helical tomotherapy had better conformality and uniformity than IMRT for patients with endometrial carcinoma, as reflected in the dose-volume histogram for organs at risk with decreasing doses (Table 2A). Helical tomotherapy decreased the mean dose successfully by 6 Gy to the rectum, 6 Gy to the bladder, and 7 Gy to the intestines when compared with IMRT, which was similar to the results with arc therapy reported by Cozzi et al.[32] For patients treated with whole pelvic irradiation followed by brachytherapy, the normalized total dose for the planning target volume was similar in both groups ($P = 0.93$). The benefits of dose-volume histogram data in helical tomotherapy were accompanied by a lower percentage of acute grade 2 diarrhea (10%). Furthermore, no significant surgical sequelae occurred, and no grade 3 or 4 acute or late toxicities, such as proctitis or genitourinary or gastrointestinal disturbance, were noted after adjuvant whole pelvic IMRT or whole pelvic helical tomotherapy. Overall, only one (3%) of 31 patients who received adjuvant radiotherapy developed acute grade 3 leucopenia during concurrent chemoradiation therapy. There were no late grade 3 or 4 hematologic toxicities. IMRT and helical tomotherapy as adjuvant radiotherapy can reduce the incidence of complications from postoperative endometrial cancer, and helical tomotherapy has a better dosimetric contribution for organs at risk.

There are some limitations to our current study. First, the number of cases and the retrospective study design make any statistical conclusions very tentative. Second, our brachytherapy system was not image-based, so could not provide the 1 cm^3, 2 cm^3, and 5 cm^3 volumes for the bladder, intestines, and rectum.[33,34] However, we compared the data for all patients, including those treated with whole pelvic IMRT or helical tomotherapy followed by brachytherapy. We also provide the normalized total doses for planning target volumes to explain the benefit of whole pelvic helical tomotherapy. Third, the follow-up time was short, and long-term results with close monitoring are required.

Conclusion

The present report represents one of the earliest studies analyzing the outcomes of IMRT and helical tomotherapy for adjuvant treatment of endometrial cancer. Whole pelvic helical tomotherapy is as effective as whole pelvic IMRT, and has better conformal and uniformity indices and critical organ sparing than whole pelvic IMRT. Concurrent chemoradiation therapy could be considered as one of the treatment options for advanced endometrial carcinoma. Prospective clinical trials are needed to evaluate the comparative efficacy of IMRT versus helical tomotherapy.

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Disclosure

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