

Scientific Article

Treatment Outcomes and Prognostic Factors of Metastasis-Directed Radiation Therapy for Oligometastatic Endometrial Cancer

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Purpose: To evaluate outcomes and prognostic factors associated with metastasis-directed radiation therapy (MDRT) for oligometastatic endometrial cancer.

Methods and Materials: We retrospectively analyzed 101 patients (203 lesions) with ≤ 5 metastatic lesions treated with MDRT between 2015 and 2025. Oligometastatic states were classified according to the European Society for Radiotherapy and Oncology –European Organisation for Research and Treatment of Cancer framework. Endpoints were overall survival (OS), progression-free survival (PFS), and local failure-free survival. Prognostic factors were assessed using multivariable Cox regression, and toxicities were graded using the National Cancer Institute Common Terminology Criteria for Adverse Events v5.0.

Results: At a median follow-up of 36.4 months, 3-year OS, PFS, and 2-year local failure-free survival rates were 76.3%, 24.5%, and 64.7%, respectively. Multivariable analyses revealed that favorable oligometastatic disease classification, endometrioid histology, favorable radiation therapy (RT) response, and maximum dose ≥ 40 Gy (equivalent dose in 2 Gy fractions, $\alpha/\beta = 10$) were independently associated with improved OS. All factors, except for histology, were significant for PFS. In a propensity-matched analysis, repeated MDRT for recurrent oligometastases showed a trend toward improved OS compared with a single course. One grade 3 event occurred with no grade ≥ 4 toxicity.

Conclusions: MDRT yielded favorable outcomes in oligometastatic endometrial cancer. Oligometastatic classification, histology, and RT response were major prognostic factors. MDRT may be a viable option within a multidisciplinary framework for de novo and recurrent oligometastases, but validation in prospective multicenter studies is warranted.

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Introduction

Endometrial cancer is the most common gynecologic malignancy in developed countries, including South

Korea,¹ and its global incidence continues to rise.² Although most patients present with early-stage disease and achieve favorable outcomes, some occasionally develop recurrent or metastatic disease with a poor prognosis.³ Systemic therapies, including hormonal therapy,⁴ immunotherapy,⁵ and cytotoxic chemotherapy,⁶ remain the standard management for metastatic diseases.

The concept of oligometastasis, defined as a limited number of metastatic lesions with potentially indolent biology,⁷ has reshaped metastatic cancer management. For carefully selected patients, local therapies such as surgical resection

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and metastasis-directed radiation therapy (MDRT), including stereotactic body radiation therapy (SBRT), can achieve durable local control, extend systemic therapy-free intervals, and potentially improve survival with acceptable toxicity.⁸ The joint European Society of Gynaecological Oncology–European Society for Radiotherapy and Oncology–European Society of Pathology (ESGO–ESTRO–ESP) guidelines recommend radiation therapy (RT) as a local ablation option for oligometastatic endometrial cancer (OEC).⁹

However, the evidence supporting the use of local ablative therapies for OEC remains limited.^{10,11} Most previous studies combined heterogeneous gynecologic malignancies with endometrial cancer, representing only a few cases.^{12–15} Furthermore, patients who benefit the most from local therapy remain unknown because of the biological heterogeneity of endometrial cancer and the diversity of oligometastatic presentations. The ESTRO and European Organisation for Research and Treatment of Cancer (ESTRO-EORTC) consensus classifications underscore the need to integrate the disease context and kinetics into treatment selection.⁷

Therefore, this study aimed to investigate the treatment outcomes and safety of local RT for OEC and identify potential factors associated with patient prognosis.

Methods and Materials

Patient selection

This retrospective, single-institution study included patients with pathologically confirmed endometrial cancer at the time of staging laparotomy who underwent RT for oligometastatic disease at the Yonsei Cancer Center between June 2015 and February 2025. Eligible patients had 5 or fewer metastatic lesions consistent with an oligometastatic state and were categorized as synchronous, metachronous, oligoprogressive, or induced oligometastatic according to the ESTRO-EORTC classification for each RT course.⁷ The exclusion criteria were as follows: (1) suboptimal initial treatment; (2) RT performed in a polymetastatic setting; or (3) RT delivered solely for palliation. This study was approved by the Yonsei University Health System Institutional Review Board (IRB No. 4-2025-1193). The requirement for informed consent was waived owing to the retrospective design of the study. In accordance with the journal's guidelines, we will provide our data for independent analysis by a team selected by the editorial team for the purposes of additional data analysis or for the reproducibility of this study in other centers if such is requested.

Treatment and follow-up

Oligometastatic lesions were identified using computed tomography (CT) or positron emission tomography

(PET)-CT at diagnosis or during follow-up. Treatment plans were determined by a multidisciplinary tumor board, including gynecologic, medical, and radiation oncologists, diagnostic radiologists, and nuclear medicine specialists. RT decisions were made by considering the lesion number and location, disease kinetics, and the patient's general condition.

Patients were immobilized and simulated using institutional protocols. A 4-dimensional CT simulation was used for thoracic and upper abdominal lesions subject to respiratory motion, using abdominal compression or active breathing control for respiratory management when feasible. The dose and fractionation were individualized for each patient. The most commonly used dose scheme was 5 to 8 Gy per fraction in 3 to 5 fractions. SBRT was defined as RT delivered in ≤ 5 fractions with a fractional dose of ≥ 5 Gy. For larger tumors or those adjacent to organs at risk (OARs), smaller fractional doses (over 10–15 fractions) were used. Patients with chained nodal metastases occasionally underwent involved-field conventional RT. For OAR constraints, bowel $D_{2cc} \leq 55$ Gy and duodenum $D_{2cc} \leq 50$ Gy were applied with other OARs following the constraints proposed by Timmerman.¹⁶ Gross tumor volume was delineated from CT and PET-CT, and internal target volume (ITV) accounted for motion. Planning target volume (PTV) margins were 3 to 5 mm for conventional RT, and $PTV = ITV$ for SBRT. OAR proximity prompted the exclusion of a 2-mm margin from the PTV.

Patients were evaluated 1-month post-RT and every 3 months for the first 2 years and subsequently at every 6 to 12 months, with clinical examination and imaging (CT, magnetic resonance imaging, and/or PET-CT) performed. Tumor response was assessed using the Response Evaluation Criteria in Solid Tumors version 1.1.¹⁷ In cases of progression, salvage treatment was discussed at the multidisciplinary board, and repeat local therapy was considered if the progression was oligometastatic.

Study endpoints and statistical analyses

The study endpoints were overall survival (OS), progression-free survival (PFS), and local failure-free survival (LFFS). OS was defined as the time from the diagnosis of the first oligometastasis to death or the last follow-up. PFS was measured from oligometastasis diagnosis to progression, death, or last follow-up. LFFS was the duration between RT initiation and local recurrence or the last follow-up date.

Survival outcomes were estimated using the Kaplan-Meier method and compared using the log-rank test. Cox regression analyses were used to identify prognostic factors influencing OS, PFS, and LFFS. All clinically relevant variables and those with P values $< .20$ in univariate analyses were included in the multivariate analyses. Complete

or partial response was defined as a favorable RT target response, whereas stable or progressive disease was defined as an unfavorable RT target response. Molecular classification was assessed in patients with available data using POLE mutation status, mismatch repair status, and p53 expression.⁹ The ESTRO-EORTC oligometastatic disease classification system, which incorporates clinical course and systemic therapy exposure, was used to stratify patients into risk subgroups. Induced oligorecurrence, synchronous oligometastasis, and metachronous oligorecurrence, those arising in the absence of ongoing systemic therapy, were classified as favorable, whereas others were classified as unfavorable, as previously reported.¹⁸ Favorable subtypes are generally associated with indolent tumor biology, preserved therapeutic sensitivity, and improved survival.¹⁸ Factors with P values $<.05$ were considered statistically significant. To compare outcomes between patients receiving a single versus multiple MDRT courses, propensity score matching was performed based on pathologic subtype, oligometastatic classification, maximum RT dose (equivalent dose in 2 Gy fractions using α/β ratio of 10 [EQD₂($\alpha/\beta=10$)]) among all irradiated target sites, and RT target site response. The analyses were performed in Python 3.10.12 using pandas, numpy, matplotlib, scipy, sklearn, lifelines, sksurv, and psmPy. Toxicities were graded using the National Cancer Institute Common Terminology Criteria for Adverse Events v5.0.

Results

This study included 101 patients with OEC, encompassing 203 irradiated lesions. The baseline characteristics are summarized in Table 1. Endometrioid adenocarcinoma was the most common histologic subtype ($n = 60$, 59.4%). At the time of RT, metachronous oligorecurrence was the most frequent ($n = 32$, 31.7%), followed by repeat oligorecurrence ($n = 30$, 29.7%), repeat oligoprogression ($n = 20$, 19.8%), and synchronous oligometastasis ($n = 11$, 10.9%). Among the patients, 59 (58.4%) had lymph node involvement. Systemic chemotherapy was administered before or after RT in 64 patients (63.4%). Overall, 150 independent RT courses were administered. Sixty-nine patients (68.3%) received RT for a single episode of oligometastatic disease, 17 (16.8%) for 2 distinct episodes, and 15 (14.9%) for 3 or more episodes.

Among the 203 lesions, the median fractional RT dose was 6 Gy (range, 2-30 Gy) in 5 fractions (range, 1-35 fractions). Lymph nodes ($n = 91$, 44.8%) were the most frequently involved lesions. Systemic therapy was most commonly administered before and after RT (65 lesions, 32.0%), with paclitaxel combined with cisplatin or carboplatin being the most frequently used regimen ($n = 60$, 29.6%). A favorable RT target response (complete or partial response) was observed in 123 lesions (60.6%), whereas 80 lesions (39.4%) demonstrated an unfavorable response

(stable or progressive disease). During follow-up, disease progression occurred in 168 lesions (82.8%), most commonly as out-of-field failures (95 lesions, 46.8%).

The median follow-up of total lesions from RT initiation was 17.6 months (range, 1.6-75.4 months). The 2-year LFFS rate was 64.7% among all treated lesions (Fig. E1A). Univariate analysis of local failures (Table E1) revealed that endometrioid pathology, favorable oligometastatic disease classification, and favorable RT target responses were significantly associated with improved local control (Fig. E1B-F), which also remained significant in the multivariate model (endometrioid pathology: hazard ratio [HR], 0.59; 95% confidence interval [CI], 0.35-0.98; $P = .043$; favorable oligometastatic disease classification: HR, 0.28; 95% CI, 0.13-0.60; $P = .001$; favorable RT target response: HR, 0.55; 95% CI, 0.33-0.90; $P = .017$).

The median follow-up of all patients from RT initiation was 36.4 months (range, 1.6-75.4 months). The 3-year OS and PFS rates were 76.3% and 24.5%, respectively (Fig. 1). Univariate analysis revealed that pathology, oligometastatic disease classification, and RT target response were significantly associated with OS (Table 2; Fig. 2). Multivariate analyses showed that endometrioid pathology (HR, 0.35; 95% CI, 0.15-0.84; $P = .019$), favorable oligometastatic disease classification (HR, 0.28; 95% CI, 0.09-0.90; $P = .033$), favorable RT target response (HR, 0.16; 95% CI, 0.06-0.45; $P = .001$), and total EQD₂($\alpha/\beta=10$) ≥ 40 Gy (HR, 0.35; 95% CI, 0.14-0.87; $P = .024$) were significantly associated with improved OS. For PFS, endometrioid pathology, favorable oligometastatic classification, favorable RT target response, and repeated RT were significantly associated in univariate analyses (Fig. 3). In the multivariate PFS model, favorable oligometastatic classification (HR, 0.36; 95% CI, 0.20-0.65; $P = .001$), favorable RT target response (HR, 0.31; 95% CI, 0.18-0.51; $P < .001$), and total EQD₂($\alpha/\beta=10$) ≥ 40 Gy (HR, 0.49; 95% CI, 0.28-0.85; $P = .011$) were statistically significant (Table 2). Regarding molecular classification among patients with available data, the no specific molecular profile subtype was associated with significantly improved OS and PFS compared with the p53 aberrant subtype, whereas no statistically significant differences were observed among the other molecular subgroups (Fig. E2A). Multivariable Cox regression analyses for OS and PFS (Fig. E2B) and for LFFS (Fig. E2C) are presented as forest plots, and patient characteristics according to total EQD₂($\alpha/\beta=10$) are summarized in Table E2.

Patients were matched using propensity score for pathology, oligometastatic disease classification, RT response, and total EQD₂($\alpha/\beta=10$), yielding 2 balanced cohorts, namely single- and multiple-course RT ($n = 32$ per group). After matching, the 3-year OS in patients receiving multiple RT courses (85.4%) was higher than that in patients receiving a single RT course (51.8%), with marginal statistical significance ($P = .084$; Fig. E3). Subgroup analyses stratified using oligometastatic disease classification

Table 1 Patient and lesion characteristics

Patient characteristics		Lesion characteristics	
Characteristic	N (%)	Characteristic	N (%)
Total, No.	101	Total, No.	203
Age, y, median (range)	61 (28-79)	Fractional dose, Gy, median (range)	6.0 (2.0-30.0)
Pathology		Number of fractions, median (range)	5 (1-35)
Endometrioid G1	13 (12.9)	Total EQD2 _($\alpha/\beta=10$) , Gy, median (range)	48.0 (12.0-100.0)
Endometrioid G2	26 (25.7)	Subsites	
Endometrioid G3	21 (20.8)	Lymph node	91 (44.8)
Serous	9 (8.9)	Vaginal stump	25 (12.3)
Clear cell	5 (5.0)	Lung	26 (12.8)
Mixed epithelial	10 (9.9)	Liver	6 (3.0)
Others	17 (16.8)	Peritoneum	16 (7.9)
Initial treatment		Bone	12 (5.9)
Op alone	21 (20.8)	Muscle	8 (3.9)
Op >RT	31 (30.7)	Whole pelvis	5 (2.5)
Op >CTx	26 (25.7)	Semiextended field	1 (0.5)
Op >CTx >RT	13 (12.9)	Extended field	6 (3.0)
CTx alone	3 (3.0)	Others	7 (3.4)
CTx >RT/Op	7 (6.9)	RT course sequence	
Oligometastasis classification		1	142 (70.0)
Synchronous oligometastasis	11 (10.9)	2	43 (21.2)
Induced oligorecurrence	2 (2.0)	3	16 (7.9)
Metachronous oligorecurrence	32 (31.7)	4	1 (0.5)
Metachronous oligoprogression	1 (1.0)	5	1 (0.5)
Repeat oligorecurrence	30 (29.7)	SBRT	
Repeat oligoprogression	20 (19.8)	No	121 (59.6)
Induced oligopersistence	1 (1.0)	Yes	82 (40.4)
Induced oligoprogression	4 (4.0)	Type of failure after RT	
Number of total RT courses		No failure	35 (17.2)
1	69 (68.3)	In-field	12 (5.9)
2	17 (16.8)	Out-field	95 (46.8)
3	14 (13.9)	Both	61 (30.0)
5	1 (1.0)	RT target response	
Molecular classification		CR	24 (11.8)
POLE mutant	0 (0.0)	PR	99 (48.8)
MMR deficient	9 (8.9)	SD	49 (24.1)
P53 aberrant	19 (18.8)	PD	31 (15.3)
NSMP	22 (21.8)	Peri-RT systemic treatment	
N/A	51 (50.5)	Paclitaxel + Cis/carboplatin	60 (29.6)
PD-L1 (CPS)		Pembrolizumab + lenvatinib	12 (5.9)
High-positive	8 (7.9)	Pembrolizumab or nivolumab	11 (5.4)
Low-positive	17 (16.8)	Adriamycin + Cis/carboplatin	19 (9.4)

(continued on next page)

Table 1 (Continued)

Patient characteristics		Lesion characteristics	
Characteristic	N (%)	Characteristic	N (%)
Negative	15 (14.9)	Hormonal Tx	20 (9.9)
N/A	61 (60.4)	Others	21 (10.3)
		No systemic Tx	60 (29.6)
		Peri-RT systemic treatment sequence	
		Systemic Tx >RT	49 (24.1)
		Systemic Tx >RT >systemic Tx	65 (32.0)
		RT >systemic Tx	29 (14.3)
		No systemic Tx	60 (29.6)

Abbreviations: CPS = combined positive score; CR = complete response; CTx = chemotherapy; EQD2_(α/β=10) = equivalent dose in 2 Gy fractions; MMR = mismatch repair; N/A = not applicable; No. = number; NSMP = no specific molecular profile; Op = operation; PD = progressive disease; PR = partial response; RT = radiation therapy; SBRT = stereotactic body radiation therapy; SD = stable disease; Tx = therapy.

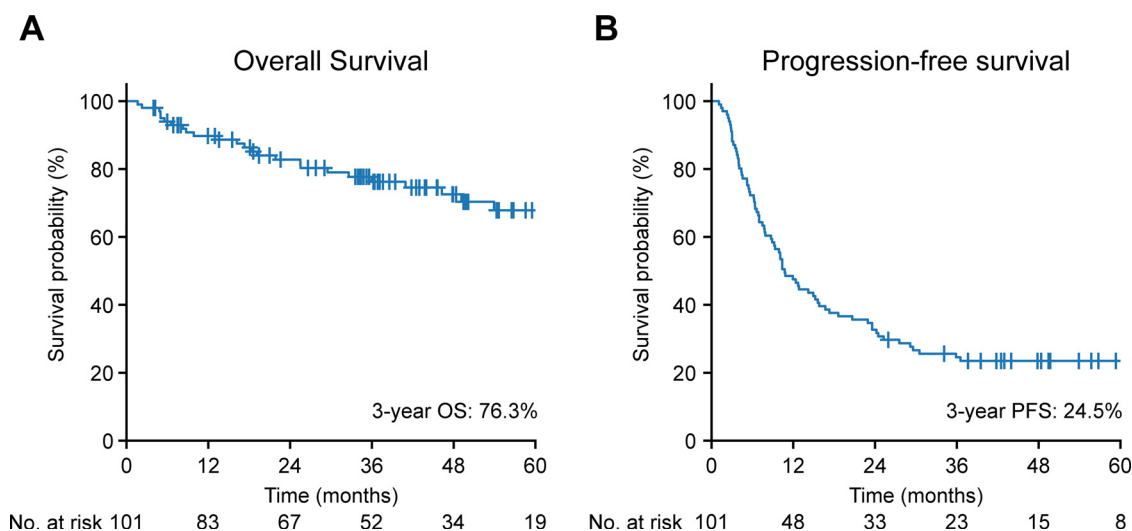


Figure 1 Kaplan-Meier survival curves for (A) overall survival and (B) progression-free survival after metastasis-directed radiation therapy (MDRT) for oligometastatic endometrial cancer.

revealed that in patients with a favorable initial oligometastatic classification (n = 45), the 3-year OS was comparable between single (91.1%) and multiple RT courses (100.0%, P = .116; Fig. E4A). In contrast, in the unfavorable group (n = 56), the 3-year OS in patients with multiple RT courses was 81.5% compared with 45.1% in patients with a single RT course (P = .038; Fig. E4B).

The treatment-related toxicities per RT course are summarized in Table E3. Most adverse events were grade 1 to 2 with no grade 4 to 5 toxicities. Nausea of any grade occurred in 22 patients (14.7%), followed by anorexia (17 patients, 11.3%), urinary frequency (15 patients, 10.0%), fatigue (12 patients, 8.0%), and diarrhea (7 patients, 4.7%). One patient experienced grade 3 diarrhea during RT for pelvic nodal metastases.

Discussion

MDRT for oligometastases in endometrial cancer demonstrated promising OS and PFS compared with historical data on metastatic and recurrent endometrial cancer treated with systemic therapy alone,⁵ while maintaining acceptable toxicity. The survival outcomes were comparable to those reported in previous studies of MDRT for OECs, which showed OS ranging from 40% to 80%.¹⁰⁻¹⁵ Furthermore, we identified oligometastatic disease classification, pathologic subtype, and RT target response as significant prognostic factors for OS and PFS. The prognostic value of favorable RT response and endometrioid histology for OS and PFS is consistent with previous findings that associated

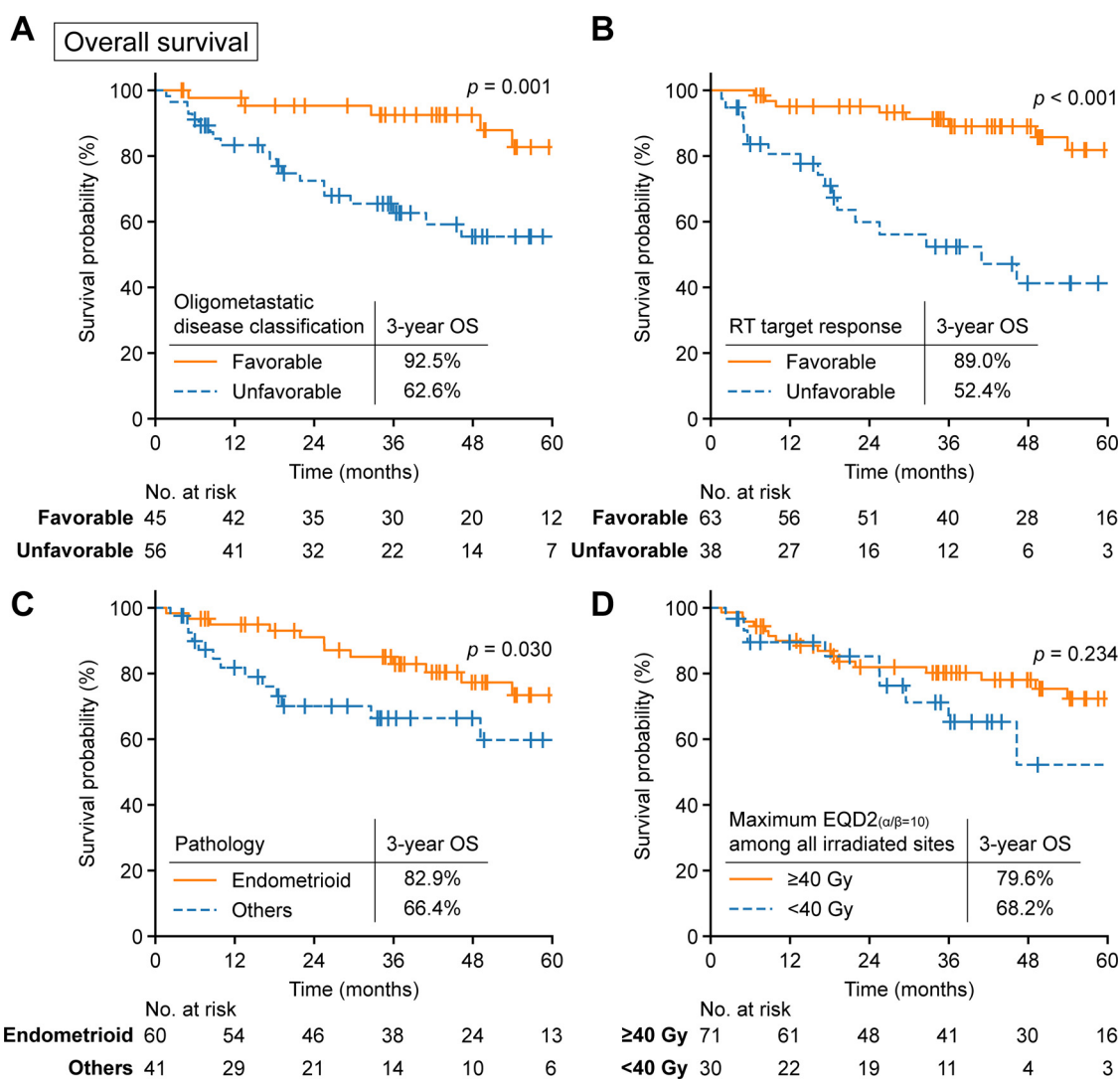


Figure 2 Kaplan-Meier survival curves for overall survival (OS) stratified according to (A) oligometastatic disease classification, (B) radiological response at radiation therapy (RT) target site, (C) pathologic subtype, and (D) maximum EQD2_($\alpha/\beta=10$) among all irradiated target sites. P values were calculated using log-rank tests. Abbreviations: EQD2_($\alpha/\beta=10$) = equivalent dose in 2 Gy fractions using α/β ratio of 10; No. = number.

these features with improved outcomes¹¹ and indolent tumor biology.¹⁹

Systemic therapy has traditionally been the cornerstone of treatment for recurrent or metastatic endometrial cancer; however, the outcomes remain modest, with limited therapeutic options. Although the combination of lenvatinib and pembrolizumab has demonstrated clinical benefit,⁵ effective salvage options remain limited for patients who have already received carboplatin plus paclitaxel.⁶ Therefore, optimizing the use and sequencing of available systemic regimens is crucial. To overcome these therapeutic limitations, MDRT for oligometastatic disease⁷ may help delay disease progression, preserve systemic treatment options, and improve survival.⁸ The efficacy of MDRT has been explored in various gynecologic malignancies, including a recently published

prospective study in ovarian cancer,²⁰ but most studies remain small-sized retrospective studies.¹²⁻¹⁵ Moreover, these studies were not specifically focused on endometrial cancer, limiting the generalizability of their findings to this disease entity. For example, a large multicenter retrospective study including 215 patients reported excellent local control with minimal toxicity after SBRT, but fewer than half of the patients had endometrial cancer.¹³ In contrast, this study exclusively includes patients with endometrial cancer. To date, 1 large multicenter retrospective study has evaluated SBRT specifically in OEC, reporting favorable treatment outcomes.¹¹ Nevertheless, this study primarily evaluated outcomes following a single course of MDRT and did not address the role of RT for recurrent oligometastases across the entire disease course, despite the high clinical demand for such an approach. Because

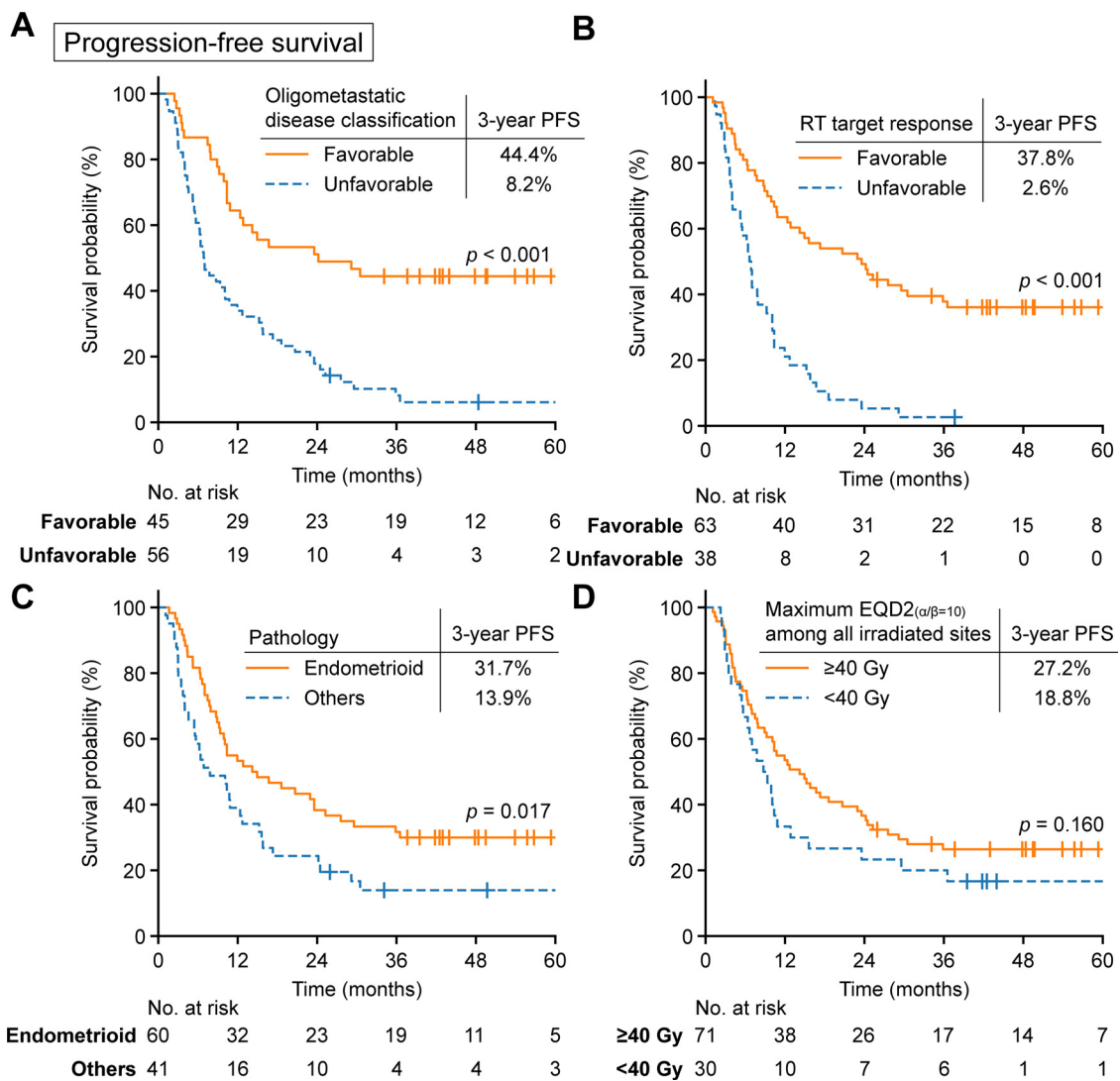


Figure 3 Kaplan-Meier survival curves for progression-free survival (PFS) stratified according to (A) oligometastatic disease classification, (B) radiological response at radiation therapy (RT) target site, (C) pathologic subtype, and (D) maximum EQD_{2(α/β=10)} among all irradiated target sites. P values were calculated using log-rank tests. Abbreviations: EQD_{2(α/β=10)} = equivalent dose in 2 Gy fractions using α/β ratio of 10; No. = number.

oligometastatic disease often occurs repeatedly over time, the role of repeated MDRT is a clinically relevant but understudied aspect of disease management.

In the present study, approximately one-third of the patients received multiple MDRT courses for recurrent oligometastases. Patients who underwent multiple MDRT courses showed numerically improved OS after propensity score matching. Subgroup analyses further revealed that this benefit was more pronounced in patients with unfavorable oligometastatic disease. Unfavorable subtypes tend to harbor resistance to systemic therapy and exhibit earlier and more frequent recurrences, where repeated MDRT may help delay disease progression and allow systemic therapy to be reserved for when it is most needed. Although selection bias cannot be excluded, repeated MDRT may be effective in addressing aggressive behavior

in unfavorable oligometastatic disease subtypes, warranting validation in larger controlled cohorts.

SBRT may offer greater clinical utility by integrating MDRT with systemic therapy schedules. Because of its short treatment duration, SBRT can be conveniently administered between systemic therapy cycles and remains the cornerstone for recurrent or metastatic endometrial cancer. Moreover, its small treatment volume and limited normal tissue exposure enhance the feasibility of subsequent reirradiation, even in cases of in-field progression, making SBRT the preferred MDRT approach for recurrent oligometastatic diseases.

Additionally, SBRT use may further enhance disease control. In this study, the 2-year LFFS rate was 64.7%, at the lower end of the 60% to >90% range reported in previous studies.^{10-13,15} This difference may be attributed to

Table 2 Univariate and multivariate Cox regression analyses for OS and PFS

Variables	OS						PFS					
	Univariate			Multivariate			Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value	HR	95% CI	P value	HR	95% CI	P value
Age (per 1 y increase)	1.01	0.97-1.05	.690	1.01	0.97-1.06	.541	1.02	1.00-1.05	.089	1.02	0.99-1.05	.178
Pathology (endometrioid vs others)	0.43	0.20-0.94	.035	0.35	0.15-0.84	.019	0.58	0.37-0.91	.019	0.64	0.39-1.06	.082
Lymph node involved (yes vs no)	1.21	0.56-2.65	.625	1.53	0.55-4.20	.414	0.85	0.54-1.33	.479	1.45	0.77-2.74	.253
Lung involved (yes vs no)	0.45	0.11-1.92	.280	0.24	0.04-1.60	.142	0.80	0.40-1.61	.533	0.90	0.36-2.24	.822
Vagina involved (yes vs no)	0.78	0.27-2.27	.653	0.88	0.24-3.30	.850	1.07	0.60-1.91	.821	0.66	0.30-1.44	.295
Oligometastasis classification (favorable vs unfavorable)	0.22	0.08-0.59	.003	0.28	0.09-0.90	.033	0.34	0.21-0.56	<.001	0.36	0.20-0.65	.001
RT target response (favorable vs unfavorable)	0.16	0.07-0.38	<.001	0.16	0.06-0.45	.001	0.29	0.18-0.47	<.001	0.31	0.18-0.51	<.001
Maximum total EQD _{2(α/β=10)} (≥40 Gy vs <40 Gy)	0.61	0.27-1.38	.238	0.35	0.14-0.87	.024	0.71	0.44-1.15	.161	0.49	0.28-0.85	.011
Repeated RT (multiple vs single)	0.99	0.44-2.22	.975	0.46	0.18-1.20	.114	2.04	1.28-3.24	.003	1.41	0.81-2.43	.221
SBRT (yes vs no)	1.14	0.51-2.57	.750	1.64	0.63-4.29	.312	1.00	0.62-1.61	.995	0.99	0.57-1.74	.981
Peri-RT immunotherapy (yes vs no)	0.90	0.21-3.80	.883	0.92	0.16-5.26	.922	1.28	0.61-2.67	.510	1.05	0.40-2.75	.924

Abbreviations: CI = confidence interval; EQD_{2(α/β=10)} = equivalent dose in 2 Gy fractions using α/β ratio of 10; HR = hazard ratio; OS = overall survival; PFS = progression-free survival; RT = radiation therapy; SBRT = stereotactic body radiation therapy.

the inclusion of conventionally fractionated RT in our cohort compared with that in previous SBRT studies in OEC,¹¹ as patients treated since 2015 were included when SBRT adoption was limited. Although SBRT showed only marginal significance for local control in our cohort, which may be attributable to the relatively modest dose in our cohort, recent studies in oligometastatic disease in gynecologic malignancies highlighted effective local control by SBRT.^{11,13,20}

Notably, radiation dose emerged as an independent prognostic factor for OS and PFS in multivariate analyses, despite not being significant in univariate analyses, likely reflecting imbalances in baseline characteristics, as the high-dose group included a higher proportion of patients with nonendometrioid histology. The observation that the radiation dose was associated with OS and PFS but only marginally with LFFS suggests several possible explanations. Improved OS and PFS may be driven by selection bias, as patients with better performance status, smaller tumor burden, or favorable metastatic sites were more likely to receive higher doses. Notably, lung metastases, for which ablative doses can be more readily administered, comprised a larger proportion of the high-dose group in our cohort, and are known to show relatively favorable outcomes.²¹ Alternatively, a true improvement in LFFS may not have been detected due to limited statistical power related to the relatively small sample size or insufficient dose escalation. Another intriguing possibility is that radiation may exert systemic biological effects beyond local control. Radiation stimulates systemic antitumor immune responses,²² and achieving an adequate dose and fractionation, particularly with SBRT,²³ may be critical for eliciting such effects.

This study has some limitations. It was a single-institution retrospective analysis of a heterogeneous group of patients with metastatic lesions, including nodal and vaginal recurrences. Although a recent prospective trial has demonstrated favorable outcomes with RT-based approaches for isolated pelvic recurrences,²⁴ a substantial proportion of lesions in the present study were distant organ metastases beyond the pelvis. Importantly, neither lymph node nor vaginal involvement emerged as an independently favorable prognostic factor in multivariable analysis, suggesting that the observed benefit of MDRT was not limited to locoregional recurrences. Such recurrence patterns, including intrapelvic involvement, are commonly encountered in real-world clinical practice among patients with endometrial cancer.²⁵ The treatment regimens were heterogeneous as well, reflecting the evolution of RT practices from conventional fractionation to SBRT during the study period. In addition, the relatively small sample size in the propensity score–matched analysis limited the ability to account for all potential confounding variables, such as tumor burden, sequencing of systemic therapy, and patient performance status. Moreover, molecular classification, which has recently emerged as a crucial prognostic framework for endometrial

cancer,²⁶ was available only in a limited subset of patients, limiting its interpretability in the present analysis. Furthermore, treatment selection was influenced by multiple patient-specific and disease-related factors, including the lesion site, disease extent, treatment preference, and clinical course, which introduced potential confounders in interpreting survival-associated variables.

Despite these limitations, this study represents one of the largest single-institution analyses of MDRT treatment outcomes in OEC to date. Our results suggest that even in a metastatic setting, RT can yield promising survival outcomes with acceptable toxicity in multidisciplinary discussions tailored to individual patients. Moreover, we identified several prognostic factors, such as oligometastatic disease classification, pathologic subtype, and RT response, which may help stratify patients most likely to benefit from MDRT. A subset of patients with such favorable oligometastatic features achieved durable disease control, suggesting the possibility of sustained remission in carefully selected cases. Similarly, we showed that repeated MDRT for recurrent oligometastases is feasible and may improve outcomes, particularly in patients with a high likelihood of early recurrence.

To our knowledge, this is the first study of endometrial cancer to demonstrate the prognostic significance of the ESTRO-EORTC oligometastatic disease classification system,⁷ supporting its clinical utility in treatment selection and decision making. Our results indicate that appropriately selected patients with OEC can achieve durable disease control and long-term survival after MDRT. Moreover, our findings suggest that higher SBRT doses may improve local control and boost systemic antitumor responses in OEC, enhancing OS and PFS. Future prospective studies with larger cohorts are necessary to validate the effect of SBRT on disease control in such patients and define optimal dose fractionation schedules.

Conclusions

We analyzed a notable cohort of patients with OEC and suggested that MDRT can achieve favorable local control with acceptable toxicity when delivered in a coordinated multidisciplinary setting. A subset of the patients experienced long-term survival, underscoring the therapeutic potential of MDRT in carefully selected cases. Favorable oligometastatic disease classification, endometrioid histology, and favorable RT response were significantly associated with improved OS and PFS, suggesting their potential value as selection criteria for MDRT. Moreover, repeated MDRT for recurrent oligometastases may provide additional benefits by extending disease control and survival in selected patients. Prospective multicenter studies are warranted to validate these findings, refine patient selection, and establish the role of SBRT in the management of OEC.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work the authors used ChatGPT (OpenAI) in order to assist with English language editing and improve clarity and readability of the manuscript. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Disclosures

None.

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Won Hee Lee performed the statistical analysis.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.adro.2026.102058.

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