WM Radiotherapy Clinical Protocol

Gynaecological: Uterine Cancer

Revision History

Version	Date	Summary of changes
1.0	06.11.2020	Approved by EAG
2.0	24.11.23	Accepted comments/change of documentation dates
2.1	3.3.26	Amendments made at protocol review group meeting – for consultation
3.0	14.4.26	Approved by EAG pending a few final changes made off-line
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Approved By

This document was ratified by the Radiotherapy Expert Advisory Group (EAG) at its 14 April 2026 meeting.

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1. Purpose

To provide a standardised protocol for planning and delivery of radiotherapy (RT) for uterine cancers within the West Midlands.

Radiotherapy for gynaecological cancers is delivered across the West Midlands as part of collaborative partnership working:

- SaTH, RWH and UHNM, where brachytherapy is delivered at RWH and UHNM
- UHB, UHCW and WAH, where brachytherapy is delivered at UHB and UHCW.

2. Information & Consent

- Each patient should be consented with individualised information of planned treatment, individualised risk / benefits and toxicities
- Booking form and consent completed by IR(ME)R practitioner
- Patients should also receive a local patient information sheet or Macmillan information booklets

3. Responsibilities

To comply with the Ionising Radiation (Medical Exposure) Regulations 2017, the following roles are defined:

- *Referrer and Practitioner*: The Consultant Clinical Oncologist is responsible for the care of the patient, including consent, prescription and treatment authorisation as per departmental IR(ME)R procedures
- *Operators*: Radiographers, Physicists and Technologists are responsible for the plan production, verification and treatment delivery as per departmental IR(ME)R procedures and under the auspices of the Practitioner.
- For brachytherapy, practitioners should be IR(ME)R licencees, issued by ARSAC for each type of procedure they carry out, or working under protocol from the IR(ME)R licenced clinician

4. Diagnosis and staging

All patients should have histological confirmation of uterine cancer. Staging investigations including trans-vaginal ultrasound scan (or trans-abdominal ultrasound scan if trans-vaginal is not feasible) should be routinely performed. MRI scan of the abdomen and pelvis is considered the technique of choice for staging of endometrial cancer[1].

Patients unable to tolerate MRI scanning should undergo CT scan of the abdomen and pelvis.

CT scan of the thorax abdomen and pelvis is recommended to exclude metastatic disease if high grade disease is present on initial biopsy, or if MRI shows locally advanced disease.

PET CT scan staging may be useful for evaluation of metastatic disease or when other imaging is equivocal.

FIGO and TNM staging of endometrial carcinoma

FIGO Stage	TNM stage
1A	T1a (< 50% myometrial invasion) N0 M0
1B	T1b (≥ 50 myometrial invasion) N0 M0
2	T2 (involvement of cervical stroma) N0 M0
3A	T3a (involvement of uterine serosa or metastasis to ovary or fallopian tube) N0 M0
3B	T3b (parametrial or vaginal involvement) N0 M0
3C1	T1-T3 N1 (pelvic lymph node metastasis) M0
3C2	T1-3 N2 (para-aortic lymph node [with or without pelvic lymph node] metastasis) M0
4A	T4a (Involvement of bladder or rectal mucosa) Any N M0
4B	Any T Any N M1 (distant metastasis including inguinal lymph nodes)

5. Primary treatment of endometrial carcinoma

Surgery is the recommended primary treatment for all patients unless the cancer is inoperable or there are contra-indications to surgical management (medical co-morbidities, poor performance status, or patient choice). Surgical management should be performed as clinically indicated in keeping with published guidelines and following discussion in the MDT.

Patients presenting with stage 4B disease, with small volume metastatic disease, may be suitable for surgical management if complete cytoreduction can be achieved. All such cases should be discussed in the gynaecology oncology MDT. Patients may be treated with neo-adjuvant chemotherapy to improve the chances of achieving complete cytoreduction. Patients achieving complete cytoreduction should be offered adjuvant treatment.

6. Adjuvant treatment following surgery

Adjuvant pelvic external beam radiotherapy (EBRT) reduces the risk of pelvic recurrence but does not improve overall survival.

Following publication of the PORTEC-2 trial, vaginal vault brachytherapy (VVBT) remains the standard of care in high-intermediate risk endometrial cancer; this was defined in the trial as stage 1b, grade 1-2, age > 60 years or stage 1a, grade 3 and age > 60 years. Women with high grade serous or clear cell carcinoma were excluded from the trial. 10 years results from PORTEC-2 trial show no statistically significant difference in rates of vaginal recurrence, isolated pelvic recurrence, distant metastases or overall survival for VVBT compared to EBRT.

Whilst PORTEC-2 excluded women high grade serous carcinoma and clear cell carcinoma, and those with stage 2 diseases, VVBT provides a reasonable option for adjuvant treatment where bilateral pelvic lymph node dissection (BPLND) has been undertaken and there is no evidence of lymph node metastases.

The presence of lymphovascular space invasion (LVSI) is an independent prognostic factor for increased risk of lymph node involvement and increased risk of cancer recurrence [4, 5]. The presence of LVSI, especially if BPLND has not been undertaken, should prompt consideration of EBRT as adjuvant treatment.

The results of the PORTEC-4A trial demonstrate that hypermutations in the POLe gene confers an excellent prognosis in intermediate and high-intermediate risk endometrial

carcinomas. This reflects data from retrospective analyses of the PORTEC-3 RCT. Based on results of the PORTEC 4A trial, the option of no adjuvant treatment can be considered in patients with intermediate or high-intermediate risk endometrial carcinomas.

Updated results of the PORTEC-3 trial demonstrate a 5.3% improvement in overall survival in favour of the addition of chemotherapy to radiotherapy (RT) in the adjuvant setting. The benefit was seen in women with stage 3 disease and in high grade serous carcinoma; 5-year overall survival for addition of chemotherapy was 78.5% compared to 68.5% for radiotherapy alone (HR 0.63 [95% CI 0.41-0.99], p = 0.043). There was no statistically significant benefit in stage 1 and stage 2 disease (HR 0.84 [0.52-1.38], p=0.5)[6].

The addition of chemotherapy to radiotherapy should be considered standard of care for women with stage 3 disease and those with high grade serous carcinoma, provided there are no contra-indications to chemotherapy. The addition of chemotherapy may be considered for other non-endometrioid subtype's e.g. clear cell, carcinosarcoma (patients with carcinosarcoma were excluded for PORTEC-3).

P53 mutations prognostically have a higher risk of disease recurrence and therefore for low grade endometrioid carcinomas with P53 mutations, it is reasonable to discuss systemic therapy with patients

Patients with high grade non-endometrioid subtypes who have no residual disease following hysterectomy and no lymph node involvement (stage 1A disease) may be spared adjuvant treatment following discussion in the gynaecology oncology MDT.

7. Management of inoperable disease at presentation

Surgery remains the curative treatment for endometrial cancer. However, patients with endometrial carcinoma may not be suitable for primary surgical management due to stage of disease, medical co-morbidities or poor performance status.

The management of each patient should be discussed in the gynaecology oncology MDT to confirm inoperability and discuss management options.

There is a paucity of clinical trials to guide evidence-based surgical or radiotherapy management of patients with inoperable disease.

Options for management include:

1. Neoadjuvant chemotherapy e.g. for high grade serous cancers, with a view to surgery if rendered operable[7]
2. Intrauterine brachytherapy (IUBT) e.g. in stage 1 cancer

3. High dose pelvic EBRT (with or without concurrent weekly cisplatin chemotherapy) based on tumour factors, patient performance status, and following discussion at MDT, with or without IUBT for stage 2-4a disease
4. Palliative hypofractionated EBRT for symptom control
5. Palliative chemotherapy with paclitaxel, carboplatin, and either dostarlimab or pembroluzimab is considered the first line treatment option for patients presenting with *de novo* stage 4B disease or patients with residual disease following surgery which is not amenable to attempt at adjuvant treatment with curative intent [8, 9]
6. Palliative treatment with hormonal treatment e.g. progestogens, aromatase inhibitors
7. Consider referrals to clinical trials
8. Referral for palliative care

8. Management of recurrent disease

8.1 Adjuvant RT not given previously

Patients with an isolated vaginal recurrence can achieve an excellent outcome with EBRT and vaginal brachytherapy thus avoiding the need for pelvic exenteration. Referral for interstitial brachytherapy should be considered where clinically appropriate.

Surgical resection of pelvic and or para-aortic lymph nodes, provided there are no contra-indications, prior to radiotherapy should be discussed in the gynaecology oncology MDT. Where surgery is not feasible, simultaneous integrated boost to suspicious lymph nodes with EBRT may be considered.

8.2 Adjuvant radiotherapy given previously

Patients with an isolated vaginal recurrence may be offered surgical management following discussion in the gynaecology oncology MDT; often this involves pelvic exenteration.

Patients with vaginal recurrence not suitable for surgery may be offered treatment with EBRT (if not contra-indicated), brachytherapy including interstitial brachytherapy or SABR. Patients with isolated lymph node metastasis may be offered treatment with SABR where suitable.

8.3 Recurrent disease not amenable to treatment with surgery or radical radiotherapy

Patients may be treated with palliative radiotherapy for symptom management as clinically indicated. Options for systemic therapy include chemotherapy, immunotherapy, or endocrine therapy. Patients should be offered participation in clinical trials where appropriate.

8.4 Uterine sarcoma

Patients with clinical/ radiological suspicion of uterine sarcoma should be staged with a CT scan of the thorax, abdomen and pelvis as there is a high propensity for lung metastases at presentation in high grade uterine sarcoma. An MRI of the abdomen and pelvis and PET CT scan can provide additional staging information.

Surgery remains the mainstay of treatment for uterine sarcoma. Patients should be referred to the regional sarcoma MDT once a diagnosis of uterine sarcoma is confirmed. There is no evidence that adjuvant treatment reduces recurrence or improves survival following surgery; pelvic EBRT may be considered in the presence of high risk features.

Treatment of recurrent disease is dictated by histology. Low grade endometrial stromal sarcomas respond well to endocrine therapy. Surgical resection of oligo metastatic disease should be considered where feasible. Palliative treatments options include systemic therapies and radiotherapy for symptom control. Patients should be referred for clinical trials where suitable.

9. Planning Technique

- Local CT scanning protocols to include scanning levels and patient immobilisation
- In stage 3c2 disease or stage 3 with ovarian or common iliac node involvement [10], the CT scan should extend superiorly to permit treatment of para-aortic lymph nodes
- Patients should be Supine with arms on chest with a full bladder approx. 200-400ml
- Local protocols for Bladder & Bowel prep
- IV contrast (unless contraindications) to delineate nodal chains

10. Target Delineation

10.1 Post Op Adjuvant

GTV: There is usually no GTV to contour following surgery however it is sometimes not possible to remove involved lymph nodes, in which case there may be an indication to contour a separate GTV for each lymph node; this should be labelled separately e.g. GTV_N1, GTV_N2.

CTV: the CTV includes the parametrial tissues bilaterally, upper third of vagina, and pelvic lymph nodes including obturator, internal and external iliac lymph nodes. Consider treating up to the common iliac lymph nodes in stage 3C1 disease. The pre-sacral lymph nodes should be treated if there is involvement of the cervical stroma. Consider treating low para-aortic lymph nodes if there is evidence of metastasis involving the common iliac lymph nodes. In stage 3c2 disease the para-aortic lymph nodes should be treated. Consider treating the para-aortic lymph nodes in stage 3 disease where there is evidence of ovarian involvement. The whole length of the vagina, to vaginal introitus, should be treated if the disease involves mid-lower third of vagina.

A 3-7 mm margin is added to any nodal GTV to grow a nodal CTV; each should be labelled separately e.g. CTV_N1, CTV_N2

ITV: Consider adding an appropriate margin for organ movement e.g. changes in bladder filling and bowel gas.

PTV: according to departmental protocol to account for set up errors.

OAR: bladder, rectum, sigmoid, large and small bowel (can be contoured as bowel bag). If treating para-aortic nodes include spinal cord, and kidneys. May need to include other abdominal organs as appropriate.

Treatment delivery: treatment should be delivered using VMAT/ IMRT. Consider simultaneous integrated boost for any suspicious lymph nodes not surgically removed. VVBT following EBRT is recommended if there is evidence of cervical stromal involvement. Brachytherapy to the whole length of the vagina using a line source is recommended if there is involvement of the mid-to-lower third of the vagina.

10.2 Inoperable disease

GTV: The GTV_ primary includes whole uterus to include cervix and ovaries plus any extension beyond the uterus. Any lymph nodes suspicious for lymph node involvement should be contoured and labelled separately e.g. GTV_ N1, GTV _ N2

CTV: A sufficient margin should be added to the GTV_ primary to account for microscopic disease; this is usually 1-2 cm. A 3-7 mm margin is added to create the nodal CTV as above.

ITV: as above

PTV: as above

OAR: as above

Treatment delivery: VMAT/ IMRT with simultaneous integrated boost as clinically indicated. A field based treatment approach is suitable if treatment with VMAT/ IMRT offers no additional advantages. Consider IUBT where clinically appropriate and not contraindicated.

11. Critical Organ Dose constraints[11]

OAR constraints for patients with nodes are derived from Embrace II protocol

OAR constraints for patients without nodes are an informed amalgamation of other clinical protocols and Embrace II resulting in tighter constraints

Small bowel constraint practice may vary between centres. We suggest using those from EMBRACE II (see below), or constraints verified in WMCA protocols for other tumour subsites (e.g. Pancreas or upper GI Protocols).

Bone constraints (vertebral bodies) are not mandatory. Should you wish to use them, we suggest referring to local Centre planning documents or constraints verified in WM RT Network protocols for other tumour subsites.

	Without SIB		With SIB	
	Optimal	**Mandatory**	**Optimal**	**Mandatory**
Bladder (Gy)	Vol %	Vol %	Vol %	Vol %
57.5			0	
47.3		0		
45	35%	-		
40	50%	75%	75	
30	70%	95%	85	
Bowel (Gy)	Vol cc	Vol cc	Vol cc	Vol cc
57.5			0	

47.3		0		
45	78			
40		100	250	
30	200	350	500	
Spinal cord (Gy)				
48		0		0
Femoral Head (Gy)	Vol %	Vol %	Vol %	Vol %
50				0
45	5%			
40	35%			
30	50%			
Kidney				
D_{mean}	<10Gy	<15Gy	<10Gy	<15Gy
Rectum (Gy)	Vol %	Vol %	Vol %	Vol %
57.5			0	
47.3		0		
45	40%	-		
40	60%	85%	85	
30	70%	95%	95	
Sigmoid (Gy)	Vol %	Vol %	Vol %	Vol %
47.3		0		
57.5			0	
Liver (Gy)	Vol %		Vol %	
30	<30%		<30%	
D_{mean}	<28Gy		<28Gy	
Duodenum *	V55 <15cm^3			
CTV-T HR +10mm (Gy)				
46.35	0		0	

12. Dose and Fractionation

12.1 Pelvic EBRT

Appropriate dose fractionation schedules (once daily treatment) include:

- 46 Gy in 23 fractions
- 48.6 Gy in 27 fractions
- 45 Gy in 25 fractions

12.2 Brachytherapy

HDR: VVBT as sole adjuvant treatment only: 21 Gy at 5mm in 3 fractions
HDR: VVBT or vaginal brachytherapy following EBRT: 8 Gy at 5mm in 2 fractions

IUBT as primary treatment in inoperable disease: 36 Gy in 5 fractions or 37.5 Gy in 6 fractions prescribed to uterine serosa
IUBT following EBRT: 21 Gy in 3 fractions or 28 Gy in 4 fractions or 25 Gy in 5 fractions prescribed to uterine serosa

12.3 Para-aortic radiotherapy

EBRT - 45Gy in 25 daily fractions of 1.8Gy over 5 weeks

12.4 Simultaneous integrated boost to involved lymph nodes

EBRT – 55 to 60 Gy in 25 fractions

12.5 Palliative

8 Gy in single fraction
20Gy in 5 fractions
30 Gy in 10 fractions
45Gy in 25 fractions (higher dose for those not eligible for surgery, see 10.2)

13. Peer Review

Peer review should be undertaken in line with the West Midlands regional guidance agreed in December 2025 which identifies which cases should be subject (as a minimum) to peer review. Please refer to the West Midlands Peer Review guidance (December 2025).

14. Treatment Verification

- Daily 3D CBCT imaging with on line correction
- Verification imaging as per local imaging protocol

15. On Treatment Review

- Patients reviewed weekly for radiotherapy toxicities. This may be a Review Radiographer or Clinical Oncologist dependant clinical situation and local guidance.
- After completion of treatment patients are seen in out-patient clinic for regular medical review
- Eligible patients can be managed on the patient stratified follow up pathway

16. Treatment Letter

- On completion of treatment, a summary of the radiotherapy dose and toxicities experienced are documented.
- In addition, expected acute and late side effects are detailed with recommended treatments.

17. Follow up and Late Effects

Patients follow up, in keeping with departmental protocols.

Assessment of late effects should be undertaken at follow up visits. Any late effects should be managed, as clinically appropriate including referral to other relevant medical or surgical specialities.

Significant Late Toxicities include

- Vaginal stenosis associated with vaginal dryness and dyspareunia
- Vulval skin changes
- Anal canal stenosis or anal leakage
- Urinary frequency / urgency
- Diarrhoea / loose stools
- Rectal bleeding
- Renal impairment
- Haematuria
- Pelvic bone thinning and increased risk of insufficiency fractures

- Lymphedema
- Bowel stenosis /fistulation
- Risk of 2nd cancer (1-2% per 10yrs of follow up)
- Risk of infertility and early onset menopause in younger (pre-menopausal) women.

18. References

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