WM Radiotherapy Clinical Protocol

Gynaecological: Cervix Radiotherapy Protocol

Revision History

Version	Date	Summary of changes
1.0	07.05.2021	Ratified by EAG Final
2.0	13.10.2023	EAG Ratified
2.1	16.1.2025	Change request received following Interlace trial findings
3.0	14.2.25	Ratified by EAG
3.1	3.4.25	Minor change of wording to 7th bullet point in location technique section
3.2	9.7.26	Peer review wording amended
Review Date:	February 2027	

Ratified By

This document was ratified by the following people:

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Gynaecological Cancer
Cervix

Purpose

To provide a standardised protocol for planning and delivery of radiotherapy for cervical cancer 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.

Diagnosis and staging

Patients may present with symptoms or through the NHS cervical screening programme. All patients should have histological confirmation of cervical carcinoma, either with a single or multiple punch biopsies or excisional biopsy (LLETZ)[1].

Following histological confirmation of cervical cancer, MRI scan of the pelvis is the modality of choice for local staging[2]. A CT scan of the thorax abdomen and pelvis or a PET CT scan should be undertaken to exclude extra-pelvic disease in women with bulky cervical tumours or where there is suspicion of pelvic lymph node involvement on MRI staging. A CT scan of the thorax, abdomen and pelvis, or PET CT scan should also be undertaken in more aggressive cervical carcinoma variants such as serous or neuro-endocrine carcinoma. Patients unable to tolerate MRI scanning should undergo CT scan of the thorax, abdomen and pelvis.

Examination under anaesthesia, cystoscopy and/ or flexible sigmoidoscopy should be considered where there is clinical or radiological suspicion of bladder or rectal involvement, and in cases considered borderline for primary surgical management.
The revised 2018 FIGO staging system includes information obtained from imaging and pathological findings before a final stage is assigned[3]. This is summarised below.

[1] Reed N, Balega J, Barwick T, et al. British Gynaecological cancer Society (BGCS) cervical cancer guidelines: Recommendations for practice. Eur J Obstet Gynecol Reprod Biol. DOI:https://doi.org/10.1016/j.ejogrb.2020.08.020 (accessed 09/12/2020)
[2] Recommendations for cross-sectional imaging in cancer management, Second addition: Carcinoma of the cervix, vagina and vulva. Faculty of Clinical Radiology 2019. https://www.rcr.ac.uk/system/files/publication/field_publication_files/BFCR%2814%292_18_cervix.pdf accessed 09/12/2020
[3] Bhatla N, Aoki D, Sharma DN, et al. FIGO Cancer Report 2018. Cancer of the cervix uteri. Int J Gynecol Obstet 2018; 143 (Suppl. 2): 22-36

FIGO Staging of cervical carcinoma

Stage	Description
1	The carcinoma is strictly confined to the cervix (extension to the uterine corpus can be disregarded)
1A	Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion < 5mm
1A1	Measured stromal invasion < 3mm in depth
1A2	Measured stromal invasion ≥ 3 mm and < 5mm in depth
1B	Invasive carcinoma with measured deepest invasion ≥ 5 mm (greater than stage 1A), lesion limited to the cervix uteri
1B1	Invasive carcinoma ≥ 5 mm depth of stromal invasion, and < 2cm in greatest dimension
1B2	Invasive carcinoma ≥ 2cm and < 4 cm in greatest dimension
1B3	Invasive carcinoma ≥ 4 cm in greatest dimesion
2	The carcinoma invades beyond the uterus, but has not extended to the lower third of the vagina or to the pelvic wall
2A	Involvement limited to the upper two-thirds of the vagina without parametrial involvement
2A1	Invasive carcinoma < 4 cm in greatest dimension
2A2	Invasive carcinoma ≥ 4 cm in greatest dimesion
2B	With parametrial involvement but not up to the pelvic wall
3	The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or para-aortic lymph nodes
3A	Involvement of the lower third of vagina with no extension to the pelvic side wall
3B	Extension to the pelvic side wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause)
3C	Involvement of pelvic and/or para-aortic lymph nodes, irrespective of tumour size and extent
3C1	Pelvic lymph node metastasis only
3C2	Para-aortic lymph node metastasis
4	Extension beyond the true pelvis or involvement of mucosa of bladder or rectum
4A	Spread to adjacent pelvic organs
4B	Spread to distant organs

Primary treatment of cervical carcinoma

The primary treatment of cervical carcinoma is based on the clinical and radiological stage, performance status, and co-morbidities. In general terms, surgery is the preferred primary treatment option for early-stage cervical carcinoma; radiotherapy (RT), with or without concurrent chemotherapy, followed by intracavitary brachytherapy (ICBT) with or without interstitial brachytherapy (ISBT), is the preferred option for locally

advanced cervical cancer (LACC). RT followed by ICBT, or ICBT alone, is an option for patients with early-stage cervical cancer deemed to be unsuitable for surgical management due to medical co-morbidities or performance status, and those who decline surgery.

Where feasible, patients should be treated with single modality treatment as dual modality treatment is associated with an increased risk of morbidity. Consideration of treatment within clinical trials should be encouraged where clinically appropriate.

Stage 1A1 to 1B1

Patients are managed surgically as clinically appropriate, based on stage of cancer, presence of lymphovascular space invasion (LVSI) and patient desire to retain fertility.

Stage 1B2

Surgery and RT have similar outcomes[4]. Surgical management, where feasible, should be considered to avoid the potential late effects of RT.

Stage 1B3 and 2A

Concurrent chemo-radiation (CCRT) followed by ICBT, with or without ISBT, is the preferred treatment option however surgery may be an option in patients where RT or CCRT may be associated with increased risk of morbidity (e.g., inflammatory bowel disease, renal transplant).

Stage 2B-4A

CCRT followed by ICBT, with or without ISBT, is the preferred treatment option for women with LACC. Pelvic exenteration may be an option for patients with stage 4A cervical cancer with central disease only and no evidence of pelvic side wall involvement however, the prognosis remains poor for stage 4A disease.

Neoadjuvant chemotherapy in the treatment of locally advanced cervical carcinoma

A randomised phase III trial of induction chemotherapy followed by chemoradiation compared with chemoradiation alone in locally advanced cervical cancer: The GCIG INTERLACE trial (Mary McCormack). Induction chemotherapy followed by ChemoRT significantly improves progression free survival and overall survival in locally advanced cervical cancer and should be considered as an option in selected patients.

A phase 2 trial of neo-adjuvant chemotherapy (NACT) followed by CCRT versus CCRT for LACC reported inferior progression free and overall survival at 3 years for the NACT arm[5]

In a phase 3 trial published by Gupta and colleagues, patients with stage 1B2-2B squamous cell cervical carcinoma were randomised to receive NACT with 3 cycles of standard dose paclitaxel and carboplatin (q 21

[4] Landoni F, et al. Randomised study of radical surgery versus radiotherapy for stage 1b-2a cervical cancer. Lancet 1997; **350**: 535-540
[5] da Costa et al. Neoadjuvant chemotherapy with cisplatin and gemcitabine followed by chemoradiation versus chemoradiation for locally advanced cervical cancer: a randomized phase 2 trial. J Clin Oncol 2019; 37: 3124-3131

days) followed by radical surgery or standard treatment with CCRT and ICBT. NACT was associated with a poorer 5-year disease free survival (DFS) but not overall survival (OS) when compared with CCRT[6].

The EORTC 55994 trial randomised patients with stage 1B2-2B cervical cancer to NACT followed by surgery or standard CCRT plus boost. Whilst there was no difference in 5-year OS, NACT followed by surgery was associated with increased short-term morbidity compared with CCRT. 24% of patients in the NACT arm did not proceed to surgery, either due to treatment related toxicity (34%), disease progression (24%) or insufficient tumour response (16%). 26.3% of patients required RT following surgery[7]. The results of EORTC 55994 were expected to be published in April 2019, but remain pending.

Adjuvant radiotherapy following surgery

Following radical hysterectomy, post-operative radiotherapy (PORT), with or without chemotherapy, is indicated for patients with adverse pathological factors. Following surgery, patients with high-risk disease should be offered CCRT[8]. The definition of high-risk disease includes the presence of any one of the following pathological features:

1. Positive surgical margin
2. Lymph node metastases
3. Parametrial spread

Patients with two out of three intermediate risk features benefit from PORT; CCRT may be considered taking in to account the potential benefit, risks, and side effects of the addition of chemotherapy to PORT. Intermediate risk features include:

1. Tumour size > 4cm (some authorities consider tumour size > 2cm to be an intermediate risk factor)
2. LVSI
3. Deep stromal invasion

Vaginal vault brachytherapy (VVBT) is indicated in the presence of a positive surgical margin. VVBT following PORT/CCRT may be considered in the presence of other high-risk features, excluding positive surgical margin, following a discussion with the patient about the benefit, risks and side effects of VVBT in addition to PORT/CCRT.

Intraoperative transpositioning of the ovaries high in the paracolic gutters away from the radiation fields, or insertion of spacers at the time of surgery can reduce the radiation dose received by the ovaries (if conserved at time of surgery).

[6] Gupta S, et al. Neoadjuvant chemotherapy followed by radical surgery versus concomitant chemotherapy and radiotherapy in patients with stage 1B2, 2A or 2B squamous cervical cancer; a randomised controlled trial. J Clin Oncol 2018; 16: 1548-1555

[7] Kenter et al. Results from neoadjuvant chemotherapy followed by surgery compared to chemoradiation for stage 1b2-2b cervical cancer, EORTC 55994. DOI: 10.1200/JCO.2019.37.15_suppl.5503 Journal of Clinical Oncology 37, no. 15_suppl (May 20, 2019) 5503-5503 accessed 25/05/2023

[8] Peters et al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. J Clin Oncol 2000; **18**: 1606-1613

Adjuvant chemotherapy following concurrent chemo-radiotherapy for locally advanced cervical carcinoma

There is conflicting evidence for the benefit of adjuvant chemotherapy (ACT) following CCRT and ICBT for the treatment of LACC. In a phase 3 randomised controlled trial published in 2011, patients receiving 2 cycles of ACT with cisplatin and gemcitabine following CCRT (with cisplatin and gemcitabine) and ICBT had improved PFS and OS compared to standard treatment[9]. ACT was associated with significantly increased toxicity.

In the OUTBACK trial, patients were randomised to receive standard treatment or standard CCRT and ICBT followed by four cycles of ACT with standard dose paclitaxel and carboplatin[10]. There was no difference in OS; ACT was associated with increased toxicity.

On the basis of current evidence, ACT following CCRT and ICBT should not be routinely recommended as part of the management of LACC.

Management of Stage 4B/ recurrent cervical cancer

The management of patients with recurrent cervical carcinoma should be discussed in the gynaecology oncology MDT as some patients, particularly those with an isolated central recurrence or oligometastatic disease, may benefit from a more aggressive treatment approach. Entry into clinical trials should be offered to patients where appropriate.

Stage 4B disease

Following publication of the Keynote 826 randomised controlled trial, patients with a good performance status, and no contraindications, and a CPS of ≥ 1, should be treated with pembrolizumab, paclitaxel and carboplatin chemotherapy, with or without the addition of bevacizumab[11]. Standard treatment entails 6 cycles of chemotherapy, pembrolizumab with or without bevacizumab, followed by maintenance pembrolizumab with or without bevacizumab for up to a total of 35 cycles.

Patients who are not eligible for treatment with pembrolizumab (CPS < 1), or where there are contraindications to treatment with immunotherapy, can be treated with bevacizumab and taxane based chemotherapy[12].

Isolated central recurrence

Patients with an isolated central recurrence following RT can be treated with pelvic exenteration. Patients who have previously been treated with surgery alone can be treated with RT or CCRT and brachytherapy. Patients may benefit from treatment with ISBT.

[9] Dueñas-González, et al. J Clin Oncol 2011; **29**: 1678-1685
[10] Mileshkin et al. lancet Oncol 2023; **24**: 468-482
[11] Colombo N, et al. Pembrolizumab for persistent, recurrent, or metastatic cervical cancer. N Eng J Med 2021; **385**: 1856-1867
[12] Tewari K, et al. Improved survival with bevacizumab in advanced cervical cancer. N Eng J Med 2014; 370: 734-743

Isolated nodal recurrence

Patients with isolated pelvic nodal recurrence can be treated with surgery if technically feasible. Patients who have not been treated with RT previously can be offered PORT following surgery. Where surgery is not feasible and patients have not been treated with RT previously, RT or CCRT with simultaneous integrated boost (SIB) to involved nodes is an option.

Patients with isolated para-aortic lymph nodal recurrence may benefit from retroperitoneal lymph node dissection. If patients have not been treated with RT previously, then PORT following surgery may be a treatment option. If surgery is not technically feasible or is contraindicated due to patient factors, RT or CCRT with SIB is an option.

Patients with oligometastatic nodal recurrence who have received RT previously and are not suitable for surgery should be considered for treatment with stereotactic ablative radiotherapy (SABR).

Palliative radiotherapy

Palliative RT, including re-irradiation, provides a good option for symptom control including pain and bleeding.

Management of uncommon/rare histological variants

The management of patients presenting uncommon or rare histological variants, e.g. serous, clear cell or mesonephric adenocarcinoma, neuroendocrine carcinoma (small cell or large cell carcinoma) and cervical sarcoma should be discussed in the gynaecology oncology MDT. The management of such cases may vary from the standard protocol with treatment being driven by the histological variant including consideration of NACT and combined modality treatment.

Concurrent chemoradiation and intracavity brachytherapy

CCRT followed by ICBT represents the standard of care in LACC. The addition of chemotherapy to RT resulted in improved progression and overall survival[13]. CCRT with 5-6 cycles of weekly cisplatin (40 mg/m^2) remains the gold standard of care[14][15]. There is a paucity of data from clinical trials to recommend other chemotherapy

[13] Green J, et al. Survival and recurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix: a systematic review and meta-analysis. Lancet 2001; **358**: 781-786
[14] Rose et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. N Eng J Med 1999; **340**: 1144-1153
[15] Keys H, et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage 1B cervical carcinoma. N Eng J Med 1999; **340**: 1154-1161

regimens for CCRT to treat LACC; where treatment with weekly cisplatin is contraindicated due to renal function or patient performance status, treatment with weekly carboplatin (AUC 2) may be an option.

ICBT following RT or CCRT is an integral component of treatment of cervical cancer and failure to treat patients with ICBT results in a poorer outcome[16]. MRI based image guided brachytherapy (IGBT) is considered the gold standard method of delivering ICBT as it permits more accurate delineation of the tumour compared to CT based IGBT[17]. IGBT potentially improves pelvic control and survival rates in LACC[18]. ISBT with ICBT potentially improves the therapeutic ratio in LACC, particularly if there is a larger burden of residual disease following CCRT[19].

Patients with LACC being treated with RT or CCRT should ideally undergo a MRI in the final week of treatment to assess response to treatment and to assess the need for ISBT.

Cervical squamous cell carcinomas are categorised as RCR category 1 cancers[20]. The overall treatment time should not exceed 56 days. Delays in treatment should be avoided by treating patients on alternative RT machines or by treating patients on weekends. Where this is not feasible, any missed fractions should be compensated for by hyper fractionated RT, ensuring a minimum of 6 hours between RT fractions. The haemoglobin concentration should ideally be maintained above 120g/L throughout treatment.

Failure to treat with ICBT results is sub-optimal treatment. In such cases patients may be considered for adjuvant/salvage hysterectomy if there has been a sufficient response to enable surgical management[21]. Where surgery is not appropriate, patients should be treated with further RT.

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

Responsibility

[16] Banerjee R, et al. Brachytherapy in the treatment of cervical cancer: a review. Int J Womens Health 2014; **6**: 555-564
[17] The Royal College of Radiologists. Implementing image-guided brachytherapy for cervix cancer in the UK. London: The Royal College of Radiologists 2009
[18] Sturdza A, et al. Image guided brachytherapy in locally advanced cervical cancer: Improved pelvic control and survival in RetroEMBRACE, a multicentre cohort study. Radiother Oncol 2016; **120**: 428-433.
[19] Fokdal L, et al. Image guided adaptive brachytherapy with combined intracavitary and interstitial technique improves the therapeutic ratio in locally advanced cervical cancer: Analysis from the retroEMBRACE study. Radiother Oncol 2016; **120**: 434-440
[20] The Royal College of Radiologists. The timely delivery of radical radiotherapy: guidelines for the management of unscheduled treatment interruptions, fourth edition. London: The Royal College of Radiologists, 2019.
[21] Walji et al. Is there a role for adjuvant hysterectomy after suboptimal concurrent chemoradiation in cervical carcinoma? Clin Oncol 2010; **22**: 140-146

- To comply with the Ionising Radiation (Medical Exposure) Regulations 2017 the following roles are defined:
- Referrer & Practitioner: The consultant clinical oncologist is responsible for the care of the patient including correct referral for treatment consent, justification prescription and treatment authorization as defined in departmental protocol but in accordance with this regional protocol.
- Operators: Radiographers, physicists and technologists Consultant clinical Oncologists and other medical staff are responsible for individual tasks associated with the plan production, verification and treatment delivery as per departmental protocols but in accordance with this regional protocol and are undertaken on the auspices of the practitioner.
- It is the responsibility of department management teams to ensure departmental protocols are consistent with this regional protocol and that any disagreement with the content of this protocol is raised through the West Midlands EAG.

Localisation Technique

- Local CT scanning protocols to include scanning levels and patient immobilisation
- In stage 3c2 disease/ high risk cervical carcinoma (involvement of common iliac lymph nodes) the CT scan should extend superiorly to permit treatment of para-aortic lymph nodes
- Patients should be Supine with arms on chest/ away from the treatment area with a full bladder approx. 200-400ml
- Local protocols for Bladder & Bowel prep
- IV contrast (unless contraindications) to delineate nodal chains
- MRI of the pelvis or abdomen and pelvis in treatment position should be considered; where feasible, this should be merged with the planning CT scan to assist with delineation of the GTV. Where an additional planning MRI scan is not feasible, the diagnostic MRI scan can be merged with the planning CT scan. Special attention should be taken in to ensure MRI/CT merging is as optimal as possible (may need to merge to tumour rather than bone).
- Planning CT scan with bladder full and empty rectum should be used. An additional CT scan with an empty bladder can provide additional information and assist with RT planning; this is imperative when adding individualised internal target volumes (ITV) as opposed to using a fixed ITV for RT planning.

Target Delineation

A number of guidelines and atlases exist to help define the target volumes for treatment of cervical cancer with RT[22]. The Interlace Trial and EMBRACE2 trial[23] radiotherapy protocols are being used in a number of departments to develop the delivery of Intensity Modulated Radiotherapy (IMRT) and Image Guided Radiotherapy (IGRT) for the treatment cervical cancer. It must be noted that both protocols have been developed as part of clinical trials and each department must decide if their use for contouring and planning treatment is appropriate before publication of trial results.

[22] Toita T et al. A consensus-based guideline defining clinical target volume for primary disease in in external beam radiotherapy for intact uterine cervical cancer. Jpn J Clin Oncol 2011; **41**: 1119-1126
[23] https://www.embracestudy.dk/Public/Default.aspx?main=1&sub=3&embrace=embrace accessed 18/01/2021

Each department must decide how to best deliver RT for the treatment of cervical cancer based on local expertise and resources. The following are provided as guidelines for contouring:

Conformal RT/ IMRT

GTV-T	Cervical tumour (based on clinical examination and radiological findings)
CTV-T	Cervix, uterus, proximal vagina, parametrium, broad and proximal utero sacral ligaments (other pelvic organs may need to be included, e.g. bladder, rectum, lower third of vagina) based on clinical assessment and radiological findings
CTV-N	This includes the following lymph pelvic lymph node groups: obturator, external, internal and common iliac, and pre-sacral. The para-aortic lymph nodes should be included if the common iliac lymph nodes are involved and in stage 3c2 disease. The inguinal lymph nodes should be included if there is involvement of the lower third of vagina.
ITV-T	Consider adding this to account for organ motion. A fixed margin of 10-15 mm in the superior/inferior and anterior/posterior direction and 5mm lateral margin may be added if the CTV-T is expanded to ITV-T.
PTV-T	Based on department protocol to account for set up errors and organ motion is ITV-T not used.
PTV-N	Based on departmental protocol to account for set-up error

EMBRACE2 protocol

GTV-T	Extension of the primary cervix tumour (inside and outside the cervix. Defined by T2 weighted MRI, supported by clinical investigation and FDG PET-CT information if available). GTV will be difficult to identify on a planning CT alone.
CTV-T HR	GTV-T and any remaining cervix
CTV-T LR	Initial CTV-T HR, the complete parametria bilaterally, the entire uterus, uninvolved vagina with a 20mm margin measured from the most inferior position of the initial HR CTV-T along the vaginal axis (not starting at the fornix), CTV-T HR plus a margin of about 5mm anterior and posterior towards bladder and rectum (excluding the non-involved walls),In case of involvement of the pelvic wall sacro-uterine ligaments, meso-rectum or other involved structures a 20mm margin around the HR CTV-T will be extended into these structures.
ITV-T	Either a fixed margin approach to CTV-LR (10-15mm in anterior/posterior and superior/inferior direction and 5mm laterally) or individualised margin approach to CTV-LR based on organ motion (e.g. planning CT scan with full and empty bladder)
GTV-N	The outer-contour of lymph node and visible (macroscopic) extra capsular extension seen on MRI or CT (each lymph node must be contoured and labelled separately e.g.GTV_N1, GTV_N2, etc.)
CTV-N	GTV N plus 0-3mm (label each lymph node separately e.g. CTV_N1, CTV_N2, etc.)
CTV-E	Elective nodal regions dependant of risk of spread
ITV 45	ITV-T plus CTV-E (containing CVT-N)
PTV 45	ITV 45 with 5 mm margin
PTV-N	CTV-N plus 5 mm margin (each labelled separately e.g. PTV_N1, PTV_N2) for purposes of treating LN with SIB

INTERLACE protocol

CTV1	Whole cervical tumour and local extension (GTV)
CTV2	Proximal half of the uterosacral ligament, bilateral parametria and upper half of the vagina, or 2cm below known vaginal disease. If there is uterosacral involvement, the entire ligament should be encompassed.
CTV Nodes	The external iliac, obturator, internal iliac and common iliac nodes are also included in this volume. The superior extent is at the aortic bifurcation. The nodal areas are defined by using 7mm around blood vessels. Extend to include visible disease and lymphoceles. Modify to exclude bone, psoas muscle, bladder and bowel. The subaortic presacral nodes can be covered by connecting the nodal areas either side of S1 and S2 with a 10mm strip volume.
CTV3 (Extended field)	Where nodes at the aortic bifurcation or at the level of the common iliac vessels are positive (histology/CT PET /> 15mm on imaging) the most superior extent will be at the renal hilum. In general, a margin of at least 2cm should be added above the highest involved lymph node region.
PTV1	Add 15-20mm to CTV1 anterior/posterior/superior/inferior and 7-10mm laterally.
PTV2	Add 7-8mm to CTV2.
PTV3	Add 5-7mm to CTV3.

Virtual simulation

Treatment with virtual simulation is rarely indicated for the radical treatment of cervical cancer but may be appropriate for palliative RT or in emergencies (e.g. haemorrhage).
Field edges are defined by;

Superior:	L4 - L5 junction for distal common iliac nodes
Inferior:	Include upper half of vagina or 3cm below disease
Anterior:	Ant ⅓ of the symphysis (must cover GTV-T if present and common iliacs)
Laterals:	1.5-2cm from pelvic brim.
Posterior:	2cm from GTV-T (includes posterior extension, utero-sacral ligaments, upper presacral nodes, commonly situated 0.5cm posterior to anterior S2-3 junction).

Shield anterior superior field corners for small bowel, and lateral fields for sacral nerve root.

Adjuvant RT

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, external iliac and common iliac, and pre-sacral lymph nodes.
CTV-N: 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.

Organs at risk (OAR)

The bladder, rectum, sigmoid, large and small bowel (can be contoured as bowel bag), and hips should be routinely contoured as OAR. If treating para-aortic nodes include spinal cord, and kidneys and other abdominal organs as appropriate.

Treatment delivery

Each department must decide whether to deliver treatment using conformal RT or IMRT/VMAT, based on local expertise and capacity. Consider SIB for any suspicious lymph nodes. ICBT with or without ISBT following RT/CCRT remains the standard of care. 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. Patients should be treated with VVBT following RT/ CCRT in the adjuvant setting.

Critical Organ Dose Constraints[24]

	No Nodes		With Nodes	
	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	
CTV-T HR +10mm (Gy)				
46.35	0		0	

[24] EMBRACE II study protocol, v.2 01/08/17

Dose and Fractionation[25]

Dose fractionation options for RT/CCRT as primary treatment include:

40 Gy in 20 fractions over 4 weeks
45 Gy in 25 fractions over 5 weeks
50 Gy in 25 fractions over 5 weeks
50.4 Gy in 28 fractions over 5.5 weeks

Involved pelvic and para-aortic lymph nodes:

55-60 Gy in 25-28 fractions over 5-5.5 weeks using SIB

Parametrial disease that cannot be encompassed by ICBT and ISBT

55-60 Gy in 25-28 fractions over 5-5.5 weeks
65 Gy in 28 fractions over 5.5 weeks using SIB

ICBT and ISBT

High-dose rate brachytherapy (HDR)
28 Gy in 4 fractions or
6-7.5 Gy per fraction for 3-5 fractions
Aim to deliver >85Gy equivalent to HR CTV when treating with IGBT.

Adjuvant RT

40 Gy in 20 fractions over 4 weeks
45 Gy in 25 fractions over 5 weeks
50 Gy in 25 fractions over 5 weeks
50.4 Gy in 28 fractions over 5.5 weeks

Vaginal vault brachytherapy post RT in adjuvant setting:

8 Gy in 2 fractions (using HDR)
6 Gy in 1# or 12Gy in 2# (using HDR)
19 Gy at 1Gy per hour in 1 fraction

Palliative radiotherapy

20 Gy in 5 fractions over 1 week
30 Gy in 10 fractions over 2 weeks
8 Gy in 1 fraction

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).

Treatment Verification

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

[25] The Royal College of Radiologists. Radiotherapy dose fractionation, fourth edition. London: The Royal college of Radiologists, 2024

On Treatment Review

- Patients reviewed weekly for radiotherapy toxicities. This may be a Review Radiographer or Clinical Oncologist dependant clinical situation and local guidance.
- Patients treated with CCRT require pre-chemotherapy bloods in keeping with departmental policy
- Ideally patients should undergo a MRI in the final week of RT/CRRT to assess response and determine if patients would benefit from ISBT
- After completion of treatment patients are seen in out-patient clinic for regular medical review in keeping with departmental protocol

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.

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). Patients should be commenced on hormone-replacement therapy as clinically appropriate.