Clinical Oncology

The Royal College of Radiologists expert panel recommendations for radiotherapy treatment for vulval cancer

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The Royal College of Radiologists

Contents

Introduction

Authors

Alexandra J Stewart[a,b] Patricia Baird[c] Eleanor Dyke[a], Melanie Powell[d] Alexandra Taylor[e], Ursula McGivern[c], Jeffrey Summers[f], Anupama Gore[g], Audrey Cook[h] Jennifer Forrest[i], Louise Hanna[j],

Affiliations

[a]St Luke's Cancer Centre, Royal Surrey Hospital NHS Foundation Trust, Guildford, UK

[b]University of Surrey, Guildford, UK

[c]Belfast City Hospital, Belfast, UK

[d]Barts Health NHS Trust, London, UK

[e]The Royal Marsden NHS Foundation Trust, London, UK

[f]Maidstone and Tunbridge Wells NHS Trust, Maidstone, UK

[g]Leicester Royal Infirmary, Leicester, UK

[h]Gloucestershire Hospitals NHS Trust, Gloucester, UK

[i]Royal Devon University Hospital Trust, Exeter, UK

[j]Velindre University NHS Trust, Cardiff, UK

Corresponding author

Dr Alex Stewart, St Luke's Cancer Centre, Royal Surrey Hospital NHS Foundation Trust, Guildford, GU2 7XX, UK

Alexandra.stewart@nhs.net

Declarations of interest

Alexandra Stewart has received speakers' honoraria from Elekta in 2019 and 2022. All other authors state no conflict of interest.

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Abbreviations

5FU	5-fluorouracil
α/β	Alpha/beta ratio
AUC	Area under the curve
BGCS	British Gynaecological Cancer Society
BMI	Body mass index
CTV	Clinical target volume
CT	Computed tomography
CTV_Elective	Clinical target volume elective lymph nodes
CTV_Node boost	Clinical target volume involved lymph nodes boost
CTV Tumour bed	Clinical target volume postoperative tumour bed
CTV_Vulva	Clinical target volume vulva
CTV_Vulva boost	Clinical target volume boost to vulval tumour
Dmax	Maximum radiotherapy dose
Dmean	Mean radiotherapy dose
DVH	Dose volume histogram
Dx%	Dose received by x% of volume
EQD_2	Equivalent dose in 2 Gray per fraction
ESGO	European Society of Gynaecological Oncology
F	Fractions
FIGO	Fédération Internationale de Gynécologie et d'Obstétrique
FNA	Fine-needle aspiration
GTV_Node	Gross tumour volume involved lymph nodes
GTV_Vulva	Gross tumour volume vulva
Gy	Gray
HPV	Human papilloma virus
IF	Inguinofemoral
IMRT	Intensity-modulated radiotherapy
IV	Intravenous
IVC	Inferior vena cava
LN	Lymph nodes
MDT	Multidisciplinary team
MPD	Mid-plane dose
MRI	Magnetic resonance imaging
NICE	National Institute for Health and Care Excellence
PET	Positron emission tomography
PTV_Elective	Planning target volume elective lymph nodes
PTV_Node boost	Planning target volume involved lymph nodes boost
PTV_Tumour bed	Planning target volume tumour bed
PTV_Vulva	Planning target volume vulva
PTV_Vulva boost	Planning target volume boost to vulval tumour
RCR	The Royal College of Radiologists
SIB	Simultaneous integrated boost
UK	United Kingdom
VSIM	Virtual simulation
Vx	Volume receiving x Gy

Guideline writing process

An expert panel was convened by The Royal College of Radiologists (RCR). A systematic literature review was conducted and current international vulval cancer guidelines were reviewed. Draft guidelines were reviewed by the expert panel over a series of online meetings and offline review and consensus reached. A contouring panel consisting of clinical oncologists with a wide range of experience treating vulval cancer was also convened by the RCR. This group performed contouring on two sample cases prior to seeing the guidance then repeated contouring after receiving the guidance. Concordance was reviewed and the guidelines were modified to ensure clarity.

Scope of document

These guidelines address the management of squamous cell carcinoma of the vulva. They do not address the management of other histological subtypes such as Paget's or Bartholin's adenocarcinoma since these have a different aetiology and treatment course.

01 Treatment rationale

Vulval cancer is a rare cancer with approximately 1,400 cases per year in the UK[1] and 90% of cases are squamous cell carcinoma. There is an association with human papilloma virus (HPV) infection, but a proportion of cases are not linked to HPV, such as those associated with lichen sclerosus and chronic inflammation. Guidelines for screening, diagnosis and surgical treatment are published by the British Gynaecological Cancer Society (BGCS), the National Institute for Health and Care Excellence (NICE) and the European Society of Gynaecological Oncology (ESGO).[2–4]

- **Radical surgery** is the primary treatment for vulval cancer, with wide local excision and sentinel node biopsy for tumours under 4 cm or inguinal nodal dissection for larger tumours or those with suspicious features.
- **Radical radiotherapy** refers to treatment courses which use radiation doses that take surrounding tissues up to, or close to, normal tissue tolerance. These are usually curative in nature and include both definitive and adjuvant radiotherapy in these recommendations.
  - **Definitive radiotherapy**, with chemotherapy for medically fit patients, is recommended to treat patients with potentially curable tumours that are unresectable (defined as stage II and above), with proximity to urethra, vagina, anus and/or large positive lymph nodes (LN) at diagnosis or patients who are not fit for surgery/anaesthesia.[2,3,5]
  - **Adjuvant radiotherapy** refers to treatment courses given after surgery to decrease the risk of recurrence.
- **Palliative radiotherapy** refers to treatment courses that use lower radiation doses aiming for symptom control and/or disease shrinkage and are generally recommended for less fit patients or those with distant metastatic disease.

The indications for **adjuvant radiotherapy ± chemotherapy** are:[2,3]

- Positive/close margins (≤0.3 cm) and further surgery not feasible.[6–9]
- Involved LN:
  - >1 involved lymph node is a definite indication for chemoradiation.
  - There is evidence for a survival advantage with adjuvant radiotherapy when there is 1 involved lymph node, but evidence for concomitant chemotherapy is not proven.[10]
  - 1 lymph node with micrometastases in the setting of full LN dissection is a relative indication for adjuvant radiotherapy.
- Extracapsular lymph node spread.
- Inguinofemoral radiotherapy is recommended instead of nodal dissection surgery for patients with an involved sentinel lymph node with micrometastases (≤2 mm).[11]

02 Essential investigations and staging

2.1. Examination and investigations

Clinical staging and investigations:[12,13]

- Examination of vulva and LN areas and biopsy results.
- Biopsy or fine-needle aspiration (FNA) of suspicious inguinal LN can be considered depending on imaging review.
- Full blood count, biochemistry and liver function.
- Computed tomography (CT) thorax, abdomen, pelvis for patients proceeding straight to surgery.
- Magnetic resonance imaging (MRI) pelvis and whole vulva and positron emission tomography-computed tomography (PET-CT) scan for patients proceeding straight to radical radiotherapy or potentially operable patients with radiologically positive LN.

The patient should be discussed at the gynaecological multidisciplinary team (MDT) meeting with clinical oncologist, gynae-oncology surgeon, specialist radiologist, specialist pathologist and clinical nurse specialist present.

2.2. Cancer staging (FIGO 2021)

Table 1. FIGO staging of vulval cancer (2021)[14]

Stage	Description	
I	**Tumour confined to the vulva**	
	IA	Tumour size ≤2 cm and stromal invasion ≤1 mm
	IB	Tumour size >2 cm or stromal invasion >1 mm
II	**Tumour of any size with extension to lower one-third of the urethra, lower one-third of the vagina, lower one-third of the anus with negative nodes**	
III	**Tumour of any size with extension to upper part of adjacent perineal structures, or with any number of non-fixed, non-ulcerated LN**	
	IIIA	Tumour of any size with disease extension to upper two-thirds of the urethra, upper two-thirds of the vagina, bladder mucosa, rectal mucosa, or regional lymph node metastases ≤5 mm
	IIIB	Regional lymph node metastases >5 mm (inguinal and femoral)
	IIIC	Regional lymph node metastases with extracapsular spread
IV	**Tumour of any size fixed to bone, or fixed, ulcerated lymph node metastases, or distant metastases**	
	IVA	Disease fixed to pelvic bone, or fixed or ulcerated regional lymph node metastases
	IVB	Distant metastases

03 Position and imaging for radiotherapy planning and localisation

Prior to the pretreatment CT planning scan, the clinician will assess the diagnostic imaging and clinical assessment information to decide on patient positioning. A 'frog-leg' position allows sparing of the skin in the upper inner thigh, though the clinician may prefer to treat the patient in a straight-leg position, preferably with the legs slightly apart. Immobilisation is very important as there can be nodal or tumour movement if immobilisation is poor, particularly if the hip position varies between fractions. It is recommended that a 'vac-bag' is used if treating in the frog-leg position and it may also be helpful in the straight-leg position. Bolus may be used to cover the entire extent of the primary lesion, areas with gross nodal disease or sites of excised LN with extranodal extension. In cases with multifocal disease, consideration can be given to placing bolus over the entire vulva ± mons pubis region. Wire markers, placed by a clinician or specialist radiographer, may help to define margins of primary tumour or postoperative scars. The placement of fiducials can be helpful.

A bladder-filling protocol is recommended; for example, consuming 450 ml fluid and waiting 30 minutes before the planning scan. A rectal preparation protocol is not usually required but consider repeat scanning following enema or laxatives if rectal diameter is >4 cm for volumes that include the pelvis.

The recommended planning CT scan thickness is 0.25–0.3 cm. Suggested scan levels are from the superior border of L2 vertebra to 5 cm below the ischial tuberosities, ensuring the whole vulva is included. The use of virtual bolus or 'false bolus' may help with optimisation of dose during the planning process. For radical treatment, registration of a diagnostic MRI with the planning CT is recommended for volume definition, particularly for urethral and vaginal definition. T2-weighted images are most useful for definition of the vulval tumour and invasion into surrounding structures.[15]

For palliative treatment, volume-based CT planning is recommended and intensity-modulated radiation therapy (IMRT) should be considered, therefore patients should be positioned accordingly. This decreases hot spots and improves dose homogeneity, thus decreasing acute and late toxicity. Virtual simulation may be considered if patient performance status is poor or predicted survival is limited.

Peer review of contours is encouraged by the RCR. The use of consistent colours and names for structures within the department is also encouraged.

04 Volume definition and critical structures

4.1. Radical radiotherapy

Clinicians should refer to the diagnostic imaging to aid with target volume definition and contouring. For postoperative patients, the pathology should be reviewed and any areas of positive or close margin determined and compared with imaging and clinical findings. The aid of other members of the MDT such as radiologist, histopathologist and surgeon can be valuable in determining target volumes. Diagnostic imaging fusion with the planning CT may be helpful. Complex cases may require modification of these guidelines with the assistance of the MDT. Table 2 presents the terminology and volume definition for radical radiotherapy. Table 3 presents the specific volumes to be included in the CTV for definitive radiotherapy or in postoperative cases where the CTV_Vulva will form part of the target volume.

Table 2. Volume definition for radical radiotherapy

Name of volume	Abbreviation*	Definition**
GTV_Vulva	**GTV_V**	Primary vulval tumour/s – MRI and physical examination may be required to define this
GTV_Node	**GTV_N**	Macroscopic involved nodes defined by imaging/FNA – consideration can be given to individual labelling GTV_N1, GTV_N2 etc
CTV_Vulva	**CTV_V**	Intact: GTV_Vulva + 10 mm expanded to include whole vulva, to skin surface (use of bolus at clinician discretion)[13,15,16] and to include associated structures as listed in Table 3 Postoperative: See Table 3
CTV_Tumour bed	**CTV_TB**	Postoperative tumour bed + 0–5 mm. This may be the vulval and/or nodal excision site. Consideration can be given to individual labelling CTV_TB1, CTV_TB2 etc If positive LN were in the area where a seroma subsequently forms, it may be appropriate to include the whole seroma
CTV_Vulva boost	**CTV_VB**	GTV_Vulva + 5 mm
CTV_Node boost	**CTV_NB**	GTV_Node + 0–5 mm
CTV_Elective	**CTV_EN**	Elective LN as per Table 4 and Appendix Table D To also include GTV_Node + 2–5 mm
PTV_Vulva	**PTV_V**	CTV_Vulva + 7–10 mm isotropic expansion
PTV_Tumour bed	**PTV_TB**	CTV_Tumour bed + 5 mm if using daily online imaging CTV_Tumour bed + 10 mm if no daily online imaging
PTV_Vulva boost	**PTV_VB**	CTV_Vulva boost + 5 mm if using daily online imaging CTV_Vulva boost + 10 mm if no daily online imaging

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Volume definition and critical structures

PTV_Node boost	**PTV_NB**	GTV_Node + 5 mm if using daily online imaging GTV_Node + 7–10 mm if no daily online imaging
PTV_Elective	**PTV_EN**	CTV_Elective + 5–7 mm isotropic expansion

*The abbreviation column uses terminology which is consistent with other RCR contouring guidelines but the consensus group recognised that use of the full word may be clearer in these guidelines.

**Note PTV margins may vary by centre with local practice and equipment taken into consideration. Variation may occur due to factors including, but not limited to, image registration, set-up imaging and margins to account for swelling on treatment.

Contouring vulval volumes

Table 3. Specific volumes to include in CTV_Vulva for radical radiotherapy

Anatomic area of tumour involvement		Anatomic site to include in CTV_Vulva
Vulva (intact) See Figure 1		Labia majora and minora, clitoris, vestibule, urethral meatus, introitus, perineum*
Mons pubis (intact) **(skin bridge between the vulva and inguinal lymph node bilaterally)** See Figure 2		Include whole mons if tumour is involving the mons; also include when treating a primary/postoperative vulval tumour and LN** 5 mm from skin surface if no bolus and to skin surface if bolus
Vaginal involvement See Figure 3		At least 3 cm of caudal vagina (with consideration of including the entire vaginal length)
Anal or rectal involvement See Figure 4	**No involved rectum or mesorectal LN**	Whole anus and caudal 5 cm of mesorectum
	Involved rectum and/or mesorectal LN	Anus and whole mesorectum
Urethral involvement See Figure 5	Urethral meatus or distal ⅓ of urethra	At least 2 cm of urethra
	Middle ⅓ and/or proximal ⅓ of urethra	Entire urethra and bladder neck
Periclitoral lesions		Clitoral crus extending to pubic bone* See Appendix Figure C for description of clitoral anatomy
Vulva (postoperative) See Figure 6		Remaining labia majora and minora, clitoris, vestibule, urethral meatus, introitus, perineum Or an individualised target based on the tumour bed with margin of at least 5 mm*** If there is perineural invasion or lymphovascular invasion it is recommended to treat the whole vulva and mons

See Appendix Table C for anatomic boundaries of normal female genitalia and nearby structures.

*The CTV_Vulva also includes the GTV_Vulva +10 mm. Consideration can be given to excluding some areas from this expansion such as the legs or outside the body. 5 mm inside the bone can be included in this expansion, to cover potential periosteal involvement.

**It is acceptable not to include the mons in CTV_Vulva if there is a small vulval lesion that lies behind the posterior vaginal wall, even if there are positive inguinal LN.

***The tumour bed is defined using the operative note and pathology report and pre-surgical imaging or clinical findings.

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Volume definition and critical structures

Figure 1. Contouring the intact vulva with a tumour in vulva

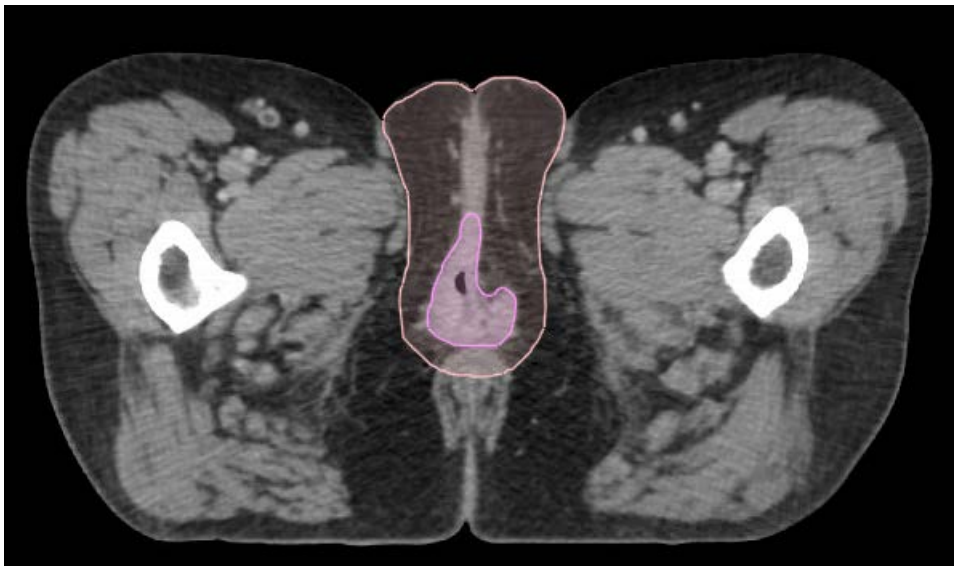

Figure 1A. Axial CT image showing the cranial aspect of vulva contours, including labia majora and minora and perineum (GTV_Vulva shown in purple, CTV_Vulva shown in pink). Here, the CTV_Vulva extends to the skin surface. At the mons, the CTV_Vulva expands to skin with bolus, or 5 mm within skin if tumour does not extend to skin. A sagittal image may be helpful to determine at what point to move the contour inwards from the skin surface/apply bolus (see Figure 2D).

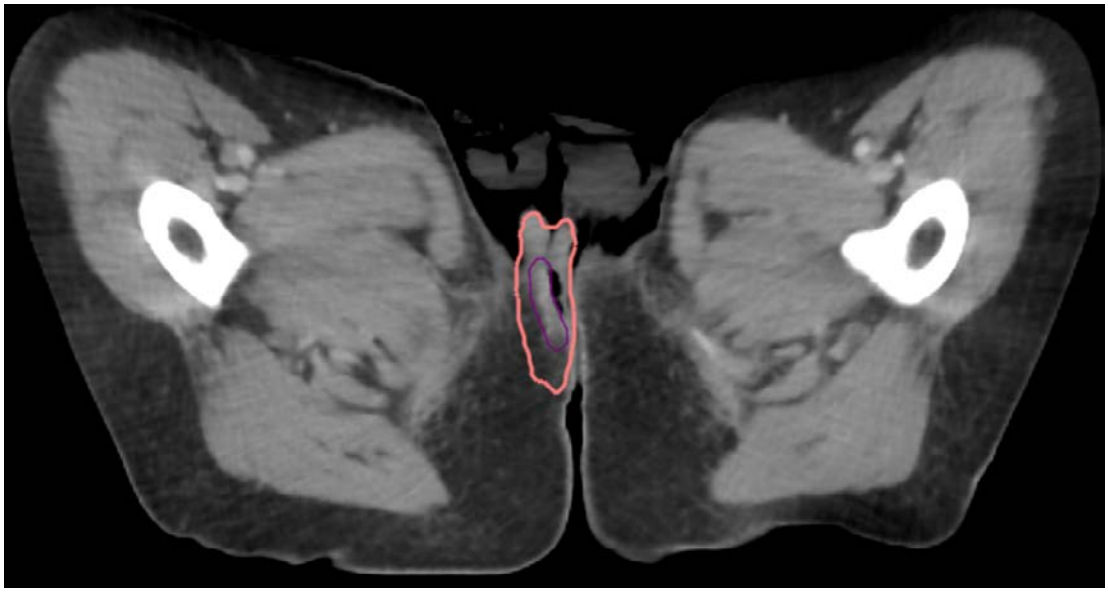

Figure 1B. Axial CT image showing caudal aspect of vulva contours, including labia majora (GTV_Vulva shown in purple, CTV_Vulva shown in pink, bolus anteriorly). When adding a 10 mm expansion to the GTV_Vulva for inclusion into the CTV_Vulva it may be appropriate to edit the expansion to one side of the vulva only, and this can be determined clinically. Bolus is added due to skin involvement.

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Volume definition and critical structures

Figure 2. Contouring the mons pubis

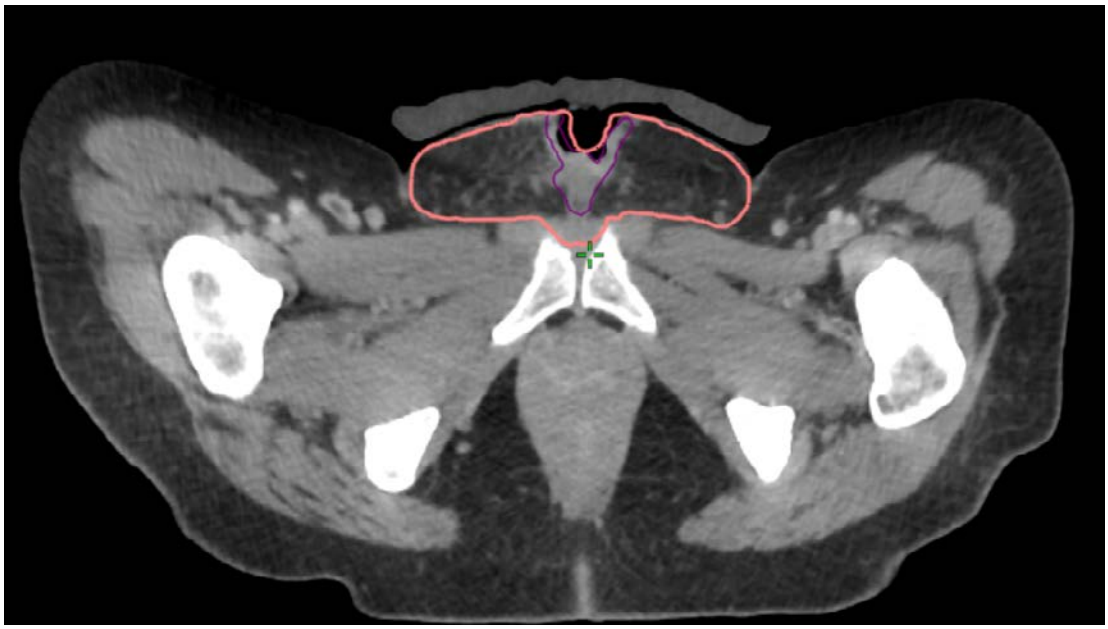

Figure 2A. Axial CT image showing contouring when the tumour lies in the mons pubis. The tumour is contoured as GTV_Vulva (purple line). The CTV_Vulva (pink line) includes the mons and clitoris and bolus is added due to skin involvement. CTV_Vulva extends to skin surface, CTV_Vulva edited off bone and muscle, except in the area of the GTV_Vulva + 10 mm.

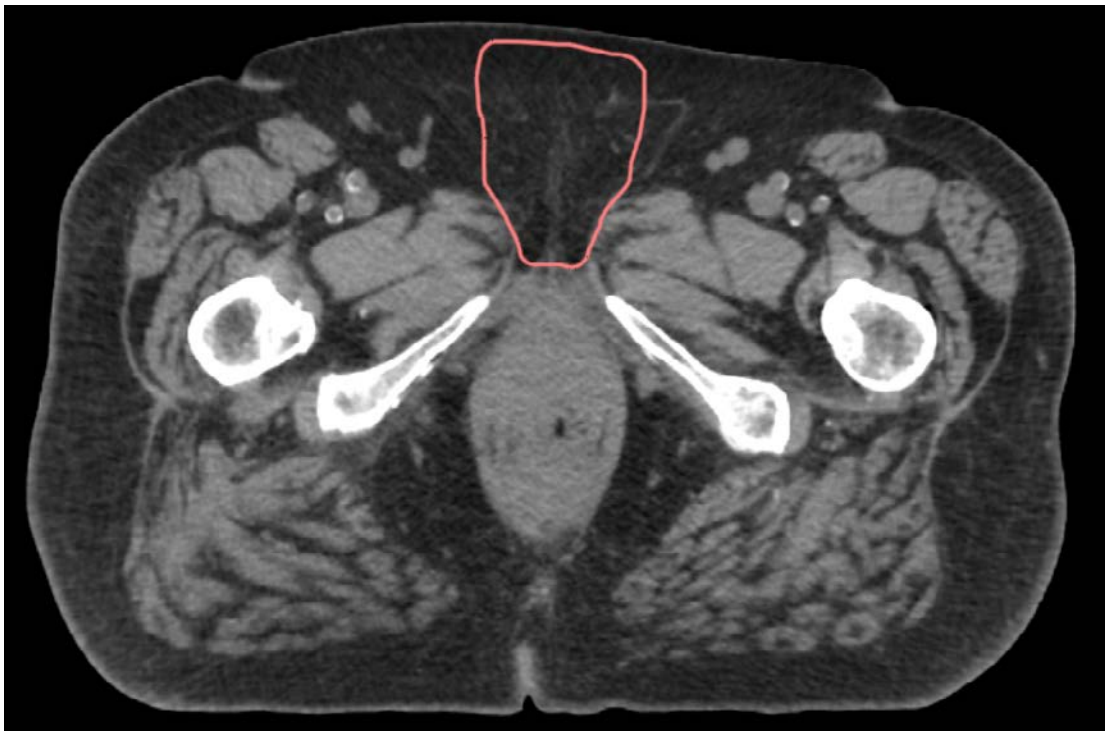

Figure 2B. Axial CT image showing contouring the mons in a patient with a high body mass index (BMI). Cranial aspect of the mons showing CTV_Vulva (pink line). Sagittal images are used to define most cranial slice to contour (see Figure 2D). The mons extends laterally to where the medial aspect of the inguinal LN contour will lie.

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Volume definition and critical structures

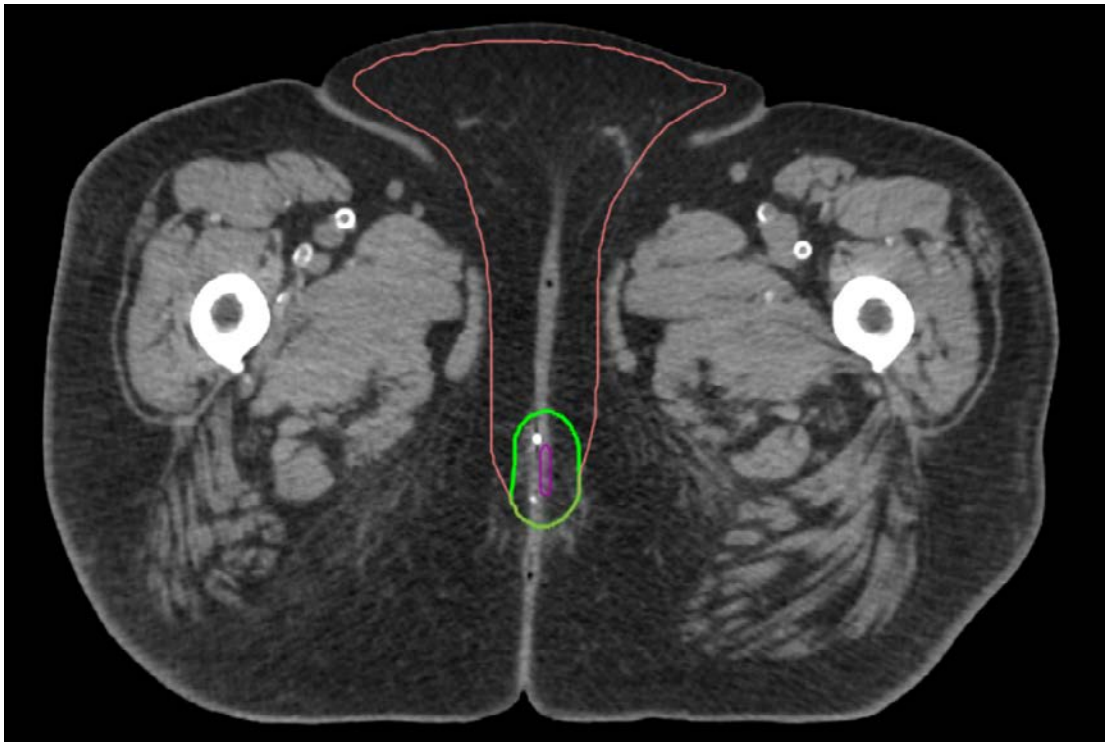

Figure 2C. Axial CT image showing a more caudal aspect of CTV_Vulva (pink line) demonstrating lower aspect of the mons, extending to the labia. The CTV_Vulva includes the GTV_Vulva which is visible posteriorly (purple line) with wire marking the scar following local excision of polypoid lesion with incomplete resection. A 10 mm expansion is added to the GTV_Vulva (green line).

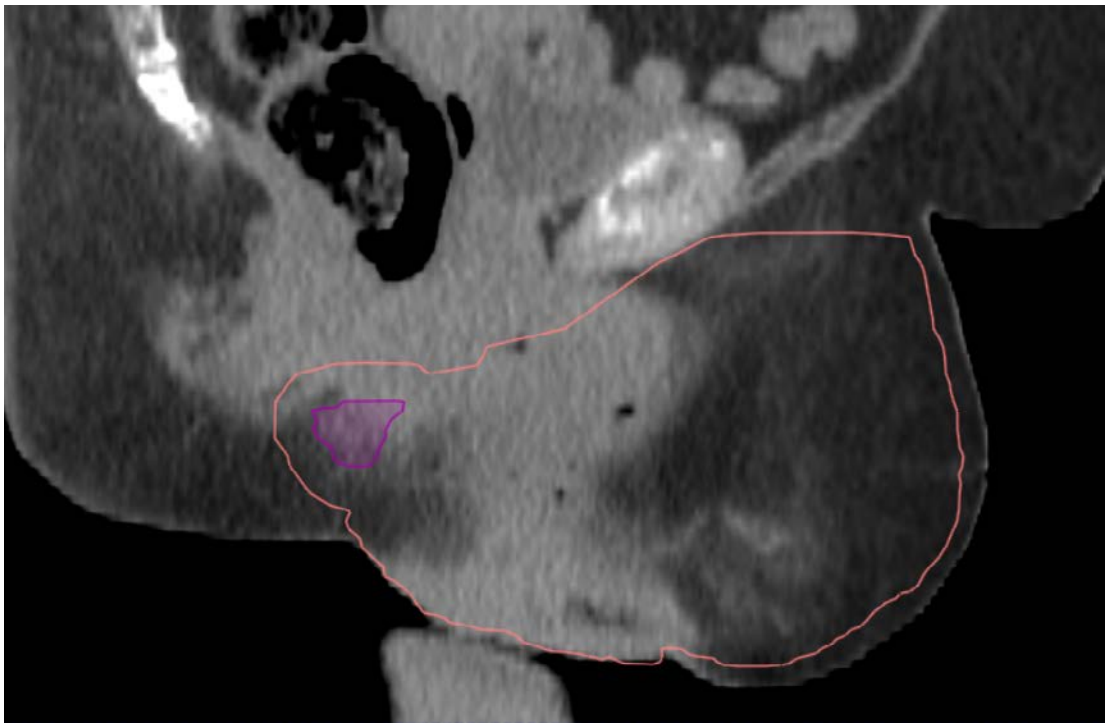

Figure 2D. Sagittal CT image in a patient with a high BMI. The sagittal image is used to define the superior extent of the mons, just inferior to the abdominal pannus. This is often at the level of the mid-pubic symphysis. The GTV_Vulva is shown in purple and the CTV_Vulva is shown in pink.

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Volume definition and critical structures

Figure 3. Contouring a tumour with vaginal involvement

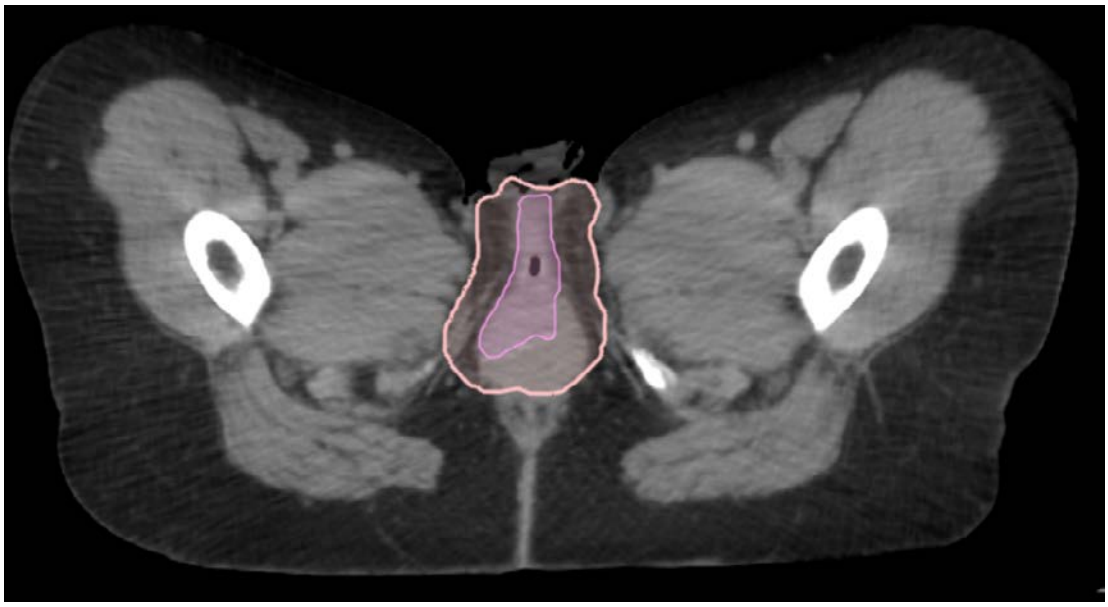

Figure 3A. Axial CT image. This more caudal image demonstrates GTV_Vulva (purple line) for a tumour that extends into the vagina postero-laterally. CTV_Vulva (pink line) is expanded to include GTV_Vulva + 10 mm, the labia, urethra and vagina. Bolus is present on the vulva due to skin involvement.

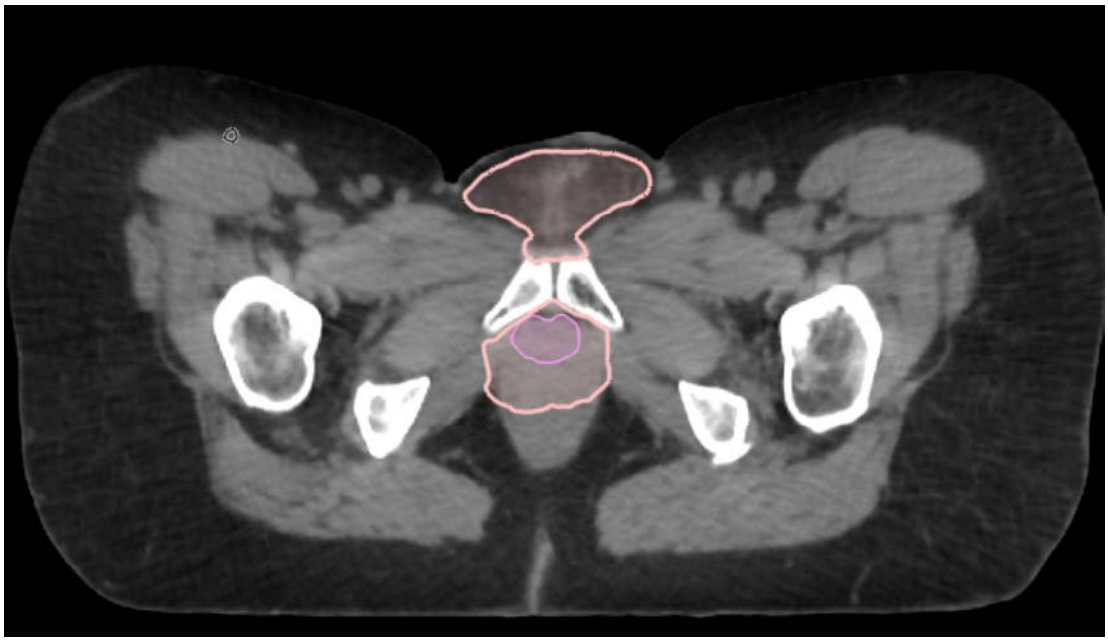

Figure 3B. Axial CT image. This more cranial image shows involvement of the upper urethra in the GTV_Vulva + 10 mm (purple line) and inclusion of the vagina posteriorly in the CTV_Vulva (pink line). Muscle and bone have been excluded from CTV_Vulva. At the area of 10 mm expansion on GTV_Vulva, consideration should be given to including 5 mm inside the bone to cover potential periosteal invasion. In this plan, the mons is not involved, and the anterior part of the contour lies 5 mm within the skin surface.

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Volume definition and critical structures

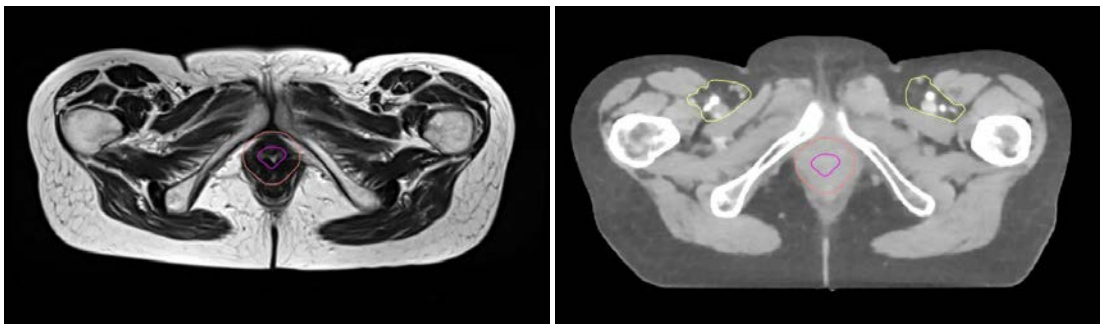

Figure 3C. Axial T2-weighted MRI (left) and CT planning (right) images demonstrating the use of MRI fusion to determine the GTV_vulva (purple line) and CTV_Vulva (pink line) for a vulval tumour invading the vagina. The structures were contoured on the MRI (left), which was fused with the planning CT (right). The CTV_Elective nodal volume is also shown in the CT planning image in yellow.

Figure 4. Contouring vulva with anal involvement

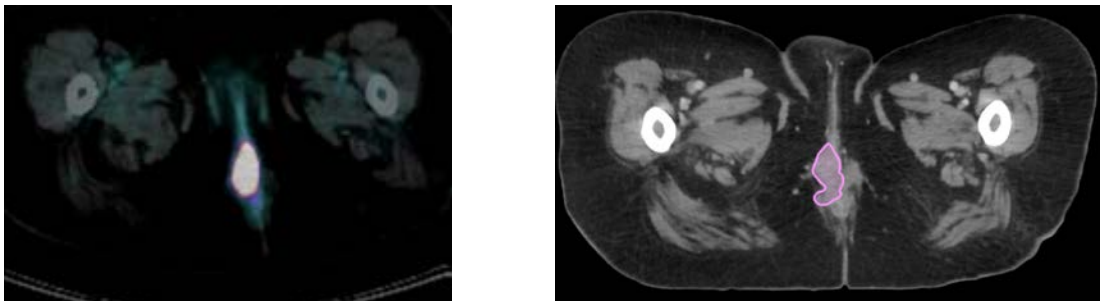

Figure 4A. Axial PET-CT (left) and planning CT (right) images demonstrating the proximity of the anus to the tumour. The tumour had visible and palpable anal extension. The planning CT scan (right) demonstrates the GTV_Vulva (purple line).

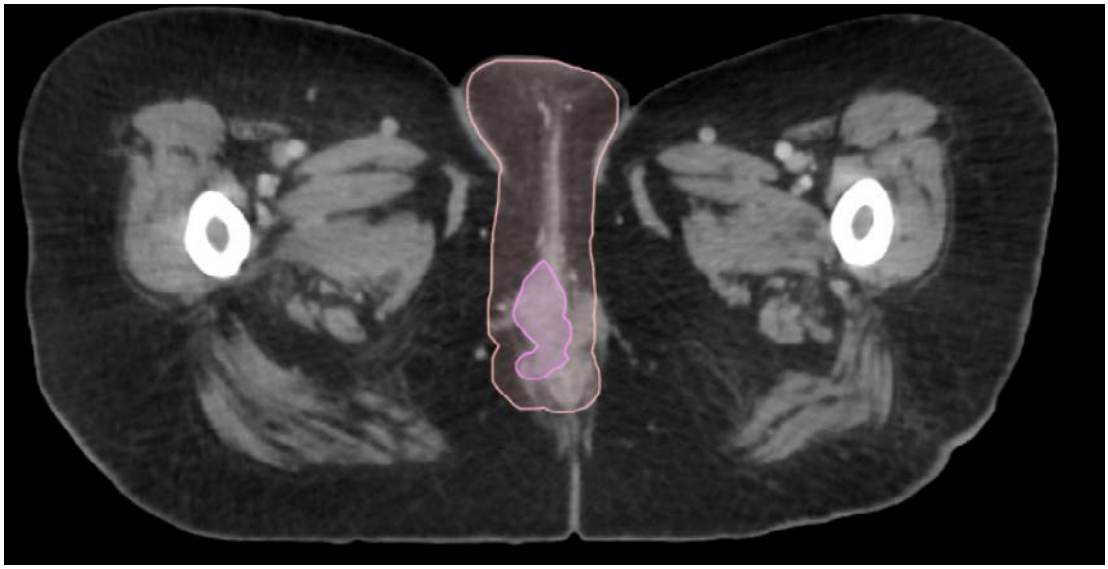

Figure 4B. Axial CT imaging showing a more cranial aspect of GTV_Vulva (purple line) with expansion of CTV_Vulva to include the anal canal (pink line). If the rectum is involved, the anus and mesorectum will be included in CTV_Vulva – the caudal 5 cm if there is no involvement of the rectum or mesorectal LN or the whole mesorectum if the rectum and/or mesorectal LN are involved.

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Volume definition and critical structures

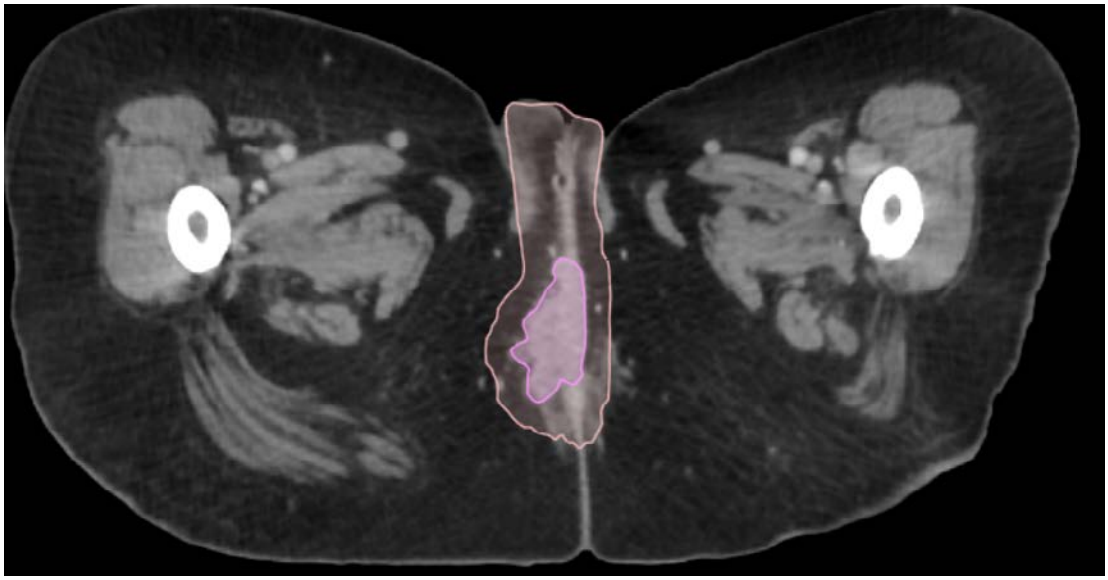

Figure 4C. Axial CT image showing a more caudal aspect of GTV_Vulva (purple line) with CTV_Vulva expanded to include the anal verge (pink line).

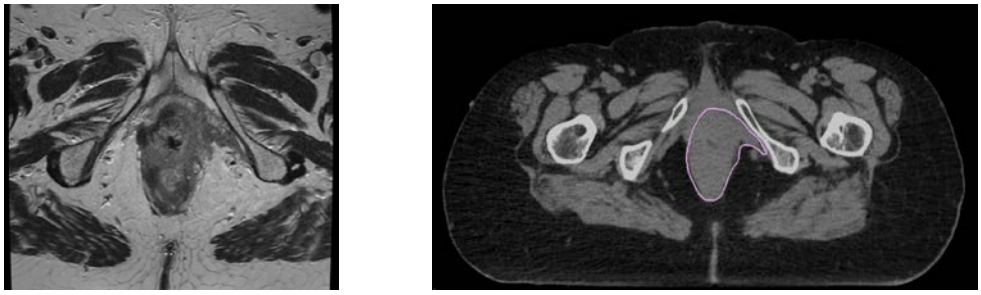

Figure 4D. Axial T2-weighted MRI (left) and CT planning (right) images showing the use of MRI in a tumour with multiple sites of local extension. The MRI image (left) demonstrates a vulval tumour invading the anal canal, perineum, vaginal introitus and pelvic side wall, and the CT image (right) demonstrates the GTV_Vulva (purple line).

Figure 5. Contouring a tumour with urethral involvement

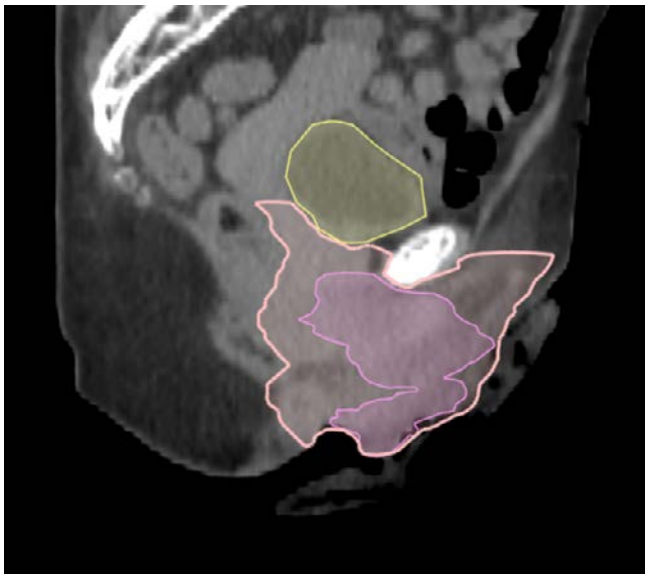

Figure 5. Sagittal CT image showing inclusion of the whole urethra to the bladder base in the CTV_Vulva shown in pink (bladder shown in yellow). This patient also had vaginal invasion so the whole vagina to the cervix is included in CTV_Vulva. The GTV_Vulva is shown in purple, and bolus is used.

04

Volume definition and critical structures

Contouring lymph node volumes

Definitive radiotherapy

- General guidelines for which LN groups should be included in the nodal CTV:[16,17]
  - Include any involved LN regions.
  - Treat the 'echelon above' the highest involved LN.
  - LN regions contoured as per Appendix Table D.

In general, LN coverage for the CTV includes the same LN regions on each side. Ipsilateral nodal irradiation can be considered in certain situations, for example small, lateralised tumours, or in the postoperative setting micrometastases in the sentinel LN with full negative lymphadenectomy on the contralateral side.[18]

Table 4. Nodal CTV volumes to include by position of primary tumour[16,18]

Anatomical involvement of primary tumour	Inguino-femoral LN	External iliac LN	Internal iliac LN	Obturator LN	Common iliac/ presacral LN	Mesorectal LN
Vulva only	✓	✓	✓	✓		
Lower ⅓ vagina	✓	✓	✓	✓		
Upper ⅔ vagina	✓	✓	✓	✓	✓	
Anus	✓	✓	✓	✓		✓
Periurethral	✓	✓	✓	✓		
Periclitoral	✓	✓	✓	✓		

All nodal irradiations should consider factors such as performance status, co-morbidity, tumour size and site of involved LN, any of which may result in acceptable variations of nodal volumes.

It is noted that the consensus group agreed that presacral lymph nodes refers to the LN region anterior to the lower lumbar vertebra and sacrum from the bifurcation of the common iliac arteries to the S2/3 junction. This can be included if there is upper vaginal involvement; it is not usually included in other cases, but this may vary with pelvic nodal involvement. Any presacral nodal area caudal to S2/3 falls into the mesorectum and therefore the whole mesorectum should be contoured if there is nodal involvement there.

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Volume definition and critical structures

Figure 6. Contouring the elective lymph nodes for a radical case

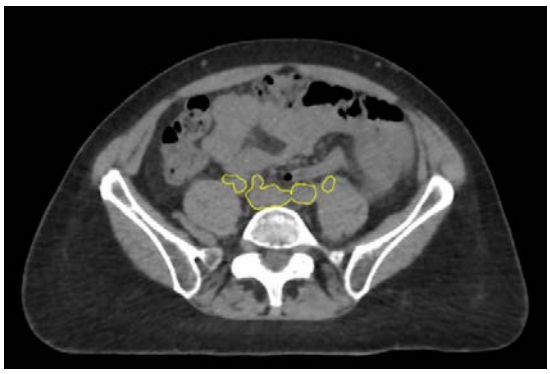


Figure 6A. Axial CT image at a more cranial level showing vessels (yellow line) contoured from the bifurcation of common iliac arteries.

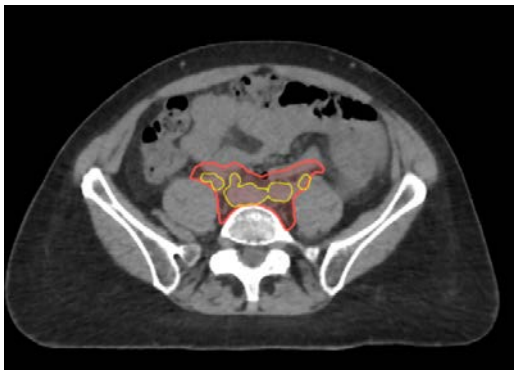


Figure 6B. Axial CT image showing the vessels (yellow line) expanded by 0.7 cm and muscle and bone excluded to form CTV_Elective (red line).

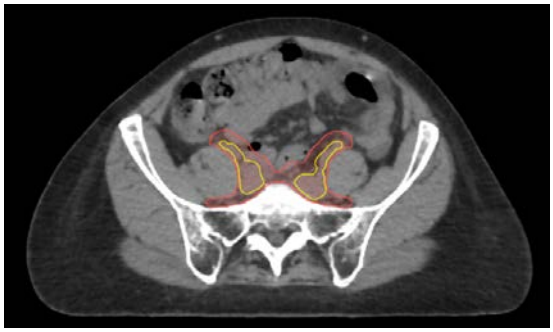


Figure 6C. Axial CT image showing the level at which the volumes would split laterally if the presacral LN are not included.

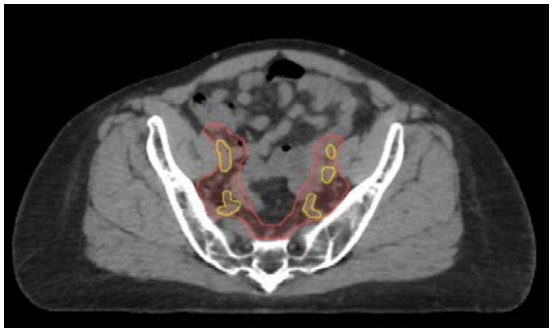
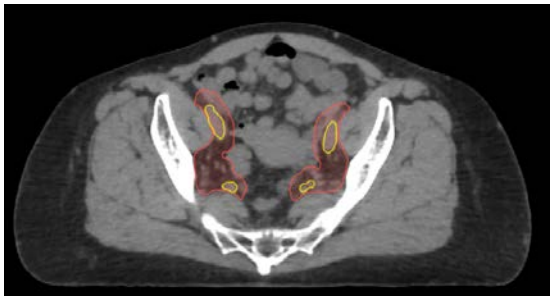
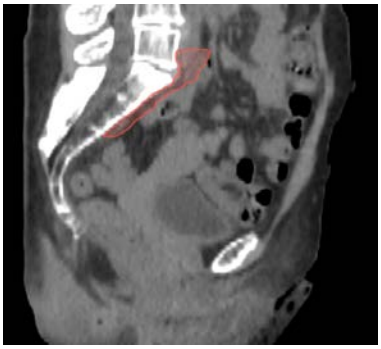


Figure 6D. Axial CT image showing the contours progressing more caudally. Vessels are shown in yellow and the CTV_Elective (red line) may be expanded to include the presacral LN posteriorly if required.

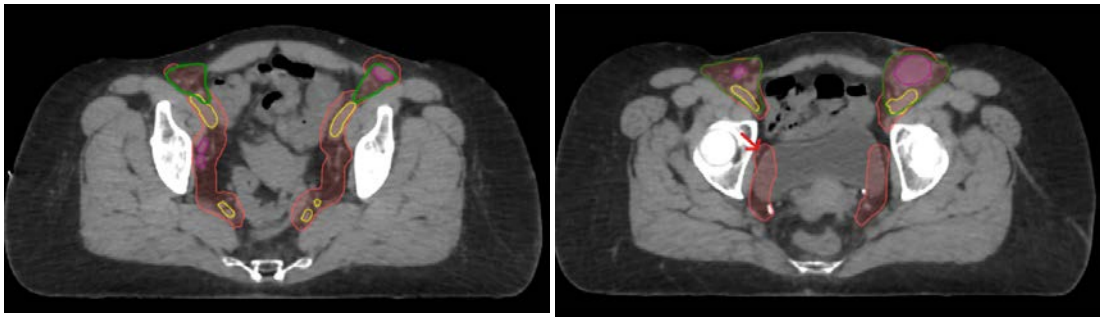




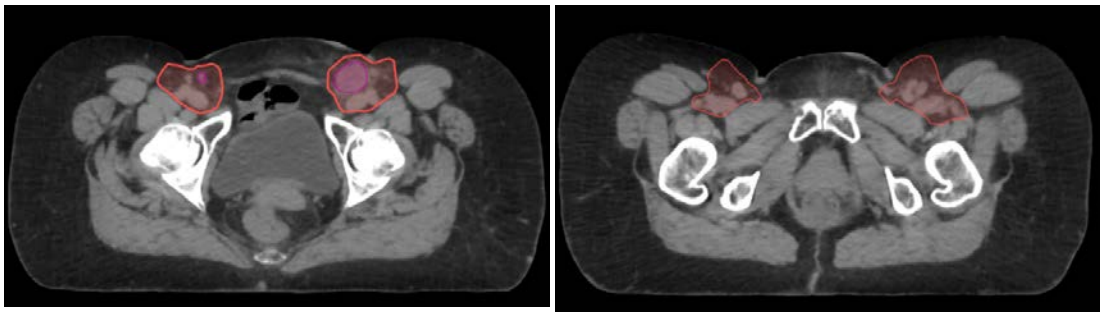
Figures 6E and 6F. Axial (Figure 6E) and sagittal (Figure 6F) CT images. The presacral nodal area between the internal and external iliac vessels is included with a 1.5 cm 'roller-ball' caudally until the S2/3 level, at which point the CTV_Elective volume splits laterally.

04

Volume definition and critical structures



Figures 6G and 6H. Axial CT images showing the inguinal nodal contouring (green line) commencing as the external iliac vessels exit the pelvis. Involved LN are contoured in purple (GTV_Node). A margin is added to GTV_Node, muscle and bone are excluded, and this volume is included in CTV_Elective (red line). This may result in parts of CTV_Elective passing closer than 0.5 cm to the skin, and the physician must assess whether bolus is required in that instance. Vessels are contoured in yellow. The inguinal and obturator nodal areas split as the obturator vessel passes anteriorly out of the pelvis (red arrow in Figure 6H).



Figures 6I and 6J. Axial CT images showing the inguinal nodal regions contoured caudally with skin creases excluded. GTV_Node (purple line) is incorporated within the CTV_Elective (pink line)

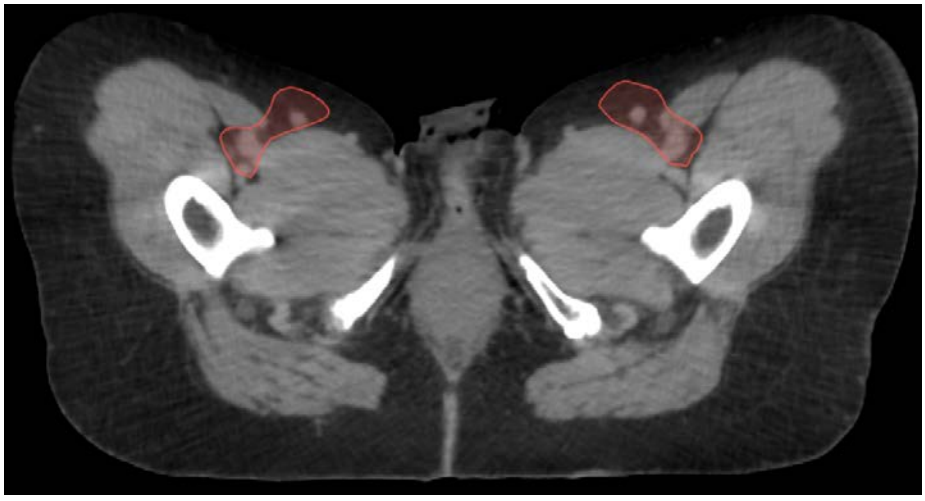


Figure 6K. Axial CT image showing the lower level of the CTV_Elective contours that finish caudally at the inferior aspect of the lesser trochanter. The posterior aspect of the contours is defined by the pectineus and iliopsoas (IP), adductor longus (AL) and vastus medialis/intermedius (VI) muscles. There is also bolus over the anterior vulva in this image.

04

Volume definition and critical structures

Postoperative involved nodal bed

Postoperative involved nodal bed refers here to the anatomic location of macroscopic and/or microscopic LN involvement. This will be a smaller volume than the relevant elective nodal CTV. It is recognised that defining the involved tumour bed may be challenging. Therefore, it is important to refer to preoperative imaging, surgical notes and histopathologic descriptions to determine the position of involved nodes. Additional margins may need to be added if there is uncertainty as to exact position. Surgical clip placement at the time of surgery may help with volume definition if appropriate.

Figure 7. Postoperative nodal irradiation with tumour bed

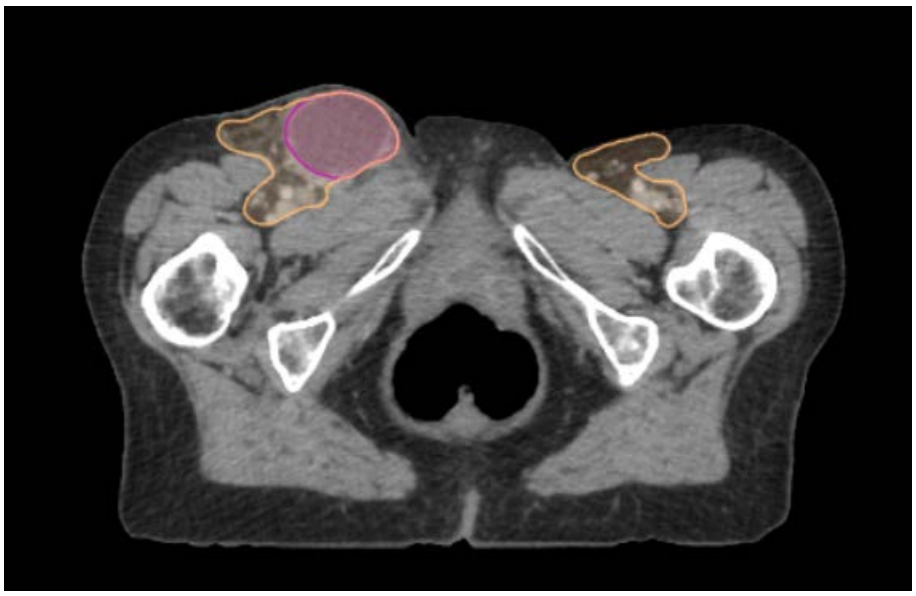


Figure 7. Axial CT image postoperatively, the CTV_EN is contoured (orange line) and will include seromas. The tumour bed is mapped using preoperative imaging, surgical findings and histopathologic results. Placement of surgical clips may help to define this. If the positive LN are in the area where a seroma subsequently forms, it may be appropriate to include the whole seroma as the CTV_Tumour bed boost volume (shown in purple).

Adjuvant nodal irradiation

The GROINSS-V II study indicates that it is acceptable to treat the 'inguinal nodal region' (comprising the inguinal and lower external iliac LN) only when there are micrometastases in the sentinel LN ≤2 mm.[11] There is no consensus on whether the LN only can be treated (and vulva omitted) if there are LN metastases >2 mm or if there is extracapsular extension and if there are clear negative margins on the vulval specimen (generally interpreted as >8 mm). Therefore, it is acceptable to take either approach – including or omitting the vulval volume. It is noted that it may be difficult to match radiotherapy fields in the future if there is recurrence in the vulva or elsewhere in the pelvis when using limited elective nodal treatment fields as an initial approach.

04

Volume definition and critical structures

Contouring the 'groins only' inguinofemoral volume as per GROINSS-V II trial

For contouring the inguinofemoral volume, the inguinofemoral CTV_EN (referred to in the GROINSS-V II trial protocol as 'groins only') is the inguinal nodal region and the lower half of the external iliac LN. See Appendix Table D for anatomic boundaries.

Figure 8. Inguinofemoral elective nodal contouring guidance

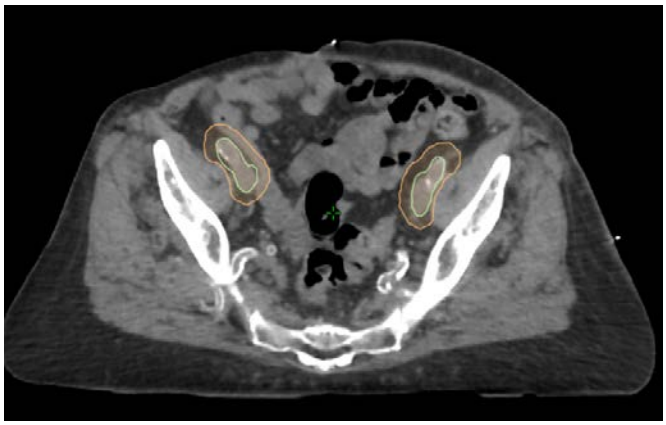


Figure 8A. Axial CT image showing caudal extent contours that start halfway along the external iliac artery (external iliac vessels shown in green), expanding by 7 mm and excluding bone and muscle to form inguinofemoral CTV_Elective (orange line).

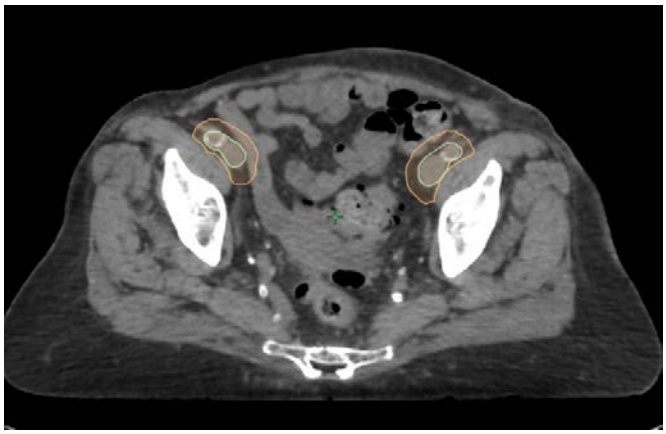
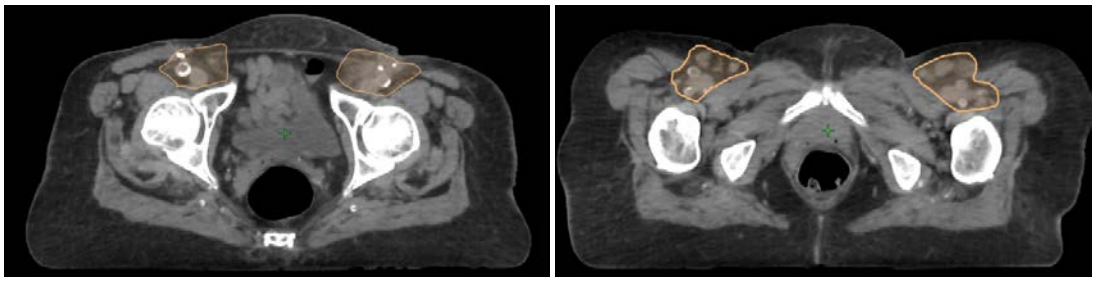


Figure 8B. Axial CT image to demonstrate inguinofemoral CTV_Elective (orange line) at the superior aspect of the acetabulum as the external iliac vessels exit the pelvic brim. External iliac vessels are contoured in green.



Figures 8C and 8D. Axial CT images, at the mid-inguinal level demonstrating bilateral postoperative seromas that should be included in the inguinofemoral CTV_Elective (orange line).

04

Volume definition and critical structures

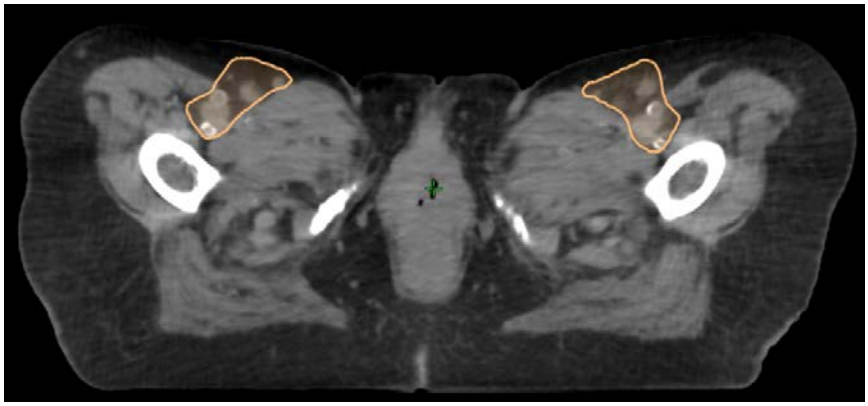


Figure 8E. Axial CT image of caudal extent of inguinofemoral CTV_Elective (orange line). Contours finish at inferior aspect of lesser trochanter of femur; postoperative seromas are included. The green cross shows the position of the introitus.

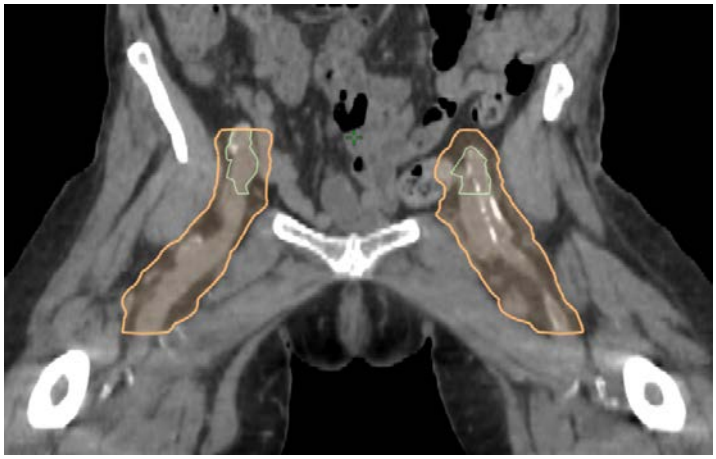


Figure 8F. Coronal CT image demonstrating CTV_Elective for inguinofemoral contouring (orange line). External iliac vessels in green.

Organs at risk

Organs at risk (OAR) include:[16,18]

- Urethra, bladder, anus, rectum, non-rectal bowel, femoral heads, pelvic bones, skin folds and kidneys (for higher fields). See Appendix Tables A and B.

If an organ is involved with tumour, it is no longer defined as OAR and therefore dose constraints do not apply.

4.2. Palliative treatment

- Aim to cover macroscopic disease with at least a 1.5–2 cm margin.[19,20]
- Use of 3D conformal radiotherapy is recommended with IMRT planning if clinically appropriate.
- Brachytherapy alone may be considered to deliver biologically similar doses in a fractionated treatment course.[21]

05 Dose prescription

5.1. Radiotherapy

Table 5. Dose prescription for radical radiotherapy

Indication	Planning technique	Dose and fractionation	
Adjuvant treatment	IMRT	**Resection margin for vulval tumour**	
		≤1 mm	PTV_Vulva boost at least 60 Gy_{10} EQD_2 [22]
		1–3 mm	PTV_Vulva boost of 56 Gy_{10} EQD_2 [22]
		>3 mm	45–50.4 Gy in 25–28 fractions to PTV_Vulva boost [23]
		All	45–50 Gy in 25 fractions to PTV_Elective and PTV_Vulva
		Lymph node involvement	
		Micrometastatic positive sentinel LN ≤2 mm	50 Gy in 25 fractions to PTV_Elective (as per GROINSS_VII) [11]
		Fully resected, no extracapsular spread	Boost to involved nodal bed of at least 56 Gy_{10} EQD_2 [11,22], though 50 Gy_{10} EQD_2 may be sufficient, GROINSS-V III results awaited
		Extracapsular spread	Boost to involved nodal bed of at least 60 Gy_{10} EQD_2 [22]
Radical treatment – inoperable disease	IMRT	PTV_Elective and PTV_Vulva	45–50.4 Gy in 25–28 fractions
		PTV_Vulva boost and PTV_Node boost	60–68 Gy in 30–34 fractions [23]
		Brachytherapy boost	The RCR guidance recommends a minimum of EQD_2 60 Gy_{10} EQD_2 but if disease is more vulvo-vaginal in nature, up to 80 Gy_{10} EQD_2 may be appropriate[24–26]
Palliative treatment	VSIM/3D planning	Dose/fractionation selected according to performance status and co-morbidity. These are suggested dose schemes, but other dose schemes are acceptable: • 8 Gy in 1 fraction • 16 Gy in 2 fractions over 2 weeks (or longer break) • 20 Gy in 5 fractions daily over 1 week • 30 Gy in 10 fractions over 2 weeks • 36–40 Gy in 15 fractions daily over 3 weeks • 24–36 Gy in 4–6 fractions over 4–6 weeks	

05

Dose prescription

Management of boosts

Traditionally treatment has been planned to use a two-phase technique with a sequential boost. Phase one treats a wider field including all elective areas. Phase two then narrows the treatment field to the boost areas. Using this approach, an MRI can be considered during week 4 to define the boost volume, enabling smaller volume fields accounting for tumour shrinkage in response to treatment. In this situation a planning CT scan is usually performed in week 5, allowing a smaller volume for the boost if there has been tumour shrinkage.
For smaller, more superficial tumours, use of electrons may deliver a boost treatment in a conformal manner with less toxicity. For deeper tumours, brachytherapy may deliver a more conformal boost while sparing OAR.

When planning a boost, the use of a simultaneous integrated boost (SIB) can be considered. However, it is important to recognise that the RCR guidance for management of unscheduled gaps does not recommend treating twice daily if the dose is above 2.2 Gy per fraction. It is noted that it is not acceptable to systematically stop treatment early, but it is considered that use of a SIB may preclude finishing a treatment course earlier (for example, in a two-phase technique stopping the radiotherapy after a boost dose of 60 Gy instead of 66 Gy due to severe skin toxicity) because the minimum dose will not have been received by the wider treatment field.

Local planning teams should take into account factors such as imaging technique, immobilisation and hot spots when using calculated conversion doses for SIB.

Table 6. Suggested equivalent doses when using simultaneous integrated boosts

Equivalent doses in Gy to tumour for different fractionations (α/β=10)

Required fractions	Original fractionation				
	45 Gy/25F	50.4 Gy/28F	54 Gy/30F	60 Gy/30F	66 Gy/33F
25	n/a	49.6	52.6	58.4	63.2
28	45.7	n/a	53.5	59.4	64.4
30	46.0	50.9	n/a	n/a	65.1
33	46.5	51.5	54.7	60.8	n/a

α/β=alpha/beta ratio; F=fractions

05
Dose prescription

5.2. Chemotherapy

Concurrent chemotherapy is recommended for all patients who are considered fit for radical treatment. In the postoperative setting when using a dose of 50 Gy in 25–28 fractions it is reasonable to treat with radiotherapy alone. The GROINSS-V II study only used concomitant chemotherapy in 11% of patients in the sentinel lymph node micrometastases ≤2 mm cohort.[11] There is insufficient evidence to state what benefit concomitant chemotherapy may add in other postoperative scenarios and whether the GROINSS-V II data can be extrapolated. There is insufficient evidence regarding the role of neoadjuvant chemotherapy but it is recognised that it may be used occasionally.

Dose:

- Weekly cisplatin 40 mg/m^2 for 4–6 cycles.[5]
- If cisplatin is contraindicated consider:[27]
  - Weekly carboplatin AUC 2 for 4–6 cycles.[28,29]
- If any platinum-containing chemotherapy is contraindicated consider:
  - Mitomycin 10–12 mg/m^2 day 1 with 5-FU 1,000 mg/m^2 over 24 hours continuous infusion for 4 days weeks 1 and 5.[30–32]

Consider dose reduction in the following situations: older than 70 years, deteriorating renal function, grade 3 haematological toxicity.[29]

Contraindications to chemotherapy include frailty and existing immunosuppression.

06 Care on treatment

Radical patients should be treated as Category 1[33] and gaps compensated for. Weekly review by a clinician, specialist nurse or specialist radiographer during the period of radiotherapy treatment should be performed. Full blood counts, renal and liver profile should be checked weekly during treatment for all chemoradiotherapy patients and are also recommended for all radiotherapy alone patients. Following treatment, regular review is recommended until skin reactions have resolved. Skin care should be considered in advance.[34] Analgesia should be optimised during treatment, including use of opiates as required. Patients may require hospital admission for analgesia or skin care if the reaction is marked or if they are unable to adequately provide skin care at home.

07 Recommendations

These guidelines are expert panel recommendations for vulval cancer radiotherapy treatment based on current practice in the UK and published evidence. It is recommended that data are collected prospectively for vulval cancer patients to enable future recommendations to be based on evidence of efficacy and minimising toxicity.

A1 Appendix

A1. Organs at risk and tolerance doses

Table A. Organs at risk

Organ at risk	Anatomic location
Urethra	Bladder base to urethral meatus
Bladder	Outer wall
Anus	Outer wall – 3 cm caudally from anal verge; can use anal marker
Rectum	Outer wall of rectum from rectosigmoid junction to anus
Bowel	All non-rectal bowel loops up to and including at least 1 cm superior to PTV; use of oral contrast allows delineation of small and large bowel separately
Femoral heads	Femoral head and neck to the inferior aspect of lesser trochanter
Pelvic bones	These can be contoured as a surrogate for active bone marrow; all bones contoured from superior border of L4 and finish inferiorly 1 cm below the level of ischial tuberosities
Skin folds	These can be contoured for avoidance of 'hot spots'
Kidneys	May be required if low-lying kidneys and common iliac LN included; contour entire kidney

A1

Appendix

Table B. Suggested organ at risk tolerances to use for radiotherapy planning

Organ at risk	Hard dose constraints*	Soft dose constraints
Bowel	Dmax <105% in regions outside 15 mm from PTV_NB	V40 Gy <250 cc** V30 Gy <500 cc** Bowel space Keep as low as possible. Volume outside PTV receiving >45 Gy should be <195 cm^3 (grade 2 toxicity). **Gr 0** **Gr 1** V45 Gy 78 cc 158 cc V50 Gy 17 cc 110 cc V55 Gy 14 cc 28 cc V60 Gy 0.5 cc 6 cc V65 Gy 0 cc 0 cc
Bladder	Dmax <105% in regions outside 15 mm from PTV_NB	V30 Gy <80%** V40 Gy <60%** V50 Gy ≤50% V60 Gy ≤25% V74 Gy ≤5%
Rectum	Dmax <105% in regions outside 15 mm from PTV_NB	V30 Gy ≤80% V40 Gy ≤75% V50 Gy ≤55% V60 Gy ≤40% V65 Gy ≤30% V70 Gy ≤15% V75 Gy ≤3%
Femoral heads	Dmax <50 Gy	Dmean <40 Gy
Kidney	Dmean <15 Gy	Dmean <10 Gy V12 Gy ≤55% V20 Gy ≤32% V28 Gy ≤20%
Body	Dmax <107% in regions outside 15 mm from PTV_NB	
Anus		No defined constraint D50% <45 Gy may be appropriate
Weight-bearing bone		V50 Gy ≤50%

*The Dmax percentages refer to the main prescription (not boost volumes).

**Soft constraints that can be used in the treatment plan optimisation; these values are based on dose volume histogram (DVH) parameters of EMBRACE II cervix cancer patients entered in the study before June 2017 and from the IMRiS trial, which was used for sarcoma patients with similar dose prescriptions to those used in vulval cancer.[35,36] The constraints are not supposed to be fulfilled in all patients but in ~70–80% of them.

Other normal tissue structures may require delineation, depending on the specific anatomical location. Accepted normal tissue tolerance constraints should be taken into account at all times. Reference can be made to consensus guidelines as outlined by Emami *et al* [37] and the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) documents.[38]

A1

Appendix

A2. Contouring notes for normal female anatomy

Figure A

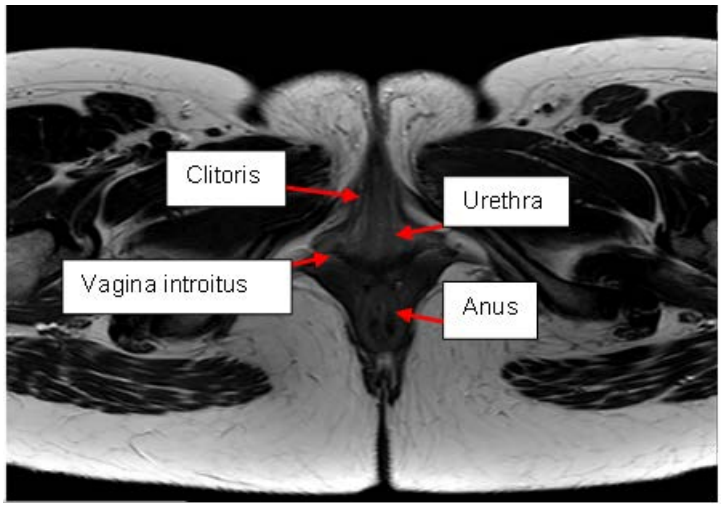
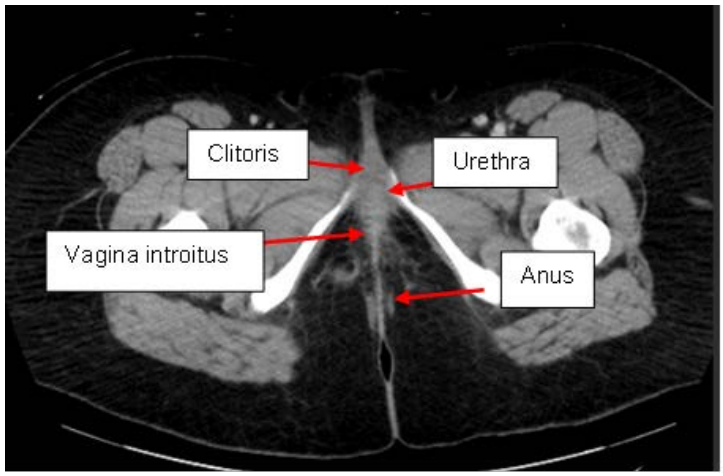


Figure B



Figures A and B. Axial images using MRI T2 weighted (Figure A) and CT (Figure B) to demonstrate the anatomy of the normal female urogenital and anal regions.

Mons pubis

The mons pubis should be included in CTV_Vulva where primary and nodal areas are treated. It is acceptable not to include the mons in CTV_Vulva if there is a small vulval lesion that lies behind the posterior vaginal wall, even if there are positive inguinal LN.

Table C. Anatomic boundaries of normal female genitalia and nearby structures

	Superior	Inferior	Lateral	Medial	Anterior	Posterior	Notes
Clitoris[39]	Labia minora	External urethral meatus and vaginal introitus	Inferior ramus of the ischium and labia minora	*Body:* medial aspect of clitoral body *Clitoral crus:* external urethral meatus and vagina	Anterior border of clitoris	Clitoral neurovascular bundles (ischiopubic ramus to pubic symphysis) and mid part of anterior aspect of pubic symphysis	Two crura alongside the inferior pubic rami unite and form the corpora cavernosa, which converge to form the body.
Urethra[40]	Internal urethral meatus at the bladder neck	External urethral meatus	Clitoral crus and puborectalis muscle		Posterior aspect of pubic symphysis	Anterior aspect of vaginal wall	Approximately 4 cm in length. Difficult to delineate on CT, it has a target-like appearance on T2 weighted MRI imaging.
Vagina[41]	Cervix	Vulva	Levator ani and pelvic fascia		Posterior aspect of urethra and bladder	Denonvilliers fascia of the mesorectum and the pouch of Douglas	Narrow fibro-muscular tube with a length of 6–8 cm.
Mons pubis [42]	Approximately mid-pubic symphysis	Labia majora	Inguinal lymph node area		Skin	Anterior aspect of mid-pubic symphysis	Often better defined clinically, especially in patients with a high BMI.
Labia majora[43]	Mons pubis	Posterior vulval commissure	Skin of upper thigh			Perineal body	In the midline the labia majora meet at the pudendal cleft; can often be seen on CT.
Labia minora[43]	Inferior border of the clitoral hood	Posterior fourchette	Labia majora				
Anal canal[44]	Anorectal junction	Anus	External sphincter		Transverse perineal muscles/ urogenital triangle	Coccyx	This is the most caudal aspect of the gastrointestinal tract, measuring approximately 3–4 cm in length.
Mesorectum [45,46]	Bifurcation of inferior mesenteric artery to sigmoid artery or S2/S3	Levator ani muscle insertion into external sphincter muscles	Sigmoid colon, terminal ileum		Bladder, vagina, rectovaginal septum	Sacrum	We recommend adding 1 cm of the anterior tissue (usually vagina) to allow for organ movement. [(46)]

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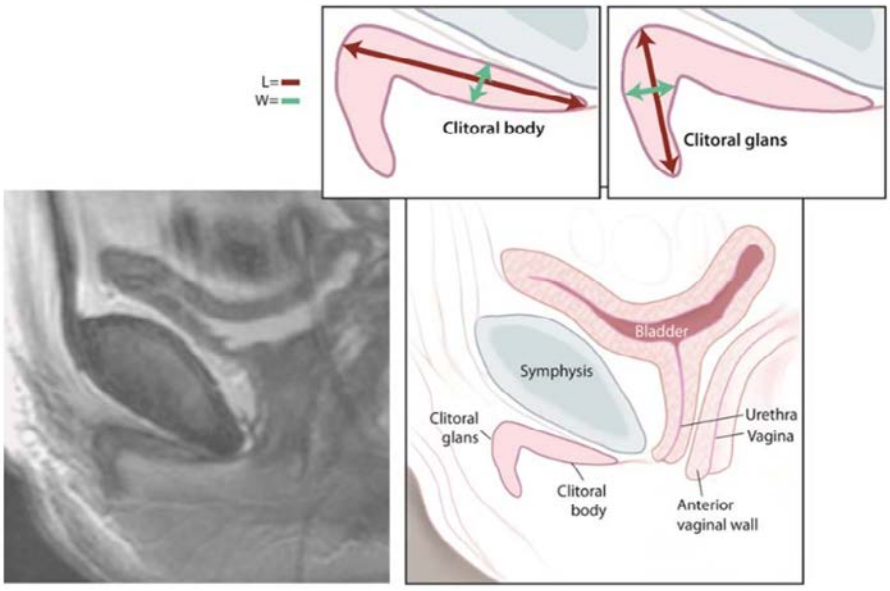
Appendix

Figure C. The anatomy of the clitoris. Images courtesy of Elsevier[39]

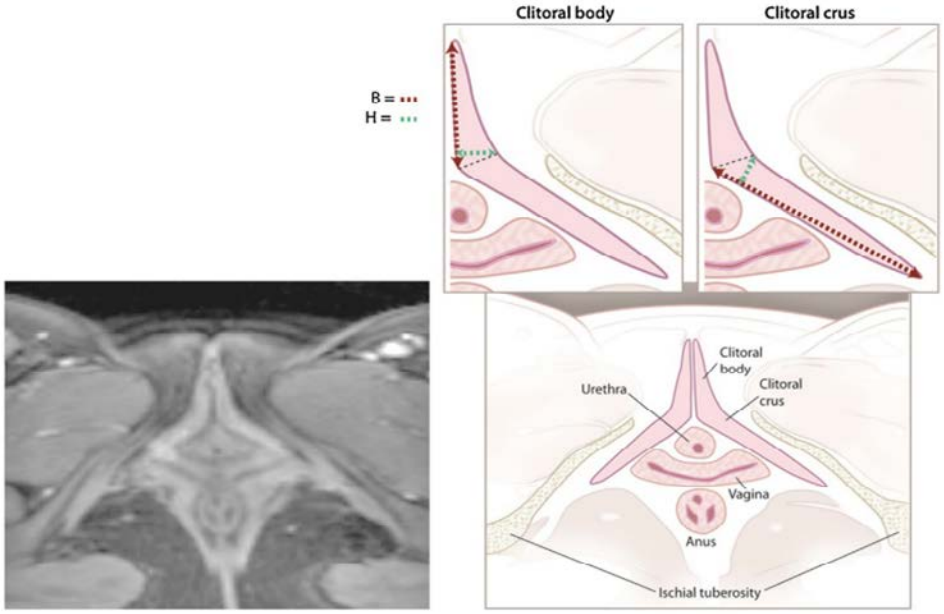
Saggital view



Sagittal pelvic MRI

Clitoral glans and body measurement (LxW)

Axial view



Axial pelvic MRI

Clitoral body and crus measurement (1/2 x B x H)

Table D. Elective lymph node compartment borders

Site	Superior	Inferior	Lateral	Medial	Anterior	Posterior
Common iliac nodes	Bifurcation of the aorta	Bifurcation of the common iliac arteries	Iliopsoas muscle	7 mm uniform expansion around common iliac vessels	7 mm uniform expansion around common iliac vessels	Anterior border of vertebral body
Internal iliac nodes	Bifurcation of common iliac vessels	Insertion of levator ani into obturator fascia and obturator internus	*Upper pelvis:* iliopsoas muscle *Lower pelvis:* obturator internus muscle	*Upper pelvis:* 7 mm medial to internal iliac vessels *Lower pelvis:* mesorectum and presacral space	*Upper pelvis:* 7 mm anterior to internal iliac vessels *Lower pelvis:* obturator internus muscle or bone	Bony pelvis
External iliac nodes	Bifurcation of common iliac vessels	Superior aspect of femoral head	Iliopsoas muscle	7 mm uniform expansion around external iliac vessels	7 mm anterior to external iliac vessels	Internal iliac LN group
Inguinal femoral nodes	Superior aspect of femoral head	Inferior aspect of lesser trochanter	Medial edge of sartorius or iliopsoas	Include all visible LN or lymphoceles Medial third to half of pectineus or adductor longus muscle	5 mm from skin surface	Pectineus, adductor longus and iliopsoas
Mesorectal nodes	Rectosigmoid junction	Anorectal junction, where levator ani muscles fuse with external anal sphincter	*Upper pelvis:* internal iliac LN *Lower pelvis:* levator ani		1 cm within vagina, cervix and uterus to account for organ movement	Presacral space
Presacral nodes	Sacrum level S1	Sacrum level S3	Sacroiliac joints		10–15 mm anterior to anterior sacral border encompassing any LN or presacral vessels	Anterior border of sacrum
Obturator nodes	Where obturator artery branches off internal iliac artery	Obturator canal, where obturator artery leaves pelvis	Obturator internus muscle	10–15 mm from pelvic wall	Most anterior extent of obturator internus	Internal iliac artery

A1
Appendix

A3. Suggested contouring workflow

Table E. Suggested contouring workflow

Step	Description	Volume label
1	Contour primary vulval cancer or postoperative tumour bed	GTV_Vulva CTV_Tumour bed
2	Add margins to GTV_Vulva or CTV_tumour bed	CTV_Vulva boost and PTV_Vulva boost or PTV_Tumour bed
3	Contour involved LN	GTV_Node
4	Add margins to GTV_Node	CTV_Node Boost and PTV_Node Boost
5	Contour vulval CTV according to involved structures	CTV_Vulva
6	Create elective nodal volume using pelvic vessels + 7 mm and inguinal nodal compartments	CTV_Elective
7	Add margins to CTV_Vulva and CTV_Elective	PTV_Vulva PTV_Elective
8	Contour OAR	Bladder, bowel, femoral heads, anus, rectum, bone, kidneys

References

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The Royal College of Radiologists
63 Lincoln's Inn Fields
London, WC2A 3JW, UK

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+44 020 7405 1282
enquiries@rcr.ac.uk
rcr.ac.uk

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