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Klinik für Radio-Onkologie

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SELECTION AND DELINEATION OF TARGET VOLUMES IN DEFINITIVE EBRT OF CERVICAL CANCER

General principles

- Concepts and terms of the ICRU Report 89, EMBRACE 2 study protocol and ESTRO teaching course on gynecological malignancies are respected in this manual.
- Prior to selection and delineation, all simulator imaging modalities should be co-registered based on skeletal anatomy. Registration accuracy should be reviewed, verified & approved.
- Ideally, the OAR should be contoured and reviewed prior to selection and delineation of the TV. After completion of TV contouring, the OAR delineations should be reviewed again for inconsistencies, i.e. unintended overlap with CTV, and edited if necessary.
- While contouring is performed in the axial plane, all imaging planes should be taken into account during the procedure. Digitally reconstructed radiographs may provide useful additional information.
- All clinical, endoscopy, radiological and pathological information should be reviewed and considered during selection and delineation of the target volumes.
- Structure contouring template with predefined structure names and colours should be used.
- Uninvolved rectum, bladder, bowel, bones and muscles should not be included in the TV.

Concepts of selection & delineation

Selection & delineation are different concepts that should be addressed systematically and separately for each TV. This paradigm is reflected in the present manual.

- *Selection* of the TV implies the decision-making process during which the regions to be treated to certain dose levels are selected for contouring. Selection refers to two major tasks:
  - Selection of GTVs: distinguishing between grossly malignant and benign changes (i.e. metastatic vs. non-involved lymph nodes or involved vs. non-

involved parametrium). Selection of GTVs is done directly on the images, based on radiological and clinical findings.
    - Selection of CTVs: Assignment of the level of risk for microscopic involvement within anatomic compartments (i.e. cervix, uterus, vagina, parametria, pelvic nodal stations, paraaortic region…). Selection of CTVs is a cognitive task, based on the clinical and radiological context.
- *Delineation (contouring)* signifies drawing of contours around selected TVs.

Role of simulator imaging modalities in selection and delineation:

- T2w FSE MRI is the primary modality for both selection and delineation of the target volumes.
- 18-FDG PET and functional MRI (i.e. DWI) are used for selection of GTVs - they help distinguish between malignant and benign tissues at the primary tumor site and in lymph nodes. Functional imaging complements contouring, but it is not the main modality for TV delineation.
- CT, due to its poor soft-tissue depiction quality, plays a limited role during TV selection and delineation. It is the principal modality for treatment planning and dose calculation. Therefore, the result of delineation on MRI and functional imaging should be transferred, reviewed and adapted on CT prior to approval of contours and dose planning.

GTV-T init: Initial Gross Tumor Volume of the primary tumor

Label: GTV Primary

IDs / Names:

- GTV T init MRI
- GTV T init CT
- GTV T init PET
- GTV T init DWI (optional)

Type: GTV

Color: red

Selection:

- Primary cervical tumor (inside and outside cervix)
- Imaging modalities for GTV selection:
  - Clinical examination (drawing, description)
  - Tw2 FSE MRI (high-signal-intensity lesion)
  - 18-FDG PET
  - T1w FSE MRI with contrast (enhancing lesion)
  - Functional MRI (i.e. DWI)

Delineation:

- Use T2w FSE MRI as the primary modality (high-signal-intensity lesion) to delineate GTV T init MRI without a margin (Figure 1).
- Use registered PET, DWI MRI and CT as complementary imaging methods for contouring and name the GTV accordingly (see Structure properties).
  - Due to poor soft tissue depiction, these modalities are not useful for detailed delineation. However, in addition to their role in GTV selection they inform about GTV motion, since they represent anatomy snapshots at different times. Estimation of internal motion is needed for generation of ITV from CTV (see ITV section). GTV is the most relevant part of the CTV; therefore, adequate margins for internal motion are especially important around the GTV region of CTV.

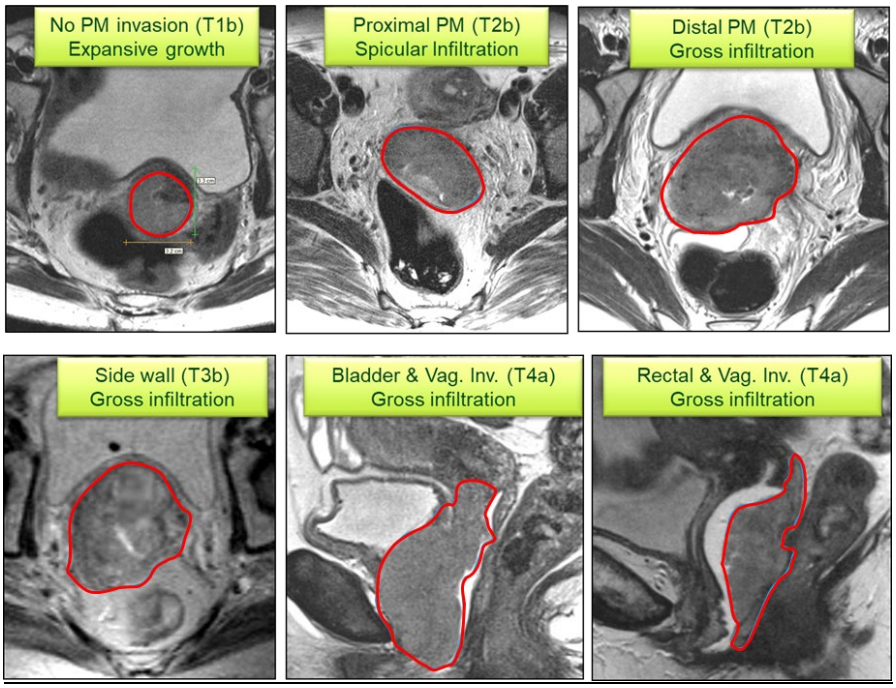

Figure 1: GTV T delineation on pelvic T2w FSE MRI. Representative slices in axial or sagittal plane of six different cases are shown. The cases are selected to demonstrate various patterns and extents of GTV infiltration into surrounding tissues. GTV contour encompasses the high-signal intensity lesion inside and outside the cervix, without a margin.

Formatiert: Englisch (Vereinigte Staaten)

CTV-T HR init: Initial High-Risk Clinical Target Volume of the primary tumor

Label: CTV High Risk

ID / Name:

- CTV T HR MRI init

Type: CTV

Color: magenta

Selection:

- CTV-T HR MRI init contour should always encompass:
  - GTV T
  - Any remaining normal-appearing cervix not infiltrated by the tumor. Knowledge of normal anatomy of the cervix is required (Figures 2 and 3).

Delineation:

- Use T2w FSE MRI as the primary modality for delineation.
- Delineate CTV T HR MRI as the union of GTV T and normal-appearing cervix without additional margin as presented in examples in Figures 4 and 5.

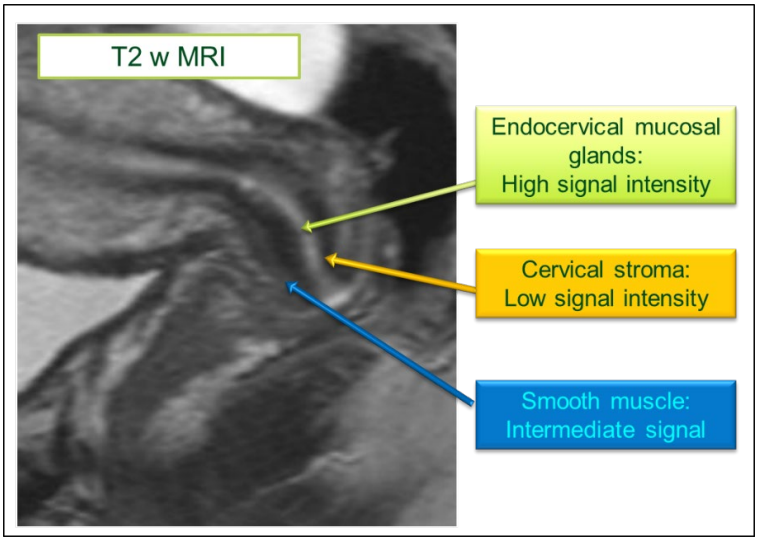

Figure 2. Normal cervical anatomy with three layers on T2w FSE MRI.

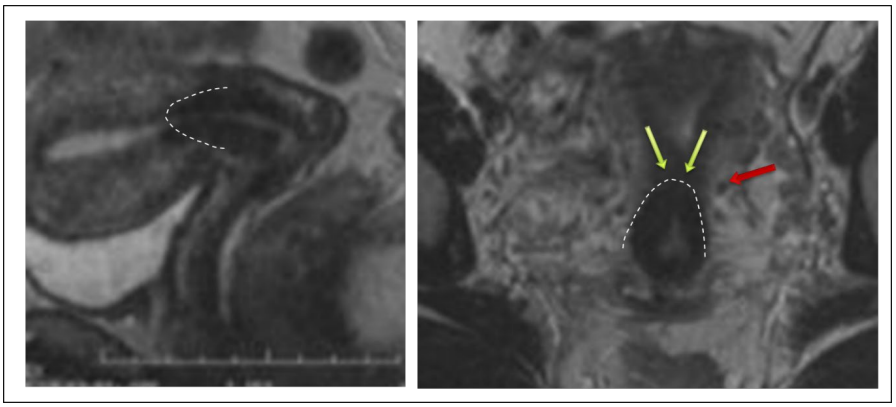

Figure 3. Normal cervical anatomy on T2w FSE MRI. Cranial border towards the uterine body is conical in shape (white dotted line and green arrows) and located around the level of the entry of uterine arteries (red arrow). Laterally, the cervix borders to parametria and caudally to vagina.

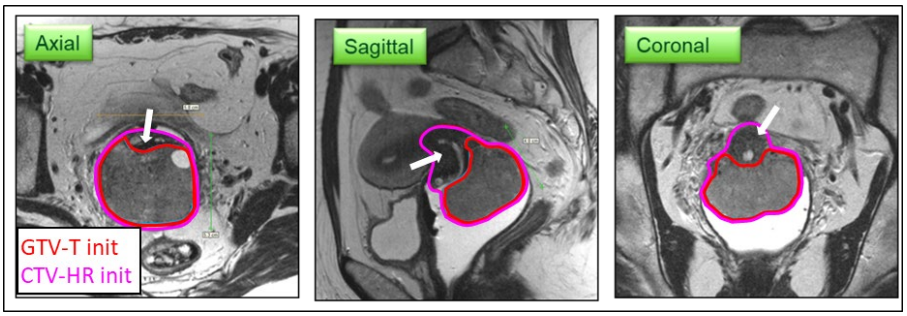

Figure 4. Delineation of CTV T HR init. Pelvic T2w FSE MRI in a patient with an exophytic cervical cancer, FIGO stage IB3. Representative slices in 3 main orientations are shown. Gel was injected into the vagina to improve depiction of the regions of interest. The tumor is in the caudal aspect of posterior lip of the portio. Delineation of CTV T HR init encompasses the GTV T init (high-signal intensity lesion) and the remaining normal appearing cervix (white arrows), without additional margins. Note the conical shape of the cranial cervical border – compare with Figure 3 and 4.

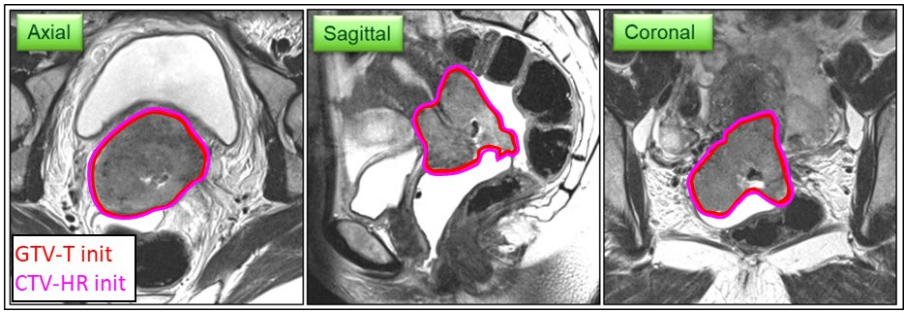

Figure 5. Delineation of CTV T HR init. Pelvic T2w FSE MRI in a patient with an infiltrative cervical cancer, bilateral parametrial spread, invasion of lower uterine segment and posterior vaginal fornix. Stage T2bN0 M0 (FIGO IIB). Representative slices in three main image orientations are shown. Gel (bright signal) was injected into the vagina to improve depiction of the regions of interest. In this case, delineation of CTV T HR init encompasses GTV T init (high-signal intensity lesion) without additional margins. There is no remaining normal appearing cervical tissue present. Therefore, CTV HR init is identical to GTV T init.

CTV T match: Initial High-Risk Clinical Target Volume of the primary tumor, transferred to the CT images and matched to the CT anatomy.

Label: CTV High Risk

ID / Name:

- CTV T match

Type: CTV

Color: dark magenta

Selection:

- GTV T
- Any remaining normal-appearing cervix not infiltrated by the tumor.

Delineation:

- Start by creating CTV T match by applying a 0 mm margin to CTV T HR init.
- Adapt the delineation to correspond to the outer contour of the cervix and GTV as much as they can be estimated on CT.

V homogen: Initial High-Risk Clinical Target Volume of the primary tumor, transferred to the CT images and matched to the CT anatomy.

Label: CTV High Risk

ID / Name:

- V homogen

Type: CTV

Color: white

Selection:

- V homogen = CTV T match with a margin

Delineation:

- V homogen = CTV T + 1 cm

CTV-T LR init: Initial Low-Risk Clinical Target Volume of the primary tumor

Label: CTV Low Risk

IDs / Names:

- CTV T LR MRI
- CTV T LR CTfb (full bladder)
- CTV T LR CTeb (empty bladder)

Type: CTV

Color: green

Selection:

- CTV-T LR always includes the following components:
  - CTV T HR init
  - Complete parametria bilaterally
  - Entire uterus
  - Uninvolved vagina & paracolpia with a 20 mm caudal margin measured from the most inferior position of the CTV T HR init along the vaginal axis.
  - When present, the tissue anteriorly and posteriorly of CTV T HR towards bladder and rectum/mesorectal fascia should be included. Organ walls should be excluded, unless they are infiltrated by tumor.

Delineation:

- Use T2w FSE MRI as primary contouring modality.
  - There is no need to delineate each component individually – the CTV T LR MRImay be contoured as one contiguous volume.
  - To delineate CTV T LR MRI, it is important to have knowledge of the MRI appearance and anatomical borders of its components (Figures 6-9).
  - When there is space between CTV T HR MRI init and bladder and rectum/mesorectum, up to 5 mm margin should be added anteriorly and posteriorly to the CTV T HR MRI init when delineating CTV T LR MRI.
  - If organ wall is infiltrated, a 20 mm margin from CTV T HR MRI init should be added along that wall (Figure 10).
  - If sacro-uterine ligaments, meso-rectum, pelvic wall or other structures are involved, a 20 mm margin from initial CTV T HR MRI init should be added in direction of spread similar as described for the organ wall above.
- Use full- and empty-bladder CT as secondary contouring modality.
  - Delineate CTV T LR CTfb and CTV T LR CTeb on registered full and empty bladder CT scans. Due to poor soft tissue depiction, CT is not optimal for detailed delineation. However, CT-based delineation is important for understanding of CTV location under different anatomical conditions and is needed for the generation of ITV from CTV (see ITV section).

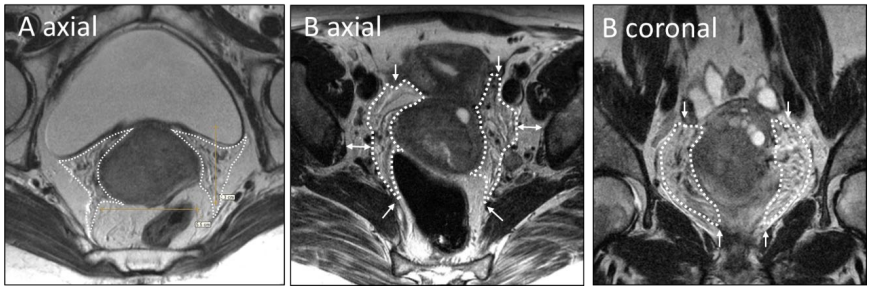

Figure 6. Parametrial borders on T2w FSE MRI in two patients (A and B). Parametria are depicted with white dotted line. (*A axial):* Case with full bladder, slice level at pubic symphysis. Ventral border = bladder; dorsal = mesorectal fascia; medial = cervix/tumor; lateral = vascular compartment at the pelvic wall. (*B axial):* Case with empty bladder; slice level above femoral heads. The ventral border is the peritoneal space, other borders are as in A. (*B coronal):* cranial (upper limit of broad ligament) and caudal border (pelvic floor) are depicted by white arrows.

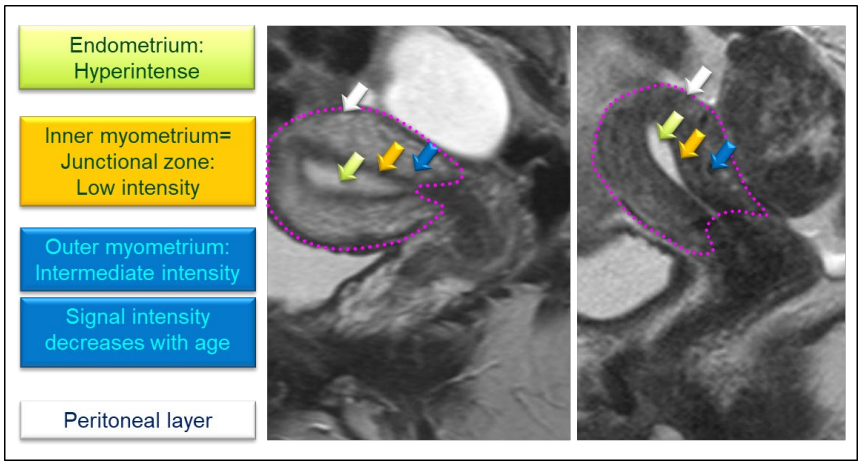

Figure 7. Uterine anatomy on pelvic T2w FSE MRI of two patients. Borders of normal uterus are depicted with magenta dotted line and zonal anatomy with arrows (color legend on the left). Note the conical shape of cervico-uterine border.

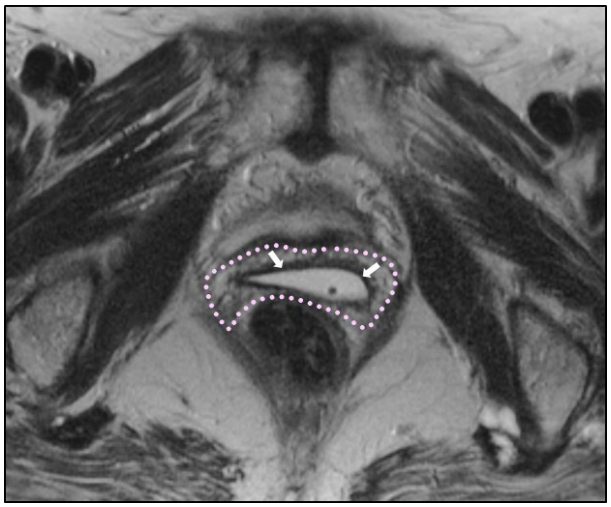

Figure 8. Vaginal anatomy on axial T2 FSE MRI. Gel (bright signal) was injected into the vagina to improve depiction of low-signal intensity vaginal wall (white arrows). Vagina and paravaginal tissue is contoured with dotted pink contour. Anteriorly, this region borders to bladder/urethra, posteriorly to mesorectal fascia and lateraly to the pelvic floor muscles/ischiorectal fossa.

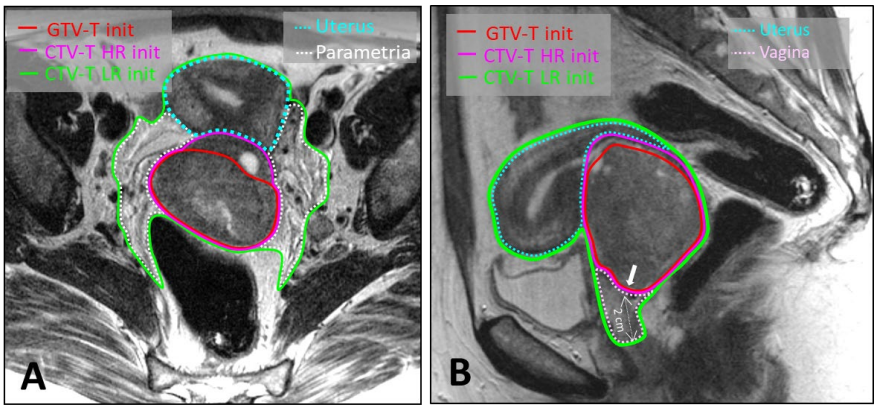

Figure 9. (A) Delineation of CTV T LR MRI on axial slice of pelvic T2w FSE MRI in a cervix cancer patient with a large T2B primary tumor. Components of CTV T LR MRI are depicted (GTV T init, CTV T HR init, uterus and parametria). (B) The principle of inclusion of uninvolved vagina into CTV T LR MRI is demonstrated: lowermost border of the CTV T HR init is identified (solid arrow). From this point, CTV T LR contour is extended for 2 cm along the vaginal axis. In practice, there is no need to delineate the parametria, uterus and vagina as individual sructures; CTV LR init contour should encompass all these regions (green contour).

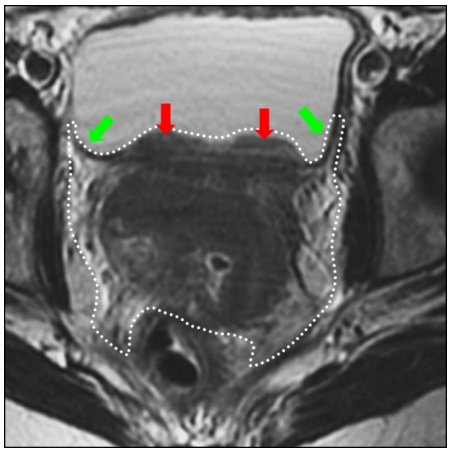

Figure 10. Adding a safety margin along tumour-invaded organ wall during CTV T LR MRI contouring. Axial T2W FSE MRI of a cervix cancer patient with bladder wall infiltration (stage T4a) is shown. CTV T LR MRI is delineated by dotted white contour. Note that the CTV T LR MRI contour extends from the area of gross bladder invasion (red arrows) to include a safety margin of 20 mm of normal-appearing bladder wall (green arrows). Note that urine is excluded from this safety margin.

GTV-N: Initial Gross Tumor Volume of the pathologically involved lymph node(s)

Label: GTV Nodal

IDs / Names:

- GTV N MRI 1, 2, 3, …etc. (separate GTV for each involved lymph node)
- GTV N CT 1, 2, 3, …
- GTV N PET CT 1, 2, 3, …
- GTV N DWI 1, 2, 3, …

Type: GTV

Color: red

Selection:

- Imaging modalities for GTV N selection (Figure 11):
  - Tw2 FSE MRI (high-signal-intensity lesion)
  - 18-FDG PET
  - Functional MRI (i.e. DWI)
- Lymph node(s) are considered positive when they have the following characteristics (Figure 12):
  - 18-FDG PET positive
  - Short axis diameter ≥10 mm on CT or MRI
  - Diameter of 5-10 mm with pathological morphology on MRI: irregular border, high signal intensity and/or round shape and/or restricted diffusion.
  - Clinical and radiological context needs to be considered when selecting suspicious nodes for GTV N (number, size and vicinity of evidently positive lymph nodes, local extent and pattern of growth of the primary tumor…).

Delineation:

- Use T2w FSE MRI as the primary modality to delineate GTV N. Name them GTV N MRI 1, 2, 3, …etc. (each involved node should be a separate structure).
- Include any visible extracapsular extension.
- Use CT to contour GTV N CT 1, 2, 3,... by transferring information from co-registered MRI.
- Use registered PET and DWI MRI as complementary imaging methods (Figure).
  - Due to poor soft tissue depiction, these modalities are not useful for detailed delineation but are needed for selection of involved nodes and for assessment of their movement. Actual contouring of GTV N on complementary modalities is not mandatory but it is helpful for delineation on primary modality (MRI). When performed, the structures should be named accordingly (i.e. GTV N PET 1).

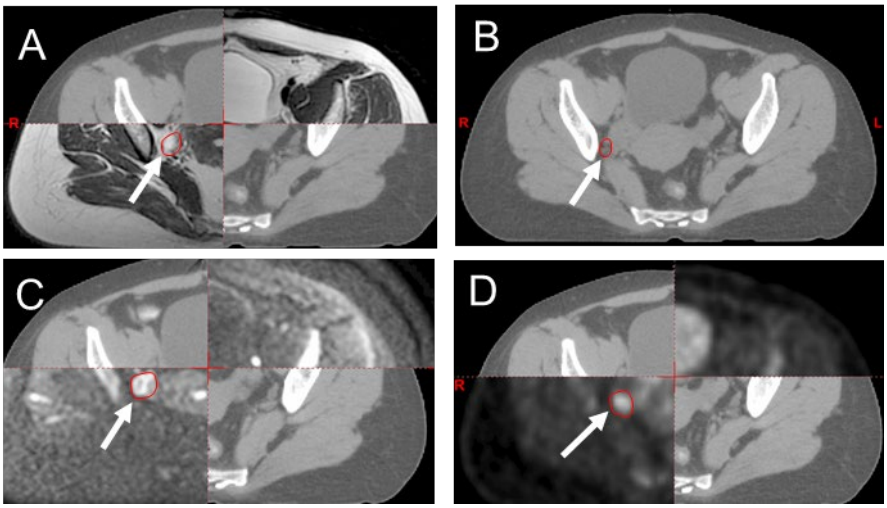

Figure 11. Role of co-registered modalities in selection and delineation of GTV N. (A) T2W FSE MRI is the primary modality for selection and delineation: a pathological lymph node (<10 mm but with pathological morphology) is contoured. (B) CT has limited role in selection and delineation of GTV N. (C) DWI confirms the selection of the lymph node which shows restricted diffusion, but it doesn't show soft tissue details and is therefore of limited value for delineation. (D) 18-FDG PET additionally confirms the selection of the lymph node, but it is also of limited value for detailed delineation due to limited soft-tissue depiction. (A-D) Information from all modalities is considered when contouring on primary modality (MRI).

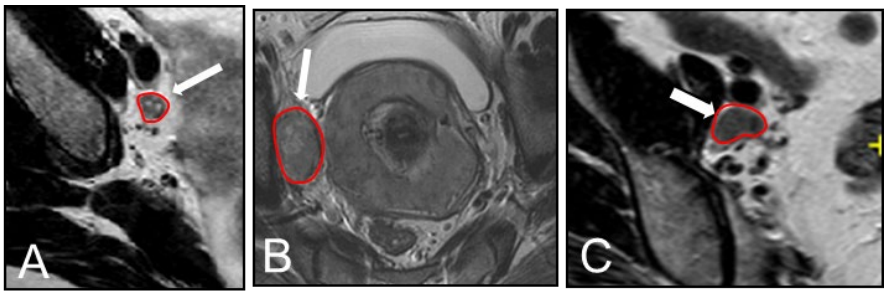

Figure 12. Three examples of GTV-N selection and delineation on T2W FSE MRI. (A) Small lymph node which is not suspicious based on dimension (<1 cm short axis); however, it has irregular border and high, inhomogeneous signal. It was also PET positive. (B) Large hyperintense inhomogeneous and irregular metastatic lymph node. (C) Medium sized (>1 cm) metastatic lymph node with irregular border and intermediate signal intensity.

CTV-N: Clinical Target Volume of the pathologically involved lymph node(s)

Structure properties:

Label: CTV Nodal

IDs / Names:

- CTV N 1, 2, 3, …etc. (separate CTV for each involved lymph node)

Type: CTV

Color: cyan

Selection:

- CTV N 1, 2, 3, …etc. correspond to GTV N 1, 2, 3, …etc. plus margin.

Delineation:

- Numbering of CTV N should be consistent with numbering of GTV N (CTV N 1,2,3…etc.)
- The CTV N should encompass the maximum extension of GTV N as visible on co-registered CT and MRI and complementary imaging modalities (PET CT, DWI). In principle, CTV N 1, 2, 3…, etc. is the GTV N 1, 2, 3…, etc. plus a margin of approximately 0-3 mm.
- Consider the partial volume effects of the upper and lower boundary of GTV N on CT and MRI when adding cranial and caudal margins.
- Take possible progression of GTV N during treatment planning interval into account.
- Uninvolved bowel, muscles, bones, bladder… should be excluded from the CTV N contours.

CTV-E: Elective Clinical Target Volume for nodal regions

Label: CTV Low Risk

IDs / Names:

- CTV E

Type: CTV

Color: blue

Selection:

CTV E should include the nodal regions with assumed microscopic disease. The regions to be included depend on the probability of spread and are selected according to the risk-group allocation (Table 1 and Figure 13).

Risk Group	Definition	Lymph node regions to be included in CTV-E
Low risk (LR LN)	*All conditions satisfied:* • Tumor size ≤ 4 cm • Stage IA/IB1/IIA1 • N0 • Squamous cell carcinoma • No uterine invasion	**Small pelvis:** • Internal iliac • External iliac • Obturator • Presacral
Intermediate risk (IR LN)	Not low risk Not high risk	**Large pelvis:** • Small pelvis • Common iliac (incl. aortic bifurcation) • Inguinal (if distal vagina involved) • Mesorectal (if m. nodes involved or local invasion to m. space)
High Risk (HR LN)	• ≥ 1 involved node at common iliac or above • OR ≥ 3 involved nodes	**Large pelvis + Para-aortic** • Large pelvis • Paraaortic region
In cases that qualify for IR group according to the general definition above but demonstrate some outstanding clinical features (i.e. large lymph node size), allocation to HR group should be considered. Inguinal nodal region (deep and superficial group) should be selected for delineation in cases with invasion of the lower third of vagina with the primary tumor and/or positive inguinal lymph node(s).		

Table 1. Allocation of nodal region risk group based on disease characteristics.

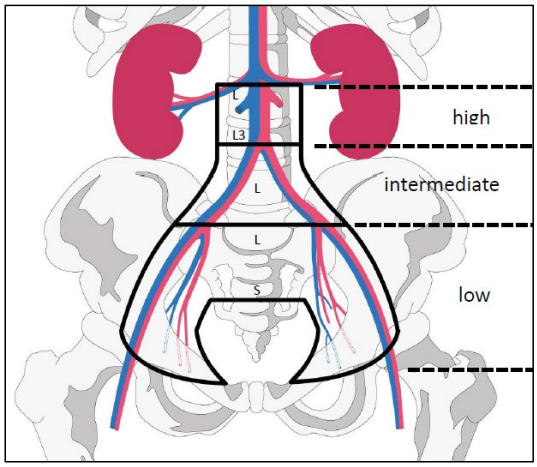

Figure 13. Schematic diagram of nodal regions to be included in the CTV E according to allocation of risk for microscopic nodal spread (see Table 1 for definitions).

Delineation:

- General principles
  - Perivascular compartments containing the lymph nodes can be identified on high-quality MRI.
  - In the pelvis, use T2w FSE MRI as primary contouring modality and combine it with CT: visualize the MRI-based delineations on CT and adapt the contours if needed (exclusion of organs, inclusion of clips and cysts, etc.).
  - Above the pelvis, MRI is usually not available, and CT alone is used for delineation.
  - Delineate the selected nodal regions according to risk allocation (see selection).
  - In case of CT-only delineation, the nodal perivascular region is not visible. In that case, follow the Taylor (3) recommendations: In principle, a 7 mm margin around the vessels is required to delineate the nodal regions. Larger margin is needed in certain regions (see region-specific instructions)
  - Include any visible normal lymph nodes within the regions.
  - Include any pathological lymph nodes. CTV N 1, 2, 3, …etc. should be encompassed by the CTV E contour.
  - Exclude uninvolved bowel loops, bladder, muscle and bone from the CTV E.
  - Include pertinent clips and/or lymphocysts (in case of prior lymphadenectomy). If lymphocists shrink during EBRT, re-contouring and re-planning should be considered. Situations with excessively large lymphocists can be challenging and should be addressed individually.

- Region - specific instructions
  - *Obturator region (Figure 14):*
    - Inferior border of delineation is the caudal limit of the obturator region, which corresponds to the upper edge of the obturator foramen where

branches of iliac vessels leave or enter true pelvis. This is usually around the level above pubic symphysis.

- Superior border: the obturator region is continuous with the inter-iliac region cranially.
- Medial border: parametrium
- Lateral border: obturator muscle
- Anterior and posterior borders vary with the level.
    - Caudally, the region approximately from anterior to posterior edge of obturator muscle is delineated.
    - Cranially, the region borders to internal (posteriorly) and external (anteriorly) iliac groups.

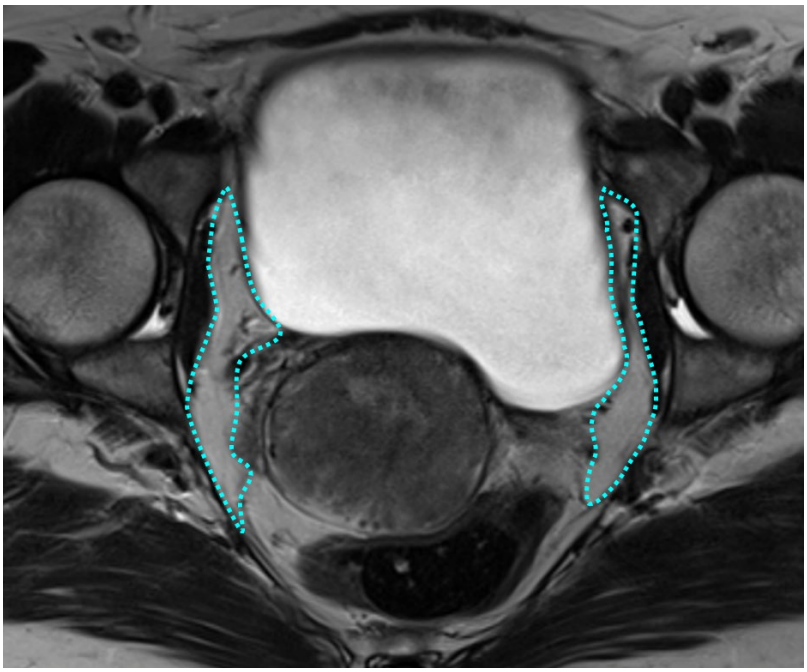

Figure 14. Delineation of obturator regions as part of the CTV-E on axial T2w FSE MRI.

- *External iliac region (Figure 15):*
    - Inferior border: start including the lateral group of external iliac lymph nodes above the inguinal ligament (usually corresponds to the level above the femoral heads).
    - Superiorly, the external iliac region merges with internal iliac group (inter-iliac region) and become continuous with common iliac group.
    - Lateral border: iliopsoas muscle, anterior aspect of obturator muscle and iliac bone.
    - Medial border: parametrium and peritoneal cavity.

- Anterolaterally, the margin from external iliac vessels should be up to 10 mm.
- Posteriorly, the external iliac group is continuous with obturator region (inferior part) and internal iliac group (superior part).
- Internal and external iliac regions should be joined together medially to the pelvic sidewall to ensure inclusion of obturator and inter-iliac nodes. Here, the distance from medial contour to the muscle/bone can be up to 18 mm.

- *Internal iliac region (Figure 15):*
  - Inferior border: at the level of the ischial spine where internal iliac vessels leave and enter the true pelvis.
  - Superiorly, the internal iliac region merges with external iliac group (inter-iliac region) and become continuous with common iliac group.
  - Lateral border: posterior border of obturator muscle, endopelvic fascia, piriform muscle, iliac bone, sacroiliac joint, sacral bone.
  - Medial border: parametrium, mesorectum, peritoneal cavity
  - Anteriorly, the internal iliac group is continuous with obturator region (inferior part) and external iliac group (superior part).
  - Posterior border: posterior limit of vascular compartment seen on the MRI; in principle, 7 mm from the posterior branches of internal iliac vessels.
  - Internal and external iliac regions should be joined together medially to the pelvic sidewall to ensure inclusion of obturator and inter-iliac nodes. Here, the distance from medial contour to the muscle/bone can be up to 18 mm.

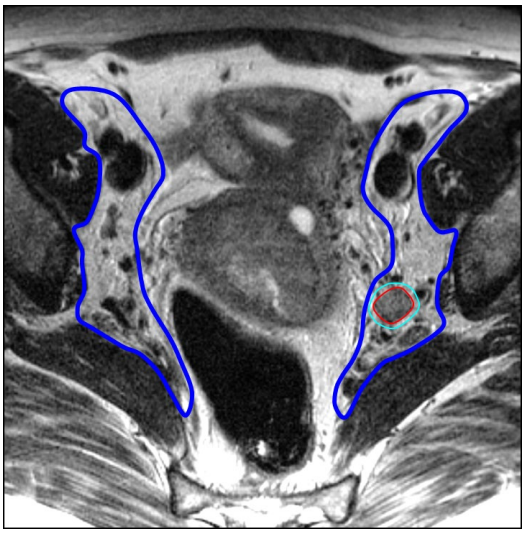

Figure 15. Delineation of external and internal iliac regions as part of the CTV-E on axial T2w FSE MRI. Combined delineation of both regions (blue) is created by joining the external and internal iliac regions. There was a nodal metastasis present in this patient. GTV-N is delineated in red and CTV-N in cyan. Note that CTV-N is entirely encompassed in CTV-E.

- *Common iliac region* (Figure 16):
  - Inferior border: bifurcation of the common iliac vessels.
  - Superior border: aortic bifurcation.
  - Lateral border: psoas muscle or bone.
  - Medial border: not applicable. Join the left and right common iliac regions medially in front of lumbar vertebrae (typically L4-5).
  - Anterior border: peritoneal space. In general, delineate a belt of tissue in front of the lumbar vertebrae, so that the left and right common iliac regions are connected and continuous with the presacral region inferiorly and paraaortic region superiorly.
  - Posterior border: lumbar vertebrae. Include the tissue in posterolateral triangle between the psoas muscle and the lumbar vertebra.

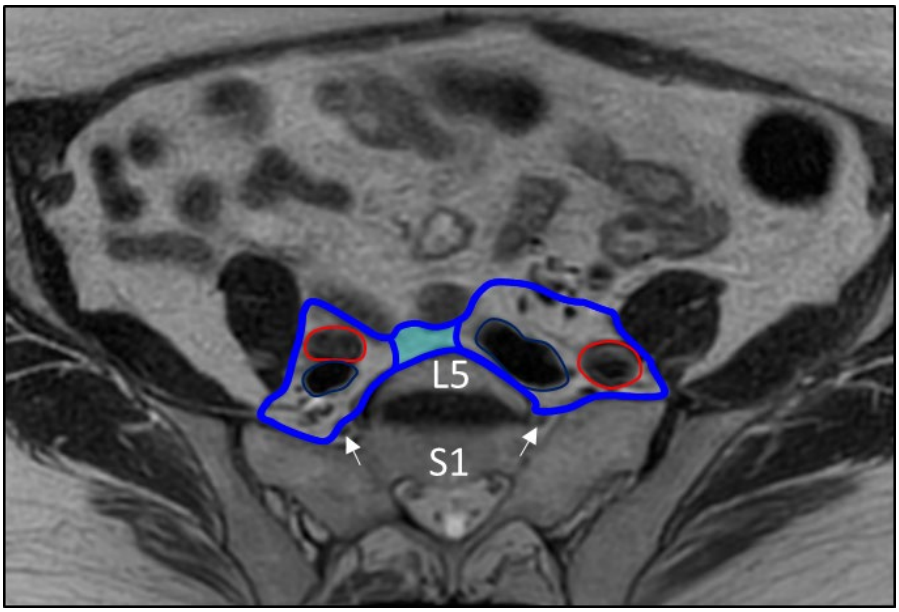

Figure 16. Delineation of common iliac regions as part of the CTV-E on axial T2w FSE MRI. Common iliac artery (red) and vein (dark blue) are indicated. Combined contour (blue) is created by joining the common iliac regions of both sides in front of the lumbar vertebra (marked with transparent cyan - subaortic inter-iliac region). Bowel loops and sacral nerve roots (arrows) are excluded from the contour. The area behind the vessels between the vertebra and the psoas muscle is included.

- *Presacral region* (Figure 17):
  - Inferior border: around S2/S3 junction.
  - Superior border: promontorium. Above promontorium, the presacral region is continuous with the region between the common iliac groups.

- Lateral border: presacral region should be delineated so that it is continuous with internal iliac regions of both sides.
- Medial border: not applicable.
- Anterior border: peritoneal space. In general, aim to delineate a belt of presacral tissue so that anterior contour is 10 mm in front of the sacrum. It is useful to check the continuity of the presacral 10 mm belt on sagittal view. If it is not continuous, consider adapting the contours in axial plane accordingly.
- Posterior border: anterior plates of S1-S2.

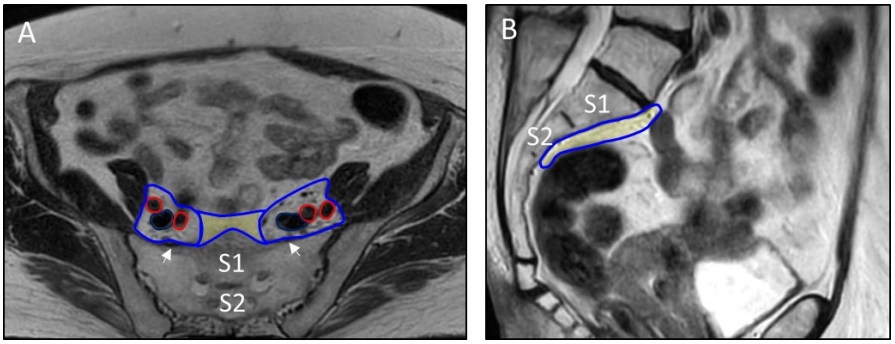

Figure 17. Delineation of presacral region as part of the CTV-E on axial (A) and sagittal (B) T2w FSE MRI. External and internal iliac arteries (red) and common iliac veins (dark blue) are indicated on both sides. Combined delineation of presacral and iliac regions (blue) is created by joining the iliac regions of both sides in front of the second and third sacral vertebra. Presacral region (transparent yellow) is located between the iliac regions and in front of S2 and S3 vertebrae. Bowel loops and sacral nerve roots (arrows) are excluded from the contour.

- *Paraaortic region* (Figure 18):
  - Inferior border: aortic bifurcation. Here, PAN region is continuous with the common iliac group.
  - Superior border: as a minimum at the level of renal veins (usually incl. L2) and at least 3 cm cranial of the highest pathological node.
  - Lateral border: extend the contour postero-laterally along the vertebral body to anterior border of the psoas muscle.
  - Medial border: not applicable.
  - Posterior border: anterior border of vertebral bodies and anterior border of psoas muscle.
  - Anterior border: peritoneal space. In general, 7 mm in front of the vessels.

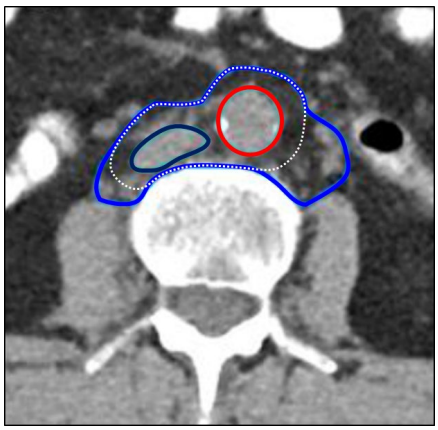

Figure 18. Delineation of paraaortic region as part of the CTV-E on axial T2w FSE MRI; figure modified from EMBRACE 2 protocol. Aorta (red) and vena cava (dark blue) are shown. White dotted line marks the 7-mm extension from the large vessels. Blue line is the final CTV-E delineation, obtained by extending the white dotted line postero-laterally along the vertebral body to the psoas muscles.

- *Inguinal region* (Figure 19):
  - Inguinal nodal region is divided into superficial and deep group, divided by the cribriform fascia.
  - Inferior border: 2 cm caudal to saphenous/femoral junction.
  - Superior border: superiorly, the region is continuous with the lateral group of external iliac region.
  - Lateral border: sartorius, rectus femoris and iliopsoas muscles. In the inferior-most part of the inguinal region, vastus medialis muscle contributes to lateral border of the region.
  - Medial border: adductor longus and pectineus muscles.
  - Posterior border: pectineus and iliopsoas muscles.
  - Anterior border of the superficial inguinal group is superficial fascia. Anterior border of the deep inguinal group is cribriform fascia.

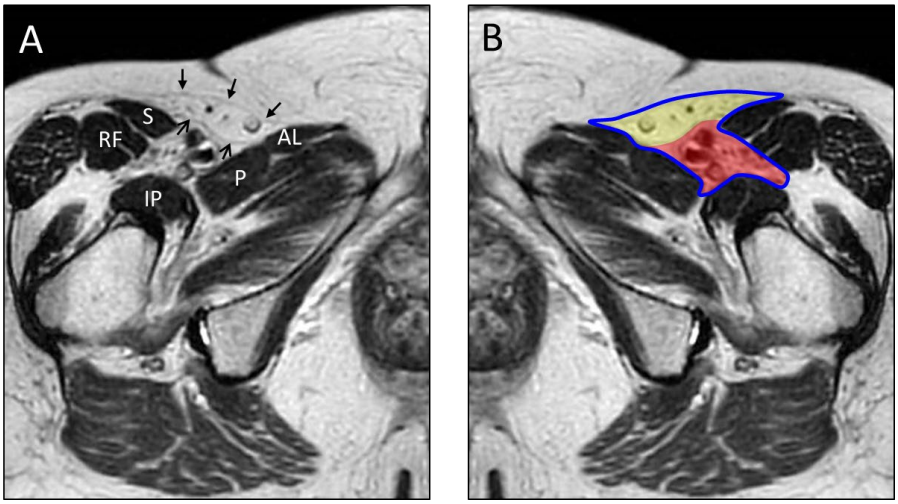

Figure 19. Delineation of Inguinal region as part of the CTV-E on axial T2w FSE MRI. (A) Selected anatomical landmarks relevant for delineation of inguinal region are marked. S – sartorius muscle; RF -rectus femoris muscle; IP – iliopsoas muscle; P – pectineus muscle; AL- adductor longus muscle; closed arrows – superficial fascia; open arrows – cribriform fascia. (B) Inguinal region is delineated with blue line. Superficial (yellow transparent) and deep (red transparent) inguinal groups of the inguinal region are indicated.

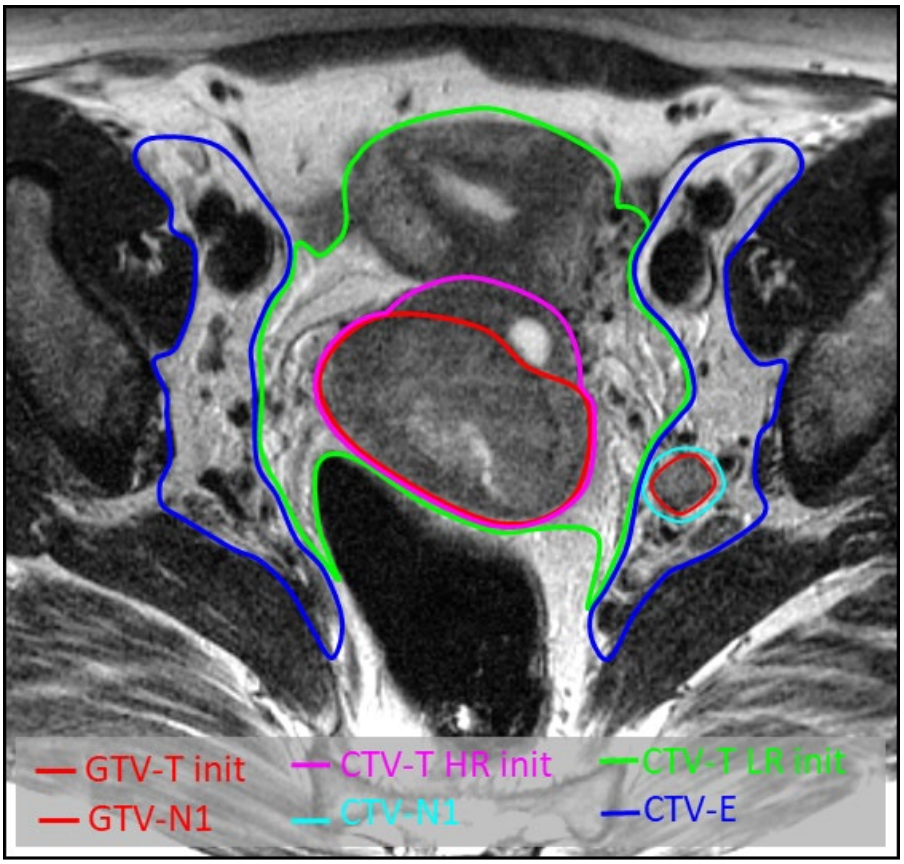

Figure 20. Summary of the delineation of GTVs and CTVs on a representative axial MRI slice.

ITV 45/25: Internal target volume to be treated to 45 Gy in 25 fractions

Structure properties:

Label: ITV

IDs / Names:

- ITV 45/25

Type: ITV

Color: pink

Selection:

ITV should be individualized based on multiple pre-treatment imaging series that allow the assessment of internal target motion range.

- ITV 45/25 includes:
  - ITV T LR, which consists of:
    - CTV T LR MRI
    - CTV T LR CTfb (full bladder)
    - CTV T LR CTeb (empty bladder)
    - CTV T LR on other modalities, when available
  - CTV E

Delineation (Figure 21):

- First, create ITV T LR with Boolean operators from the CTVs listed in the selection.
- Use Boolean operators to create the ITV 45/25 as the union of ITV T LR listed and CTV E.
- After automatic ITV delineation, consider additional careful manual adaptations of obtained contours. Clinical judgement and input from all available imaging series play an important role in this process:
- In cases with full rectum on pre-treatment imaging, extension of the ITV posteriorly may be needed to consider the potential target motion due to variation of rectal filling.
- GTV is the most relevant part of the CTV T LR; therefore, it is prudent to assess the ITV margin around the GTV region, especially in the anterior and posterior directions. This is best visualized in sagittal and axial views. If tight margins around the GTV were obtained with automatic ITV generation, manual expansion of ITV in this region may be considered. During this process, the standard motion ranges should be kept in mind (5-10 mm anterior-posterior).
- In addition to simulator images, the patients will typically have other pre-treatment imaging series available (i.e. diagnostic PET CT and MRI) that may not be registered with the simulator images. It is useful to study those series to obtain additional information about the target motion and potentially adapt the ITV delineations based on the findings.
- In cases with pronounced anterior position of the uterus on image series with empty bladder, inclusion of the entire uterus in the ITV may be unnecessary, because such anatomical situation is unlikely to occur during treatment with a drinking protocol. However, caution is

needed in cases with extensive tumors, especially with uterine invasion. In addition, studies indicate that the average bladder volume decreases during EBRT.

- Do not include uninvolved muscle and bone in ITV delineations.
- Do not add caudal margin below the vaginal portion of the CTV T LR.
- ITV delineations may need to be modified (expanded, shrunk or differentially adapted) during treatment if daily CBCT reveals different target motion than that assumed from pre-treatment imaging (intermediate level of IGRT).

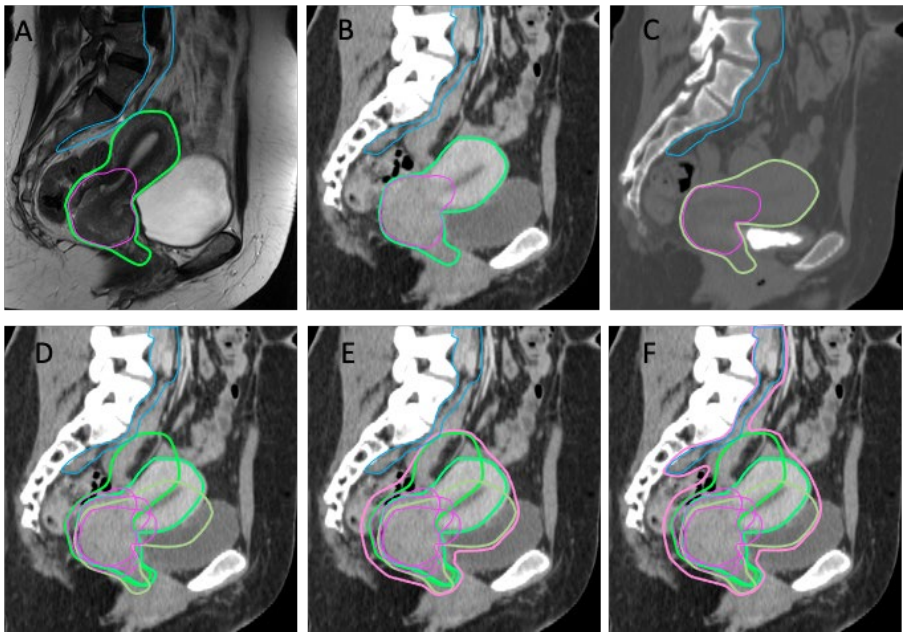

Figure 21. Delineation of ITV 45/25. Contrast enhanced CT with full bladder with all three CTV T LRs transferred on the image. (A-D) Green: CTV T LR, magenta; CTV T HR init, blue: CTV-E. (A) T2w FSE MRI simulator image with full bladder. CTV T LR MRI is contoured in green. Note the extended position of the uterus due to full bladder. (B) Contrast enhanced CT simulator image with full bladder. CTV T LR CT fb is contoured in light green. Note that the bladder, in spite of instructions to the patient is less full than in MRI, resulting in a different topography of the CTV T LR. (C) Contrast enhanced CT simulator image with empty bladder. CTV T LR CT eb is contoured in olive green. The uterus is anteverted, resulting in a different topography of CTV T LR when compared with the full-bladder MRI and CT. (D) The main contouring and planning image data set - the contrast enhanced CT with contrast - with all three CTV T LRs co-registered. (E) ITV T LR is contoured in pink as a union of all three CTV T LRs. The contour is manually edited by adding approximately 5 mm in the posteriorly and anteriorly of the ITV T LR region which contains the three CTV HRs (magenta). The aim of this edit is to ensure adequate coverage of the CTV HR, which is the most relevant part of the ITV. (F) ITV 45/25 is finally created as a union of CTV E and ITV T LR.

ITV 55/25 and ITV 57.5/25: Internal target volume to be treated to 55 and 57.5 Gy in 25 fractions

Structure properties:

Label: ITV

IDs / Names:

- ITV 55/25
- ITV 57.5/25

Type: ITV

Color: pink

Selection:

- ITV 55/25 should encompass CTV N 1, 2, 3, …etc. of lymph nodes within true pelvis (external iliac, internal iliac, obturator regions).
- ITV 57.5/25 should encompass CTV N 1, 2, 3, …etc. of lymph nodes outside true pelvis (common iliac, para-aortic, inguinal).
-

Delineation:

- Use Boolean operators to automatically create ITV 55/25 and ITV 57.5/25 as the union of individual CTV Ns as defined under selection.
- Do not add any margin from CTV N to ITV.

Further reading

1. International Commission on Radiation Units and Measurements. ICRU Report 89: Prescribing, Recording, and Reporting Brachytherapy for Cancer of the Cervix. Journal of the ICRU 2013; 13 (1-2). Oxford University Press.
2. Protocol writing committee. EMBRACE II study protocol. https://www.embracestudy.dk/UserUpload/PublicDocuments/EMBRACE%20II%20Protocol.pdf
3. Taylor A, Rockall AG, Rodney HR, et al. Mapping pelvic lymph nodes: guidelines for delineation in intensity-modulated radiotherapy. Int J Radiat Oncol Biol Phys 2005;63(5):1604-1612.

LIST OF ABBREVIATIONS

Abbreviation	Term
18-FDG-PET	18-fluorodeoxyglucose positron emission tomography
CBCT	Cone beam computed tomography
CT	Computed tomography
CTV	Clinical target volume
DWI	Diffusion weighted imaging
E	Elective
eb	Empty bladder
EBRT	External beam radiotherapy
EMBRACE	External beam radiochemotherapy and MRI based adaptive brachytherapy in locally advanced cervical cancer
fb	Full bladder
FIGO	International federation of gynecology and obstetrics
FSE	Fast spin echo
GTV	Gross tumor volume
HR	High risk
ICRU	International commission on radiation units and measurements
ID	Identification
Init	Initial
ITV	Internal target volume
L	Lumbar
LR	Low risk
MRI	Magnetic resonance imaging
N	Nodal / Node
OAR	Organ(s) at risk
PAN	Paraaortic nodes
PM	Parametrium
S	Sacral
T	Tumor
T2w	T2 weighted
Vag.	Vaginal