

Nordic Society for Gynecological Oncology
Advisory Board of Radiotherapy
Guidelines for *postoperative* irradiation of cervical cancer



Contents:

1. Treatment planning for EBRT.....	2
2. Target definition for EBRT.....	2
3. Dose, fractionation and over all treatment time of EBRT.....	3
4. Technique for EBRT.....	4
5. BT.....	4
6. Hemoglobin.....	4
7. Chemotherapy.....	4
8. Minimal standards for quality assurance.....	5
9. Minimal standards for documentation.....	5

EBRT = External Beam Radiotherapy

BT= Brachytherapy

The board of NSGO has approved these guidelines.

The guidelines should be perceived as minimal standards and should not replace independent medical judgment or the use of more advanced technique where this is possible or needed based on the clinical situation.

These guidelines should not be used for patients with macroscopic tumor remaining or diagnosed after radical hysterectomy!

1. Treatment planning for EBRT

It is recommended to perform target delineation based on 3D CT data set performed using both oral and intravenous contrast. Slide thickness of the CT scanning should not exceed 5 mm, and dose planning should be performed on a 3D dose planning system. Before dose planning CT, a marking of the vaginal vault with silver seeds or metal clips is recommended. Fixation is optional but should at least include knee cushions to ensure reproducible patient positioning. To minimize internal motion emptying of bladder and rectum before dose planning CT is also recommended unless bladder and rectum volume can be controlled by other methods.

2. Target definition for EBRT

Target definition should be based on integrated information obtained by CT (MRI) and gynecological examination.

The volumes of interest (VOI) should be defined according to ICRU:

GTV: Gross Tumor Volume (*not present*).

CTV: Clinical Target Volume = GTV + microscopic tumor extension.

ITV: Internal Target Volume = CTV + internal margins to compensate for internal motions.

PTV: Planning target Volume = ITV + set-up margin.

To evaluate competing dose plans it is recommended to define volumes of organs at risk, (primarily bladder, rectum and intestines) and to add internal and set-up margins using the same principles as for PTV to obtain the Planning Organ at Risk Volume.

IMPORTANT: The standard margins used for defining VOI should be modified when more precise knowledge is available.

T-target (tumor-bed)

- Definition of CTV-T is **optional** and only relevant in cases where a dose increment to the tumor bed is required because of close parametrical and/or vaginal margins.
- CTV-T: Vaginal vault and/or preoperative tumor extension based on gynecological examination and CT-scan (MR-scan). Alternatively the CTV-T may be defined as the upper 1/3 of the vagina and/or remaining parametrical tissue/scar tissue.
- ITV-T: CTV-T + 0.0 cm in all directions.
- PTV-T: ITV-T + 0.5 cm in all directions.

P-target (pelvic nodes, vagina and parametrical tissue)

Elective irradiation of the upper part of vagina, parametrical tissue and all pelvic lymph nodes including iliaca interna/obturatoria, iliaca externa, sacral and iliaca communis (1).

- CTV-P: For patients with positive lymph node or parametrical invasion (pIIB) the cranial border is 1 cm below the L4-L5 interspace. Proximal border is at the promontorium for patients treated purely on the basis of unfavorable tumor parameters (2). Caudal border (vagina) is at least 2 cm below the vaginal vault. Ventral and lateral borders are defined by the iliac vessels with a margin of 0.5-2 cm in the loose connective tissue as described by Chao and Lin (3). The iliac external vessels are included from above the inguinal ligament. The muscular rim of the pelvic cavity, excluding fossa ischio-rectalis, defines dorsal-caudal border. If CTV-T is defined it should always be fully include in CTV-P.
- ITV-P: CTV-P + 0.0 cm
- PTV-P: ITV-P + 0.5 cm in all directions. A larger set-up margin laterally should be considered for obese patients.

3. Dose, fractionation and over all treatment time of EBRT

Irradiation is given with five fractions per week and a dose per fraction of 1.8-2.0 Gy.

Unintended dose variation should be less than +/- 5% in 98% of PTV. **Intended maximal treatment time is 35 days.** Two daily external beam radiotherapy (EBRT) fractions at least 6 hours apart should be used to compensate for unplanned treatment breaks. The cumulative dose of EBRT should not exceed 12 Gy per week to avoid consequential late damage.

T-target (tumor-bed)

- 50 Gy in 25 fractions (optional) (2;4).

P-target (pelvic lymph nodes and vagina)

- 45 Gy in 25 fractions (4;5).

4. Technique for EBRT

- Iso-centric technique, normally a combination of box techniques.
- No standard fields. Beam shaping should be individualized according to target definitions, MLC recommended.
- If relevant, the edge of beams used to cover PTV-T should be set with no margin for penumbra, as PTV-T is included in PTV-P.
- Bladder and rectum should be empty before irradiation unless bladder and rectum volume is controlled by other methods.

5. Brachytherapy

Brachytherapy is not recommended as standard (4), but may be used to substitute EBRT dose increment to the vaginal vault (CTV-T) (2). Thus, if vaginal intracavitary BT is considered, maximal dose of EBRT is 45 Gy (6). Dose of vaginal BT can either be prescribed according to institutional standards or as follows: For HDR three application of 5 Gy is generally advocated. For LDR, the surface dose is in the range 25-30 Gy (6). BT should preferentially be initiated one week after completion of EBRT. The temporal separation between BT applications should optimally not be less than one week, especially if BT is administered during EBRT.

6. Hemoglobin

Hemoglobin should be monitored weekly and kept within institutional limits unless otherwise specified in particular protocols.

7. Chemotherapy

Concomitant EBRT and cisplatin is standard unless otherwise specified in particular protocols.

- The schedule is weekly cisplatin 40 mg/m² for as long as radiotherapy is given. No more than 6 series should be applied.

- Chemotherapy should be initiated on the same day or the day after administration of the first EBRT fraction.
- Blood tests are repeated once a week. Treatment with cisplatin should be withheld if the total white blood cell counts falls below $2.5 \cdot 10^9$ (alternatively granulocytes $< 1.0 \cdot 10^9$) or platelets below $50 \cdot 10^9$. Cisplatin can be resumed once the blood counts exceed these limits.
- Nausea and vomiting grade 4 (CTC version 2), reduce Cisplatin by 25%
- Neurotoxicity grade 2 (CTC version 2), reduce Cisplatin by 25%
- Neurotoxicity grade 3-4 (CTC version 2), discontinue Cisplatin
- Nephrotoxicity with GFR < 50 ml/min or creatinine > 177 μ mol/l, discontinue Cisplatin

8. Minimal standards for quality assurance

- Verification films of EBRT at start and mid time through treatment.
- In vivo dosimetri for EBRT.
- If BT is applied orthogonal X-rays should be performed for each application.
- If BT is applied in vivo rectal and/or bladder dosimetri is recommended for each application.

9. Minimal standards for documentation

- Dose plans and simulator and verification films must be stored for inspection.
- ICRU point dose.
- Maximal dose, minimal dose and SD in the targets.
- Maximal dose to bladder and rectum.
- Total dose, dose per fraction and total treatment time.

Reference List

- (1) Martinez-Monge R, Fernandes PS, Gupta N, Gahbauer R. Cross-sectional nodal atlas: A tool for the target definitions of clinical target volumes in three-dimensional radiation therapy planning. *Radiol* 2002; 211:815-828.
- (2) Sedlis A, Bundy BN, Rotman MZ, Lentz SS, Muderspach LI, Zaino RJ. A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: A Gynecologic Oncology Group Study. *Gynecol Oncol* 1999; 73(2):177-183.
- (3) Chao CKS, Lin P. Lymphangiogram-assisted lymph node target delineation for patients with gynecologic malignancies. *Int J Radiat Oncol Biol Phys* 2002; 54:1147-1152.
- (4) Peters WA, III, Liu PY, Barrett RJ, Stock RJ, Monk BJ, Berek JS et al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. *J Clin Oncol* 2000; 18(8):1606-1613.
- (5) Thomas GM, Dembo AJ. Is there a role for adjuvant pelvic radiotherapy after radical hysterectomy in early stage cervical cancer? *International Journal of Gynecological Cancer* 1991; 1:1-8.
- (6) Chadha M. Gynecological brachytherapy-II: Intravaginal brachytherapy for carcinoma of the endometrium. *Sem Radiat Oncol* 2002; 12:53-61.