



Patterns of care in cervical cancer

## Patterns of care survey: Radiotherapy for women with locally advanced cervical cancer



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### ABSTRACT

**Background and purpose:** Regarding latest developments, the need of a radiotherapy 'Patterns of Care' survey was expressed by the Dutch National Platform Radiotherapy for Gynaecological Cancer (LPRGT). Therefore, this study investigated current practice for cervical cancer in all 16 radiation oncology centres in the Netherlands specialised in gynaecological oncology.

**Material and methods:** A structured 'patterns of care' questionnaire was completed and followed by an in-depth interview with radiation oncologists from all radiotherapy centres specialised in gynaecological oncology. Specific topics addressed were: definition of target volumes, treatment preparation, imaging for treatment planning, treatment planning, and image-guided adaptive radiotherapy for external beam radiotherapy and brachytherapy.

**Results:** Current radiotherapy practice in the Netherlands for cervical cancer appears to be in accordance with international standards. However, at the time of the survey some differences were revealed that might have relevant clinical impact. For instance: 1) Half of the centres acquired positron emission tomography combined with CT (PET-CT) for staging and target delineation for every patient, 2) The definition of upper border of the para-aortal lymph node area and dose prescription for external beam radiotherapy varied between the centres, and 3) 12 centres used a single treatment plan for delivering EBRT, and four used a plan-of-the-day strategy with a library of 3–4 treatment plans.

**Conclusions:** Most differences were found at the cutting edge of clinical evidence. However, the majority of these uncertainties are topics being addressed in current and planned (inter)national studies.

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In the last decades, the radiotherapy community has made successful efforts to reduce radiation toxicity by tailoring the required dose to the tumour while reducing undesirable dose to the normal organs at risk (OAR). This became increasingly feasible due to high-precision radiation techniques such as Intensity-Modulated Radiation Therapy (IMRT), Volumetric-Modulated Arc Therapy (VMAT) and image-guided adaptive brachytherapy (IGABT) [1,2].

High-precision radiotherapy techniques require precise target definition of both tumour and OAR. This is accomplished by registration by means of various radiological modalities (such as CT with MRI and/or PET) supported by guidelines for contouring and planning of external beam radiotherapy (EBRT) [3–5]. When taking into account the interfractional motion of the uterus due to daily variation of bladder and rectal filling, target coverage can be

maintained while the dose to OAR is reduced [6–8]. By making use of image-guided adaptive radiotherapy techniques (IGART), further dose reduction to OAR can be achieved [9].

International guidelines, as well as the GEC-ESTRO recommendations/ICRU-89 report, encourage progression to more advanced techniques, while achieving uniform recording and reporting of the delivered radiotherapy dose [10–12]. Recently, the EMBRACE initiatives reported the results of world-wide data on dose delivery and subsequent outcome [13–15]. In the EMBRACE II protocol, even more uniformity will be pursued since image guidance, radiotherapy techniques and dose prescriptions are a part of the protocol.

In response to latest developments, the necessity of a 'Patterns of Care' survey for radiation oncology practice was expressed by the Dutch National Platform Radiotherapy for Gynaecological Cancer (LPRGT). Therefore, the present study aims to investigate the current radiotherapy practice, for women with locally advanced cervical cancer, in all radiotherapy centres in the Netherlands specialised in gynaecological oncology.

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## Material and methods

### Survey

A 'Patterns of Care' survey was developed in mutual discussion with all authors and tested for further fine-tuning in both the Academic Medical Centre Amsterdam and the University Medical Centre of Utrecht. The survey addressed topics concerning EBRT and brachytherapy (BT); both being part of the curative treatment consisting of radiotherapy with concomitant chemotherapy for patients with locally advanced stage (FIGO stage IB2, IIA2-IVA) uterine cervical cancer. The questionnaire addresses important factors that might influence EBRT and BT treatment dose:

- Imaging for treatment planning and delineation
- Definition of target volumes
- Planning objectives and planning constraints
- Appraisal of the treatment plan
- Radiotherapy technique
- Treatment delivery and position verification

### Centres

All 16 radiotherapy centres in the Netherlands specialised in gynaecological oncology were invited and consented to participate in a structured 'Patterns of Care' interview. A questionnaire was submitted in advance to be completed (preferably) by both a radiation oncologist and a medical physicist radiotherapy, with a minimum of one radiation oncologist per centre answering the questionnaire. During the interview, the first author (P.B.) went interactively through all the questions with the respondents to ensure that all questions and answers were understood correctly and completed, and to allow additional comments on specific choices.

## Results

All 16 centres completed the questionnaire (March to September 2015) and 14 were visited for face-to-face interviews; due to busy schedules, two centres were only available for an extensive interview and discussion by telephone. All data were stored in a database and the clinically most important outcomes/answers are described below; the remaining answers are summarised in [Supplementary Table S1](#). To improve the readability of [Table S1](#), answers to the questionnaire are divided, per subject, according to the largest, smaller, and the smallest number of centres.

### EBRT

#### Imaging for target delineation and treatment planning

In agreement with the national guideline for treatment of patients with cervical cancer, all centres reported to acquire a treatment planning computed tomography (CT) in treatment position with laser for positioning. All 16 centres used magnetic resonance imaging (MRI) for staging; of these, three performed MRI in radiotherapy position and, of these, one centre used laser for positioning on MRI.

At the time of the survey, half of the centres acquired a positron emission tomography combined with CT (PET-CT) for staging and target delineation for every patient. The other half performed a PET-CT if patients had lymph nodes with pathological features on MRI or CT and were, therefore, at increased risk of distant lymph node or organ metastasis. If a PET-CT was performed, 7 of the 16 centres used laser for positioning.

Thirteen centres treated patients in supine 'face-up' position because they found this a more reproducible and comfortable posi-

tion compared to prone 'face-down'. Three centres treated patients in prone position in combination with a belly board, aiming to push the small bowel away from the high-dose area.

To visualise the vagina on planning CT, 13 centres used contrast-enhancing methods: four used a coated lead wire, three a catheter or tube, two a tampon soaked in contrast fluid, and four centres used contrast fluid containing ultrasound gel. The remaining three centres used MRI to determine anatomy properly.

### EBRT technique

Five, seven and one centre(s) reported using IMRT, VMAT and tomotherapy, respectively. Three centres used a 3D conformal technique for EBRT; however, these centres were likely to introduce a more advanced technique within one year.

### Adaptive strategies

At the time of the survey, 12 centres used a single treatment plan for delivering EBRT, and four choose each day the most favourable treatment plan out of a library of 3–4 treatment plans.

Bladder filling: seven centres did imaging for treatment planning with a full or near-full bladder, but comfortably filled. The rationale for a comfortably filled bladder is to achieve a better reproducible filling, particularly during the last week of the treatment when acute bladder/urinary toxicity is beginning to interfere with the filling goals. Nine centres performed separate imaging series; of these, eight centres performed one with a full or comfortably filled bladder and one with an empty bladder, and one centre performed three different imaging series with a full, empty, and an intermediately filled bladder. In these nine centres, four made a library of treatment plans whereas the other five aim to do so in the near future.

Rectal filling: 14 centres did not take any specific measures. One centre advised a specific diet aiming to reduce hard lumpy stools that can increase rectal volume. Another centre prescribed bisacodyl laxative on a regular basis during treatment.

### Delineation of targets and organs at risk

At the time of the survey, 13 centres delineated primarily on CT, two primarily on PET-CT, and one centre on MRI. All centres based their delineations on the consensus guidelines by the Radiation Therapy Oncology Group, by European colleagues, and on training at specific courses such as the ESTRO Image-guided radiotherapy in cervical cancer radiotherapy course [3,5,7,16,17]. In 2014 before implementation of EMBRACE II was initiated, a delineation atlas based on these papers was issued by the LPRGT; nine of the 16 centres were using this atlas in their daily practice [18].

The survey revealed differences in the cranial treatment border, mainly in case of para-aortic irradiation. The indication for inclusion of the para-aortic lymph node region was the same for all centres: pathologic lymph node(s) in the common iliac lymph node region or higher. When there is an indication for including the para-aortic lymph node region, the cranial border ranged from the lower border of the 12th thoracic (Th12) to the lower border of the 3rd lumbar vertebrae (L3). In five centres the upper border is at the level of the renal veins which should (roughly) be situated at the lower border of L1-L2. One centre did not include levels higher than the lower border of L3, six centres the lower border of L2, one centre the lower border of L1, and four centres used the lower border of Th12 as surrogate for the upper border of their elective para-aortic CTV. If there was no indication for para-aortic irradiation 14 centres had the upper border at the bifurcation of the aorta, whereas two centres had the upper border at the confluence of the common iliac veins.

The margin for interfractional motion of the uterus/cervical region, often referred to as internal target volume (ITV), varied among the centres. Three centres did not use an ITV while perform-

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