Impact of the filling status of the bladder and rectum on their integral dose distribution and the movement of the uterus in the treatment planning of gynaecological cancer

André Buchali*, Stefan Koswig, Stefan Dinges, Peter Rosenthal, Jürgen Salk, Gundula Lackner, Dirk Böhmer, Lorenz Schlenger, Volker Budach

Universitätsklinikum Charité, Campus Berlin-Mitte, Klinik für Strahlentherapie, Schumannstrasse 20/21, 10117 Berlin, Germany

Received 19 January 1999; received in revised form 15 April 1999; accepted 17 May 1999

Abstract

Purpose: Determination of the impact of the filling status of the organs at risk (bladder and rectum) on the uterus mobility and on their integral dose distribution in radiotherapy of gynaecological cancer.

Methods: In 29 women suffering from cervical or endometrial cancer two CT scans were carried out for treatment planning, one with an empty bladder and rectum, the second one with bladder and rectum filled. The volumes of the organs at risk were calculated and in 14 patients, receiving a definitive radiotherapy, the position of the uterus within the pelvis was shown using multiplanar reconstructions. After generation of a 3D treatment plan the dose volume histograms were compared for empty and filled organs at risk.

Results: The mobility for the corpus uteri with/without bladder and rectum filling was in median 7 mm (95%-confidence interval: 3–15 mm) in cranial/caudal direction and 4 mm (0–9 mm) in posterior/anterior direction. Likewise, cervical mobility was observed to be 4 mm (1–6 mm) mm in cranial/caudal direction. A full bladder led to a mean reduction in organ dose in median from 94–87% calculated for 50% of the bladder volume ($P < 0.05$, Wilcoxon’s matched-pairs signed-ranks test). For 66% of the bladder volume the dose could be reduced in median from 78 to 61% ($P < 0.005$) and for the whole bladder from 42 to 39% ($P < 0.005$), respectively. No significant contribution of the filling status of the rectum to its integral dose burden was noticed.

Conclusion: Due to the mobility of the uterus increased margins between CTV and PTV superiorly, inferiorly, anteriorly and posteriorly of 15, 6 and 9 mm each, respectively, should be used. A full bladder is the prerequisite for an integral dose reduction. © 1999 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Radiotherapy; Cervical and endometrial cancer; Bladder; Rectum; Clinical target volume; Planning target volume; Dose volume histogram

1. Introduction

During irradiation of cervical and endometrial cancer different filling status of the organs at risk may result in considerable tumour mobility within the pelvis. As a consequence the clinical target volume (CTV) may not completely be encompassed by the daily treatment volume. This may result in a reduction in local tumour control in gynaecological cancer up to 30% [15].

The daily filling status of the organs at risk are variable and thus total acquired dose levels during radiation treatment may also be quite variable.

The integral dose delivered to the organs at risk during radiotherapy of gynaecological cancers may contribute to the incidence of late radiation damage such as chronic cystitis, proctitis, fistulas and stenosis. The severity of late rectal sequelae depends critically on the integral dose, while for the bladder there is no or only a marginally correlation [17,18]. The integral dose to the organs at risk is one of the limiting factors for dose escalation studies.

The aim of this study was to determine to what extent filling status of the organs at risk can be related to simultaneous movement of the uterus during fractionated external beam irradiation and to modification of their integral dose.

2. Material and methods

Twenty-nine women were included in this study. The patients suffered from cervical or endometrial cancer, necessitating a definitive or post-operative radiotherapy.
Just before the treatment planning CT a catheter was inserted into the urinary bladder. The bladder was completely emptied and the catheter was blocked during the scan. All patients were investigated in prone position on a belly board.

A spiral CT (PQ 2000, Picker) was used to generate the scans with a slice thickness of 4 mm covering a volume from the upper rim of the 5th lumbar vertebral body to the anal channel.

After the first series of CT-scans women remained in position and the bladder was filled to the maximally tolerated extent, using a mixture of NaCl 0.9% and iopromide containing contrast medium. After the rectum was filled in a similar procedure, a second series of CT-scans was carried out.

The uterus was outlined in each slice of the CT studies involved in definitive radiotherapy. Moreover the clinical target volume (CTV), planning target volume (PTV), bladder and rectum were outlined in each CT slice using the AcQSim software (Picker Inc.) [5].

The CTV included the uterus and parametric tissue or the tumour bed with a safety margin, the obturator and common iliac lymph nodes and in women with cervical cancer also the external iliac lymph nodes. The PTV was defined as CTV plus a margin of 1 cm. Moreover the bladder and rectum were outlined including the mucous membrane, the rectum was contoured from the level of anal channel up to the rectosigmoid flexure.

All studies were processed and further evaluated by the same physician to avoid interindividual differences [6,14]. Empty and full organs at risk were compared to the outline of the target volumes to reduce intraindividual errors.

Axial, sagittal and coronal digital multiplanar reconstructions were generated to determine the position of the cervix and corpus uteri in relation to bony landmarks such as promontorium, upper margin of the symphysis and lateral pelvic wall in 14 patients, receiving a definitive radiotherapy (Fig. 1a,b)

The data were transferred to the planning system CADPLAN (Dosethek) for physical 3D treatment planning. An experienced physicist generated all plans. The standard technique used three fields (two wedged bilateral and one posterior portal) for 20 MV-photons allowing an individual field shaping by the use of multi leaf collimators (MLC). The dose distribution was calculated according to ICRU 50 [10,12].

The field weights and wedges were individually optimised in order to achieve best PTV homogeneities, but no modifications were allowed for the comparative dose planning in the same patient.

Dose volume histograms were generated for the PTV, bladder and rectum.

All values given here are mean values ± standard deviations (SD) for volumes of bladder and rectum and median values and 95%-confidence interval (CI95%) for mobility and dose specification of the organs. For statistical comparison of the results with empty and filled risk organs the Wilcoxon’s matched-pairs signed-ranks test was used. A P-value of less than 0.05 was considered statistically significant.

3. Results

Among all patients included in this study 17 suffered from cervical and 12 from an endometrial carcinoma, respectively. Fourteen patients had definitive, 15 patients post-operative radiotherapy. Tumour stages are listed in Table 1.

The rotational set-up error comparing sagittal, transversal and longitudinal axis in both CT studies of each patient was

---

Fig. 1a,b. Sagittal multiplanar reconstructions showing the position of the corpus and cervix uteri within the pelvis. (A) Distance between promontorium and the anterior margin of the cervix. (B) Distance between promontorium and the posterior margin of the cervix. (C) Distance between upper margin of the symphysis and the lower margin of the cervix. (D) Distance between promontorium and the anterior margin of the corpus. (E) Distance between promontorium and the upper margin of the corpus. (F) Distance between right uterus and pelvic wall (not demonstrated). (G) Distance between left uterus and pelvic wall (not demonstrated).
The mean bladder and rectum filling volumes were 175 ± 40 ccm and 71 ± 49 ccm (mean ± SD), respectively. The corresponding mean organ volumes of emptied and filled bladder and rectum after outlining were 50 ± 34 ccm versus 236 ± 67 ccm and 74 ± 27 ccm versus 93 ± 41 ccm (mean ± SD), respectively.

A significant uterus mobility with bladder and rectum filled could be observed in cranial direction. The corpus uteri moved upward in median 7 mm (CI95%: 3–15 mm) and the cervix 4 mm (−1–6 mm). Additionally a posterior movement of the corpus uteri of 4 mm (0–9 mm) was detected. No significant anterior/posterior movement of the cervix or lateral movement of the cervix or corpus uteri was observed (Table 2).

A correlation between the extent of the differences in bladder volumes prior to and after organ filling and the degree of cranial/caudal or anterior/posterior movement of the uterus could not be established. Decreasing radiation dose levels with increasing bladder volumes were observed. For one half of the bladder volume the dose level decreased significantly from 94% (CI95%: 82–93%) to 87% (73–86%) (P < 0.05, Wilcoxon’s matched-pairs signed-ranks test), respectively, of the total isocentre dose. For two thirds and the whole bladder volume the percent total dose diminished from 78% (69–84%) to 61% (57–72%) (P < 0.005) and from 42% (40–52%) to 39% (36–39%) (P < 0.005), respectively. No dose sparing was shown for one third of the bladder volume. The dose reduction was more pronounced in patients with a definitive than with a postoperative radiotherapy (Table 3). There was no distinct correlation between the difference in bladder volumes and the reduction of the bladder dose.

For the rectum no reduction of the integral dose was observed with increased filling. A small insignificant increase of the median rectum dose, calculated for 1/2, of the rectum volume of 3% and decrease, calculated for 3/3 of the rectum volume of 4% was found (Table 4).

The treatment volumes were not significantly different between empty and filled organs at risk.

### Table 1

<table>
<thead>
<tr>
<th>Tumour stages of patients (n = 29)</th>
<th>Definitive radiotherapy</th>
<th>Post-operative radiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>Corpus</td>
<td>Cervix</td>
</tr>
<tr>
<td>T1N0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>T2N0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>T2N1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>T3N0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>T3N1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>T4N0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>T4N1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>1</td>
</tr>
</tbody>
</table>

1.7 ± 1.6°, 0.1 ± 2.5° and 1.7 ± 2.0° (mean ± SD), respectively.

The mean bladder and rectum filling volumes were 175 ± 40 ccm and 71 ± 49 ccm (mean ± SD), respectively. The corresponding mean organ volumes of emptied and filled bladder and rectum after outlining were 50 ± 34 ccm versus 236 ± 67 ccm and 74 ± 27 ccm versus 93 ± 41 ccm (mean ± SD), respectively.

A significant uterus mobility with bladder and rectum filled could be observed in cranial direction. The corpus uteri moved upward in median 7 mm (CI95%: 3–15 mm) and the cervix 4 mm (−1–6 mm). Additionally a posterior movement of the corpus uteri of 4 mm (0–9 mm) was detected. No significant anterior/posterior movement of the cervix or lateral movement of the cervix or corpus uteri was observed (Table 2).

A correlation between the extent of the differences in bladder volumes prior to and after organ filling and the degree of cranial/caudal or anterior/posterior movement of the uterus could not be established. Decreasing radiation dose levels with increasing bladder volumes were observed. For one half of the bladder volume the dose level decreased significantly from 94% (CI95%: 82–93%) to 87% (73–86%) (P < 0.05, Wilcoxon’s matched-pairs signed-ranks test), respectively, of the total isocentre dose. For two thirds and the whole bladder volume the percent total dose diminished from 78% (69–84%) to 61% (57–72%) (P < 0.005) and from 42% (40–52%) to 39% (36–39%) (P < 0.005), respectively. No dose sparing was shown for one third of the bladder volume. The dose reduction was more pronounced in patients with a definitive than with a postoperative radiotherapy (Table 3). There was no distinct correlation between the difference in bladder volumes and the reduction of the bladder dose.

For the rectum no reduction of the integral dose was observed with increased filling. A small insignificant increase of the median rectum dose, calculated for 1/2, of the rectum volume of 3% and decrease, calculated for 3/3 of the rectum volume of 4% was found (Table 4).

The treatment volumes were not significantly different between empty and filled organs at risk.

### 4. Discussion

The patients set-up error between the two CT-studies was small. Important factors contributing to these results were catheter insertion prior to the first CT-scan and the stable positioning of all women during organ filling and CT-scans.

The differences in bladder volumes before and after organ filling is a function of the volume of contrast medium applied. The differences for rectum volumes were in some cases substantially smaller than the injected volume of contrast medium, because of a retrograde outflow into the rectosigmoid and sigmoid.

The mean bladder filling volumes of 190 ml as achieved in this study were relatively small compared with the physiological bladder capacity, which is usually more than 500 ml in healthy volunteers [1]. One possible reason might be the fast and unphysiological external filling procedure. The dynamics of the physiological filling is slow and the urine temperature is always identical to the body temperature. Moreover women undergoing postoperative radiotherapy have a known reduced bladder volume during the weeks after hysterectomy [20]. The planning procedure was carried out with the patient in prone position on a belly board.

A considerable mobility of the corpus uteri depending on the filling status of the organs at risk was observed. During

### Table 2

| Significant mobility of the cervix and corpus uteri with empty and full organs at risk (median values and 95%-confidence interval (CI95%) in mm) (n = 14) |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Cervix: lower margin − symphysis | Empty organ | Full organ | Differences (full versus empty organ) | P-value |
| Median | CI95% | Median | CI95% | Median | CI95% | Median | CI95% |
| C: cervix | 10 | 5 to 17 | 14 | 7 to 21 | 4 | −1 to 6 | <0.05 |
| F: corpus | 34 | 2 to 59 | 35 | 21 to 55 | 5 | 0 to −9 | <0.05 |
| 0: corpus | 92 | 70 to 100 | 108 | 76 to 112 | 7 | 3 to 15 | <0.05 |
the filling procedure a cranial movement of the corpus and cervix and a posterior movement of the corpus uteri occurred. The precise determination of the mobility in cranial/caudal direction depends on the thickness of the CT slices, which was 4 mm in our investigation. The measurements of the distance between upper margins of the symphysis and corpus uteri revealed a difference from the reality of up to 3 mm. The position of the upper extension of corpus uteri and symphysis inside a 4 mm CT slice is incidental. The determination of the mobility shows a random error, which is lower than the measured differences of the distances between upper margins of the symphysis and corpus uteri. The influence of the bladder filling is predominant to the filling of the rectum concerning the direction of the mobility of the corpus uteri. The differences of organ volumes prior and after filling procedures were > 2.5 fold higher for the bladder compared with the rectal volume. No other studies in the literature with a same or similar design match this study. Two workgroups examined the variations of the cervix in gynaecological brachytherapy. Both discussed changes of the position of the bilateral prescription point A, which can be used as a reference point for the mobility of the applicator and cervical channel. The authors found differences between two applications of about 5 mm for the cranio-caudal direction. The movements in the anterior-posterior and lateral direction were about 2 mm each. [8,11]. These results are also comparable to our results for the cervix. Comparable results of prostate mobilities in male patients showed an anterior-posterior movement of the prostate of up to 20 mm in patients with a prostate cancer [2,3,9,21,22]. A possible reason could be the relatively loose fixation of the prostate within the pelvis compared to the cervix. Additionally the uterus movement is limited in women with a tumoural infiltration of the parametric tissue. We could not verify this hypothesis because of the small number of patients. The outlining procedure for the CTV in CT slices should take into account the mobility of the uterus. The normal margin between CTV and PTV in cranial direction should be therefore increased to about 15 mm depending on the thickness of CT slices. Likewise the margin between CTV and PTV should also be increased by 9 mm in anterior and posterior direction with respect to the filling conditions during planning CT scans. The caudal margin of cervical PTV should be extended by about 6 mm.

A full bladder is an important factor for sparing dose burden for this organ, particularly if more than one third of the bladder is taken into consideration. In our examination one third of the bladder was located inside of the PTV in most cases. Therefore we found no reduction of the dose for this volume level. The reduction of the radiation dose levels at three different volume levels was small, but significant. Calculating to our treatment schedule of 50.4 Gy to
the whole pelvis during first external beam series, the dose reduction for daily irradiation with filled bladder in comparison with empty bladder was about 11 Gy and 4 Gy for two thirds and whole bladder volume, respectively.

The tolerance dose for the bladder is not well established, especially the dose-volume relationship. Severe side effects are published after total doses over 65 Gy for the whole bladder [7]. For definitive irradiation of an advanced stage of cervical carcinoma 50–60 Gy external beam radiotherapy and an additional brachytherapy boost is needed. An analysis of women treated for advanced cervix carcinoma with higher total doses showed clinical relevant rates of moderate or severe bladder complications [19]. For this group of patients distinct bladder protection is an important factor for reducing the incidences of severe late sequelae. The severity of late sequelae is not positively related to the integral dose burden [17,18].

The dose level as shown from the dose volume histograms (DVH) reflects the immediate planning CT situation. The reproducibility during the treatment series however is not guaranteed.

A maximum bladder filling cannot be maintained during a whole course of external beam radiotherapy, due to the frequently developing acute cystitis. The dose volume histograms show a decreasing integral bladder dose when a high filling grade is achieved. An emptied bladder could lead to an excellent reproducibility but implies a considerable higher integral dose burden. A medium filled bladder during planning CT scan leads to a moderate mobility of the uterus and cervix in all directions during daily treatment fractions. Thus, an extreme deviation of the normal position of the uterus within the pelvis can be avoided. The uterus and cervix were surely encompassed in the safety margin for the planning target volume during daily set-up to achieve a high local control [15]. The CT scans for radiation treatment planning should therefore be carried out with the bladder filled to a moderate extent in patients with radiotherapy of gynaecological tumours, e.g., a slight urinary distress. However, the late toxicity of the bladder is not the major complication after radiotherapy of gynaecological cancers.

The protection of the rectum is of even higher relevance than that of the bladder, because of the lower tolerance dose. The incidence of moderate and severe late radiation effects is therefore of higher probability [4,13,19]. In this study the filling status of the rectum had no protective effect. In some cases an even higher but not significant total dose burden was observed with rectum filling. In patients with prostate cancer Lebesque et al. also found an independence of the DVH curve from rectum filling irrespective of the total rectum volume or the rectum wall volume being considered [16].

A critical issue in this study is the filling of both, the bladder and rectum. In an additional study we therefore plan to fill the bladder only due to the insignificant dose sparing effects of rectum filling.

References

