Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/rpor

Original research article

Does ITV vaginal procedure ensure dosimetric coverage during IMRT of post-operative gynaecological tumours without instructions concerning rectal filling?

Ramona Verges[a,*], *Alexandra Giraldo*[a], *Alejandro Seoane*[b], *Elisabet Toral*[a], *M. Carmen Ruiz*[a], *Ariadna Pons*[a], *Jordi Giralt*[a]

[a] *Radiation Oncology Department, Vall d'Hebron University Hospital, Barcelona, Spain*
[b] *Medical Physics Department, Vall d'Hebron University Hospital, Barcelona, Spain*

ARTICLE INFO

Article history:
Received 14 September 2017
Received in revised form
9 December 2017
Accepted 22 January 2018

Keywords:
Vaginal ITV
ITV coverage
Organ motion
Bladder filling
Rectal filling

ABSTRACT

Aim: To find out whether the internal target volume (ITV) vaginal procedure ensures dosimetric coverage during intensity-modulated radiation therapy (IMRT) of post-operative gynaecological tumours without instructions on rectal filling.

Background: The ITV vaginal procedure does not necessarily include all movements of the bladder, and does not include changes in the rectal volume. We should know if the vaginal ITV is a useful tool in maintaining CTV coverage during treatment.

Materials and methods: A retrospective analysis of 24 patients treated between July 2012 and July 2014 with adjuvant IMRT for gynaecological cancer. All patients underwent empty and full bladder CT on simulation (CT-planning) and three weeks later (CT-control). ITV displacement was measured and the 3D vector was calculated. ITV coverage was then evaluated by comparing the volume covered by the prescription isodose on both CT's. Patients were asked to have full bladder but they did not follow recommendations for the rectum.

Results: The mean 3D vector was 0.64 ± 0.32 cm (0.09–1.30). The mean ITV coverage loss was $5.8 \pm 5.7\%$ (0–20.2). We found a significant positive correlation between the 3D vector and the loss of coverage (Pearson correlation, $r = 0.493$, 95% CI: 0.111–0.748, $p = 0.0144$). We did not find any significant correlation between the bladder and rectal parameters with the 3D vector and loss of dosimetric coverage. We found a trend between the maximum rectal diameter in CT-planning and 3D vector ($r = 0.400$, 95% CI: −0.004 to 0.692, $p = 0.0529$).

Conclusion: ITV vaginal procedure contributed to ensuring a good dose coverage without instructions on rectal filling.

* *Corresponding author at*: Servei de Oncologia Radioteràpica, Hospital Universitari Vall d'Hebron, P° Vall d'Hebron 119-129, 08035 Barcelona, Spain.
E-mail address: rverges@vhebron.net (R. Verges).
https://doi.org/10.1016/j.rpor.2018.01.006

1. Background

The need for adjuvant treatment in high-risk patients treated with hysterectomy for cervical or endometrial cancer is well-established.[1–7]

Adjuvant pelvic radiotherapy, however, increases the side effects such as gastro-intestinal (GI), genito-urinary (GU) and hematologic toxicity.[1–3] In 40–60% of cases, whole "conventional" pelvic irradiation of up to 45–50 Gy results in acute GI grade 2 side effects, and in 26% of cases, this procedure is associated with late GI toxicity. Severe complications occur in 3% of cases, mainly in patients who have experienced an acute adverse event (grade 2 or higher). In a randomised study[5] comparing the addition of cisplatin-based chemotherapy (CT) to pelvic radiation therapy (RT), Grades 3 and 4 hematologic and gastrointestinal toxicity were more frequent in the Radiotherapy plus chemotherapy group with 27 episodes of grade 4 toxicity in 21 of 122 patients, most of which were hematologic.

The use of intensity-modulated radiation therapy (IMRT) in sparing the surrounding normal tissues has been reported by several investigators.[8–13] Two prospective Phase II trials[14,15] together with an international multicentre study[16] confirm that pelvic IMRT reduces GI acute toxicity grade 2 or higher in up to 28% of patients.

The standardisation of the pelvic IMRT has been performed, but with its rapid dose fall-off around the PTV and internal movement of organs during treatment, it may cause a dosimetric coverage loss of the target and unnecessary OAR inclusion into high dose regions.

At the time of defining the vaginal clinical target volume (CTV), in the adjuvant setting for IMRT in gynaecological tumours, we must take into account the movement of pelvic organs between fractions during treatment. The position of the vagina can vary greatly depending on the different volumes of the bladder and rectum. This is why RTOG introduced internal target volume (ITV) in order to individualise the movement of the vagina associated with bladder filling.[17] Even so, this method does not necessarily include all movements of the bladder, and does not include changes in the rectal volume.[18]

2. Aim

We investigated the extent of vaginal shifts of our patients treated with postoperative IMRT for gynaecological tumours. We used instructions for the bladder filling during treatment and gave no recommendation regarding the rectum. We assessed whether the movement of the vaginal ITV entails the loss of dosimetric coverage, and we have sought the correlation between that loss of dosimetric coverage, with vaginal motion, and the volumes of the bladder and rectum during treatment.

3. Materials and methods

3.1. *Patient characteristics*

24 consecutive patients treated with adjuvant pelvic IMRT, after undergoing hysterectomy for endometrial or cervical cancer, were evaluated between July 2012 and July 2014 with institutional review board approval. In accordance with our treatment protocol, the patients were treated with IMRT, 45 Gy in 25 fractions of 1.8 Gy. Adjuvant chemotherapy was given to 10 of 24 patients.

3.2. *CT simulation and treatment planning*

Patients were instructed to attend the planning-CT (p-CT) session and subsequent daily treatment sessions in full bladder conditions. To accomplish this, patients were asked to empty the bladder and drink 33 cc of water in 15 min, 1 h before the planning-CT. Patients were not given instructions concerning rectal filling. Treatment position was supine decubitus, using a knee cushion to immobilise the hip and the legs. Patients were then scanned from the upper abdomen to below the perineum, with a slice width of 3.75 mm (LightSpeed RT; General Electric, Fairfield, CT, USA) (full bladder CT). After this first scan, patients emptied their bladder and, immediately, a second scan was acquired in the same position (empty bladder CT). Both CT scans were then rigidly registered and vaginal CTV was contoured following RTOG guidelines for each scan.[19] ITV was then constructed on the full bladder CT as the Boolean union of both CTVs. Fig. 1 summarises the whole image procedure followed in the study. Additionally, nodal CTV was also contoured following the consensus guidelines described by Small et al.[17] Planning target volume (PTV) was created by adding a 7 mm margin to ITV and nodal CTV, according to RTOG protocol. The following organs at risk (OAR) were delineated on both CTs: rectum, bladder, femoral heads and peritoneal cavity.

Treatment was planned in Eclipse (Varian Medical Systems, Palo Alto, CA) on the full bladder p-CT. All treatment plans consisted of nine equispaced 6 MV photon beams with dynamic intensity modulation, and were calculated to deliver the prescription dose to 97% of the PTV. Version 10 of the Dose Volume Optimizer and the Analytical Anisotropic Algorithm were used for the fluence optimisation and dose calculation, respectively, with a dose resolution of 2.5 mm.

On week 3 of treatment, a second set of full and empty CT scans were acquired, and the volumes were contoured again (*control-CT, c-CT*) by the same radiation oncologist.

To investigate whether the full/empty bladder CT simulation process prevents tumour loss coverage along the treatment, p-CT and c-CT full bladder scans were rigidly registered in ARIA registration workspace. Afterwards, original plans were recalculated on the full bladder c-CT using the same beam parameters and fluence (Fig. 1).

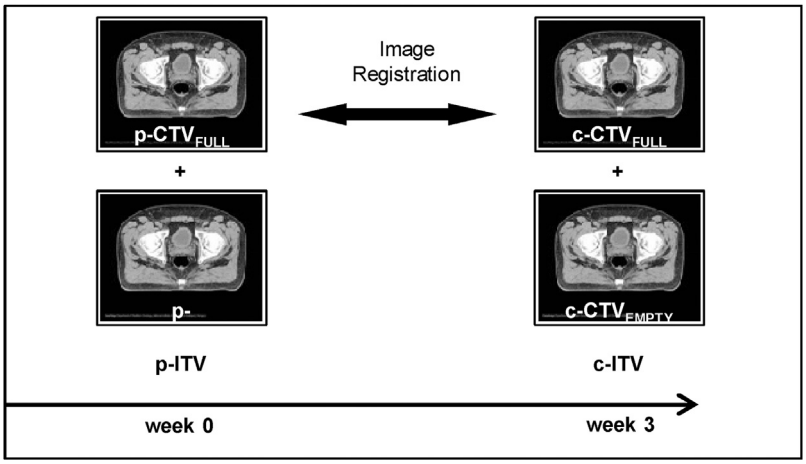

Fig. 1 – Creation of ITV from full and empty bladder CT. p: planning CT; c: control CT; FULL: full bladder CT; EMPTY: empty bladder CT; CTV: clinical target volume; ITV: internal target volume.

ITV dose coverage loss was then assessed by subtracting the ITV volume covered by the prescription isodose in p-CT and c-CT.

To quantify the ITV movement between p-CT and c-CT, two parameters were calculated: the coordinates' difference between the centre-of-mass of both ITVs, and the 3D vector calculated as the square root of the sum of the squares of the coordinates difference.

3.3. *Statistical analysis*

To know the relationship between the movement of the ITV and its loss of coverage with the main organs at risk, bladder and rectal volumes were calculated from each planning and control scan. The parameters evaluated were: the ratio between the organ volumes in both CTs, and the difference of the volumes between them. Other parameters evaluated were the maximum rectal diameter and the maximum anteroposterior (AP) rectal diameter at the coccyx level in both CTs and, finally, the ratio between the AP rectal diameter at the coccyx level in both CTs.

A descriptive analysis was carried out calculating frequencies and percentages for qualitative variables and mean (standard deviation), median and range for quantitative variables. A Pearson correlation analysis was performed to evaluate the relationship between ITV coverage loss and 3D vector.

Results are presented in a scatter plot, and a linear regression is fitted. All analysis were carried out in Stata 13.1.

4. Results

The mean age was 60 years (range 37–77). The patient and tumour characteristics of the 24 patients are summarised in Table 1.

The ITV displacements obtained are shown in Table 2 for the three main axes. Mean 3D vector was 0.64 ± 0.32 cm (range 0.09–1.30).

Table 1 – Patient characteristics.

Characteristic	Number of patients (%)
All patients	24(100)
Age (years)	
Mean	60
Range	37–77
Primary tumour	
Cervix	3 (12.5)
Endometrium	20 (83.3)
Nodal relapse	1 (4.2)
Histology	
Endometriod	15 (62.5)
No endometrioid	7 (29.2)
SCC	2 (8.3)
Chemotherapy	
Yes	10 (41.7)
No	14 (58.3)
EBRT[a] (fractions × Gy)	
25 × 1.8	23 (95.8)
28 × 2.12	1 (4.2)
Brachytherapy	
Yes	14 (58.3)
No	10 (41.7)

[a] EBRT: external beam radiation therapy.

4.1. *ITV coverage loss*

The mean ITV coverage loss was 5.8 ± 5.7% (range 0–20.2). 11 of 24 patients (45.8%) showed a 3D vector of <0.7 cm. For these patients, the loss of coverage was less than 10%.

The remaining 13 patients (54%) had a 3D vector of > 0.7 cm, but only 16.7% (4/24) had a loss of coverage higher than 10% (range 16.4–20.2%).

We found a significant positive correlation between the 3D vector and the loss of coverage (Pearson correlation = 0.493, 95% CI: 0.111–0.748, $p = 0.0144$) (see Fig. 2).

4.1.1. *Bladder volumes*

The results of the analysis of bladder volumes can be seen in Table 3.

Table 2 – ITV displacements.

Axis	Mean (cm)	Standard deviation (cm)	Range (cm)
Left/right	0.17	0.12	0.01–0.50
Superior/inferior	0.35	0.28	0.00–0.93
Anterior/posterior	0.41	0.31	0.03–1.26

Table 3 – Bladder and rectal volumes.

	p-CT[a]				c-CT[b]			
	Bladder vol (ml)		Rectal vol (ml)	Max rectal diameter (cm)	Bladder vol (ml)		Rectal vol (ml)	Max rectal diameter (cm)
	Full	Empty			Full	Empty		
Mean	204.8	42.2	72.2	5.1	220.2	49.4	69.4	5
Median	217.7	42.6	65	5	225.6	50.8	61.6	5.4
Max value	536.8	86.1	132	7.3	523.2	97.2	202.6	8.8
Min value	51.26	23.2	37.6	3.8	64.7	22.8	33.4	3

[a] p-CT: planning CT.
[b] c-CT: control CT.

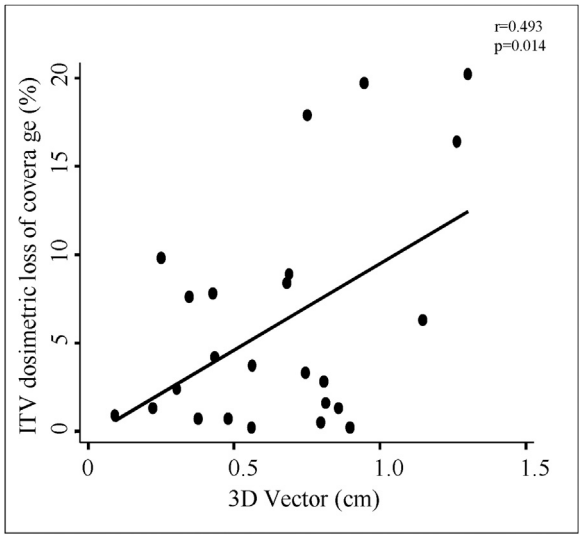

Fig. 2 – ITV dosimetric loss of coverage (%) vs 3D vector (cm).

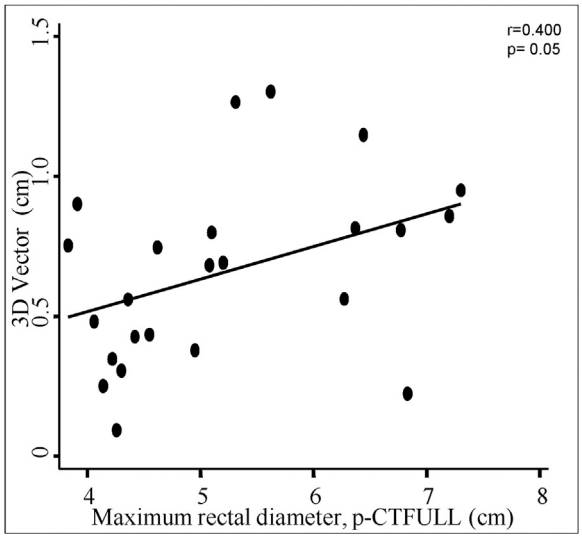

Fig. 3 – 3D vector (cm) vs maximum rectal diameter in planning CT full bladder (p-CT).

Despite written and oral instruction, only 7 of 24 (29.2%) patients had consistent bladder volume, with a variability of <50 ml between both full bladder CTs. 12 of 24 (50%) patients achieved bladder volumes in control CT that were greater than the volumes at the initial full-bladder simulation. However, despite this great variability, the median bladder volume in both CTs was similar.

We analysed the correlations between bladder volumes, the ratio and differences between bladder volumes in planning CT and control CT. We did not find any significant correlation between these parameters and the 3D vector or loss of dosimetric coverage.

4.1.2. *Rectal volumes*

The results of the analysis of rectal volumes can be seen in Table 3.

Parameters such as mean and median of the rectal volume and maximum rectal diameter in both CTs were similar. We did not note a decrease in rectal filling over time, even in those patients who presented GI toxicity.

We did not find any significant correlation between rectal parameters and 3D vector or loss of dosimetric coverage. We only found a trend between the maximum rectal diameter in planning CT and 3D vector that can be seen in Fig. 3 (Pearson correlation 0.400, 95% CI: −0.004 to 0.692, $p = 0.0529$). However, we did not find correlation between the loss of coverage and the maximum rectal diameter (Fig. 4A and B) in any of the CTs.

Finally, we did not find any correlation between changes in bladder volume in the planning CT and control CT, and rectal volume change.

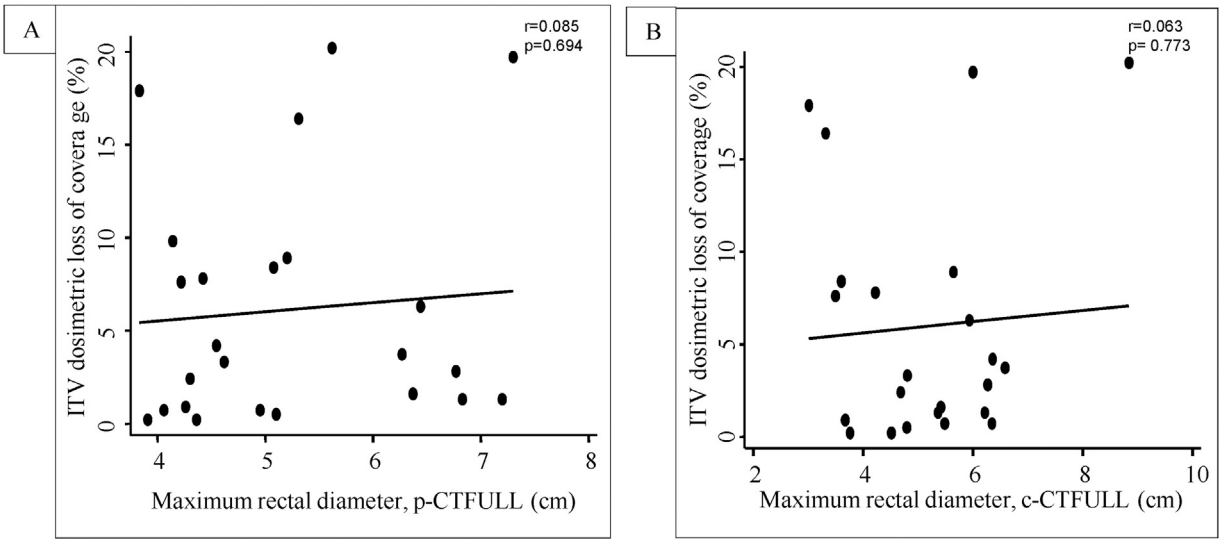

Fig. 4 – ITV dosimetric loss of coverage (%) vs maximum rectal diameter in planning CT full bladder (p-CTFULL) (A) and control CT full bladder (c-CTFULL) (B).

5. Discussion

Adjuvant treatment with IMRT for the gynaecological neoplasms has proven to be better than conventional treatment with conformal radiotherapy on the basis of lower morbidity without compromising control of the disease. Even so, with IMRT, the motion of internal organs can cause dose gradients around the CTV, so it may be displaced from the high dose area in some treatment fractions. The vaginal CTV is located between the bladder and rectum and is therefore subject to the movement of these organs during treatment. This movement varies greatly from patient to patient, meaning that it is necessary to customise strategies for managing movement during treatment.

Accordingly, from the first implementation of adjuvant IMRT in pelvic gynaecological cancer on a multi-institutional level, the RTOG recommended creating a vaginal ITV delineated on CT' with empty and full bladder. With the aim of maintaining constant bladder volume during treatment, patients were instructed to ingest a consistent volume of water 60 min before each treatment session.

With the widespread use of adjuvant IMRT in gynaecological tumours we analysed our data regarding the control of vaginal motion and vaginal ITV strategy.

Jhingran et al.,[18] using the ITV procedure, obtained twice weekly CT scans during treatment of 16 patients and reported median shifts of 0.64 cm in the AP dimension, 0.62 cm in the SI dimension, and 0.23 cm in the right-left plane. In 11 of 16 cases the shifts of the vaginal apex correlated with changes in the volume of the bladder and rectum. We did not find any correlation between bladder volumes and 3D vector as surrogate of ITV vaginal movement.

Rash et al.[20] reported the impact of rectal filling on 145 images from 5 patients treated with adjuvant IMRT for endometrial or cervical cancer, and ITV procedure used at simulation. The mean rectal distention was 3.7 cm (SD 1.8 cm), ranging from 2.05 cm to 6.01 cm. They established a correlation between rectal distention and AP movement of the vaginal cuff marker. To prevent rectal motion, some authors have recently used rectal balloons during radiotherapy. Taku et al.[21] reported the vaginal motion on 18 patients treated with ITV procedure at simulation and placement of an endorectal balloon (ERB) during radiotherapy. They found an inter-treatment fiducial A/P movement with a mean of 2.8 mm (SD = 2.5 mm, range 0–11.8 mm) and suggested that the stability in rectal volumes was provided by ERB placement. They recommend treatment with ERB for patients to benefit from smaller A/P margins and potentially reduced toxicity to the rectum. Our patients, without instructions for rectal filling and without ERB, achieved similar or slightly higher shifts in A/P movement (mean of 4.1 mm, SD = 3.1 mm, range 0.3–12.6 mm). We found a weak correlation between the maximum diameter of the rectum in the planning CT and 3D vector. We did not find correlations with any of the rectal measurements and loss of dosimetric coverage. According to our results, we do not consider it necessary to use the ERB for patients that have a high probability of having small bowel toxicity at any level during radiotherapy.

Some authors solve the problem of organ movements with generous margins, but the PTV margins are another field of controversy. The RTOG recommended 0.7 cm in its Phase II trial, but does not give specifications regarding the margin in the closed Phase III trial and the consensus guidelines recommend either 1–1.5 cm, or for each institution to decide for itself.

Chopra et al.[22] reported that 4.1 mm, 10.6 mm and 10.3 mm, for left-right, craniocaudal and AP margins respectively, could encompass 95% of the observed displacements. Shih et al.[23] reported clinical outcomes in endometrial cancer and Folkert MR et al.[24] in cervical cancer treated with adjuvant pelvic IMRT. They used vaginal contrast to improve the visualisation of the vaginal cuff allowing a better contour of the organ. It was expanded by 2 cm to generate the vaginal cuff CTV. An additional 1 cm expansion was applied to create the vaginal

cuff PTV. On the other hand, in the French study,[15] the PTV was generated from the CTV by adding a 7 mm margin without ITV procedure, which can cause a loss of vaginal coverage. They tried, however, to counterbalance this risk of vaginal infradosification with a brachytherapy boost.

Our study of 24 patients, even understanding the small sample size and the observational study design, allowed us to vary our care practice, allowing patients to go to daily treatment sessions with comfortable bladder and without firm instructions, thus avoiding patient discomfort. The fact that we found no clear relationship between changes in rectal volume and the loss of coverage, has allowed us to continue not giving instructions related to the rectum.

As we found a weak correlation between the maximum diameter of the rectum in the p-CT and 3D vector, we should consider the possibility of applying a non-isotropic margin, in A/P direction, to those patients with major rectal maximum diameter on simulation. Notwithstanding, the conclusions of our study must be considered within the context of its limitations, especially regarding the number of CT scans per patient.

6. Conclusions

Although vaginal movement was observed for the majority of patients, only a few of them showed a significant loss of coverage as a result of this movement. The absence of correlation between bladder volumes and vaginal ITV supports the case for using ITV procedure to ensure adequate dose coverage, even so, we advise patients to maintain comfortable bladder during treatment without fixed instructions, as following a strict bladder-filling protocol does not necessarily achieve stable bladder volumes. Without instructions regarding rectal-filling, we found a weak correlation between rectal volume and 3D vector, allowing us to infer that the diameter of the rectum could be a predictor of ITV vaginal motion.

Conflict of interest

None declared.

Financial disclosure

None declared.

REFERENCES

1. Creutzberg CL, van Putten WL, Koper PC, et al. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial. PORTEC Study Group. Post-Operative Radiation Therapy in Endometrial Carcinoma. *Lancet* 2000;**355**:1404–11.
2. Blake P, Swart AM, Orton J, et al. Adjuvant external beam radiotherapy in the treatment of endometrial cancer (MRC ASTEC and NCIC CTG EN.5 randomised trials): pooled trial results, systematic review, and meta-analysis. *Lancet* 2009;**373**:137–46.
3. Keys HM, Roberts JA, Brunetto VL, et al. A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol* 2004;**92**:744–51, http://dx.doi.org/10.1016/j.ygyno.2003.11.048.
4. Rotman M, Sedlis A, Piedmonte MR, et al. A phase III randomized trial of postoperative pelvic irradiation in Stage IB cervical carcinoma with poor prognostic features: follow-up of a gynecologic oncology group study. *Int J Radiat Oncol Biol Phys* 2006;**65**:169–76, http://dx.doi.org/10.1016/j.ijrobp.2005.10.019.
5. Peters 3rd WA, Liu PY, Barrett 2nd RJ, 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**:1606–13, http://dx.doi.org/10.1200/JCO.2000.18.8.1606.
6. Colombo N, Creutzberg C, Amant F, et al. ESMO-ESGO-ESTRO consensus conference on endometrial cancer: Diagnosis, treatment and follow-up. *Radiother Oncol* 2015;**117**(3):559–81, http://dx.doi.org/10.1016/j.radonc.2015.11.013.
7. Harkenrider MM, Adams W, Block AM, Kliethermes S, Small Jr W, Grover S. Improved overall survival with adjuvant radiotherapy for high-intermediate and high risk Stage Iendometrial cancer. *Radiother Oncol* 2017;**122**(3):452–7, http://dx.doi.org/10.1016/j.radonc.2016.12.003.
8. Corn BW, Lanciano RM, Greven KM, et al. Impact of improved irradiation technique, age and lymph node sampling on the severe complication rate of surgically staged endometrial cancer patients:a multivariate analysis. *J Clin Oncol* 1994;**12**:510–5, http://dx.doi.org/10.1200/JCO.1994.12.3.510.
9. Mundt AJ, Lujan AE, Rotmensch J, et al. Intensity-modulated whole pelvic radiotherapy in women with gynecologic malignancies. *Int J Radiat Oncol Biol Phys* 2002;**52**(5):1330–7, http://dx.doi.org/10.1016/S0360-3016(01)02785-7.
10. Mundt AJ, Mell LK, Roeske JC. Preliminary analysis of chronic gastrointestinal toxicity in gynecology patients treated with intensity-modulated whole pelvic radiation therapy. *Int J Radiat Oncol Biol Phys* 2003;**56**(5):1354–60, http://dx.doi.org/10.1016/S0360-3016(03)00325-0.
11. Roeske JC, Bonta D, Mell LK, Lujan AE, Mundt AJA. dosimetric analysis of acute gastrointestinal toxicity in women receiving intensity-modulated whole-pelvic radiation therapy. *Radiother Oncol* 2003;**69**(2):201–7, http://dx.doi.org/10.1016/j.radonc.2003.05.001.
12. Mell LK, Kochanski JD, Roeske JC, et al. Dosimetric predictors of acute hematologic toxicity in cervical cancer patients treated with concurrent cisplatin and intensity-modulated pelvic radiotherapy. *Int J Radiat Oncol Biol Phys* 2006;**66**(5):1356–65, http://dx.doi.org/10.1016/j.ijrobp.2006.03.018.
13. Tierney RM, Powell MA, Mutch DG, Gibb RK, Rader JS, Grigsby PW. Acute toxicity of postoperative IMRT and chemotherapy for endometrial cancer. *Radiat Med* 2007;**25**(9):439–45, http://dx.doi.org/10.1007/s11604-007-0163-1.
14. Jhingran A, Winter K, Portelance L, et al. A phase II study of intensity modulated radiation therapy to the pelvis for postoperative patients with endometrial carcinoma: Radiation Therapy Oncology Group Trial 0418. *Int J Radiat Oncol Biol Phys* 2012;**84**(1):e23–8, http://dx.doi.org/10.1016/j.ijrobp.2012.02.044.
15. Barillot I, Tavernier E, Peignaux K, et al. Impact of post-operative intensity modulated radiotherapy on acute gastro-intestinal toxicity for patients with endometrial cancer: results of the phase II RTCMIENDOMETRE French multicentre trial. *Radiother Oncol* 2014;**111**(1):138–43, http://dx.doi.org/10.1016/j.radonc.2014.01.018.
16. Klopp AH, Yeung AR, Deshmukh S, et al. A Phase III Randomized Trial Comparing Patient-Reported Toxicity and Quality of Life (QOL) During Pelvic Intensity Modulated Radiation Therapy as Compared to Conventional Radiation

Therapy. S3 Proceedings of the 58th Annual Meeting of the American Society for Radiation Oncology. *Int J Radiat Oncol Biol Phys* 2016;**96**(2):S3, http://dx.doi.org/10.1016/j.ijrobp.2016.06.024.
17. Small Jr W, Mell LK, Anderson P, et al. Consensus guidelines for delineation of clinical target volume for intensity-modulated pelvic radiotherapy in postoperative treatment of endometrial and cervical cancer. *Int J Radiat Oncol Biol Phys* 2008;**71**(2):428–34, http://dx.doi.org/10.1016/j.ijrobp.2007.09.042.
18. Jhingran A, Salehpour M, Sam M, Levy L, Eifel PJ. Vaginal motion and bladder and rectal volumes during pelvic intensity-modulated radiation therapy after hysterectomy. *Int J Radiat Oncol Biol Phys* 2010;**82**(1):256–62, http://dx.doi.org/10.1016/j.ijrobp.2010.08.024.
19. Radiation Therapy Oncology Group website. Available from: http://www.rtog.org/CoreLab/Contouring/Atlases/GYN.
20. Rash D, Hagar Y, Cui J, Hunt JP, Valicenti R, Mayadev J. Interfraction motion of the vaginal apex during postoperative intensity modulated radiation therapy: are we missing the target? *Int J Gynecol Cancer* 2013;**23**(2):385–92, http://dx.doi.org/10.1097/IGC.0b013e3182791f24.
21. Taku N, Dise J, Kenton O, et al. Quantication of vaginal motion associated with daily endorectal balloon placement during whole pelvis radiotherapy for gynecologic cancers. *Radiother Oncol* 2016;**120**(3):532–6, http://dx.doi.org/10.1016/j.radonc.2016.05.005.
22. Chopra S, Patidar A, Dora T, et al. Vaginal displacement during course of adjuvant radiation for cervical cancer: results from a prospective IG-IMRT study. *Br J Radiol* 2014;**87**:20140428, http://dx.doi.org/10.1259/bjr.20140428.
23. Shih KK, Milgrom SA, Abu-Rustum NR, et al. Postoperative pelvic intensity-modulated radiotherapy in high risk endometrial cancer. *Gynecol Oncol* 2013;**128**(3):535–9, http://dx.doi.org/10.1016/j.ygyno.2012.11.020.
24. Folkert MR, Shih KK, Abu-Rustum NR, et al. Postoperative pelvic intensity-modulated radiotherapy and concurrent chemotherapy in intermediate- and high-risk cervical cancer. *Gynecol Oncol* 2013;**128**(2):288–93, http://dx.doi.org/10.1016/j.ygyno.2012.11.012.