Objectives. The aim of this pilot study is to evaluate the feasibility of 3D-conformal radiotherapy (3D-CRT) in the adjuvant postoperative radiotherapy of the vaginal cuff and upper third of present vaginal tissue.

Methods. The representative patient (FIGO IB; PH: squamous cell carcinoma) was referred for adjuvant post-hysterectomy radiotherapy. A whole pelvis irradiation with concomitant high-dose-rate intracavitary brachytherapy (HDR-ICBT) was applied. HDR-ICBT total dose of 24 Gy in four fractions/one fraction per week was delivered to the vaginal cuff using two Fletcher-Suit ovoids. The feasibility of change from HDR-ICBT to CRT was evaluated by generating of three different plans using 10 MV photon beams shaped by multileaf collimator.

Results and discussion. The referent volume received HDR-ICBT prescribed dose. The maximum ICBT percentage dose to the rectum and urinary bladder was 101% and 106% respectively. In all 3D-CRT plans almost 100% of planning target volume (PTV) was covered by 95% therapy isodose surface. From 12-13% of the rectum and 1-3% urinary bladder volume were covered by 100% isodose surface, with the highest maximum dose of 104% and 101%, respectively. Comparison of the PTV dose coverage and the maximum dose to the rectum and urinary bladder for HDR-ICBT and 3D-CRT plans showed no major difference.

Conclusion. 3D-CRT could be considered as adequate replacement for ICBT in the adjuvant postoperative treatment of the vaginal cuff and upper third of present vaginal tissue. Time-dose-fractionation pattern for HDR-ICBT may be safely applied for 3D-CRT.

Key words: cervical cancer, conformal radiotherapy, brachytherapy, radiotherapy, treatment planning

INTRODUCTION

Number of patients with the diagnosis of early stages of cervical carcinoma (FIGO stages I to IIA), worldwide rapidly grows in contrary to those with advanced stages (FIGO stages IIB to IV). There are treatment strategy variations for patients with the early stages of cervical carcinoma but the primary therapy in these patients is surgery. Adjuvant radiotherapy has been shown to improve local and loco-regional control rates in patients with adverse prognostic factors (bulky disease, adverse histology, high grade, node involvement, positive surgical margin, parametrial invasion etc.)1,2. Usually, dose of about 40-56 Gy in 20-28 consecutive daily fractions is delivered to the pelvic nodal area using photon fields. The energy varies from 6 MV to 18 MV mostly depending on patient characteristics and radiotherapy center energy assortment. Fields arrangement varies from pair of parallel opposite fields, trough "4-field box" to conventional3-5, arc 3D-conformal (3D-CRT)6 and intensity modulated techniques (IMRT)7-9. In patients with bulky disease, positive surgical margin and high tumour grade, intracavitary brachytherapy (ICBT) is used to treat the vaginal cuff and the vaginal cuff with upper third of present vaginal tissue to additional dose of 25-40 Gy. ICBT doserate patterns vary from low- to high-dose-rate (HDR). Unfortunately, ICBT may not be possible in some patients due to co-morbid and other conditions or even because of lack of brachytherapy equipment in RT centre. Mitchell et al.10 pointed out that about one third of the elderly cervical cancer patients have been unable to receive ICBT in their institution. In Serbia, majority of patients with stage I and IIA are treated with the radical extended hysterectomy. Patients with at least one adverse prognostic factor are subjected to adjuvant postoperative whole pelvis irradiation (WPRT) with HDR-ICBT. At the Institute for Oncology and Radiology of Serbia the WPRT dose of about 40-45 Gy in 20-24 consecutive daily fractions (4 factions per week) is delivered to the pelvic area using photon fields.
on a linear accelerator. Additional HDR-ICBT to the vaginal cuff and upper third of present vaginal tissue is delivered using two Fletcher-Suit ovoids (sphere diameter 2-2.5 cm) with Microselectron HDR (Nucletron BV, The Netherlands). Total ICBT dose of 24-30 Gy in 4 fractions/one fraction per week is applied on the referent volume that encompass 0.5 cm area lateral to ovoid plastic. HDR-ICBT dose specification and reporting to the rectum and urinary bladder are done following the ICRU 38 recommendations.11 The aim of this pilot study is to analyze dose distribution to the vaginal cuff and upper one third of present vaginal tissue, when it is delivered by CRT and to compare it with dose distribution delivered by HDR-ICBT. To our knowledge there has been no attempt to analyze possibilities of implementation of conventional 3D-CRT as a replacement for HDR-ICBRT in this patient group. A successful attempt of stereotactic boost irradiation for patients with isolated tumor recurrences in the abdomen and pelvis was done by Wulf et al.12

PATIENT AND METHOD

This pilot study was done for representative patient with cervical squamous cell carcinoma, grade II, in stage: FIGO IB/TNM stage: T1N0M0, previously underwent the radical extended hysterectomy. Combined radiotherapy plan consisted of the WPRT to the total dose of 45 Gy to be given in 24 daily fractions/4 fractions per week and the concomitant HDR-ICBT to the total dose of 24 Gy in 4 fractions/one fraction per week. After application of Fletcher-Suit ovoids (sphere diameter 2 cm), as well as, a rectal marker and Foley catheter in the urinary bladder (filled with 7 cm³ of 60% urographine contrast) following ICRU 38 recommendations9, patient was transferred to radiotherapy simulator (Mevasim S, Siemens, Germany). Reconstruction of catheters and tissues of interest was done from two oblique radiographs (angles: 45 and 315 deg.). Since, only tumour bed and surrounding tissue was present, the Recommendations from GYN GEC-ESTRO Working Group13 were not applied for treatment planning. The ICBT isodose distribution (Fig. 1) was generated by NPS-BPS V.6 (Nucletron BV, The Netherlands) using standard iridium-192 source positions: 2, 4, 6, and 8 in both catheters that enabled full coverage of the referent volume. Volumes encompassed with 300%, 200%, 110%, 100%, 95%, 90% and 80% of the referent ICBT dose were calculated and recorded. The maximum dose to the rectum (point R1 on Fig.1) and urinary bladder (point B on Fig.1) were recorded, too. The patient (representative patient) received planned WPRT and HDR-ICBT and was aware of the study character and completed an inform consent. For preparation of 3D-CRT isodose plan, the representative patient was simulated in supine position, because ICBT was done in that position. The patient’s legs and knees were immobilized using Combifix-Sys (Sinmed, The Netherlands). A computer tomography (CT) scan was obtained using a General Electric CT scanner (GE Medical Systems, Milwaukee, USA), with a flat table-top insert.

FIGURE 1. ISODOSE DISTRIBUTION FOR TWO FLETCHER-SUIT OVOIDS; LATERAL VIEW.

FIGURE 2. DRR WITH THE MARKED CORRESPONDENT STRUCTURES OF INTEREST (RED-PTV; BLUE-LOWER 2/3 OF VAGINA; YELLOW-RECTUM; PURPLE-URINARY BLADDER).

The scanning was done from the L4 vertebral body to 5 cm below the ischial tuberosities with 5 mm slice thickness. The CT data set was transferred to the planning computer. Referent volumes, following ICRU 50 recommendations14, consisted of clinical target volume-CTV (contours of present vaginal tissue - upper 4 cm) and planning target volume-PTV (CTV + 1.0 cm margins in anterior/posterior and caudo/cranial direction, as well as, 0.7 cm in LL dir.). Added margins took into account possible interfraction organ motion and set-up uncertainty. CTV, PTV, the rectum and urinary bladder were contoured on all axial CT slices.
Lateral digitally reconstructed radiograph (DRR) with the marked correspondent structures of interest is shown on Fig. 2.

The planning goal in this study was to achieve maximum therapy dose coverage of the PTV that fully corresponds to the ICBT referent volume (including ovoid spheres volume), while minimizing volume of the rectum and urinary bladder irradiated by CRT. Also, the CRT maximum dose to the rectum and urinary bladder should have to be kept less than or, as least as, those from the ICBT. For treatment of the vaginal cuff and upper third of present vaginal tissue, 3 separate CRT plans were generated using 3D computer planning software (PrecisePlan, Ver. 1.10-102.87, USA). Field arrangements in these plans are shown on Fig. 3. First plan (PLAN1) assumed 4 fieldbox technique: 2 anterior/posterior and 2 latero-lateral fields (Fig. 3A). Second plan (PLAN2) consisted of 4 field oblique technique: 2 anterior (beam angle: 60 and 300 deg.) and 2 posterior direction (beam angle: 120 and 240 deg.) (Fig. 3B). Finally, third plan (PLAN3) was created using 6 fields: 2 latero-lateral fields and 4 oblique field arrangement (Fig. 3C), generated as a mix from PLAN1 and PLAN2. Field with was about 7 cm and height about 5-6 cm for all fields applied. The isocenter was placed in the center of PTV for all plans and inhomogeneity correction was enabled. X-ray beam energy was 10 MV for all beams and MLC was used to shape field forms applied.

No special dose and volume restrains on rectum and urinary bladder were set. Dose volume parameters for PTV were derived from dose volume histograms (DVH), recorded and compared among generated CRT plans. Maximum and average CRT dose for the rectum and urinary bladder were compared to the correspondent ICBT doses. In our opinion, the best CRT plan should have to include both adequate coverage of PTV and, at least, to correspond to ICBT plan when the rectum and urinary bladder doses were considered, as well as, to be relative simple to perform.

RESULTS

The referent therapy volume of about 45 cm$^3$ (vaginal tissue volume of about 37 cm$^3$) received HDR-ICBT therapy dose when the Fletcher-Suit ovoids were inserted. There were substantial volumes that received higher doses during HDR-ICBT due to high dose gradient around ovoid, i.e. outer ovoid surface contact dose could be equal to 3 times referent dose, and about 8 cm$^3$ of vaginal tissue received 2 times referent dose. Volume of about 260 cm$^3$ received one third of referent dose that was comparable to one fraction of external WPRT dose.
Maximum ICBT percentage dose to the rectum and urinary bladder was 101% and 106% respectively, i.e. full therapy dose. This was in agreement with previous studies\textsuperscript{15,16}, that has shown impact of patient individual anatomy on the maximum rectum and urinary bladder dose regardless on reconstruction and optimization technique. We considered that further rectum and urinary bladder dose optimisation, by changing source positions, would have impact on the referent therapy volume.

The PTV dose coverage for all 3 CRT plans was adequate, as it could be seen on Fig. 4A. Precisely, 99.8 % and 99.9 % of PTV was covered by 95% therapy isodose surface with the dose range 94-103 % for PLAN1 and PLAN2, respectively. For PLAN3 99.8 % of PTV was covered by 95% therapy isodose surface with the dose range 94-100 %.

The dose coverage of the rectum is shown on Fig. 4B. For PLAN1 and PLAN2, 13 % and 10 % of the rectum volume was covered by 100% isodose surface, respectively, with maximum dose of 104 %. The dose coverage of urinary bladder is shown on Fig. 4C. About 1.3 %, 3 % and 2.2 % of the urinary bladder volume was covered by 100%, 101 % and 100 % isodose surface, with maximum dose of 101 %, 103 % and 102 % for PLAN1, PLAN2 and PLAN3, respectively. Comparison of the referent volume/PTV dose coverage for HDR-ICBT and all three CRT plans is shown in Table 1, and the maximum rectum and urinary bladder dose in Table 2. All three plans showed almost the same PTV coverage. The PTV coverage homogeneity for PLAN2, shown on Figure 5., seemed slightly better than for other two CRT plans. PLAN 2 showed better CTV coverage than other two plans (Table 1).

**DISCUSSION**

In selected case (FIGO IB), the ICBT referent volume, enveloped with 6 Gy dose surface (Fig. 1), strongly corresponds to the CTV (Fig. 2). This enabled adequate dose-volume analysis for ICBT and CRT plans. In accordance with the ICRU 50 recommendations\textsuperscript{14}, there were no differences among chosen irradiation techniques/plans regarding PTV enveloped in 100% dose. Volumes covered with 95, 90, 80% dose envelope were remarkable lower for ICBT than for applied CRT plans.

Related DVHs showed no major differences in CRT plans. There were no major differences between the maximum dose for the rectum and urinary bladder among all techniques/plans used. Comparative cumulative DVHs for the rectum and urinary bladder showed no differences in high dose region whichever CRT plans have been used. Margin added to CTV (PTV = CTV + margin) did not show impact to the PTV 100% dose coverage for CRT compared to ICBT. On the other hand, the volume that received one third of the referent dose (comparable to one fraction of external WPRT dose) for the CRT was remarkably grater than for ICBT.

However, when change from ICBT to CRT is considered, CRT-PLAN 2 points certain advantages over other two CRT plans. PTV 100% dose coverage in CRT-PLAN2 is slightly lower than for other two CRT plans, while other parameters stay almost the same. In combination with relative performance simplicity, and smaller irradiated volume (IR) than for PLAN1 and PLAN3, PLAN2 can be considered as adequate replacement for ICBT in the adjuvant postoperative treatment of the vaginal cuff and upper third of present vaginal tissue. Since dose weighting of all fields was the same, time-dose-fractionation pattern for the CRT of the vaginal cuff and upper third of present vaginal tissue could be the same as for HDR-ICBT. In this particular case the rectum and urinary bladder would have received the same maximum dose regardless of the irradiation technique applied (HDR-ICBT or CRT).

Dose to the small bowel seemed to be sufficiently low, due to low fields’ localization. Modification of the WPRT fraction size (from 2.00 Gy to 1.8 Gy) would additionally make the CRT of the vaginal cuff and upper third of present vaginal tissue safer. An alternative usage of 6 MV or higher X-ray energy beam may be considered without major changes in field arrangement and time-dose-fractionation pattern.
CONCLUSION

The CRT presented is simple to perform, enable precise delivery of adequate dose to target volume and sufficiently sparing of healthy tissue. All presented CRT techniques could be used in highly selected group of patients (FIGO IB) to boost the vaginal cuff and upper third of present vaginal tissue. The main problem in application of CRT techniques of the vaginal cuff upper third of present vaginal tissue seems to be the precise definition of target volume (PTV) regarding the rectum and bladder movement.

Time-dose-fraction pattern for HDR-ICBT may be safely applied for CRT. Seemingly the answer to a question: Could CRT replace ICBT in the adjuvant postoperative treatment of cervical cancer? is yes. We see no technical, dosimetric and clinical obstacles for such statement when this patient group is considered. In contrary, when patients with advanced disease stages, treated with radical (definitive) radiotherapy are considered, the answer is not so simple, even may be: Should it, that is in agreement with position of Mundt and Roeske.

We strongly believe that investigation of application of IMRT instead of CRT in the investigated group of patients would show improvement of doses to organ of risk. As possible, some questions remained unanswered so further examinations are required.

SUMMARY

KLASIČNA KONFORMALNA RADIOTERAPIJA U POREĐENJU SA INTRAKAVITARNOM BRAHITERAPIjom KOD ADJUVANTNOG POSTOPERATIVNOG LEČENJA KARCINOMA CERVIKSA KOMPARATIVNA DOZIMETRIJSKA STUDIJA

Cilj preliminarne dozimetrijske studije je da ispita priremenost klasične konformalne radioterapije u postoperativnoj radiotherapiji operativnog ožiljka i gornje trećine ostatka vase.


Rezultati i diskusija. Referentni brahiterapijski volumen primio je planiranu dozu zračenja, pri čemu doza zračenja na mokraćnu bežiku i rektum iznosi 101% odnosno 106% ukupne brahiterapijske doze zračenja. Kod sva tri generisana konformalna radioterapija doza na mokraćnu bežiku i rektum iznosi 101% odnosno 106% ukupne brahiterapijske doze zračenja. Kod sva tri generisana plana za konformalno lečenje skoro 100% planiranog volumena mete obuhvaćeno je sa 95% izodoznom površinom, pri čemu je 12-13% tkiva rektuma i 1-3% tkiva mokraćne bežike obuhvaćeno sa 100% izodoznom površi.

Maksimalne doze na rektum i mokraćnu bežiku nisu bile veće od 104% odnosno 101% ukupne terapijske doze zračenja. Uporedjivanjem pokrivenosti planiranog volumena mete i maksimalnih doza na rektum i mokraćnu bežiku kod brahiterapijskog i sva tri generisana konformalna radioterapijska plana nije uočena značajna razlika.

Zaključak. Klasična konformalna radioterapija bi se mogla uzeti u obzir kao odgovarajuća zamena za intrakavitarnu brahiterapiju kod postoperativnog lečenja operativnog ožiljka i gornje trećine ostatka vase.

U ovom slučaju, način frakcioniciranja kod brahiterapijskog tretmana bi se bezbedno mogao primeniti i kod klasične konformalne radioterapije.

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OBSERVATION

Intracavitory brachytherapy in postoperative combined radiotherapy in patients with cervix uteri carcinoma is standard, efficient and relatively safe treatment modality. In cases when intracavitory brachytherapy could not be applied, the total dose delivered by external beam radiotherapy could be elevated with a moderate risk of disease control failior followed by higher risk of postirradiation sequel occurrence. In these cases, classical conformal radiotherapy confined to the brachytherapy target volume could be therapy method of choice. Comparing of dosimetric characteristics for intracavitory brachytherapy of vaginal cuff and upper third of vagina with corresponding dosimetric parameters for conformal radiotherapy, authors are in position to conclude that in these cases, intracavitory brachytherapy could be efficiently swept with conformal radiotherapy, without additional risk for patient. Fractionation scheme could be preserved, too.

NOTE

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