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Chapter

Dosimetric and Radiobiological Evaluation of Combined Radiotherapy of Cervical Cancer Based on the VMAT Technique

Evgeniia Sergeevna Sukhikh and Leonid Grigorievich Sukhikh

Abstract

A dosimetric and radiobiological investigation of the possibility to replace the traditional combined radiation therapy (3D-CRT + high-dose-rate brachytherapy (HDR-BT)) of cervical cancer with the following combinations, ^{60}Co + VMAT, 3D-CRT + VMAT, and VMAT + VMAT, without change of total course dose and the number of fractions is described. For the investigation, the data of 11 patients with a diagnosis of cervical cancer (stages $T_{2b}N_xM_0$ and $T_3N_xM_0$) who received a course of combined radiotherapy was used. The 3D-CRT + high-dose-rate brachytherapy (HDR-BT) combination of dose delivery techniques was used as the basic one. The following fractionation regimes for combined radiotherapy were simulated: external beam radiation therapy (RT) (EBRT) of the first stage, total dose 50 Gy and fractional dose 2 Gy (25 fractions), and the second stage—total dose 28 Gy and fractional dose 7 Gy (4 fractions). Total combined RT course dose amounted to EQD_2 = 89.7 Gy. Simulation results show that there is a technical possibility of replacing the second stage of combined RT of cervical cancer by EBRT based on the VMAT technique. Implementation of the VMAT technique allows increasing the uniformity of irradiated volume coverage compared with traditional high-dose rate. While using the VMAT technique, the tolerant levels of organs at risk are not exceeded.

Keywords: intracavitary brachytherapy, external beam radiation therapy, cervical cancer, intensity-modulated radiotherapy, combined radiotherapy

1. Introduction

In the treatment of cervical cancer, the main methods include surgical treatment, chemotherapy, and radiation therapy (RT), which can be used either separately or in combination with each other [1–3]. The combination of two consecutive stages of irradiation with different dose delivery techniques, i.e., external beam radiotherapy (EBRT) and intracavitary high-dose-rate brachytherapy, is called combined RT [1–6]. At the first stage of combined RT, the clinical tumor volume and regional lymph nodes are irradiated in total doses up to 44–50 Gy with fraction dose equal to 2 Gy depending on the widespread nature of the process. At the second stage of the combined RT, the clinical tumor volume is irradiated in the

mode of dose boost when the dose per fraction is increased to 6–7.5 Gy delivered in 4 or 5 fractions resulting in the total dose equal to 28–30 Gy. The goal of the total combined RT course is to achieve a total EQD_2 dose equal to 90 Gy delivered to the clinical tumor volume in less than 50 days of treatment [2–7].

From the point of view of dose delivery technologies, the first stage of combined RT is EBRT based on one of the methods: conventional RT, 3D conformal RT (3D-CRT), or methods with intensity-modulated radiation (IMRT and VMAT) [8, 9]. The photon radiation sources used are gamma apparatus with ^{60}Co sources and photon energy of 1.25 MeV or linear electron accelerators (linacs) with a photon energy equal to 6 or 10 MeV. When using conventional irradiation with gamma apparatus, there are difficulties in creating a conformal dose field that reduces the dose loads on critical organs, and, consequently, it is hard to improve the uniformity of coverage with a dose of the target volume; therefore, this technique, at present, is not very popular. However, from the point of view of operation and maintenance, the gamma apparatus is simpler and more convenient than linacs. According to IAEA, there are 240 gamma apparatuses in Russia and only 197 linacs. For comparison, in Germany, there are 523 linacs and only 20 gamma apparatuses [10]. From this point of view, the development of techniques for the best possible use of gamma apparatuses is an important task for Russia and other developing countries.

The second stage of combined RT is usually implemented using intracavitary HDR-BT based on gamma-emitting radionuclides ^{60}Co or ^{192}Ir [2–7]. The advantages of BT are the possibility of delivering a high dose to a clinical tumor volume with a relatively low dose load on OARs (bladder and rectum). Most of the radiotherapy departments in Russia are equipped with equipment that allows performing BT in HDR mode. However, BT has several significant drawbacks compared with EBRT. The main one is the substantial heterogeneity of the coverage of the clinical target volume, where doses in the range from 90 to 300% of the prescribed dose are delivered. BT is also a less comfortable procedure for patients because they experience painful sensations when inserting implants into the uterine cavity, which requires anesthesia. Dosimetric planning of BT needs conduction of topographic preparation using CT or magnetic resonance tomography (MRI) with implants inserted followed by a tight vaginal tamponade, to prevent their possible displacement inside the patient during transportation to the treatment table [2–3, 5]. Optimization of the dose distribution in BT can be regulated only by introducing sectoral blocks into a Manchester (Fletcher)-type applicator (nozzle with an intra-uterine endostat) or additional needles for interstitial implantation, which is even more complicated and requires anesthetic management. On the other hand, with BT, no additional margin from the clinical tumor volume (CTV) is required, which should consider the inaccuracy of dose delivery from fraction to fraction, i.e., creating a planned target volume (PTV), which is mandatory for EBRT. Because irradiation occurs from the inside, and not from the outside, in the case of movement of the organ with the implant inserted, the implant will move along with the organ [2–6].

The development of EBRT technologies has led to the widespread implementation of IMRT and VMAT dose delivery techniques, which allow delivery of single doses of up to 7 Gy to a target without exceeding tolerant levels for OARs. The VMAT method with large dose fractions is widely used, for example, in the treatment of prostate carcinomas [11–22]. The first investigations devoted to the study of the possibility of replacing BT with EBRT during the second stage of combined RT started in 2012 [18]. The goal of such investigations was to change BT with EBRT in hypofractionation mode for patients for whom BT was not possible for various reasons.

The aim of this work was to carry out a dosimetric and radiobiological planning of the replacement of traditional combined radiation therapy (3D-CRT + HDR BT) by combinations of ^{60}Co + VMAT, 3D-CRT + VMAT, and VMAT + VMAT while preserving the value of the total dose delivered and the number of fractions. The paper presents a comparison of radiation loads on tumor volumes and critical organs using different combinations of irradiation at the first and second stages, namely, 3D-CRT + HDR BT, conventional RT ^{60}Co + VMAT, 3D-CRT + VMAT, and VMAT + VMAT. The study was conducted using tomographic data of 11 patients with cervical cancer.

2. Combined radiotherapy

Anatomical data of 11 patients with cervical cancer (squamous carcinoma) stages $T_{2b}N_0M_0$ (six patients) and $T_3N_0M_0$ (five patients) were used for investigation. The patients received no surgery due to the fact that for stages T_2 and T_3, the surgery is not the best treatment [13]. The patients were selected randomly between the patients who have received combined radiotherapy for half a year at Tomsk Regional Oncology Center. Patients' age was in the range from 55 to 57 years. All patients had received courses of standard combined radiotherapy using EBRT with 3D-CRT (Elekta Synergy linac, 10 MeV, AB Elekta) or conventional radiotherapy based on ^{60}Co (Theratron Equinox 100) followed by HDR BT (Multisource HDR, Bebig). The prescribed total dose for EBRT amounted to 50 Gy given in 25 fractions (2 Gy/fr). During the HDR BT, the total dose amounted to 28 Gy given in 4 fractions (7 Gy/fr). The total course dose assuming $\frac{a}{b} = 10$ Gy for the tumor was equal to BED = 107.6 Gy and EQD$_2$ = 89.7 Gy, which agreed with Refs. [2–7]. All patients received concomitant cisplatin chemotherapy weekly.

Different irradiation techniques were compared for dosimetric investigation. During the first stage of combined radiotherapy, we used conventional RT with ^{60}Co, 3D-CRT using 10 MeV photons, and VMAT technique with 10 MeV photons. The second stage modalities included either HDR BT or VMAT with 10 MeV photons. The total dose values, as well as the fractionation regimen, were the same as during irradiation.

The OARs included bladder and rectum. The irradiation constraints are listed in **Table 1**. During the study, we assumed that $\frac{\alpha}{\beta} = 8$ Gy for the bladder and $\frac{\alpha}{\beta} = 3.9$ Gy for the rectum [11]. The data were taken from the QUANTEC protocols [23, 24], RTOG 0415 [25], GYN GES ESTRO [4], and other recommendations.

Organ at risk	QUANTEC [12, 13]	RTOG 0415 [14]	EBRT+BT
Rectum	$V_{50} < 50\%$	$V_{59} < 50\%$	$D_{2cc} < 75Gy$ [3, 15]
	$V_{60} < 35\%$	$V_{64} < 35\%$	$D_{2cc} < 70Gy$ [2, 4]
	$V_{65} < 25\%$	$V_{69} < 25\%$	
	$V_{70} < 20\%$	$V_{74} < 15\%$	
	$V_{75} < 15\%$		
Bladder	$V_{65} < 50\%$	$V_{64} < 50\%$	$D_{2cc} < 90Gy$ [2–4, 15]
	$V_{70} < 35\%$	$V_{69} < 35\%$	
	$V_{75} < 25\%$	$V_{74} < 25\%$	
	$V_{80} < 15\%$	$V_{79} < 15\%$	

Table 1.
The tolerant levels of critical organs for all radiotherapy courses which include EBRT and BT or only the EBRT for two stages based on QUANTEC [23, 24], RTOG 0415 [25], GYN GES ESTRO [4], and other recommendations [26].

The data in **Table 1** are presented as $V_x < y\%$, which means that the organ volume equal to y% of the total volume should not receive a dose greater than x Gy EQD_2. Late third-grade radiation reactions are possible for the bladder if each of these levels is exceeded. For the rectum, second-grade (<15%) and third-grade reactions (<10%) are possible if the levels are exceeded [23, 24]. The data presented in **Table 1** for EBRT are taken from the statistics of radiation complications obtained during the treatment of prostate carcinomas. Because EBRT is widely used to treat this disease, we used these data, while we found no data for EBRT used along with treatment of cervical cancer due to the extremely rare use of EBRT for the second stage of combined radiotherapy.

2.1 The first-stage EBRT

Patient data for the first stage EBRT were obtained using the CT Toshiba Aquilion (Toshiba, Japan). The scanning step was equal to 3 mm. Patients were in the supine position due to the better immobilization possible [2–5]. A contrast substance was used during topometric preparation for the better identification of structures of interest: vessels, involved lymph nodes, tumor, bowel, bladder, and vagina. The rectosigmoid and the bladder were treated according to international recommendations [2–5] to minimize internal motion and ensure reproducibility during dose planning and treatment.

Because of the use of CT, only the CTV-T included the whole uterus. The PTV-T safety margin was approximately equal to 10 mm to ensure full coverage of the CTV during treatment course [2–5].

The pelvic lymph node (CTV-N) region included parametrial, para-rectal, internal iliac, external iliac, presacral, and iliaca communis. PTV-N included CTV-N plus an additional 10 mm margin. In the case of anatomical barriers such as the bone or uninvolved muscle/fascia, a smaller margin value was used [2–5].

PTV-T and PTV-N were joined to PTV-TN, and the prescription was defined for PTV-TN as follows: D95 ≥ V95% and D107 ≤ V2%. The average volumes amounted to CTV-T = 198 ± 120 cm^3, PTV-T = 475 ± 180 cm^3, CTV-N = 334 ± 140 cm^3, and PTV-TN = 1323 ± 300 cm^3.

The first-stage EBRT dosimetric treatment planning was carried out in the XIO dosimetry planning system (version 5.1, Elekta AB) using the conventional RT ^{60}Co with Theratron Equinox 100 gamma apparatus and 3D-CRT technique at the Elekta Synergy linac at 10 MeV. Dosimetric planning of conventional RT ^{60}Co and 3D-CRT was carried out using the superposition calculation algorithm based on modified four-field irradiation. For conventional RT, lateral irradiation on the right and left was complemented by the "field-in-field" irradiation technique and the distribution of weight dose loads to improve the target coverage. For 3D-CRT, the upper and lower fields were divided into subfields with turns at gantry angles of 340° and 20° to reduce the radiation load on the OARs while keeping an acceptable level of target coverage.

The first-stage EBRT dosimetric treatment planning based on the VMAT technique was carried out using the Monaco dosimetric planning system (v. 5.10.04, Elekta) at the Elekta Synergy linac at 10 MeV. For the VMAT technique, the inverse algorithms based on the Monte Carlo method were used. The dose delivery was realized using three full arches. The grid step was 0.3 cm, the minimum width of the segment was 1 cm, and the uncertainty of the entire calculation was 0.8% during the dose simulation.

In **Table 2**, one can see the results of dosimetric planning of the first-stage EBRT averaged over all patients.

Dose, %	^{60}Co, V%	3D-CRT, V%	VMAT, V%
90	97.9 [96.9–99.0]	99.2 [99.0–99.4]	98.8 [98.4–99.2]
95	89.0 [85.6–92.3]	95.7 [95.2–96.2]	97.0 [96.1–97.9]
98	72.7 [64.0–81.4]	87.2 [85.3–89.0]	93.5 [91.5–95.5]
99	62.1 [50.8–73.4]	81.5 [78.5–84.4]	90.4 [87.0–93.7]
100	47.9 [34.8–60.9]	71.8 [66.5–77.1]	84.5 [78.9–90.1]
110	0 [0–0]	0 [0–0]	1.5 [0–4.4]

Table 2.
PTV-TN dose coverage for the first stage of combined RT.

From **Table 2**, one can see that, as expected, the use of a more complex and higher gradient dose delivery technique (VMAT) leads to an increase in the irradiation of the tumor and the regional-iliac lymph nodes. The VMAT method allows reaching the level of coverage of 95% of the prescribed dose delivered in 97% of the irradiation volume, which can be considered a very good indicator of the coverage uniformity. It should be noted, however, that even the use of a conventional RT ^{60}Co on a gamma device allows one to confidently exceed the coverage level of 90% of the prescribed dose delivered to 90% of the irradiation volume, ensuring even the level of 90% of the dose to 97.9% of the volume. At the same time, for 95% of the prescribed dose, the average irradiated volume is 89%, which should also be recognized as a good result for the conventional ^{60}Co technique. The 3D-CRT technique allows obtaining a coverage level of 95–95%, which fully satisfies the prescription.

2.2 HDR for the second stage

To prepare for HDR BT, the patients were scanned using the CT scanner in a supine position with inserted Manchester-type CT-compatible implants (rigid direct central intrauterine endostat and two rigid lateral intrauterine endostats with ovoid) that were sufficiently fixed.

CT scans give poor visualization of the tumor, which is why the whole uterus (whole cervix) was chosen as CTV for BT (CTV-B). No additional safety margins are needed to take into account internal movement during BT because the applicator moves together with the CTV [2–5]. Although there are some uncertainties for setup (applicator reconstruction), these seem to be rather negligible, if the systematic error can be kept below 2 mm and the slice thickness below 5 mm (random error) [3]. In the present study, we assumed that no margins should be added to CTV-B, resulting in CTV-B = PTV-B.

For compensation of possible changes of target and OAR localization with respect to the position of the applicator, each BT implant insertion was followed by a new CT study with the applicator in situ and a new dose plan calculation. Contouring for both CTV and OARs was performed for each insertion/implant of BT applicators.

The treatment planning goal for HDR BT was prescribed to deliver more than 90% of the dose to 90% of the volume (D90% ≥ V90%). DVHs were used for the analysis of the planning results.

The dose limitations to OARs were set for the bladder and rectum according to the limits listed in **Table 1**. The whole organs were contoured based on CT images without division on parts.

For OAR, it was important to specify the position of the hot spots in the bladder (D_{2cc}) because this small volume may have an impact on the clinical outcome, and

so delineation of full organs based on CT images and dose was estimated in any location whose accordance did not exceed the tolerance level (see **Table 1**).

The dosimetric planning of the HDR BT of the second stage was carried out using the HDRplus 3D BT dose-planning system (version 3.4) for the MultiSource HDR apparatus with ^{60}Co source (Bebig, Germany).

During the planning procedure, the implant was carefully reconstructed, and the conventional standard loading pattern matching the prescribed dose to point A was applied. From this starting point, dose optimization was performed with the goal of adapting the dose to the CTV-B. The optimization of CTV-B dose coverage and OAR dose constraints was carried out using the following steps:

- Dose point optimization

- Manual dwell time or dwell weight optimization

- Graphical optimization ("dose shaping") combined with manual verification and adjustments for unnecessarily large deviations from standard loading patterns

There is the task of summation of the doses from the first-stage EBRT and the second-stage HDR BT. This was done based on the assumptions given by GYN GEC ESTRO recommendation [3]. According to Ref. [3], it is assumed that CTV and OARs receive the full dose from the EBRT course. Thus, it was assumed that the dose in the small volumes of interest for BT (anterior-lateral walls of the rectum and sigmoid, posterior-inferior wall of the bladder, and wall of the vagina adjacent to macroscopic disease) receives the EBRT prescribed dose for CTV-T and CTV-N.

2.3 VMAT for the second stage

The VMAT technique with three full arches was used as EBRT of the second stage. The dosimetric planning was carried out using the same CT scans as for the first-stage EBRT because no specific patient scanning was done after the first-stage EBRT. The PTV tumor for the second stage was assumed to be equal to CTV-T of the first stage plus 5 mm safety margin. In our opinion, it is sufficient estimation, taking into account the fact that the tumor shrinks after the first-stage EBRT.

The second-stage VMAT dosimetric planning was carried out using the Monaco dosimetric planning system (v. 5.10.04, Elekta) at the Elekta Synergy linac at 10 MeV. For the VMAT technique, the inverse algorithms based on the Monte Carlo method were used. The dose delivery was realized using three full arches. The grid step was 0.3 cm, the minimum width of the segment was 1 cm, and the uncertainty of the entire calculation was 0.8% during the dose simulation.

2.4 Summation of the first- and second-stage results

When planning a combined RT in the EBRT + BT format, the question of DVH summation arises because the DVHs were calculated by different planning systems that are completely incompatible. Therefore, we assumed that during the first stage, the CTV-T was irradiated uniformly up to the prescribed dose of 50 Gy. The DVH from the second-stage HDR BT was added to that dose value [2–6]. The damage to the OARs was assessed by the criterion of the total EQD_2 delivered to 2 cm^3 from both courses of EBRT and HDR BT because the summation of DVHs for OARs is illegal because of OAR shape changes while inserting the implants [2–5, 18]. For

combined therapy in the EBRT + VMAT format, the EQD_2 DVHs from the EBRT and VMAT course were summed up for CTV-T and OARs.

3. Results and discussion

Figure 1 shows examples of the planned dose distribution for the first and second stages of combined radiotherapy.

Let us further consider the results of the total combined RT course. **Figure 1** shows an example of DVHs for CTV-T, for one of the patients. **Figure 2** shows all considered irradiation combinations (3D-CRT + HDR-BT, ^{60}Co + VMAT, 3D-CRT- + VMAT, VMAT + VMAT).

In **Figure 2**, one can see that with the use of HDR BT, the dose distribution over the target volume is nonuniform, i.e., there are proportions of the volume of radiation that receive doses substantially higher than prescribed.

Table 3 shows the resulting dose coverage for the total treatment course as the mean value obtained for 11 patients and a confidence interval [27].

From **Table 3**, one can see that combined RT based on HDR BT results in 90% of prescribed dose delivered to 95.9% of the target volume, which is a rather good result. However, HDR BT results in irradiation of the significant target volumes by doses that are significantly higher than the prescribed dose. In this case, 150–200% of the prescribed dose was delivered to 44.6 and 19.7% of the volume, respectively.

The use of VMAT as the second stage of the combined RT significantly improves the situation. Regardless of the dose delivery technique used during the first stage dose, 95% of the prescribed dose is delivered to 97% of the volume. The hot spots do not exceed 110% of the prescribed dose delivered in less than 9% of the volume for the VMAT + VMAT combination. It should be noted that even the use of the conventional RT based on ^{60}Co in combination with VMAT allows one to achieve such a high level of target coverage.

Figure 3 shows examples of bladder and rectum DVHs in the case of the VMAT technique used as the second stage of combined RT. Statistical data on the irradiation of critical organs are given in **Table 4** for the bladder and in **Table 5** for the rectum.

From **Table 4**, one can see that the dose load on the bladder using ^{60}Co + VMAT or VMAT + VMAT combinations allows meeting the tolerant levels, avoiding third-degree radiation complications (see **Table 1**). For the combination of 3D-CRT + VMAT, there is a slight exceeding of the tolerant levels for the dose levels of 65 Gy and 70 Gy. This dose overload is caused by the high level of the dose coverage during the first stage when 95% of the prescribed dose was delivered to 95% of the volume (see **Table 2**). In the case of conventional irradiation, the dose load meets the tolerant levels because the first-stage dose coverage is lower than the 95–95% prescription. The use of VMAT techniques reduces the dose loads due to modulation of the radiation intensity.

According to the criterion of the maximum dose delivered to the volume of 2 cm^3 of the bladder, all the methods of dose delivery meet the constraints, although the best result was obtained with the use of HDR BT. When using VMAT + VMAT technology, there are individual cases exceeding the tolerant dose of 90 Gy per 2 cm^3 volume, which is caused by escalation of the dose in the target. In this case, it is difficult to judge whether this will lead to radiation complications because the irradiation levels of parts of the bladder do not exceed the tolerant levels of QUANTEC.

Table 5 shows the radiation loads on the rectum for the different combinations of dose delivery techniques. From **Table 5**, one can see that the use of the VMAT + VMAT combination does not exceed the tolerance levels established by the
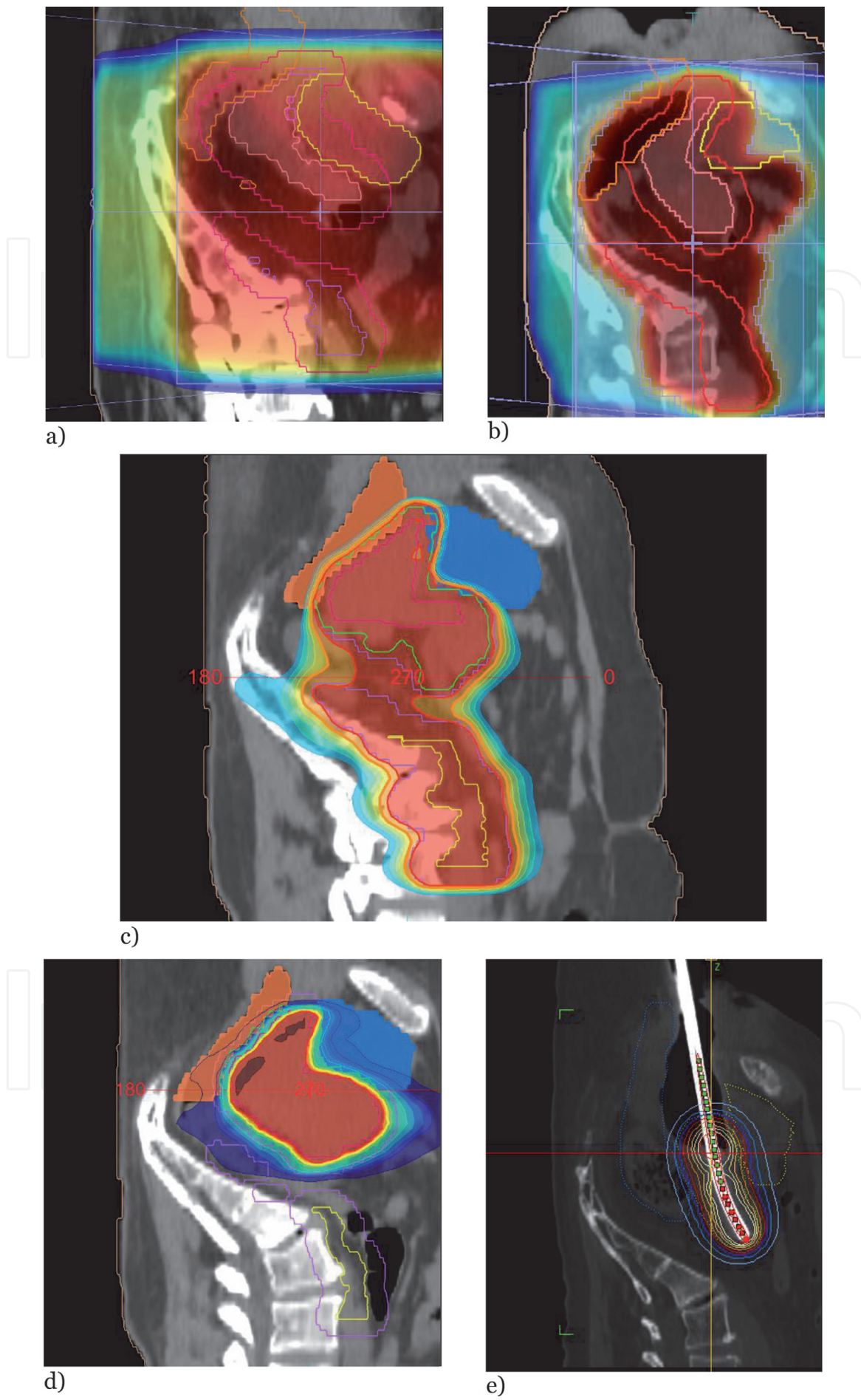
Figure 1.
Dose distributions of treatment plans: (a) ^{60}Co, (b) 3D-CRT, (c) VMAT for the first stage, (d) VMAT for the second stage, and (e) HDR.
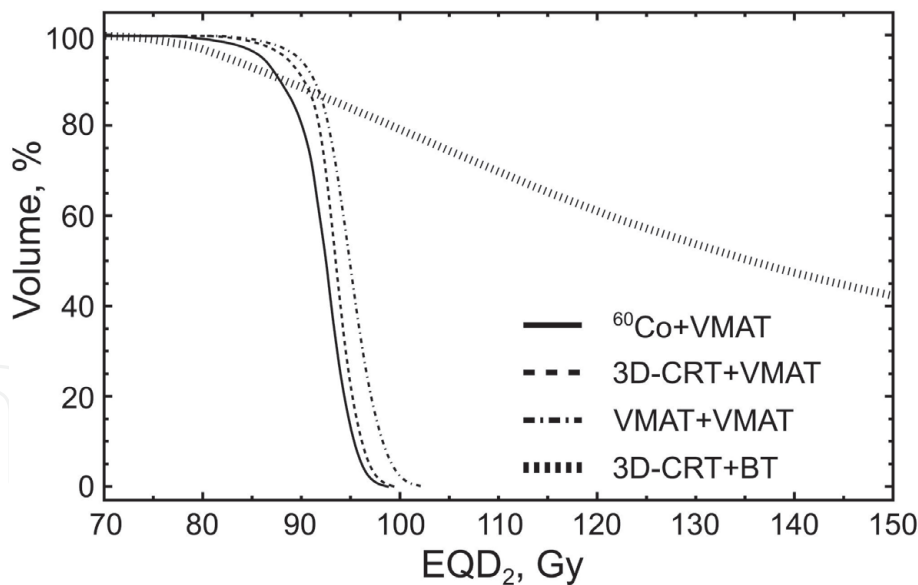
Figure 2.
Example of DVHs calculated for target volume for different variants of combined therapy at prescribed dose EQD2 = 89.7 Gy.

Dose, %	3D-CRT + BT, volume %	^{60}Co + VMAT, v %	3D-CRT + VMAT, volume %	VMAT+VMAT, volume %
90	95.9 [94.8–96.9]	99.3 [98.9–99.6]	99.6 [99.4–99.8]	99.7 [99.6–99.8]
95	91.8 [90.5–93.2]	97.1 [96.1–98.0]	98.0 [97.4–98.5]	98.8 [98.4–99.3]
98	88.8 [87.2–90.3]	92.4 [90.4–94.3]	94.7 [93.3–96.0]	97.0 [96.1–97.9]
99	87.7 [86.1–89.4]	89.4 [86.8–91.9]	92.5 [90.6–94.4]	95.8 [94.6–97.0]
100	86.7 [85.0–88.4]	85.0 [81.4–88.7]	89.2 [86.6–91.8]	93.9 [92.2–95.5]
110	75.7 [73.3–78.2]	2.1 [0.9–3.4]	2.6 [1.2–4.1]	8.8 [5.4–12.1]
150	44.6 [41.8–47.4]	—	—	—
200	27.4 [25.2–29.6]	—	—	—
250	19.7 [17.7–21.6]	—	—	—

Table 3.
Target coverage for different courses of combined RT.

QUANTEC protocol. In the case of ^{60}Co + VMAT and 3D-CRT + VMAT combinations, there is an exceeding of tolerant levels. In these cases, 60 Gy EQD$_2$ is delivered to more than 35% of the volume and 50 Gy EQD$_2$ to more than 50%. This can lead to late second- and third-grade complications. Such results appear due to large irradiation volumes. During the first-stage irradiation, PTV is close to the anterior rectal wall, which leads to its irradiation. The use of the VMAT technique allows reducing the radiation load during the implementation of high-gradient plans. To reduce the exposure of the rectum, it is necessary to reduce the margin between
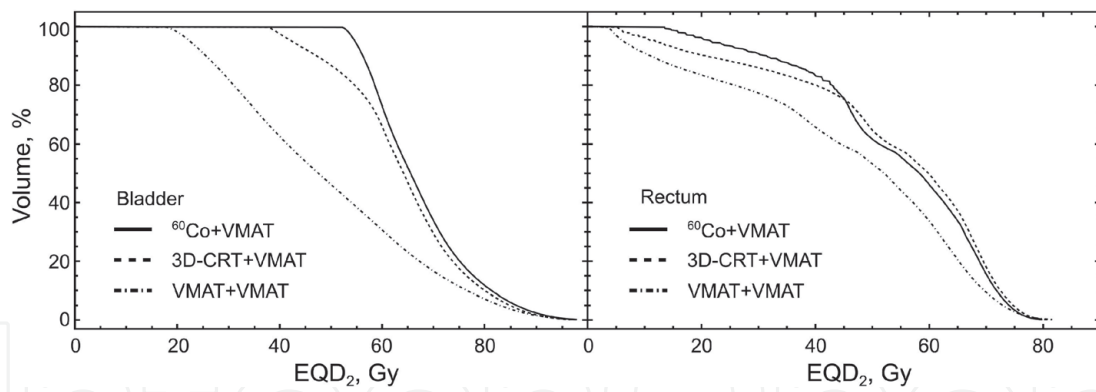
Figure 3.
Example of DVHs calculated for bladder and rectum for one of the patients.

EQD$_2$/volume % QUANTEC	3D-CRT + BT, volume %	^{60}Co + VMAT, volume %	3D-CRT + VMAT, volume %	VMAT+VMAT, volume %
80 Gy/15%	—	12.1 [7.1–17.0]	12.7 [7.4–18.0]	11.8 [7.0–16.6]
75 Gy/25%	—	19.7 [13.6–25.9]	23.3 [15.3–31.4]	18.6 [12.5–24.7]
70 Gy/35%	—	29.1 [22.1–36.1]	37.0 [26.5–47.5]	26.0 [19.1–32.8]
65 Gy/50%	—	40.4 [31.4–49.5]	52.3 [41.4–63.2]	33.5 [26.2–40.8]
Volume	3D-CRT + BT, EQD$_2$, Gy	^{60}Co + VMAT, EQD$_2$, Gy	3D-CRT + VMAT, EQD$_2$, Gy	VMAT+VMAT, EQD$_2$, Gy
2 cm^3 < 90 Gy EQD$_2$	82.2 [74.6–89.8]	87.2 [84.4–90.0]	87.7 [85.0–90.4]	88.9 [85.8–92.2]

Table 4.
Bladder dose loads for different courses of combined RT.

EQD$_2$/volume % QUANTEC	3D-CRT + BT, volume %	^{60}Co + VMAT, volume %	3D-CRT + VMAT, volume %	VMAT+VMAT, volume %
75 Gy/15%	—	2.6 [0.9–4.3]	2.5 [0.9–4.0]	2.1 [1.2–3.0]
70 Gy/20%	—	9.4 [3.9–15.0]	8.5 [3.3–13.7]	6 [3.4–8.6]
65 Gy/25%	—	22.3 [12.4–33.3]	20.3 [9.8–30.7]	13.2 [7.8–18.5]
60 Gy/ 35%	—	42.1 [30.1–54.2]	38.4 [25.5–51.3]	22.6 [15.4–29.9]
50 Gy/ 50%	—	77.3 [67.9–86.8]	73.3 [65.0–81.7]	44.3 [35.4–53.1]
Volume	3D-CRT + BT, EQD$_2$, Gy	^{60}Co + VMAT, EQD$_2$, Gy	3D-CRT + VMAT, EQD$_2$, Gy	VMAT+VMAT, EQD$_2$, Gy
2 cm^3 < 75 Гр EQD$_2$	70.9 [67.1–74.7]	71.9 [69.5–74.4]	72.4 [69.9–74.9]	71.5 [69.3–73.7]

Table 5.
Rectum dose loads for different courses of combined RT.

PTV-T and CTV-T for the displacement of organs, which requires fixing the position of the target, the rectum, and the stability of the filling of the bladder.

In **Table 5**, one can see that there is no exceeding of the rectum tolerant level by 2 cm³ parameter for any combination of the techniques simulated. It should again be noted that the criterion of 2 cm³ has a much lower accuracy than the DVH estimate.

The combined RT for cervical cancer can be realized using different combinations of the first- and second-stage irradiation techniques. The efficiency of the total course can be analyzed using two parameters, which are dose coverage of the target (both tumor and nodes during the first stage) and the dose loads on the OARs.

Thus, from the point of view of target coverage, the ^{60}Co + VMAT and 3D-CRT + VMAT combinations are very similar because with ^{60}Co + VMAT, coverage is 95% of the prescribed dose, 97.1% of the volume, and with 3D-CRT + VMAT, 95% of the dose, 98% of the volume. Unfortunately, the use of the gamma apparatus loses in the first stage of the combined RT because the coverage of the volume of PTV is only 95% of the dose—89% of the volume—and with 3D-CRT 95% of the dose, 95.1% of the volume. Despite this, it can be pointed out that using a gamma apparatus for EBRT can be effective for a combined RT when followed by VMAT, providing good coverage of the target with a 10–15% chance of late second- and third-grade complications to the rectum and bladder. When using the VMAT + VMAT combination, a coverage level of 98–97% is achieved without exceeding the tolerant levels for all critical organs.

Obviously, the values of radiation loads will depend on the accuracy of contour creation for both the target and for critical organs, as well as the offset space used. Therefore, the results of irradiation substantially depend on the degree of immobilization of the patient, which includes maintaining the mutual position of the internal organs by introducing a Foley catheter, as well as minimizing and controlling their displacement during breathing (e.g., abdominal press).

The main advantage of using the VMAT technique for the second stage of combined RT is to simplify the treatment procedure, to reduce the painful sensations typical for BT in the process of topometric preparation and treatment, as well as to reduce the time of the irradiation session. When using VMAT technology, the radiotherapist's labor costs (no need for implants) are reduced, but the work of the topometrist (the need for more accurate contouring) and the medical physicist (more complex dosimetric planning and the need for dosimetry quality assurance) increases.

One of the effective ways to implement the use of the VMAT technique for the second-stage irradiation is to use both CT and MRI for the topographic preparation of the patient after the first-stage irradiation.

4. Conclusion

In the considered examples, it can be seen that the use of the VMAT dose delivery technique for the second stage of combined RT of cervical cancer allows a significant increase in the irradiation uniformity, to exclude overexposure of large volumes with high doses (more than 115% of the prescribed dose) and to deliver the prescribed dose to the target with a high coverage level (95.8% of the target volume can be irradiated with a dose higher than 99% of the prescribed dose), not exceeding the dose loads to OARs.

In Tomsk Regional Oncology Center, HDR brachytherapy is not fully equipped by implants of different types needed for effective treatment of the cervical cancer. Also we do not have the equipment for the gynecological interstitial brachytherapy

that significantly limits our possibilities. At the same time, Tomsk Regional Oncology Center has good competences in the EBRT VMAT treatment planning, QA, and delivery. The results of presented study show that the VMAT dose delivery could be effective enough to replace HDR brachytherapy in some case.

There are different patients that could benefit from the change of HDR BT to VMAT. These are the patients with challenging cervical dilation, perforation risk, patients with asymmetric tumor invasion, and patients with personal reasons to avoid the BT procedure.

The results of this study that have shown the technical possibility of HDR BT replacement were the basis to start this method in the clinical practice. These days, five patients are treated with VMAT for the second stage of combined radiotherapy with cisplatin chemotherapy. The patients chosen have intolerance to procedure, asymmetric tumor invasion, and religious contradictions to the intracavitary BT.

Due to the focus of the present study on the dosimetric and radiobiological evaluation of the radiotherapy using different dose delivery techniques, we cannot discuss the advantages of the different treatment methods that include surgery, adjuvant or neoadjuvant therapy, etc. These treatment modalities should be carefully examined for each patient. In the case when RT can be performed, the HDR BT could be examined to the possibility to be replaced by the VMAT technique. In this case, it does not matter which treatment modality is used, postsurgery + EBRT, chemotherapy + EBRT, etc.

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