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ORIGINAL ARTICLE

Dosimetric study of a hybrid plan technique for external beam radiotherapy in patients with cervical cancer

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Abstract
The aim of this study was to investigate the effect of a hybrid technique which results from combining intensity modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) for the treatment of cervical cancer patients. Plans made with the hybrid technique and pure IMRT and VMAT were retrospectively compared in 20 patients with cervical cancer at different stages. All plans were made using the same contours based on the original computed tomography (CT) scans. Conformity (CI) and homogeneity (HI) indices of the planning target volumes (PTVs) were calculated for each technique in order to evaluate plan quality. All techniques were compared in terms of dose to organs at risk (OARs), number of monitor units (MUs) and treatment time. It turned out that plans made with the hybrid technique had improved dose conformity and homogeneity compared to plans made only with IMRT and VMAT ($p < 0.001$). Regarding the OARs, the maximum dose (D_{max}) delivered to the bladder, rectum and femoral heads was lower for the hybrid plans compared to the IMRT and VMAT plans ($p < 0.001$). The volumes irradiated to doses of 50 Gy (V_{50Gy}) for rectum, bladder and bowel were lower for the hybrid plans ($p < 0.001$, $p = 0.002$). Furthermore, the treatment time and MU values for the hybrid plans were found to be between of the values for the IMRT and VMAT plans. It is concluded that, as compared to IMRT and VMAT plans, the hybrid plan technique allowed a better conformity and homogeneity for the dose distribution in the PTV and a dose reduction to the OARs.

Keywords Cervical cancer · Radiotherapy · IMRT · VMAT · Hybrid

Introduction

Cervical cancer is a neoplasm that represents a serious threat to the lives of women, being the second most common type of diagnosed cancer. About 90% of deaths related to this disease occur in developing countries (Vaccarella et al. 2017).

Radiation therapy (RT) is an essential treatment option for the management of cervical cancer and it is used in up to 60% of patients (Guy et al. 2016). Previously, 3-dimensional conformal radiation therapy (3D-CRT) was the standard treatment for cervical cancer. However, this technique was not capable of significantly reducing the dose to organs at risk (OARs) (Wu et al. 2019). Technological advances have allowed for the development of superior treatment techniques for the protection of OARs. Intensity modulated radiation therapy (IMRT) (Bucci et al. 2005) was an important breakthrough, since it allows delivery of radiation to the tumor region to be treated while maximizing the protection to the OARs (Randall and Ibbott 2006; Van Rij et al. 2008; Korreman et al. 2010). Despite the advantages mentioned above, the use of IMRT results in certain drawbacks, namely, prolonged treatment duration due to the high number of required monitor units (MUs) (Verbakel et al. 2009), and the presence of scattered radiation from the collimator which could result in an increased risk of secondary cancers (Hall 2006). Volumetric modulated arc therapy (VMAT) is another intensity modulated technique (Otto 2008) where the movement of the gantry and the multi-leaf collimator (MLC) is performed simultaneously during irradiation while the dose rate is varied. VMAT has been used for the treatment of a wide variety of malignant tumors (Teoh et al. 2011; Quan et al. 2012; Yin et al. 2012; Akbas et al. 2019) and produces almost identical homogeneity and conformity in comparison to IMRT, but with less MUs and treatment time (Hall

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2006; Verbakel et al. 2009). There are many works where the dosimetric differences between IMRT and VMAT were compared for cervical cancer patients (Sharfo et al. 2015; Deng et al. 2017). Furthermore, these two techniques can be combined to treat certain types of tumors. This combination is called "Hybrid plan" (Lin et al. 2015; Akbas et al. 2019) because in some cases, neither the IMRT nor the VMAT are sufficient to obtain the desired result. The hybrid plan technique has the potential benefit of obtaining better dosimetric outcomes compared to IMRT and VMAT, because it uses the advantages present in both techniques. However, to the best of the authors' knowledge a hybrid plan has not yet been implemented in cervical cancer patients. The present study was designed to compare the hybrid plan technique with plans made with pure IMRT and VMAT in terms of plan quality, that is, to evaluate if it results in improved conformity, homogeneity, lower doses to the OARs, or in a lower treatment time.

Materials and methods

Delineation of target volumes and OARs

Twenty patients with cervical cancer were retrospectively selected. Patients were 33–83-years old, with a mean age of 58.6 years. The staging system for cervical cancer developed by the International Federation of Gynecology and Obstetrics (FIGO) was used (Bhatla et al. 2019). According to this system, two cases were stage I, two cases were stage II, eight cases were stage III, and eight were cases stage IV. The patients underwent CT scans that were acquired with a 3 mm slice thickness, extending from T10-L1 to the proximal third of the femur, without oral or intravenous contrast. Patients were positioned supine. The contoured OARs included the bladder, rectum, bowel bag, and femoral heads. All clinically identifiable disease was marked as gross tumor volume (GTV). The clinical target volume (CTV) was then defined as the GTV plus the potential microscopic disease, lymph node areas (common, internal iliac, external iliac and presacral nodal groups), uterus and parametrial tissues. No para-aortic lymph nodes were included. The inguinal lymph nodes were included to clinical judgment of the radiation oncologist. The CTV was customized to exclude the vertebral body, obturator muscle, psoas muscle, bowel, bladder and rectum (if the last two were not involved). Finally, a planning target volume (PTV) was generated by expanding the CTV 7–10 mm in all directions, where the whole pelvic field was defined superiorly above the bifurcation of the common iliac vessels or at level of L5-S1 and inferiorly above the inferior extent of the obturator foramen. All contouring was done by the same radiation oncologist.

Constrains to OARs were: bladder $V_{40Gy} < 40\%$ and $D_{max} < 55$ Gy, rectum $V_{40Gy} < 40\%$ and $D_{max} < 55$ Gy, bowel bag $V_{45Gy} < 195$ cm^3 or $V_{40Gy} < 30\%$ and femoral heads $D_{max} < 50$ Gy and $V_{30Gy} < 15\%$. Dose prescription to the PTV was from 50 to 50.4 Gy with 1.8–2 Gy per fraction.

Planning techniques

An IMRT, a VMAT, and a hybrid plan were created for each patient on the same CT image by the same medical physicist. The main objective of the planning process was to achieve 95% of the prescribing dose delivered to 95% of the PTV volume for all plans. This makes 5% of the PTV to be slightly under-dosed, improving normal tissue sparing (Pötter et al. 2018). It was also sought to reduce the dose to the OARs as much as possible. Treatment plans were generated by the Eclipse (v. 15.6, Varian Medical Systems; Palo Alto, CA, USA) treatment planning system (TPS) including an AAA (anisotropic analytical algorithm) on a Varian VitalBeam linac equipped with a 120- leaf MLC, using 6 MV coplanar beams.

For the IMRT plans, nine coplanar fields separated by 40° were used, the gantry angles were 0°, 40°, 80°, 120°, 160°, 200°, 240°, 280° and 320°. A collimator rotation angle of 0° was chosen to reduce the dose to the OARs, as described by Fung et al. (2005). A fixed dose rate of 600 MUs/minute was maintained in all plans, along with the sliding window technique. Dose priorities were defined similarly in the optimization algorithm. Dose delivery to the PTV received the highest priority followed by dose limitation to the OARs, particularly to the rectum and bladder. Nine IMRT fields were used since for 6 MV photon beams, this is the minimum number of fields recommended to produce dose distributions similar to those that would be obtained with higher voltages (Pirzkall et al. 2002). This is because for deep-seated targets, as in the case of cervical cancer, voltages of 10 MV are preferable, particularly for larger patients (Laughlin et al. 1986). Thus, nine fields of 6 MV were used to compensate for the use of a lower voltage. In addition to the above, Pirzkall et al. suggested that the use of six or fewer IMRT fields with 6 MV photon beams could result in an increased dose for regions distant from the PTV (e.g., near the skin surface). Other reports in the literature suggest that no dosimetric improvements were found with the use of more than nine IMRT fields (Roeske et al. 2000). The use of nine IMRT fields for pelvic tumors is the standard treatment at the workplace of the authors, where generally better dosimetric results are observed with this field arrangement. This is consistent with what was discussed above.

The VMAT plans had the same voltage as those of IMRT, with a maximum dose rate of 600 MUs/minute. For each patient, four coplanar arc fields were used, which consisted of four complete arches, each 358° in length. Two of these arches were placed from 179° to 181° (counter-clockwise) and the other two from 181° to 179° (clockwise). Four fields were chosen to optimally cover the PTVs without exceeding the recommended 15 cm field size (Ugurlu and Temelli 2020). The selected collimator angles were 30° and 330°. The couch angle in all arcs was set to 0°. It is recommended not to exceed a field size of 15 cm because this allows both sides of the MLC to reach anywhere inside the field, resulting in a better optimization and target coverage. The pairs of fields in both rotation direction (and with collimator angles set at 30° and 330°) are necessary to reduce possible under-dosing caused by the Tongue-and-Groove effect (Huang et al. 2014). Due to its dimensions, none of the PTVs for the investigated patients could be correctly covered by only one or two 15 cm fields, which is why it is necessary to use four VMAT fields. To make a fair comparison with the plans made in IMRT, the optimization template used was the same in both types of plans, as well as the optimization goals.

Hybrid plans were made by combining IMRT's 9-field plans and VMAT's 4-arc plans. For the plans that had a prescribing dose of 50.4 Gy in 28 fractions, the total number of fractions was divided equally for each type of plan, that is, 14 fractions of IMRT and 14 of VMAT. For patients with a dose prescription of 50 Gy in 25 fractions, a division of 13 fractions of IMRT and 12 of VMAT was used. These proportions resulted in the best overall results. The original nine IMRT fields and the four VMAT fields were not changed at all. The dose distribution and the conformities of the hybrid plans were evaluated in the plan sum. The ratio of use between IMRT and VMAT can be modified when creating hybrid plans to improve either homogeneity or conformity. This methodology is similar to that used by Akbas et al. (2019).

Dosimetric evaluation

A dose–volume histogram (DVH) was generated for all PTVs and OARs for dosimetric analysis. The homogeneity index (HI) was calculated with Eq. (1) (Wu et al. 2019):

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}}, \tag{1}$$

where $D_{2\%}$, $D_{98\%}$ and $D_{50\%}$ represent the doses received by 2% (near maximum dose), 98% (near minimum dose), and 50% of the volume of the PTV, respectively. An HI of 0 indicates that the absorbed-dose distribution was almost homogenous.

The conformity index (CI) was also calculated (Eq. 2) (Lin et al. 2015):

$$CI = \frac{V_{PTV,ref}}{V_{PTV}} \times \frac{V_{PTV,ref}}{V_{ref}}, \tag{2}$$

where $V_{PTV,ref}$ refers to the volume of the 95% of the prescribed dose that covers the PTV, V_{PTV} refers to the volume of the PTV, and V_{ref} is the volume of the 95% prescribing dose curve. The CI value is between 0 and 1, and the closer it is to 1, the better the conformity is. The following parameters were recorded for each of the plans: percentage of dose that covers 100, 98, 50, 2 and 1% of the PTV ($D_{100\%}$, $D_{98\%}$, $D_{50\%}$, $D_{2\%}$ and $D_{1\%}$, respectively), and maximum and mean dose delivered to the PTV (PTV_{Dmax} and PTV_{Dmean}, respectively). For all OARs (except both femoral heads) the following dosimetric parameters were recorded: percentage of volume that receives a dose of 10, 20, 30, 40, 50 Gy (V_{10Gy}, V_{20Gy}, V_{30Gy}, V_{40Gy} and V_{50Gy}, respectively), the maximum dose delivered to each organ (D_{max}), and the volume in cubic centimeters of bowel to which a dose of 45 Gy (V_{45Gy}) is delivered. The treatment time in minutes was measured as the time interval in which the first to the last field was delivered including gantry rotation but not patient positioning. MUs were also recorded for the three types of treatment for comparison.

Statistical analysis

To analyze the dosimetric differences between the three planning techniques, the Friedman test was used. When a significant difference was found ($p < 0.05$), the difference between each of these three types of plans for each effect was further investigated using the Wilcoxon signed rank test. The statistical analyses were performed using the OriginPro Software Version 2018 (OriginLab Corporation, Northampton, MA, USA).

Results

The mean PTV volume for the 20 patients was 1775.46 ± 335.89 cm^3. All plans made with the three techniques had clinically acceptable dose distributions. Typical dose distributions for the three techniques are shown in Fig. 1; axial, coronal and sagittal views (from left to right) are shown for a patient with cervical cancer. The red structure is the PTV, and the isodose curves corresponding to 47.88, 45.36, 40.32, 35.28, 30.24 and 25.20 Gy of the prescription dose are also shown.

For the PTV, the mean value for HI, CI, $D_{100\%}$, $D_{98\%}$, $D_{50\%}$, $D_{2\%}$, $D_{1\%}$, PTV_{Dmean}, and PTV_{Dmax}, along with their standard deviations (SD) are presented in Table 1. The p values where there is statistical significance between the three planning techniques are in bold format.

The quality indices (HI and CI) revealed that there were significant differences between the three types of plans, which suggest that the hybrid plan has better conformity and homogeneity compared to the pure IMRT and VMAT

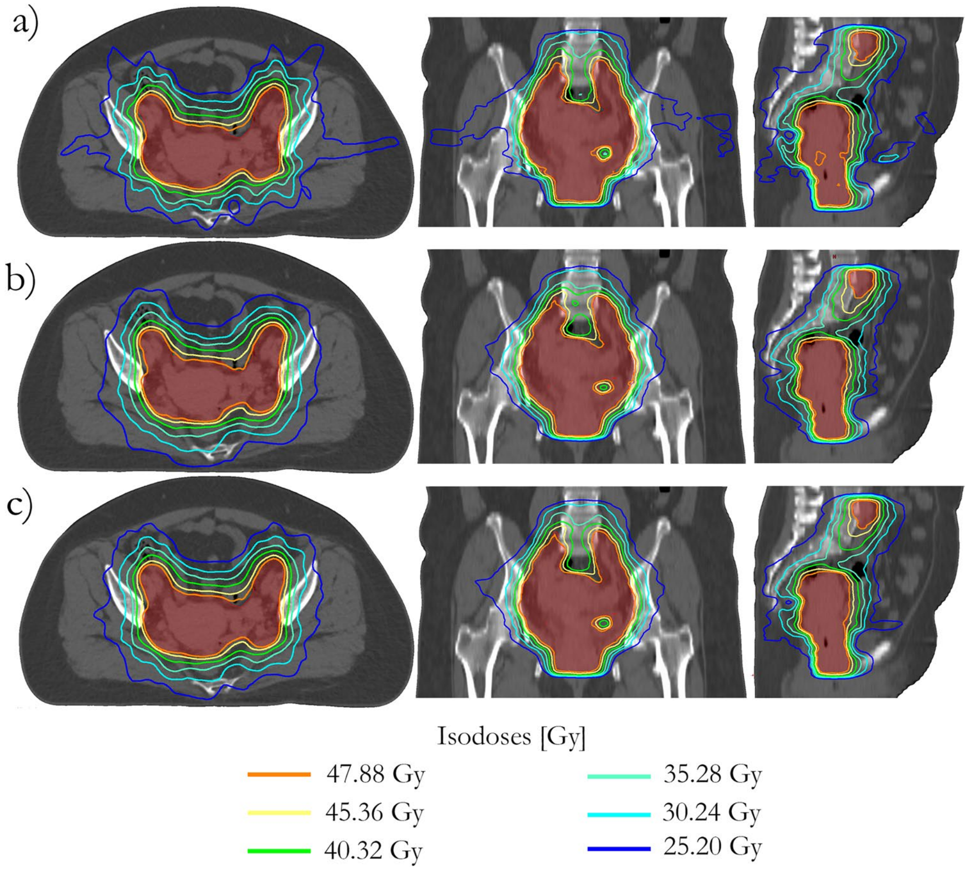

Fig. 1 Dose distribution on axial, coronal, and sagittal views for one cervical cancer patient: **a** IMRT, **b** VMAT, and **c** hybrid plan. Planning target volumes are shown in red

Table 1 PTV Dosimetric parameters for IMRT, VMAT and hybrid plans; SD—standard deviation; HI—homogeneity index (Eq. 1); CI—conformity index (Eq. 2); bold *p* values indicate statistical significance between the three planning techniques

Item	IMRT (mean ± SD)	VMAT (mean ± SD)	HYBRID (mean ± SD)	*p* value
HI	0.0855 ± 0.0176	0.0837 ± 0.0184	0.0770 ± 0.0173	**< 0.001**
CI	0.8809 ± 0.0254	0.8945 ± 0.0232	0.9006 ± 0.01884	**< 0.001**
$D_{100\%}$ (cGy)	3827.35 ± 599.89	3931.33 ± 599.61	3905.73 ± 606.51	**< 0.001**
$D_{98\%}$ (cGy)	4694.93 ± 38.38	4674.80 ± 46.63	4687.395 ± 47.83	**< 0.001**
$D_{50\%}$ (cGy)	4943.29 ± 37.64	4961.93 ± 35.18	4939.61 ± 27.63	**< 0.001**
$D_{2\%}$ (cGy)	5118.23 ± 66.53	5090.73 ± 58.19	5068.16 ± 50.98	**< 0.001**
$D_{1\%}$ (cGy)	5139.20 ± 70.79	5109.62 ± 65.16	5084.29 ± 54.06	**< 0.001**
PTV_{Dmean} (cGy)	4939.28 ± 36.30	4946.07 ± 32.70	4927.90 ± 26.19	**< 0.001**
PTV_{Dmax} (cGy)	5285.16 ± 159.51	5209.05 ± 80.71	5183.42 ± 104.22	**< 0.001**

plans. The average HI value for the IMRT technique was 0.0855 ± 0.0176, for the VMAT plan it was 0.0837 ± 0.0184 and for the hybrid plan it was 0.0770 ± 0.0173 ($p < 0.001$). The mean value of HI for the hybrid plan was the lowest of all the three types of plans, so this indicates that it has the best dose homogeneity.

The mean CI value for the IMRT technique was 0.8809 ± 0.0254, for the VMAT technique it was 0.8945 ± 0.0232 and for the hybrid plan it was 0.9006 ± 0.01884 ($p < 0.001$). The CI value closest to a value of 1 was the one that belonged to the hybrid plan. This suggests that the hybrid technique produces plans with better conformity compared to the other two techniques. There were statistically significant differences between these three methods for all dose values that were delivered at a certain percentage of volume, mean dose and maximum dose received to the PTV. For $D_{100\%}$ and PTV_{Dmean} the VMAT technique gave the highest value ($p < 0.001$), for $D_{98\%}$ the IMRT technique gave the highest dose value ($p < 0.001$). In contrast, the hybrid technique showed the best results for the control of high doses, i.e., the corresponding values of $D_{2\%}$, $D_{1\%}$ and PTV_{Dmax} were the smallest in all three types of plans ($p < 0.001$).

The dosimetric comparison of the OARs is shown in Table 2. The p values with statistical significance are again in bold format. For V_{10Gy}, V_{20Gy}, V_{40Gy} of the rectum, V_{10Gy}, V_{40Gy} of the bladder, and V_{10Gy} and V_{20Gy} of both femoral heads, no significant difference was observed ($p > 0.05$). In contrast, the maximum dose (D_{max}) for all OARs was significantly reduced for hybrid plans compared to pure IMRT plans, with a decrease of 1.38, 1.45, 4 and 5.96% for rectum, bladder ($p < 0.001$), right and left femoral heads, respectively ($p = 0.015$; 0.026). Similarly, for the comparison between the hybrid plan and pure VMAT there was a decrease in maximum dose for all OARs: 0.6, 0.19, 0.87 and 0.01% for rectum, bladder ($p < 0.001$), right and left femoral heads, respectively ($p = 0.015$; 0.026). In addition, the plans made with the hybrid technique consistently showed the best results for V_{50Gy} for the rectum, bladder ($p < 0.0.01$) and bowel ($p = 0.002$). Subsequently, V_{30Gy}, in all organs ($p < 0.001$) and for V_{10Gy} ($p < 0.001$), V_{20Gy} ($p < 0.001$), V_{30Gy} ($p = 0.002$), V_{40Gy} ($p < 0.001$), V_{45Gy} ($p < 0.001$) and V_{50Gy} ($p = 0.002$) of the bowel, the VMAT technique had the smallest values. Finally, for V_{20Gy} of the bladder, the IMRT technique received the lowest dose values. The average dose–volume histograms (DVHs) of PTV and OARs are shown in Fig. 2.

The MUs and treatment time of the three planning techniques are shown in Table 3. The p values with statistical significance are in bold format. The MUs and treatment time values for the hybrid plan were intermediate between those of the plans made with IMRT and VMAT, being higher than those of VMAT but lower than those of IMRT.

Discussion

Optimizing a radiotherapy treatment for gynecological tumors faces the challenge of a treatment region being close to many healthy tissues, such as rectum, bladder, bowel and femoral heads. Radiotherapy treatment can lead to the presence of toxicity in patients, since it includes external beam radiotherapy and brachytherapy later. Initially, cervical cancer treatment consisted of a two-dimensional irradiation of the entire pelvis, which was associated with severe

Table 2 OARs dosimetric parameters for IMRT, VMAT and hybrid plans; bold p values indicate statistical significance between the three planning techniques

Organ	Parameter	IMRT (mean ± SD)	VMAT (mean ± SD)	HYBRID (mean ± SD)	p value
Rectum	D_{max} (cGy)	5120.78 ± 68.29	5081.04 ± 73.42	5049.95 ± 52.65	**< 0.001**
	V_{10Gy} (%)	98.29 ± 4.29	98.11 ± 4.52	98.21 ± 4.39	0.350
	V_{20Gy} (%)	95.81 ± 7.38	96.39 ± 6.79	96.50 ± 6.83	0.142
	V_{30Gy} (%)	70.35 ± 12.78	75.01 ± 9.82	71.94 ± 10.88	**< 0.001**
	V_{40Gy} (%)	33.19 ± 8.68	33.64 ± 7.45	33.01 ± 7.78	0.584
	V_{50Gy} (%)	1.06 ± 1.21	0.875 ± 1.34	0.4 ± 0.75	**< 0.001**
Bladder	D_{max} (cGy)	5169.43 ± 82.60	5104.04 ± 64.73	5094.40 ± 60.13	**< 0.001**
	V_{10Gy} (%)	100 ± 0	100 ± 0	100 ± 0	1
	V_{20Gy} (%)	96.91 ± 3.62	99.63 ± 1.14	99.23 ± 1.91	**< 0.001**
	V_{30Gy} (%)	67.08 ± 14.46	72.43 ± 10.38	69.23 ± 12.85	**< 0.001**
	V_{40Gy} (%)	34.72 ± 15.38	34.74 ± 15.45	34.43 ± 15.47	0.151
	V_{50Gy} (%)	2.74 ± 4.17	1.84 ± 3.13	1.37 ± 2.36	**< 0.001**
Femoral head right	D_{max}(cGy)	4162.94 ± 321.57	4031.23 ± 229.12	3996.21 ± 263.95	**0.015**
	V_{10Gy} (%)	94.80 ± 14.42	96.16 ± 11.29	95.50 ± 12.86	0.638
	V_{20Gy} (%)	75.58 ± 17.46	73.43 ± 24.27	76.93 ± 21.64	0.542
	V_{30Gy} (%)	9.08 ± 3.64	6.43 ± 3.57	7.08 ± 3.25	**< 0.001**
Femoral head left	D_{max} (cGy)	4135.29 ± 263.84	3889.34 ± 250.63	3885.93 ± 234.61	**0.026**
	V_{10Gy} (%)	94.94 ± 13.61	95.55 ± 12.05	95.41 ± 12.60	0.705
	V_{20Gy} (%)	72.49 ± 17.97	75.16 ± 24.44	76.48 ± 21.01	0.074
	V_{30Gy} (%)	9.29 ± 3.65	5.95 ± 3.40	6.99 ± 3.32	**< 0.001**
Bowel	V_{45Gy} (cm^3)	87.32 ± 49.48	78.74 ± 48.11	79.71 ± 47.86	**< 0.001**
	V_{10Gy} (%)	76.16 ± 6.32	74.05 ± 6.11	75.24 ± 6.20	**< 0.001**
	V_{20Gy} (%)	59.07 ± 9.94	54.55 ± 8.32	56.80 ± 9.19	**< 0.001**
	V_{30Gy} (%)	26.55 ± 9.86	25.10 ± 8.75	25.24 ± 9.02	**0.002**
	V_{40Gy} (%)	10.59 ± 4.62	9.78 ± 4.49	9.92 ± 4.44	**< 0.001**
	V_{50Gy} (%)	0.53 ± 1.03	0.58 ± 1.000	0.355 ± 0.84	**0.002**

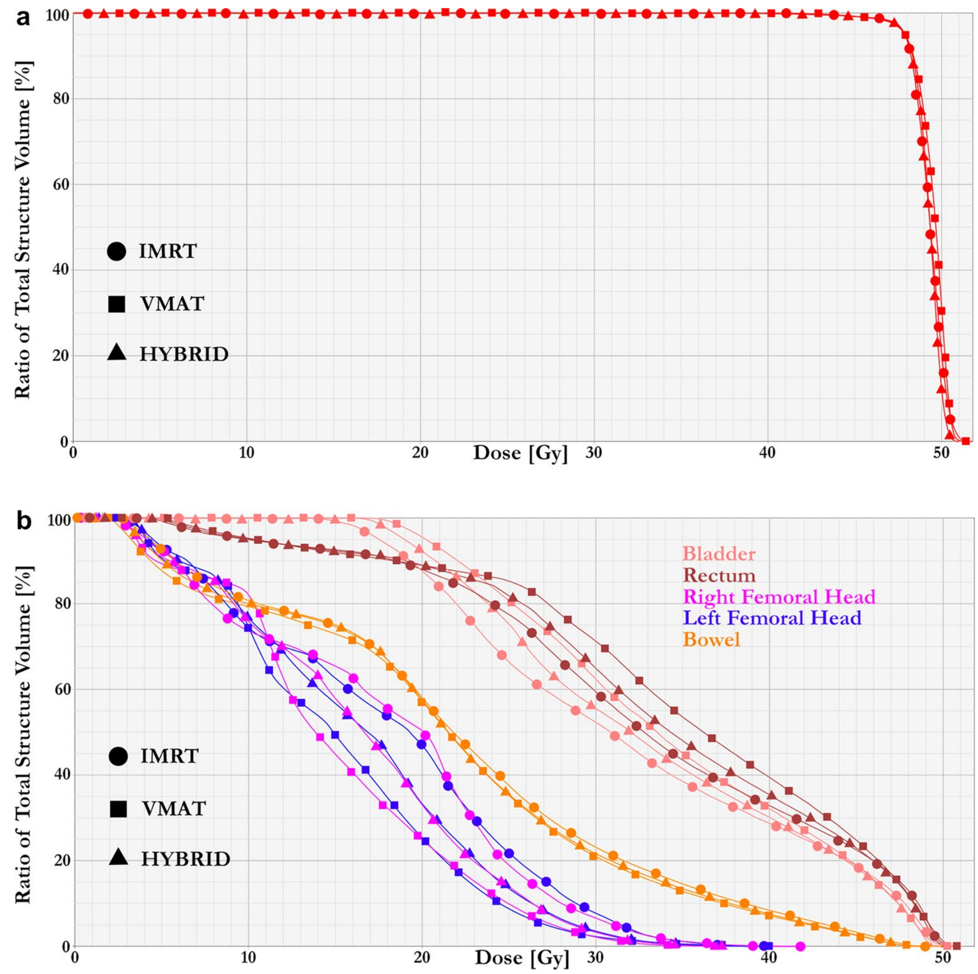

Fig. 2 Representative dose–volume histograms of target volumes **a** and OARs **b**

short- and long-term toxicities. The subsequent advancement of technology led to the development of 3D-CRT and IMRT, which soon demonstrated its superiority compared to 3D-CRT being applied extensively to the treatment of cervical cancers (Morris et al. 1999; Chang et al. 2016). IMRT has advantages over 3D-CRT: improvement in dose distribution to target volumes and decreased radiation delivered to OARs. However, it is associated with some disadvantages, mainly with a higher number of MUs, and consequently with longer treatment times (Lesnock et al. 2013). This is potentially detrimental to the patient, since prolonged treatment times result in discomfort and consequently increases the possibility of patient motion (both external motion and internal organ filling/emptying, such as bowel and rectum), which would impact the accurate delivery of the radiation dose. The subsequent development of the VMAT technique came to remedy these disadvantages in a certain way, since this technique is also a modulated intensity technique capable of producing plans that are dosimetrically equivalent to IMRT, but it delivers fewer MUs, thus reducing the treatment time (Wu et al. 2019). However, there are reports where the dosimetric quality of the plans made with VMAT is lower than those made with IMRT. This occurs particularly in complex geometries, such as those of head and neck tumors (Guckenberger et al. 2009; Popple et al. 2010). In addition, the design of a treatment in VMAT is usually more complex than that in IMRT, therefore requiring more developing time (Jin et al. 2013). However, despite all the advantages offered by

Table 3 MU values and delivery time of treatment for IMRT, VMAT and hybrid plans; SD—standard deviation; bold *p* values indicate statistical significance between the three planning techniques

Parameters	IMRT (mean ± SD)	VMAT (mean ± SD)	Hybrid (mean ± SD)	*p* value
MUs	1999.4 ± 253.71	637.16 ± 133.37	1318.96 ± 187.93	**< 0.001**
Time (min)	5.54 ± 0.41	4.54 ± 0.34	5.07 ± 0.36	**< 0.001**

both techniques, there is the possibility that neither of these techniques is sufficient by itself to meet certain dosimetric requirements. Earl et al. proposed the idea of combining the virtues of IMRT and VMAT in a hybrid scheme (Earl et al. 2007). Matuszak et al. obtained treatment plans with significant improvements for pancreas, prostate and brain cases through an IMRT/VMAT hybrid optimization strategy where IMRT intensity modulation at certain angles was combined with single VMAT arches (Matuszak et al. 2013).

In the present study, a hybrid planning technique based on the combination of IMRT and VMAT techniques is proposed for patients with cervical cancer. The plans made with the hybrid technique showed substantial improvements in the irradiation homogeneity and conformity of the target volumes, as well as a decrease in the maximum doses of all the OARs. There are several studies in the literature where a hybrid technique is applied to various regions of the body. Zhao et al. conducted a study comparing two-arch VMAT, 9-field IMRT, and hybrid IMRT/VMAT plans for nasopharyngeal cancer. Their hybrid plan consisted of seven IMRT fields and a full VMAT arc (Zhao et al. 2015a). They found that the hybrid IMRT/VMAT technique improved the target dose homogeneity and conformity compared with nine field IMRT and two-arch VMAT, while reducing the dose delivered to the temporomandibular joints, and mandible and temporal lobes. They also reported fewer MUs compared to 9-field IMRT and smaller doses delivered to parotids, brainstem, and spinal cord compared with the two-arch technique. For irradiation of the whole-breast left-sided early breast cancer Lin et al. made a plan comparison between seven fields of IMRT, two coplanar arcs of VMAT and a hybrid plan composed of two tangential fields of IMRT and two coplanar arcs of VMAT, where the proportion of the prescription dose for IMRT was 75%. In their work, the hybrid plans obtained the best results in dose conformity and homogeneity, while the ipsilateral lung volumes that received 20 Gy (V_{20Gy}) and 5 Gy (V_{5Gy}) were significantly less in comparison to the other techniques. They even reported a fewer number of MUs for the hybrid plan with respect to pure IMRT and VMAT plans (Lin et al. 2015). Regarding pelvic tumors, Robar and Thomas reported an improvement in conformity for hybrid plans (composed of VMAT/IMRT fields) in comparison to pure VMAT plans, but not to those made only with IMRT fields. They also reported an improvement in the homogeneity of the PTV, as well as a reduction in the maximum dose delivered to the rectum and bladder (Robar and Thomas 2012).

These results are similar to those obtained in the present work, that is, the implementation of a hybrid plan resulted in improved homogeneity and conformity to the PTV compared to the other techniques. OARs such as rectum, bladder and femoral heads show a reduction for high dose values (D_{max} and V_{50Gy}), which could be an advantage for a subsequent brachytherapy treatment. Significant reductions in the dose received for certain OARs for various treatment regions using hybrid IMRT/VMAT treatment schemes have also been reported in the literature by other authors. For example, Akbas et al. reported a substantial improvement in the sparing of serial organs such as the brainstem and spinal cord in patients diagnosed with nasopharyngeal cancer (Akbas et al. 2019). This has clinical relevance, since lower doses to the OARs, along with the right PTV coverage result in a smaller probability of acute toxicities as well as better local control of the tumor. According to what was reported by Berger et al. (Berger et al. 2019) there is a correlation between radiation exposure and the presence of morbidities, in terms of dose and volume, that is, a lower volume of irradiated organs significantly reduces gastrointestinal and genitourinary toxicities, as well as symptoms such as fatigue, resulting in an improvement in overall quality of life. This shows the potential merit of implementing a hybrid plan, since all these benefits could be achieved without compromising the coverage to the target volume, while at the same time, a better dosimetric quality is obtained.

One of the possible reasons why the hybrid plan presented better dosimetric results is that it combines useful features of both IMRT and VMAT techniques, by making compromises in different aspects. The IMRT technique has a limited angular sampling but achieves a reasonable dose distribution by modulating beam intensity. This is useful to improve dose homogeneity. However, intensity modulation alone, in general, is not enough to produce the desired dose distribution. In fact, another important factor is the correct number of angular sampling, which leads to a high target volume conformity, particularly for complex cases, since a sufficient angular sampling allows the high dose regions to be correctly curved. This is the main advantage of the VMAT technique, which is characterized by an abundant angular sampling. However, this technique does not have intra-beam intensity modulation in some or all directions, thus limiting dose uniformity, since each arc beam is limited to a single aperture value. Using multiple arcs is a way to partially solve this problem, but this increases the treatment time, without solving the requirement for field modulation. For this reason, neither the IMRT nor VMAT techniques are totally satisfactory for a wide spectrum of cases.

The hybrid plan is suggested as an optimal treatment scheme since it potentially includes the advantages of both techniques: sufficient angular sampling, beam modulation, delivery efficiency while obtaining superior dosimetric results with low doses to the OARs. As it was mentioned before, it is suggested that the hybrid plan achieves all of the above by making a compromise between IMRT/VMAT techniques in such a way that the advantages of both are exploited. To summarize, the modulated intensity of the

IMRT achieves a good dose distribution even with limited angular beam sampling. However, this sparse angular sampling could limit obtaining a good dose conformity to the target. In contrast, beam angle sampling in VMAT is abundant, but it is limited by its inability to modulate dose intensity in certain beam directions. Both factors (beam sampling and intensity modulation) determine the quality of the final dose distribution. This suggests that the hybrid technique produces treatment plans with better dose conformity and homogeneity, since it combines the advantages of both techniques, that is, it increases the freedom to find the optimal combination between intensity modulation and beam angular sampling (Zhao et al. 2015a).

The MU values and treatment delivery times for the hybrid plan in the present work were found between those of IMRT and VMAT, being lower than those of the former but higher than those of the latter. There are two factors that could explain the reason for this result: the complexity of the multi-leaf collimator sequence in the IMRT component of the hybrid plan and the average apertures of the optimized field size for the VMAT component. For all the plans of the present study, the PTVs were close to OARs whose dose restrictions are demanding (such as bladder and rectum). Therefore, the field apertures would be forced to block the aforementioned OARs, thus requiring more MUs to deliver a specific dose to the PTV. It was previously mentioned that the VMAT technique is superior to IMRT in terms of required treatment time and MUs. This has been reported in various studies where both techniques were compared in cervical cancer treatments (Guy et al. 2016; Wu et al. 2019). However, planning for a VMAT plan is generally more complex than for an IMRT plan, due to the additional factors that must be controlled in its optimization. That is why the hybrid plan is proposed as an alternative to compensate for the disadvantages of both techniques, since it requires fewer MUs than a pure IMRT plan, while its planning process is less intricate than that of a VMAT plan.

There are still areas where more research on the subject of developing an IMRT/VMAT hybrid plan is required. For instance, there is still no consensus regarding the appropriate ratio between the IMRT component and the VMAT component. For patients with non-small cell lung cancer Zhao et al. used different proportions between both techniques to generate a hybrid plan and found that the best results regarding plan quality and decreased delivery of high doses to healthy lung tissue were achieved when the ratio of VMAT to IMRT was 2:1. This result was obtained, however, at the cost of increasing low doses to the healthy part of the lung (V_{5Gy} and V_{10Gy}) (Zhao et al. 2015b). On the other hand, Bedford et al. stated the opposite, that is, that by increasing the portion of IMRT the dosimetric quality of the PTV was improved, while at the same time the volume of rectum irradiated to 65 Gy was substantially reduced (Bedford et al. 2016). In the present study, the ratio between the IMRT/VMAT for the developed hybrid plan was 1: 1. That is, half of the prescribed dose was delivered by each of the techniques, with the exception of five patients where the dose prescription was delivered in an odd number of fractions (50 Gy in 25 fractions). For these cases, it was decided to deliver 13 fractions in IMRT and the remaining 12 fractions in VMAT. Because the difference was only one fraction, no significant dosimetric differences were found. This proportion was selected since it had the best results in terms of quality of plan and dose to OARs, in addition to agreeing with the results of Akbas et al. for nasopharyngeal cancer. These authors had also reported of having used the same ratio for the generation of their hybrid plan (Akbas et al. 2019). All the studies mentioned above show that the way in which a hybrid plan is designed and implemented as well as the results that it delivers can vary for each case.

Conclusions

Application of a hybrid planning technique, which combines the IMRT and VMAT techniques, considerably improved both the target dose homogeneity and conformity in comparison to pure IMRT and VMAT plans for patients with cervical cancer. The maximum doses for OARs such as rectum, bladder and femoral heads were reduced, while the required monitor units and treatment times showed intermediate values between the other two techniques, being lower than those of IMRT, but higher than those of VMAT. It is concluded that the hybrid planning technique is a viable option of radiotherapy treatment for patients with cervical cancer.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This research work complies with the considerations issued in the Nuremberg Code, the Declaration of Helsinki promulgated in 1964 and its various modifications, including the update of Fortaleza, Brazil in 2013, as well as the international guidelines for medical research with human beings adopted by WHO and the Council for International Organizations for Research with Human Beings; In Mexico, it complies with the provisions of the General Health Law and the INAI (Instituto Nacional de Transparencia, Acceso a la Información y Protección de Datos Personales) on Research for Health and Protection of Personal Data, respectively.

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