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RADIATION THERAPY IN CERVICAL CANCER: COMPARATIVE STUDY OF 3D ADVANCED CONFORMAL TECHNIQUE AND CLASSIC «BOX TECHNIQUE

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ABSTRACT

Backrgound and purpose: The treatment of locally advanced cervical cancer is external beam radiotherapy to the pelvis alone or in combination with chemotherapy, followed by intracavitary brachytherapy. The objective of this study was to evaluate the role of a new Three-Dimensional Conformal Radiation Therapy (3DCRT) technique in reducing the dose to organs at risk (OARs) as compared with the classic 3DCRT plan which is the box technique with respect to target volume coverage. **Methods:** We conducted a comparative planning study of forty one patients with cervical cancer treated with radiation therapy, between April 2017 and November 2017 at the National Institute of Oncology in Rabat .Two plans in 3DCRT were done for every patient; one using 6 beams and the second one using the conventional box technique (4 beams). Then, the two plans were compared adopting dose volume histograms (DVH) analysis for the planning target volume (PTV), bladder, rectum and both femoral heads. **Results:** Comparing different plans of treatment, it was shown that the planning target volume was sufficiently covered in both plans, although, it was demonstrated that the 6 beams conformal radiation therapy technique decreased doses reaching all OARs. **Conclusion:** From the present study, it is concluded that 6 beams CRT technique spared more adequately OARs than box technique. Hence, it might be a good solution in centres don't yet have intensity- modulated radiation therapy (IMRT).

KEYWORDS: Cervical cancer, Radiation therapy, Gynecologic cancers, Dosimetric techniques, 3DCRT.

INTRODUCTION

The treatment for locally advanced cervical cancer (stage IB2-IVA) is either external beam radiotherapy alone to the pelvis or in combination with chemotherapy, followed by intracavitary brachytherapy (ICT).

Actually, the most commonly used radiotherapy technique is the conventional 4-field technique which contains anterior, posterior and 2 lateral fields, while the advanced nature of these tumors necessitates more advanced techniques allowing a better coverage of the tumor without increasing the toxicity to the organs at risk, especially if the brachytherapy cannot be performed, then a boost by radiotherapy would be necessary.

The intensity-modulated radiation therapy (IMRT) allows delivery of radiation dose in a more conformal manner than conventional three-dimensional radiation therapy (3DCRT) by varying the radiation beams spatially or temporally.[1,2] An optimal use of 3D conformal radiation therapy would be an interesting alternative when IMRT isn't available, increasing the number of fields (more than 2 fields) in treatment planning process improves the conformity index.

To our knowledge; this is the first study that reports dosimetric comparison between the 4-field technique (4FT) and an advanced conformal 3D technique (ACT) based on the multiplicity of treatment fields in patients with squamous cell carcinoma of the cervix.

MATERIALS AND METHODS

CT Simulation, target volumes and organs at risk delineation

This is a comparative planning study of forty-one patients with cervical cancer treated with radiation therapy, between April and November 2017 at the National Institute of Oncology in Rabat. Informed verbal consent was obtained from all patients.

Patients were simulated in the supine position and immobilized with contention devices. A CT simulator (Siemens Simulator Scanner) with 5-mm thick slices was performed and used for the delineation of target volumes and organs at risk (bladder, rectum, bowel and femoral heads). The delineation was performed by one radiation oncologist for all patients. The clinical target volume (CTV-T) includes: The cervix, entire uterus, parametrial/ paravaginal tissues, and 1/3 proximal vagina is included if there is no vaginal tumor extension, the upper 1/2 is included if involvement of the 1/3 proximal vagina, the entire vagina is included if there is involvement of more than the proximal 1/3 of the vagina. The nodal clinical target volume (CTV-N) includes: the bilateral internal and external iliac, the presacral and the primitive s iliac areas, they were delineated by applying 0.7cm margin around internal and external iliac vessels according to RTOG recommendations.

Treatment methods

Two different treatment plans were performed by the same medical physicist, using the superposition algorithm of the Treatment planning system (XiO Radiation Therapy Planning System 5.0.0; CMS, St. Louis, MO) and generated 6MV and 18MV photon beams by ELEKTA Synergy linear accelerator with an 80-leaf MLC (**Figure. 1**). The prescription dose was 46 Gy, 2Gy/fraction, 5 fractions/ week to the total planning target volume (PTV).

1. **Technique 1: 4-field technique (4FT)**(figures 1c-1d)

It consisted of using four 18MVfields conformed to the total PTV: anterior, posterior and 2 lateral fields.

2. **Technique 2: Advanced 3D conformal technique(ACT)** (figures 1a-1b)

This technique is composed by six fixed fields (0°,35°,90°,180°,270° and 325°) covering the PTV. The fields with an oblique beam direction (35° and 325°) are limited to one side of the target volume and enable in this way an adoption to its biconcave shape.

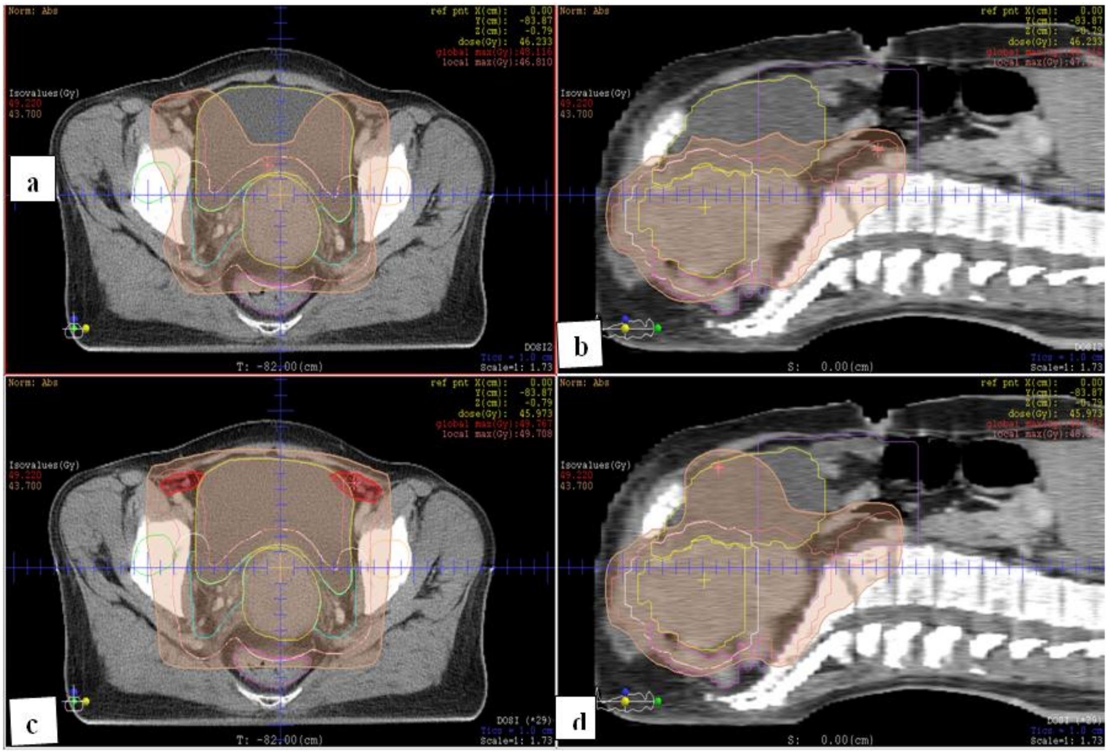

Figure 1: Axial and sagittal reconstruction planning CT slices of the two irradiation techniques:ACT (a-b), 4FT(c-d); Display of the 95% and 107%isodose of the prescribed dose.

Treatment plans analysis

XIO was used to generate treatment plans. 95% of the PTV should receive 95% to 107% of the prescribed dose to consider plan acceptable. For each plan, the dose-volume histogram (DVH) was used to generate target volumes (PTV) and OARs (bladder, rectum, bowel and femoral heads) parameters (maximum dose (D max), mean dose (D mean), homogeneity index (HI), conformity index (CI) and volume of OAR receiving xGy (VxGy)).

The degree of conformity has been evaluated by calculating the RTOG conformity index, defined as: $CI_{RTOG} = V_{RI}/V_{PTV}$

Where $V_{RI:}$ reference isodose volume and V_{PTV}: PTV volume.

The Homogeneity index was calculated using the folowing formulae:

* Homogeneity index (HI1) $= D_5 - D_{95}/D_{50}$ where D_{50}: minimum dose in 50% of PTV, D5.dose in 5% of PTV,

indicating the maximum dose, and $D_{95:}$ dose in 95% of PTV, indicating the minimum dose. The ideal value is 0.[3]

Statistical analysis

Statistical analysis was performed using SPSS software, version 20. Comparison was done using student t test. The p-value of less than 0.05 was considered significant.

RESULTS

Regarding the coverage of the PTV as shown in **table.1** the two techniques offered a good coverage, while the ACT reduced significantly the 95% isodose volume (p<0.0001) and resulted in the best conformity index with 1.61±0.15 (P<0.0001) **(Fig.2)**.

Organ at risk parameters according to irradiation techniques were summarized in **table.2**.

Regarding dose to the bladder and rectum, the ACT decreased the Dmax, V45 and V40 significantly in comparison with the 4FT. For the bladder:V40;V45 and Dmax with 86.76±10.48 (p<0.0001), 38.65±14.73 (p<0.0001) and 47.57±0.63(p<0.0001) respectively. For the rectum: V40; V45 and Dmax with 86.19±9.50 (p<0.0001), 47.48±17.37(p<0.0001), and 46.66±0.52 (p<0.0001),

Concerning femoral heads, the ACT decreased significantly the Dmax and V45. However, no difference was found between both techniques according V40. Furthermore, we note a significant decrease of V40 and V45 in abdominal cavity with ACT **(Fig.3)**.

Table 1: Dosimetric comparison of target volumes parameters according irradiation techniques.

		4FT	ACT	p
Total PTV	95% Isodose volume	2167.95±418.12	1789.16±372.23	0.001
	PTV volume	1129.15 ± 287	1129.15±287	-
	D95%	99.70±0.23	99.45±0.50	0.002
	Conformity index	1.91±0.36	1.61±0.15	<0.0001
	Homogeneity index	0.06±0.01	0.06 ±0.007	0.25

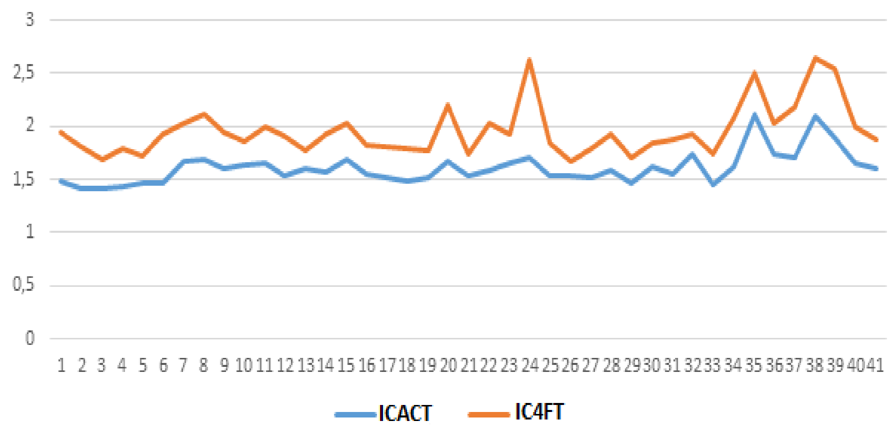

Figure 2: Total PTV conformity index of all patients according to irradiation techniques.

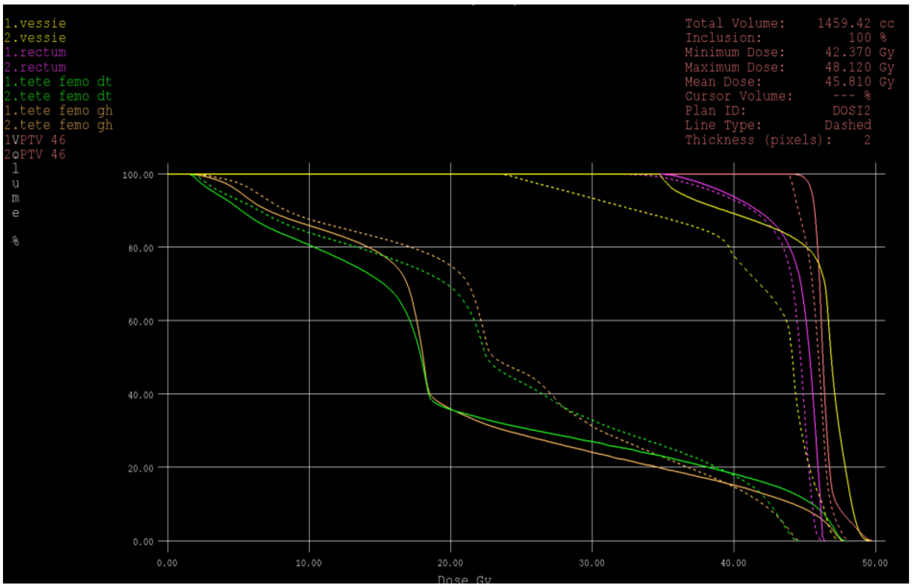

Figure.3: dose-volume histogram of the rectum, bladder and femoral heads according to irradiation techniques (----4FT, ….. ACT).

Table 2: Dosimetric comparison of OAR parameters according irradiation techniques.

		4FT	ACT	P
Bladder	**V20 (%)**	100	100	**-**
	V30 (%)	100	98.38±3.27	**-**
	V40 (%)	92.37±7.27	86.76±10.48	**<0.0001**
	V45 (%)	82.15±12.14	38.65±14.73	**<0.0001**
	Dmax	48.67±0.91	47.57±0.63	**<0.0001**
Rectum	**V20 (%)**	99.82±1.09	99.49±1.84	**0.168**
	V30 (%)	99.16±2.78	98.38±3.27	**0.002**
	V40 (%)	90.54±7.74	86.19±9.50	**<0.0001**
	V45 (%)	69.76±15.00	47.48±17.37	**<0.0001**
	Dmax	47.40±0.60	46.66±0.52	**<0.0001**
Abdominal cavity	**V15 (cc)**	1304.34±606.63	1355.77±642,44	**-**
	V30 (cc)	937.57.84±468.00	767.22±418.62	**<0.0001**
	V40 (cc)	588.79±362.84	552.13±346.59	**<0.0001**
	V45 (cc)	444.95±312.26	314.83±250.06	**<0.0001**
Right femoral head	**V20 (%)**	40.72±14.26	87.26±14.74	**-**
	V30 (%)	24.89±10.87	32.58±12.98	**-**
	V40 (%)	14.13±7.77	14.23±7.36	**0.725**
	V45 (%)	6.99±5.51	0.56±0.93	**0.0001**
	Dmax	47.16±1.02	45.17±0.84	**0.0001**
Left femoral head	**V20 (%)**	41.81±13.23	89.42±12.66	**-**
	V30 (%)	25.57±10.49	34.21±11.59	**-**
	V40 (%)	14.57±7.97	15.05±7.56	**0.027**
	V45 (%)	7.40±5.50	0.92±3.25	**<0.0001**
	Dmax	47.09±1.20	45.12±0.63	**<0.0001**

DISCUSSION

Cervix carcinoma is a common cancer in females in the developing world, and radiotherapy is the cornerstone of treatment at all locally advanced stages.[4] The treatment modality for these are radiotherapy in combination with chemotherapy. Radiation treatment consists of combination of external beam RT and intracavitary brachytherapy.[5]

The most common technique for whole pelvic irradiation has been the 2-field, anterior and posterior fields (AP/PA). However, the 4-field box technique has gained increasing acceptance by the radiation oncologists. The advantage of 4-field radiation to the pelvis is that the use of lateral portals spares a portion of the small bowel anteriorly and a portion of rectum posteriorly from radiation. The advances in technology, such as computed tomography (CT) scans have further optimized this technique.[5] Despite of all this, we estimate that the 4F box technique remains insufficient because of a large irradiated volume of normal tissue, thus increasing the risk of treatment-related toxicity, especially if the brachytherapy cannot be performed; then a boost by external radiotherapy would be necessary.

Modern techniques of precision radiation delivery like IMRT allow the dose to be "sculpted" to the tumor volume while at the same time minimizing the dose to adjacent dose-limiting normal tissues[6], thereby offering greater locoregional control and leading to fewer side effects. IMRT is associated with lower gastrointestinal and haematological toxicities than is conventional RT (c-RT) in treatment of cervical cancer, and it is therefore used more widely.[7,8] However, the potential advantages of IMRT for treating cervical cancer remain unclear.[9]

In this study, we compared two conformal techniques, the conventional 4FT and an advanced 3DCT in the treatment of 41 patients with intact cervical cancer referred to our department, to assess the dosimetric advantages of this innovative conformal technique.

The dosimetric comparison showed that ACT reduced significantly the 95%isodose volume (p<0.0001), thus improved the conformity index by 16% (1.64 vs 1.95). However, IMRT allows a more conformal dose distribution, Du XL et al[10] reported that IMRT produced approximately a 30% improvement in the conformity relative to the conventional-RT techniques, a statistically significant difference which is of potential clinical significance.

IMRT can decrease the risk for radiation-induced toxicity in patients after pelvic or para-aortic irradiation with conventional RT.[11–13] In the present study, we found that, for the same PTV dose, ACT gave a significant lower dose to OAR than 4FT. ACT decreases the rectal and bladder volume absorbing more than 45Gy with over 30 and 50% respectively. Du XL et al[10] in their comparative study found that IMRT caused less rectum exposure than conventional techniques: median exposure was 21.3% and 49.7%, respectively. The doses received by the bladder and small intestine were also significantly lower. Our results also showed that the ACT reduced significantlyV40 and V45 of the abdominal cavity. Iğdem et al[14] compared IMRT and 4FT planning in 10 women with gynecologic malignancies; IMRT reduced the volume of small bowel receiving more than 45 Gy in all patients. The average absolute volume of small bowel receiving 45 Gy was significantly reduced from 318 cc to 33 cc. No significant increase in the volume of small bowel receiving less than 20 Gy was observed.

Furthermore, according to a 2012 systematic review and meta-analysis by Yang et al. based on 13 studies[15], IMRT significantly reduced the average proportion of irradiated volume of the rectum and small bowel compared with 3D-CRT in patients with gynaecologic malignancies.

These results indicate that ACT may provide an encouraging dosimetric benefits for cervical cancer patients, we suggest that this innovative technique could be a good alternative to the IMRT when it’s unreachable.

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