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Vulvar Cancer: Dosimetric Comparison of Advanced 3D Conformal Radiation Therapy Technique with Anteroposterior and Posteroanterior Irradiation Techniques

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ABSTRACT

Introduction: The commonly used technique of radiation therapy for vulvar cancer consists of anteroposterior (AP) and posteroanterior (PA) fields. This is the first study that reports the dosimetric comparison between the AP-PA techniques and the new 3D advanced conformal technique (3D-ACT) based on the multiplicity of treatment fields in patients with squamous cell cancer of the vulva in the postoperative setting.
Material and Methods: This comparative planning study was conducted on15 patients with vulvar carcinoma treated with adjuvant radiation therapy at the National Institute of Oncology in Rabat, Morocco. Three treatment plans were performed, corresponding to three techniques, namely photons with source-skin distance inguinal supplement, modified segmental boost technique and 3D advanced conformal technique. For each plan, the dose-volume histogram was used to generate planning target volumes (total and inguinal PTV) and organs at risk (bladder, rectum, bowel and femoral heads) parameters.
Results: The 95% isodose volume was significantly reduced with the advanced conformal technique (P<0.0001) without compromising the total PTV coverage (P= 0.94). This technique resulted in the best conformity and homogeneity index. The 3D-ACT decreased significantly the PTVs D_{max} and D_{mean} (P<0.0001), and offered better homogeneity for inguinal PTV (i.e., 1.07±0.01, P<0.0001).The 3D-ACT decreased the rectum absorbed dose, V40 (volume receiving ≥40Gy), V45, and D_{max}to50.21±27.21, 22.81±10.22, and 46.56±1.11, respectively. With regard to femoral heads, the 3D-ACT decreased the D_{max} and V45 in comparison to the other two techniques.
Conclusion: The 3D-ACT seems to be an alternative to the AP-PA irradiation techniques in postoperative setting when IMRT is unavailable.

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Introduction

Vulvar cancer is a rare type of cancer, which accounts for 1-2% of all cancers in women and about 3-4% of all gynecologic malignancies. In this regard, surgery is considered as the major treatment in the adjuvant setting of patients with close or positive margins, deep invasion, lymphatic-vascular invasion, or with inguinal lymph node metastasis [1, 2].

The radiation therapy consists of anteroposterior "AP" and posteroanterior "PA" fields. The AP photon field is wide enough to cover the pelvis, the primary tumor, and inguinal areas. On the other hand, the PA photon field is narrow, which could only encompass the pelvis. A third anterior electron field is also used to deliver the missing dose into inguinal nodes [3]. However, the main disadvantages of this technique are the large volumes of irradiated normal tissues with low conformity index and dose inhomogeneity across the photon-electron junction of the field at the level of the inguinal area.

The intensity-modulated radiation therapy (IMRT) is a modern radiation technique with higher precision in the delivery of radiation dose. The IMRT allows more conformity by varying radiation beams spatially or temporally [4.5]. However, the 3D radiation therapy technique remains an interesting tool when it is used technically. One way to improve the conformity index of IMRT is to increase the number of fields (more than 2 fields) in the treatment planning process.

To the best of our knowledge, this is the first study that reports the dosimetric comparison between the AP-PA techniques and the 3D advanced conformal

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technique (3D-ACT) based on the multiplicity of treatment fields in patients with squamous cell cancer of the vulva in postoperative setting.

Materials and Methods

CT Simulation and target contouring

This comparative planning study was conducted on 15 patients with vulvar carcinoma treated with adjuvant radiation therapy between April, 2015 and November, 2016 at the National Institute of Oncology in Rabat, Morocco. In line with ethical considerations, verbal informed consent was obtained from all patients.

Patients were simulated in the supine position with an immobilization device. A planning computed tomography CT (Siemens Simulator Scanner, Siemens AG, Erlangen, Germany) with 5-mm thick slices was used for the delineation of target volumes and organs at risk (bladder, rectum, bowel, and femoral heads) without using a contrast agent. The delineation was performed by one radiation oncologist for all patients. The tumoral clinical target volume (CTV-T) included the operative bed with 1-cm margin, while the nodal CTV-N included the bilateral internal, external iliac nodal areas by applying 0.7-cm margin around internal and external iliac vessels. The CTV-N also included inguinal lymphnodes, which were delineated, according to the radiation therapy oncology group (RTOG) recommendations, as a "compartment" [6]. The total planning target volume (PTV) resulted in a 1-cm expansion around CTV-T and CTV-N.

Treatment methods

Three 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 6 and 18MV photon beams by (ELEKTA Synergy linear accelerator, Elekta AB, Stockholm, Seweden)with an 80multileaf collimator (MLC) as can be seen in Figure 1. A total dose of 46Gy (i.e., 2Gy/fraction, 5 fractions/week) was prescribed to the total PTV and if required a boost range of 10-14 Gy to PTV-T and/ or PTV-N was considered.

Technique 1 (photons with source-skin distance inguinal supplement) (figure 1a)

Technique 1 consisted of using a wide 6MV AP pelvic field that includes the inguinal nodes, a narrower 18MV PA pelvic field sparing the femoral heads. It also involved two additional 6MV anterior fields setup at the standard source-skin distance (SSD) of 100 cm, angled to match the divergence of the lateral borders of PA field, to boost the dose to the inguinal nodes (Figure 1a).

Technique 2 (modified segmental boost technique "MSBT") (figure 1b)

This technique, as reported by Moran et al [7], is a modification of technique 1. The two anterior inguinal boost fields were generated using the same isocenter. The gantry of each field was angled 7°-9°.

Technique 3 (3D Advanced conforma technique « 3D-ACT ») (figure 1c)

This technique included 8 open fields to cover the PTV from 5 fixed gantry angles: 30°, 95°, 180°, 265°, and 330°, weighted differently with three fields (95°, 180°, and 265°) as segments to minimize hot spots.

Treatment plans analysis

The treatment plans were generated by XIO. The 98% of the PTV should receive 95%-107% of the prescribed dose to consider the plan acceptable. For each plan, the dose-volume histogram was used to generate planning target volumes (total and inguinal PTV) and organs at risk (OAR; e.g., 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 [V_{xGy}]).

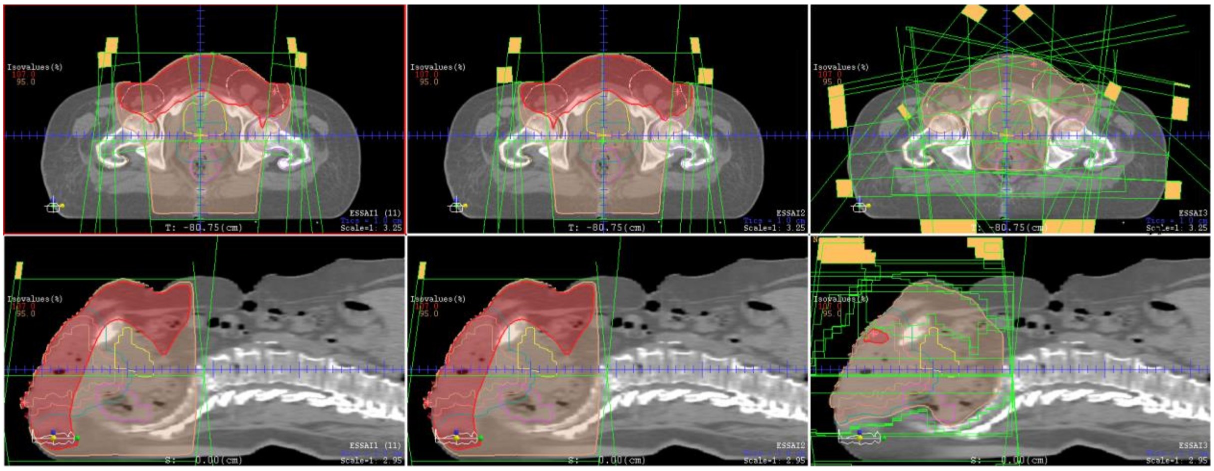

Figure1. Axial and sagittal reconstruction planning CT slices of SSD (left: a), MSBT (middle: b), and 3D-ACT (right: c) display of the 95% (brown) and 107% (red) isodoses of the prescribed dose

The degree of conformity has been evaluated by calculating the RTOG conformity index, defined as:

$$CI_{RTOG} = V_{RI} / V_{PTV} \quad (1)$$

Where, V_{RI} denotes reference isodose volume and V_{PTV} signifies PTV volume.

The Homogeneity index was calculated using two different formulae:

a/Homogeneity index (HI1) $= D_5 - D_{95}/D_{50}$ (2)

Where, D_{50} is the minimum dose in 50% of PTV; D5refers to the minimum dose in 5% of PTV, indicating the maximum dose, and D_{95}refers to the minimum dose in 95% of PTV, indicating the minimum dose. The ideal value is zero.

b/ Homogeneity index (HI2) $= D_5/D_{95}$.

(3)

The ideal value is one, and it increases as the plan become less homogeneous [8].

Statistical analysis

Statistical analysis was performed running ANOVA and post hoc test in SPSS software, version 20. P-value less than 0.05 was considered statistically significant.

Results

The 95% isodose volume was significantly reduced with the advanced conformal technique ($P<0.0001$) without compromising total PTV coverage (P= 0.94).As figures 1, 2, and 3 illustrate this technique result in the best conformity and homogeneity index (HI1 and HI2) values as 2.33±0.37, 0.08±0.008, and 1.08±0.001, respectively ($P<0.0001$). Furthermore, as Table 1 shows the 3D-ACT decreased significantly the PTVs D_{max} and D_{mean} to 49.51±0.69 and 46.49±0.45, respectively ($P<0.0001$), and offered better homogeneity (HI1 and HI2) for inguinal PTV with the values of 0.07±0.01 and 1.07±0.01, respectively ($P<0.0001$).

Table 1. Dosimetric comparison of target volume parameters with regard to the irradiation techniques

			SSD	MSBT	3D-ACT	p
total PTV	95% Isodose volume		4716.75±976.11	4711.11±976.41	2650±1000	<0.0001
	D95%		98.39±1.18	98.38±1.19	98.50±0.53	0.94
	Conformity index		3.87±0.77	3.86±0.87	2.33±0.37	<0.0001
	Homogeneity index	HI 1	0.13±0.02	0.13±0.02	0.08±0.008	<0.0001
		HI 2	1.14±0.03	1.14±0.03	1.08±0.001	<0.0001
	Dmax		55.19±1.82	55.46±1.99	49.51±0.69	<0.0001
	Dmean		48.51±0.94	48.56±0.94	46.49±0.45	<0.0001
inguinal PTV	Dmax		54.78±1.92	55.21±2.14	49.07±0.62	<0.0001
	Dmean		49.55±1.07	49.69±1.06	46.2±0.8	<0.0001
	Homogeneity index	HI 1	0.12±0.04	0.13±0.03	0.07±0.01	<0.0001
		HI 2	1.13±0.05	1.14±0.04	1.07±0.01	<0.0001

PTV: planning target volume
SSD:source skin distance
MSBT:modified Segmental Boost Technique
3D-ACT: advanced conformal technique

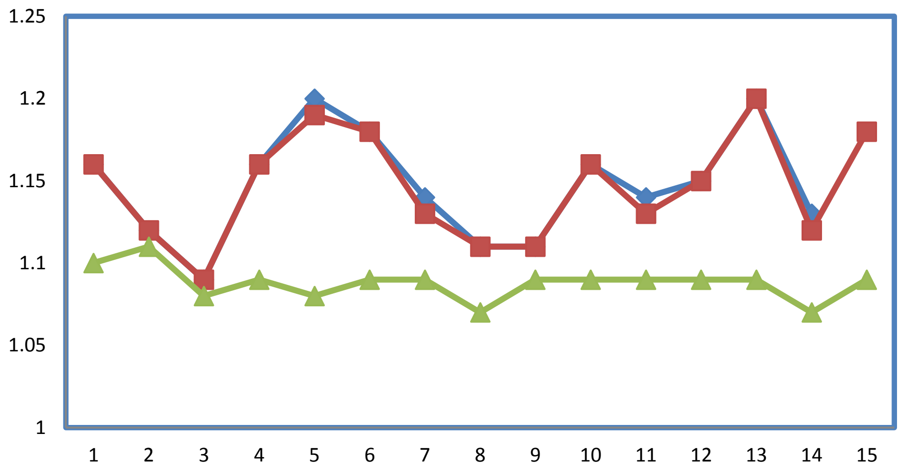

Figure 2. Total PTV homogeneity index (HI 2) of all patients with regard to irradiation techniques (SSD: red, MSBT: blue, 3D-ACT: green)

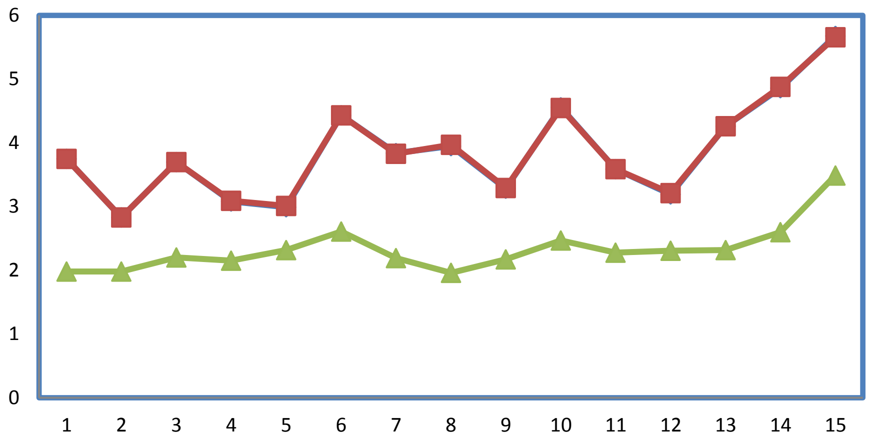

Figure 3. Total PTV conformity index of all patients with regard to irradiation techniques (SSD: red, MSBT: blue, 3D-ACT: green)

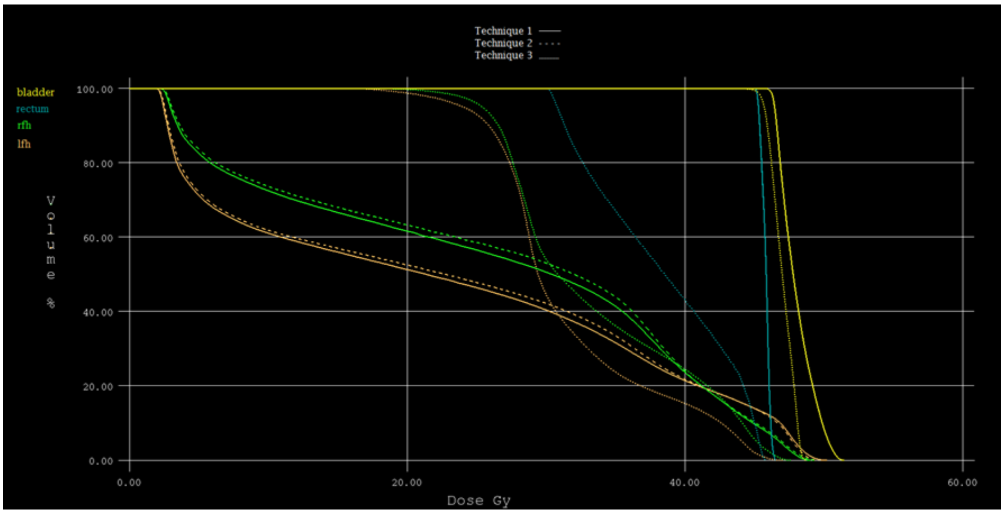

Figure 4. Dose-volume histogram of the rectum, bladder, and femoral heads with regard to irradiation techniques (1: SSD, 2: MSBT, 3: 3D-ACT)

The parameters of OAR with regard to the irradiation technique were summarized in Table 2. As can be seen, there was nosignificant difference among the three irradiation techniques regarding bladder. The 3D-ACT revealed that rectum absorbed dose decreased significantly in terms of V40 (volume receiving ≥40Gy), V45, and D_{max} to 50.21±27.21 (P=0.002), 22.81±10.22 (P<0.0001) and 46.56±1.11 (P= 0.003), respectively. Considering femoral heads, the 3D-ACT significantly decreased the D_{max} and V45 in comparison to both SSD and MSB techniques. However, the V20 increased up to 93.49±8.48 (P<0.0001). The D_{max} of small bowel reduced by 6% with the 3D-ACT. Moreover, the values associated with V45 and V40 decreased in this technique; however, their decrease was not statistically significant (Figure 4).

Table 3 shows the analysis of correlation for the irradiation techniques. There was a significant correlation between femoral heads parameters and the distance from groin skin to the deeper aspect of PTV inguinal ("PTV inguinal Depth" 6.59±0.97cm). In this regard, 3D-ACT showed the highest correlation for V30 (LFH r: 0.64, p: 0.009. RFH r: 0.67 p: 0.006) and V40 (LFH r: 0.66, p: 0.0047. RFH r: 0.60 p: 0.01).

There was no significant difference between SSD and MSBT regarding conformity and homogeneity index, target volumes coverage, and OAR parameters.

Table 2. Dosimetric comparison of OAR parameters with regard to irradiation techniques

		SSD	MSBT	3D-ACT	difference % (3D-ACT/MSBT)	p
Bladder	V10 (%)	100	100	100	-	-
	V20 (%)	97.48±6.96	97.48±6.96	100	-	0.35
	V30 (%)	93.09±12.04	93.01±12.03	99.99±0.02	-	0.09
	V40 (%)	85.94±19.6	85.94±19.6	87.68±14.44	-	0.95
	V45 (%)	78±28.79	78.08±28.79	60.49±35.25	-	0.21
	Dmax	49.27±1.8	49.27±1.8	48.2±1.7	-	0.14
Rectum	V10 (%)	99.81±0.7	99.81±0.7	100	-	0.61
	V20 (%)	96.41±7.91	96.41±7.91	99.74±0.87	-	0.27
	V30 (%)	92.2±14.88	92.21±14.86	91.35±11.95	-	0.98
	V40 (%)	81.93±25.24	81.94±25.23	50.21±27.21	- 39	0.002
	V45 (%)	73.94±34.18	74.05±34.18	22.81±10.22	- 69.2	<0.0001
	Dmax	48.16±1.52	48.18±1.53	46.56±1.11	- 5.2	0.003
Small bowel	V15 (cc)	266.43±114.87	266.41±114.6	293.5±122.13	-	0.76
	V30 (cc)	221.58±77.21	228.3±97	221.58±77.21	-	0.97
	V40 (cc)	204.7±89.86	311.32±82.6	175.84±72.37	-	0.35
	V45 (cc)	182.81±85.68	182.76±85.66	128.83±74.5	-	0.12
	Dmax	51.74±1.34	51.73±1.35	48.99±0.67	-6	<0.0001
Right femoral head	V20 (%)	69.9±16.8	68.7±17	93.49±8.48	+35	<0.0001
	V30 (%)	60.52±16.6	57.64±15.56	57.58±14.34	-	0.84
	V40 (%)	32.14±10.87	31.78±10.96	33.12±11.19	-	0.94
	V45 (%)	12.37±5.48	12.79±5.75	7.16±4.71	- 43	0.01
	Dmax	48.48±1.32	48.51±1.18	47.14±0.77	- 3	0.002
Left femoral head	V20 (%)	72.47±15.23	71.2±15.34	93.64±7.7	+ 30	<0.0001
	V30 (%)	61.9±15.05	59.22±14.91	56.04±13.42	-	0.54
	V40 (%)	30.32±10.21	30±10	29.31±10.21	-	0.96
	V45 (%)	10.41±5.79	11.18±5.61	2.36±1.95	- 79.8	<0.0001
	Dmax	48.13±1.23	48.35±1.37	46.47±0.99	- 3.7	<0.0001

SSD:source skin distance
MSBT: modified Segmental Boost Technique
3D-ACT: advanced conformal technique

Table 3: Analysis of correlation between femoral heads parameters and PTV inguinal Depth

		Left femoral head					Right femoral head				
		V20	V30	V40	V45	Dmax	V20	V30	V40	V45	Dmax
MSBT	r	0.55	0.56	0.34	-0.26	-0.32	0.62	0.57	0.52	0.57	-0.03
	p	0.03	0.28	0.21	0.34	0.25	0.01	0.02	0.04	0.02	0.89
SSD	r	0.58	0.62	0.39	-0.31	-0.25	0.61	0.58	0.53	0.55	0.13
	p	0.02	0.01	0.14	0.24	0.35	0.01	0.02	0.04	0.02	0.62
3D-ACT	r	0.44	0.64	0.66	-0.28	-0.31	0.59	0.67	0.60	0.67	0.16
	p	0.09	0.009	0.007	0.3	0.24	0.02	0.006	0.01	0.002	0.55

SSD: source skin distance
MSBT: modified Segmental Boost Technique
3D-ACT: advanced conformal technique

Discussion

Adjuvant radiotherapy decreases locoregional relapses and improves survival in patients with close margins, positive margins, or inguinal lymph node involvement [9]. The radiation therapy was mostly delivered using an “AP” and “PA” fields. The AP photon field was wide enough to cover the pelvis, primary tumor, and inguinal areas. On the other hand, the PA photon field was narrow, which could only encompass the pelvis. A third anterior electron field was also used to deliver the missing dose into inguinal nodes. This technique suffers from the demerits of the hotspots and dose heterogeneity across the match line, which can potentially result in tardive toxicity.The dose homogeneity across the match line could be increased by setup errors. The therapist enters the room several times to reposition the patient to treat inguinal areas. Another limitation of this technique is using higher energy electrons necessary to reach the inguinal nodal depths of 5–7 cm, which can induce skin reactions [10]. Both SSD and MSBT delivered the missing dose in groin areas with photons, which can reduce skin complications. However, the dose inhomogeneity across the match line is a great concern even with avoiding the couch shifts for groin nodes treatment in the MSBT technique. In order to resolve this problem, it is suggested to use more than 2 treatment fields with different gantry angulations.

The dosimetric comparison confirmed that the 3D-ACT, either on total or inguinal PTV, was more conformal. In addition, this technique could significantly improve dose homogeneity. Regarding OAR, this approach reduced the dose at the rectum, small bowel, and femoral heads. To the best of our knowledge, this is the first study that reports a dosimetric advantage of another 3D radiation technique in the postoperative treatment of vulvar cancer.

According to the findings of previous studies, reductions in the volume of irradiated normal tissues may reduce the risk of treatment-related toxicity in patients who received conventional doses [10]. Therefore, there is a need for ongoing studies on the conformal treatment technique. It is worth mention that the main inconvenient with AP-PA techniques is the large irradiated volume of normal tissue. In the current study, the conformity index was a little lower than 4 either with SSD or MSB techniques, where as the 3D-ACT reduced this index by 40% (2.33 vs 3.87). The IMRT provided a more conformal dose distribution as Khosla et al [3] reported a CI=1.4. In addition, the 3D-ACT improved dose homogeneity (1.08 vs1.14). These improvements were available either for total or inguinal PTV without compromising target volume coverage.

Regarding OAR, the 3D-ACT reduced up to the volume of 70% absorbing more than 45Gy and up to 5% the maximum dose in the rectum. Heron et al [11] compared IMRT and conventional (AP-PA) planning in seven women undergoing adjuvant pelvic irradiation; the percentage of the rectum that received 30Gy or more by conventional planning was 92.8% versus 32% with IMRT, corresponding to a reduction about 60%. The 3D-ACT reduced the D_{max}, V40, and V45 of the small bowel; however, the threshold of significance was not reached for V40 and V45. This reduction was much better with IMRT as reported by Khosla et al [3]. As expected, there was no significant reduction of the bladder absorbed dose due to the anatomic location of the bladder, a larger number of anterior than posterior fields, and heaveir anterior fields. This is the major difference between our technique 3D-ACT and IMRT. As Beriwal et al [10] reported the mean volume of the bladder that received doses in excess of 30Gy was significantly reduced with IMRT compared with 3D CRT.

Electron beams can be used to treat a superficial target with sharp dose fall-off rather than high-energy photons. For example, with 12 MeV electron beam the dose is 90% of max at 3 cm; however, it falls to approximately 10% at 6cm[12]. Koh et al. used 50 pre-treatment CT to define the depth of the femoral vessels and found a mean depth of 6.1 cm [13]. In the current study, the PTV inguinal depth was 6.59±0.97cm and it seemed that the irradiation of groin nodes with electron could be associated with the probability of missing the target. Therefore, we treated all patients with photons. The main disadvantage associated with the photon in this location was the increase in the femoral heads absorbed dose. The recommended dose was less than 10% of femoral head received more than 50Gy [14] which be treated either with the both AP-PA techniques or the 3D-ACT. However, the latter modality allowed a significant decrease of the delivered dose to femoral heads (V45: 2.36±1.95). Therefore, the advanced conformal technique can be proposed as an alternative to the AP-PA irradiation techniques in postoperative setting when IMRT equipment is unavailable.

Conclusion

The 95% isodose volume was significantly reduced with the 3D-ACT without compromising total PTV coverage. This new technique resulted in the best conformity and homogeneity index comparing to AP-PA irradiation techniques. The new technique seems to be an alternative to the AP-PA irradiation techniques in postoperative setting when IMRT is not available.

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