The African Review of Physics (2020) **15**:0020

Megavoltage X-Ray Volumetric Modulated Arc Therapy and Multi-Entrance Three Dimensional Conformal Radiation Therapy for Prostate Cancer

F. Assaoui[1], A. Lachgar[2] and N. Benjaafar[2]
[1]*Medical Physics Unit, Radiotherapy Department, National Institute of Oncology, Rabat, Morocco;*
[1]*The Abdus Salam International Center for Theoretical Physics, Trieste, Italy*
Email: Assaoui2003@yahoo.fr
[2]*Radiotherapy Department, National Institute of Oncology, Rabat, Moroco*

We investigate the dual arc volumetric modulated arc therapy (VMAT) technique and its pretreatment quality control for patients with prostate cancer. The forward technique multi-entrance three-dimensional conformal radiation therapy (ME-3DCRT) and VMAT technique were compared with respect to plan quality (homogeneity and conformity indexes, and the organs at risk doses) and treatment efficiency (i.e., treatment time, monitors unity) for Eleven high risk prostate cancer patients treated with dual-arc volumetric modulated arc therapy (one fraction per day and five times a week) in the National Institute of Oncology Rabat-Morocco, between 2017 and 2019. Furthermore, the statistical analysis and the VMAT dosimetric evaluation were done.

1. Introduction

The prostate cancer is the most common visceral cancer in male patients and is the second cause of cancer-related deaths [1]. The randomized phase three studies demonstrated that dose escalation provided better disease-free survival in prostate cancer patients [2]. This effect was found especially in intermediate and high-risk prostate cancer patients [3]. However, Zelefsky MJ et al [4] and Peeters ST, et al [5] showed that escalated doses caused more side effects, particularly the late grade-2 gastrointestinal toxicity. The introduction of the new radiotherapy techniques such as IMRT and VMAT reduced the side effects as a result of less number of organs at risk in the volume of treatment area [6, 7]. From this viewpoint IMRT and VMAT were considered more in the curative treatment of prostate cancer [8-14]. However, in high dose radiotherapy applications, volumetric modulated arc therapy approaches have been found better than IMRT [15, 16-18], especially for the busy center because of the long treatment time constraint of IMRT technique [19-24].

The aim of this work is to find answer to questions from our study statistical analysis and volumetric dose studies for the organ at risk of prostate cancer [25]. The first question was about the feasibility of the modern techniques (IMRT, VMAT) in a busy clinic and the comparison of treatment planning and delivery times required for modern and classical approaches. The second question was about the acute and late complications of the prostate cancer treatment. Its answer will be in our clinical study which we have already started for the same patients. Furthermore, the dosimetric comparison of the target and organs at risk doses for forward techniques ME-3DCRT and VMAT as well as the evaluation of the VMAT treatment plans.

2. Methods and Materials

CT datasets of 11 patients with high risk prostate cancer were prospectively selected for this comparative planning study. The prescribed dose was 76Gy for 10 patients with a conventional fractionation (2Gy per fraction) and a hypo-fractionated regimen 66.25Gy over 25 fractions was for one patient. All patients underwent CT with a 3 mm slice thickness and reconstructed with 1 mm using a Siemens Scanner (16 barrettes and FOV of 82 Cm). Prior to imaging, the patients were instructed to have a full bladder and to empty their bowels using mild laxatives. To minimize the setup variability, a custom immobilization device (knees rest and foot wedges) was used in supine position. Three positional markers were placed in anatomically stable regions, one anterior and two lateral points to assure identical positioning of the patient during computed tomography and irradiation. An MRI with the same position as the planning CT was done for all patients.

The target volumes (CTV, PTV) and the OARs (Rectum, Bladder, bowel, left and right femur heads and penile bulb) were delineated with aid of diagnostic MRI and CT using Monaco Sim. The prostate +/- seminal vesicles (PSV/P) and prostate plus seminal vesicles and pelvic lymph nodes (PSVN) contours denoted as the clinical target volumes CTV_1

and CTV_2, respectively. The PTV_1 (High risk) was generated by adding a 10 mm to the CTV_1 in all directions, except in the posterior position, where a 5 mm margin was used. The PTV_2 (low risk) was PTV_1 plus PTVN where the PTVN was the CTV nodes with a 7 mm margin. The treatment dose was 56 Gy (50 Gy) on PTV_2, and an overdose of 20 Gy (16.25 Gy) on PTV_1. The two treatment plans VMAT and the ME-3DCRT were created using the Monaco treatment planning system (TPS) version 5.11.02. The primary goal during planning was to reach similar PTV coverage for both approaches and then, as a secondary goal, to reduce the dose in OARs to avoid the radiation complexations. The dosimetric indices were assessed according to the criteria of the International Commission on Radiation Units and Measurements (ICRU) Report 83 [26].

2.1. VMAT treatment plan

The VMAT plans were generated for a 6 MV Elekta Versa HD equipped with 160 MLC (leaf width 5 mm at the iso-center). The planning was calculated using Monte Carlo Algorithm at 2.5 mm dose grid space, 1% statistical uncertainty per calculation, 5 mm as minimum segment width and 360 control points per Arc. The PTV_2 was planned to receive 56Gy (50Gy) in 38 (25) fractions of 1.47Gy (2Gy) with the integrated boost volume PTV_1 receiving 76Gy (66.25Gy) simultaneously (simultaneous integrated boost SIB technique). All plans were optimized to cover more than 95% of the PTVs with the 95% of the prescribed dose and to have less than 107% of the prescribed dose in 2% of the PTVs. The prescription was done in 50% of the PTV_1. The iso-center was the center of the PTV_2 because of the pretreatment quality control's constraint (such that the all beamlet projections were on the MatriXX^{Evolution} phantom (24x24) cm^2 to collect the maximum data).

2.3. ME-3DCRT treatment plan

TheME-3DCRT plan was consisted of 10 fields 18 MV as follows: Four direct fields (Anterior, posterior, and 2 laterals opposed) on PTV_2 for the first phase of the 46Gy and then 30Gy (20 Gy) as boost with 6 fields (45º, 90º, 135º, 225º, 270º, 315º) on PTV_1. The weights of the individual fields were optimized to maximize the dose uniformity in the PTVs and sparing the OARs (in the first course two thirds of the dose with anti-post and the one third with the laterals. For the second dose, 18%, 11%, 17%, 21%, 11%, 18%, respectively and 4% for one segment of the field 135º. The iso-center and the dose point were the center of the PTV_1.

2.4. Data analysis and statistical study

The dose volume histograms (DVHs) were calculated for the PTVs and the OARs. The homogeneity within the PTV_1 and the dose conformity index (HI and CI) were calculated and compared in both techniques with: $HI = (D_{2\%} - D_{98\%}) / D_{50\%}$, where, $D_{n\%}$ is the dose in n % of the volume of the PTV (the ideal is close to zero). CI = TV / PTV, where TV is the target volume covered by the reference dose (the ideal is One).

The t-test student method was used for statistical analysis where the p value is significant for the results <=0.05. The D_{max}, D_{mean} and $D_{95\%}$ of the PTVs were compared and evaluated between the two approaches. The mean percent's with 60Gy and 74Gy (60Gy and 75Gy) of the rectum and (bladder) volumes, respectively, were calculated and compared. We also computed and analyzed the mean of the dose on 200cc, 300cc and 400cc of the volume of the bowel, the dose in 50% for the penile bulb and the dose received by 50% of the left and right femur heads. The pretreatment quality control for the VMAT plans was also evaluated using the My QA patient system and Matrixx ^{Evolution}.

3. Results

The isodose lines on the transversal slice of the hypo-fractionated case and on the Transversal, Sagittal and Coronal slices of one patient with the conventional fractionation for both techniques are shown in Figs.1a and 1b, respectively. As seen in the Figs.1, the isodose 95% of the prescribed doses are conforming to the shape of the PTVs and reducing at the volume of the neighboring normal critical structures for the VMAT treatment planning. In contrast, the ME-3DCRT plan results show that the OARs are included in the isodoses 95% of the prescribed doses.

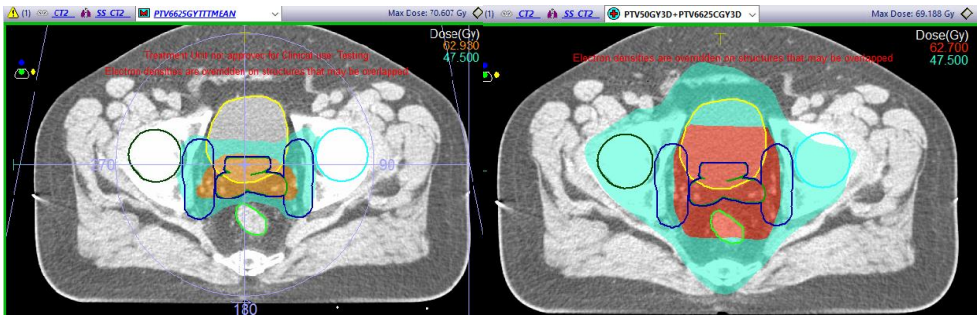

Fig.1a: Transversal CT image with isodoses distribution 95% of the prescribed dose 66.25Gy (Brown) and 50Gy (Cyan) from the VMAT (left) and the ME-3DCRT (Right) plans superimposed. The PTV_1, PTV_2, Bladder, Rectum, left and right Femur heads indicated in Green, blue, Yellow, Light green, Cyan and Dark Green, respectively.

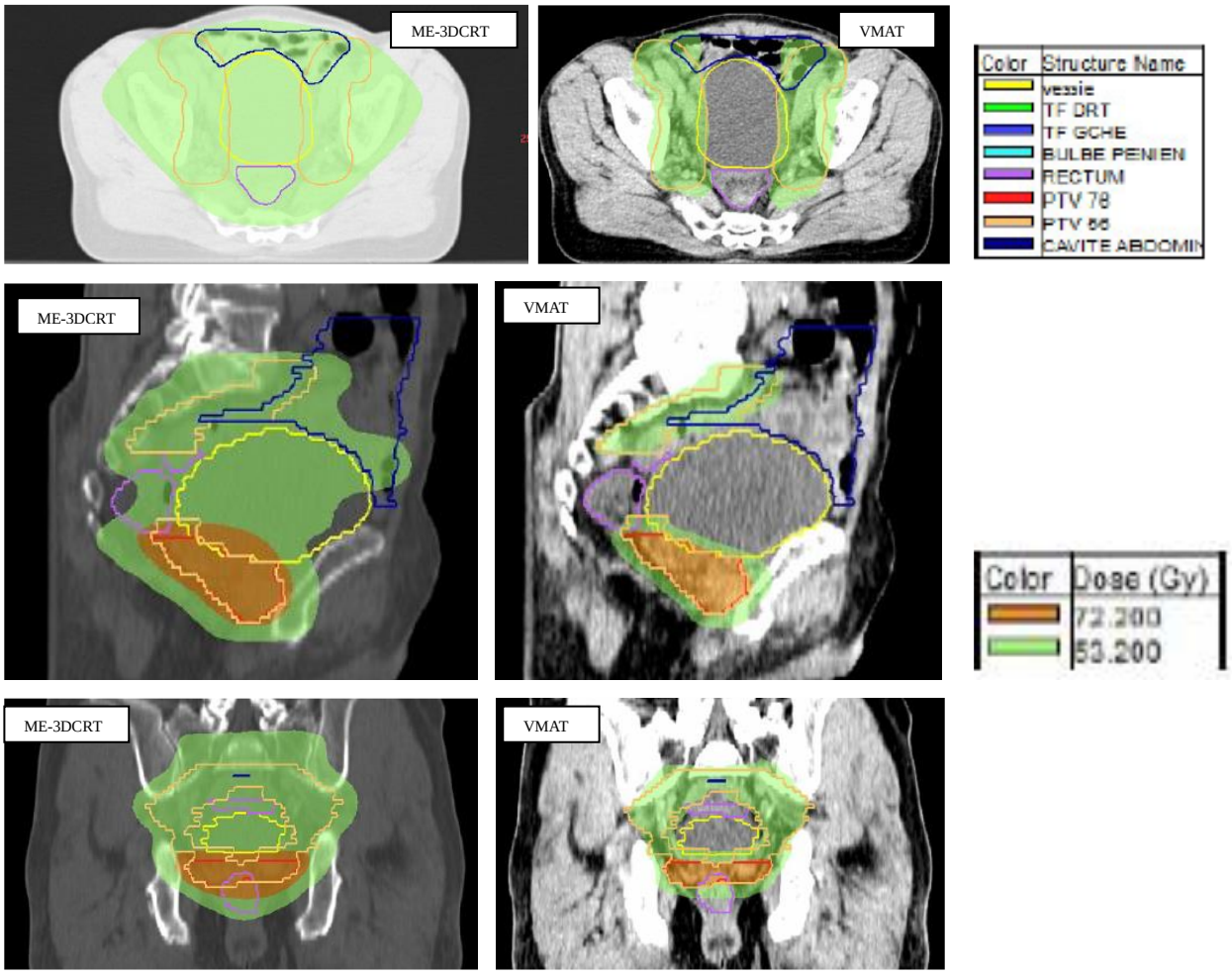

Fig.1b: Transversal, Sagittal and Coronal CT images with isodoses distribution 72.2Gy and 53.2Gy (95% of the prescribed doses were respectively76Gy and 56Gy) from the ME-3DCRT (left) and the VMAT (Right) plans.

The DVHs in Fig.2 show that the coverture of the PTVs with the ME-3DCRT is better than VMAT. But there is a large difference between the doses received by the OARs.

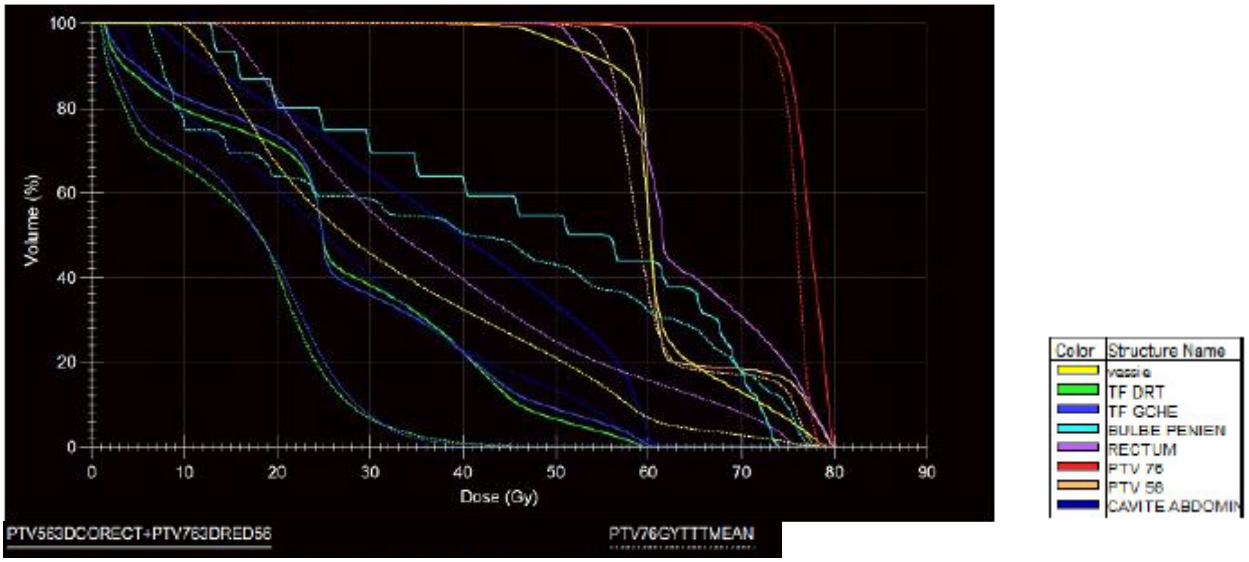

Fig.2: DVHs for VMAT (solid) and ME-3DCRT (dashed), the colors correspond to the PTVs and OARs are shown in the right of the image.

The mean of the CI and the HI for the High risk planning target volume were 0.99/0.97 and 0.08/0.086, respectively with the p value 0.73 and 0.57 (Table.1**)**, so the difference were not significant.

PTV_1	*ME-3CRT*	*VMAT*	*P Value*
Conformity index mean	0.99	0.97	0.73
Homogeneity index mean	0.08	0.086	0.57

Table.1: The conformity and the homogeneity index of the PTV_1 for the both approaches

Table.2 shows the results of the $PTV_{1,\,2}$ doses with ME-3DCRT and VMAT. The difference between the two $D_{max\ PTV1,2}$ were not statistically significant p = 0.517 and 0.525, respectively, and without hot spots for the both techniques (D_{max} < 107% of the prescribed dose). The coverage of the $PTV_{1,\,2}$ (with the 95% of the prescribe dose) were adequate with these two approaches but better with the ME-3CRT and the difference was significant for the PTV_1, p = 0.02 and p = 0.011 for the PTV_2. The $D_{mean\ PTV1,\,2}$ were 77.056/76.031 and 60.11/63.83 with the p value 0.33 and 0.036, respectively, the difference was significant for the PTV_2.

	Average		*P value*
	ME-3DCRT	*VMAT*	
Dmean PTV1 (Gy)	77.056	76.031	0.33
Dmax PTV1 (Gy)	79.43	80.16	0.517
V PTV1 (95% of Prescribed Dose) (%)	99.67	97.74	*0.02*
Dmean PTV2 (Gy)	60.11	63.83	0.036
Dmax PTV2 (Gy)	79.44	80.15	0.525

V PTV2 (95% of Prescribed Dose) (%)	99.99	98.68	*0.011*

Table.2: The $D_{mean\ PTV1,2}$, $D_{max\ PTV1,2}$ and $V_{PTV1,2}$ received 95% of the prescribed dose for the both techniques.

3.1. Organs at Risk

The difference between the ME-3DCRT and VMAT plans is significant, for the DVHs of the OARs, rectum, bladder, left and right femur heads, bowel and penile bulb, see Fig.2. The mean of the V_{60Gy} and V_{74Gy} of the rectum were 78.112% / 25.525%, and 34.562% / 4.283%, with a p value 0.8 10^{-7} and 0.003, respectively. For the bladder the mean of V_{60Gy} and V_{75Gy} were 57.46% / 29.766% (p = 0.001) and 14.447% / 11.088% (p = 0.038), respectively. The volume of the Left (Right) femur heads received 50 Gy was 18.018 % / 2.234%, (18.491% / 1.444%) with a p value 0.001 (0.001). So, the difference was very significant for rectum, bladder and femur heads, Table.3. For the bowel and the penile bulb there is an important difference between the both techniques but statistically not significant. The dose in 200, 300 and 400 cc of the bowel was 39.654Gy / 34.269Gy (p=0.161), 45.183Gy / 40.996Gy (p=0.086) and 33.635Gy / 26.337Gy (p=0.128), respectively. Concerning the dose in the penile bulb, the volume received 50Gy was 92.77% / 74.865% of the structure with the p value 0.046.

	Average		*P value*
	ME-3DCRT	*VMAT*	
V60Gy Rectum (%)	78.112	25.525	0.000008
V74Gy Rectum (%)	34.562	4.283	0.003
V60Gy Bladder (%)	57.46	29.766	0.001
V75Gy Bladder (%)	14.447	11.088	0.038
V50Gy Left Femoral Head (%)	18.018	2.234	0.001
V50Gy Right Femoral Head (%)	18.491	1.444	0.001
D200cc Bowel (Gy)	39.654	34.269	0.161
D300cc Bowel (Gy)	45.183	40.996	0.086
D400cc Bowel (Gy)	33.635	26.337	0.128
V50Gy Penile Bulb (%)	92.77	74.865	0.046

Table.3: The doses received by the OARs using the ME-3DCRT and VMAT approaches.

3.2 Monitor units and treatment time for each technique

For plan efficiency, number of Monitor units (MUs) and treatment time (TTT) were considered. The mean of the MUs and the TTT were 459.636 / 592.499 and 4.125mn/6.038mn for ME-3DCRT and VMAT respectively, with a p= 0.02 and 0.1 10^{-4}, as shown in the following Table.

	ME-3DCRT	*VMAT*	*P Value*
MUs mean	459.636	592.499	0.02

TTT mean (mn)	4.125	6.038	$0.1\ 10^{-4}$

Table.4: The mean of the MUs and TTT of the ME-3DCRT and VMAT approaches.

3.3. Pretreatment quality control for the VMAT:

A dosimetric evaluation of VMAT was performed using the 2D-array with angle correction in a homogeneous phantom, the gamma index analysis showed for the 3% / 3 mm a mean passing pixel percentage of 99.4% (ranges from 97.7% to 100%).

4. Discussion

Advancement in treatment delivery techniques in external beam radiation therapy (EBRT) has significantly improved the conformal radiation dose distributions of the tumor while reducing dose to the critical structures. These have played an important role in the treatment of high risk prostate cancer. Dose escalation in prostate treatments has been demonstrated to improve local control [2, 3] [18]. In [20-23], the authors concluded that the initial pelvic IMRT is the most important strategy in dose escalation and critical organs sparing. The long treatment time is the constraint of the IMRT [19-24].

The volumetric modulated arc therapy is the technique which achieves the IMRT quality plans with shorter treatment time. K. Otto et al. showed that the dual arc –VMAT achieved the best dosimetric quality, homogeneity and conformity index, with shortest treatment time and the lowest MUs comparing to the IMRT and single arc-VMAT [27]. With ME-3DCRT (prescribed doe 70Gy) for the patients with high risk prostate cancer the OARs were tolerated, the mean of V_{60Gy} and V_{70Gy} of the rectum (bladder) were 31.53% and 2.00% (32.22% and 2.68%), respectively, and the mean of V_{50Gy} and V_{40Gy} of the femur heads were 0.19% and 4.21% [25]. We increased the prescribed dose to 74Gy and from our National Institute of Oncology-Rabat's experience using ME-3DCT, the OARs were always tolerated which is not the case with 76Gy as we show in this study. The mean of the V_{60Gy} and $V_{74\ (75)Gy}$ of the rectum (bladder) were 78.112% and 34.56% (57.46% and 14.447%) respectively, and the mean V_{50Gy} of the Left (Right) femur heads was 18.018% (18.491%) with the ME-3DCRT technique, in contrary the dose in all of these OARs was very low using the dual-arc VMAT. The mean of the V_{60Gy} and $V_{74\ (75)\ Gy}$ of the rectum (bladder) were 25.525% and 4.283% (29.766% and 11.088%), respectively, and the mean V_{50Gy} of the Left (Right) femur heads was 2.234% (1.444%) with the VMAT approach. Our results are similar to those of the Adam et all [28]. It may be concluded that the escalade of dose is especially for the volumetric modulated arc therapy [28, 18, 29].

5. Conclusion

In high dose radiotherapy applications, dual arc-VMAT technique have been found better than ME-3DCRT for the high risk prostate cancer with the pelvic nodal irradiation. This investigation demonstrates the dual arc-VMAT achieves superior normal tissue and OARs protection as compared to ME-3DCRT and with similar dose to the planning target volumes. Clinical results are pending.

Acknowledgements

The corresponding author would like to thank the Head of the ICTP Medical Physics Section Professor Luciano Bertocchi and the Director of the ICTP Professor Fernando Quevedo, the International Atomic Energy Agency, the Italian Government and UNESCO for hospitality at the Abdus Salam International Centre for Theoretical Physics (ICTP), Trieste-Italy. This work was supported by the Associated and Federation Schemes of the Abdus Salam International Center for Theoretical Physics (ICTP), Trieste-Italy.

Conflict of Interest

The Authors declare that they have no competing interest associated with this manuscript.

References:

[1] Cooperberg MR, Cowan J, Broering JM, Carroll PR, World. J. Urol. 26, 211-218 (2008).
[2] Viani GA, Stefano EJ, Afonso SL, Int. J. Radiat. Oncol. Biol. Phys. 74, 1405-1418 (2009).
[3] Kuban DA, Tucker SL, Dong L, Starkschall G, Huang EH, et al, Int. J. Radiat. Oncol. Biol. Phys. 70, 67-74 (2008).
[4] Zelefsky MJ, Levin EJ, Hunt M, Yamada Y, Shippy AM, et al, Int. J. Radiat. Oncol. Biol. Phys. 70, 1124-1129 (2008).
[5] Peeters ST, Heemsbergen WD, van Putten WL, Slot A, Tabak H, et al, Int. J. Radiat. Oncol. Biol.

Phys. 61, 1019-1034 (2004).
[6] Amin N, Konski AA, Expert. Rev. Pharmacoecon. Outcomes. Res. 12, 447 - 450 (2012).
[7] Dinan MA, Robinson TJ, Zagar TM, Scales CD, Int. J. Oncol. Biol. Phys. 82, e781-e786 (2012).
[8] Kupelian PA, Reddy CA, Carlson TP, Altsman KA, Willoughby TR, Int. J. Radiat. Oncol. Biol. Phys. 53, 904-912 (2002).
[9] Kupelian PA, Reddy CA, Carlson TP, Willoughby TR , Cancer. J. 8, 62-66 (2002).
[10] Shunichi N, Shigeto I, Tatsuo T, Sadafumi K, Masaaki K, et al, Jpn. J. Clin. Oncol. 36, 224-230 (2006).
[11] Sanguineti G, Cavey ML, Endres EJ, Franzone P, Barra S, et al, Strahlenther. Onkol. 182, 543-549 (2006).
[12] Veldeman L, Madani I, Hulstaert F, De Meerleer G, Mareel M, et al, Lancet. Oncol. 9, 367-375 (2008).
[13] Zelefsky MJ, Fuks Z, Happersett L, Lee HJ, Ling CC, et al, Radiother. 55, 241-249 (2000).
[14] Zelefsky MJ, Fuks Z, Hunt M, Lee HJ, Lombardi D, et al, J. Urol. 166, 876-881 (2001).
[15] Berrin Inanc, Kubilay Inanc, Bilgehan Coskun, Ahmet Uyanoglu, Orhan Kizilkaya and Birsen Yucel, J. Nucl. Med. Radiat. Ther. 9,370 (2018).
[16] Palma D, Vollans E, James K, Nakano S, Moiseenko V, et al, Int J Oncol Biol Phys 72: 996-1001 (2008).
[17] Davidson MT, Blake SJ, Batchelar DL, Cheung P, Mah K, Int. J. Oncol. Biol Phys. 80, 1550-1558 (2011).
[18] Wolff D, Stieler F, Welzel G, Lorenz F, Abo-Madyan Y, et al, Radiother. Oncol. 93, 226-233 (2009).
[19] David Palma, Emilly Vollans, Kery James, Sandy Nakona, Vitali Moissenko, Richora Shaffer, Michael Mckenzie, James Moris and Karl Otto, Int. J. Radiation. Oncology. Biol. Phys. 72, No.4, 996 (2008).
[20] C. M. Nutting et al., Int. J. Radiat. Oncol. Biol. Phys. 48, 649 (2000).
[21] M. J. Zelefsky, Z. Fuks and S. A. Leibel, Semin. Radiat. Oncol. 12, 29 (2002).
[22] D. E. Heron et al, Gynecol. Oncol. 91, 39 (2003).
[23] G. Luxton, S. L. Hancock and A. L. Boyer, Int. J. Radiation Oncol. Biol. Phys. 59, 267 (2004).
[24] Henry C. K. Sze et al., Medical Dosimetry 37, Issue 1, 87 (2012).
[25] F.Assaoui, A.Bazine and T.Kebdani, African Review of Physics Journal. 8.0063, p. 477-487 (2013).
[26] ICRU, Report 83. Prescribing, recording, and reporting Intensity-Modulated Photon-Beam. Bethesda: International Commission on Radiation Units and Measurements; (2010).
[27] K. Otto, M. Milette and J. Wu, Int. J. Radiat. Oncol. Biol. Phys. 69 (suppl.) S703 (2007).
[28] D. Adam, M. D. Suditu, R. Popa, R. E. Ion, V. Ciocalitei, Romanian Report in Physics. Vol.66, No.2, P. 394-400 (2014).
[29] Tsai CL, Wu JK, Chao HL, Tsai YC, Cheng JC, Med. Dosim. 36, 264-271 (2011).

Received: 23 November, 2020

Accepted: 19 February, 2021