International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Dosimetric Advantage of VMAT Technique in Bone Marrow Sparing Than IMRT in Treatment of Cervical Cancer

Jayapalan Krishnan[1,2], Jayarama Shetty[2], Suresh Rao[1], Sanath Hegde[1], Shambhavi[1]

[1]Department of Radiation Oncology, Mangalore Institute of Oncology, Mangalore, India.
[2]Department of Radiation Oncology, K.S.Hegde Medical Academy, Mangalore, India.

Corresponding Author: Jayapalan Krishnan

ABSTRACT

Aim: Aim of this study was to compare bone marrow (BM) sparing at different dose and volume level of two state of the art technique VMAT and IMRT in the treatment of Ca.Cervix.
Methods and Materials: 20 patients with carcinoma of cervix were selected and each patient was simulated in head first supine position using a thermoplastic mask and/or vaclock. Computed tomographic images with a thickness of 3 mm were acquired with state of full bladder condition. The prescribed dose was 50 Gy in 25 equal fractions for 5weeks concurrently chemotherapy with cisplatin from second week of radiotherapy was administered. Two set of plans, one set of VMAT and another set of IMRT were generated and optimized with similar planning objectives to each patient. Dose of all plans of both techniques was calculated for 6MV photon using AAA with calculation grid size of 2.5mm. Dosimetric score of both techniques plans were evaluated and compared using student 't' test at 5% significant level.
Results: All of the patients in this study received VMAT technique treatment. The all patient VMAT plan satisfied with better DVH scoring, technical parameters as well as better Unified Dosimetry Index score. Both techniques achieved good target coverage. Moreover, CN(95%) ($p=0.001$) and V107% ($p=0.006$) of target were significantly better with VMAT. Bone marrow dose was significantly lesser ($P<0.001$) with VMAT than IMRT at the same time, without compromise, the sparing of other OARs also was achieved.
Conclusion: In the treatment of cervical cancer, the VMAT technique can be delivered highly conformal dose to the target with better OARs sparing. It helps to reduce hematological toxicity by reducing the bone marrow irradiation dose and volume to avoid the treatment gap due. The un-interruption treatment helps to be continued chemoradiotherapy without delay to achieve better tumor control.

Key words: VMAT, IMRT, Bone marrow, Cervical cancer

INTRODUCTION

Cervical cancer is highly prevalent in developing nations and it is estimated that close to 500,000 women worldwide develop this tumour and 233,000 die of the disease. [1] In the management of the cervical cancer, Concurrent chemoradiotherapy is used as a standard treatment protocol. In this treatment protocol, the radiation dose can be delivered to the tumour with external beam using Anteroposterior and posteroanterior fields or four field box techniques addition of chemotherapy and followed by intracavity brachytherapy. [2-3] Concurrent

chemoradiotherapy improved tumor control and overall survival and progression-free survival. [2] Many studies have been reported that the planned dose delivered to the tumour using conventional techniques 2D and 3DCRT can be irradiated more volume of bone marrow and delivered higher dose to the bone marrow. [4-5] The BM more than 50% is located in the pelvic and neighbouring bones in the adults, which is irradiated during the pelvic radiotherapy can cause blood counts dropping. [4] In the treatment of cervical cancer, the concurrent pelvic radiotherapy and chemotherapy increase the hemotological toxicity (HT) particularly leukopenia, neutropenia and thrombocytopenia. This (HT) can lead to interrupt the scheduled radiotherapy or to reduce the chemotherapy cycles from planned no.of cycles. The prolonged treatment time due to this unplanned interruption and reduced chemo cycle can reduce the tumour control and increase the tumor prognosis. [6]

To overcome these issues, IMRT technique has been used widely to reduce bone marrow dose and volume irradiation than 3DCRT technique with significant benefit. [4-5,7] However, no consensus was reached on the ability of IMRT compared with 3DCRT. [7] At the same time, there is no unique dose volume objectives of bone marrow sparing have been recommended to reduce the HT. [8-10] RTOG 0418 phase II trial shown that the HT associates with mean dose and higher dose irradiation volume of BM. [11] In some other studies resulted that the HT is associated with V_{10Gy}% and V_{20Gy}%. [12-13] Since there is different dose volume recommendation for the BM sparing, we planned to identify the better sparing level of bone marrow (BM) at different dose volume objectives by two state of art techniques Rapid Arc and IMRT and to compare the achieved dosimetric results of the BM.

METHODS AND MATERIALS

Patient Selection

20 patients of ca. cervix were selected for this study based on purposive sampling method. It includes a median age of 61.61 years (range 50-78years). Table 1 shows the descriptive data of patients. This study was approved by the ethics committee and informed consent for treatment was obtained from all the patients. For all patients VMAT and IMRT plans were generated for unbiased comparison of plan quality so, each patient can serve as his own control for the all parameters comparison.

Volume Definition and treatment planning

All patients were simulated in head first supine position using a thermoplastic mask and/or vaclock. Patients were instructed to drink 8oz water one hour before simulation to maintain full bladder condition while acquiring CT-images. Axial CT images with a thickness of 3mm were acquired using GE-NXi High-Speed CT scan. PET-CT images and/ or MRI images also acquired for few patients at the simulated position.

All images were transferred to Eclipse Planning system (10.0.39) and fused each other modality images using rigid registration algorithm for delineation of targets volume and OARs on CT images. Gross Tumour volume (GTV) defined, gross tumor extent and positive lymph nodes shown by the image. CTV was defined, based on the primary tumor extent and positive node involved with an additional margin for including microscopic spread. PTV was created from the CTV with an additional margin of 5mm in all direction. Based on standard Radiation Therapy Oncology Group guidelines (RTOG), [14-16] OARs bladder, rectum, both femoral head, small bowel and bone marrow were included. Bone marrow was delineated as the marrow cavity 2cm above and below the PTV. The rectum was outlined up to sigmoid flexure. The small bowel included the entire peritoneal cavity (not individual loops of bowel) up to L3. The healthy tissues were created by subtracting all

targets from body volume. The prescribed dose to PTV was 50Gy in 25 fractions (2Gy/fraction) and from second week of radiotherapy 50mg/m^2/week cisplatin chemotherapy was administered for five weeks.

Table 1 Summary of patients characteristics at treatment start		
Number of Patients		20
Diagnosis	Ca.Cx	20
Sex	Female	20
Age(Years)	Median (Range)	61.61 (50-78)
Stage	II	11
	III	6
	IV	3
Chemotherapy	CisPl	20
	50mg/m^2/week	
Radiation Dose		
Prescription	50Gy in 25 fraction	20

Ca.Cx: Carcinoma Cervix, CisPl: Cisplatin

To the each patient, two set of plans were generated for 6MV photon energy delivered by Varian UNIQUE Performance which has equipped with 120 mlc (5mm spatial resolution for the central 20cm and 10mm spatial resolution for both outer sides 10cm (2X10cn) at isocentre level). One set of dual arc VMAT plan and another set of IMRT plan with seven to nine beams were generated for all patients in eclipse planning system (10.0.39). For both techniques plan, similar planning objectives were used for optimization and dose of both plans was calculated at 2.5mm grid size using AAA algorithm.

Plan Evaluation:

All plans were Evaluated based on dose-volume histogram (DVH) scoring values of PTV and OARs and ranked using Unified Dosimetry Index(UDI) scoring values. The UDI scoring value collectively accounts the conformity index, coverage index, homogeneity index, and dose gradient index of the dose distribution.

The Unified Dosimetry Index (UDI) [17] scoring values of all plans were ranked between the both techniques. The lesser UDI scored plan was considered as a better plan of the patient. The Unified Dosimetry Index (UDI) score values calculated using the following formula,

$$UDI=\{\pi_{k=1}^{4} W_k.\{|1.0 - DI\ k| + 0.1\}\} \times 10^4$$

For ideal plan, Unified Index (UDI) is equal to 1

UDI=UDI(C)XUDI(CF)XUDI(HI)XUDI(G)=1.0

where C-coverage index($DI_{1)}$, CF-conformity index(DI_2), HI-Homogeneity Index(DI_3) and DG-gradient index(DI_4). Hilary Akpati et.al [17] explained full detail about Unified dosimetry Index (UDI). In addition, the bone marrow dose was analysed with different dose volume objectives since there is no exact dose volume objective of sparing level has been recommended.

The independent student 't' test was used to compare the both techniques plans. p-value <0.05 was considered statistically significant. The statistical values were calculated using SPSS (version 16.0.0, SPSS, Chicago, USA).

RESULTS

In our study, VMAT technique plans of all patients scored better UDI, DVH, and technical parameters than IMRT plans. Table 2 and 3 give the details of the UDI score values and bone marrow dose of all plans. Figure 1 shows the axial, sagittal and coronal view of dose distribution and refers to one patient. Figures 2 and 3 show the comparison DVH for PTV and OARs respectively.

The mean dose of PTV50Gy was achieved in both techniques adequately with better sparing of OARs with VAMT techniques. The UDI score of all plans with VMAT shown lesser than IMRT. Bone marrow mean and D40% dose with VMAT and IMRT were 30.128±1.94 and 34.399±2.09; 32.216±2.72 and 37.397±2.87 respectively.

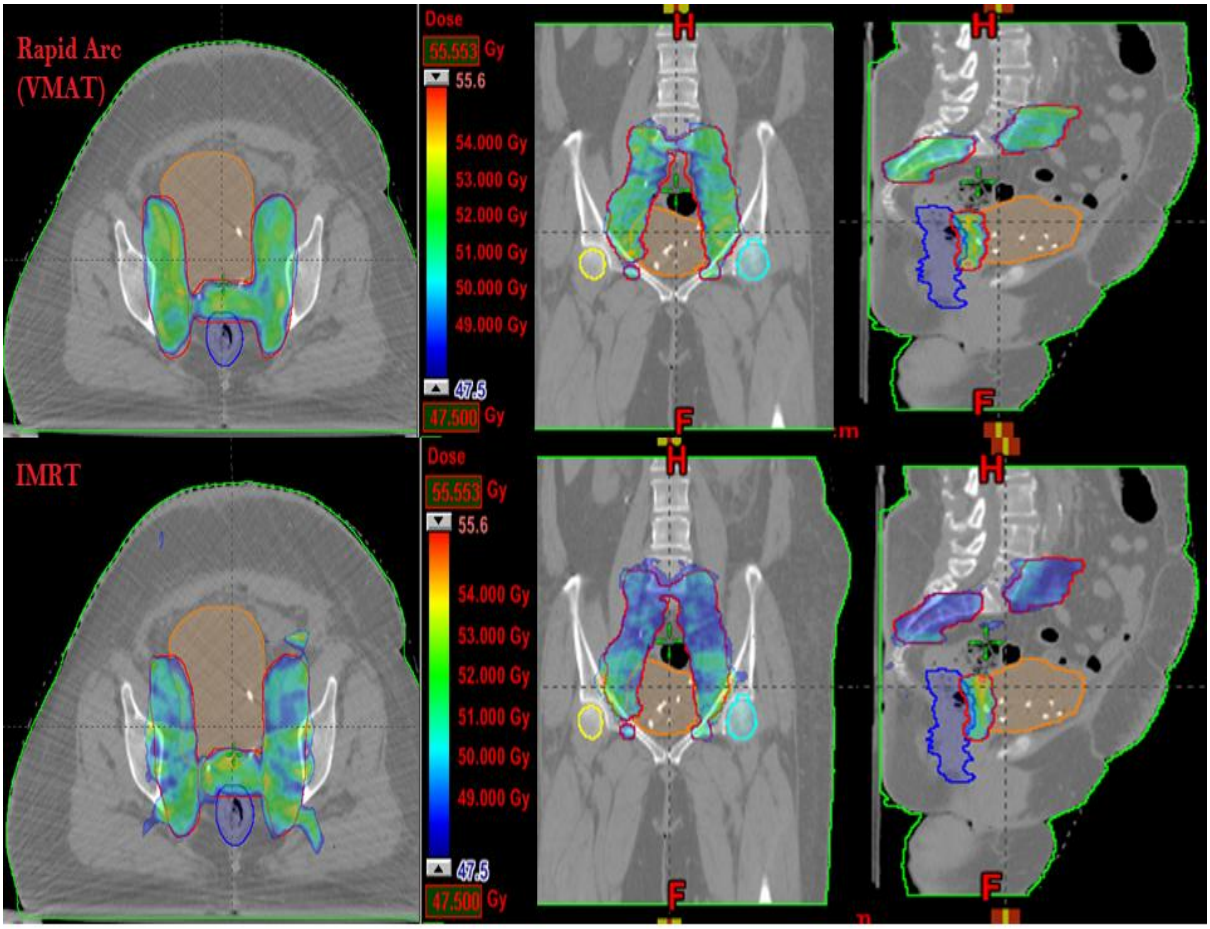

Figure1: Dose Distribution for one patient under study for axial, coronal and sagittal views

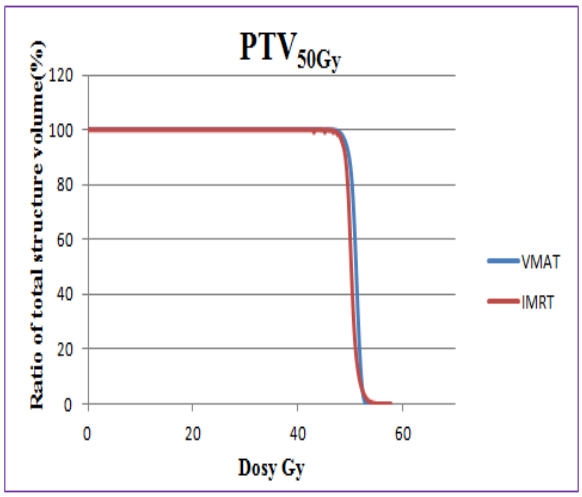

Figure 2: DVH for PTV_{50Gy} of a patient's plans.

Table 2: Unified Dosimetry Index(UDI) of all plans of all patients, the all patients were treated with VMAT technique.

Parient #	Unified Dosimetry Index	
	VMAT	IMRT
1	48.091	102.854
2	79.318	93.767
3	78.624	187.874
4	82.704	159.077
5	47.034	120.231
6	41.040	80.161
7	44.092	112.468
8	48.636	107.584
9	42.592	57.758
10	49.572	65.468
11	52.658	56.210
12	57.982	72.475
13	45.412	73.958
14	42.397	51.662
15	59.332	60.251
16	52.923	70.868
17	60.251	80.332
18	58.153	67.541
19	57.320	62.044
20	58.473	64.321

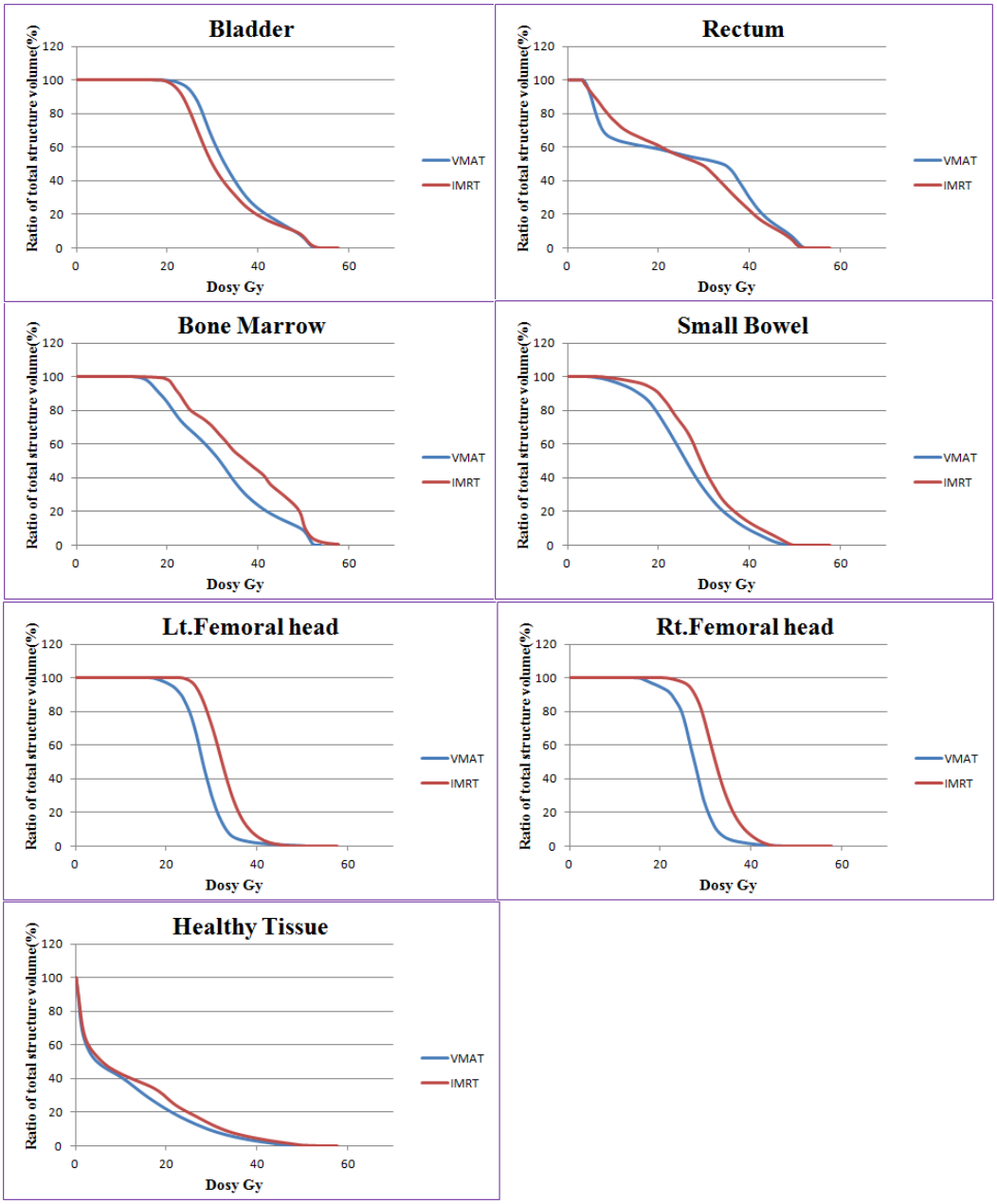

Figure 3: DVH for OARs of a patient's plan. All critical organs were spared better with Rapid arc than IMRT. Irradiated healthy tissue volume by higher dose was lesser with Rapid Arc and no significant difference found in the low dose irradiation volume.

Table 3: Average Bone Marrow dose of different volume of both techniques.

Dose/volume	Technique	Mean	Std. Deviation	Sig. (2-tailed)
Mean(Gy)	RA	30.128	1.94	
	IMRT	34.399	2.09	<0.001
D40	RA	32.216	2.72	
	IMRT	37.397	2.87	<0.001
V10	RA	99.693	0.68	
	IMRT	99.893	0.18	0.217
V15	RA	95.934	3.57	
	IMRT	99.216	0.93	<0.001
V20	RA	82.961	6.35	
	IMRT	93.800	5.07	<0.001
V25	RA	64.366	6.90	
	IMRT	76.960	6.55	<0.001
V30	RA	46.580	7.31	
	IMRT	60.792	9.11	<0.001
V35	RA	30.529	7.15	
	IMRT	44.055	11.42	<0.001

Table 3:- Continued…				
V40	RA	17.585	6.21	
	IMRT	30.181	11.46	<0.001
V45	RA	9.611	4.56	
	IMRT	17.114	8.57	0.002
V50	RA	3.401	2.09	
	IMRT	4.934	4.19	0.155

Vx%= Volume receiving at least X% of the prescribed dose Dx% = dose received by the X% of the volume.

DISCUSSION

The comparison between the volumetric modulated arc therapy with IMRT in different sites have been published by various authors. [18-21] The study published by Richard et al. [22] Shows VMAT had shorter Beam-On time and more homogeneous dose distribution compared with 7 fields step and shoot IMRT for prostate cancer. In an another study published by Mahantshetty Swamidas Jamema et al. [23] shows that with Rapid Arc technique the dose distribution to the target is adequate with high target homogeneity sufficient sparing of organs at risk and minimization of patient moment compared to IMRT.

In our study the dose of PTV50Gy received adequately with both techniques however the unified dosimetry index (UDI) was lesser with VMAT. It implies that the PTV coverage with conformity and homogeneity of the prescribed PTV dose along with higher dose gradient for better sparing of OARs was achieved with VMAT plan better than IMRT and it has agreed with many other studies results. [18-21]

John C. Roeske et al reported that the volume of the PTV receiving at least 110% of the dose in a BM-sparing plan was 15.9% compared with 12.9% (p = .09) with standard IM-WPRT planning and the BM sparing cannot be achieved without some compromise in the dose distribution. [24]

However in this study VMAT plan spared the bone marrow significantly at different dose and volume level (p<0.001) than IMRT at the same time small intestine also spared without compromised. Especially higher dose irradiation of bone marrow volume was significantly reduced with VMAT. Mell LK et al shown in some of their studies that chemotherapy delivery is improved in patients by decreased BM irradiation. [4]

The RTOG 0418 phase II clinical trial showed that the mean dose and more than 40 Gy received volume of bone marrow is related to the haematological toxicity of concurrent chemoradiotherapy for cervical cancer. [11] Similarly some of the studies have reported that the volume of bone marrow irradiation dose of 30 to 50 Gy needed an extended time to recover and sometimes experienced irreversible damage. [9-10] Therefore the higher dose volume irradiation has to be reduced. In our study the sparing of bone marrow with VMAT at different dose and volume level was significantly better than IMRT. Further studies need to be continued to analyze the correlation between the achieved dosimetric results with complete blood test results of every week of treatment. The functional Bone Marrow has to be delineated to achieve better conformal sparing and identified the association between dose volume and haematological toxicity grade.

CONCLUSION

In the treatment of cervical cancer the VMAT technique can be delivered highly conformal dose to the target with better OARs sparing. It helps to reduce hematological toxicity by reducing the bone marrow irradiation dose and volume to avoid the treatment gap due. The un-interruption treatment helps to be continued chemoradiotherapy without delay to achieve better tumor control.

REFERENCES

1. Hoskins WC Perez CA Young RC eds. principles and practice of gynaecologic oncology 4th ed. Philadelphia: Lippincott Williams & Wilkins 2005.

2. Green JA Kirwan JM Tierney JF et al. Survival and recurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix: a systematic review and meta-analysis. Lancet. 2001;358:781-786.
3. Chemoradiotherapy for Cervical Cancer Meta-analysis Collaboration (CCCMAC). Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: individual patient data meta-analysis. The Cochrane Library 2010;1:5-12.
4. Mell LK Kochanski JD Roeske JC et al. Dosimetric predictors of acute hematologic toxicity in cervical cancer patients treated with concurrent cisplatin and intensity-modulated pelvic radiotherapy. Int J Radiat Oncol Biol Phys. 2006; 66:1356-1365.
5. Collaboration CfCCM-A. Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: a systematic review and meta-analysis of individual patient data from 18 randomized trials. J Clin Oncol. 2008; 26:5802-5812.
6. Vaupel P Thews O Hoeckel M. Treatment resistance of solid tumors: role of hypoxia and anemia. Med Oncol. 2001;18:243-259.
7. Beina Hui et al Association Between Bone Marrow Dosimetric Parameters And Acute Hematologic Toxicity In Cervical Cancer Patients Undergoing Concurrent hemoradiotherapy Comparison Of Three-Dimensional Conformal Radiotherapy And Intensity-Modulated Radiation Therapy. Int J Gynecol Cancer. 2014 Nov;24(9):1648-52.
8. Albuquerque K Giangreco D Morrison C et al. Radiation-related predictors of hematologic toxicity after concurrent chemoradiation for cervical cancer and implications for bone marrowYsparing pelvic IMRT. Int J Radiat Oncol Biol Phys. 2011;79:1043-1047.
9. Sacks EL Goris ML Glatstein E et al. Bone marrow regeneration following large field radiation. Influence of volume age dose and time. Cancer. 1978;42:1057-1065.
10. Mauch P Constine L Greenberger J et al. Hematopoietic stem cell compartment: acute and late effects of radiation therapy and chemotherapy. Int J Radiat Oncol Biol Phys. 1995;31: 1319-1339.
11. Klopp AH Moughan J Portelance L et al. Hematologic toxicity in RTOG 0418: a phase 2 study of postoperative IMRT for gynecologic cancer. Int J Radiat Oncol Biol Phys. 2013;86:83-90.
12. Lhomme´ C Fumoleau P Fargeot P et al. Results of a European Organization for Research and Treatment of Cancer/Early Clinical Studies Group phase II trial of first-line irinotecan in patients with advanced or recurrent squamous cell carcinoma of the cervix. J Clin Oncol. 1999;17:3136-3142.
13. Mell LK Schomas DA Salama JK et al. Association between bone marrow dosimetric parameters and acute hematologic toxicity in anal cancer patients treated with concurrent chemotherapy and intensity-modulated radiotherapy. Int J Radiat Oncol Biol Phys. 2008;70:1431-1437.
14. Albuquerque K Giangreco D Morrison C et al. Radiation-related predictors of hematologic toxicity after concurrent chemoradiation for cervical cancer and implications for bone marrowYsparing pelvic IMRT. Int J Radiat Oncol Biol Phys. 2011;79:1043-1047.
15. Small W Jr Mell LK Anderson P Creutzberg C De Los Santos J Gaffney D *et al.* Consensus guidelines for delineation of clinical target volume for intensity-modulated pelvic radiotherapy in postoperative treatment of endometrial and cervical cancer. Int J Radiat Oncol Biol Phys 2008;71:428-34.
16. Lim K Small W Jr Portelance L Creutzberg C Jürgenliemk-Schulz IM Mundt A *et al.* Consensus guidelines for delineation of clinical target volume for intensity-modulated pelvic radiotherapy for the definitive treatment of cervix cancer. Int J Radiat Oncol Biol Phys 2011;79:348-55.
17. Akpati et al.Unified dosimetry index(UDI): a figure of merit for ranking treatment plans. *Journal of applied clinical medical physics vol.9No. 3 Summer 2008.*

18. Cozzi L Dinshaw KAShrivastava SK et al. A treatment planning study comparing volumetric arc modulation with Rapid Arc and fixed field IMRT for cervix uteri radiotherapy. *Radiother Oncol* 2008;89:180-91.
19. Palma D vollans E James K et al. Volumetric Modulated arc therapy for delivery of prostate radiotherapy. Comparision with intensity modulated radiotherapy and three-dimensional conformal radiotherapy. *Int J Radiat oncol Biol Phys* 2008;72:996-1001.
20. Clivio A Fogliata A Franzetti -Pallanda A et al. Volumetric-modulated arc radiotherapy for carcinomas of the anal canal: a treatment planning comparison with fixed field IMRT. *Radiother Oncol* 2009;92:118-24.
21. Wagner D Christiansen H Wolff H Vorwerk H. Radiotherapy of malignant gliomas: comparison of volumetric single arc technique and 3D conformal technique. *Radiother Oncol* 2009;93: 593-6.
22. Richard et al. A dosimetric comparison of volumetric modulated arc therapy with step-and-shoot intensity modulated radiation therapy for prostate cancer. *Practical radiation oncology* 20155 11-15.
23. Mahantshetty Swamidas Jamema et al. Whole abdomen radiation therapy in ovarian cancers: a comparison between fixed beam and volumetric arc based intensity modulation. *Radiother Oncol* 20105:106.
24. John C. Roeske et .al. Bone marrow – sparing IMRT Intensity modulated radiation therapy- A clinical perspective *BC Decker 2005.*

How to cite this article: Krishnan J, Shetty J, Rao S et al. Dosimetric advantage of VMAT technique in bone marrow sparing than IMRT in treatment of cervical cancer. Int J Health Sci Res. 2017; 7(8):102-109.

****