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RESEARCH ARTICLE
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VMAT VS BRACHYTHERAPY IN GYNECOLOGICAL TUMORS

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Abstract

Background: According to data, gynecological tumors is a big problem for woman health and is second most common cancer in women in the world. Generally, gynecological cancers are being treated with 3D conformal radiotherapy treatment followed by intracavitary brachytherapy treatment.

Purpose: To investigate this question that VMAT could be option for gynecological tumors in some scenarios where some complications making brachytherapy an impossible option like brachytherapy machine is not available in some remote regions, brachytherapy apparatus insertions is not possible due to fibrosis, edema, bleeding and sometime patient is not willing to undergo painful insertion procedure.

Materials and Methods: Ten patients were selected who were treated according to normal workflow treatment with four field EBRT and sequential 3D brachytherapy.

We have chosen the normal scan before the insertion of first brachytherapy and we have delineated the target volumes on the basis of MRI and CT scan reports. We have contoured the organ at risk including bladder, rectum, small bowel and sigmoid colon. Also we have contoured the some target volumes within treatment volume so we can produce the dose gradients in VMAT just like brachytherapy. Then we have planned with VMAT and try to give dose from 85Gy-95Gy to the delineated target with 45Gy in 25 fractions followed by 50.1Gy in 15 fractions. At the end, a comparison of evaluating parameters, including volume coverage, conformity index, homogeneity index and organ doses was made.

Results: We obtained analogous results of target coverage factor and homogeneity index from VMAT and brachytherapy plans. VMAT was really efficient in organ sparing but conformity of brachytherapy is better than VMAT.

Conclusions: On basis of results obtained, it was concluded that VMAT treatment planning should be chosen if brachytherapy is not possible. There are many pros and cons of both techniques but VMAT can be opted in some scenarios as mentioned above.

1: Introduction

1.1: Treatment for Gynecological Tumors

Treatment of early stage cervical cancer is curative but in most cases patient comes on later stage. Clinical data shows that chemotherapy is the standard treatment for cervical cancer [1]. Mostly localized tumor are cured with combinations of surgery and radiotherapy treatment especially when disease is progressed to lymph nodes [2].

Mostly cervical cancer at advance stage are treated with external beam therapy (EBRT) with ICBRT and Chemotherapy. Generally endometrial cancer can be cured by surgery along with radiotherapy depending on the stage of disease. In early stage mostly ICBRT is only treatment, but for advanced stage EBRT get involved. For endometrial cancer recurrence in vaginal wall is treated with only ICBRT [3].

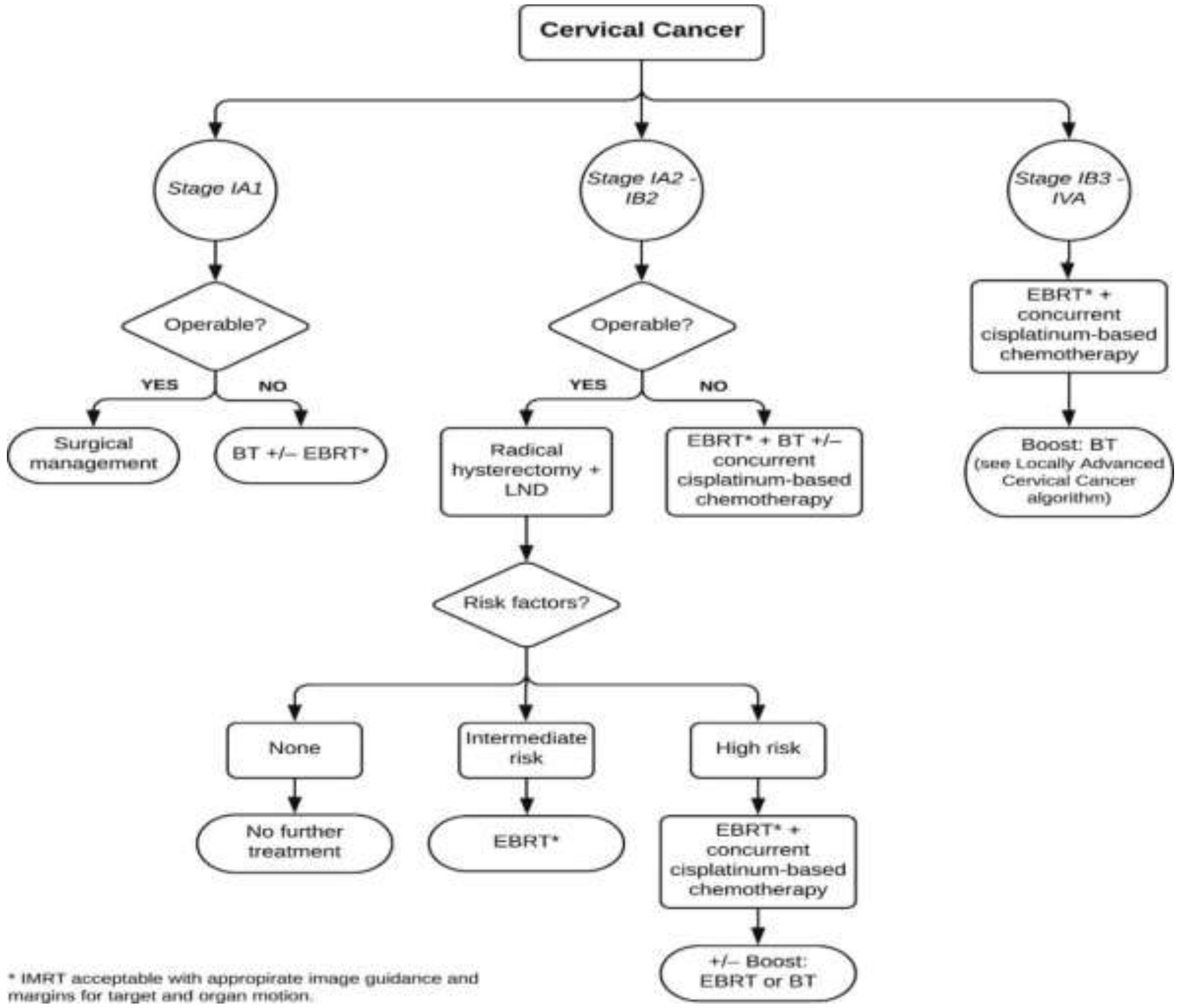

***Figure 1*: Cervical Cancer Algorithm *[4]*.**

1.2: External Beam Radiotherapy

External beam radiotherapy deliver the dose to target area noninvasively and minimizing the dose to adjacent organs at risk. According to ICRU 42 recommendations 2% accuracy in low dose gradient and 2 mm accuracy in high dose gradients should be achieved. Suggestion for brachytherapy is that 5% to 10% accuracy at distance of 0.5 cm should be achieved [5].

1.3: Brachytherapy

Brachytherapy is a radiotherapy treatment procedure, in which we use sealed source from catheters, radioactive sources deliver radiation by putting them in, on or around the tumor. In this technique

dose is delivered with high dose rate but radiation is given in fractions due to which better radiobiological result are met as compared to low dose rate brachytherapy [6].
In limited cases, ICBRT cannot be recommended due to technical limitations and rapid fall-off the dose for irregular geometry of target and large sized tumor. For above scenarios intensity modulated dose (IMRT) can be used as alternative approach. IMRT is beneficial for high dose delivery to irregular shape and concave volume of target. In present era IMRT is widely used for whole-pelvis radiotherapy treatment to avoid much toxicity to the bowel delineation of critical area. In present time study of boost IMRT as alternative approach of ICBRT has been started [3].

1.4: Volume Modulated Arc Therapy

VMAT is the noval technique of IMRT with rotational gantry mode. For VMAT technique MLC bidirectional motion makes volume modulation possible. There are two prominent benefits of VMAT
1: Through VMAT treatment can be delivered at all angles about complete rotation of 360 degree with more conformity than IMRT.
2: VMAT has an edge delivering treatment in shorter time of treatment [6].
There are some options in VMAT technique such like dose rate variation, multi-leaf collimator position and gantry speed, which interpolate between control points. In VMAT technique beam should be stable and we should ensure beam flatness and symmetry by monthly basis quality assurance [7].

2: Materials and Methods

In this report 10 patients chosen for data analysis which were previously diagnosed with gynecological cancer. The role of external beam therapy and intracavitary brachytherapy in gynecological tumors is very significant. Our selected cases were treated with external beam radiotherapy plus ICBRT. For some early stage cancers patient is treated with only ICBRT, but when disease was in advanced stages then patient treatment is planed with EBRT plus ICBRT. In certain cases, ICBRT can't be performed due to some limitations related to insertion procedure of the cervix and irregular tumor's geometry, large size diseased area and rapid fall-off dose [3]. VMAT is also conformal technique in which dose distribution area is specified.

2.1: Patient Evaluation and CT simulation

For ICBRT treatment patients were first scanned on CT simulation in supine position with 2mm slice thickness. The target volume which were selected includes intermediate risk clinical target volume (IR-CTV) and high-risk clinical target volume (HR-CTV)[8].

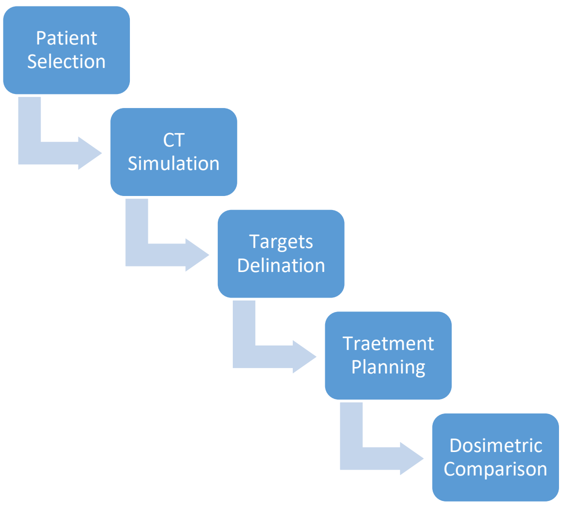

***Figure 2*: Flow Chart of Report**

The patient evaluation is made on examination, assessment of disease spread and the area of morbidity should be delineated on CT images. There are different modalities for simulation i.e. MRI and CT scan which is used for this project.

2.2: Targets Delineation/Image Segmentation

For target delineation clinical target volume (CTV) is marked which includes the visible and extent of microscopic disease. In brachytherapy we are just marking the CTV volume these volumes includes HR CTV and IR CTV. But for the sake of understanding and easy comparison between intra-cavity brachytherapy and VMAT plans we have labeled them as IR CTV 60, HR CTV 85 and HR CTV 100.
IR CTV 60 encompasses areas susceptible to microscopic tumor spread in locally advanced cervical cancer, including the whole parametria, uterus, upper vagina, and anterior/posterior spaces.
HR CTV 85 is the volume that includes the GTV and the surrounding tissue at high risk of microscopic disease. It encompasses the GTV-Tres—the residual tumor visible or palpable at the time of brachytherapy—along with any adjacent residual pathologic tissue, such as edema or fibrosis, that may surround it.
HR CTV 100 is basically the gross tumor volume (GTV) that includes the macroscopic tumor assessed by clinical, imaging, and/or pathological investigations.
For treatment planning dose of CTV should be optimized to D90 and we should minimize dose to normal organs. We are going to check dose limits of sigmoid colon, bladder, femoral head and rectum. Doses of organ at risk should be checked at volume of 2 cm^3. The dose distribution should be optimized to improve our target coverage and sparing of organ at risk. In brachytherapy dose to areas adjacent to source channel goes beyond the limit of 150% of prescribed dose. Mostly dose volume histogram are used for assessment of volumetric dose distribution. For radiation therapy total tumor dose is prescribed in range 70 Gy and 85 Gy for CTV [9].

2.3: Treatment Planning

In EBRT we are using four field technique with dose of 45 Gy in 25 fractions. In EBRT PTV Intermediate Risk is being irradiated with same dose rate as PTV-High Risk. For dose tolerance of OARs we are using QUENTEC data for standard reference. We are making comparison of OARs doses by noting dose to 2 cm^3, 15% volume of total volume and maximum dose of organ.
The single fraction of brachytherapy plan is prescribed with the dose of 7 Gy per fraction to HR CTV for 4 fractions exported from Brachyvision (Varian Medical systems, Palo Alto, CA). In Eclipse Treatment Plan system the sigmoid colon, femoral heads, bladder, rectum, GUT, IRCTV and HRCTV were contoured [10].
In gynecological tumors external beam radiation was made by VMAT with two arcs and 6 MV energy is being used. For gynecological tumors CTV consist of tumor volume, uterus, parametrial, cervix, vagina, ovaries and pelvic lymphatic drainage. In gross tumor volume (GTV) positive lymph nodes are included and for planning. Mostly dose prescribed to PTV is 45 Gy in 25 fractions and in case of boost it goes to 60 Gy. The dose limitations for the organ at risk were as follows: rectum V30<50%, bladder V30<50%, Kidney V20<20%, small intestine V40<30%, femoral head V20<50%, spinal cord D1cm3<40Gy and liver mean dose <15 Gy [11].
The objective of our treatment plan was; 90% of HR volumes should receive the prescribed dose total prescribed dose (7 Gy) and 90% of IR volumes should receive the 75% of prescribed dose (5.2 Gy). We should look at dose distribution and dose volume histograms (DVHs) and check dose gradient. In plan target coverage should assessed by D90% and D95%. For dose homogeneity in the target volume is made by homogeneity Index (HI). For assessing the dose to OARs bladder, rectum, GUT, sigmoid colon was D2cc were evaluated and for femoral head sparing maximum dose point is considered [8].

2.4: Statistical Analysis

Conformity Index (CI) is used for checking the conformity of dose coverage of PTV-HR Volume. Its formula as used in Lee et. al is given as

$$CI = \frac{VRI}{TV} \qquad 2.\ 1$$

Where VRI is Volume of reference isodose curve overlaped by 95% isodose level and TV is Total Volume of Target. The value of CI should be close to 1 for a plan having better conformity. Homogeneity Index (HI) parameter accounts for homogeneity within the target volume. Its formula is given as

$$HI = \frac{D_5}{D_{95}} \qquad 2.\ 2$$

Where D_5 = Maximum dose to 5% of PTV-HR volume.
D_{95} = Maximum dose to 95% of PTV-HR volume.

Ideally, its value should be close to 0 for better homogeneity in any plan. Coverage Factor parameter accounts for coverage of Target volume. Its formula is given as

$$CF = \frac{D_{min}}{D_p} \qquad 2.\ 3$$

Where D_{min} is minimum dose to target and $D_p$is prescribed dose to the target.

3: Result and Discussion

Conventionally patients diagnosed with cervical cancer goes for treatment with external beam radiotherapy antecedent four fractions of 7 Gy intracavitary brachytherapy. The complications and lack of resources of brachytherapy are the major reasons which based for our project. To deal with above scenarios of brachytherapy treatment we are looking the pros and cons of treatment, if we opt to irradiate patient of gynecological tumor by VMAT.

3.1: Dose Coverage of Target Volumes

In the whole world patient of gynecological tumor are being treated conventionally with external beam therapy (EBRT) and intracavitary brachytherapy (ICBT). In EBRT we are using four field technique with dose of 45 Gy in 25 fractions. In four field EBRT, the target is PTV-High Risk with dose limit of 45 Gy in 25 fractions. In EBRT PTV-Intermediate Risk is being irradiated with same dose rate as PTV-High Risk. For brachytherapy planning it was conventionally treated such that volume of CTV-High risk should be covered in 7Gy isodose level. For DVH we should check 90% volume of CTV-High should get 7Gy dose. For coverage of our created inner volume which is CTV-100 we should check isodose level of 8.82 Gy. For intermediate volume of brachytherapy we should check isodose level of 4.2 Gy. For VMAT planning maximum dose to CTV-High Risk is 95.1 Gy. In this project dose is 45 Gy in 25 fractions to PTV-High Risk and PTV-Intermediate Risk. After that boost plan for CTV-100 with 50.1 Gy in 15 fractions is being delivered.

***Table 1*: Doses of Target volumes in EBRT+ICBT and VMAT Planning**

	External beam Therapy (EBRT) + Intracavitary Brachytherapy (ICBT)		Volume Modulated Arc Therapy (VMAT)	
	Average Dose (Gy)	Standard Deviation	Average Dose (Gy)	Standard Deviation
HR-CTV100-D95	92.07	3.20	96.45	1.89
HR-CTV100-D90	96.13	4.14	97.75	2
HR-CTV100-Mean	158.17	10.97	106.7	2.13
HR-CTV85-D95	80.88	2.18	86.51	1.59
HR-CTV85-D90	85.35	1.23	88.85	1.91
HR-CTV85-Mean	138.64	5.57	100.6	1.78
IR-CTV60-D95	68.32	2.07	64.82	3.33
IR-CTV60-D90	70.76	2.37	67.62	5.03
IR-CTV60-Mean	108.24	4.52	89.84	2.15

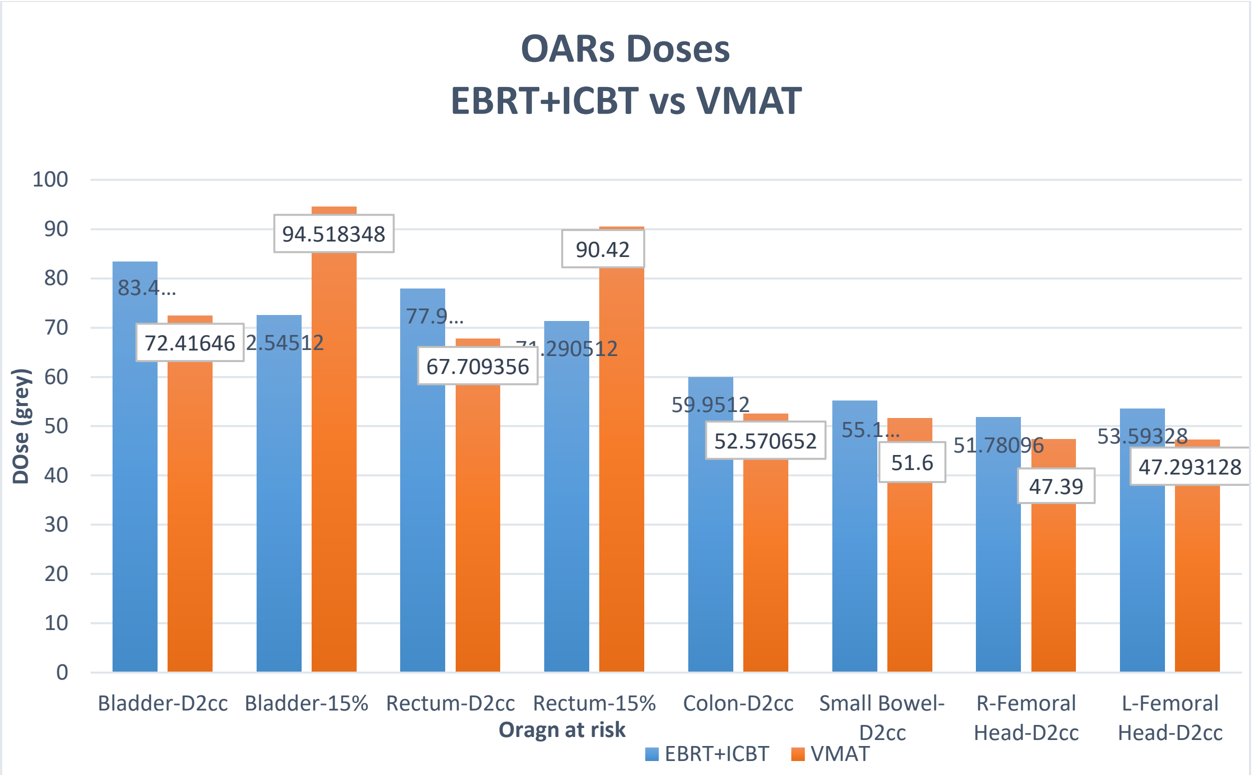

Figure 3: Comparison of doses to D90 of CTV-100 in EBRT+ICBT vs VMAT plan

3.2: Doses of OARs

For dose tolerance of OARs we are using quentec data for standard reference. We are making comparison of OARs doses by noting dose to 2cm^3, 15% volume of total volume and maximum dose of organ.

***Table 2*: Average Doses of OARs and their Standard deviation**

	External beam Therapy (EBRT) + Intracavitary Brachytherapy (ICBT)		Volume Modulated Arc Therapy (VMAT)	
	Average Dose (Gy)	Standard Deviation	Average Dose (Gy)	Standard Deviation
Bladder-D2cc	83.41	5.44	72.42	4.56
Bladder-15%	72.55	4.24	94.52	7.16
Bladder-Max	112.5	18.3	86.06	4.63
Rectum-D2cc	77.91	6.36	67.71	6.97
Rectum-15%	71.29	3.04	90.43	5.62
Rectum-Max	99.18	7.38	79.9	4.95
Colon-D2cc	59.95	5.98	52.57	11.3
Colon-Max	70.05	13.1	43.32	8.15
Small Bowel-D2cc	55.16	2.03	51.65	9.92
Small Bowel-Max	59.59	4.64	59.53	13.5
R-Femoral Head-D2cc	51.78	2.73	47.39	3.87
R-Femoral Head-Max	55.63	2.68	55.14	4.04
L-Femoral Head-D2cc	53.59	3.38	47.29	2.24
L-Femoral Head-Max	58.15	3.74	56.17	3.36

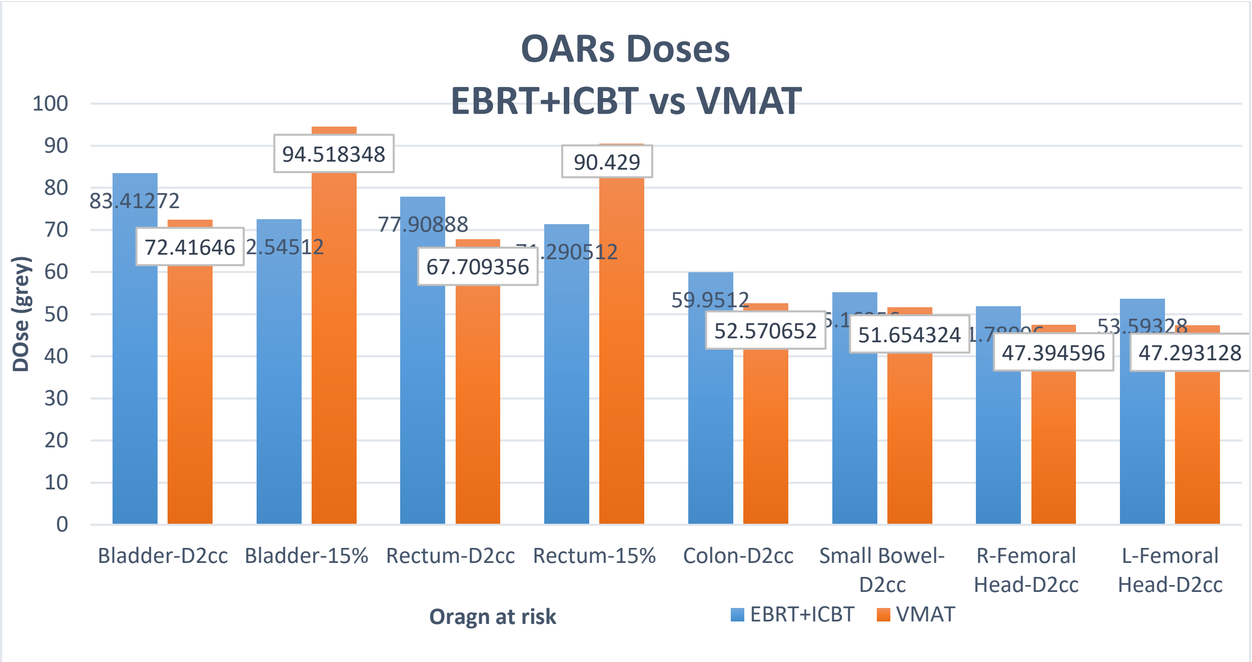

Figure 4*: Comparison Doses of OARs *We are able to optimize our VMAT plan to limit the dose of OARs to their tolerance doses according to QUENTEC data.

3.3: Statistical Analysis of Quality parameters

We are going to make comparison of three parameters including Conformity index, Coverage factor and Homogeneity index.

***Table 3*: Quality Parameters of EBRT+ICBT and VMAT**

	VMAT			EBRT+ ICBT		
	CI Average	CF Average	HI Average	CI Average	CF Average	HI Average
CTV_100	1.41	0.92	1.05	0.83	0.51	5.76
CTV_85	1.49	0.91	1.15	0.91	0.54	6.08
CTV-60	3.29	0.92	1.53	0.93	0.58	6.27

CI= conformity Index, CF= Coverage factor and HI= Homogeneity index

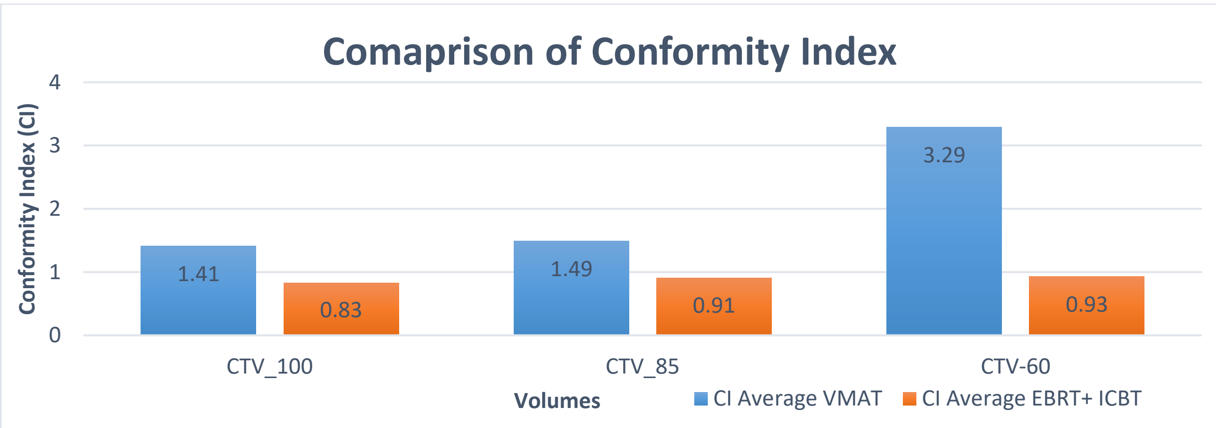

***Figure 5*: Comparison of Conformity Index (CI).**

Analysis of VMAT Planning and ICBT treatment is made by comparing their conformity index. Ideal value of CI should be equal to 1. For VMAT Planning the conformity of target is greater than 1. For target of CTV_100 and CTV_85 are is 1.41 and 1.49 respectively the reason of this deviation is due to high dose gradient which is going to be created in our plans. The higher conformity index (CI) for

CTV-60 is due to the delivery of a 50.1 Gy dose from 360-degree angles, which results in a large spill of low-dose area. Conformity of conventional treatment is better than VMAT but it is lower than ideal value 1, which means that our target is going to be under-dose in some cases like patient has very large volume of disease that cannot be covered with tandem and ovoids. The conformity index value is below than 1 because of dose tolerance of OARs which can't be compromised. Mostly for brachytherapy system we are looking for D90 should receive 7 Gy due which little bit conformity is compromised.

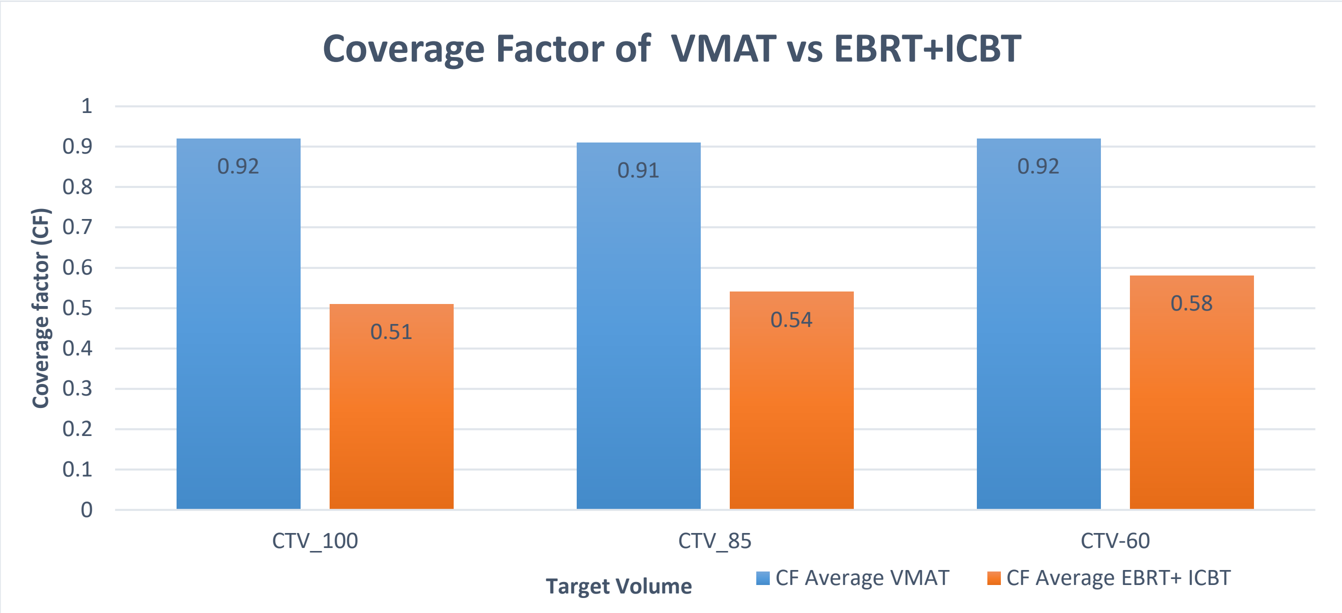

Figure 6: Comparison of Coverage Factor (CF).

The dose coverage factor is basically the uniformity of dose to the target. CF is the ratio of minimum dose and prescribed dose. Its value should be ideally 1. For VMAT planning CF factor is very near to the ideal value which means that by VMAT planning we can achieve very good uniformity. For brachytherapy treatment CF value is very low than Ideal value because of high gradient of dose in brachytherapy.

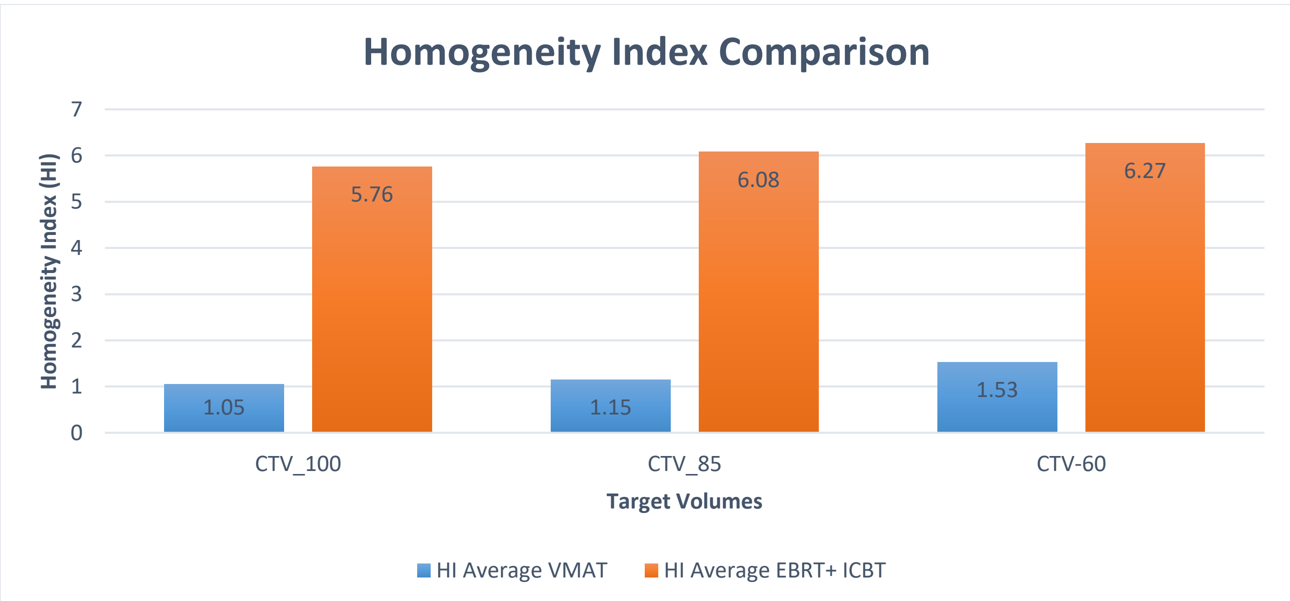

Figure 7: Comparison of Homogeneity Index (HI).

The homogeneity index is the ratio of D_5 to D_{95}, tells us about the dose gradient in the dose coverage volume. For VMAT the dose gradient is very small for all volumes with different doses such as 50.1 Gy to HR CTV 100, 38 Gy to HR CTV 85 and 17 Gy to IR CTV 60.. For homogeneity index the ideal value is 1. For volume of lower dose HI is going to be increased. The reason for such higher value of HI is that the higher dose sharp fall off can't be made with just like a single boundary line. For brachytherapy homogeneity is very bad because of inserted source. The presence of source inside the volume give big fall off coverage in the target due to which the homogeneity can't be expected as ideal as in EBRT.

4: Conclusion and Future Recommendations

4.1: Conclusion

The dosimetric comparison of VMAT and brachytherapy is made in this project. For giving dose gradient in VMAT planning we have drawn three different volume of different dose level. In VMAT we have achieved the other doses comparatively same as in Brachytherapy but the mean dose of ICBT is higher than the mean dose of VMAT. We are achieving comparatively good result in VMAT with sparing of OARs to maximum limit. For better dose gradient in VMAT we have to generate more volumes inside the CTV to give higher dose gradient. Till present time under this progess report we can go for the VMAT treatment planning at that hospitals where Brachytherapy system is not present. For the above scenarios when ICBT is not possible and patient can't move to other areas so then we should go for VMAT planning with prescribed dose of 95 Gy to the CTV. But condition is that OARs doses are the most critical thing that we have to consider.

4.2: Future Recommendation

For future first of all we have to make our dose coverage better in brachytherapy because of dose constraints of OARs lowering the CI value. For better assessment of volumes we to make rigid registration based on tissue density. We are facing the problem of a lower mean dose in VMAT, which requires to increase the dose to the innermost area just like brachytherapy by creating a region with a higher dose within the CTV-100. If we want to set up study that VMAT can be alternative option of ICBT in some scenarios, then we should get larger number of patients to make VMAT as recommended treatment.

5: References

[1] J. M. Tayyiba Wasim, "Gynecological malignancies at tertiary care hospital, Pakistan A five year review," *Pak J Med Sci,* vol. 37, 2021.

[2] S. E. Waggoner, "Cervical Cancer," *NATURE,* vol. 28, pp. 17-25, 2003.

[3] V. L. C. L. A. J.-F. O. Valentina Pinzi, "IMRT and brachytherapy comparison in gynaecological cancer treatment: thinking over dosimetry and radiobiology," *The National Center for Biotechnology Information advances science and health by providing access to biomedical and genomic information.,* vol. 13, 2019.

[4] M. M. A. M. P. unzo Chino, Radiation Therapy for Cervical Cancer: An ASTRO Clinical Practice Guideline, 2020.

[5] P. Faiz M. Khan and P. John P. Gibbons, The Physics of Radiation Therapy, London: Library of Congress Cataloging-in-Publication Data, 2014.

[6] P. Faiz M. Khan, P. John P. Gibbons and M. M. F. Paul W. Sperduto, Khan's treatment Planning in Radiation Oncology, Hongkong: Library of Congress Cataloging-in-Publication Data, 2016.

[7] P. A. A. P. W. M. JAMES L. BEDFORD, "COMMISSIONING OF VOLUMETRIC MODULATED ARC THERAPY (VMAT)," *Elsevier,* vol. 73, p. 537–545, 2009.

[8] A. M. H. R. M. D. Lila Mahmoud Walia, "A dosimetric comparison of Volumetric Modulated Arc Therapy (VMAT) and High Dose Rate (HDR) brachytherapy in localized cervical cancer radiotherapy," *IOS Press and the authors,* p. 11, 2018.

[9] S. Beriwall, "American Brachytherapy Society consensus guidlines for interstial brachytherapy for vaginal cancer," *Elsevier,* vol. 11, pp. 68-75, 2012.

[10] C. Merrow, "VMAT for treatment of gynecological malignancies for patients unable to receive HDR brachytherapy," *Journal of applied Clinical medical physics,* vol. 15, p. 5, 2014.

[11] Y. Yuan, "Long term follow up of volumetric modulated arc therapy in definitive radiotherapy for cervical cancer A single-center retrospective experience," *Elsevier,* 2020.

[12] L. U. P Blake (Royal Marsden Hospital, "Adjuvant external beam radiotherapy in the treatment of endometrial cancer pooled trial results, systematic review,," *Lancet,* vol. 373, pp. 137-146, 2009.

[13] F. Todd Pawlicki PhD, D. J. S. PhD and F. F. F. George Starkschall PhD, Hendee's Radiation Therapy Physics, New Jersey: John Wiley & Sons, 2016.