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RESEARCH ARTICLE

COMPARATIVE STUDY OF CONFORMAL HDR BRACHYTHERAPY WITH ICRU POINTS DOSES AND TOXICITY ASSESSMENT

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Abstract

Background: Toxicity assessment is done by comparing HDR brachytherapy with ICRU point doses. D2cc doses of OAR in HDR brachytherapy is slightly more than ICRU point doses.

Objectives: The primary objective is volumetric dose assessment and toxicity comparison between ICRU point doses and HDR brachytherapy.

Materials and Methods: It is a prospective comparative study. The total number of patients enrolled in the study is 20. After obtaining informed consent, then patients were enrolled in the study. All patients were diagnosed with H.P.E. positive squamous cell carcinoma of the Cervix from stage IIB to IIIB.

Results: HDR brachytherapy-based D2cc of Rectum is more than ICRU point doses of the rectum. bladder doses does not show any significant changes.

Conclusion: Comparatively HDR D2cc doses are more than conventional doses for rectum.

Introduction:-

The fourth most frequent cancer in the world is carcinoma of the cervix, whereas carcinoma of the breast is the second most frequent cancer in India. Cervical cancer is moderately common. Programmes, CARCINOMA CERVIX IS. But Due to lack of awareness of the disease and screening systems, cervical cancer has remained a serious health issue in underdeveloped nations. In underdeveloped nations, 40 to 45 percent of patients present with a locally advanced stage.

Aim of study:-

The primary endpoint of the study is to compare computer tomography HRCTV volumetric-based calculation and (I.C.R.U.) international commission on radiation units and measurements Reference points estimation of radiation doses to bladder, rectum, and sigmoid in the patient of carcinoma cervix treated with HDR brachytherapy. Toxicity assessment of OAR.

Place of study:
Government general hospital/ Guntur medical college

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Study design:
A prospective comparative study.
Sample size: 20 patients
Study duration: 1 year.

Inclusive criteria:
1. A histopathological proven Diagnosed squamous cell carcinoma of the uterine cervix.
2. Age 32-65 years.
3. The stage included advanced IIB to IIIB carcinoma.
4. Previously not exposed to any chemotherapy and radiation.
5. ECOG Score 0, 1.
6. No major life-threatening comorbidities.

External criteria:
1. Tumor of vagina, vulva endometrium.
2. Abnormal LFT and RFT, CBP.
3. Metastatic, recurrent disease.
4. Patient not given consent.

Materials and Methods:-

All patients enrolled in the study of IIB to IIIB received EBRT under LINAC of 50GY /25 fractions after completion of EBRT, CT simulation-based HDR intracavitary brachytherapy. For each institution, a comparison of mean Dose D2cc bladder and rectum doses with I.C.R.U. Bladder rectal doses were calculated using a paired test.

Equipment
EBRT under LINAC Varian Eclipse treatment planning system
I.C.R. – remote after loading with Iridium 192 source –HDR brachytherapy.

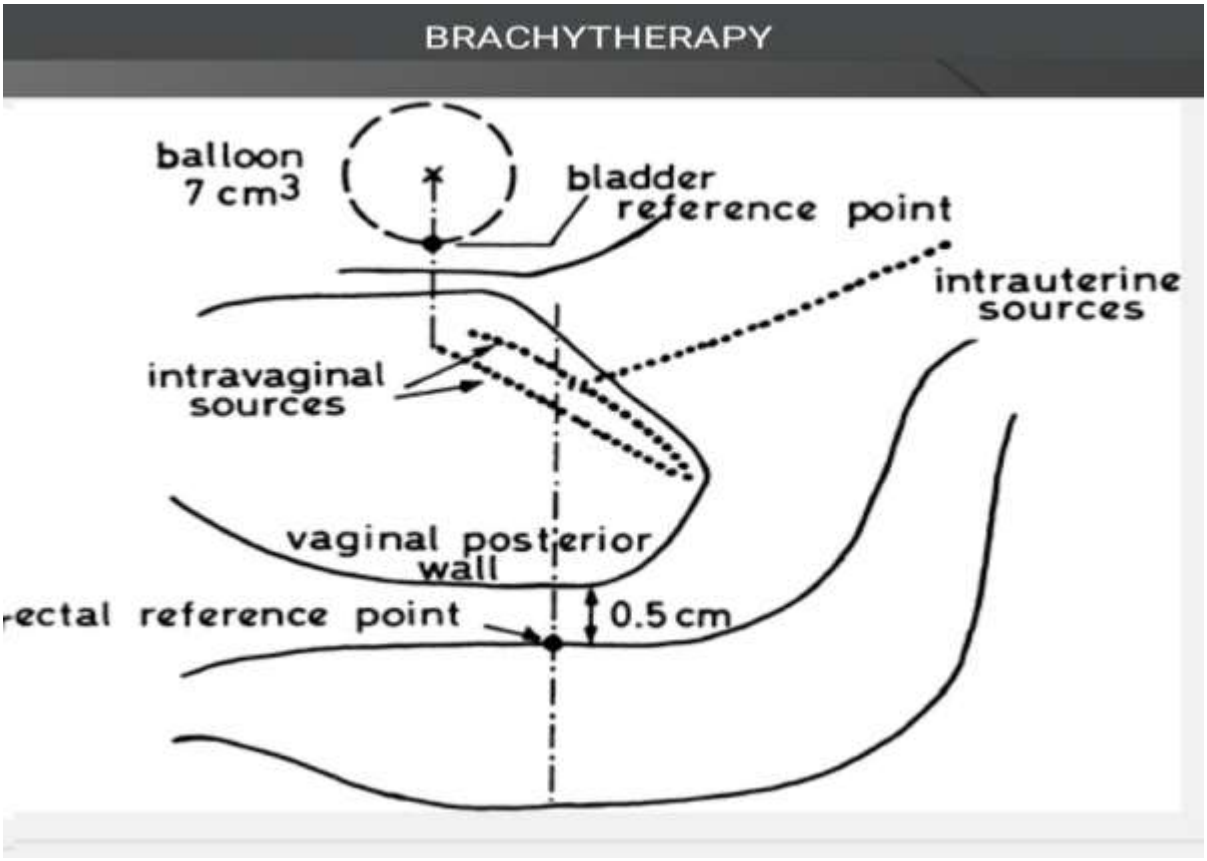
External Beam Radiation Simulation
1. Under LINAC, using conformal 3DCRT
2. The patient was simulated under C.T. with bladder protocol.
3. 3DCRT – whole pelvic – uterus, cervix, vagina, parametrium, along with a pelvic and iliac group of lymph nodes.
4. V95-95 % achieved.
5. (O.A.R.) Bladder, Bowel, And Rectum Doses Are Within the Prescribed Doses.

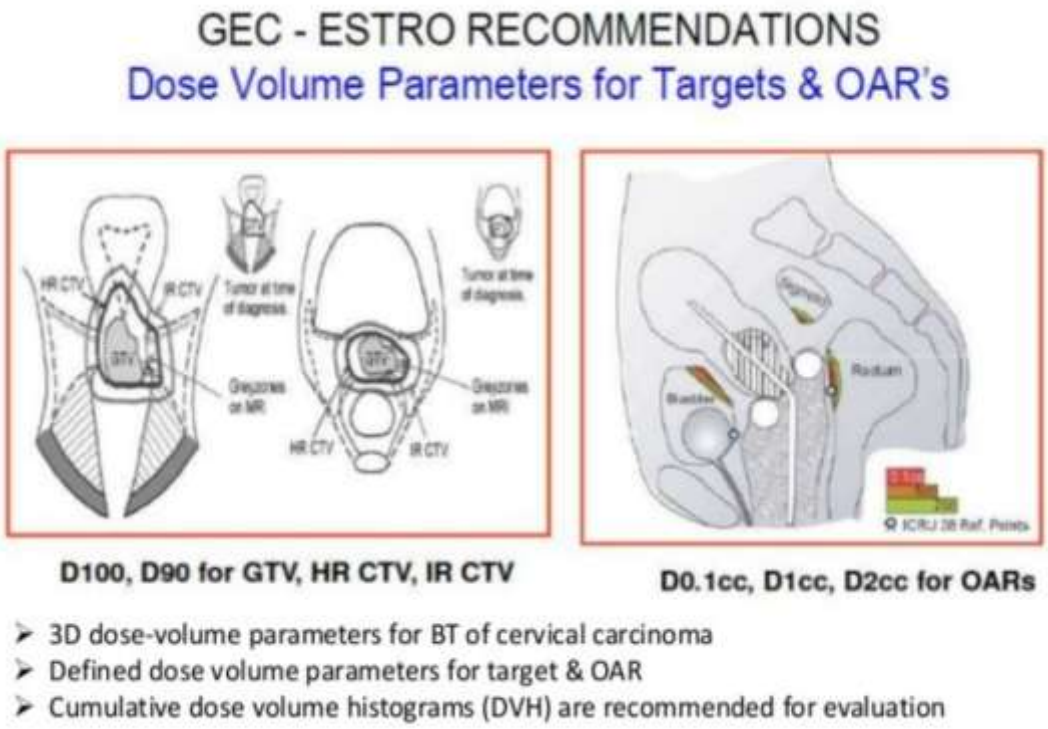
Treatment EBRT
1. CBCT was done on the initial day of treatment and weekly once for setup verification, and CTV, PTV bladder and rectal position were verified in relation to planning CT.
2. EBRT dose of 50GY/25 fractions, 2GY /fraction daily for five days a week for five weeks given.
3. Delivery of homogenous doses distribution to the entire pelvic organ for microscopic disease. Central Residual diseases addressed by brachytherapy. Parametrium and gross nodal disease were addressed by a boost of 10GY five fractions, 2GY per fraction.
4. Weekly assessment of toxicity of Gastrointestinal and Genitourinary followed by symptomatic management.

HDR brachytherapy:
After completion of EBRT, patients were clinically assigned for a response, then patients who are fit of I.C.R. or taken for application HDR. fractionation doses at 5^{th}, 6^{th}, 7^{th} week 3 fraction 7GY per fraction.

Application of brachytherapy
Each application of brachytherapy done under local anaesthesia or spinal anaesthesia patient was kept in a lithotomy position, external genitalia cleaned and draped, foleys catheter was inserted into the bladder with 5cc normal saline 2cc contrast for identification of bladder reference point.
1. Clinically assessed for residual tumour and parametrium with a uterine sound length of uteri cavity determined.

2. Fletcher suit application with central tandem with flange, with an ovoid paired used and fixed applicators.
3. Packing is done anteriorly and posteriorly around the applicators to push the bladder and rectum away.
4. Applicators stabilised with 'T' bandages tapped to the patient's abdomen.
5. C.T. simulation was done for pelvic to mid-thigh 3mm slice thickness exported to T.P.S. (treatment planning system).
6. A dose of 7GY prescribed to point A is placed 2cm above and 2cm lateral to the stopper/ tandem at the external os. I.C.R.U. bladder and rectal points are noted based on I.C.R.U. 38.
7. The rectal point at the level of the flange or tandem anterior position line draws from a tandem 5mm position to the posterior wall of the vagina. Following above and below, four additional points are noted. The highest rectal dose was recorded at these points, max dose at one of these points.
8. I.C.R.U. bladder point most positioned of the foleys catheter balloon.
9. An optimisation is done until the optimal plan result is achieved.
10. High-risk CTV contoured by using GEC ESTRO guidelines, clinically and C.T. assessment followed by the contour of the rectum and bladder outer wall of the rectum from ischial tuberosity inferiority to lower end of sigmoid colon superiorly.
11. The outer wall of the bladder was contoured from the base of the bladder contract filled by a Foley catheter to the apex. The sigmoid colon and contoured according to guidelines.





1. Planning was done using brachytherapy planning systems D.V.H. calculated for HR CTV, rectum, and bladder. A total of three fractions, 7GY/fraction, was given for three weeks. The minimum dose of rectum and bladder receiving for 2cc doses recorded HRCTV D90% recorded additional doses were recorded for rectum above and below. These doses are compared with 2cc doses of I.C.R.U. Points.
2. A total dose of E.B.R.T. and HDR brachytherapy normalised to 2GY/ fraction.
3. O.A.R. alpha/beta ratio was 3GY, Tumor alpha/beta ratio was 10GY.
4. B.E.D. biologically effective dose calculated by using
   BED = nd [1+d(α/β)]
   N= number of frictions
   D=dose/friction
   Alpha/beta = dose at lines quadratic positions are equal
   EQD2 =BED/[1+2/α/β]

Response:
After completion of treatment, patients were assessed for response to at 8weeks treatment response arrangement done with resist criteria complete, partial, stable, progressive disease. Toxicity assessment by using RTOG grading system. Patients' response assessment is done with history, physical and Imaging with CECT. Patients are kept under follow-up for one year.

Results:-

Patients enrolled in this study are 20, who are presented with Histopathology positive for carcinoma of cervix squamous cell, locally advanced stage from 2021, follow u for one year.

Patient characteristics
Total sample size : 20
1. Age of patients in years

Age in years	Number of patients
30-40	4
41-50	10
51-60	6

Mean age group is 46years.

2.Performance status

ECOG	Number of patients
0	15
1	5

3.Hemoglobin levels at the time of diagnosis

Hemoglobin gm%	Number of patients
<10	3
10-11	10
>11	7

4.FIGO staging

FIGO STAGE	Number of patients
II B	10
IIIA	6
III B	4

5.Parametrial extension

Parametrial extension	Number of patients
Unilateral	15
Bilateral	5

Medial overall treatment time is 50- 60 days.

1. All patients received EBRT under LINAC with a dose of 50GY/ 25 fractions,2GY per fraction. Patients with parametrium positive and nodal positive are boosted with 2 GY per fraction for 5 fractions.
2. After completion of EBRT all patients are assessed for HDR, patients enrolled in this study received 7 Gy per fraction for 3 fractions, total 21 Gy to HRCTV and point A.
3. The mean dose to point A is kept 7Gy and the mean EQD2 was 83.12±0.12Gy. α/β ratio is 10 for tumors.
4. The mean dose of rectum with 2cc is more compared to mean ICRU. Mean D max for rectum is 4.68±1Gy and mean EQD2 was 68.73±4.02. the mean rate of D 2cc rectum to D ICRU rectum was 1.35 for all fractions. P value is significant p< 0.005.
5. For bladder mean dose, EQD2 at 2cc is higher compared to ICRU bladder dose. mean ratio of D 2cc and DICRU bladder is 1.3. which is not significant difference. P value (0.20).

Dose parameters	Mean dose of individual fractions (Gy)
Rectum Dmax DICRU D2CC	 4.62±1.01 3.56±0.5 4.60±1.02
Bladder DICRU D2CC	 4.26±1.03 4.01±1.04

Dose parameters	Mean isoeffective dose in 2Gy per fraction
Rectum Dmax DICRU D2cc	 62.6±1.7 67.5±3.02 68.1±6.1
Bladder	

DICRU D2cc	73.1±16.4 80.8± 10.3

Response to treatment

Stage	Number of patients	Complete response	Partial response
IIB	10	10	0
IIIA	6	5	1
IIIB	4	2	2
Total	20	17	3

Toxicity: By RTOG Grading System

RTOG toxicity	Grade 1	Grade 2
Bladder	3	2
Rectum	3	2

Discussion:-

Brachytherapy for cervical cancer has progressed in the new era over since last 2 decades, with the introduction of image-guided brachytherapy. In developing countries like India, point A-based ICR was standard, with the introduction of image-guided brachytherapy. The doses of OAR and addressing of residual disease is properly validated.

Traditional brachytherapy application was done and dose to point A prescribed based on orthogonal x-ray film, with respect to the applicator. In CT Simulation after image guidance dose to point to A was also prescribed. As CT scan is less representative of residual disease. Point A prescription-based bladder and rectum on ICRU38.

These points cannot be the best estimate to forecast late complications to organs at risk because numerous studies have revealed discrepancies between them and volumetric image-based 3D dose calculations (Ling et al., 1987;Schoeppel and colleagues (1993); Barillot and colleagues (1994); van der Bergh et al. (1998); Fellner and colleagues (2001); Jason et al. (2003); Kirisits and colleagues (2005); Pelloski and colleagues (2005); Tan et al. (2009); Vinod et al. (2011)

Image-guided or conformal brachytherapy using HRCTV and 2CC doses to bladder and return showed. It provides anatomy, of OAR tumor features and response with time. 3D crossectional image reconstructive done of CT simulations. Critical OAR-delineated doses were optimized accordingly. Dose escalation to target volume HRCTV, respecting normal tissue tolerances.

According to a study done by Takenada T.et al 2012 , point A prescription dose will over-treat small tumours and under-treat large tumor with the new applications of brachytherapy. We could improve the doses adjusted to tumor and OAR for better clinical outcomes with decreasing toxicities.

Similar studies were done by Tan LT and colleagues for 3 years using image-guided doses with good pelvic control of 96% and reduced late toxicities. Increase in disease-specific survival by 81%. This study showed individual patient-adjusted doses by adaption using images guided brachytherapy.

By using the linear quadratic model for incomplete mono exponential sublethal damage repair to compare the effect of different dose rates and fraction size of conformal EBRT and brachytherapy, dose to point is equal to 82.1 ± 0.1 by GEC -ESTRO the results given in this study with isoeffective (equivalent) doses 2Gy/ fraction.

In this study we found significant difference for rectum D2cc and DICRU, with difference of 0.83Gy. But there is no significant difference with Dmax and D2cc. Bladder D2cc and DICRU does not show any significant difference.

Mean isoeffective dose is 68.1±6.1gy with α/β it was 75% from prescribed dose to point A.

These maximum point doses were mostly (47%) reported in the vicinity of 6 mm superior to the ICRU rectal points and only 25% the maximal dose is the ICRU dose. This is not in agreement with studies done by Deshpande (1997) and Mahan Shetty (2008) where they reported the maximum rectal dose point was the ICRU rectal point and found no significant difference the two points. Our result however is in good agreement with a study done by Jason C and colleague (2003), who reported the maximal rectal dose during ICBT was at the proximal rectum and found correlation between the maximal rectal doses with rectal complications. In our study, the dose to the 2 cc volume of bladder and the ICRU point dose did not differ significantly. The mean difference was 0.17 .

For the bladder, the DICRU and D2cc had good correlations. There is a strong association between bladder DICRU and D2cc, according to two investigations (Kirisits et al., 2005). But before our investigation, two other studies found a substantial difference between the two doses (Pelloski et al., 2005; Kim et al., 2007).

The dose to Point A, as determined by the linear-quadratic model to calculate the dose received by the tumour, was calculated to be 82.12 Gy / 10. However, based on our data, the average rectum received 77% and the average bladder received 92% of the prescribed dose, resulting in expected higher doses received by the rectum and bladder than our normal dose constraint.

Conclusion:-

Our findings from this study imply that DVH criteria-assessed organ at-risk doses was greater than ICRU point doses. The predicted dosage to the ICRU bladder point might be about equivalent to D2cc for the bladder and Dmax for the rectum in terms of rectal dose. However, it doesn't seem like the dose at the rectal point is a good substitute for the D2cc of the rectum. In traditional point-based planning, the dosages to organs at risk, especially the rectum, were underestimated.

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