Significance of ovoid separation with various applications of high-dose-rate-intracavitary radiotherapy in carcinoma of uterine cervix: A study from rural centre of Maharashtra, India

ABSTRACT
Aims: To analyze the differences in dose distribution, with ovoid separation in various applications, by different radiotherapists in the same patient of carcinoma of the uterine cervix treated by multiple fractions of high-dose-rate (HDR) intracavitary Radio therapy (ICRT).
Settings: Pravara Rural Hospital and Rural Medical College.
Design: Retrospective study.
Materials and Methods: Retrospective analysis of six cases of carcinoma uterine cervix, randomly chosen in the period from January 2004 and December 2007. Three selected radiotherapists performed the applicator placement for ICRT on the aforementioned patients in a consistent pattern-three consecutive ICRT treatments separated by weekly intervals. Ovoid separation was categorized into three groups: <25 mm, 26-35 mm and >36 mm. Prescribed point 'A' isodose lines with maximum separation laterally in right and left parametrium and antero-posteriorly in lateral plane was calculated for all 36 isodose charts for the 18 ICRT applications.
Results: In this study, there proves to be a significant difference in the ovoid separation between the applications of the different radiotherapists in the same patient with multiple fractions of HDR-ICRT. The applications done by 'A' radiotherapist resulted in an ovoid separation of <25 mm more often, 'B' radiotherapist of >36 mm while, 'C' radiotherapist fell in between the two.
Discussion and Conclusion: With more ovoid separation, lateral dose to parametrium was improved; however, antero-posterior dose was not significantly affected. In order to determine the best dose distribution, as evident in the dose charts of 'C' radiotherapist, it is recommended to choose the optimum ovoid separation in accordance to the patient's anatomy.

KEY WORDS: Carcinoma cervix, high-dose-rate brachytherapy, radiotherapy

INTRODUCTION
Carcinoma of the uterine cervix (Ca. Cx.) is the most common malignancy in women in developing countries as India. Accordingly, it is also the most prevalent carcinoma in females reported in our center, located in a rural area of Maharashtra, India. As in most cases, patients present at advanced stages such as stage III and IV in which surgery is not possible, radiotherapy holds a significant role in treatment. Indeed, the combination of external beam irradiation and brachytherapy has been shown to be an effective treatment for carcinoma cervix patients. The success of brachytherapy requires the delivery of a high dose of radiation to the tumor, while sparing the surrounding normal tissue to some degree.
This study is aimed to analyze the difference in dose distribution with ovoid separation in the applications by three different radiotherapists in the same patient with carcinoma of the uterine cervix treated by multiple fractions of high-dose-rate (HDR) intracavitary Radiotherapy (ICRT). Brachytherapy treatment was delivered by HDR/PDR remote after loader Gamma-med unit, in which there is a single high stepping iridium ($^{192}$Ir) source of 10ci with the active dimensions of 0.6 mm diameter and 3.5 mm length. The $^{192}$Ir source was encapsulated in a stainless steel capsule, which forms a total diameter of 1.1 mm and 5.1 mm length. Dwell positions can be adjusted from a distance of 1 mm to 10 mm apart and dwell times can be adjusted to 0.1 sec. to 999 sec, according to the desired treatment plan.

MATERIALS AND METHODS
Between January 2004 and December 2007, a total
of six cases of carcinoma uterine cervix, all having completed their external beam radiotherapy (EBRT) and HDR-ICRT in time, were randomly selected for the retrospective analyses. Three different radiotherapists, referred to as A to C, following the pattern of three consecutive treatments in weekly intervals, performed the applicator placement for ICRT. All six cases were histo-pathologically confirmed and investigated for routine hematological and biochemical examinations, chest X-ray, as well as Ultrasonography of the abdomen and pelvis before starting the radiotherapy treatment. Additionally, all the patients were examined and clinically staged in accordance to the International Federation of Gynecologists and Oncologists (FIGO) staging system. Three patients proved to be in stage IIB, and the other three were in stage IIIIB.

Radiation therapy- All six patients were treated by Anterior-posterior/Posterior-anterior (AP/PA) fields with cobalt 60 unit, to a mid plane dose of 5000 cGy in 25 fractions. Five fractions per week were administered for duration of five to six weeks without any midline block.

Brachytherapy- After completion of the external radiotherapy, the cases were scheduled for brachytherapy; 12 to 18 days later. All were given three fractions of HDR-ICRT at weekly intervals, but a different radiotherapist did the applicator placement. Fixed length three channel Fletcher applicator insertion was done under general/spinal anesthesia. A Foley’s catheter was inserted and the balloon was filled by 7 cc diluted Urograffin to identify the bladder neck region. A rectal catheter with lead wire inside was inserted into the rectum to visualize rectal mucosa for rectal points. In all applications, small size ovoids (colpostats) were placed. After applicator insertion, the vagina was packed by regular betadine soaked gauze packs to push the bladder and rectum away, stabilizing the applicator. Once the procedure is over, with the help of jig, AP and lateral semi orthogonal marker X-ray, films were taken by C-arm. Semi orthogonal X-ray films were reconstructed, and future planning was done with the Abacus treatment planning system (Program version-3.1; Germany). Dose was prescribed to point “A” - a point 2 cm up from the cervical os point of the intra uterine tube (tandem) and 2 cm lateral to the uterine source. Using bladder and rectal reference points, the doses given to the urinary bladder and rectum were calculated.

On the lateral radiograph, an antero-posterior line was drawn through the Foley’s catheter balloon center and the bladder reference point was taken on this line, at the posterior surface of the balloon (as per ICRU-38). The resulting bladder reference points were marked on the anterior radiograph at the center of the balloon. Rectal reference points, on the other hand, were found using a rectal catheter with a marker lead wire inside not the ideal recommendation as per ICRU-38, but used for its convenience and cost effectiveness. Multiple rectal reference points were delineated on a lateral radiograph: The R3 rectal point from an anterior-posterior line drawn through the lower end of the uterine source to 5 mm anterior to the rectal marker, and rectal points R1 to R5 taken 1-1 cm above and below the R3 point. All points are in the line of the rectal marker.

The doses delivered were 21 Gy to point “A” by HDR, in three fractions at weekly intervals (per fraction dose was 7 Gy). Bladder and rectum doses were limited to 80% of prescribed point “A” dose, as per ICRU-38 recommendations. Isodose charts for antero posterior (AP) and lateral (Lat.) plane were analyzed for ovoid separation and dose distribution. Additionally, a total of 36 AP and Lat. plane isodose charts were evaluated for the 18 ICRT applications. Ovoid separation was categorized into the three groups of <25 mm, 26-35 mm and >36 mm. The prescribed point ‘A’ isodose lines for maximum separation laterally in right and left parametrium and antero-posteriorly in lateral plane was calculated for all 36 isodose charts.

The bladder and rectal doses were calculated with reference to point “A” dose and grouped in three groups - dose less than 80% (<80%), 80-100% and above 100% (>100%).

RESULTS

In all six patients, A, B and C radiotherapist did the applicator placement. The total of 18 applications for six patients were analyzed as stated previously. In all the applications, the bladder doses were below 80%. The rectum doses were below 80% in 5, 4 and 5 applications, 80-100% in 0, 1 and 0 applications and above 100% in 1, 1 and 1 applications respectively [Table 1]. Ovoid separation, as calculated from isodose charts, proved to be different in all the applications, though the patients were same for all the three radiotherapists. Ovoid separation by A, B and C radiotherapists were <25 mm in 5, 1 and 1 applications, 26-35 mm in 1, 2 and 4 applications and >36 mm in 0, 3 and 1 applications respectively. As a whole, the ovoid separation ranged from 20 to 47 mm. Details are shown in Table 2 and in Figures 1 and 2. Prescribed point ‘A’ isodose line with maximum separation laterally in Antero-posterior plane was put into three groups-less than 60 mm (<60 mm), 61-70 mm and more than 70 mm (>70 mm). The maximum separation was 78 mm, while the minimum was 55 mm. Similarly, antero-posteriorly in lateral plane maximum separation was grouped in three categories-less than 35 mm (<35 mm), 36-40 mm and more than 40 mm (>40 mm). The maximum separation was 49 mm, and minimum was 34 mm. The details are shown in Table 3 and Figures 3-5.

Table 1: Details of bladder and rectal doses in respect to point “A” dose, in shared applications by different radiotherapists

| Radiotherapist | Pt. no. and no. of applications | Bladder dose | Rectal dose |
|----------------|---------------------------------|--------------|-------------|
|                |                                 | <80% | 80-100% | >100% | <80% | 80-100% | >100% |
| A              | 6                               | 6    | 0       | 0     | 5     | 0       | 1     |
| B              | 6                               | 6    | 0       | 0     | 4     | 1       | 1     |
| C              | 6                               | 6    | 0       | 0     | 5     | 0       | 1     |
Table 2: Details of ovoid separation as calculated from isodose charts in all the applications, by the different radiotherapists

| Radiotherapist | Pt. no. and no. of applications | Ovoid separation in mm |
|----------------|---------------------------------|------------------------|
|                |                                 | <25  | 26-35 | >35 |
| A              | 6                               | 5    | 1     | 0   |
| B              | 6                               | 1    | 2     | 3   |
| C              | 6                               | 4    | 1     | 1   |

The isodose distribution groups with less ovoid separation had a lower later dose distribution when analyzed (<50 mm), but more for antero-posterior distribution (>40 mm). This indicates that going for more ovoid separation improves the lateral dose to parametrium, leaving the antero-posterior dose largely unaffected. Difference in dose distribution in one patient for all three applications in AP and Lat. Plane for point 'A' isodose line (7 Gy) is shown in Figures 1 and 2.
DISCUSSION

Radiotherapy is an effective treatment modality for all the stages of carcinoma of the cervix and is widely used in developing countries.\textsuperscript{[1]} The success of brachytherapy requires delivery of high radiation dose directly to the tumor, while sparing the surrounding normal tissues, to some degree.\textsuperscript{[1]} Though HDR-ICRT (HDR-ICBT) is an acceptable, efficient, and safe alternative to traditional Low Dose Rate (LDR), ICRT requires multiple applications. The American Brachytherapy Society (ABS) recommends multiple HDR insertions for progressive tumor volume reduction, allowing more effective disease coverage with subsequent applications. Four to eight fractions of HDR-ICRT with a dose range of 5.3 to 7.5 Gy per fraction and a total dose by EBRT from 20 Gy to 50.4 Gy, depending on the disease state, as well as ICRT was given during EBRT (but EBRT is not given on the day of HDR).\textsuperscript{[1]}

Since the patients were uneducated and financially poor, it was preferred to perform three fractions of HDR-ICBT after the completion of EBRT. In our institution, where only three to four radiotherapists are working, the same radiotherapist does not generally do multiple applications in the same patient. There is an observed difference even when the same radiotherapist does all applications for the patient, and this becomes greater if done by different radiotherapists. Excluding patient factors, such a difference, may be attributable to ignoring the vaginal assessment and previous application notes before the next applicator placement.

Administering a dose to point “A” is commonly used for prescribing and reporting in gynecological radiation therapy and this point is related to applicator positioning. Thus, the applicator position intrauterine probe (tandem) and colpostat probes play a significant role with respect to dose distribution given to the parametrium, bladder and rectum. One can improve dose distribution by changing dwell position, dwell times and step distance with the help of the computers and various planning systems, but this has its own limitations.

In this study, there is a lot of difference in the ovoid separation with the application by the different radiotherapists in the same patient with multiple fractions of HDR-ICRT. Ovoid separation in the different applications by ‘A’ radiotherapist was often $<25$ mm, by ‘B’ radiotherapist was more times $>36$ mm and by ‘C’ radiotherapist in between the A and B. With less ovoid separation, lateral dose distribution to parametrium is less (\(<50\) mm), but more (\(>40\) mm) for antero-posterior distribution. This indicates that the lateral dose to parametrium can be improved by going for more ovoid separation, but antero-posterior dose stays largely unaffected. Dose to bladder was less than 80% of the prescribed point ‘A’ dose in all applications, while to the rectum exceeded the limit of 80% in once case by all the radiotherapist applications due to the patient’s short and narrow vagina. Possible outcome would be best with ‘C’ radiotherapist application due to good parametrial dose as well as less chances of complications.

Per vaginal, per rectum and per speculum examination under anesthesia before the starting applicator placement procedure is important, as it provides an idea of the vaginal space, residual lesion and amount of fibrosis. Once the uterine length is known with the help of the uterine sound, the scale decision of using an intrauterine probe of appropriate length is taken. In patients in which the vagina is roomy and the fibrosis is less than the appropriate size, colpostat (ovoid) should be fixed to colpostat probes, while the intrauterine applicator is fixed to the central clamping device before applicator placement. In patients in which the vagina is small and fibrosis is more than appropriate, one should be more careful in deciding size of the colpostat as well as in ensuring that the colpostat remains below the cervical stopper. Maintaining the latter reduces the chances of vaginal trauma/tearing.

CONCLUSION

With more ovoid separation, lateral dose to parametrium was improved, but the antero-posterior dose was not affected much. To get the best dose distribution, as obtained by C radiotherapist dose charts, one should go for optimum ovoid separation according to the patient’s anatomy. Less ovoid separation gives a 15-25 mm difference of dose to parametrium. More ovoid separation increases the likelihood of vaginal trauma. During applicator placement, especially for ovoids, the most important factors are the patient’s age, disease stage, duration between EBRT and HDR-ICRT, and anatomy. However, these differences can be minimized to some extent by careful application, choosing the proper size ovoids, and proper ovoid separation, thereby improving dose to parametrium.
Jain, et al.: Radical radiotherapy treatment (EBRT+HDR-ICRT), in carcinoma of the uterine cervix

ACKNOWLEDGEMENT

I was helped by excellent institutional facility in rural Maharashtra, India. To submit this article I was helped by Dr. S. N. Jangle and Mr. Sanjeev Kulkarni. I thank them sincerely.

REFERENCES

1. Saibishkumar EP, Patel FD, Sharma SC. Evaluation of late toxicities of patients with carcinoma of the cervix treated with radical radiotherapy: An audit from India. Clin Oncol 2006;18:30-7.
2. Nag S, Erickson B, Thomadsen B, Orton C, Demanes JD, Petereit D. The American Brachytherapy society recommendations for High-Dose-Rate Brachytherapy for Carcinoma of the Cervix. Int J Radiation Oncology Biol Phys 2000;48:201-11.
3. Foroudi F, Bull CA, Gebski V. Radiation therapy for Cervix Carcinoma: Benefits of Individualized Dosimetry. Clin Oncol 2002;14:43-9.
4. Sunder S, Symonds P, Deehan C. Tolerance of Pelvic organs to radiation treatment for Carcinoma of Cervix. Clin Oncol 2003;15:240-7.
5. King M, McConkey C, Latief TN, Hartley A, Fernando I. Improved survival after concurrent weekly cisplatin and radiotherapy for cervical carcinoma with assessment of acute and late side effects. Clin Oncol 2006;18:38-45.
6. Lorvidhaya V, Tonusin A, Changwiwit W, Chitapanarux I, Srisomboon J, Wanwilairat S, et al. High dose rate after loading brachytherapy in carcinoma of the cervix: An experience of 1992 patients. Int J Radiat Oncol Biol Phys 2000;46:1185-91.
7. Arai T, Nakano T, Morita S, Sakashita K, Nakamura YK, Fukushima K. High dose rate remote after loading intracavitary radiation therapy for cancer of the uterine cervix. Cancer 1992;69:175-80.
8. Shivkumar SS, Solomon JG, Supe SS, Vadhiraaj BM, Rao KK, Vidaysagar MS. A Physical optimization technique in high dose rate brachytherapy for cervical carcinoma. J Med Phys 2002;27:51-7.
9. Shang-Wen C, Ji-An L, Lian-Shung Y, Shih-Neng Y, An-Cheng S, Fang-Jen L. Comparative study of reference points by dosimetric analyses for late complications after uniform external radiotherapy and high-dose-rate brachytherapy for cervical cancer. Int J Radiat Oncol Biol Phys 2004;60:663-71.
10. Jain VS, Sarje MB, Singh KK, Umbarkar R, Shrivastava R, Jain SM. High-dose-rate-intracavitary brachytherapy applications and the difference in the bladder and rectum doses: A study from rural centre of Maharashtra, India. J Cancer Res Ther 2007;3:116-20.
11. Jain VS, Singh KK, Shrivastava R, Saumsundaram KV, Sarje MB, Jain SM. Radical radiotherapy treatment (EBRT + HDR-ICRT) of the carcinoma of the uterine cervix: Outcome in patients treated at a rural centre in India. J Cancer Res Ther 2007;3:211-7.

Source of Support: Nil, Conflict of Interest: None declared.