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COMBINED IRRADIATION OF PELVIS AND INGUINALNODAL REGIONS USING MODIFIED SEGMENTAL BOOST TECHNIQUE: A PROSPECTIVE STUDY.

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ABSTRACT **AIM:** To describe a novel Modified Segmental Boost Technique (MSBT) for combined irradiation of pelvis and inguinal nodes and to compare the dosimetry of the new method with that of other traditional methods of radiation treatment and IMRT. **METHODS AND MATERIALS**: Total 30 patients who required combined irradiation of pelvis and inguinal regions are included in our study to illustrate details and advantages of MSBT. Conventional photons with enface electrons design was created first with two opposing parallel fields and four field box. MSBT plans are generated and patient is treated with this technique to TD 45-50Gy for 5-6 weeks duration. A step-and-shoot inverse IMRT planning was subsequently generated. For dosimetric comparison, these treatment techniques were evaluated by dose-volume histogram (DVH) of PTV and OARs. Dose profiles at different depths from each treatment planning were generated for comparison. **RESULTS:** Comparing the modified segmental boost technique with conventional two opposing and four field box technique, we have found out that the target coverage, dose homogeneity index (DHI) and femoral head sparing is superior in modified segmental boost technique compared to other conventional approaches. And also the patients had better clinical response of both primary and the nodes with minimal skin morbidity when compared with conventionally treated patients data. DHI and target coverage of MSBT was comparable with that of IMRT. **CONCLUSION:** To cover pelvis and inguinal/femoral nodes, MSBT is technically simple to simulate, plan, and execute. Dosimetric study has demonstrated that it achieves comparable PTV coverage compared with other approaches while at the same time significantly sparing the surrounding OAR .It also has dose homogeneity comparable with IMRT and can be a nearer alternative for IMRT, in centers which are not having the facility and where the patient load is higher.

KEYWORDS : Modified segmental boost technique, femoral head sparing, dose homogeneity index, inguinal node coverage.

INTRODUCTION

The prognosis and failure patterns of pelvic malignancies depend upon the regional nodal involvement. Combined radiation of both the pelvic and inguinal nodal regions are indicated in a number of malignancies such as advanced carcinoma vulva, carcinoma anal canal, carcinoma vagina, carcinoma uterine cervix, metastasis inguinal lymphadenopathy of undetected primary, carcinoma penis and few other occasions either in definitive settings or in adjuvant settings. Groin irradiation is most commonly practiced nowadays compared to inguinal dissection for the associated morbidity. Combined treatment of inguinal lymph nodes along with pelvis is an alternative option or a definitive option to morbidity driven nodal dissection and sterilizes the node in elective and prophylactic settings[1]. True positive rate of clinically suspicious inguinal nodes are 70-75 percent when found by biopsy or fine needle aspiration cytology (FNAC) to have nodal metastasis. Pelvic lymph nodes are found positive in 30-35% of patients having positive inguinofemoral nodes. Adjuvant or neo adjuvant irradiation or even the definitive irradiation of inguinal lymph nodes may benefit patients with positive inguinal nodes[1,2].

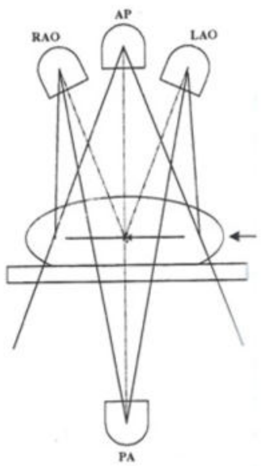

FIGURE1: MSBT FIELD SET UP

Most commonly used techniques in treating pelvis and inguinal lymph nodes is conventional two opposing AP/PA ,four field box with inguinal nodal boost with electrons, partial transmission block technique. Because of the problems associated with abutting treatment fields, new technique known as segmental boost technique (SBT) was developed using a single isocentric setup. The hot spots due to field overlap along the match line were the main disadvantage. To avoid the hot spots, Watson et al postulated this new technique Modified Segmental Boost Technique [Fig-1]. It is a simpler and straightforward technique to simulate, plan and also to execute and reproduce.

AIM

To describe a novel Modified Segmental Boost Technique (MSBT) for combined irradiation of pelvis and inguinal nodes and to compare the dosimetry of the new method with other methods of radiation treatment.

MATERIALS AND METHODS

Total 30 patients[Table-1] treated at our institution during May 2018-October 2019 were included in our study.MSBT plans are generated and patient is treated with this technique to TD-45-50Gy for 5-6 weeks duration.Conventional technique was created first with two opposing fields and four field box. A step-and-shoot inverse IMRT planning was subsequently generated. For dosimetry comparison, these techniques were evaluated by dose-volume histogram (DVH) of PTV and OARs. Dose profiles at different depths from each treatment planning were generated for comparison.

TABLE 1:PATIENT STATISTICS

CLINICAL DIAGNOSIS	NO
VULVAL CANCER	2
STAGE II	1
STAGE III	1
VAGINAL CANCER	8
STAGE II	3
STAGE III	5
ANAL CANCER	12
STAGE II	6
STAGE III	6
Cervical CANCER	7
STAGE III A	7
RECTAL CANCER	1
STAGE III	1
TOTAL	30
TOTAL DOSE 45-50 Gy	28

STUDY DESIGN

COMPARED TECHNIQUES

1. Two opposing AP/PA technique with electron boost fields; AP field extended to include inguinal and femoral nodes.
2. Four field box technique with electron boost fields for inguinal region.
3. Intensity modulated radiation therapy.

INCLUSION CRITERIA

All patients requiring combined irradiation of pelvis and inguinal region; ECOGPS ≤2,Haemoglobin>10gm/dl,confirmed histopathologically, previously untreated, Informed consent.

EXCLUSION CRITERIA

Patient with distant metastasis except in case of carcinoma uterine cervix with inguinal lymphadenopathy; Poor PS; Treated previously for the same condition; Patient not willing to sign informed consent.

PRIMARY ENDPOINTS

1. Femoral head sparing
2. Dose homogeneity index.
3. Inguinal node dose distribution.
4. Skin dose.

SECONDARY ENDPOINTS

1. Clinical response of node and primary.
2. Acute toxicity.
3. Treatment time
4. Contouring modifications.
5. Monitor units per fraction (MU).

MSBT-SIMULATION AND CT PLANNING

Patient is first immobilized in a conventional simulator with an immobilization device under the buttocks and lower extremities in a supine frog legged position. This position helps in stretching the inguinal folds using immobilization devices thereby preventing dose inhomogeneity and skin reactions. The isocenter is defined at the midplane of the pelvis. For planning CT the pelvis is scanned from T12 vertebrae to the mid-thigh region with 0.5 cm slice thickness. The primary tumor and nodal disease are contoured and CTV is obtained for each patient depending on the primary.PTV is then contoured by adding a margin to CTV. The OAR which includes the femoral head, bladder, small bowel, bone marrow and external genitalia is also contoured[3].

STEPS IN TREATMENT PLANNING

The field borders are defined and AP field is set up with 15 MV x-ray energy and is narrower and includes the pelvis alone. PA field is then defined from the posterior field. The width is extended to include the inguinal nodal regions. A 6MV x-ray energy beam is used for the wide AP field which also includes the pelvis and the inguinal nodal regions.MLCs are used to shape the collimator settings of AP and PA fields. Anterior inguinal boost fields use the same isocenter. While designing the left anterior inguinal boost field, using the exit shape of AP and PA beams on body, the Y2 jaw of anterior field is reduced to coincide with the superior border of the left inguinal nodes as it block all portions of the anterior field except the inguinal area of interest. After this, MLCs are now added to the fields and fitted to the medial border of the left inguinal nodes. Now the MLCs are manually retracted to match with the divergence of the posterior pelvic field with the help of field exit shape beams on body.

In other words, the MLC position of PA field is used to define the medial border of the inguinal boost field. Still there may be minimal field overlaps causing hotspots as in segmental boost technique. Now the gantry is tilted to an angle (6-8 degrees) such that inguinal node boost field matches exactly with the divergent beam of posterior pelvic field thereby preventing hot spots along the match lines as depicted below (Figure 2).

The boost segments thus formed are much smaller than the full anterior pelvic field but are also within the larger anterior segment[4,5,6].The same planning process is repeated to define the right inguinal boost field (Figure 3).

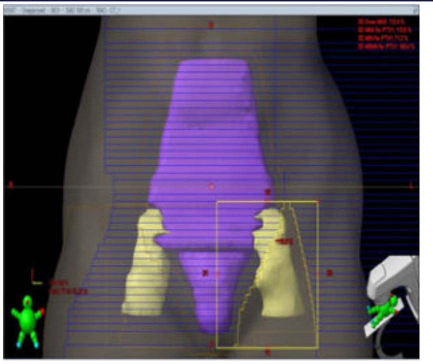

FIGURE2: LEFT ANTERIOR BOOST FIELD

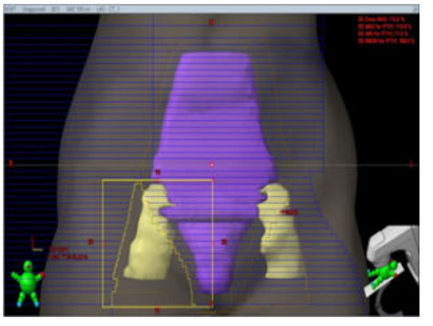

FIGURE 3: RIGHT ANTERIOR BOOST FIELD

The anterior and posterior fields were then normalized to the isocentric Inguinal node depths have varied from 3 cm to as much as 8 cm in the cases studied and verified using a diagnostic or treatment planning CT study of the pelvis to determine exact depths bilaterally. The actual prescribed dose to the isocenter as well as to depth of bilateral inguinofemoral nodes can be delivered by adjusting the field weightage[7]. The depth of prescription dose that is the isocenter is usually 10 cm in the pelvis and 5 cm in the inguinal nodes. Approximate field weighting was then applied to the corresponding fields such that 100% of the prescribed dose was seen at isocenter with another goal of reaching 100% of the prescribed dose to the inguinal depths. This weighing was usually in the amounts of 50% for the anterior and posterior fields and 30% to the subsequent boost segment fields. The MU needed for the technique are obtained from treatment plans and total no of MU is recorded. Treatment time is also recorded. The purpose of assigning lower photon energies to the anterior field segments was to ensure increased doses to the skin surface, thus maintaining the goal of treatment to the superficial node chains and/or surgical scar sites. Bolus was also defined to increase skin doses to superficial node regions or surgical scars[6,7]. Careful consideration was given in noting the bolus location relative to the point of normalization and calculation. Dose grid levels were then adjusted to include all areas of interest within the contours selected and a computer generated isodose calculation was performed giving the resulting isodose distributions.

RESULTS

DOSE HOMOGENEITY INDEX

MSBT has a very good dose homogeneity (0.16) comparable with IMRT (0.11) and superior than conventional techniques such as two opposing (0.20) and four field (0.22) (Table 2).

PTV COVERAGE

TECHNIQUE	D98 (Gy)	D2 (Gy)	D50 (Gy)	D95 (Gy)	DHI	MAX (Gy)	MIN (Gy)	MEAN (Gy)
2 OPP	44.9	55.5	52.5	47.5	0.20	57	32.3	51.8
4FBOX	43.7	54.9	51.9	48.2	0.22	56.6	31.6	49.8
MSBT	46.9	55.3	52.1	48.7	0.16	58.1	32.2	49.7
IMRT	48.9	55.1	52.7	50.2	0.11	58.7	33.0	52.6

STATISTICAL ANALYSIS

The techniques were analyzed using 'one way anova' method. There is a statistically significant difference in femoral head constraints V30, V40 and V50, mean femoral head dose, inguinal dose mean, D95 of inguinal nodes, dose homogeneity index (DHI), mean PTV dose and skin mean. Now after comparing for the difference between different techniques, MSBT is compared with each of the other technique for statistical significance using independent sampling test.

MSBT and two opposing techniques:

Results

P value is significant for MSBT in femoral head dose V30, V40, V50, PTV mean dose, PTV D95, DHI, inguinal mean dose, skin mean dose compared to two opposing technique and MSBT is statistically significant (P value =0.000) than two opposing technique[8].

MSBT and four field box technique

Results

P value is significant for MSBT in femoral head dose V30, V40, Results: P value is significant for MSBT in femoral head dose V30, V40, V50, PTV mean dose, PTV D95, DHI, inguinal mean dose, skin mean dose compared to four field box technique and MSBT is statistically significant (P value =0.030) than four field box technique[8].

MSBT AND IMRT TECHNIQUES

DISCUSSION

FEMORAL HEAD DOSE

Femoral head fracture is a potential complication of combined irradiation of pelvic and inguinal lymph node regions which was due to obliterative endarteritis, atrophy of the bone secondary to cellular damage and osteoporosis giving rise to stress or fatigue fractures. Although confounded by factors like age, smoking, alcohol, menopause, osteoporosis, steroid use etc., femoral head fracture is always higher than unirradiated population. Abe et al found that 27 out of 80 cancer cervix patients had femoral head fracture and risk was estimated at 34%.Emami et al postulated that absolute complication risk of femoral head exists when the dose exceeded its tolerance dose of 52Gy and it is 5% at 5years. Brown et al compared different techniques like conventional two opposing with electron tags or boost and PTB but found no significant difference between them.Grisgsby.et al evaluated the crude incidence of femoral head fractures and found it to be 5% and mean radiation dose is 52Gy. In a study by Mallinckrodt institute of radiology, per patient incidence of femoral head fracture was 4.8%and the actuarial incidence was 11% and 15% at 5 and10 years[11,12]. There is very good femoral head sparing in MSBT compared to other techniques. MSBT has met the RTOG constraints of V30, V40 and V50 as shown in DVH. The Dmax, Dmin, and Dmean of MSBT are 50.6Gy, 4.9Gy and 29.4Gy respectively compared to other techniques as illustrated by DVH (figure 4).

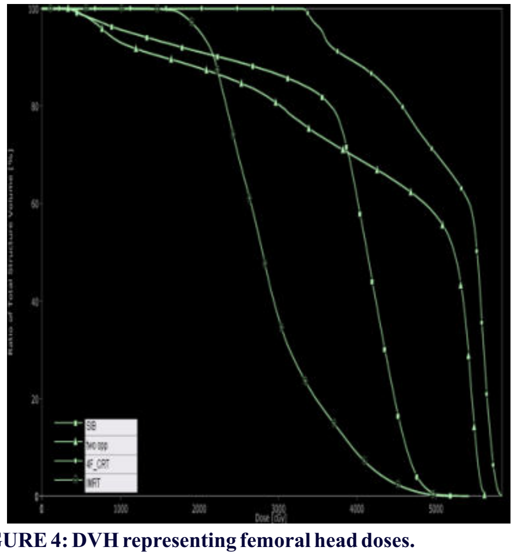

FIGURE 4: DVH representing femoral head doses.

Conventional techniques deliver very high doses to the femoral head and did not meet the RTOG constraints. Dmean is also very high. Although it can be reduced by using electrons, due to fields overlap dose inhomogeneity arises[13].

Dose homogeneity index

DHI is a tool to quantify the dose homogeneity between the various techniques. MSBT produces more uniform dose distribution compared to conventional techniques. The feathering of field junction is not needed in MSBT. The reason for that is MLCs with rounded edges do not produce a very sharp penumbra as it does not follow the beam divergence. MSBT is relatively very easy to set up and extremely well reproducible and treatment is completed soon in 3-4 minutes as there is no interruption. Conventional techniques using electrons lead to dose inhomogeneity. The field overlap causes hotspots ultimately leading to dose inhomogeneity. The reproducibility is difficult as the electron fields are designed manually leading to set up errors and inhomogeneity. This leads to numerous complications due to hot spots such as chronic pain, fibrosis, lymphedema, femoral head fracture, and avascular necrosis of the femur (figure 5).

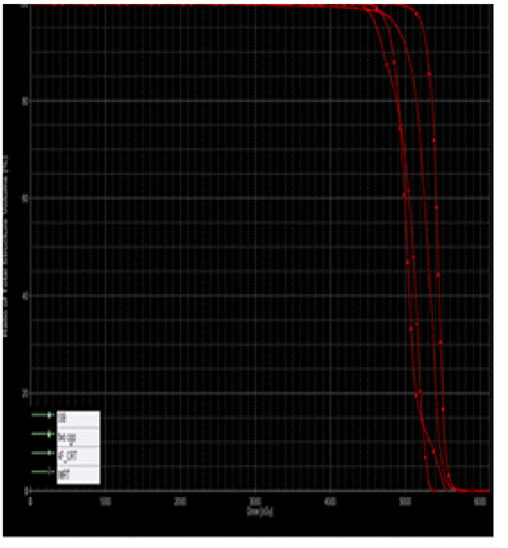

FIGURE 5: DVH representing dose homogeneity.

INGUINAL NODE COVERAGE

MSBT produces an excellent inguinal node coverage compared to conventional techniques. The Dmax, Dmin, Dmean of the inguinal nodes are 58.4Gy, 27.2Gy 52.2Gy respectively. The inguinal node depth can be ascertained in the CT scans during treatment planning. Dose prescription to the depth can be done resulting in desired PTV coverage. MSBT allows for the right and left nodal depth to differ during dose prescription so that a higher dose can be prescribes to one side in case of unilateral positive nodes (figure 6,7). MSBT can be used where inguinal nodes dose should be around 45-50Gy and where dose prescription is >50Gy the additional doses can be supplemented by electrons.

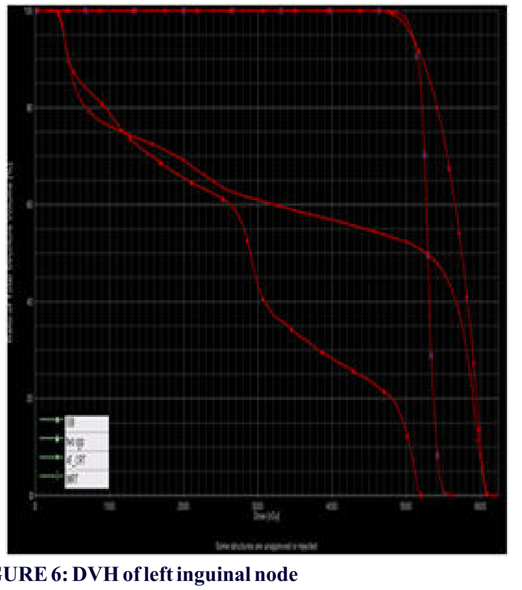

FIGURE 6: DVH of left inguinal node

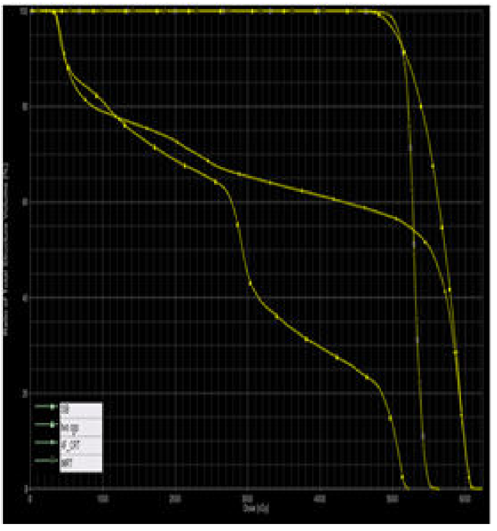

FIGURE 7: DVH of right inguinal node

INGUINAL NODE DEPTH:

It is measured from the skin surface to anterior surface of pectineus muscle. It is usually measured at two levels, one at the junction of pubic ramus and pubic symphysis and second at the pubic symphysis. Alternatively, the femoral vessel depth was selected as the indicator of maximal depth. The mean depth of both the values is also calculated (figure 8). In our patients, the depth varied from 1.5cms to 8cms. The mean depth is 4.5cm. With MSBT, we could prescribe dose to the actual depth of the nodes[16].Inguinal node depth measurement should be given to utmost importance during treatment planning.

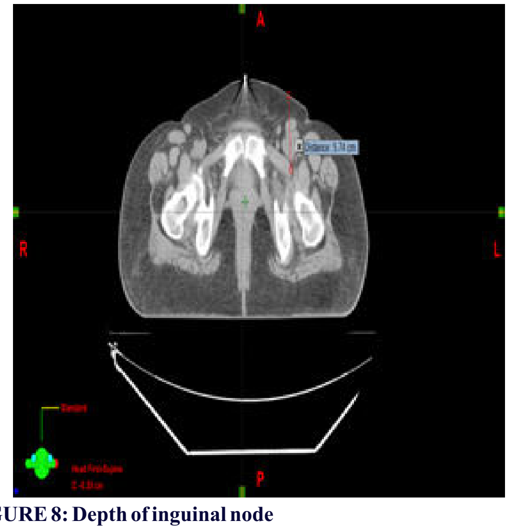

FIGURE 8: Depth of inguinal node

SKIN DOSE

The skin dose in MSBT is comparatively lower than conventional techniques. Bolus can be added if we need to boost the skin or biopsy scars. Like conventional techniques, MSBT does not require electrons boost which increases the skin dose (figure 9). In conventional techniques to comprehensively treat the deep inguinal nodes one has to use high energy electrons leading to skin reactions which are more pronounced in obese patients. It leads to treatment breaks prolonging the treatment. Khan postulated that, as latent depth increases, the electron beam experiences a sharp dose fall off which is attributed to elastic and inelastic collisions with atomic electrons and nuclei.

CONTOURING MODIFICATIONS

When there is unilateral or bilateral positive inguinal nodes, contours can be extended to the skin surface. Though bolus can be applied slight contouring modification can be incorporated to ensure skin coverage. Adaptive radiotherapy was not routinely done in our institute. But in few cases in our study, patients with bulky primary and node, carcinoma cervix with fluid collections and also in situations where we have to spare critical normal structures, repeat CT was done at 30Gy and depending on the tumor regression or fluid, patients were contoured again and treatment is planned again.

MSBT OVER IMRT

IMRT is a highly conformal technique that produces optimum intensity modulated profiles. The dose volume constraints for PTV and OAR are defined and adjusted to ensure optimum target coverage and minimizing the normal tissue toxicity. IMRT planning is done for dosimetric comparison with MSBT. The isodose distribution of IMRT and MSBT for PTV and also DVHs of OAR are analyzed (figure 10).

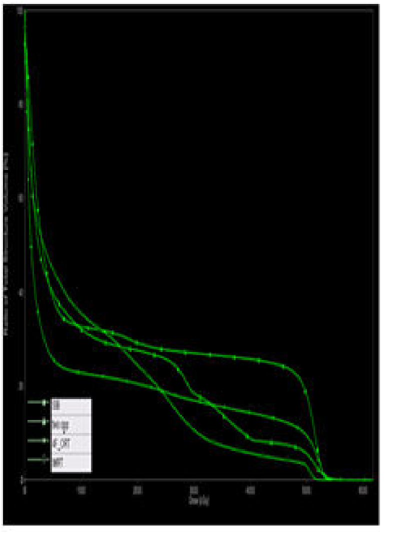

FIGURE 9: DVH of skin dose.

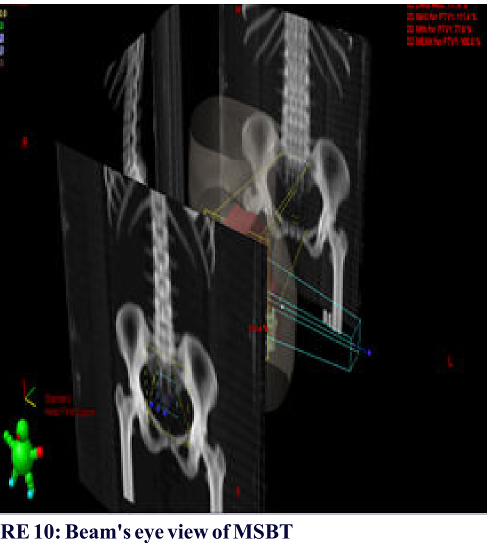

FIGURE 10: Beam's eye view of MSBT

IMRT significantly reduces the mean doses to bowel, bladder etc. compared with other techniques and Dmean dose to the OARs in MSBT are comparatively higher than IMRT. IMRT planning is labor intensive for both the radiation oncologist and physicist and the time taken up for IMRT is 6 hours but for MSBT is 40minutes. IMRT is always known to reduce the dose to OARs and thereby preventing acute and chronic toxicity[9,10]. But till date, there is no validated phase III prospective or randomized study for acute or chronic toxicities. IMRT contouring requires expertise, precision and accurate guidelines for routine use of IMRT in pelvic malignancies has not come yet. The total no. of MUs needed in MSBT plan was 300 MU/day but in IMRT it is 1900 MU/day leading to very prolonged treatment time. IMRT gives rise to higher integral dose resulting in very excessive low dose volume to the normal tissues as shown below contributing to second malignancies. It can be prevented by reducing the margins; but organ motion presents a major problem given the very high dose gradient of IMRT. RTOG 0529 study stated that the IMRT plans devised in the treatment of patients with anal canal cancer along with chemotherapy were all inadequate and required revisions of plan before starting treatment. It signifies that the accurate self-reproducible IMRT planning of PTV and nodal regions is often troublesome. RTOG formed a new panel to devise new contouring guidelines indicating the needed detailed research. The scenarios where MSBT is more preferred than IMRT are high risk of geographical miss, need for underdosing the target, locally advanced vulvar cancers as the perineal region can be treated extensively, difficult to delineate the tumors, patients with high risk of second malignancies, contouring expertise in pelvic malignancies is not optimal. IMRT is best suited for treating tumors with no target motion, tumors which require total dose >50Gy, patients receiving re-irradiation, to avoid a critical structure during pelvic irradiation such as pelvic kidney, Cohn's disease or ulcerative colitis. MSBT can used be used as alternative to IMRT where patient load is higher[9,10].

TOXICITY PROFILE

MSBT provides a comparable PTV coverage to that of the conformal techniques and at the same time spares the normal tissues (OAR) and the expected side effects are diarrhea, anemia, neutropenia, proctitis, cystitis and skin reaction. Toxicities were graded using RTOG grading system. Most of the patients developed perineal reactions but no skin reactions were observed in the external genitalia. Treatment breaks were given for grade II hematological toxicity, severe gastrointestinal toxicity and painful subcutaneous and moist desquamation skin reaction. The mean treatment delay was 4 days. Though grade I and II were seen, no grade III skin reactions were observed. The gastrointestinal side effects also follow the same trend as that of the skin toxicity as seen in 11(36.7%) patients. Myelosuppression were very less encountered as bone marrow was contoured and constraints were set at V20<70%. Acute radiation proctitis were seen in 6 cases (20%) and resulted in treatment delay (not more than 4 days) only in 4 cases. Acute radiation cystitis was seen in only 2(7%) patients and managed conservatively and did not result in any treatment breaks. Other side effects such are slow abdominal pain, giddiness, burning micturition, frequency of urination were rarely reported and did not cause any treatment breaks[14,15].

CLINICAL RESPONSE

Patients are examined clinically for the treatment response during end of 30Gy and at 50Gy. Almost all patients have responded to the treatment. Second clinical assessment was done at first follow up, after 6 weeks by clinical examination, imaging and pathological studies (if needed).22 patients achieved complete response proven by imaging and clinical examination. Two anal canal patients had partial response and one patient defaulted for further treatment and one patient was effectively salvaged and disease free henceforth.

FOLLOW UP

No patients treated with MSBT were lost to follow up. Most of the recurrences occur in the first 3 years and patients are followed very closely in this period.2 monthly follow up for next 6 months and 3 monthly follow up until 3 years and then 6 monthly until 5 years and yearly thereafter. Patient will undergo clinical examination, imaging and further studies once in a year or if clinically indicated.

CONCLUSION

We used modified segmental boost technique in the treatment of combined irradiation of pelvis and inguinal nodal regions and we achieved significantly higher femoral head sparing, dose homogeneity index, inguinal nodal coverage with minimal skin toxicity compared to other conventional techniques and is almost comparable to IMRT.MSBT is easy to simulate, plan, execute and reproduce and also time efficient. It provides good clinical response of the primary and node. MSBT can be readily used in hospitals with limited resources or higher patients load.Long term follow up is needed to study the clinical efficacy of this technique, disease free survival and overall survival.

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