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The Gulf Journal of Oncology

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Dosimetric Comparison Between Bone Marrow Sparing Intensity-Modulated Radiation Therapy And Conventional Techniques In The Treatment Of Cervical Cancer: A Retrospective Study

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⁴Department of Physics, Bharathiar University, Coimbatore, India

Abstract

Purpose

The purpose of this study was to compare the AP/PA (2F), four-field box (4FB), 6MV and 15MV intensity-modulated radiation therapy (6MV-IMRT and 15MV-IMRT) techniques in the treatment of cervical cancer. In particular, each technique’s ability to spare the bone marrow was of primary interest.

Materials and methods

Nine patients with squamous cell carcinoma of cervix were analyzed in this retrospective study. All the nine patients were earlier treated using 4FB technique. All the plans were created with the intention of having similar dose distributions and all plans were normalized such that 95% of PTV is covered by 99% of prescribed dose. In addition, different homogeneity indices, mean dose-volume histograms and mean doses were kept as close as possible. Volumetric parameters for iliac bone marrow (IBM), lumbo-sacral bone marrow (LSBM), lower pelvic bone marrow (LPBM), bladder, rectum and unspecified tissue (UT) were evaluated at different dose levels and compared between the different techniques.

Results

The 6MV and 15MV-IMRT plans were more conformal (1.205, 1.183) when compared with 2F and 4FB techniques (1.501, 1.405). For IBM, 6MV-IMRT plans reduced $V_{10}$, $V_{15}$, $V_{20}$ and $V_{30}$ by 0.154%, 4.008%, 9.975% and 0.557% respectively when compared with 4FB. But, IBM was most spared in 2F technique at these low dose levels. The volume of LSBM receiving different dose levels ($V_x$) were considerably reduced in IMRT plans when compared to 2F and 4FB techniques.

IMRT plans reduced bladder and rectal high doses volumes ($V_{30}$, $V_{40}$ and $V_{46}$) when compared with 2F and 4F techniques. The bladder and rectal volumes receiving 40Gy or more ($V_{40}$) were 84.678 Gy and 80.366 Gy respectively in 6MV-IMRT when compared with 2F and 4FB plans (all values are 100.000 %). The $V_{46}$ of the rectum was 54.991% using 6MV-IMRT, a reduction of 45.009% and 40.587% from that using the 2F and 4FB plans respectively.

For all OAR’s, statistical significance was not observed between 6MV and 15MV IMRT plans and hence differences due to energy are small.

Conclusions:

IMRT reduced LSBM dose at all dose-levels than 2F and 4FB techniques. IMRT also reduced the IBM dose than 4FB technique together with better sparing of other OAR’s, unlike 2F technique. The differences between high and low energy IMRT plans were not significant. Thus, IMRT might reduce acute hematologic toxicity (HT) when compared with conventional techniques.

Keywords

Bone marrow, Cervical cancer, Intensity modulated radiation therapy, Sigma index.
Introduction

Cervical cancer is a leading cause of cancer incidence and mortality among women. Concomitant chemo-radiotherapy is the primary treatment choice for patients with locally advanced cervical cancer. Concomitant chemo-radiation improves overall survival when compared with radiotherapy (RT) alone (1-3). Nevertheless, this is frequently associated with acute hematologic toxicity (HT) due to the fact that most of the total body bone marrow is located within the lumbar spine and pelvic bones (4, 5). Approximately 40% of the patient’s total bone marrow lies within the pelvic bones (5, 6). Thus, one of the reasons for the HT may be due to irradiation of large volume of pelvic bone marrow which also limits further chemotherapy to maximize tumor control. The main cause of myelosuppression is due to the destruction of bone marrow stem cells which are highly radiosensitive. Moreover, pelvic radiotherapy impairs the ability to deliver chemotherapy in the future in patients who develops metastatic disease.

The other organs-at-risk (OAR) include bladder, rectum and small bowel. The well-known complications with administration of conventional techniques followed by intracavitary brachytherapy include proctitis, fistula and stenosis for rectum and cystitis and contracture for bladder. Normal tissue injury also limits total radiation dose administered to patients. While conventional doses are good for most patients in achieving good tumor control, there is a non-negligible proportion of patients who may benefit from dose escalation, notably cervical cancer patients for whom brachytherapy cannot be administered (unfavorable anatomy, bulky residual disease, comorbid conditions and multiple medical problems) and women with documented lymph node involvement (7). However, higher doses are not practical with conventionally radiation techniques without unacceptably high rates of toxicity.

The reduction of radiation doses to critical organs in the initial whole pelvis radiation therapy might reduce the hematologic toxicity, bladder and rectal complications after the completion of external beam RT and brachytherapy (BT). Modern techniques of precision radiation delivery like intensity modulated radiation therapy (IMRT) allow the dose to be “sculpted” to the tumor volume while at the same time minimizing the dose to the adjacent dose-limiting normal tissues. This offers the opportunity to increase the therapeutic ratio. Several studies have demonstrated the ability of IMRT to reduce the bladder and rectum doses (8, 9). However, the ability of IMRT to reduce the bone marrow dose compared with conventional techniques has not been fully investigated.

The purpose of this study was, therefore to quantify the potential advantages of intensity modulated radiation therapy (IMRT) relative to antero-posterior (2F) and 4 field box (4FB) conventional techniques which are routinely employed. In particular, each technique’s ability to spare pelvic bone marrow (PBM) was of primary interest in this study. PBM consists of lumbo-sacral bone marrow (LSBM), iliac bone marrow (IBM) and lower pelvic bone marrow (LPBM). Bladder, rectum and unspecified tissue (UT) were also studied in view of their documented relevance in the literature.

Another objective of this work was to determine the differences, if any between high and low energy intensity modulated radiation therapy plans.

Methods and Materials

Nine patients with cervical cancer were selected for this retrospective analysis. All patients had intact cervical cancer with FIGO stage IIB in 7 and IIIB in 2. All the 9 patients were already treated with 4FB technique using 15 MV photons. The mean age of the patients was 59.5 years. The same CT datasets were chosen for creating 15 MV antero-posterior (2F), 6 MV intensity modulated radiation therapy (6MV-IMRT) and 15 MV intensity modulated radiation therapy plans (15MV-IMRT).

Simulation

All patients were immobilized with customized thermoplastic sheets adequately encompassing the upper and lower pelvic regions of the body before a CT scan of the pelvic region
was performed (Brilliance 16, Philips Medical Systems). Scan parameters consist of large field-of-view protocol with a 4mm slice thickness. The CT scans were acquired from L3 level to 4cm below the ischial tuberosities. Intravenous and rectal contrast was administered at the time of scanning to aid in the delineation of normal and target tissues.

**Target definition**

The clinical target volume (CTV) and critical organs were contoured on individual CT slices following ICRU50 recommendations (10). The CTV consisted of pelvic and presacral lymph nodes, uterus and cervix, upper vagina and parametrical tissue. In general, 1 cm margin was used around the vessels but it was reduced in select cases according to physician’s discretion. All plans had uniform 1cm CTV-PTV margin.

**Normal tissue delineation**

Normal tissues included lumbo-sacral BM (LSBM), iliac BM (IBM), and lower pelvic BM (LPBM), bladder, rectum and unspecified tissue (body minus delineated organs). The external contour of the pelvic bones was delineated on the planning CT scan to define BM, as described in detail elsewhere (11). The descriptive statistics of volume of OAR’s are given in (Table1).

**Treatment Planning**

For each patient, in addition to 4FB technique (used to treat the patients earlier), 2F (AP/PA), 6MV-IMRT and 15MV-IMRT plans were created. 2F and 4FB techniques were created with 15 MV X-rays. All the plans were generated using a commercial planning system (PrecisePlan version 2.03, Elekta Medical Systems, Crawley, UK). A 40 pair multileaf collimator having a width of 1cm at the isocentre distance was used for all plans. A uniform field margin of 1cm was used for PTV, to account of beam penumbra to obtain the desired PTV coverage. The dose calculation was done using an irregular field algorithm based on Clarkson’s technique (area integration algorithm). For step and shoot inverse IMRT plans, the segmental inverse optimizer in PrecisePlan planning system was used. The prescribed dose to PTV was 46 Gy in 23 fractions.

In 4FB plans, the fields consisted of anterior, posterior, left lateral and right lateral beam directions. 2F plans were created by removing the right and left fields. In 2F and 4FB plans,

<table>
<thead>
<tr>
<th>OAR</th>
<th>Range</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV (cm³)</td>
<td>1039.80 - 1589.30</td>
<td>1274.08 ± 164.97</td>
</tr>
<tr>
<td>LSBM (cm³)</td>
<td>205.10 - 351.30</td>
<td>280.88 ± 53.79</td>
</tr>
<tr>
<td>IBM (cm³)</td>
<td>265.20 – 492.70</td>
<td>379.44 ± 70.05</td>
</tr>
<tr>
<td>LPBM (cm³)</td>
<td>239.80 – 394.50</td>
<td>286.21 ± 47.80</td>
</tr>
<tr>
<td>Bladder (cm³)</td>
<td>50.90 – 556.10</td>
<td>251.39 ± 176.27</td>
</tr>
<tr>
<td>Rectum (cm³)</td>
<td>20.40 – 134.70</td>
<td>50.83 ± 42.11</td>
</tr>
<tr>
<td>UT (cm³)</td>
<td>6424.60 – 10419.60</td>
<td>8155.24 ± 121.06</td>
</tr>
</tbody>
</table>

Table 1: Volume statistics of OAR’s
beam weights were adjusted to maximize target uniformity and to minimize hot spots.

The beam placement angles of 0°, 50°, 90°, 150°, 180°, 210°, 270° and 310° were used for IMRT plans. This beam angle configuration was found to provide the most bone marrow sparing without compromising the PTV coverage (12-13). 3D view of beam arrangement is shown in (Figure 1). Inverse planning was performed to optimize PTV dose uniformity and to minimize the doses to the organs-at-risk (OAR’s). PTV coverage was not compromised as a result of overlap with the OAR’s.

The dose volume constraints for the segmental inverse optimizer are mentioned in (Table 2). Each structure had a priority factor defining the relative importance of the given constraint. In segmental inverse optimizer, the priority can be varied from 1 to 999.

In order to study the differences between low (6MV) and high energy (15 MV) photons in IMRT plans, all other plan parameters like gantry angles, collimator angles, number of segments, shape of the segments, dose constraints etc. were kept constant between 6MV-IMRT and 15MV-IMRT plans.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Dose-volume Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>V100 &gt; 95%, V95 &gt; 99%</td>
</tr>
<tr>
<td>LSBM</td>
<td>V10 &lt; 75%, V30 &lt; 50%</td>
</tr>
<tr>
<td>IBM</td>
<td>V10 &lt; 75%, V30 &lt; 50%</td>
</tr>
<tr>
<td>LPBM</td>
<td>V10 &lt; 75%, V30 &lt; 50%</td>
</tr>
<tr>
<td>Bladder</td>
<td>As low as possible</td>
</tr>
<tr>
<td>Rectum</td>
<td>As low as possible</td>
</tr>
<tr>
<td>UT</td>
<td>Maximum dose of 48 Gy</td>
</tr>
</tbody>
</table>

Table 2: Dose-volume constraints used in the optimizer

**Treatment plan evaluation**

In order to facilitate the comparison between all four techniques, the plans were generated such that they deliver similar dose distributions to the PTV. This can be achieved by normalizing the plans such that 95% of the PTV is covered by 99% of the prescribed dose. The similar dose distributions can be further ascertained by keeping very similar mean doses, homogeneity and conformity indices etc. Mean dose volume histograms (MDVH) of all 9 patients were generated and used for comparing the different techniques. BIOPLAN (14) software was used for generating the MDVH’s.

**Plan parameters: PTV**

Many indices (15, 16, 17, and 18) were available to evaluate the homogeneity. Nevertheless, most of them are not reliable and have inherent limitations. Such indices are briefly described here followed by a better index recently proposed by Yoon et al (19). Because of similar naming conventions of different homogeneity indices and to avoid ambiguity, we have adopted a simple terminology as given in (Table 3).

The robustness of the index increases from

<table>
<thead>
<tr>
<th>ELSEWHERE TERMINOLOGY</th>
<th>DEFINITION</th>
<th>USED TERMINOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>primitive H-index</td>
<td>D_{max} / D_p</td>
<td>HI-1</td>
</tr>
<tr>
<td>modified H-index</td>
<td>D_5 / D_p</td>
<td>HI-2</td>
</tr>
<tr>
<td>HI-index</td>
<td>((D_{2} - D_{98}) / D_{5}) x 100%</td>
<td>HI-3</td>
</tr>
<tr>
<td>modified HI-index</td>
<td>((D_{5} - D_{95}) / D_{2}) x 100%</td>
<td>HI-4</td>
</tr>
</tbody>
</table>

Table 3: Existing and presently used naming convention for different homogeneity indices and their definitions. D_{x} is the dose to x% volume of the target, D_p is the prescribed dose and D_{max} is the maximum dose.
HI-1 to HI-4 as can be easily seen from (Table 2). HI-1 relies on just two points ($D_p$ and $D_{\text{max}}$) in the cumulative DVH (CDVH) curve. HI-2 is very similar to HI-1 with reduced range ($D_i$ instead of $D_{\text{max}}$ thus clipping the tail portion). HI-3 and HI-4 further reduces the curve by clipping the low and high dose regions of the CDVH. However, all the four indices are point sensitive (depending on just two point doses on CDVH curve). For the first two indices, a value close to unity indicates a better homogeneous dose. For the penultimate and the last indices, the lower the value, the better is the homogeneity. Since they are point-based they have inherent limitations and they fail occasionally. This was best illustrated with examples by Yoon et al (19) who proposed a new index called sigma-index (SI). Further illustrations and examples can be found in the work by Sundaram et al (20).

**Sigma-index (SI) is defined as**

$$s-index = D_{\text{SD}} = \sqrt{\sum (D_i - D_{\text{mean}})^2 \times \frac{v_i}{V}}$$

where $D_{\text{SD}}$ represents the standard deviation about the mean dose, $D_{\text{mean}}$ is the mean dose to PTV, $D_i$ is the dose to the $i^{th}$ bin having a volume $v_i$ and $V$ is the total volume of the target. It is apparently evident from the expression of sigma-index that it takes lot of dose points on the differential dose volume histogram (DDVH) unlike the other indices. Thus this index is expected to be more accurate than the other indices. All the above homogeneity indices were evaluated for all 9 patients and mean ± SD values are reported for the four techniques.

Conformity index is defined as the ratio of the volume of the body receiving the prescription dose to the volume of the PTV receiving the same dose. The mean conformity indices along with SD are reported for all four techniques.

As cited earlier, the plans were designed in such a way that, the MDVH’s and mean doses are very similar and hence leads to similar dose distributions for PTV. Thus, the homogeneity indices are also expected to be similar. Mean doses and all HI’s were reported for all four techniques.

Figure 3: Axial dose distributions for 2F, 4F, 6MV-IMRT and 15MV-IMRT techniques respectively
Table 3(a): Descriptive statistics of DVH parameters for different structures. The values are reported as mean \( \pm \) SD averaged over the sample size (n=9). For each structure, statistical p values are listed beneath. ‘NS’ value for p stands for non significance and indicates the zero value of standard deviation for the corresponding groups.
Table 3(a): Descriptive statistics of DVH parameters for different structures. The values are reported as mean ± SD averaged over the sample size (n=9). For each structure, statistical p values are listed beneath. ‘NS’ value for p stands for non significance and indicates the zero value of standard deviation for the corresponding groups.
Plan parameters: OAR’s

The percent volume of the OAR’s (LSBM, IBM, LPBM, Bladder, Rectum and UT) were obtained at different dose levels (5 Gy, 10 Gy, 15 Gy, 20 Gy, 30 Gy, 40 Gy) for all four techniques and the mean ± SD values were reported (representative of all 9 patients).

Statistical analysis

The mean values of all delineated structures were then compared for the 2F, 4FB, 6MV-IMRT and 15MV-IMRT techniques. Student’s t-test was used for statistical analysis. A p-value of < 0.05 was considered statistically significant.

Results

A quantitative comparison of DVH’s between different techniques (and plans) is most meaningful when similar target doses are achieved. This was accomplished by normalizing the plan such that 95% of the PTV is covered by 99% of the prescribed dose. In addition, the mean doses of PTV for all the plans were also kept very similar. Table 3 summarizes the descriptive statistics of DVH parameters. Of note in the Table is the fact that there are significant differences observed for the OAR’s between the conventional plans (2F, 4FB) and the conformal plans (6MV-IMRT, 15MV-IMRT) at low dose regions of the DVH (atleast for IBM and LSBM). These findings are consistent with other studies (11, 21) which suggests significant association of acute hematologic events with V10 and V20 for patients undergoing concurrent chemotherapy and IMRT.

PTV coverage

The MDVH of PTV is shown in (Figure 2a). Very similar dose coverage for all techniques is quite evident. Concerning conformity of dose, figure 3 shows the prescription dose (pink colorwash) for 2F, 4FB, 6MV-IMRT and 15MV-IMRT plans respectively. 6MV and 15MV-IMRT plans result in sculpturing (conform) of prescribed isodose line to the shape of the PTV.

While planning, emphasize was given to create almost similar dose distributions in all plans. Nevertheless differences were observed and they arise because of inherent characteristics of the individual techniques. The p-values of all the evaluated parameters (HI-1, HI-2, HI-3, HI-4, SI, CI and mean dose) showed statistical significance for the following plan comparisons: 2F versus 4FB, 2F versus 6MV-IMRT, 4FB versus 6MV-IMRT.

The sigma index values of 2F, 4FB, 6MV and 15MV-IMRT plans were 2.104, 1.737, 2.745, and 2.637 respectively. Sigma index is considered more reliable and robust since it takes the entire differential DVH curve into account unlike the other indices (HI-1, HI-2, HI-3 and HI-4). Thus homogeneity decreases in the following order: 4FB – 2F – 15MV-IMRT – 6MV-IMRT; However, the other homogeneity indices do almost follow the same trend, in general, except for close values of conventional plans (2F and 4FB).

As expected, IMRT plans had better conformity index values (1.205, 1.183) than conventional plans (1.501, 1.405).

4FB showed better values for SI, CI and mean doses (1.737, 1.405, 4.712.220) when compared with 2F (2.104, 1.501, 4713.556). 15MV-IMRT showed marginally better values for HI-I, HI-2, HI-3, HI-4, SI, CI and mean dose (1.127, 14.753, 1.084, 10.756, 2.637, 1.183 and 47.395) when compared with 6MV-IMRT (1.134, 14.894, 1.087, 10.771, 2.745, 1.205 and 47.513) though statistically not significant. Among conformal plans (6MV-IMRT and 15MV-IMRT), differences were in general small and not significant as is evident from high p-values in (Table 3a).

Dose distribution for bone marrow

IBM

The axial CT datasets in the plane of isocentre are shown in figure 3 for the four techniques. 2F being parallel opposed, produced a sharp fall-off beyond the field edge thus reducing the IBM dose in particular, below a threshold dose of 60% of prescribed dose as is clearly evident from (Figure 2c). 4FB technique was more conformal than 2F. Significant reduction in different volumetric parameters was observed in 2F. The \( V_{5} \), \( V_{10} \), \( V_{15} \) and \( V_{20} \) values were 70.054%, 63.486%,
Dosimetric Comparison between IMRT and Conventional Techniques, T. Sundaram, et. al.

60.866% and 56.930%, respectively, using the 2F plans, a reduction of 28.782%, 34.920%, 33.716%, 35.672%, respectively, from that using the 4F plans. 6MV-IMRT plans reduced $V_{10}$, $V_{15}$, $V_{20}$ and $V_{30}$ by 0.154%, 4.008%, 9.975% and 0.557% respectively when compared with 4FB. Thus, IBM was most spared in 2F technique at these low dose levels. However, the bladder and rectal doses were high in 2F plans. Not much difference was observed between 6MV and 15MV-IMRT plans.

**LSBM**

The values of all volumetric parameters ($V_x$) are 100% in 2F technique as it completely encompasses LSBM. 4FB spares the posterior part of LSBM and hence exhibits comparatively less $V_x$ values (100.00%, 100.00%, 98.890%, 97.200%, 68.110% and 48.008%) than in 2F technique. IMRT plans conforms the dose further and hence $V_x$ values are lower than conventional plans. A reduction of 3.904%, 12.144%, 19.722%, and 25.780% was observed in $V_{15}$, $V_{20}$, $V_{30}$ and $V_{40}$ respectively with 6MV-IMRT when compared with 4FB plans.

All p-values are <0.05 and hence showed statistical significance when conventional plans are compared between them or with 6MV-IMRT plan. 6MV and 15MV-IMRT plans showed no statistical significance at $V_5$, $V_{10}$, $V_{20}$, $V_{40}$ and mean dose (p > 0.05) and hence the differences due to energy are small. (nine patients is too small group to conclude statistical significance)

**LPBM**

IMRT plans showed superior sparing of LPBM at high doses (Fig. 2d). p-values of < 0.005 for $V_{30}$, $V_{40}$, $V_{45}$ and mean dose shows the statistical significance (except for IMRT plan comparison). Between the IMRT plans, the differences are small for all volumetric parameters (p > 0.031).

**Bladder, Rectum and UT**

The mean ± SD value of bladder volume is 251.39 ± 176.27 cm$^3$ (Table 1). Not much difference (p values are not significant) was observed for bladder in the conventional techniques (2F versus 4FB). This is not consistent with the results reported by Mell et al (22) in which V30 and V40 were 97.8% and 89.8% in 4FB against 100% for 2F and could be due to large bladder volumes and subsequent anterior sparing. However, bladder volume was not reported.

At low dose levels ($V_5$, $V_{10}$, $V_{15}$ and $V_{20}$), statistical insignificance was observed between different techniques for rectum (p = NS). However, the rectal mean doses with 2F, 4FB, 6MV and 15MV-IMRT techniques were 49.136 Gy, 46.007 Gy, 42.717 Gy and 42.246 Gy respectively.

IMRT plans reduced bladder and rectal high doses volumes ($V_{30}$, $V_{40}$ and $V_{46}$) when compared with 2F and 4F techniques. The bladder and rectal volumes receiving 40Gy or more ($V_{40}$) were 84.678% and 80.366% respectively in 6MV-IMRT when compared with 2F and 4F plans (all values are 100.00%). The V46 of the rectum was 54.991% using 6MV-IMRT, a reduction of 45.009% and 40.587% from that using the 2F and 4FB plans respectively.

For both rectum and bladder, differences were small for all parameters between low and high energy IMRT plans (p > 0.05).

The mean doses of UT (body minus delineated organs) are 8.052 Gy, 8.170 Gy, 7.368 Gy and 6.970 Gy for 2F, 4FB, 6MV and 15MV-IMRT plans.

**Discussion**

The purpose of this study was to evaluate the impact of IMRT on bone marrow doses when compared with conventional techniques. Several lines of evidence are available for acute hematologic toxicity and possible causes in women with gynecologic malignancies who underwent concurrent chemoradiation treatments. High radiosensitivity of hematopoietic stem cells is well documented in multiple in vitro and in vivo animal studies (6). Up to 50% of patients BM is distributed within the os coxae, proximal femora, sacrum and lower lumbar spine and is usually encompassed by conventional pelvic treatment fields (23) and damage to hematopoietic stem cells could be significant contributor to
myelosuppression and low peripheral blood cell counts (24). The potential of radiation to induce acute and chronic pathologic and radiographic changes to BM at low doses are well documented (25, 26) and the level of damage is dependent on both dose and volume (27, 28).

It is found in this study that the IMRT plans and 2F resulted in large reductions in the volume of IBM irradiated when compared with 4FB. This may be attributed to sculpturing of dose in IMRT and sharp fall-off beyond the field edge in 2F plans. It was also found that IMRT plans reduced LSBM doses at all dose levels. IMRT also considerably reduced LPBM doses only at higher doses. Since large dose reductions are seen in IBM, this could well be the significant contributor for reduction in acute HT. These results are consistent with the findings of Brixey et al (5) and Mell et al (22). Lujan et al (29) have analyzed the IBM as a individual organ and they found that at 30 Gy level, average volume of BM irradiated was 38% using bone marrow sparing IMRT compared with 54.9% and 52.9% for conventional and normal-IMRT plans. Hence in the present study, IBM, LSBM and LPBM were delineated as individual organs and optimizer constraints were used for IMRT plans thus widening the scope for optimizer to handle the IBM effectively.

The doses to BM can be further reduced by some conventional approaches like reducing CTV-PTV margin etc. However, considering the significant uncertainties associated with inter- and intrafractional motions in the pelvic region, it is not safe to follow such approaches. Image guidance could well allow some reduction in planning margins. Rather the use of potentially more promising method like intensity-modulated proton therapy (IMPT) may be a good solution to reduce the low doses to BM (30).

To achieve meaningful reductions in HT, some issues must be addressed. Delineation of bone marrow is an approximation as the entire bony landmarks are usually contoured. Also BM is not uniformly distributed throughout the pelvis. Functional imaging modalities like magnetic resonance imaging (MRI), SPECT-CT and PET could be useful for delineating BM by fusing them with primary CT datasets.

Concurrent chemoradiation has become a standard regimen for cervical patients and has led to increased tumor control at the expense of increased toxicity. The potential or predicted advantages of IMRT are still unclear from HT perspective. There is a definite reduction of high dose in bone marrow sparing IMRT but the reduction at low dose is modest. Also many trials have used 4FB technique and not IMRT. The reported acute HT with whole pelvis RT and concurrent chemotherapy in cervical cancer trials has been variable, with acute Grade 3 or greater HT ≥ 35% in some studies (31). Others (32) have reported much lower values.

Such reductions in IMRT plans could well augment the tolerance of bladder and rectum during intracavitary brachytherapy applications.

Normal tissue irradiation (Unspecified tissue, UT) was reduced in IMRT plans because of multiple beams which disperse the treatment load in eight fields but increased the volume of normal tissue irradiated to low doses.

Another finding of this study is that the differences due to energy are small in IMRT plans. The p-values in the last column of (Table 3) clearly show that there is no statistical significance observed between 6MV and 15MV-IMRT plans. The neutron contamination at photon energies greater than 10 MV is well-known. Thus this work augments the present practice of using low energy photons for IMRT. These results are consistent with the findings of Sundaram et al (20) and Boer et al (33).

**Conclusion**

This study is retrospective and dosimetric in nature and hence suffers from inherent limitations in that approach. There was no follow-up (as IMRT plans were created retrospectively) and clinical differences because of BM sparing were not quantified. However, IMRT plans can significantly reduce the BM doses and are expected to reduce the HT. Further investigations are necessary to address the aforementioned problems.
There were small differences observed between 6MV and 15MV-IMRT plans for cervical cancer. Because of well-known neutron contaminations in high energy photons, this study recommends using low energy photons for clinical IMRT plans.

**References**


