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FULL PAPER

Simultaneous integrated boost (SIB) of the parametrium and cervix in radiotherapy for uterine cervical carcinoma: a dosimetric study using a new alternative approach

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Objective: To compare the dose distributions of intensity-modulated radiotherapy (IMRT) and volumetric-modulated arc therapy (VMAT) using the simultaneous integrated boost (SIB) technique with that of the traditional midline block (MB) technique for boosting the parametrium in patients with cervical cancer.

Methods: Treatment plans using VMAT or IMRT with the SIB technique (VMAT-SIB and IMRT-SIB) and IMRT followed by the MB technique (IMRT-MB) were generated for each of the 10 patients with cervical cancer. For the SIB plans, 45-Gy and 50-Gy dose levels in 25 equal fractions were set for the pelvic planning target volume 45 (PTV₄₅) and the parametrial boost volume (PTV₅₀), respectively. For the IMRT-MB plans, the parametrium was sequentially boosted with the MB technique (5.4 Gy in three fractions) after pelvic IMRT (PTV₄₅).

Results: Volume receiving 100% of the prescribed dose or more coverage of the PTV₅₀ was significantly better for

VMAT-SIB and IMRT-SIB than that for IMRT-MB (99.08 and 99.31% compared with 91.79%, respectively; $p < 0.05$). VMAT-SIB and IMRT-SIB both generated significantly greater doses to the organs at risk (OARs) except for the volume receiving 50 Gy or more doses, which were significantly lower for the bladder and bowel. Comparable results were achieved with VMAT-SIB and IMRT-SIB.

Conclusion: The VMAT-SIB and IMRT-SIB techniques are promising in terms of dose distributions and tumour coverage, although these approaches might result in slightly higher doses of radiation to the OARs.

Advances in knowledge: This is the first study to examine the feasibility of the SIB technique using IMRT or VMAT to boost the parametrium. The techniques dosimetrically produced better target coverage but resulted in slightly higher doses to the OARs.

INTRODUCTION

Anatomically, the parametrium is a fibrous tissue of the supravaginal portion of the uterine cervix. It separates in front from the bladder and extends laterally on between the layers of the broad ligament.¹ During uterine cervix carcinoma progression, the parametrium is usually the first, and sometimes the only, site of extracervical tumour invasion. It is thus at greater risk of harbouring subclinical disease and unrecognized gross tumours than any other pelvic structure. For these reasons, the cervix and parametrium should be examined together and considered integral structures.

Pelvic external beam radiotherapy (EBRT) followed by parametrial boost with midline block (MB) and intracavitary brachytherapy (ICBT) have long been a standard treatment for advanced cervical cancer. Over the past two

decades, EBRT has evolved into intensity-modulated radiotherapy (IMRT), and image-guided intracavitary brachytherapy (IGBT) is the main competitor of the conventional Point A-based Manchester system. These changes might have contributed to improved dose distribution, decreased toxicity and better local control.²⁻⁴ However, to date, the use of an MB or a stepping wedge through two-dimensional anteroposterior/posteroanterior parallel-opposed ports remains a common clinical practice for the parametrium boost. According to a survey by the Gynecologic Oncology Group from 56 affiliated institutions, 76% of participants used an MB, 21% participants used customized blocks and 3% participants used a stepping wedge.⁵ The boost was delivered without full knowledge of the parametrium anatomy. This practice might yield an unpredictable dose distribution to the tumour and the

adjacent organs at risk (OARs), as recently reported by Fenkell *et al*.⁶

Simultaneous integrated boost (SIB), which is occasionally known as “dose painting”, is a new radiotherapy strategy that allows for the simultaneous delivery of different dose levels to the target volumes. Recent studies have demonstrated that this technique produces improved dose distribution and offers radiobiological advantages,^{7,8} and clinical applications to head and neck cancers,⁹ breast cancers¹⁰ and high-grade gliomas,¹¹ among others, have been reported with satisfying results.

Currently, studies of volumetric-modulated arc therapy (VMAT) or IMRT using the SIB technique (VMAT-SIB or IMRT-SIB) to boost the entirety of the parametrial tissue are not available. Given this background, we completed this study to compare the dose distributions of IMRT-SIB with those of the traditional MB technique and test the clinical feasibilities of VMAT and IMRT-SIB.

METHODS AND MATERIALS

Patient selection

10 patients with cervical cancer treated with definitive concurrent chemoradiotherapy at our institution between March and December 2014 were selected. The median age was 55.5 years (range, 48–76 years). All of the patients had intact uterus with International Federation of Gynecology and Obstetrics (2010 edition) stage, IIB stage in nine patients and IB2 stage in one patient.

Planning objectives

CT images of all of the patients were obtained by using our CT simulator (LightSpeed RT16; GE Medical System, Milwaukee, WI) with a 5-mm slice thickness. The simulation was performed in the supine position. Patient contours were delineated by a single physician to minimize interpersonal variation.

Three treatment plans, *i.e.* VMAT-SIB, IMRT-SIB and IMRT-MB, were generated for each patient. The VMAT-SIB and IMRT-SIB plans consisted of two dose levels administered by means of simultaneously integrated boosts delivered in 25 equal fractions. A 45-Gy dose level was set for the pelvis planning target volume (PTV₄₅) and a 50 Gy level was set for the parametrial boost volume (PTV₅₀). In the IMRT-MB plan, the parametrium was sequentially boosted with the MB technique (5.4 Gy in three fractions) after pelvic IMRT (PTV₄₅).

The OARs, including the bladder, rectum, bowel, femoral heads and bone marrow, were identified on individual CT slices. The bone marrow was delineated according to Mell *et al*¹² method, in which the ilium, lower pelvis and lumbosacral spine are used as surrogates for the bone marrow. The clinical target volume (CTV) and PTV margins are listed in Table 1. The CTV-primary, CTV-nodal and CTV-parametrium were determined according to the Radiation Therapy Oncology Group (RTOG) guidelines,^{13,14} whereas the posterior margin of the CTV-parametrium was adjusted according to the Japan Clinical Oncology Group (JCOG) guidelines¹⁵ to provide stage-specific schemes. Briefly, the anterior border of the CTV-parametrium was defined as the posterior bladder wall or the posterior border of the external iliac vessel; the lateral border was the medial edge of the internal obturator muscle or the ischial

ramus bilaterally; the cranial border was the top of the fallopian tube or broad ligament; and the caudal border was the urogenital diaphragm. The rectum was not included in the posterior border of the CTV-parametrium. For Stage IB2 disease, the anterior portion of the mesorectal fascia was included. For Stage IIB or greater disease, the border was further extended along the uterosacral ligaments depending on the involvement of the disease.

We presumed that the 10-mm margin area of the CTV-primary would be optimally covered by ICBT. Therefore, CTV for the parametrium boost (CTV-PM boost) was defined as CTV-parametrium excluding CTV-primary with a 10-mm margin. The PTV margins varied for different CTVs (15 mm for PTV-primary, 7 mm for CTV-nodal and 10 mm for CTV-parametrium).¹⁶ These three PTVs were then merged to form PTV₄₅, and PTV₅₀ was defined as a PTV-PM boost with a 10-mm margin. The dose constraints used in this study are listed in Table 2. The constraints for the bladder and rectum were tighter than those given in the Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC). QUANTEC indicates a volume receiving 50 Gy or more (V_{50}) of <50% for the rectum and a V_{65} of <50% for the bladder. Most of the information mentioned in QUANTEC is related to prostate cancer radiotherapy. We have individualized the constraints and attempted to make them tighter for our study of patients with cervical cancer.

A 4-cm MB was used for the midline-blocked technique. With the anteroposterior/posteroanterior parallel-opposed ports, the superior margin was the inferior aspect of the sacroiliac joints, the lower margin was the lower border of the obturator foramen and the lateral margin was 1 cm beyond the widest part of the pelvic brim.

Treatment planning

Three sets of plans (VMAT-SIB, IMRT-SIB and IMRT-MB) were generated with Pinnacle3[®] treatment planning system (TPS) (v. 9.2, Philips, Fitchburg, WI, USA) and then compared. The VMAT-SIB plans were composed of two coplanar arcs of 360° and delivered with opposite rotations. Co-planar seven-field IMRT was designed for the IMRT-SIB plans and the pelvic IMRT portion (CTV₄₅) of the IMRT-MB plans. Seven gantry angles of 0°, 50°, 100°, 150°, 210°, 260° and 310° were used with the couch angle set to 0°. The MB technique was performed using the multileaf collimator. The VMAT and IMRT plans were normalized to cover ≥99% of the PTV with 90% of the prescription dose and ≥95% of the PTV with 100% of the prescription dose. All sets of plans were created using the same 10-MV photon beams from a Varian Clinac[®] (Palo Alto, CA, USA) iX linear accelerator equipped with a 60-leaf multileaf collimator (0.5-cm leaf in the central 20 cm of the field and a 1-cm leaf in the outer 20 cm of the field).

Statistical analysis

We used the Paddick conformity index (CI)¹⁷ to evaluate the conformity of the PTV coverage to the prescription isodose volume for the two sets of plans. The CI was calculated using the

equation: $CI = \frac{TV_{PV}^2}{V_{PTV} \times V_{TV}}$, in which V_{PTV} is the volume of PTV, V_{TV} is the volume covered by the prescription dose and TV_{PV} is the volume of V_{PTV} within V_{TV} . A larger CI value indicated better conformity.

Table 1. Clinical target volume (CTV) components and planning target volume (PTV) margins

CTV	CTV components	PTV margins (mm)
CTV-primary	GTV, entire cervix, entire uterus and vagina ^a	15 ^b
CTV-nodal	Common iliac, external iliac, internal iliac, presacral and obturator lymph nodes	7 ^b
CTV-parametrium	Parametrium	10 ^b
CTV-PM boost	(CTV-parametrium) – (CTV-primary + 1-cm margin)	10 ^c

GTV, gross tumour volume.

^aUpper half of the vagina for the minimal or no vaginal extension, upper two-thirds of the vagina for upper vaginal involvement and entire vagina for extensive vaginal involvement.

^bThe PTV-primary, PTV-nodal and PTV-parametrium were merged to generate the PTV₄₅ for which 45 Gy in 25 fractions was prescribed.

^cPTV-PM boost = PTV₅₀, for which 50 Gy in 25 fractions was prescribed and delivered using simultaneous integrated boost.

CI and dose–volume histograms (DVHs) for the PTVs and OARs were compared for all of the three plans. Repeated-measures analysis of variance was used, and the Bonferroni correction was chosen for the *post hoc* pairwise comparisons. The differences were considered statistically significant at $p < 0.05$.

RESULTS

The axial and coronal dose distributions of the three techniques in one representative case are shown in Figure 1. The average DVHs of the PTVs between the three techniques are presented in Figure 2a,b, and the average DVHs of the OARs including the rectum, bladder, bowel, femoral heads and bone marrow are shown in Figure 2c–h. Table 3 summarizes the comparisons of the CI and numerical findings from DVH analysis on the PTV and OARs.

Dose distribution for planning target volumes

As shown in Table 3, the average coverage for the volume receiving 100% of the prescribed dose or more of PTV₅₀ was significantly better for VMAT-SIB and IMRT-SIB than that for IMRT-MB (99.08% and 99.31% compared with 91.79%, respectively; $p < 0.05$), and the volume for PTV₅₀ receiving 110% of the prescribed dose or more) was less for VMAT-SIB and IMRT-SIB than that for IMRT-MB (0.02% and 0%

compared with 1.51%, respectively; $p = 0.008$). The average coverage for volume receiving 100% of the prescribed dose or more of the PTV₄₅ was significantly better for VMAT-SIB than that for IMRT-SIB, although the difference was subtle (98.90% compared with 98.53%; $p < 0.001$). The DVHs are shown in Figure 2a,b. Regarding the PTV conformity to the prescription isodose volume, the CI values for both PTV₄₅ (CI indicates for the PTV₄₅) and PTV₅₀ [CI indicates for the PTV₅₀ (CI₅₀)] were compared. The VMAT-SIB and IMRT-SIB produced better results in the CI₅₀ (0.680 and 0.687 compared with 0.344, respectively; $p < 0.001$), whereas no significant difference was noted in the CI indicates for the PTV₄₅. The main factor contributing to this difference in the CI₅₀ was the significantly larger treatment volume (V_{TV}) for the IMRT-MB than that for the two SIB plans (651.47 ml compared with 389.17 and 385.01 ml for VMAT-SIB and IMRT-SIB, respectively).

Organs at risk

The constraints were met for all of the OARs except for the bone marrow. The average volume receiving 10 Gy or more (V_{10}) was 93.18, 94.65 and 94.39% for VMAT-SIB, IMRT-SIB and IMRT-MB, respectively, and the average volume receiving 20 Gy or more (V_{20}) was 75.79, 76.00 and 75.99%, respectively. All of the values were higher than the preset constraints of $V_{10} < 90\%$ and $V_{20} < 75\%$.

Compared with IMRT-MB, the VMAT-SIB technique significantly increased the volume receiving 40 Gy or more (V_{40}) for the rectum, the volume receiving 30 Gy or more (V_{30}) and V_{40} for the bone marrow, the V_{20} for the right femoral head and the V_{40} for the left femoral head. Regarding the bladder, the V_{30} and V_{40} were increased, whereas the V_{50} was decreased. For the bowels, the V_{10} , V_{30} and V_{40} were increased, whereas the V_{20} and V_{50} were decreased. Detailed numerical findings and p -values are listed in Table 3.

Compared with IMRT-MB, the IMRT-SIB technique significantly increased the V_{40} for the rectum, and the V_{30} and V_{40} for the bone marrow, bilateral femoral heads, bladder and bowels. The V_{50} was decreased for the bladder and the bowels.

The differences between the two SIB plans were subtle. The VMAT-SIB technique significantly lowered the V_{10} for the bilateral femoral heads (76.13% compared with 86.92% for

Table 2. Dose constraints to the organs at risk

Organ	Constraints
Rectum ^a	$V_{50} < 35\%$
Bladder ^a	$V_{50} < 50\%$
Bowel ^b	$V_{45} \leq 250$ cc and maximum $< 115\%$
Bone marrow ^c	$V_{10} < 90\%$ and $V_{20} < 75\%$
Femoral head ^d	$V_{50} < 5\%$

^aModified from Quantitative Analysis of Normal Tissue Effects in the Clinic. The values were individualized to be tighter for our patients in the study with cervical cancer.

^bContoured as a bowel bag (based on the entire potential space within the peritoneal cavity). Bowel loops posterior to the uterus in the lower pelvis within the planning target volume were excluded (according to the constraint used at the University of California, San Diego).³⁷

^cFollowed by Mell et al¹² method and constraints. The ilium, lower pelvis and lumbosacral spine were used as surrogates for bone marrow.

^dAccording to the Radiation Therapy Oncology Group Genitourinary (GU) consensus.³⁶

Figure 1. An actual plan (axial CT slices) for a patient with International Federation of Gynecology and Obstetrics Stage IIB cervical cancer: the three techniques are indicated. (a), (d), and (g) for IMRT-MB plan; (b), (e), and (h) for IMRT-SIB plan; (c), (f), and (i) for VMAT-SIB plan. The solid red line (thick arrow) is representing the isodose line for the 100% prescribed dose of the parametrial boost and the solid green line (thin arrow) is representing the isodose line for 45 Gy. PTV 45 is shown in the colour-washed green area (hollow triangle), and PTV 50 is shown in the colour-washed red area (solid triangle). The black asterisks (d) and (g) are indicating areas where the intensity-modulated radiotherapy (IMRT)-midline block (MB) plan failed to provide optimal coverage. SIB, simultaneous integrated boost.

IMRT-MB

IMRT-SIB

VMAT-SIB

the left, $p = 0.001$; and 72.43% compared with 86.19% for the right, $p < 0.001$). Detailed numerical findings and p -values are listed in Table 3.

DISCUSSION

Traditionally, the parametrial boost has been used to treat gross or subclinical diseases at or near the pelvic side wall that would not be optimally covered by Point-A-based IGBT. This approach compensated for the fall-off dose distant to the central cervix. In recent years, the use of IGBT has emerged, and the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) guidelines^{18,19} have recommended this strategy as the standard of care for IGBT. The guidelines introduced the concept of high-risk CTV, which indicates areas of residual macroscopic disease. In the era of IGBT,

several solutions to compensate for the distal fall-off have been proposed, including the addition of interstitial needles to IGBT^{20–22} or concomitant external IMRT/IGBT boost.^{23,24} For these reasons, Lindegaard and Tanderup²⁵ suggested parametrial boost retirement. According to the survey from Gynecologic Cancer Intergroup in 2009, however, 78% of the selected Gynecologic Cancer Intergroup members in Japan, Korea, Australia, New Zealand, Europe and North America still prescribe doses for Point A,²⁶ and it is possible that the percentage would be higher if underdeveloped countries were taken into account.

Although solutions using additional interstitial implants with IGBT or concomitant external IMRT/IGBT boost are possible, these approaches are largely invasive and time-consuming, which might not be practical for patients who are senile or those

Figure 2. (a, b) The average dose-volume histogram (DVH) for the planned target volumes (PTV₄₅ and PTV₅₀) comparing volumetric-modulated arc therapy (VMAT)-simultaneous integrated boost (SIB), intensity-modulated radiotherapy (IMRT)-SIB and IMRT-midline block (MB), and (c-h) the average DVHs for organs at risk.

Table 3. Dose-volume comparisons of the planning target volumes (PTVs) and organs at risk

Parameter	IMRT-MB ^a	IMRT-SIB ^a	VMAT-SIB ^a	<i>p</i> -value ^b
PTV ₄₅				
V _{100%}	98.70 ± 0.16	98.53 ± 0.21	98.90 ± 0.20 ^c	<0.001 ^d
PTV ₅₀				
V _{100%}	91.79 ± 1.23	99.31 ± 0.18 ^e	99.08 ± 0.28 ^f	<0.001 ^d
V _{110%}	1.51 ± 0.38	0.00 ± 0.00 ^e	0.02 ± 0.21 ^f	0.003 ^d
Rectum				
V ₁₀	99.47 ± 0.41	99.49 ± 0.41	99.59 ± 0.41	0.334
V ₂₀	98.42 ± 0.72	98.68 ± 0.62	98.79 ± 0.68	0.240
V ₃₀	96.08 ± 1.29	97.78 ± 0.86	97.93 ± 0.80	0.042 ^d
V ₄₀	75.10 ± 3.79	89.27 ± 1.37 ^e	88.62 ± 1.66 ^f	<0.001 ^d
V ₅₀	6.85 ± 1.91	7.14 ± 1.35	6.97 ± 1.52	0.948
Bladder				
V ₁₀	100.00 ± 0.00	100.00 ± 0.00	100.00 ± 0.00	1.000
V ₂₀	99.82 ± 0.18	100.00 ± 0.00	100.00 ± 0.00	0.387
V ₃₀	89.99 ± 2.28	99.46 ± 0.33 ^e	98.87 ± 0.66 ^f	0.001 ^d
V ₄₀	65.83 ± 3.73	74.53 ± 3.00 ^e	74.55 ± 3.33 ^f	<0.001 ^d
V ₅₀	17.18 ± 3.39	7.31 ± 1.68 ^e	8.35 ± 1.87 ^f	0.002 ^d
Femoral head (left)				
V ₁₀	82.85 ± 4.85	86.92 ± 2.28	76.13 ± 1.61 ^c	0.039 ^d
V ₂₀	34.31 ± 1.45	36.40 ± 1.53	38.31 ± 2.01	0.097
V ₃₀	20.27 ± 1.48	24.95 ± 1.61 ^e	22.47 ± 1.63	0.006 ^d
V ₄₀	7.13 ± 1.10	11.16 ± 1.13 ^e	10.08 ± 1.17 ^f	<0.001 ^d
V ₅₀	0.28 ± 0.11	1.33 ± 0.38	0.73 ± 0.25	0.022 ^d
Femoral head (right)				
V ₁₀	84.06 ± 4.31	86.19 ± 2.24	72.43 ± 1.32 ^c	0.005 ^d
V ₂₀	35.05 ± 1.66	37.31 ± 1.81	37.40 ± 1.87 ^f	0.033 ^d
V ₃₀	20.85 ± 1.72	24.39 ± 1.89 ^e	23.43 ± 1.88	0.008 ^d
V ₄₀	07.83 ± 1.02	11.08 ± 1.03 ^e	10.23 ± 1.28	0.003 ^d
V ₅₀	0.26 ± 0.15	0.99 ± 0.38	0.39 ± 0.20	0.159
Bone marrow				
V ₁₀	94.40 ± 0.84	95.13 ± 0.43	93.18 ± 0.43	0.072
V ₂₀	75.99 ± 0.39	76.00 ± 0.46	75.79 ± 0.45	0.803
V ₃₀	61.04 ± 0.68	62.27 ± 0.64 ^e	63.09 ± 0.69 ^f	<0.001 ^d
V ₄₀	39.07 ± 1.12	41.74 ± 1.27 ^e	43.11 ± 1.16 ^f	<0.001 ^d
V ₅₀	6.17 ± 0.29	6.23 ± 0.67	5.21 ± 0.42	0.240
Bowel ^g				
V ₁₀	1152.99 ± 181.54	1158.02 ± 182.90	1178.23 ± 189.36 ^{c,f}	0.012 ^d
V ₂₀	918.18 ± 121.70	917.84 ± 122.21	887.82 ± 119.86 ^{c,f}	0.006 ^d
V ₃₀	609.16 ± 63.54	641.89 ± 68.76 ^e	654.81 ± 73.80 ^f	0.001 ^d
V ₄₀	277.01 ± 25.67	366.58 ± 34.90 ^e	368.24 ± 31.11 ^f	<0.001 ^d

(Continued)

Table 3. (Continued)

Parameter	IMRT-MB ^a	IMRT-SIB ^a	VMAT-SIB ^a	<i>p</i> -value ^b
V ₅₀	27.88 ± 4.07	0.26 ± 0.13 ^c	0.39 ± 0.24 ^f	<0.001 ^d
CI				
CI ₄₅	0.735 ± 0.008	0.740 ± 0.010	0.736 ± 0.010	0.794
CI ₅₀	0.344 ± 0.029	0.687 ± 0.022 ^e	0.680 ± 0.019 ^f	<0.001 ^d

CI₄₅ and CI₅₀, conformity index indicates for the PTV₄₅ and PTV₅₀; CI, conformity index; IMRT, intensity-modulated radiotherapy; MB, midline block; SIB, simultaneous integrated boost; V₁₀, V₂₀, V₃₀, V₄₀ and V₅₀, volumes receiving 10, 20, 30, 40 and 50 Gy or more; V_{100%} and V_{110%}, volumes receiving 100% and 110% of the prescribed dose or more.

^aMean volume [% ± standard error (SE)].

^bRepeated-measures analysis of variance was used, and *post hoc* analyses with the Bonferroni correction were completed.

^cStatistically significant difference in the comparison of VMAT-SIB and IMRT-SIB.

^dStatistically significant difference between the three groups.

^eStatistically significant difference in the comparison of IMRT-SIB and IMRT-MB.

^fStatistically significant difference in the comparison of VMAT-SIB and IMRT-MB.

^gAbsolute volume (cubic centimetre ± SE).

with significant comorbidities. In addition, the extra cost of high technical facilities such as an MR simulator might not be economically feasible in many institutions in underdeveloped countries with high cervical cancer prevalence.

The potential advantages of the SIB technique are understandable. It is a simple extension of the existing external beam technique. Its delivery saves time and is known to be safe when applied to other cancer sites.^{9–11} Treatment of both the parametrium and the central cervix can be completed using external beam therapy on the same day, leading to a shortening of overall treatment time by 3–5 days or more. This therapy is radiobiologically advantageous in terms of local tumour control.^{27,28}

There are some reports on the use of the SIB technique to boost cervical primary tumours or gross lymph nodes. Lindegaard et al²⁹ compared the results from the Nordic Cervical Cancer (NOCECA) study (*i.e.* NOCECA cohort) with those of an image-guided adaptive brachytherapy (IGABT) cohort and found that IGABT improved the overall survival and reduced the morbidity. In the NOCECA cohort, whole-pelvic three-dimensional conformal EBRT with SIB *via* lateral fields to the primary tumour and uterus was used and followed by ICBT. In the IGABT cohort, VMAT or IMRT were used for EBRT, followed by IGABT, and only pathological nodes were boosted. Although the SIB technique was utilized in both cohorts, it was not meant to boost the parametrium (PM). Vandecasteele et al³⁰ reported an experience of the application of VMAT with SIB to the macroscopic tumours of irresectable cervical cancer. The SIB in this study was also not meant to boost the PM. Marnitz et al³¹ presented a report of the use of helical tomotherapy with the SIB technique to boost the PM and clearly demonstrated that the technique is feasible and associated with a low rate of acute toxicities. Based on successful results from the helical tomotherapy experience, our study sought to investigate the possibility of using the more affordable IMRT or VMAT techniques to achieve comparable results.

In this study, we mostly followed the RTOG guideline for contouring of the parametrium. To date, two consensus-based guidelines (the RTOG and JCOG guidelines) and one single institutional guideline (the Postgraduate Institute guideline) are

available to delineate CTVs for intact cervical carcinomas.^{14,15,32}

There are small differences in these systems for parametrium contouring. The main differences are noted for the definitions of cranial and posterior borders between the systems and are summarized in Table 4.

The RTOG system remains the most commonly used system worldwide. We adopted, in part, the JCOG guidelines to contour the posterior border of the parametrium. The JCOG guideline was stage-specific for the posterior margin of the parametrium and preserved more rectum in advanced cases, although the patients in our study did not present with advanced disease. This approach agreed with our departmental policy to decrease rectal complications and personalize treatment plans. Therefore, we felt comfortable and justified in the use of the hybrid RTOG and JCOG system.

Reported doses for parametrial boost in the literature using the midline-blocked technique varied considerably, ranging from 5.4 to 20 Gy,²⁶ and the optimal doses for parametrial boost remained undefined. Interestingly, Rajasooriyar et al³³ treated 193 positron emission tomography-staged cases to whole pelvis 40 Gy without a parametrial boost and found that pelvis relapse rates were similar in early and advanced cases, suggesting that 40 Gy is adequate for the parametrium.

In this study, we prescribed 45 Gy for the central cervix and pelvic lymphatics and 50 Gy for the parametrium. These doses were delivered in 1.8- and 2-Gy daily treatments, respectively. The patients in our study were mainly International Federation of Gynecology and Obstetrics Stage IIB cases with no lymph node involvement. However, in cases with gross lymph nodes or more advanced diseases with invasion into the pelvic sidewall, dose escalation is somehow necessary. Vargo et al³⁴ demonstrated that a dose of 55 Gy in 25 fractions (2.2 Gy daily) was effective at eradicating disease in involved nodes, and previous work by Huang et al³⁵ demonstrated that parametrium dose of 54 Gy or higher is predictive of enterocolitis and proctitis. We generally agreed with Rajasooriyar et al's view that an exceedingly high dose to the parametrium is not necessary. Currently, escalation of the parametrial boost to >2 Gy daily (2.1–2.2 Gy) is not used in our daily practice unless the node is positive.

Table 4. Main differences in delineation of the parametrium clinical target volume between the three guidelines

Characteristic	RTOG	JCOG	Postgraduate Institute of Medical Education & Research (PGIMER)
Country or institution	USA	Japan	India PGIMER
Authors	Lim et al ¹⁴	Toita et al ¹⁵	Bansal et al ³²
Year	2011	2011	2013
Cranial boundary	Top of fallopian tube/broad ligament	Isthmus of uterus ^a	Where the true pelvis begins
Posterior boundary for IB2, IIA2 and IIB diseases	Uterosacral ligament and mesorectal fascia	Extend into the anterior perirectum	Mesorectal fascia
Relationship between the rectum and the posterior boundary for advanced-staged diseases ^b	Entire mesorectum should be included	The rectum is not included	Entire mesorectum should be included

RTOG, Radiation Therapy Oncology Group.

^aLevel at which the uterine artery drains into.

^bIIB or greater disease, those with extensive nodal involvement and those with uterosacral ligament involvement.

The results of our study indicated that both VMAT-SIB and IMRT-SIB provided improved coverage of the parametrium. This benefit is at the slight cost of a higher middle-dose volume (V_{20-40}) to OARs. Some factors might contribute to this result. First, the main areas where the IMRT-MB plans failed to provide optimal coverage were close to the CTV-primary (black asterisks in Figure 1). The bladder and rectum were close to this area and would inevitably receive higher doses if the area were well covered. Although the bladder and bowel received higher volumes from V_{30-40} when using the SIB technique, the volume was lower for V_{50} . These findings, together with a better CI, indicate that the VMAT-SIB and IMRT-SIB plans are likely more reliable and result in more predictable dose distributions. Therefore, fewer risks would be taken with this approach, as there would be fewer high-dose regions (dose >50 Gy) within the OARs, especially the bladder and bowel. It is difficult to predict where the dose is delivered when using the MB technique, leading to underdosing of the clinical target. Moreover, despite the fact that the treatment volume was much larger for IMRT-MB than that

for SIB plans, the overtreated areas were mostly spread in the treatment field of the obturator or the iliac lymph nodes and were not reflected in the DVHs of OARs.

Patients who needed treatment with extended field radiotherapy to cover para-aortic lymph nodes were beyond the scope of our investigation. The dose and method of ICBT were also not considered in our study.

CONCLUSION

We conducted a comparative dosimetric study to investigate the feasibilities of the VMAT-SIB and the IMRT-SIB techniques for boosting the parametrium in radiotherapy for uterine cervix carcinoma. This study revealed that both SIB techniques are promising in terms of dose distribution and tumour coverage. It is possible the SIB technique may be used as an alternative approach to radiotherapy for cervical cancer, although the use of this technique might come at the cost of slightly higher radiation doses to the OARs.

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