

The Benefit of Small Bowel and Pelvic Bone Sparing in Excluding Common Iliac Lymph Node Region from Conventional Radiation Fields in Patients with Uterine Cervical Cancer: A Dosimetric Study

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Uterine cervical cancer/Radiotherapy/Small bowel/Pelvic insufficiency fracture/Common iliac lymph node region.

The purpose of this study was to compare dose reduction to the small bowel and sacral bone by two-field and four-field techniques when the common iliac lymph node region is excluded from the radiation field in external beam radiotherapy of uterine cervical cancer. Thirteen patients with cervical cancer were entered into the study. Conventional treatment plans based on bony landmarks were made with parallel-opposed two-field technique (C2F) and four-field box technique (C4F). Modified C2F (M2F) and C4F (M4F) plans of excluding the common iliac lymph node region from the conventional radiation fields were created in reference to the bifurcations of pelvic arteries in computed tomography images. For each patient, the dose volume histograms for the small bowel and sacral bone resulting from the C2F, C4F, M2F, and M4F plans were compared. The volumes were obtained at 10 levels of prescribed dose, at increments of 10%, from 5 Gy to 50 Gy. By sparing both small bowel and sacral bone, the M2F and M4F plans were significantly better than the C2F and C4F plans at any dose level ($p < 0.05$), respectively. In addition, the M4F plan was significantly better than the M2F plan in sparing both small bowel at 10–50% of the prescribed dose ($p < 0.05$) and sacral bone at 40–100% of the prescribed dose ($p < 0.05$). The present study suggests that modified treatment planning could be useful for selected patients for reducing small bowel complications and insufficiency fracture after radiotherapy.

INTRODUCTION

Radiotherapy has an essential role in the treatment of uterine cervical cancer. Early-stage disease is highly curable by radiotherapy alone. Concurrent chemoradiotherapy improves overall survival for locally advanced cervical cancer in comparison with radiotherapy alone.^{1–6} Radiotherapy for cervical cancer consists of external beam irradiation to the primary tumor and corresponding region of lymphatic drainage, and brachytherapy for the primary tumor.⁷ The external beam component is conventionally delivered by a

two-field or four-field technique.

Small bowel complication is one of the most common side effects in gynecologic patients undergoing radiotherapy. It has been pointed out that high-dose irradiation to the small bowel of the pelvis correlates with severe intestinal complications.^{8–12} Pelvic insufficiency fracture is also a major concern after radiotherapy to the pelvis. Although radiation-induced pelvic insufficiency fracture has been considered to be rare,¹³ several recent reports revealed that it is more common than previously believed.^{14–16} Thus, pelvic bone should be excluded from radiation fields as much as possible.

Efforts for dose reduction to organs at risk (OARs) should be encouraged to achieve lower incidence of late complications without sacrificing local control. In the treatment planning of the two-field and four-field techniques, definition of the superior border of the fields varies among radiotherapy facilities. A survey of the Gynecologic Cancer Intergroup showed that the upper border of the pelvic field for cervical

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cancer was set at L4/L5 in 50% of the facilities, L5/S1 in 12%, and computed tomography (CT)-based planning in 24%.¹⁷⁾ However, the quantitative benefit of a small pelvic field for normal tissue sparing has not been well documented. Recently, treatment planning based on CT has become wide-spread, a method that enables us to define the clinical target volume (CTV) of the pelvic lymph node region more precisely by reference to pelvic vessels.

The purpose of this study was to compare the dose reduction to the small bowel and sacral bone by two-field or four-field technique when the common iliac lymph node region is excluded from the radiation field in external beam radiotherapy of uterine cervical cancer.

MATERIALS AND METHODS

Patient characteristics

Between January and October 2009, 13 consecutive patients with cervical cancer treated with radiotherapy at the Department of Radiation Oncology of Gunma University Graduate School of Medicine were selected for this dosimetric study. The median age of the patients was 63 years (range, 41–82 years). The International Federation of Gynecology and Obstetrics stage was IB in 2 patients, IIB in 7, IIIA or IIIB in 3, and IVA in 1 patient.

Imaging

Each patient underwent a planning CT scan (LightSpeed; GE Healthcare, Buckinghamshire, UK) in supine position with vaginal tampon contrast. CT images with 5-mm slice thickness were taken from the L3–L4 interspace to the perineum. Bladder content was not restricted at the time of CT data acquisition.

Delineation

Contouring was performed by a radiation oncologist. Another radiation oncologist specializing in gynecologic oncology reviewed all delineated regions of interest. All target volumes and OARs were contoured on the axial CT slices of all patients. CTV included the cervical tumor, the whole uterus, parametrium, uterine appendage, upper half of the vagina and regional lymph nodes (common nodes, internal and external iliac nodes, obturator nodes and presacral nodes). The small bowel of the pelvis and sacral bone were contoured as OARs. For the small bowel, individual loops existing below the level of the upper border of L5 vertebra were separately contoured. Common, internal and external iliac vessels were contoured as reference landmarks to identify the pelvic lymph node regions.

Treatment planning

All treatment plans and dose volume histogram (DVH) analysis were done with the treatment planning system XiO, Version 4.34 (CMS, St. Louis, MO, USA). All treatment

plans were based on a 10-MV high-energy photon beam. For each patient, 4 treatment plans were generated as follows.

First, treatment plans based on a conventional parallel-opposed two-field technique (C2F) and four-field box technique (C4F) were made. The definition was based on the commonly used design of standard portals in relation to bony reference landmarks. The borders for the anterior and posterior fields were at the interspace of the L4–L5 vertebrae superiorly, inferior border of the obturator foramen inferiorly, and 1.5–2 cm lateral to the bony pelvis.

For the lateral field, the anterior border was placed 3 cm anterior to the vessel edge and posterior edge of the pubic symphysis. The posterior margin was defined 1.5 cm from the anterior aspect of the sacral bone. Superior and inferior borders were the same as those of the anterior and posterior fields. The width of the lateral fields was maintained at 6 cm at least to ensure coverage of the lymph node regions. The typical radiation fields of the conventional plans are shown in Fig. 1.

Second, modified plans of C2F and C4F were created. The common iliac lymph nodes are adjacent to the common iliac vessels from the aortic bifurcation to the division of the common iliac artery into the external and internal iliac branches.^{18–21)} In the modified C2F (M2F) and C4F (M4F) plans, the common iliac lymph node region was excluded from the conventional radiation fields. In case of different levels of bifurcation of the common iliac artery, the most cranial one was selected as the superior border. Inferior, lateral, anterior and posterior borders were defined just as those of C2F and C4F. The typical radiation fields of the modified plans are shown in Fig. 2.

For each plan, the total dose of 50 Gy in 25 fractions at the isocenter was prescribed. The beams were weighted equally in each portal in all plans. The planning target volume (PTV) had to be covered between 95% and 107% of the prescribed dose in the isocenter plane.

DVH analysis

For the small bowel of the pelvis and sacral bone, the percent volumes irradiated in the C2F, C4F, M2F, and M4F plans were compared. The volumes were obtained at 10 levels of prescribed dose, at increments of 10%, from 5 Gy to 50 Gy.

Statistical analysis

Statistical analysis was performed by StatMateIII Version 3.17 (ATMS, Tokyo, Japan). Paired *t* test was used to compare the different treatment plans. Differences were considered significant at $p < 0.05$.

RESULTS

Example case

The M4F plan for a representative patient is shown in Fig. 3. As seen in the sagittal image of Fig. 3, the volumes of the small bowel and the sacral bone were excluded from the lat-

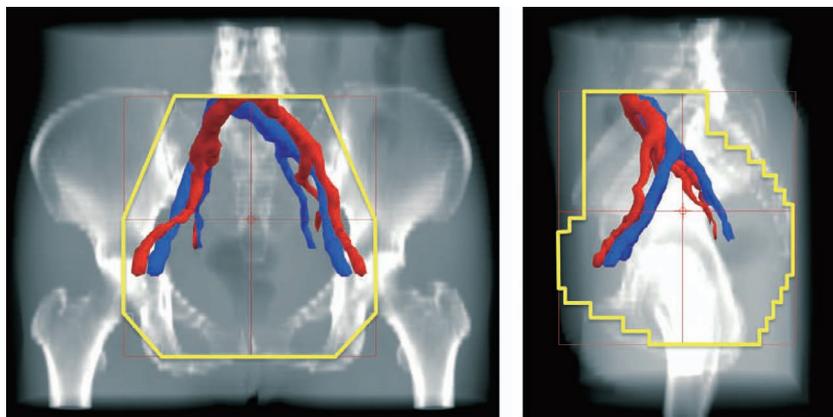


Fig. 1. Ventral and lateral radiation fields of conventional plan. Highlighted yellow lines are the border of the fields. Pelvic (common, internal and external) arteries and veins are illustrated in red and blue, respectively.

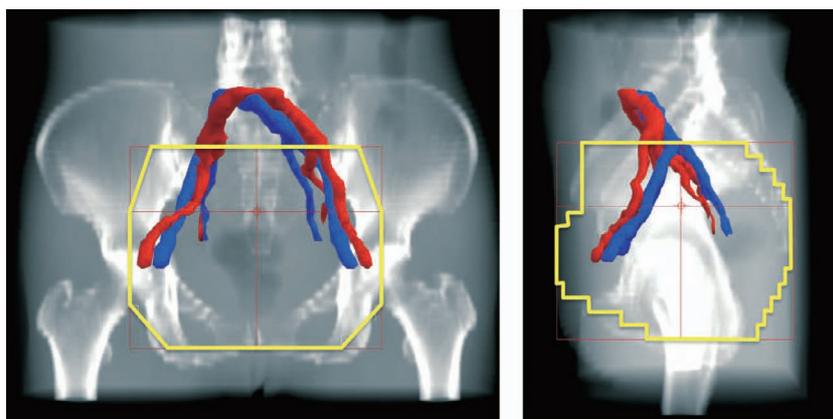


Fig. 2. Ventral and lateral radiation fields of modified plan. Highlighted yellow lines are the border of the fields. Common iliac lymph node region is excluded from the radiation fields. Pelvic (common, internal and external) arteries and veins are illustrated in red and blue, respectively.

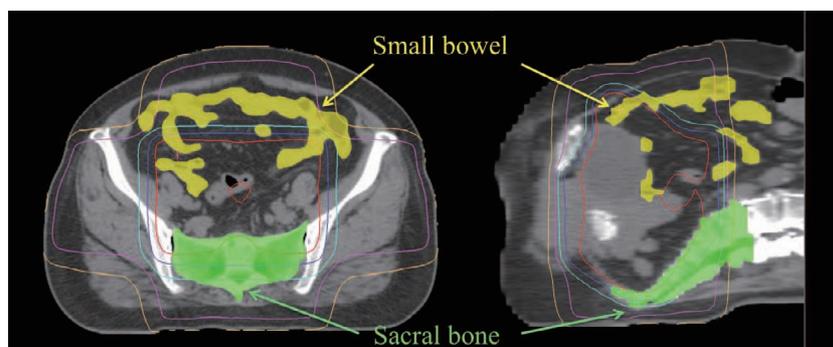


Fig. 3. Axial and sagittal images with isodose distribution in modified four-field plan. Highlighted are the 20% (orange), 50% (magenta), 70% (cyan), 90% (blue), and 100% (red) isodose lines. The small bowel and the sacral bone in these slices are shown in yellow and green, respectively.

eral radiation fields as much as possible. The average field size of 2.8 cm (range, 0.5–4.7 cm) was reduced in the longitudinal direction with the modified plans compared to the conventional plans.

Small bowel

Comparison of small bowel volumes irradiated in a representative patient is shown in Fig. 4. The volumes of the small bowel irradiated by each plan are summarized in Table 1. Compared to the C2F plan, the M2F plan was significantly better in sparing the small bowel at any dose level ($p < 0.001$). Through the total range of doses, the extent of vol-

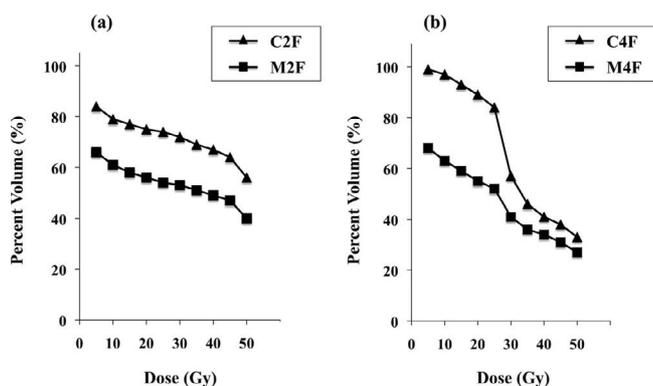


Fig. 4. Dose-volume-histogram for the small bowel. The percentages of small bowel volumes receiving different doses are shown. Comparison of conventional two-field (C2F) plan vs. modified two-field (M2F) plan is shown in (a), conventional four-field (C4F) plan vs. modified four-field (M4F) plan in (b).

Table 1. Median volumes of small bowel receiving prescribed doses with conventional and modified 2- or 4-field technique.

Dose	Median percent volume (range)			
	C2F	M2F	C4F	M4F
5	84 (76–100)	75 (47–87)	100 (99–101)	82 (52–100)
10	80 (70–100)	71 (41–84)	100 (97–101)	74 (45–100)
15	77 (67–100)	68 (37–83)	99 (89–100)	70 (40–99)
20	75 (65–98)	66 (35–81)	96 (81–98)	67 (37–97)
25	74 (63–96)	64 (33–80)	92 (72–98)	66 (34–95)
30	72 (59–88)	62 (31–79)	79 (52–92)	63 (30–90)
35	70 (55–79)	60 (29–78)	73 (38–83)	62 (27–83)
40	68 (50–77)	59 (27–77)	67 (29–77)	58 (23–80)
45	66 (43–75)	56 (24–75)	60 (20–78)	53 (17–78)
50	58 (22–69)	50 (16–69)	48 (9–75)	45 (8–75)

Abbreviations: C2F = conventional 2-field technique; M2F = modified 2-field technique; C4F = conventional 4-field technique; M4F = modified 4-field technique.

ume reduction to the small bowel irradiated was similar. Compared to the C4F plan, the M4F plan was also significantly better in sparing the small bowel at any dose level ($p < 0.001$). A large extent of volume reduction was observed at 5–25 Gy. Compared to the M2F plan, the M4F plan was significantly better in sparing the small bowel at 5–25 Gy ($p < 0.001$ at 5–20 Gy, $p < 0.01$ at 25 Gy).

Sacral bone

Comparison of sacral bone volumes irradiated in a representative patient is shown in Fig. 5. The volumes of the sacral bone irradiated by each plan were summarized in Table 2.

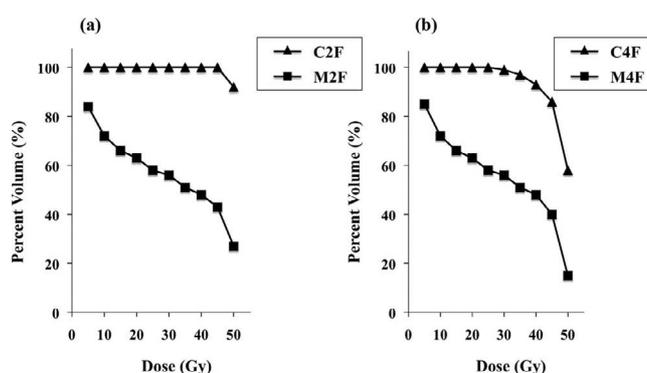


Fig. 5. Dose-volume-histogram for the sacral bone. The percentages of sacral bone volumes receiving different doses are shown. Comparison of conventional two-field (C2F) plan vs. modified two-field (M2F) plan is shown in (a), conventional four-field (C4F) plan vs. modified four-field (M4F) plan in (b).

Table 2. Median volumes of sacral bone receiving prescribed doses with conventional and modified 2- or 4-field technique.

Dose	Median percent volume (range)			
	C2F	M2F	C4F	M4F
5	100 (100–100)	98 (84–100)	100 (100–100)	98 (85–100)
10	100 (100–100)	96 (81–100)	100 (100–100)	95 (72–100)
15	100 (100–100)	93 (76–100)	100 (100–100)	91 (66–100)
20	100 (100–100)	90 (74–100)	100 (100–100)	88 (63–100)
25	100 (100–100)	87 (70–100)	100 (100–100)	85 (56–100)
30	100 (98–100)	85 (68–100)	98 (87–100)	82 (56–98)
35	100 (94–100)	82 (51–100)	93 (75–100)	77 (51–98)
40	100 (89–100)	78 (48–100)	86 (66–99)	69 (48–96)
45	99 (81–100)	70 (43–100)	77 (53–98)	57 (40–92)
50	92 (42–99)	57 (27–96)	50 (24–88)	24 (12–72)

Abbreviations: C2F = conventional 2-field technique; M2F = modified 2-field technique; C4F = conventional 4-field technique; M4F = modified 4-field technique.

Compared to the C2F plan, the M2F plan was significantly better in sparing the sacral bone at any dose level ($p < 0.05$ at 5 Gy, $p < 0.01$ at 10–25 Gy, $p < 0.001$ at 30–50 Gy). Compared to the C4F plan, the M4F plan was significantly better in sparing the sacral bone at any dose level ($p < 0.05$ at 5–10 Gy, $p < 0.01$ at 15–25 Gy, $p < 0.001$ at 30–50 Gy). Compared to the M2F plan, the M4F plan was significantly better in sparing the sacral bone at 20–50 Gy of the prescribed dose ($p < 0.05$ at 20 Gy, $p < 0.01$ at 25 Gy, $p < 0.001$ at 30–50 Gy).

DISCUSSION

The Japanese Patterns of Care Study demonstrated the patterns of definitive radiotherapy practice for patients with uterine cervical cancer between 1999 and 2001 in Japan. Pelvic external beam RT was given using an opposing anteroposterior (AP-PA) technique in 87% of the patients. The upper border of the pelvic field was at the L4–L5 interspace in 77% of the patients.²² CT simulation is widely used for radiotherapy treatment planning today. However, for uterine cervical cancer, the two-field technique based on bony landmarks is still the common treatment planning method in Japan. In the present study, we compared the dose reduction by two-field and four-field techniques when the common iliac lymph node region is excluded from the radiation field in patients with uterine cervical cancer. Our results suggest that, compared to conventional technique, the modified technique of excluding the common iliac lymph node region from the conventional field significantly reduces the irradiated volume of the small bowel and sacral bone.

The severity of acute intestinal complications has been considered to correlate with the irradiated volume of the small bowel.⁸ It has also been pointed out that high-dose irradiation to the small bowel correlates with severe late intestinal complications.^{8–12} Ohara *et al.* reported that, in the pelvis, a large amount of small bowel exists in the area ranging over 8 cm from the L4–L5 interspace and below that occupies the upper side in conventional fields.¹¹ Therefore, exclusion of the common iliac lymph node region from conventional fields could result in reduction of the irradiated volume of the small bowel. The results of our study show that the modified plans are significantly better than the conventional ones in sparing the small bowel volume irradiated at all dose levels in both two-field and four-field techniques (Fig. 4), thereby indicating that radiotherapy by the modified techniques could lead to a reduction in small bowel complications.

Radiation-induced pelvic insufficiency fracture has been regarded as a rare complication in patients with gynecologic cancer.¹³ However, recent studies have reported the incidence of pelvic insufficiency fracture as 8.2–17.9% after pelvic irradiation, a higher frequency than previously believed.^{14–16} The most common site of pelvic insufficiency

fracture is the sacral bone including the sacroiliac joints. Kwon *et al.* reported that 85% of patients with pelvic insufficiency fracture after pelvic irradiation had sacral involvement in their retrospective evaluation of MRI images.¹⁶ For this reason, we evaluated the DVHs of sacral bone in this study. The modified plans proved to be significantly better than the conventional plans in sparing sacral bone volume irradiated in both two-field and four-field techniques at all dose levels, and especially at a high-dose level (Fig. 5). Because high-dose irradiation (> 50.4 Gy) to the pelvic bone is regarded one of the risk factors of pelvic insufficiency fracture,²³ radiotherapy by the modified technique could reduce this incidence.

Which of M2F and M4F is better when both small bowel and sacral bone sparing are taken into account? As for small bowel sparing, M4F was significantly better only at a low to middle-dose level compared to M2F. Regarding sacral bone sparing, M4F showed significant benefit at a high-dose level compared to M2F. Thus, it could be concluded that the M4F technique is better for both small bowel and sacral bone sparing compared to M2F.

The upper border of the modified field depends on the position of the division of the common iliac artery into external and internal iliac branches. Greer *et al.* demonstrated the position of the common iliac bifurcation based on intraoperative retroperitoneal measurements from 100 patients.²⁴ They showed that the mean level of the bifurcation was 1.7 cm above the lumbosacral prominence on the right and 1.4 cm above on the left, that both common iliac bifurcations were cephalad to the level of the lumbosacral prominence in 87% of patients, and that the mean level of the aortic bifurcation was 6.7 cm above the lumbosacral prominence. In our study, as our standard upper border is at the L4–L5 interspace, field-size reduction in the modified plan varied from 0.5 cm to 4.7 cm (mean, 2.8 cm) in the longitudinal direction, which was relatively smaller than those in the study by Greer *et al.*

Patient selection is important in adopting radiotherapy with small bowel and sacral bone sparing technique while maintaining curability of the disease. Squamous cell carcinoma of the cervix, which constitutes approximately 80% of all cervical cancers, commonly metastasizes to lymph nodes anterogradely along vessels from paracervical lymph nodes to common iliac lymph nodes. Sakuragi *et al.* reviewed surgically treated cervical cancer cases, reporting the incidence of pelvic lymph node metastasis in stage Ib, stage IIa, and stage IIb as 12%–22%, 10%–27%, 34%–43% respectively.²⁵ They also reported a positive rate for metastasis to common iliac lymph node of 9.1% in 208 cases with stage Ib to stage IIb.²⁶ However, when focusing on early-stage squamous cell carcinoma of the cervix (Stage I/II, tumor size ≤ 4 cm), the frequency of metastasis to common iliac lymph nodes was a lower 1.5%.²⁷ In the early-stage cases, the modified technique of excluding the common iliac

lymph node region can be indicated. Further study will be needed to investigate the incidence of small bowel complications and insufficiency fracture, and failure patterns after radiotherapy with the modified technique.

Since most patients with early-stage disease will be cured, major efforts should be made to reduce long-term complications while maintaining post-radiotherapy efficacy. A small study of 33 cervical cancer patients treated after hysterectomy with intensity-modulated radiation therapy (IMRT) and concurrent chemotherapy showed decreased gastrointestinal and genitourinary side effects, with local control comparable to that in patients treated with four-field box radiotherapy.²⁸⁾ Recently, Kidd *et al.* reported clinical outcomes of 452 cervical cancer patients treated with IMRT or non-IMRT.²⁹⁾ In that report, IMRT significantly decreased toxicity while maintaining disease control. IMRT was used in 27% of the patients with gynecologic cancer in the United States in 2004³⁰⁾ and the use of IMRT for gynecological malignancy is also of interest in Japan. Therefore, comparison of the current modified plan with IMRT by excluding the common iliac lymph node region from the target will be necessary.

In conclusion, we have demonstrated that the modified radiation technique of excluding the common iliac lymph node region from the conventional radiation field has significant benefits for sparing the small bowel and sacral bone in the treatment of cervical cancer compared with a conventional two-field or four-field technique. In clinical practice, the modified technique could be useful for patients with early-stage squamous cell carcinoma of the cervix and lead to a reduction in small bowel complications and insufficiency fracture after radiotherapy.

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