Access this article online
Quick Response Code:

Website: www.pogsjournal.org
DOI: 10.4103/pjog.pjog_67_23

Adaptive extended-field intensity-modulated radiation therapy with simultaneously integrated boost for locally advanced cervical cancer with lymph node metastases

Yukihiro Hama[1], Etsuko Tate[1]

Abstract:

Performing external beam radiotherapy alone without chemotherapy or brachytherapy for locally advanced cervical cancer with multiple lymph node metastases is challenging. The purpose of this case report is to present the efficacy of high-dose adaptive extended-field intensity-modulated radiotherapy (IMRT) with simultaneous integrated boost (SIB) in treating locally advanced cervical cancer with multiple lymph node metastases. A 67-year-old woman with locally advanced squamous cell carcinoma of the uterine cervix was treated by external beam radiotherapy alone due to the refusal of chemotherapy and intracavitary brachytherapy. In order to maximize the efficacy of treatment, extended-field radiotherapy that includes the paraaortic lymph nodes as well as an adaptive IMRT-SIB plan, was applied. The treatment was successful, resulting in complete tumor disappearance without severe adverse events. In conclusion, high-dose adaptive IMRT-SIB may be an alternative treatment option for locally advanced cervical cancer with multiple lymph node metastases.

Keywords:

Image-guided radiotherapy, intensity-modulated radiotherapy, radiation dosage, uterine cervical neoplasms

Introduction

Concurrent chemoradiotherapy with intracavitary brachytherapy is the standard treatment for locally advanced cervical cancer with multiple pelvic lymph node metastases.[1,2] Surgical resection of bulky lymph nodes has been attempted optionally. If chemotherapy or brachytherapy cannot be administered or if the patient refuses these treatments, external beam radiotherapy is the treatment of choice. In the case of multiple bulky pelvic lymph node metastases or metastases in the paraaortic lymph nodes, the radiation field should be extended to the paraaortic lymph node area.[3] Despite the potential efficacy of extended-field radiotherapy, there are several concerns about serious adverse effects such as gastrointestinal, genitourinary, and hematologic toxicity due to the larger radiation field and higher radiation dose.[4]

Helical tomotherapy is a radiation therapy technique that uses a binary multileaf collimator with 64 leaves to modulate beam intensity with high speed and precision. This technique provides a helical delivery of radiation that allows a large field of view up to 40 cm × 160 cm. This feature is particularly useful in treating large tumors or lesions.[5] There are no reports

[1]Department of Radiation Oncology, Tokyo-Edogawa Cancer Centre, Edogawa Hospital, Tokyo, Japan

Address for correspondence:
Dr. Yukihiro Hama, 2-24-18 Higashikoiwa, Edogawa, Tokyo 133-0052, Japan.
E-mail: yjhama2005@yahoo.co.jp

Submitted: 17-Sep-2023
Revised: 18-Sep-2023
Accepted: 27-Oct-2023
Published: 28-Dec-2023

How to cite this article: Hama Y, Tate E. Adaptive extended-field intensity-modulated radiation therapy with simultaneously integrated boost for locally advanced cervical cancer with lymph node metastases. Philipp J Obstet Gynecol 2023;47:320-4.

of extended-field adaptive radiotherapy for locally advanced cervical cancer with lymph node metastases with tomotherapy alone. Here, we report a case of locally advanced cervical cancer with multiple pelvic lymph node metastases treated with helical tomotherapy alone with extended-field high-dose adaptive radiotherapy.

Case Report

A 67-year-old woman was referred to our institution for evaluation and treatment of squamous cell carcinoma (SCC) of the uterine cervix. The patient had already undergone a cervical biopsy at the referring hospital and was diagnosed with moderately differentiated SCC. Whole-body computed tomography (CT), pelvic magnetic resonance imaging (MRI), and ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) were performed to evaluate the extent of cervical cancer. T2-weighted images showed the heterogeneous mildly hyperintense tumor in the cervix infiltrating the vagina and bladder [Figure 1a]. Apparent diffusion coefficient maps obtained using a *b*-value of 800 s/mm^2 showed a low signal intensity lesion in the cervix [Figure 1b]. Gadolinium-enhanced volumetric interpolated breath-hold examination (VIBE) T1-weighted images showed heterogeneous enhancement of the tumor [Figure 1c]. ^{18}F-FDG PET scans showed a hypermetabolic tumor in the cervix consistent with cervical cancer [Figure 1d]. Pelvic lymph node metastases were observed in the bilateral external iliac lymph nodes and the left common iliac lymph node on MRI and PET scans [Figure 1e and f]. Several suspicious metastatic lymph nodes were found in the paraaortic and bilateral inguinal lymph nodes, but no distant metastases were detected. Serum SCC antigen (SCC-Ag) level was elevated (23.2 ng/mL; normal 0–2.5 ng/mL). Based on CT, MRI, and PET imaging findings, the patient was diagnosed with FIGO stage IVA cervical cancer. She declined chemotherapy and intracavitary brachytherapy, which were recommended as part of the treatment regimen along with external-beam radiotherapy. Therefore, we decided to administer external-beam radiotherapy only.

All procedures performed in this case report were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments. Institutional review board approval was waived because every treatment was approved by the national health insurance. Informed consent was obtained from the patient for the use of clinical data. Adaptive radiotherapy was planned to treat the multiple metastatic lymph nodes in the pelvic region and the suspected metastases in the paraaortic and bilateral inguinal lymph nodes. To compensate for the lack of chemotherapy and brachytherapy, we used intensity-modulated radiation therapy (IMRT) with simultaneous integrated boost (SIB)

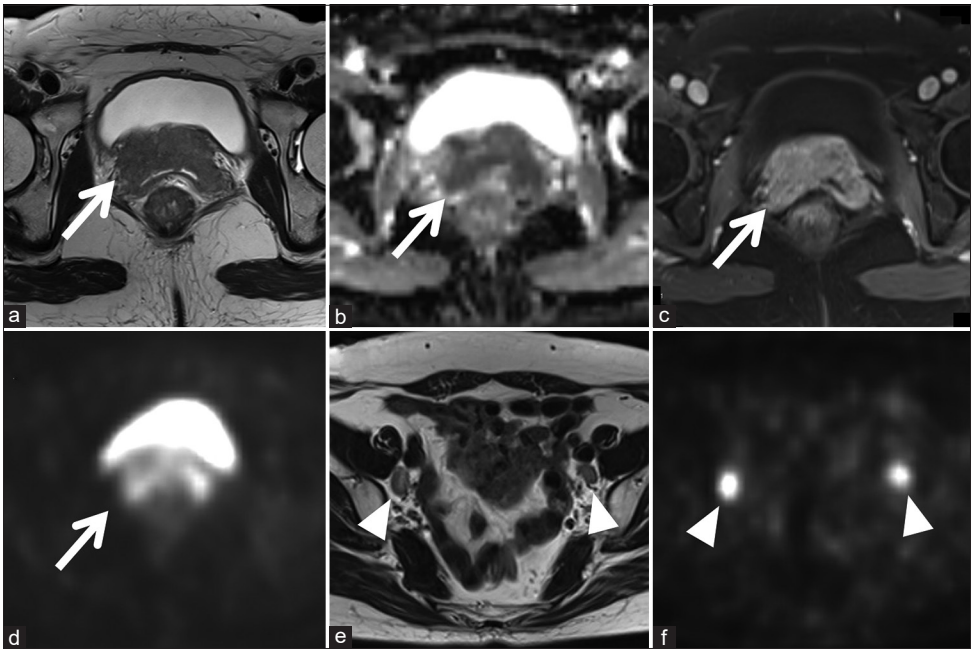

Figure 1: Magnetic resonance imaging and ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) scans before radiotherapy. (a) Transverse T2-weighted turbo spin echo image shows the heterogeneous mildly hyperintense tumor in the cervix infiltrating the bladder (arrow), (b) Apparent diffusion coefficient map obtained with a b-value of 800 s/mm^2 shows a low signal intensity lesion in the cervix (arrow), (c) Gadolinium-enhanced volumetric interpolated breath-hold examination T1-weighted image shows heterogeneous enhancement of the tumor (arrow), (d) Transverse ^{18}F-FDG PET shows significantly increased FDG uptake (arrow), (e) On T2-weighted image, bilateral external iliac lymph nodes are enlarged and shows slightly higher signal than skeletal muscle, consistent with lymph node metastasis (arrowheads), (f) ^{18}F-FDG PET scan shows markedly increased FDG uptake in bilateral external iliac lymph nodes (arrowheads)

using helical tomotherapy, which allowed us to deliver high-dose radiation therapy over a large field while reducing the risk of radiation-related adverse events. The prescribed doses were 81.4 Gy at 2.2 Gy per fraction for cervical cancer, 66 Gy at 2.0 Gy per fraction for the metastatic lymph nodes, and 45 Gy at 1.8 Gy per fraction of the extended field, including bilateral inguinal lymph nodes, pelvic lymph nodes, and paraaortic lymph node region. Gross tumor volumes (GTVs) were delineated using transverse T2-weighted turbo spin echo images and contrast-enhanced VIBE T1-weighted images. GTV was created by fusing T2-weighted images, contrast-enhanced T1-weighted images, and CT images. The planning target volume (PTV) for cervical cancer was calculated by adding a 2–3 mm margin around the cervical cancer. The PTV for metastatic lymph nodes was calculated by adding a 3 mm margin around GTV. The nodal clinical target volume included the para-aortic, common iliac, external iliac, internal iliac, obturator, presacral, and inguinal nodal basins. For the first IMRT-SIB plan, the delivered doses to cervical cancer, metastatic lymph nodes, and lymph node basins were 55 Gy, 50 Gy, and 45 Gy, respectively, in 25 fractions. After completion of the 20th fraction, CT and MRI were performed to make the adaptive plan. For the adaptive plan, the doses delivered to the cervical cancer and metastatic lymph nodes were 15.4 Gy and 14 Gy, respectively, in 7 fractions. For the final adaptive plan, the dose delivered to the cervical cancer was 15.4 Gy in 7 fractions. Radiotherapy was performed 5 times a week using helical tomotherapy. Grade 2 diarrhea and Grade 1 urinary urgency (Common Terminology Criteria for Adverse Events v5.0) were noted during radiotherapy but recovered within 1 month after radiotherapy. Six months after radiotherapy, a whole-body CT, pelvic MRI, and whole-body PET scan confirmed that all tumors had completely disappeared [Figure 2a-f]. Serum SCC-Ag levels decreased and normalized to 1.7 (normal 0–2.5 ng/mL).

Discussion

It may be difficult to control locally advanced cervical cancer with multiple lymph node metastases with radiotherapy alone without adverse events. When combined with intracavitary brachytherapy, a paracentric (point A) dose of 85 Gy or more is required for local control.[6] Due to the high recurrence rate of pelvic radiotherapy alone, extended-field radiotherapy that includes the paraaortic lymph nodes has been reported to have a lower recurrence rate than pelvic radiotherapy alone.[4,7,8] Because the radiation field for extended-field radiotherapy is larger than that for pelvic-only radiotherapy, gastrointestinal and hematologic side effects may be problematic. However, IMRT-SIB with helical tomotherapy seems to avoid this problem.[7] High-dose radiotherapy with intracavitary brachytherapy has been used to control the primary lesion

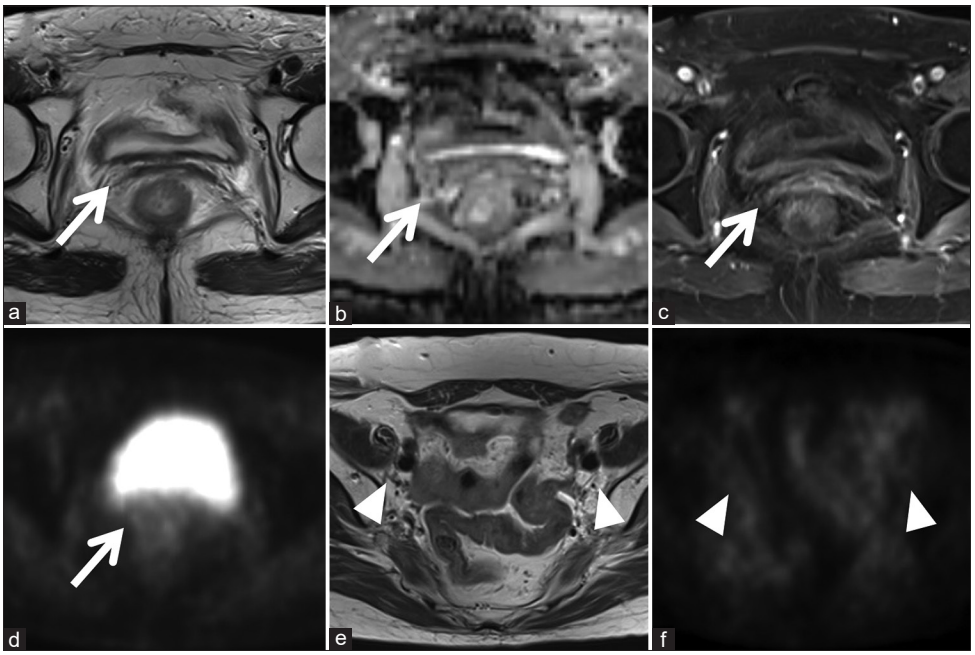

Figure 2: Magnetic resonance imaging and ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) scans 6 months after radiotherapy. (a) T2-weighted image shows no residual tumor in the cervix (arrow). Invasion into the bladder is completely relieved, (b) Apparent diffusion coefficient map obtained with a b-value of 800 s/mm2 shows a low signal intensity lesion (white arrow) in the cervix, (c) Gadolinium-enhanced volumetric interpolated breath-hold examination T1-weighted image shows no residual tumor (arrow), (d) Transverse ^{18}F-FDG PET scan shows normalization of increased FDG uptake in the cervix (arrow), (e) On T2-weighted imaging, the bilateral external iliac lymph nodes were significantly reduced and almost disappeared (arrowheads), (f) ^{18}F-FDG PET scan shows no abnormal FDG uptake in bilateral external iliac lymph nodes (arrowheads)

of cervical cancer, while extended-field radiotherapy with or without systemic chemotherapy plays an important role in controlling paraaortic lymph node metastases. If systemic chemotherapy or intracavitary brachytherapy is not available, curative doses should be safely delivered by external beam radiation alone. Adaptive IMRT-SIB with helical tomotherapy may be a solution to this problem.

This case report has several strengths. First, this case report suggests the possibility of treatment without serious side effects, even with high doses of radiation to cervical cancer, as well as extended-field radiotherapy involving paraaortic, pelvic, and bilateral inguinal lymph nodes. One reason for the treatment's success is the use of image-guided adaptive radiotherapy, which optimizes the radiation field and dose according to the shrinkage and shape of the tumor, delivering high doses of radiation precisely to the tumor while minimizing exposure to surrounding normal tissue. Second, IMRT-SIB using helical tomotherapy enables confirmation of the tumor and normal tissue shapes on CT images before radiation delivery. This feature allows for safe delivery of large doses of radiation even near normal organs whose shape is constantly changing, such as the bladder and rectum while minimizing radiation exposure to normal tissue.

There are several limitations to this case report. First, even with helical tomotherapy, the movement of the tumor and surrounding normal organs cannot be monitored during radiation delivery. MRI-guided radiotherapy may solve this limitation.[9] However, MRI-guided radiotherapy systems are not compatible with helical or rotational IMRT, such as volumetric-modulated arc therapy, and future development is warranted. Second, helical tomotherapy allows only coplanar irradiation and pelvic irradiation requires complex treatment planning to avoid irradiation of the femoral head. In addition, because helical irradiation is performed using a binary multileaf collimator, the larger the irradiation field, the longer the irradiation time. Dynamic WaveArc therapy using a gimbal-head radiotherapy system can overcome this limitation.[10]

In conclusion, although one case report cannot be generalized to other cases without further scientific validation, high-dose adaptive IMRT-SIB may be an alternative treatment option for locally advanced cervical cancer with multiple lymph node metastases.

Author's contribution

Concept: Hama Y, Tate E, Design: Hama Y, Tate E, Definition of intellectual content: Hama Y, Tate E, Literature search: Hama Y, Tate E, Clinical studies: Hama Y, Tate E, Experimental studies: N/A, Data acquisition: Hama Y, Tate E, Data analysis: N/A, Statistical analysis: N/A, Manuscript preparation: Hama Y, Tate E, Manuscript editing: Hama Y, Tate E, Manuscript review: Hama Y, Tate E.

Patient declaration of consent statement

All procedures performed in this case report were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments. Institutional review board approval was waived because every treatment was approved by the national health insurance. Informed consent was obtained from the patient for the use of clinical data.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initial will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Authorship contributions

Yukihiro Hama - Made substantial contributions to the study concept, drafted the manuscript and revised it critically for important intellectual content, approved the final version of the manuscript to be published, and agreed to be accountable for all aspects of the work.

Etsuko Tate - Made substantial contributions to the study concept, drafted the manuscript and revised it critically for important intellectual content, approved the final version of the manuscript to be published, and agreed to be accountable for all aspects of the work.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Tohyama A, Murakami M, Yoshino K. Strategies for the treatment of cervical cancer with bulky pelvic lymph nodes: An overview of the current evidence. J UOEH 2020;42:317-25.
2. Olthof EP, Wenzel H, van der Velden J, Spijkerboer AM, Bekkers R, Beltman JJ, *et al*. Treatment of bulky lymph nodes in locally advanced cervical cancer: Boosting versus debulking. Int J Gynecol Cancer 2022;32:861-8.
3. Li H, Wang S, Liu Y, Wang T, Jin S, Liu Z. Prophylactic extended-field irradiation for locally advanced cervical cancer. Gynecol Oncol 2022;166:606-13.
4. Thamronganantasakul K, Supakalin N, Kietpeerakool C, Pattanittum P, Lumbiganon P. Extended-field radiotherapy for locally advanced cervical cancer. Cochrane Database Syst Rev 2018;10:CD012301.

5. KD0123 M, Baumert J, Jazmati D, Schoroth F, Garbe S, Koch D, *et al*. Whole body irradiation with intensity-modulated helical tomotherapy prior to haematopoietic stem cell transplantation: Analysis of organs at risk by dose and its effect on blood kinetics. J Cancer Res Clin Oncol 2023;149:7007-15.
6. Lanciano RM, Martz K, Coia LR, Hanks GE. Tumor and treatment factors improving outcome in stage III-B cervix cancer. Int J Radiat Oncol Biol Phys 1991;20:95-100.
7. Wang W, Zhou Y, Wang D, Hu K, Zhang F. Prophylactic extended-field irradiation in patients with cervical cancer: A literature review. Front Oncol 2020;10:579410.
8. Ouyang Y, Wang Y, Chen K, Cao X, Zeng Y. Clinical outcome of extended-field irradiation versus pelvic irradiation using intensity-modulated radiotherapy for cervical cancer. Oncol Lett 2017;14:7069-76.
9. Hama Y, Tate E. Palliative MRI-guided intensity modulated radiation therapy (IMRT) for locally recurrent endometrial cancer. Actual Gynecol 2020;12:70-4.
10. Hiraoka M, Mizowaki T, Matsuo Y, Nakamura M, Verellen D. The gimbaled-head radiotherapy system: Rise and downfall of a dedicated system for dynamic tumor tracking with real-time monitoring and dynamic WaveArc. Radiother Oncol 2020;153:311-8.