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Magnetic resonance imaging-guided high-dose planned adaptive intensity-modulated radiation therapy for locally advanced cervical cancer

Planowa radioterapia adaptatywna o modulowanej intensywności dawki pod kontrolą rezonansu magnetycznego w leczeniu miejscowo zaawansowanego raka szyjki macicy

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Abstract

Magnetic resonance imaging-guided radiotherapy can accurately irradiate moving targets such as cervical cancer. An 82-year-old woman with locally advanced cervical cancer was referred for palliative radiotherapy. She had refused chemotherapy and brachytherapy, so she was treated with external beam radiotherapy to control her uterine bleeding and to alleviate pubic pain. Since her cervical cancer had no metastases, and she was expected to survive for a long time, curative doses of radiation (70–80 Gy/28 fractions) were administered by magnetic resonance imaging-guided planned adaptive intensity-modulated radiation therapy. Six months after intensity-modulated radiation therapy, the tumor disappeared without adverse events, and her symptoms were relieved. To the best of our knowledge, this is the first report of locally advanced cervical cancer treated with high-dose magnetic resonance imaging-guided adaptive intensity-modulated radiation therapy.

Keywords: adaptive radiotherapy, image-guided radiotherapy, MRI, radiation therapy, uterine cervical neoplasms

Streszczenie

Radioterapia pod kontrolą rezonansu magnetycznego umożliwia precyzyjne dostarczanie dawek promieniowania w leczeniu guzów ruchomych, m.in. raka szyjki macicy. Osiemdziesięciodwuletnia kobieta z miejscowo zaawansowanym rakiem szyjki macicy została skierowana na radioterapię paliatywną. Ponieważ pacjentka uprzednio odmówiła wdrożenia chemioterapii i brachyterapii, zastosowano radioterapię wiązką zewnętrzną w celu opanowania krwawienia z macicy i złagodzenia bólu w okolicy łonowej. Ze względu na brak przerzutów i spodziewane długie przeżycie chorej zastosowano lecznicze dawki promieniowania (70–80 Gy/28 frakcji) w schemacie planowej radioterapii adaptatywnej o modulowanej intensywności dawki, pod kontrolą rezonansu magnetycznego. Sześć miesięcy po zakończeniu leczenia nie stwierdzono guza ani działań niepożądanych; objawy ustąpiły. Zgodnie z naszą wiedzą jest to pierwsze doniesienie na temat miejscowo zaawansowanego raka szyjki macicy leczonego przy zastosowaniu wysokodawkowej radioterapii adaptatywnej o modulowanej intensywności dawki i pod kontrolą rezonansu magnetycznego.

Słowa kluczowe: radioterapia adaptatywna, radioterapia sterowana obrazem, MRI, radioterapia, nowotwory szyjki macicy

INTRODUCTION

Cervical cancer is the third most common gynecological malignancy in the developed populations, and predominant malignancy in developing countries[1,2]. Concurrent cisplatin-based chemoradiotherapy incorporating brachytherapy is standard treatment for locally advanced cervical cancer[3]. However, patients with serious comorbidities and the elderly do not always receive standard treatment. Magnetic resonance imaging (MRI)-guided radiotherapy not only allows visualization of the target and surrounding tissues more clearly than computed tomography (CT), but also provides real-time intrafraction motion monitoring for targets such as the uterine cervix[4]. With MR-guided radiotherapy, high doses of radiation can be accurately delivered to the uterine cervix like intracavitary brachytherapy. Here, we report a case of an elderly patient with locally advanced cervical cancer treated with high dose MRI-guided planned adaptive intensity-modulated radiation therapy (IMRT). As far as we know, this is the first report of locally advanced cervical cancer treated by MRI-guided adaptive IMRT.

CASE REPORT

An 82-year-old woman was referred to our hospital for treatment of locally advanced squamous cell carcinoma of the uterine cervix. She had a history of advanced rectal cancer and underwent laparoscopic high anterior resection with D3 lymph node dissection 8 years previously. Radiation therapy, chemoradiotherapy, and postoperative adjuvant chemotherapy for rectal cancer were not performed because of patient refusal. Contrast-enhanced whole-body CT showed no metastases in locoregional lymph nodes or in distant organs. T2-weighted MRI demonstrated a tumor which infiltrated the whole cervix circumferentially and extended into the right parametrium. Laboratory findings showed an elevated serum squamous cell carcinoma (SCC) antigen level (6.4 ng/mL, normal: <2.5 ng/mL), and cervical pathological examination revealed squamous cell carcinoma. Based on these findings, she was diagnosed with stage IIB cervical cancer (2018 FIGO Staging System). We initially recommended concurrent chemoradiation with cisplatin and brachytherapy, but the patient refused chemotherapy and brachytherapy. Consequently, we gave her palliative external-beam radiotherapy to control the uterine bleeding and to alleviate her pubic pain. Since there were no metastases or comorbidities, the patient was treated with high-dose MRI-guided IMRT to control the cervical cancer. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the institutional review board (Approval No. RO20191205), and written informed consent was obtained from the patient.

To perform sequential planned adaptive IMRT, true fast imaging with steady precession (FISP) MRI was performed before the initial plan of 40 Gy/16 fractions and during treatment for the adaptive plan of 30 Gy/12 fractions (MRIdian®,

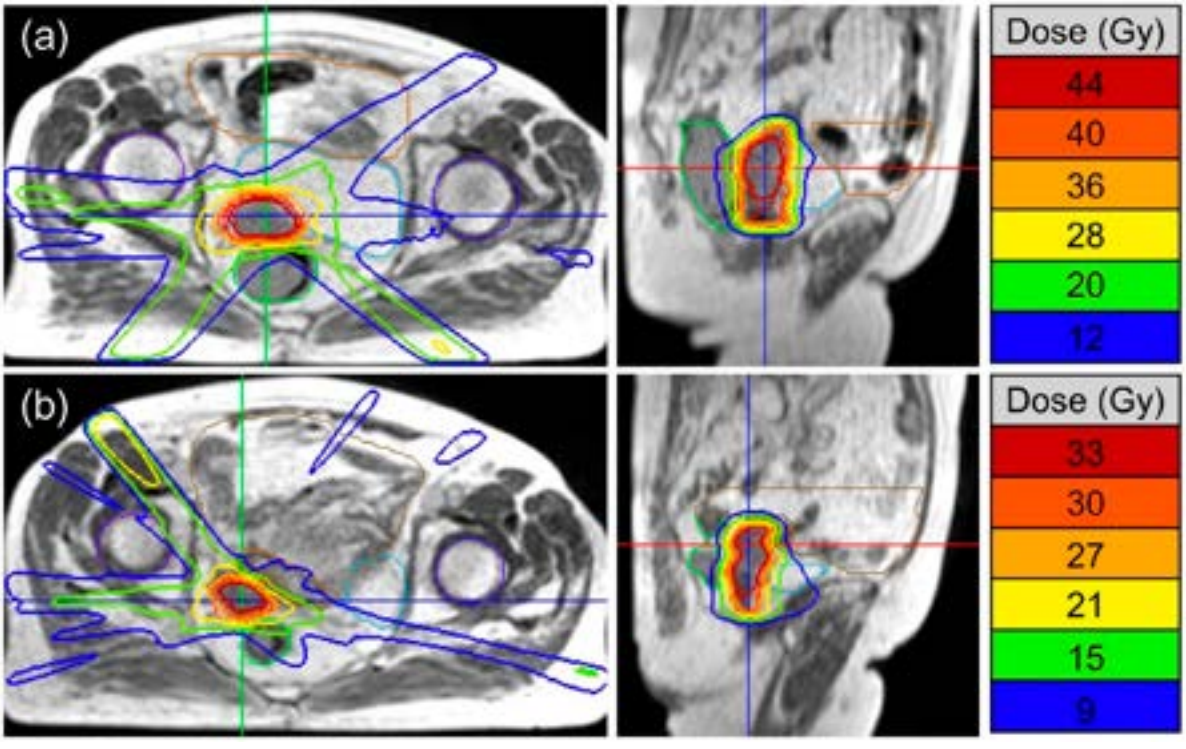

Fig. 1. MRI-guided radiotherapy isodose lines with corresponding actual radiation doses. ***A.*** *The initial plan.* ***B.*** *The adaptive plan*

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ViewRay, Oakwood Village, Ohio, USA). Gross tumor volume (GTV) was defined as the macroscopic tumor and the parametrial infiltrated lesion on true FISP images, and planning target volume (PTV) was defined by adding a 3-mm three-dimensional (3D) margin to the GTV, but avoiding overlap with the rectum. The prescribed dose to the D95% of the PTV in the initial plan (PTV1) (the dose covering 95% of the PTV1) was 40 Gy in 16 fractions (Fig. 1 A). As the tumor shrank, an adaptive plan with true FISP MRI was made at the end of 15 fractions. The prescribed dose to the D95% of the PTV in the adaptive plan (PTV2) was 30 Gy in 12 fractions (Fig. 1 B). The total prescribed dose to the D90% of the GTV was 80 Gy in 28 fractions, and the maximum dose in the GTV was 90 Gy in 28 fractions.

There were no adverse events during radiotherapy or at the 6-month follow-up. Her abnormal uterine bleeding stopped during radiotherapy, and her serum SCC antigen level decreased to 1.1 ng/mL. The tumor in the cervix disappeared, and the result of cervical cytology was negative for cancer cells. There were no recurrences or adverse events during the 6-month follow-up period.

DISCUSSION

A standard palliative radiotherapy regimen for patients with locally advanced cervical cancer has not been established. Patients with no metastases and no serious comorbidities may survive for a long time, so the aim should be local control. MRI-guided radiotherapy has been shown in pancreatic cancer to deliver high doses of radiation without increasing toxicity compared to conventional external-beam radiotherapy[5]. However, it is not yet known whether this is also true for cervical cancer. Cervical cancer is a moving target, and there are organs at risk (OARs) such as the rectum and bladder nearby. Brachytherapy has been considered the only method that can deliver high doses required to control cervical cancer without causing excessive adverse events[6]. Since MRI-guided radiotherapy enables high-dose radiation delivery while tracking moving targets and OARs, it may be able to deliver high doses of radiation as safely as brachytherapy.

There are some limitations in this study. First, the patient did not undergo radiotherapy to the pelvic lymph nodes, which is commonly performed[7]. Therefore, this study cannot be directly applied to patients undergoing curative radiotherapy for locally advanced cervical cancer. Secondary, there are no data on the concurrent use of chemotherapy and MRI-guided high-dose IMRT-SIB (simultaneous integrated boost). If MRI-guided IMRT-SIB can be performed as safely as brachytherapy, it might be as effective as brachytherapy.

In conclusions, MRI-guided adaptive IMRT-SIB may become one of the treatment options for cervical cancer. Further studies are needed to evaluate its usefulness and safety compared to brachytherapy.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations which might negatively affect the content of this publication and/or claim authorship rights to this publication.

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