Adaptive radiotherapy of locally advanced sigmoid colon cancer with intra-fractional motion using the MRIdian system: A case report

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Abstract. Neoadjuvant chemotherapy, when combined with radiotherapy, serves as an optional treatment for patients with locally advanced sigmoid colon cancer and is usually performed in conjunction with complete mesocolic excision. The substantial movement of surrounding organs in cases of sigmoid colon cancer frequently leads to toxicity in normal tissues. The present report details the case of a 76-year-old man diagnosed with locally advanced sigmoid colon cancer. Initially, treatment using the Tomotherapy Hi-Art system was selected; however, during image guidance from the first to the sixth fractions, the tumor location underwent a marked change, exceeding the range of the planning target volume. Efforts to recapture the image were unsuccessful, leading to a decision to transition the patient to the MRIdian system for daily treatment with online adaptive radiotherapy. The positional variations in the tumor were evident in each treatment using the MRIdian system, with mean shifts of 2.58 cm in the right-left direction, 1.24 cm in the cranial-caudal direction and 0.40 cm in the anterior-posterior direction. The mean time from the entry of the patient to treatment completion was 41 min. Adaptive treatment plans were performed for all 19 fractions, with two treatments repeated due to the tumor moving out of tracking range. Following irradiation using the MRIdian system, the gross tumor volume decreased by 62%. Notably, the patient experienced no side effects during treatment. A CT scan conducted 3 months after radiotherapy revealed a marked reduction in the tumor size, consistent with a partial response, leading to the scheduling of surgery. Following surgery, a CT scan after 6 months revealed no local recurrence in the surgical bed region. The findings in the present case support the feasibility of implementing an adaptive treatment plan using the MRIdian system for locally advanced sigmoid colon cancer in the context of neoadjuvant chemoradiotherapy.

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Introduction

Colorectal cancer is the third most common cancer, accounting for 10% of all cancer cases. It is also the second leading cause of cancer-related deaths worldwide. The risk factors of developing colorectal cancer include age, family history, personal history and lifestyle factors (1). Combination of neoadjuvant chemotherapy with radiotherapy is an optional treatment for patients with locally advanced sigmoid colon cancer (2), and it usually accompanies complete mesocolic excision (3,4). Considerable variation in the small intestine and bladder following pelvic and lower abdomen irradiation can lead to normal organ toxicity (5-7). Consequently, the goal of treatment is to improve the prognosis of patients, reduce toxicity and enable patients to complete treatment without interruption. At present, the principal methods to reduce the toxicity of radiotherapy for colon cancer include image-guided, intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy and treatment with a full bladder (8). To achieve these goals when treating patients with sigmoid colon cancer, the MRIdian system (ViewRay Technologies, Inc.) is employed (9). In the present study, for 1 patient with sigmoid colon cancer, the treatment plan included 50 Gy administered in 25 daily fractions. The Tomotherapy Hi-Art system (Accuray, Inc.) was used for the first six fractions. However, during the treatment, the location of the tumor differed substantially from the CT simulation image each time. Attempts to recreate the image were unsuccessful, leading to the arrangement for the patient to receive daily treatment using online adaptive radiotherapy with the MRIdian system. The online adaptive treatment plan system, employed through MRIdian system, allows medical professionals to correct for daily tumor variations in both tumor and normal tissue, and to reoptimize the treatment plan online. This correction helps to amplify the tumor dose and reduce the planning target volume (PTV), thereby reducing side effects (10,11). The MRIdian system not only offers soft tissue contrast images that surpass those of CT but also

provides real-time images to monitor and track the position of the tumor during treatment, ensuring that the treatment target is accurately positioned before treatment delivery (9). The image alignment system of the Tomotherapy Hi-Art system relies solely on megavoltage CT image guidance. The soft-tissue contrast of these images is inferior to that of MRI, making it infeasible to perform online adaptive radiotherapy and track tumors that undergo substantial position changes during treatment (12).

Case report

In October 2021, a 76-year-old man with neither a family history of illness nor any unhealthy habits presented to their local medical doctor (Pintung, Taiwan) with symptoms of diarrhea and tarry feces that had persisted for a month. The performance status was assessed as 1 based on the Eastern Cooperative Oncology Group guidelines (13). Upon a blood examination, which showed low hemoglobin levels, the attending physician referred the patient to Antai Medical Care Coorperation Antai Tian-Sheng Memorial Hospital (Pintung, Taiwan) for colonoscopy. A diagnosis of moderately differentiated adenocarcinoma, a type of sigmoid colon cancer, was made. Abdominal CT 1 day later revealed the sigmoid colon tumor and suspected metastasis to the abdominal lymph nodes (LNs) and the right lower lobe in the lung. Thus, the cancer was categorized as clinical stage cT4aN2bM1a, stage 4A cancer (American Joint Committee on Cancer 8th edition) (14). After being told the examination result, the patient came to Kaohsiung Medical University Hospital (Kaohsiung, Taiwan). Nearly 1 month later in November 2021, a subsequent colonoscopy confirmed the malignancy through a pathology report, noting that the distance of the tumor from the anal verge was 17 cm. Given the large size of the tumor (7.2 cm) and visceral peritoneum invasion, which posed challenges to safe resection, the medical team chose to administer preoperative neoadjuvant chemotherapy and radiotherapy. The chosen chemotherapy regimen was 12 cycles of FOLFIRI (180 mg/m^2 Campto + 2,800 mg/m^2/48 h 5-FU) + Erbitux (500 mg/m^2/once every 2 weeks). Radiotherapy commenced in December 2021. As the treatment was for local advanced stage cancer, the prescribed dose was 50 Gy, delivered in 2-Gy daily fractions. Initially, the Tomotherapy Hi-Art system was selected for treatment. However, during the megavoltage CT image guidance for the first six fractions, it was observed that the location of the tumor had changed by itself, exceeding the range of the PTV. This displacement rendered other control methods ineffective. After the first fraction, a CT re-simulation was arranged to correct the treatment; however, this was unsuccessful. Consequently, the decision was eventually made by the patient to switch to the MRIdian system for treatment, starting at the seventh fraction. The MRIdian system allowed for the performance of an online adaptive treatment plan, using real-time image and target tracking functions during dose delivery to ensure minimal differences in the treatment target position. Both MRI and CT were used for simulation positioning before treatment. The MRI simulation scan was conducted using the MRIdian system, with bladder protection achieved by maintaining a full bladder (the patient emptied the bladder and drank 300 ml water 30 min before treatment). The MRI magnetic field strength was 0.35 T, and the image sequence was captured using true fast imaging with steady-state free precession, scanning a field of view of 40x43x40 cm for 128 sec. The image quality sufficed for radiation oncologists to delineate targets, including critical organs, without the need for fiducial markers or contrast medium. CT images were aligned with MRI to obtain electron density for treatment planning calculations. The gross tumor volume (GTV) was defined as visible lesions on the MRI simulation image. Margins of 3 mm were used for both the clinical target volume of GTV and the PTV high (PTVH). The PTV median encompassed the regional LNs (Fig. 1). Treatment began on December 3, 2021, with six fractions of radiotherapy performed using the Tomotherapy Hi-Art system, followed by the remaining 19 fractions using the MRIdian system, and was completed on December 14, 2021. The transition between the two technologies was seamless, and the positioning of the patient remained constant throughout the treatment process.

The MRI procedure during treatment was consistent with that used during the simulation positioning phase. After aligning the image, the radiation oncologists delineated the target volume and critical organs as required by the situation, and they reoptimized the treatment plan through daily Monte Carlo calculations. Following dose calculation, a comparative evaluation was conducted between the original plan and the reoptimized plan with regard to their respective advantages and disadvantages. The plan used step-and-shoot IMRT, using a 6 MV flattening filter free beam and a dose rate of 600 MU/min. Comprising 13 angles and 123 segments, a total dose of 50 Gy was prescribed in 2 Gy daily fractions. Throughout the treatment process, slight changes occurred in the number of segments, target volume and dose volume of critical organs due to the implementation of the adaptive treatment plan. These changes were verified using online Monte Carlo calculations and gamma comparisons at 2%/2 mm locally, with a gamma pass rate >90% as the acceptance standard. Before delivery, the target tracking function was activated, and images were captured continually in the sagittal view at a rate of 8 frames per sec. The GTV was used as the tracking structure, with the boundary defined by the PTV. If the GTV exceeded 5% of the PTV, treatment was halted and resumed only when the target returned to within 5% of the PTV. In the present case, it was observed that the position of tumor varied from the image captured during each MRIdian system treatment, and the distance between the three axes and the original position in the 19 fractions was presented in a box plot. The mean distance of the shifts in the right-left direction was 2.58 cm (range, 0-10.07 cm), the mean distance of the shifts in the cranial-caudal direction was 1.24 cm (range, 0.11-6.47 cm) and the mean distance of the shifts in the anterior-posterior direction was 0.40 cm (range, 0.06-2.03 cm) (Fig. 2). The workflow and the time spent for MRIdian system treatment were as follows: Patient setup took a mean time of 4 min (range, 2-8 min), simulation and image fusion took a mean time of 10 min (range, 7-13 min), online contouring took a mean time of 9 min (range, 4-18 min), reoptimization took a mean time of 4 min (range, 3-7 min), delivery took a mean

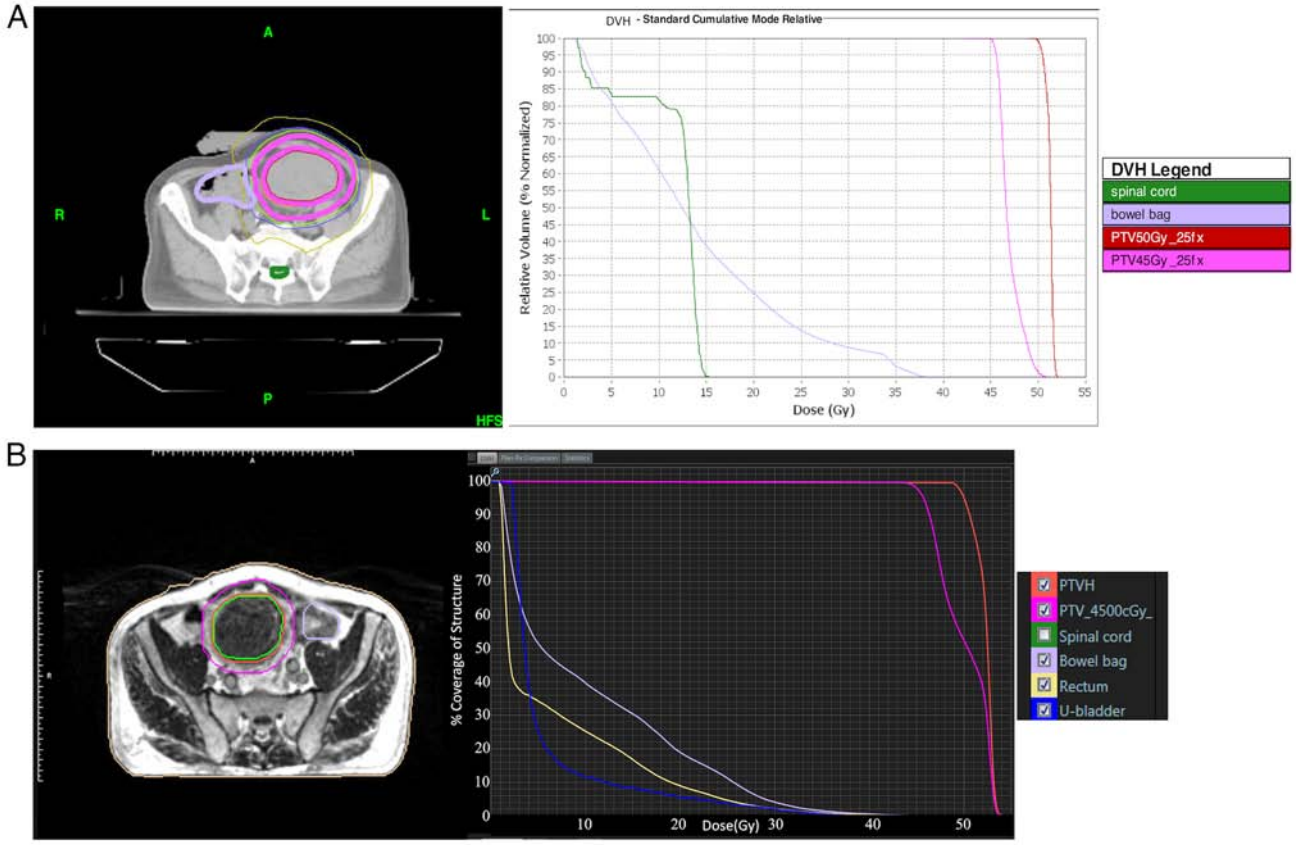

Figure 1. Simulation images based on treatment plan. (A) Treatment plan, including contour and DVH, using the Tomotherapy Hi-Art system. (B) Treatment plan, including contour and DVH, using the MRIdian system. DVH, dose-volume histogram; fx, fractions; HFS, head-first supine; PTV, planning target volume; PTVH, PTV high; PTVM, PTV median; U-bladder, urinary bladder.

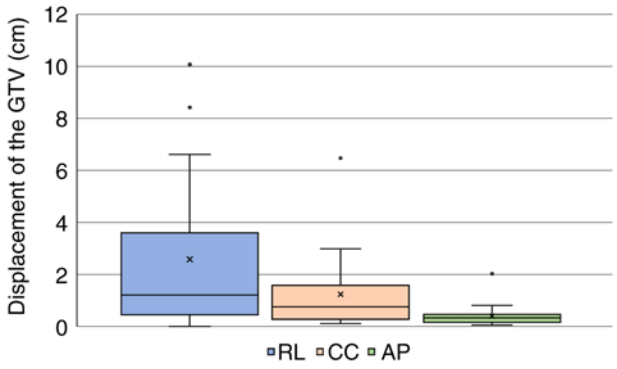

Figure 2. Displacement of the GTV during treatment. AP, anterior-posterior; CC, cranio-caudal; GTV, gross tumor volume; RL, right-left.

time of 11 min (range, 10-15 min) and patient exit from the treatment room took a mean time of 3 min (range, 2-4 min). The mean time from the entry of the patient to treatment completion was 41 min (range, 33-52 min). Adaptive treatment plans were performed in each of the 19 fractions, with two treatments repeated due to the tumor being out of tracking range. After irradiation with the MRIdian system, the GTV shrank by 62% (Fig. 3) and the PTVH shrank by 57%. During the treatment course, the patient experienced no side effects. Treatment concluded on January 2022, spanning 41 days. A subsequent CT scan in April 2022 revealed a marked reduction in tumor size, categorized as a partial response (Response Evaluation Criteria in Solid Tumours Version 1.1) (15) (Fig. 4A), leading to the scheduling of a low anterior resection in May 2022. The operation lasted 5 h and 10 min, with blood loss of 50 ml, and proceeded without complications. The total hospital stay was 19 days, and the postoperative pathological report stage was ypT3N0 (American Joint Committee on Cancer 8th edition) (14). Following surgery, a thoracoscopic examination of the right lower lung was performed in November 2022, revealing no evidence of malignancy in the pathological report. A CT scan in November 2022 (Fig. 4B) and April 2023 (Fig. 4C) indicated no local recurrence at the surgical bed region. The patient is currently alive without discomfort.

Discussion

Colorectal cancer is the third most common cancer worldwide, and the application of neoadjuvant chemoradiotherapy for locally advanced colon cancer is a common practice in Kaohsiung Medical University Hospital in Kaohsiung, Taiwan; however, clinically published cases of neoadjuvant chemoradiotherapy for locally advanced colon cancer are limited (2). The focus of the present report were the benefits of the online daily adaptive treatment plan using the MRIdian system for patients, including reduced toxicity and full coverage of the target by the PTV. Concerns regarding the process of neoadjuvant chemoradiotherapy, whether for rectal or colon cancer, typically center on excessive toxicity (16,17). However,

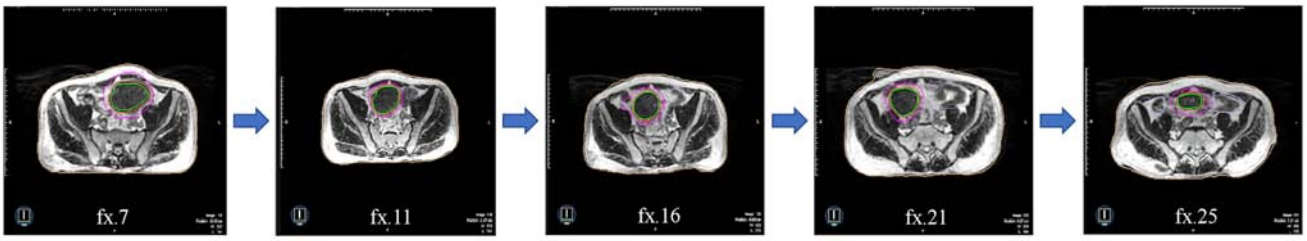

Figure 3. Progression of tumor shrinkage. Images from left to right show the seventh fraction, the eleventh fraction, the sixteenth fraction, the twenty-first fraction and the twenty-fifth fraction. Illustration of planning MRI with target definition: Gross tumor volume in green, planning target volume high in red, planning target volume median in pink, skin in beige, and small intestine in purple. fx., fraction.

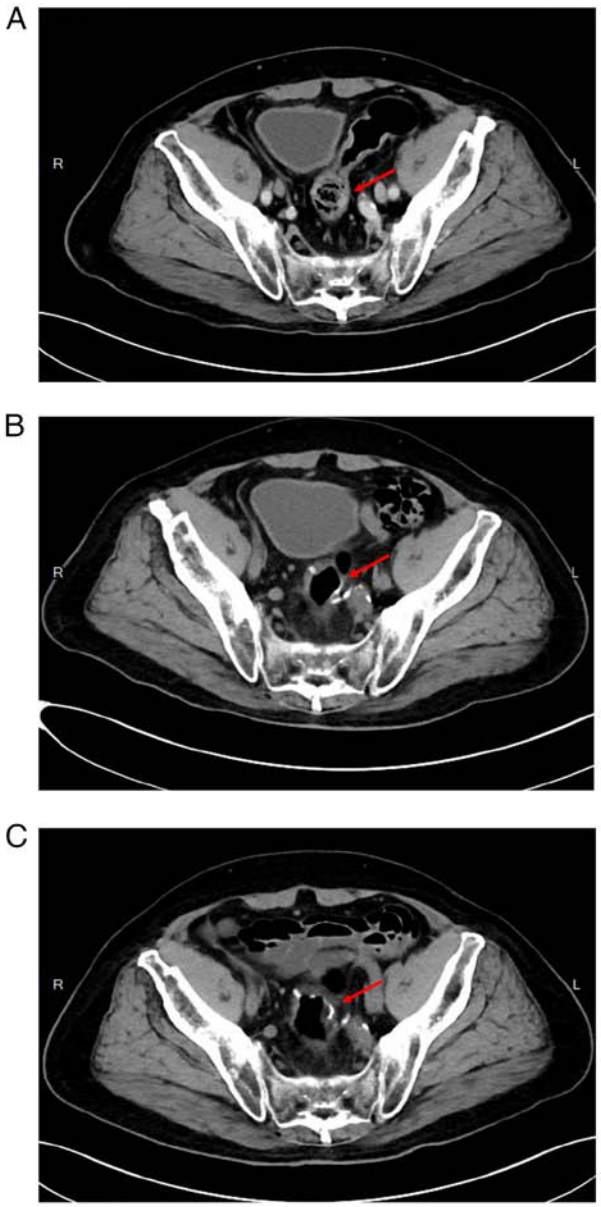

Figure 4. Abdominal CT images, with the red arrows indicating the tumor or surgical bed region. (A) After radiotherapy, before surgery, (B) 6 months after surgery and (C) nearly 1 year after surgery.

the present case demonstrated that the patient did not experience any discomfort attributable to radiotherapy during the treatment process.

When evaluating the overall duration of treatment, the scarcity of clinical case reports of colon cancer necessitates the use of rectal cancer cases with similar tumor locations as reference points. Intven *et al* (18) reported rectal cancer treatment involving five fractions with a total dosage of 25 Gy, resulting in an mean total treatment time of 48 min, which was comparable to the treatment time of the present case. Additionally, de Jong *et al* (19) found that the majority of patients with rectal cancer require ~40 min of treatment. The mean total treatment time was 41 min for the present case, reinforcing the feasibility of using the MRIdian system to treat sigmoid colon cancer.

Compared with the image quality of cone beam CT (CBCT) scans, the 0.35 T MRI of the MRIdian system potentially offers superior soft tissue contrast, thereby enhancing the accuracy of contouring (12). This quality makes online adaptive radiation therapy an alternative to CBCT imaging (20).

Abdominal organs frequently shift position during treatment due to factors such as respiration or organ volume transformation (21,22). Although methods such as breathing control, compression and fasting can manage these shifts, particularly in the upper abdomen, control of the colon to the lower abdomen is less frequently addressed. At present, no effective control method exists, making daily adaptive treatment plans with tumor tracking preferable for colon cancer surgery (23).

In the present case, the Tomotherapy Hi-Art system was initially used for treatment, and the plan was to select the treatment strategy and reposition to accommodate changes in tumor position. However, the irregular movement of the tumor rendered the chosen treatment plan ineffective. Thus, the patient was transitioned to the MRIdian system for treatment with an online adaptive treatment plan (24). The tumor consistently decreased in size throughout the treatment period, ultimately shrinking by 62%. If the treatment plan was not adapted, the PTV covering an excess volume of normal organ could lead to toxicity. Based on the outcomes in the present case, the implementation of an adaptive treatment plan with the MRIdian system was deemed feasible for locally advanced sigmoid colon cancer in neoadjuvant chemoradiotherapy. At present, studies related to radiotherapy for colon cancer are rare, and this case may be the first clinical published case using the MRIdian system with adaptive plan. The present case report contributes valuable insights and may serve as a reference for future treatment of locally advanced sigmoid colon cancer.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available to protect the privacy of the individual concerned but are available from the corresponding author on reasonable request.

Authors' contributions

CHC, TYC and MYH contributed to the conception and design of the study. CHC performed the statistical analysis and drafted the initial manuscript. CHC, TYC and MYH wrote sections of the manuscript. CHC and TYC confirm the authenticity of all the raw data. All authors were actively involved in manuscript revision. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The study received approval from the Kaohsiung Medical University Chung-Ho Memorial Hospital Institutional Review Board [Kaohsuing, Taiwan; approval no. KMUHIRB-E(I)-20230082].

Patient consent for publication

Based on the study being a retrospective study and a routine medical treatment, after institutional review board review, the requirement for a subject consent form was waived, so an informed consent form was not obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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