

## Teaching Case

# Magnetic Resonance—Guided Radiation Therapy to Boost Cervical Cancer When Brachytherapy Is Not Available: A Case Report



Mutlay Sayan, MD,<sup>a</sup> Teuta Zoto Mustafayev, MD,<sup>b</sup> Banu Atalar, MD,<sup>b</sup>  
Gorkem Gungor, MS,<sup>b</sup> and Enis Ozyar, MD<sup>b,\*</sup>

<sup>a</sup>Department of Radiation Oncology, Rutgers Cancer Institute of New Jersey, New Brunswick, New Jersey and

<sup>b</sup>Department of Radiation Oncology, Mehmet Ali Aydınlar Açıbadem University, School of Medicine, Istanbul, Turkey

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## Introduction

Cervical cancer is the fourth most common female malignancy worldwide, resulting in over 300,000 deaths annually.<sup>1</sup> Locally advanced cervical cancer has a worse prognosis compared with early-stage disease and the treatment of choice consists of concurrent chemotherapy with radiation. A Cochrane meta-analysis of 18 randomized controlled trials showed that concurrent chemotherapy with radiation was associated with a 6% improvement in 5-year survival compared with radiation therapy alone for women with locally advanced cervical cancers (hazard ratio, 0.81;  $P < .001$ ).<sup>2</sup> Brachytherapy has been considered an essential part of the locally advanced cervical cancer treatment, as it has been persistently associated with improved clinical outcomes.<sup>3</sup> However, the safe delivery of high doses of radiation therapy is difficult in patients with history of hysterectomy because brachytherapy options are limited to treatment of the vaginal vault alone.<sup>4,5</sup> When interstitial brachytherapy is not possible or simply not

available, referral to a high-volume center with expertise is recommended. Properly designed external beam radiation therapy (EBRT) boost could be considered as a last resort. Critical normal structures in the pelvis and the nonbony targets are difficult to visualize on standard cone beam computed tomography, and their positions may change between treatments.<sup>6</sup> Substantial decrease in tumor volume during the treatment necessitates the adaptive radiation therapy. Magnetic resonance—guided radiation therapy (MRgRT) resolves these problems by providing an excellent visualization of bowel and nonbony targets.<sup>6</sup> Herein, we report a case of MRgRT boost in a patient with locally advanced cervical cancer with history of supracervical hysterectomy. This case demonstrates the value and utility of MRgRT boost when brachytherapy is not an option.

## Case Presentation

Our patient was a 66-year-old woman with a history of supracervical hysterectomy in March 2016 for a benign disease. In January 2018, the patient presented to our institution with abnormal vaginal bleeding. On pelvic examination, a bilobular tumor of approximately 6 cm at the cervical stump with parametrial extension was palpated. A pelvic magnetic resonance imaging (MRI) showed a bilobular cervical stump mass, measuring 5 × 6 cm with intimate bowel contact and

Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

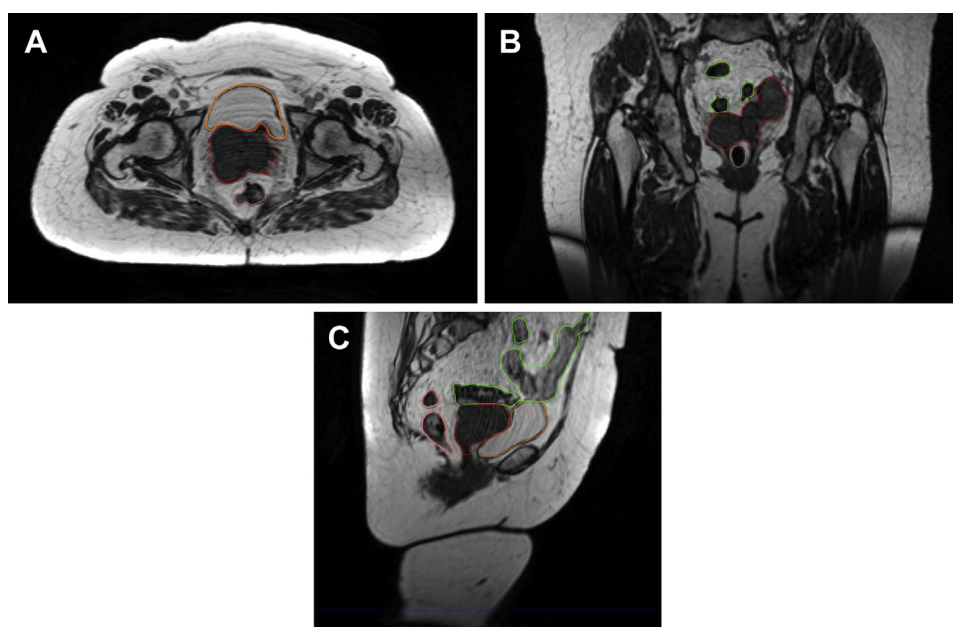
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\* Corresponding author: Enis Ozyar, MD; E-mail: [enis.ozyar@acibadem.com](mailto:enis.ozyar@acibadem.com).

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**Figure 1** A pretreatment pelvic magnetic resonance imaging (MRI) demonstrating a bilobular cervical stump mass (red) adjacent to bowel (green), rectum (pink), and bladder (orange).

without obstructive uropathy or pelvic wall involvement (Fig 1). A biopsy of the lesion demonstrated squamous cell carcinoma. Additional work-up including a positron emission tomography–computed tomography scan revealed no pelvic lymphadenopathy or definitive metastatic disease. She was clinically staged as The International Federation of Gynecology and Obstetrics IIB. The patient's case was discussed in a multidisciplinary meeting and a decision was made to treat her with concurrent chemoradiation. She received 48.6 Gy in 27 fractions to the planning target volume, which encompassed the gross tumor volume, cervix, parametrium, upper vagina, and pelvic lymph nodes. The EBRT was delivered using intensity modulated radiation therapy on

Truebeam (Varian Medical Systems, Palo Alto, CA) with concomitant chemotherapy weekly consisting of cisplatin. Gross tumor volume was 157 cm<sup>3</sup> and 115 cm<sup>3</sup> before and immediately after EBRT, respectively. Tumor volume decreased by approximately 26% during EBRT. Our center does not have the experience to deliver interstitial brachytherapy in this clinical setting. Referral to a higher volume GYN center with brachytherapy expertise was considered; however, the patient decided to proceed with EBRT boost at our institution.

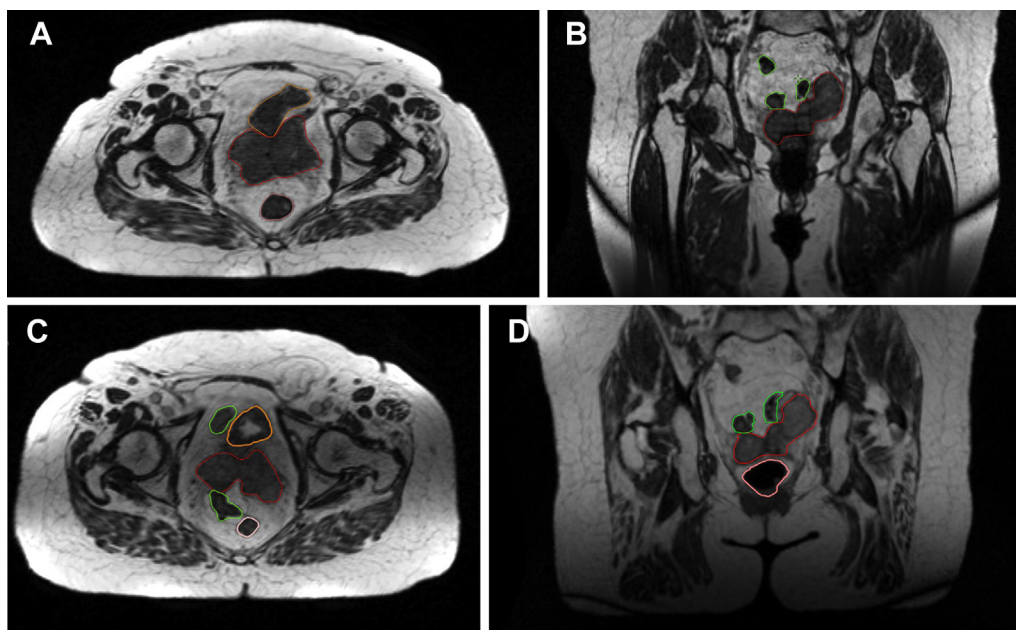
A linear accelerator-based MRgRT system (MRIdian System; ViewRay Inc, Oakwood Village, OH) was used to deliver an EBRT boost of 32 Gy in 8 fractions delivered every other day to the gross tumor volume plus 3 mm margin. The MRgRT system includes open, split-superconductor low-field (0.35 Tesla) MRI with a 50-cm field of view and double-focused multileaf collimator, with a 135-leaf–equipped linear accelerator. The MRI has 3-dimensional high-resolution modes scanning in 17 seconds to 12 minutes. MRI scans were obtained for the simulation in supine position and during daily setups to confirm the correct position of the patient. No immobilization device other than an MR-compatible knee cushion was used. The patient was instructed to have half full bladder and empty rectum before planning scans and treatments. The radiation oncologist assessed the target and organs at risk daily to detect interfractional anatomic changes for further contouring and adaptive planning. After the plan was finalized, treatment was started. During treatment delivery, cine MRI

**Table 1** Dosimetry and planning aims per GEC-ESTRO

	Patient EQD2 doses	Planning aims
HR-CTV D <sub>90</sub> (cGy)	9321	7500-9000
Bladder D2 cm <sup>3</sup> (cGy)	7420	9000
Rectum D2 cm <sup>3</sup> (cGy)	6503	7000-7500
Sigmoid D2 cm <sup>3</sup> (cGy)	6355	7000-7500

*Abbreviations:* EQD<sub>2</sub> = equieffective dose in 2 Gy; D<sub>90</sub> = minimum dose received by 90% volume; D2 cm<sup>3</sup> = minimum dose received by 2 cm<sup>3</sup> volume; HR-CTV = high-risk clinical target volume; GEC-ESTRO = The Groupe Européen de Curiothérapie and the European Society for Radiotherapy & Oncology.

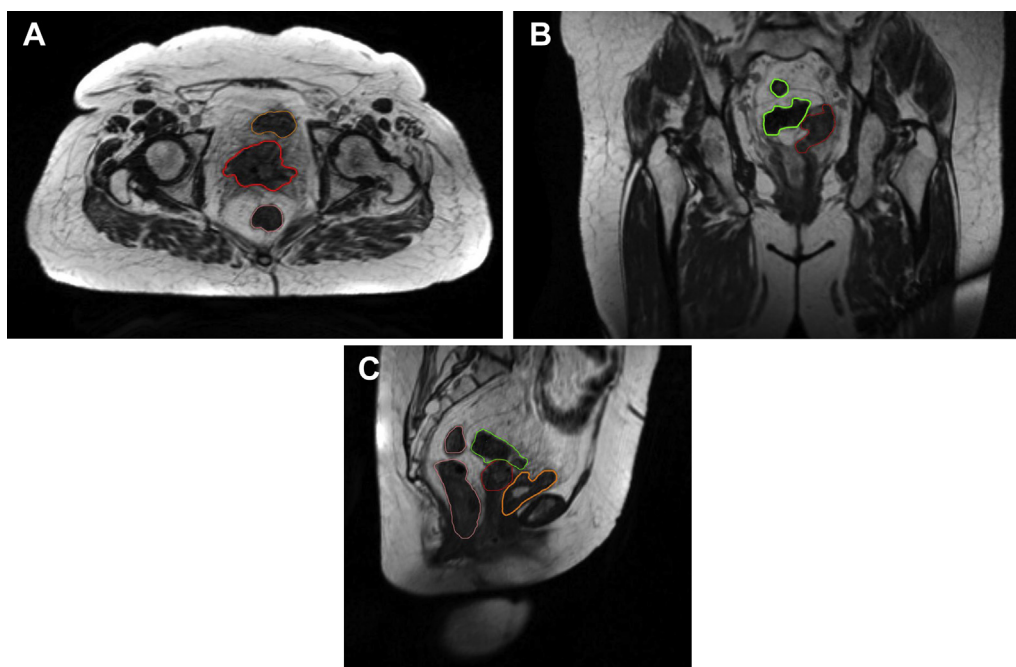
The organs-at-risk doses include combined doses from external beam radiation therapy and adaptive magnetic resonance–guided radiation therapy boost.



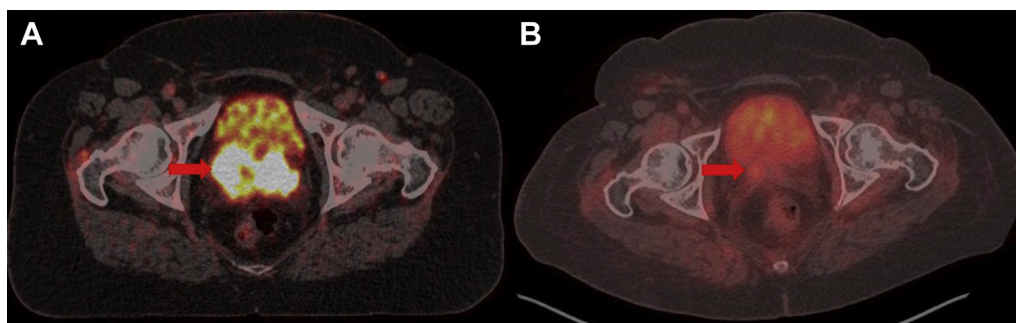
**Figure 2** Axial magnetic resonance imaging (MRI) scans of the patients before fraction 1 (A, B) and 8 (C, D) of the magnetic resonance–guided radiation therapy (MRgRT). Gross tumor volume (GTV, red) changed from 115 cm<sup>3</sup> to 83 cm<sup>3</sup> during the MRgRT boost. Visible are the bowel (green), rectum (pink), and bladder (orange).

imaging was performed through a sagittal plane to track the intrafractional motion of the target. No respiratory gating was used during the treatment as no intrafractional movement was detected. Cumulative dosimetry and planning aims are shown in [Table 1](#).

The patient tolerated the treatment well and tumor volume decreased from 115 cm<sup>3</sup> to 83 cm<sup>3</sup>, approximately 28% during the MRgRT ([Fig 2](#)). A subsequent clinical evolution at 2 months after the treatment was marked by the disappearance of bleeding and a significant



**Figure 3** A pelvic magnetic resonance imaging (MRI) 2 months after treatment demonstrated further decrease in the gross tumor volume (GTV, red). Visible are the bowel (green), rectum (pink), and bladder (orange).



**Figure 4** Positron emission tomography (PET) scan before (A) and 3 months after the treatment (B). Red arrows denote tumoral target.

further decrease in the tumor size to 32 cm<sup>3</sup>, which is an approximately 61% volume reduction since the end of MRgRt boost treatment (Fig 3). The patient received an additional 2 cycles of adjuvant chemotherapy, and a positron emission tomography–computed tomography performed 3 months after the radiation therapy revealed near total response with no major side effects (Fig 4). The patient remains asymptomatic without clinical evidence of disease 9 months after completion of treatment.

## Discussion

A concomitant chemoradiotherapy and EBRT followed by brachytherapy boost is considered to be the standard of care in patients with locally advanced cervical cancer.<sup>7</sup> Generally, it is accepted that increasing the dose to the target volume with brachytherapy will lead to increased local control. The inclusion of brachytherapy in the treatment of cervical cancer has been shown to improve local control and overall survival.<sup>3,8</sup> However, this operator-dependent technique requires specific skills and may not be available globally.<sup>9</sup> If this is not available, timely referral to a high volume GYN center with brachytherapy expertise is recommended. When brachytherapy is not available and the patient declines referral to an expert center, as in our case, properly designed EBRT boost could be considered. However, it is important to recognize that the higher dose needed for optimal outcomes cannot be achieved without brachytherapy.<sup>10</sup> In addition to its dose limitations, replacing brachytherapy with EBRT boost is associated with increased toxicity. Albuquerque et al<sup>11</sup> recently showed that the percent rectal circumference receiving 15 Gy (PRC15) from stereotactic ablative radiation therapy boost was associated with high-grade toxicity and recommended limiting the PRC15 to less than 62%. Two-year cumulative grade  $\geq 3$  rectal toxicity was 26.7%. Although PRC15 in our case was 27.8%, longer follow-up is warranted to assess late toxicities.

Bowel and nonbony targets are difficult to visualize on cone beam computed tomography daily setup, which may result in missing the target and delivering a high dose to the bowel. However, MR-guidance allows accurate visualization and alignment of the target. Furthermore, use of MRgRT provides the opportunity for daily adaptive planning to avoid critical structures, particularly the bowel, which may migrate into the field as part of normal day-to-day variation. The MRgRT also provides the best targeting available as it allows direct visualization of the tumor during treatment delivery. With the continuous imaging of the target, the patient can be coached by the therapists during treatment, or even see the real-time cine-MRI and actively adjust his or her respiratory movements, to ensure the irradiated site and the tumor site are overlapping.

## Conclusions

The MRgRT boost could be an option when brachytherapy is not available and the patient declines referral to an expert center. With accurate visualization of the anatomy on daily setups and during treatment, we felt confident in our ability to deliver precise and on-target treatment. However, it is important to acknowledge the dose limitation and increased toxicity with EBRT boost.

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