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Whole pelvic intensity-modulated radiotherapy for gynecological malignancies: A review of the literature

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Abstract

Radiation therapy has long played a major role in the treatment of gynecological malignancies. There is increasing interest in the utility of intensity-modulated radiotherapy (IMRT) and its application to treat gynecological malignancies. Herein, we review the state-of-the-art use of IMRT for gynecological malignancies and report how it is being used alone as well as in combination with chemotherapy in both the adjuvant and definitive settings. Based on dosimetric and clinical evidence, IMRT can reduce gastrointestinal, genitourinary, and hematological toxicities compared with 3D-conformal radiotherapy for gynecologic malignancies. We discuss how these attributes of IMRT may lead to improvements in disease outcomes by allowing for dose escalation of radiation therapy, intensification of chemotherapy, and limiting toxicity-related treatment breaks. Currently accruing trials investigating pelvic IMRT for cervical and endometrial cancers are discussed.
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Keywords: IMRT; Radiation therapy; Endometrial; Cervical; Gynecologic

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1. Background

Whole pelvic radiation therapy (WPRT) is commonly employed for multiple gynecologic malignancies in the neoadjuvant, adjuvant, and definitive settings. To treat involved and at-risk lymph nodes, multiple WPRT techniques have been developed, including 3D-conformal radiotherapy (3D-CRT) and more recently intensity-modulated radiotherapy (IMRT).

3D-CRT typically employs either two (AP/PA), three (PA and opposed laterals), or four (AP/PA and opposed laterals) photon fields. Such WPRT techniques, while effective in controlling disease, result in irradiation of large volumes of small bowel, rectum, bladder and femoral heads to the full prescribed treatment dose, usually 45–50.4 Gy in 25–28 fractions. In the adjuvant setting, such as following hysterectomy for endometrial cancer, small bowel may fall into the vacated space in the true pelvis, increasing bowel volume irradiated. This can increase the risks of acute and late gastrointestinal (GI) complications, limiting the dose that can be delivered to paracervical and nodal tissues at highest risk for recurrence. As a result, genitourinary (GU) and GI toxicities are commonly experienced in patients receiving conventional WPRT after hysterectomy [1,2].

1.1. Emergence of IMRT

IMRT has evolved as a technique that can treat tumor or areas at risk of recurrence and nodal metastasis, while sparing adjacent normal tissues from high-dose irradiation. IMRT is an advanced form of radiotherapy that allows a varying intensity of irradiation across the path of the treatment beam. Fig. 1 demonstrates comparison WPRT plans using standard AP/PA, 4-field (AP/PA and opposed laterals), and IMRT techniques. As opposed to conventional treatment planning techniques that utilize a variety of configurations of beams, wedges, and beam weightings until a desirable treatment plan is achieved, IMRT employs inverse planning in which dose-volume constraints and/or dose limits are inputted and an automated process derives an optimal treatment plan [3]. By selecting constraints to prioritize tumor volume coverage and normal tissue sparing, IMRT produces a more conformal treatment with irradiation to a desired target volume while decreasing dose to normal pelvic tissues, including small bowel, bladder, rectum, and femoral heads (Fig. 1). IMRT is widely utilized to achieve more conformal treatment of irregular treatment volumes, including the treatment of prostate, GI, and head and neck cancers.

The major potential advantage of IMRT in treating gynecological malignancies is the ability to shape a dose distribution that delivers a lower dose to intraperitoneal pelvic contents than surrounding pelvic lymph nodes, making it possible to reduce acute and late side effects of treatment. Dosimetrically, studies have shown that intensity-modulated whole pelvic radiation therapy (IM-WPRT) treatment plans provide highly conformal dose to areas at risk of recurrence, with considerable sparing of surrounding normal tissues [4,5], including bone marrow [6,7], bowel, kidney (with extended para-aortic treatment), spinal cord [8], rectum, and bladder [9].

2. Dosimetric studies

Early dosimetric studies sought to demonstrate the advantages of IM-WPRT. One study reported by Heron et al. [9] compared alternative plans for 10 patients with gynecologic malignancies who underwent CT-planning for adjuvant radiotherapy. 3D-CRT was set up using a four-field technique, compared with seven-field IMRT plans, and patients were treated to 45 Gy in 25 fractions to the internal, external, and common iliac nodal groups and upper 4 cm of the vagina. IMRT showed a reduced volume receiving >30 Gy compared to 3D-CRT in the following organs: small bowel reduced by 52%, rectum by 66%, and bladder by 36%. This study showed IMRT can reduce normal tissue volume irradiated, which could lead to fewer acute and late side effects in these organs.

A dosimetric study by Lujan et al. [7] presented the potential of reduced hematologic toxicity with bone marrow sparing IM-WPRT (BMS-IM-WPRT). For 10 patients with cervical or endometrial malignancies, three radiotherapy treatment plans to 45 Gy were compared: four-field WPRT plan, IM-WPRT plan, and BMS-IM-WPRT. Dose-volume histograms (DVHs) showed BMS-IM-WPRT reduced the volume of BM receiving >50% of the prescribed dose (60.0%) compared with IM-WPRT (75.7%, $p < 0.003$) and four-field WPRT (87.4%, $p < 0.001$), while still allowing for similar target coverage and normal organ sparing. BMS-IM-WPRT plans substantially reduced the volume of iliac crests irradiated to >20 Gy and allowed for more modest improvements in lumbar spine and sacrum doses. The authors of this study recommended focusing on iliac crests in consideration of BMS-IM-WPRT, especially as 50% of the total pelvic BM resides in the iliac crests. This study supports that BMS-IM-WPRT reduces BM volume irradiated while maintaining other improvements in critical structure doses achieved with non-BMS-IM-WPRT. This approach was adopted in recent IMRT trials, such as radiation therapy oncology group (RTOG) 0529 that evaluated pelvic IMRT for anal cancer [10]. Taken together, BMS-IM-WPRT may allow for improved chemotherapy compliance and further optimization of the systemic and radiation modification effects of chemotherapy [6].

3. Reports on toxicity and efficacy

Following dosimetric comparisons, clinical studies of IM-WPRT were pursued. Mundt et al. [11] compared 15 patients with gynecologic malignancies who received 45 Gy