

Intensity-Modulated Radiation Therapy in Gynecologic Malignancies: Current Status and Future Directions

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Abstract: Radiation therapy is used as either definitive or adjuvant therapy following surgery in many gynecologic malignancies. Though effective, radiation therapy is limited by the adverse sequelae that result from normal tissues receiving external-beam radiation. A novel approach, intensity-modulated radiation therapy, can overcome these limitations by sparing the tissue surrounding the malignancy through conforming the dose to the shape of the target in three dimensions. This review provides an overview of current use, published research, and ongoing studies of intensity-modulated radiation therapy.

Radiation therapy (RT) has a long history in the treatment of gynecologic cancers. In fact, RT was first used in gynecologic cancer more than a century ago.¹ Currently, RT is used as either definitive or adjuvant therapy following surgery in many gynecologic tumors, notably cervical, vulvar, and endometrial cancer. It is also combined with chemotherapy in women with locally advanced cervical tumors.

In cervical cancer patients, treatment entails a combination of external-beam pelvic irradiation followed by intracavitary brachytherapy, whereby radioactive sources are placed in close proximity to the tumor. Patients treated following surgery typically undergo pelvic RT alone, which is delivered over 4–6 weeks. In select tumors, notably endometrial cancer, brachytherapy may be delivered as the sole adjuvant therapy, particularly in women undergoing pelvic lymph node dissection. Some patients require more comprehensive treatment, including extended-field (pelvis plus para-aortic), abdomino-pelvic (“whole abdominal”), or pelvic-inguinal RT, depending on the primary site and disease involvement.

Although effective, RT has a number of limitations in gynecologic malignancies. First of all, external-beam fields encompass considerable volumes of normal tissues (small bowel, bladder, rectum, etc), resulting in a variety of adverse sequelae.^{2–4} The total dose delivered is constrained by concerns over normal tissue injury, precluding the delivery of higher and potentially more effective doses in high-risk patients, including those with unresectable tumors or involved lymph nodes.⁵ Finally, brachytherapy is not feasible or desirable in all patients, due to unfavorable anatomy, bulky tumor masses, or comorbid conditions.⁶

Keywords

Intensity-modulated radiation therapy, gynecologic malignancies, multi-leaf collimator

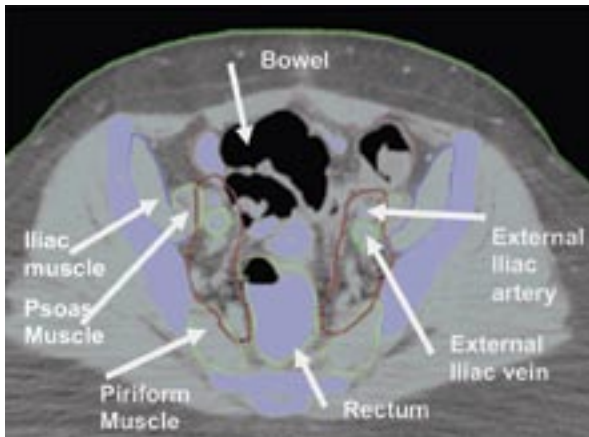


Figure 1. Axial computed tomography (CT) slice through the mid-pelvis in an endometrial cancer patient treated with intensity-modulated pelvic radiation therapy. The clinical target volume (CTV) (red) encompasses the internal and external iliac lymph node regions. Highlighted are various pelvic muscles that are used to help define the limits of the CTV. Normal tissues are also contoured and are used as avoidance structures in the planning process.

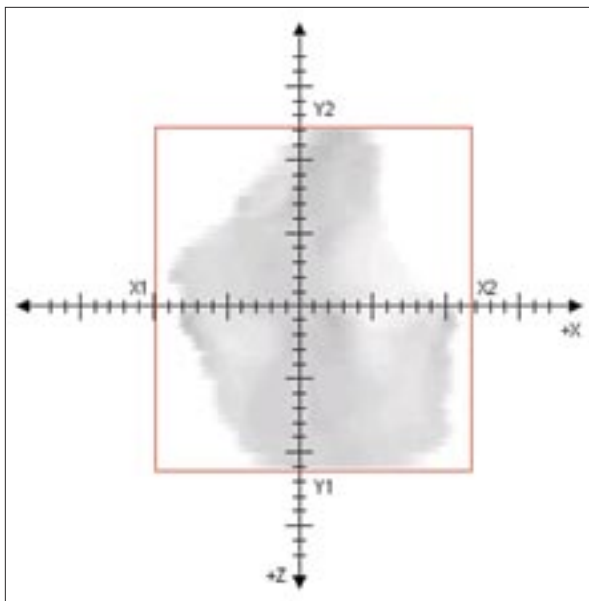


Figure 2. Intensity profile of a treatment beam in a patient undergoing intensity-modulated pelvic radiation therapy. The dark areas correspond to high-intensity regions and the light areas correspond to low-intensity regions. The other treatment beams have unique intensity profiles.

In recent years, a novel approach to the planning and delivery of external-beam RT has been introduced, known as intensity-modulated RT (IMRT), which may overcome these limitations. Unlike conventional techniques, IMRT conforms the prescription dose to the shape of the target tissues in three dimensions, thereby sparing the surrounding normal tissues.^{7,8} Highly conformal treatment plans may minimize the incidence of severe RT-related toxicity, improving patient quality of life. IMRT may also enable safe escalations of doses in high-risk patients, improving tumor control. It may even represent an alternative to, and potentially a replacement for, brachytherapy. Not surprisingly, gynecologic tumors are the fastest growing disease site treated with IMRT in the United States.⁹

The purpose of this review is to provide an overview of IMRT and its application in gynecologic malignancies. Published studies and ongoing research focusing on this novel technology in these patients are also discussed.

IMRT Planning and Delivery

Unlike conventional RT, IMRT planning is an inverse process, whereby the planner first delineates the target and surrounding normal tissues on a computed tomography (CT) scan with the patient immobilized in the treatment position. This “planning scan” is used to outline areas that require treatment (target) and those that should be avoided (normal tissues). Two separate targets are typically delineated: a gross tumor volume (GTV), consisting of the primary tumor as defined on imaging studies and physical examination, and a clinical target volume (CTV), comprised of the GTV plus areas of potential microscopic disease in regional lymph nodes and other tissues.

Target volumes differ from patient to patient based on tumor site and pathologic features. In women with cervical cancer, for example, the CTV consists of the cervix and uterus (if present), parametria, presacral region and regional lymph nodes (common, internal, and external iliacs). In vulvar cancer patients, the vulva and inguinal lymph nodes are also included. After the CTV is delineated, a planning target volume (PTV) is then generated by adding a margin to the CTV, accounting for organ motion and setup uncertainty, typically ranging from 1–2 cm (Figure 1).

IMRT treatment planning continues with the selection of dose volume constraints for the PTV and normal tissues. Such constraints are entered into a sophisticated optimization program. During the optimization process, each beam is divided into small “beamlets” of individually varied intensity. The resultant intensity profile of each beam is complex (Figure 2), unlike the homogenous beams used in conventional RT. This inverse process is in contrast to the iterative (“trial and error”) approach used in

conventional RT. The result is that whereas conventional planning produces an acceptable plan, IMRT produces the optimal plan. When cast into a patient, conformal dose distributions are achieved with rapid dose gradients outside the PTV, resulting in sparing of normal tissues (Figure 3).

IMRT is delivered at most institutions using a linear accelerator equipped with a multileaf collimator (Figure 4), whose “leaves” (0.5–1 cm in width) move in and out of the beam’s path under computer control. The longer the leaves remain open at a particular position, the greater the intensity of radiation.

Preclinical Data

Numerous investigators in the United States and abroad have presented preclinical (planning) studies of IMRT in gynecologic cancer patients. Although such studies do not include patients treated with IMRT, they are important because they demonstrate the feasibility of IMRT in various disease sites. Moreover, many compare IMRT planning with conventional techniques, illustrating potential benefits of this approach, notably in terms of both normal tissue sparing and the ability to escalate the dose, laying the foundation for clinical treatment studies.

Pelvic Radiotherapy

As the most common external-beam RT approach for treatment gynecologic malignancies, it is not surprising that most IMRT planning studies focus on pelvic RT. In their initial report, Roeske and coworkers^{10,11} at the University of Chicago compared intensity-modulated pelvic RT (IM pelvic RT) and conventional pelvic RT plans in 10 patients (5 cervical, 5 endometrial cancers). All IM pelvic RT plans were found to be highly conformal, providing excellent PTV dose coverage while reducing the volume of small bowel volume irradiated to the prescription dose by a factor of two (17.5% vs 33.8%; $P=0.005$), compared to conventional RT planning. The bladder and rectal volumes irradiated were both reduced by 23%. Others have reported similar results confirming the potential benefits of IMRT planning in patients undergoing pelvic RT (Table 1).^{10,12-15}

Although most attention has focused on the small bowel and rectum, another “organ” that could be spared using IMRT is the bone marrow (BM). Fifty percent of the total body BM reserve is located in the pelvic bones,¹⁶ within conventional pelvic RT fields. Not surprisingly, given the exquisite radiosensitivity of BM, women undergoing pelvic RT plus chemotherapy may develop significant hematologic sequelae, resulting in unplanned treatment breaks, dose reductions, and missed chemotherapy cycles. To evaluate its ability to spare the BM, Lujan and colleagues¹⁷ included the iliac crest BM in the IMRT

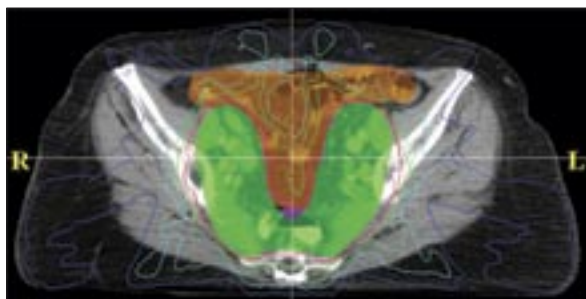


Figure 3. An intensity-modulated pelvic RT plan in a patient with cervical cancer. The different lines correspond to different dose levels (isodose lines). In this plan, the high-dose isodose lines conform to the shape of the lateral lymph nodes and the pre-sacral region, resulting in a U-shaped dose distribution that spares the centrally placed small bowel.

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optimization process and found significant sparing of the BM irradiated without compromising PTV coverage or sparing of other tissues (Figure 5). Others have reported similar favorable results.¹⁵

More Comprehensive Volumes

Multiple investigators have also reported significant benefits using IMRT planning in patients treated with more comprehensive fields. In a study of 10 patients undergoing extended-field RT, Portelance and coauthors¹⁸ compared IMRT with conventional RT planning. Although equivalent PTV coverage was achieved, IMRT reduced the volume of all normal tissues irradiated. Compared with a 2-field approach, the volume of small bowel, bladder, and rectum irradiated was reduced by 61%, 96%, and 71%, respectively. Compared with a 4-field approach, corresponding reductions were 60%, 93%, and 56%. Others have noted similar results.¹³

IMRT planning may also improve the delivery of abdomino-pelvic RT. Given the inclusion of the entire peritoneal cavity within the target volume, the benefit of IMRT planning is not just sparing of the small bowel. Rather, it is used to improve coverage of the peritoneal cavity (by obviating conventional kidney blocks), thereby improving tumor control, and to improve dose homogeneity, reducing the risk of adverse sequelae. Hong and coworkers¹⁹ compared IMRT and conventional abdomino-pelvic RT plans in 10 endometrial cancer patients. IMRT improved coverage of the peritoneal cavity, particularly near the kidneys, and it reduced dose heterogeneity. The volume of pelvic bones (and thus BM) receiving at least 21 Gy was reduced by 60%. Duthoy and colleagues²⁰ reported comparable results in ovarian cancer patients.

Beriwal and coauthors²¹ recently compared conventional and IMRT planning in 12 vulvar cancer patients undergoing pelvic-inguinal RT. The volume of the small

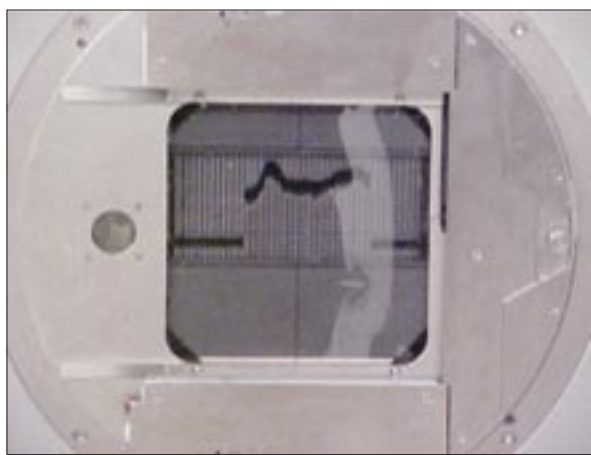


Figure 4. (Top) A modern linear accelerator equipped with a multileaf collimator. (Bottom) Multileaf collimator.

bowel, rectum, and bladder receiving at least 30 Gy was reduced using IMRT by 27%, 49%, and 26%, respectively. Surprisingly, no benefit was seen in sparing of the femoral heads. In a similar study, Garofalo and coworkers²² noted improvements in the volume of small bowel, rectum, and bladder irradiated, along with considerable sparing of the femoral heads in patients treated with pelvic-inguinal IMRT. Femoral head sparing is an important potential benefit of IMRT in this setting given the long-term risks of bone fractures in these patients.²³

Dose Escalation

Several investigators have evaluated IMRT as a means of delivering higher-than-conventional doses in patients with gynecologic malignancies. In a cohort of 10 post-hysterectomy patients, D'Souza and colleagues²⁴ reported the feasibility of escalating radiation doses to 54 Gy with IM-pelvic RT, while maintaining the volume of small bowel volume receiving at least 45 Gy below levels achieved with

conventional planning and conventional doses. Although modest, escalating dose to 54 Gy in these patients may help improve pelvic control rates in the postoperative setting. However, a concern with this approach is that small volumes of the small bowel receive doses between 55 and 60 Gy, which increases the risk of small bowel injury.

Attention has also been focused on delivering higher doses using the simultaneous integrated boost (SIB) technique, whereby higher doses per fraction are delivered to selected portions of the CTV. Such an approach is appealing because it escalates the dose delivered without increasing the overall treatment course. Lujan and coauthors²⁵ evaluated the SIB approach to escalate dose to involved pelvic nodes in patients undergoing IM pelvic RT and found that a dose of 54 Gy (in 2.14-Gy fractions) could be delivered to the involved nodes and 45 Gy (in 1.8-Gy fractions) to the remaining PTV without compromising sparing of the normal pelvic tissues. It remains unclear, however, whether this modest dose escalation is efficacious.

Investigators at Washington University have reported the feasibility of escalating doses to metastatic paraortic lymph nodes (identified on positron emission tomography [PET]) using the SIB approach.²⁶ Total doses of 59.4 Gy (in 2.12-Gy fractions) are delivered to the involved nodes, while delivering 50.4 Gy (in 1.8-Gy fractions) to uninvolved paraortic sites and the pelvis. Ahmed and coworkers²⁷ demonstrated the feasibility of delivering a dose of 60 Gy in 2.4-Gy to involved paraortic nodes, with the remainder of the paraortic region treated with 45 Gy in 1.8-Gy fractions. Kavanagh and colleagues²⁸ described a SIB approach to treating the primary tumor and involved pelvic nodes in cervical cancer patients with an intact uterus.

Alternative to Brachytherapy

IMRT as an alternative to intracavitary brachytherapy in cervical cancer patients has recently received attention.^{29,30} IMRT is an appealing approach in many patients, particularly those with bulky primary tumors and those with significant comorbidities that preclude anesthesia. In cervical cancer patients unable to undergo brachytherapy, Roeske and coworkers³¹ reported that IMRT allowed the delivery of doses as high as 81 Gy. Low and coworkers^{32,33} have developed an IMRT approach in patients with bulky cervical tumors who are inadequately treated with standard brachytherapy. As envisioned, an applicator is placed in the vagina and uterus, localizing the target tissues and reproducibly positioning the bladder and rectum. Magnetic resonance imaging or PET used to delineate the target. Treatment is delivered using high-dose schedules.

Guerrero and colleagues recently presented a SIB approach as a replacement for the conventional two-phase

approach of pelvic RT followed by brachytherapy. The proposed dose schedule is 70 Gy (in 2.8-Gy daily fractions) to the primary tumor and 45 Gy (in 1.8 Gy daily fractions) to the pelvic lymph nodes.³⁴ Investigators at the University of Colorado reported the feasibility of the SIB approach in women unable to undergo brachytherapy.³⁵

Although attractive, considerable controversy exists regarding the use of IMRT in lieu of brachytherapy, given the long history of excellent results with brachytherapy. Clinical trials are clearly needed to evaluate the efficacy of this novel approach. Until then, such approaches should be considered experimental and should not be performed in women who are eligible for traditional brachytherapy, unless under the auspices of a clinical trial.

Clinical Data

Based on these promising preclinical results, several centers in the United States and abroad have begun treating gynecology patients with IMRT. To date, most of the published clinical experience has focused on women treated with IM pelvic RT and conventional doses. Early experience in these patients has been favorable, with low rates of RT-related toxicity and excellent tumor control. In contrast, little to no clinical data exist regarding the use of IMRT in women treated with more comprehensive fields, with higher-than-conventional doses, or in place of brachytherapy.

In a series of reports,^{36,37} Mundt and coworkers at the University of Chicago evaluated acute toxicity in patients treated with conventional-dose IM pelvic RT. In their most recent report,³⁷ acute gastrointestinal (GI) toxicity in 40 IM pelvic RT patients was compared to a comparable earlier cohort of conventional RT patients. Patients receiving IM-pelvic RT experienced less grade 2 or higher acute GI toxicity (60% vs 91%; $P=.002$). Moreover, the percentage of IM-pelvic RT and conventional patients requiring no (or infrequent) antidiarrheal medications was 75% and 34% ($P=.001$). While less genitourinary toxicity (10% vs 20%) was observed, this difference did not reach statistical significance possibly due to the small number of patients evaluated.

In a subsequent report, Roeske and colleagues³⁸ analyzed factors correlated with acute GI toxicity in IM pelvic RT patients. In a multivariate analysis, the most significant factor was the volume of small bowel receiving the prescription dose, providing additional support for the IM pelvic RT approach. In a cohort of 5 high-risk endometrial cancer patients treated with IM pelvic RT, Wong and coauthors¹⁵ noted “no unplanned treatment breaks or significant sequelae.”

Mundt and coworkers³⁹ recently reported a favorable chronic GI toxicity profile in a cohort of 30 patients

Table 1. Comparative Studies: Intensity-modulated Pelvic RT versus Conventional Pelvic RT

Author	↓Volume Receiving Prescription Dose		
	Small Bowel	Bladder	Rectum
Roeske et al ¹⁰	↓50%	↓23%	↓23%
Heron et al ¹²	↓51%*	↓31%*	↓66%*
Chen et al ¹³	↓70%	↓†	↓†
Ahamad et al ¹⁴	↓40–63%‡	↓†	↓†
Wong et al ¹⁵	↓95%	NS	NS

* Reduction in percent volume receiving 30 Gy or higher.

† Percentage reduction not stated.

‡ Dependent on planning target volume expansion used.

NS = not stated; RT = radiation therapy.

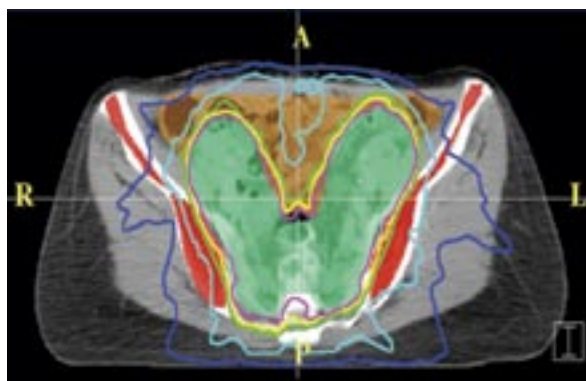


Figure 5. A bone marrow sparing intensity-modulated pelvic RT plan in a patient with cervical cancer. Compared to the non-BM sparing IMRT plan (Figure 3), this plan provides improved sparing of the bone marrow (red) by increasing the conformity of the isodose lines to the target tissues in the vicinity of the iliac crests.

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undergoing IM pelvic RT, with a median follow-up of 19.6 months. Compared to a balanced cohort of conventional pelvic RT patients, IM pelvic RT was associated with less chronic GI sequelae (11.1% vs 50%; $P=.001$). In a multivariate analysis controlling for age, stage, chemotherapy, surgery, brachytherapy, and length of follow-up, IMRT remained correlated with less GI sequelae (odds ratio, 0.16; 95% confidence interval, 0.04–0.67; $P=.01$).

Other clinical benefits of IMRT have also been reported. Brixey and colleagues⁴⁰ compared acute hematologic toxicity in patients undergoing pelvic RT with and without IMRT planning. Although sequelae were infrequent with RT alone regardless of technique, conventional RT patients receiving chemotherapy experienced more grade 2 or higher leukopenia (60% vs 31.2%; $P=.08$) and a lower white blood cell count nadir. The conventional

RT group also developed a lower neutrophil count nadir. Although the BM was not included as a constraint in the planning process, it was spared due to the highly conformal nature of the IMRT plans.

In a subsequent report, Mell and coauthors⁴¹ performed an analysis of 37 cervical cancer patients undergoing IM pelvic RT with concomitant cisplatin (40 mg/m²/week). Increased volume of the pelvic BM receiving low-dose radiation (≥ 10 Gy) was found to be predictive of an increased likelihood of acute hematologic toxicity, missed chemotherapy cycles, and reduced chemotherapy dose delivered. Importantly, this is the first report demonstrating that the benefits of IMRT may extend beyond the improved delivery and tolerance of RT to include improved delivery of chemotherapy. Current work is focused on optimizing BM-sparing IM pelvic RT plans and prospectively testing their impact on hematologic toxicity in chemoradiotherapy patients. BM-sparing IMRT approaches may not only chemotherapy dose intensification but also the use of potentially more effective multiagent regimens.

Taken together, these analyses provide strong evidence that the dosimetric benefits of IMRT planning may translate into clinical benefits, notably less RT-related toxicity. A concern, however, is whether the highly conformal IMRT plans designed to spare normal tissue may inadvertently also “spare” the tumor, adversely affecting tumor control. However, the published data to date have not supported this concern.

Kochanski and coauthors⁴² reviewed the outcome of 62 cervical cancer patients treated with IM pelvic RT at the University of Chicago. Forty-four (Group A) were treated with an intact uterus (40 received concomitant chemoradiotherapy). Eighteen (Group B) underwent primary surgery and adjuvant IM pelvic RT. At a median follow-up of 23 months, cancer recurred in 12 women, for a 3-year actuarial disease-free survival (DFS) rate of 72.7%. The 3-year DFS of Groups A and B were 67.8% and 78.9%, respectively. Group A patients with stage IB–IIA disease had a better 3-year DFS than those with stage IIB–IVA disease (80.9% vs 52.7%; $P=.049$). Five women failed in the pelvis, for a 3-year pelvic control rate of 87.5%. The 3-year pelvic control rate in Group A patients was 82.8% (93.3% stage IB–IIA, 67.4% stage IIB–IVA). In Group B, the 3-year pelvic control rate was 93.9%. These results compare favorably to published outcome studies of cervical cancer patients treated with conventional RT.

To address the same issue in endometrial cancer, Beriwal and coworkers⁴³ reviewed the outcome of 47 endometrial cancer patients treated with adjuvant IM pelvic RT and high-dose rate brachytherapy. With a

median follow-up of 20 months, no patient had pelvic recurrence. The 3-year actuarial rates of DFS and overall survival were 84% and 90%, respectively. In addition, Knab and colleagues⁴⁴ reviewed the outcome of 31 endometrial cancer patients (20 stage I–II, 11 stage III–IV) undergoing adjuvant IM pelvic RT. Seventeen (54%) had unfavorable histologies. Twelve underwent vaginal brachytherapy and 5 received neoadjuvant or concomitant chemotherapy. At a median follow-up of 24 months, 5 patients had disease recurrence, for a 3-year actuarial DFS of 80.6%. Pelvic control was excellent, with all 5 patients failing in extrapelvic sites, again demonstrating the efficacy of the IMRT approach.

Published outcome studies involving larger treatment volumes or higher doses are more limited. Beriwal and coworkers²¹ treated 12 vulvar cancer patients with intensity-modulated pelvic-inguinal RT. Seven were treated preoperatively (with concomitant chemotherapy) and 5 postoperatively. Of the 7 preoperative patients, 5 achieved a complete clinical response, of whom 3 had a complete pathologic response. None developed a local recurrence. Of the 5 postoperative patients, 3 failed locally (2 of the 3 did not receive treatment to the vulva) and were salvaged with additional treatment. Overall, grade 2 or higher dermatitis and small bowel rectal toxicities were seen in 75%, 25%, and 8.3% of patients, respectively. No late grade 3 sequelae have been noted.

Gerszten and colleagues⁴⁵ treated 22 consecutive cervical cancer patients with concurrent cisplatin and extended-field RT using IMRT. In addition to the cervix, uterus, parametria, presacral space, upper vagina, and pelvic common iliac lymph nodes, the para-aortic nodes were treated to the level of L1. The prescribed dose was 45 Gy in 1.8-Gy daily fractions delivered with a simultaneous boost to 55 Gy in 2.2-Gy fractions to involved nodes. Patients were followed weekly and assessed for toxicity. The treatment was well-tolerated as all patients completed the prescribed course. Only 2 patients required treatment breaks (for 2 and 3 days) as a result of bone marrow toxicity. Two patients had their chemotherapy held during the last week secondary to neutropenia.

Kavanagh and coworkers²⁸ treated 7 advanced, metastatic, or recurrent cervical cancer patients with a SIB approach (6 received concomitant chemotherapy). Three underwent extended-field RT and 6 received brachytherapy. Complete responses were observed in all patients. At 3 months, 4 patients were alive without evidence of disease, and 2 were alive with disease. Two grade 3 toxicities were seen, resulting in chemotherapy treatment delays. Of the remaining 5 patients, 4 developed grade 2 upper GI toxicity and 1 developed grade 2 lower GI toxicity. One patient developed a grade 2 genitourinary sequelae.

Issues and Concerns

Despite the growing data supporting the use of IMRT, clinical outcome studies in gynecology patients treated with IMRT remain limited. Moreover, the available reports consist of relatively small patient numbers, focus primarily on IM pelvic RT, and are mostly limited to assessments of acute toxicity. To date, few series have sufficiently long follow-up to assess chronic toxicity and tumor control. Additional studies are clearly needed with larger patient numbers and longer follow-up to assess whether the dosimetric benefits seen with IMRT truly translate into long-term clinical benefits. To this end, the Radiation Therapy Oncology Group (RTOG) has recently launched RTOG trial 0418, the first multi-institutional study of IM pelvic RT in cervical and endometrial cancer patients.

Prospective studies are also important in order to assess the risks of IMRT. Although IMRT reduces the volume of normal tissue receiving high doses, the volume of these tissues receiving low doses is increased. This “dose dumping” effect has raised concerns regarding second malignancies.⁴⁶ To date, no second malignancies have been reported in gynecologic IMRT patients. Nonetheless, such concerns can be allayed only by long-term, careful follow-up of large cohorts of patients.

Another potential concern with gynecologic IMRT is that treatment planning is based solely on CT imaging. More sophisticated imaging approaches may help define targets, improving IMRT planning. As noted earlier, PET-guided IMRT approaches are being explored.²⁶ Nanoparticle approaches may improve the detection of involved lymph nodes.⁴⁷ Novel imaging approaches may augment the delineation (and thus sparing) of normal tissues, including technetium Tc 99^m spectroscopy of bone marrow.⁴⁸ Image-guided approaches are also being explored to address concerns regarding organ motion and, in cervical cancer, tumor regression during a course of IMRT.⁴⁷

Perhaps one of the greatest limiting factors of the broad implementation of the use of IMRT is organ motion, which is of particular concern in patients with an intact uterus. Unfortunately as a result of both interfractional and intrafractional organ motion, the delivered dose cannot be accurately predicted. Several solutions, however, have been proposed. Maleike and coauthors⁴⁹ addressed the problems with interfractional organ motion by using stochastic properties to better account for the dose distribution and provide the physician with information about motion-related risks of different plans. This particular approach provides the physician with a diagram that shows the variability of each individual plan's dose volume histogram. Others have proposed using image-guided RT to reduce the uncertainty of the organs location prior to treatment.⁵⁰ Van de Bunt and coworkers⁵¹ have proposed

using the patient's tumor response combined with image-guided RT to customize IMRT as the tumor responds. In a study of 14 cervical cancer patients, the group found that after a dose of 30 Gy, gross tumor volumes decreased on average by 46% (range, 6.1–100%). They demonstrated that the intratreatment tumor volume remained covered by the 95% isodose line. The problem of organ motion remains a challenging one.

Finally, standards and guidelines for gynecologic IMRT need to be developed. Presently, none exists regarding any aspect of gynecologic IMRT. Numerous questions remain unanswered. Which gynecology patients should receive IMRT? Which tissues should be irradiated and which avoided? How should the CTV be delineated? What are the optimal planning constraints? What makes an IMRT plan acceptable? To address these questions, the Gynecologic IMRT Working Group was formed, consisting of 45 institutions throughout the United States, Canada, Europe, and Asia. This group is currently developing a consensus statement on IMRT planning in gynecology patients undergoing adjuvant IM pelvic RT.⁴⁸ In addition, the RTOG, Gynecologic Oncology Group, and the European Organization for Research and Treatment of Cancer recently sponsored a consensus conference on CTV design in the posthysterectomy setting, the results of which will soon be published. Such guidelines will help not only clinicians interested in adopting gynecologic IMRT. They will also aid cooperative groups in the development of prospective clinical trials.

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