Imaging across the Life Span: Innovations in Imaging and Therapy for Gynecologic Cancer[1]

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The focus of this article is radiation therapy for gynecologic cancers, with emphasis on imaging-based treatment planning and delivery. For the various gynecologic cancers, radiation oncologists rely on essential clinical information to triage treatment options, and various imaging studies are performed for treatment planning and radiation therapy delivery. A practical approach is provided to help radiologists tailor their reports for the needs of their radiation oncology and gynecologic oncology colleagues, to optimize multidisciplinary care for patients with gynecologic cancer. Template radiology reports are proposed to address the specific information needs of oncologists at each phase—before, during, and after treatment. Fueled by the rapid progress in engineering and computer sciences during the past 2 decades, remarkable advances have been made in anatomic, functional, and molecular imaging and in radiation treatment planning and delivery in patients with gynecologic cancer. Radiation therapy has evolved from a nontargeted approach to a precisely targeted, highly conformal treatment modality, to further improve treatment outcomes and reduce morbidity. High-quality imaging has become essential for staging of the disease, delineation of tumor extent for treatment planning and delivery, and monitoring therapy response. Anatomic and functional imaging has also been shown to provide prognostic information that allows clinicians to tailor therapy on the basis of personalized patient information. This field is an area of active research, and future clinical trials are warranted to validate preliminary results in the field.

Abbreviations: CTV = clinical target volume, FDG = fluorine 18 fluorodeoxyglucose, FIGO = International Federation of Gynecology and Obstetrics, GTV = gross target volume, IMRT = intensity-modulated radiation therapy, PTV = planning target volume, RECIST = Response Evaluation Criteria in Solid Tumors, SUV_{max} = maximum standardized uptake value, 3D = three-dimensional

RadioGraphics 2014; 34:1062–1081

Published online 10.1148/rg.344130099

Content Codes: CT MR OB OI

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Funding: The research was supported by the National Institutes of Health (grant number R01-CA71906).

SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

- Describe the role of radiation therapy in patients with gynecologic cancer.
- Explain the role of imaging in pretreatment evaluation and radiation therapy planning for gynecologic cancer.
- Describe the use of advanced imaging modalities for therapy in patients with gynecologic cancer.

See www.rsna.org/education/search/RG.

Introduction

Gynecologic cancer remains an important health problem for women worldwide. Uterine cancer is the most common gynecologic malignancy in the Western world, including the United States, and is the second most common cause of deaths from gynecologic cancer (1). The incidence of and mortality from cervical cancer have decreased steadily in the Western world during the past 5 decades with the implementation of successful screening programs. Cervical cancer continues to be one of the most common and fatal cancers in

TEACHING POINTS
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Table 1: Roles of Chemotherapy and Radiation Therapy in the Treatment of Gynecologic Cancers in Relationship to Surgery

Type of Therapy	Description of Therapy
Primary (definitive) therapy	A course of radiation therapy or chemotherapy (or both) without any surgery, in which the goal of treatment is curative
Neoadjuvant therapy	A course of radiation therapy or chemotherapy (or both) administered before surgery with the aim of augmenting the surgical outcome
Adjuvant therapy	A course of radiation therapy or chemotherapy (or both) administered after surgery with the aim of eradicating microscopic locoregional (radiation therapy) or distant (chemotherapy) residual cancer cells
Palliative therapy	Typically, a short course of radiation therapy or chemotherapy (or both) with the aim of reducing cancer symptoms such as pain or obstruction; typically, the patient has stage IV cancer, and cure is not possible

women in the developing world; cervical cancer led to approximately 275,000 deaths worldwide in 2008, about 88% of which occurred in developing countries (2). Although ovarian cancer is less common, it is fatal much more often than any other gynecologic tumor. Similarly, vaginal and vulvar cancers continue to pose a serious health threat worldwide.

Radiation therapy has played an important role in the treatment of gynecologic cancers. Concurrent advances in tumor imaging and treatment delivery technologies have spawned a paradigm shift in radiation therapy from two-dimensional to three-dimensional (3D) targeted treatment planning. This shift has profoundly changed the field of radiation oncology in the past 10–15 years.

Simultaneously, progress with both surgical techniques and systemic chemotherapy has improved treatment outcomes with the use of multimodality therapy. For these three key treatment modalities (radiation therapy, surgery, and chemotherapy), advanced imaging plays an essential role in the diagnosis and treatment of gynecologic cancers with a multimodality therapy strategy. Although imaging is of great importance in detecting lesions and differentiating cancer from other etiologies, the contributions of imaging to medical, surgical, and radiation therapy change once the definitive tissue diagnosis had been made with surgical or imaging-guided biopsy. After the diagnosis is made, the focus of tumor imaging shifts to staging of the disease, delineation of tumor extent for treatment planning and delivery, and monitoring response.

From a historical perspective, radiology and radiation oncology have a unique past. After divergent paths for decades, these two distinct specialties are becoming more closely related to each other for the optimal treatment of cancer. Advanced imaging is essential to radiation therapy for *(a)* the evaluation of the extent of tumor involvement for pretherapy staging and prognostic assessment, *(b)* tumor delineation for targeting in radiation therapy planning, *(c)* the evaluation of therapy response after or during the course of treatment, and *(d)* the prediction of early response and outcome, an emerging role that enables potential adaptive treatment.

Teaching Point

The purpose of this article is to encourage radiologists to provide high-quality imaging and radiology reports to facilitate collaboration with radiation oncologists and gynecologic oncologists, to provide optimum care for patients with gynecologic cancer. First, the types of radiation therapy for gynecologic cancer are reviewed, followed by the imaging modalities for pretreatment staging and prognosis. Then the principles of therapy and the role of imaging are covered for various types of gynecologic cancers, followed by the role of multimodality imaging in radiation therapy. Finally, the use of imaging for early response assessment during therapy and for early outcome prediction is discussed.

Radiation Therapy Modalities in Gynecologic Cancer

Therapeutic radiation plays an integral part in the multimodality treatment of patients with gynecologic cancers (Tables 1, 2). Several radiation-based modalities, including 3D conformal external beam radiation therapy, intensity-modulated radiation therapy (IMRT), and brachytherapy (implant radiation), as well as novel stereotactic delivery approaches, have been incorporated into the paradigm for treatment of gynecologic cancers. It is important for radiologists to understand the radiation therapy options for the specific types of gynecologic cancers and their relevant clinical information, such as clinical staging, to optimize the role of imaging at various times in the treatment.

Table 2: Radiation Therapy for Gynecologic Cancers

Site and Stage of Cancer	Role of Radiation Therapy	Area Treated with External Radiation Therapy	Brachytherapy Group
Cervix			
I–IIA	Adjuvant*	Pelvic with or without paraaortic nodes	Selected patients
IIB–IVA†	Primary	Pelvic with or without paraaortic nodes	All patients
IVB, recurrent	Palliative	Multiple sites	NA
Endometrium			
I–II	Adjuvant	Pelvic with or without paraaortic nodes	Selected patients
IIIA–IVA	Adjuvant	Pelvic with or without paraaortic nodes	Selected patients
Medically inoperable (all stages)‡	Primary	Pelvic with or without paraaortic nodes	All patients
Recurrent	Primary	Pelvic with or without paraaortic nodes	All patients
Metastatic	Palliative	Multiple sites	NA
Vagina			
I–IIA	Adjuvant	Pelvic with or without paraaortic nodes, inguinal	Selected patients
IIB–IVA	Primary	Pelvic with or without paraaortic nodes, inguinal	All patients
Metastatic	Palliative	Multiple sites	NA
Vulva			
I–II	Adjuvant	Pelvic with or without paraaortic nodes	Selected patients
Metastatic	Palliative	Multiple sites	NA
Ovary			
Recurrent	Palliative	Pelvic with or without paraaortic nodes	NA
Metastatic	Palliative	Multiple sites	NA

Note.—NA = not applicable.
*Primary radiation therapy if not suitable for surgery.
†This group includes selected patients with stage IB2 cancer.
‡Medically inoperable because of comorbidities.

3D Conformal Radiation Therapy

Among the external beam radiation modalities, in 3D conformal radiation therapy, the profile of each radiation beam is shaped to fit the profile of the target from a beam's-eye view by using a multileaf collimator and a variable number of beams. When the treatment volume conforms to the shape of the target, the relative toxicity of radiation to the surrounding normal tissues is reduced, which allows a higher dose of radiation to be delivered to the tumor than nonconformal techniques would allow. 3D conformal radiation therapy is considered a minimum standard for delivery of external beam radiation for treatment of gynecologic cancer.

Intensity-modulated Radiation Therapy

Teaching Point

IMRT advances one step beyond 3D conformal radiation therapy by using inverse treatment planning by modulating the beam's intensity. The intensity of the radiation dose is elevated in the areas of the target and is decreased in the neighboring normal tissues. Inverse treatment planning is performed by first determining the dose objectives for the tumor target, as well as the normal tissues (normal tissue constraints). With the use of iterative algorithms and cost functions, inverse planning can be used to create a set of fluence maps for each beam angle, which result in a dose distribution that conforms to the predetermined dose objectives for target and normal tissues (3). Figure 1 shows an example of IMRT treatment beam angles and the resulting isodose distribution in the axial, coronal, and sagittal planes.

IMRT-based treatment planning further improves the ability to conform the treatment volume to concave or highly complex tumor shapes, thereby delivering a higher dose to the target with less toxicity to normal tissues. The robustness of IMRT for the treatment of cervical and endometrial cancer across institutions has been recently shown in the results from a multi-institutional study (4), and the technique is now widely accepted. The preciseness of IMRT requires high-quality imaging studies; and often CT, dual-modality imaging with positron emis-

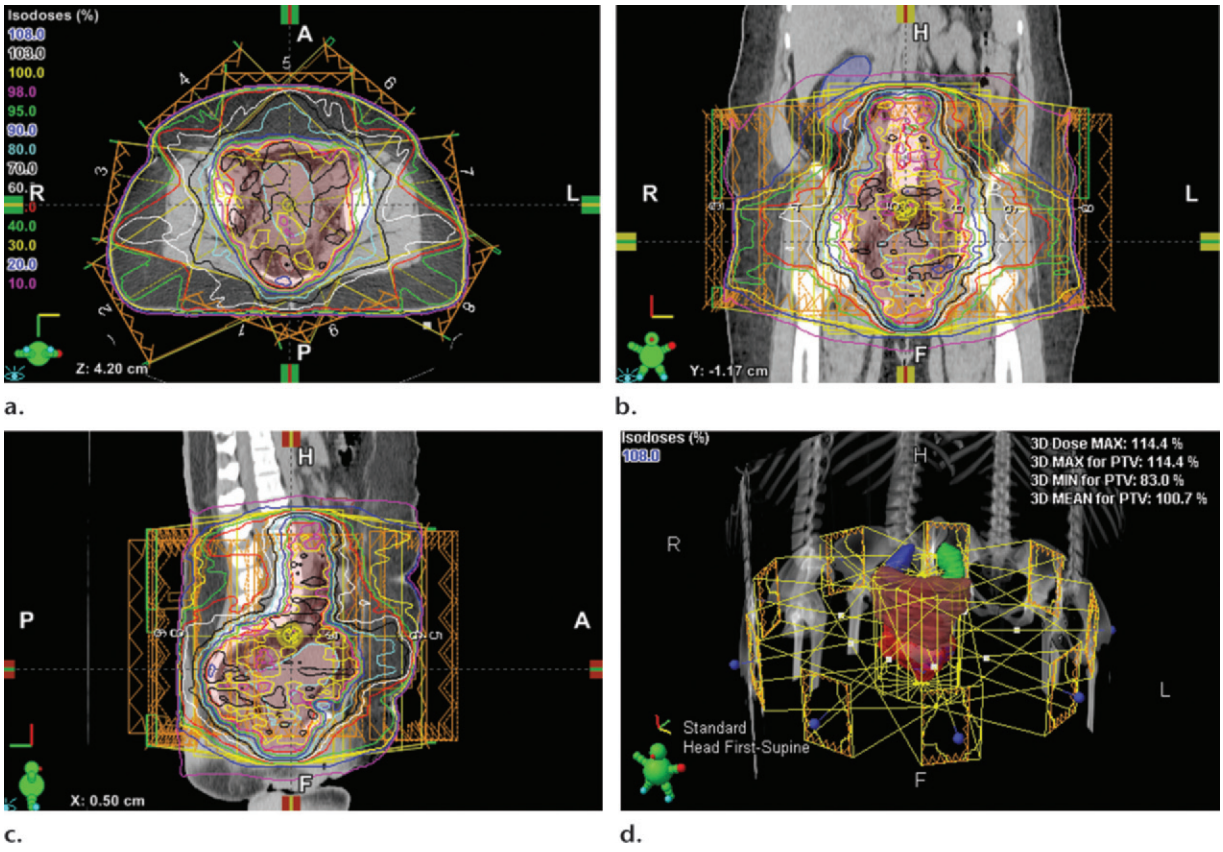


Figure 1. IMRT in a woman with cervical cancer. **(a–c)** Axial **(a)**, coronal **(b)**, and sagittal **(c)** views of treatment planning computed tomography (CT) show dose distribution with IMRT for cervical cancer. **(d)** 3D reconstruction with beam paths shows the use of multiple beam angles to achieve the fused dose distribution to focus on the planning target volume (PTV) (red area) and reduce the dose to the surrounding normal structures.

sion tomography (PET) and CT (PET/CT), and magnetic resonance (MR) imaging are all used for the purpose of treatment planning.

Stereotactic Body Radiation Therapy

Teaching Point

Stereotactic body radiation therapy refers to stereotactically delivered radiation treatments within extracranial body sites. Because stereotactic body radiation therapy delivers only a few high-dose treatments (hypofractions) and applies highly focused radiation dose distributions to a relatively small and well-defined tumor target, stereotactic body radiation therapy requires extremely detailed imaging studies, real-time monitoring of imaging, rigid immobilization devices, and, in some cases, respiratory motion control. Even though stereotactic body radiation therapy has not been commonly used in treating gynecologic cancers, its clinical efficacy for the treatment of spine, lung, and liver lesions generated great interest in the incorporation of this new treatment modality into curative and palliative treatment regimens for gynecologic malignancies (5,6); and stereotactic body radiation therapy has been used successfully for primary and recurrent gynecologic cancer. Stereotactic body radiation therapy can be performed as 3D conformal radiation therapy or IMRT. Because of the extremely high doses delivered during stereotactic body radiation therapy, more stringent dosimetric, mechanical, and imaging quality assurance measures are critical. Onboard imaging is also essential to ensure 3D target alignment before each treatment.

Imaging for Pretreatment Staging and Prognosis Assessment

Tumor staging, including the tumor volume and the extent of involvement, is essential to determine the prognosis, triage the therapy options, and design a multimodality treatment strategy. For decades, clinical staging of gynecologic cancers has been based on the International Federation of Gynecology and Obstetrics (FIGO) staging system. FIGO staging relies on clinical palpation and radiographs alone, a combination that poses inherent limitations in assessing the tumor volume, the involvement of adjacent tissues, the spread of disease to regional lymph nodes, and the distant metastatic sites in patients with gynecologic cancer (7,8). The historical reason why FIGO staging excludes advanced imaging data and relies exclusively on

the findings at clinical examination is because of the high prevalence of gynecologic cancers in the developing world and the lack of imaging resources in these geographic areas. FIGO staging has been reported to underestimate the stage in 20%–60% of the patients with cervical cancer, compared with surgical correlation (9). This partly explains why great variations of local recurrence and survival rates exist within each FIGO stage category (10). Despite its error-prone methodology, FIGO staging remains the current worldwide standard of practice. Therefore, a more accurate noninvasive method, including advanced imaging, is urgently needed to improve the tumor staging.

With the improvement of the spatial and temporal resolution to provide the much-needed anatomic detail and functional imaging capability, the advanced 3D tumor cross-sectional imaging modalities have greatly enhanced the efficacy in assessing tumor volume and the extent of involvement, and thus these advanced modalities allow further improvement in staging compared with the FIGO-based staging assignments. With the improvement in tumor delineation, the advanced imaging has become an integral part of image-guided targeted treatment planning and precise dose delivery for patient-centered individualized radiation therapy for gynecologic cancers (11,12).

CT Imaging

For decades, CT imaging has been an invaluable imaging modality for the treatment of gynecologic cancers, to identify regional involvement in pelvic and paraaortic lymph nodes and distant metastatic disease to the liver, lungs, bones, and others structures. To date, CT remains the most widely used diagnostic imaging modality for staging gynecologic cancer worldwide and remains the most used imaging modality for radiation therapy treatment planning and for targeting dose delivery. However, CT is limited in delineating the extent of tumor involvement within the uterus because of the lack of soft-tissue contrast between the tumor and the normal uterine tissue, which is critical information needed for the treatment of gynecologic cancers (13).

MR Imaging

Teaching Point

The actual tumor size, a well-established prognostic criterion in cervical cancer (10,14), is best assessed with MR imaging (15,16). With its superior soft-tissue contrast, MR imaging has been shown to be an excellent imaging modality to delineate the intrauterine tumor involvement in cervical and uterine cancer. In surgical-imaging correlation studies, MR imaging is reported to provide better staging of early-stage tumors, compared with staging from clinical examinations (15–17). MR imaging–based 3D tumor volume measurement correlates well with histologic findings obtained from digitized giant tissue sections, showing a 98% correlation (18), and attesting to a high accuracy in delineating tumor extent within the uterus in cervical cancer.

In the staging evaluation of cervical cancer, CT and MR imaging are generally equivalent for the assessment of lymph node and metastatic involvement, but MR imaging is superior in delineating tumor extent within the uterus and direct extensions of tumor to adjacent pelvic tissues (19,20), including bladder invasion, parametrial extension, and rectal and perirectal involvement. Ancillary findings that may or may not be related to the tumor but can influence the treatment approach, such as distortion or retroversion of the uterus, uterine fibroids, ovarian findings, and other pelvic abnormalities, can be readily evaluated with MR imaging. In addition, vaginal extension can be accurately delineated with MR imaging (21).

In endometrial cancer, MR imaging with a gadolinium-based contrast material provides excellent assessment of the extent of myometrial and cervical invasion of the tumor, as well as extrauterine extension (22,23), and contrast-enhanced MR imaging is the imaging modality of choice for such assessment. Differentiation between endometrial and cervical primary adenocarcinomas, a task that could be clinically and histologically challenging, can be performed with MR imaging (24).

In vaginal cancer, MR imaging is invaluable for delineating the extent of tumor invasion into the vaginal wall and paravaginal tissues. Such invasion critically influences the triage of treatment options and also the individualized treatment planning during radiation therapy.

PET/CT Imaging

The staging of cervical cancer has been further advanced by the introduction of PET/CT imaging. Most often, the biologically active molecule chosen for PET is fluorine 18 fluorodeoxyglucose (FDG), an analog of glucose. The concentrations of tracer imaged show tissue metabolic activity in terms of regional glucose uptake. Although PET/CT of cervical cancer has been studied more extensively than PET/CT of other gynecologic neoplasms in the peer-reviewed medical literature, PET/CT is also gaining acceptance in the staging of other gynecologic malignancies, including vaginal cancer and vulvar cancer. FDG PET/CT provides the most accurate assessment of pelvic and paraaortic lymph node involvement. Tumor involvement in these lymph node regions is known to be difficult to control with the combination of

Table 3: Role of Imaging for Cervical Cancer

Pretherapy staging
CT: local pelvic extent, lymph node metastases, distant metastases
MR imaging: tumor definition within the cervix or uterus, lymph node metastases, distant metastases
PET/CT: distant metastases
External beam radiation therapy planning
CT: delineation of tumor target, lymph nodes, normal tissues, establishment of clinical target volume (CTV) and PTV
MR imaging: delineation of tumor within cervix or uterus, vaginal extension, parametria, lymph nodes
Brachytherapy planning
Ultrasonography (US): intraoperative US-guided brachytherapy applicator insertion
CT: delineation of brachytherapy applicator, uterus, normal tissues for image-guided brachytherapy
MR imaging: delineation of tumor within cervix, uterus, or pelvis for image-guided brachytherapy; establishment of CTV and PTV; delineation of normal tissues, positional abnormalities (retroflexion, retroversion), fibroids
Response assessment and outcome prediction
MR imaging: tumor volumetric response; functional changes (dynamic contrast material–enhanced and diffusion-weighted MR imaging) intratherapy, posttherapy
PET/CT: primary tumor, lymph node involvement, posttherapy

radiation therapy and chemotherapy alone, and such involvement is generally associated with much-reduced overall survival. Although PET/CT findings are not included in the FIGO staging system, they have been used increasingly as a staging tool and have become critically important for multimodality therapy planning in patients with gynecologic cancer (25,26).

Recently, the American College of Radiology Appropriateness Criteria for pretreatment evaluation and follow-up of various gynecologic cancers have been published and are freely available at the American College of Radiology's Web site *(www.acr.org)*. This information is of great value for practitioners in choosing appropriate imaging modalities for the assessment of cervical cancers and endometrial cancers (27–29).

Principles of Therapy and Role of Imaging in Gynecologic Cancer

Cervical Cancer

In cervical cancer, accurate staging is critical for appropriate treatment selection and treatment planning. Imaging, including CT, MR imaging, and PET/CT, plays an important role in *(a)* refining the tumor staging and target delineation, *(b)* monitoring therapy response, and *(c)* providing an early prediction of ultimate treatment failure, as well as a basis for adaptive therapy (Table 3).

Teaching Point

A substantial proportion of cervical cancer patients are initially diagnosed with stage IIB–IVA disease, for which the combination of definitive chemotherapy with radiation therapy is the standard of care. Radiation therapy for this disease group consists of pelvic external beam radiation and brachytherapy (implant radiation). Brachytherapy is a critical therapy component to cure advanced cervical cancer. Brachytherapy provides a localized high-dose radiation boost to the cervix and uterus through implanted specialized brachytherapy applicators that require close and individualized integration with the external beam radiation to achieve the maximal effect of radiation to the residual tumor. The evolution from conventional brachytherapy with two-dimensional treatment planning to 3D image-guided brachytherapy has enabled higher and more conformal dose delivery. Early data suggest that tumor control may be further improved with image-guided brachytherapy (11,30). This change marks a paradigm shift in brachytherapy similar to the earlier advances in external beam radiation therapy from conventional two-dimensional radiation to 3D conformal radiation therapy and IMRT delivery. Since 1999, concurrent cisplatin-based chemotherapy has been incorporated into the course of radiation therapy because data from multiple randomized studies had demonstrated decreased tumor recurrence rates and improved survival with the combined chemotherapy and radiation therapy, compared with radiation therapy alone (31).

Patients with stage I–IIA cervical cancer are treated with radical hysterectomy and pelvic lymphadenectomy or with definitive radiation therapy if they are deemed poor surgical candidates (Table 2). Adjuvant postoperative radiation therapy is recommended for patients with a combination of high-risk histopathologic features, such as deep invasion of tumor into the cervix, lymphovasular space invasion, and tumor size more than 4 cm in diameter (32,33). Adjuvant chemoradiotherapy is recommended for patients with positive tumor margins, parametrial invasion, or involved pelvic lymph nodes (34). One exception is patients with stage IB2 disease. Although their disease is amenable to surgical cure, most of them would need postoperative radiation therapy, and therefore definitive chemoradiotherapy is commonly recommended

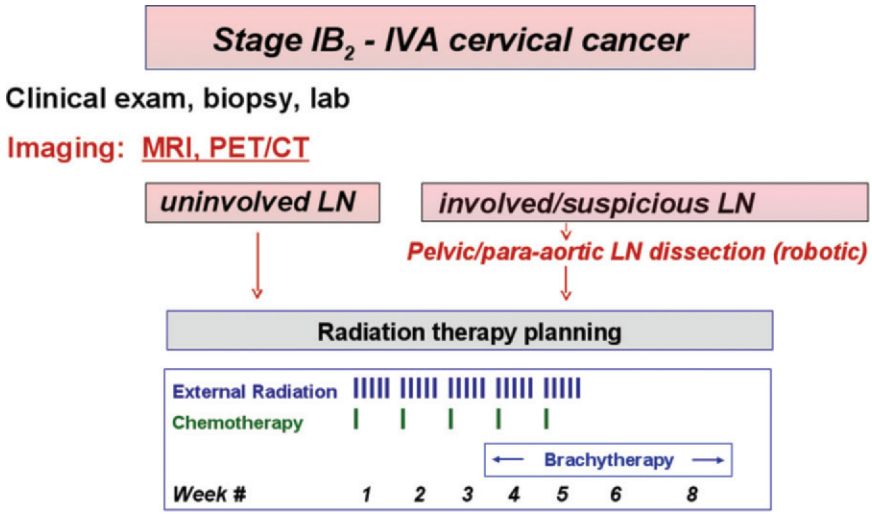


Figure 2. Diagram of the treatment algorithm for cervical cancer, showing the role of multimodality imaging. The treatment algorithm shows how tumor staging that is based on MR imaging and PET/CT helps identify patients for lymph node *(LN)* dissection and debulking of involved nodes. The robotic lymph node dissection technique allows rapid postoperative recovery and an expeditious start of definitive radiation therapy and chemotherapy, with radiation target volumes tailored according to molecular imaging and the surgical and histopathologic findings.

for these patients (35). Patients with distant hematogenous spread of disease (stage IVB) are treated mainly with palliative chemotherapy, and palliative radiation therapy may be used to treat local recurrence and complications that are not responsive to the treatment.

Surgery is not only the primary treatment for early-stage cervical cancer, but surgery also plays an important role in the management of pelvic or paraaortic lymph node involvement in all stages of cervical cancer. Involved lymph nodes are challenging to control with radiation therapy, and surgical resection could lead to a delay in therapy. Recently, minimally invasive robotic surgery has provided a new means to address this challenge by facilitating resection and allowing fast postoperative recovery. Robotic surgery is becoming increasingly available for gynecologic malignancies and allows better intraoperative visualization and improved ergonomics. Robotic surgery achieves overall tumor control (36,37) similar to that with laparotomy but with decreased blood loss, fewer wound complications, and a shorter recovery period (36). In patients with cervical cancer, the rapid postoperative recovery achieved with robotic surgery for lymph node dissection or debulking allows earlier institution of definitive radiation therapy or chemotherapy (or both) within days of the procedure, as compared with patients who undergo conventional laparotomy for lymph node dissection. An integrated algorithm used at our institution includes molecular imaging to identify involved lymph nodes, robotic lymph node dissection, and definitive therapy (Fig 2). This algorithm illustrates the importance and benefits of a judicious and individualized combination of imaging modalities to enable an integrated treatment approach.

Endometrial Cancer

In endometrial cancer, stage I disease prevails, and most patients are treated with surgery, including hysterectomy and lymph node sampling or dissection, either with laparotomy or, increasingly, with a robotic approach (36,37). However, postoperative radiation therapy is required for patients with stage I–II endometrial cancer and histopathologic high-risk features for recurrence, such as high-grade tumor, outer one-third or one-half myometrial invasion, lymphovascular space invasion, involvement of the cervix or adnexa, or older age (>70 years), as reported in the findings of several randomized trials (38,39). In patients with surgical stage III and IV endometrial cancer, chemotherapy and volume-directed radiation therapy are commonly used.

The role of imaging is the delineation of the postoperative target and normal tissue structures for conformal treatment planning, to reduce the dose and toxicity to normal tissue (Table 4). In patients with the less-common advanced endometrial cancer, imaging plays an important role in the assessment of the extent of involvement of pelvic structures, lymph nodes, and metastatic sites.

Table 4: Role of Imaging for Endometrial Cancer

Pretherapy staging (for advanced tumors)
CT: local pelvic extent, lymph node metastases, distant metastases
MR imaging: tumor definition within the uterus, myometrial invasion, delineation of primary tumor (uterus or cervix), lymph node metastases, distant metastases
External beam radiation therapy planning
CT: delineation of tumor or postoperative target, lymph nodes, normal tissues, CTV, PTV
MR imaging: delineation of tumor within cervix or uterus, postoperative target, vaginal extension, parametria, lymph nodes
Brachytherapy planning
US: intraoperative US-guided brachytherapy applicator insertion
CT: delineation of brachytherapy applicator, uterus, normal tissues for image-guided brachytherapy
Response assessment and outcome prediction
MR imaging: tumor volumetric response, myometrial invasion, intratherapy, posttherapy

Table 5: Role of Imaging for Vaginal Cancer

Pretherapy staging
CT: local vaginal, pelvic, or vulvar extent; lymph node metastases; distant metastases
MR imaging: tumor definition within the vagina, vaginal wall invasion, lymph node metastases, distant metastases
External beam radiation therapy planning
CT: delineation of tumor, lymph nodes, normal tissues, CTV, PTV
MR imaging: delineation of tumor, lymph nodes, normal tissues, CTV, PTV
Brachytherapy planning
CT: delineation of brachytherapy applicator, vagina, normal tissues for image-guided brachytherapy
MR imaging: delineation of brachytherapy applicator, vaginal invasion, normal tissues for image-guided brachytherapy
Response assessment and outcome prediction
CT: tumor response, posttherapy
MR imaging: tumor response, posttherapy

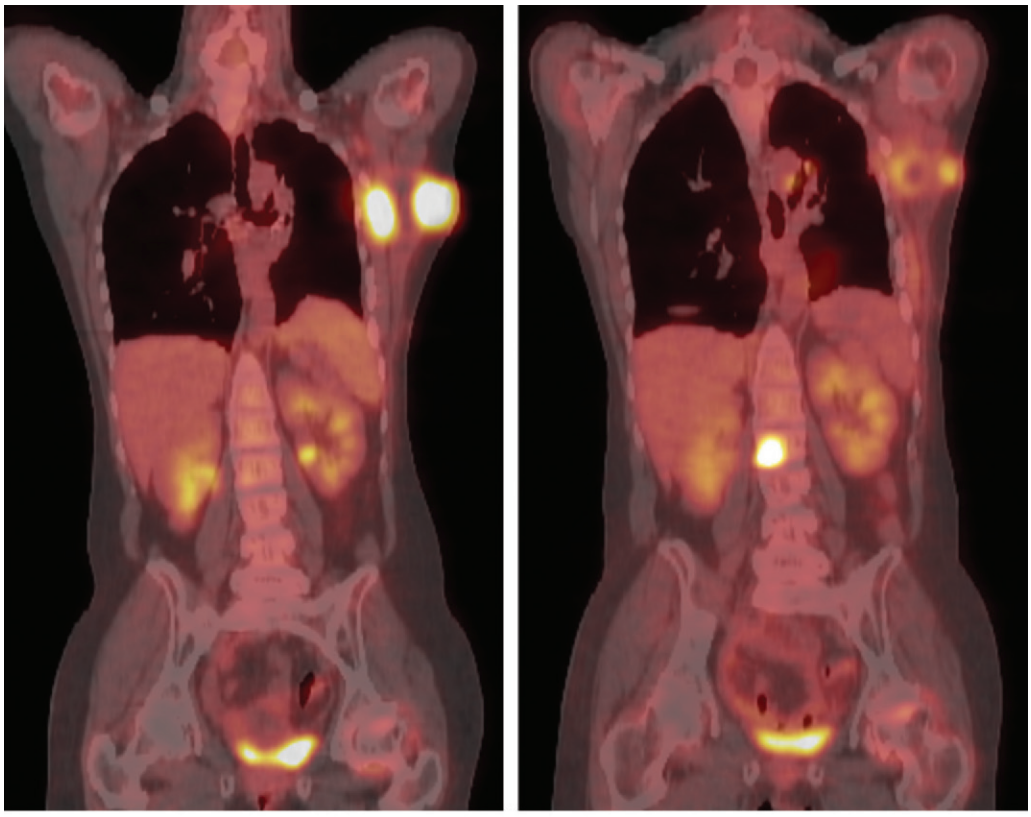
Primary radiation therapy alone without surgery is used as the curative treatment modality for patients with "medically inoperable" disease because many patients with endometrial cancer present with severe comorbidities that preclude surgical therapy. Radiation therapy in this setting again involves both pelvic external beam radiation therapy and brachytherapy. External beam radiation therapy targets the uterus, cervix, upper portion of the vagina, pelvic lymph nodes, and other involved areas. Intracavitary brachytherapy with specialized intracavitary applicators is designed to deliver a high-dose boost to the involved uterine cavity; and further targeted radiation may be delivered to other areas of involvement, requiring image-guided dose delivery. Imaging plays an important role in these patients, including *(a)* CT for staging of tumor extent and target delineation for external beam radiation therapy; *(b)* MR imaging for assessment of tumor extent within the uterine cavity, particularly diffusion-weighted MR imaging (40), and response monitoring; and *(c)* intraoperative US to guide insertion of brachytherapy applicators.

Vaginal Cancer

Vaginal cancer is rare and accounts for only 1%–2% of all gynecologic malignancies. Imaging plays an important role in the delineation of tumor involvement for treatment planning, particularly for the assessment of regional and distant metastases (Table 5). In vaginal cancer, the treatment relies largely on radiation therapy because most vaginal tumors are not amenable to surgical resection. Even in small stage I vaginal cancers (tumor confined to a limited portion of the vagina), which are treated with surgery, radiation therapy is usually required after surgery, especially for close or involved margins. The radiation therapy for stage II or higher-stage vaginal cancers includes definitive external beam radiation therapy to the pelvis, often with chemotherapy, with or without inclusion of the inguinal lymph nodes, as well as highly individualized interstitial or intravaginal brachytherapy, in which MR imaging is helpful in delineating the tumor target (Table 5) (41).

Vulvar Cancer

In vulvar cancer, the primary treatment is radical surgery (radical vulvectomy and lymph node dissection). Molecular imaging has contributed to tumor staging in high-risk disease (Fig 3) and to an innovative approach to sentinel node dissection. For radiation therapy, imaging plays an important role in delineating the extent of disease involvement for treatment planning, particularly for the assessment of regional and distant metastases. However, radiation therapy has an essential adjuvant role in women with lymph node involvement or large tumors with positive margins. The benefit of the addition of radiation therapy after radical vulvectomy and inguinal lymphadenectomy in inguinal node–positive patients was demonstrated in the Gynecologic Oncology Group's GOG-36 trial (42); adjuvant



a. b.

Figure 3. Molecular imaging for tumor staging in a woman with high-risk vulvar cancer. **(a)** Coronal fused PET/CT image obtained after resection of vulvar cancer shows increased avidity of a tumor mass in the left chest wall. This finding profoundly changed the treatment approach from treatment with curative intent to palliative therapy. **(b)** Coronal fused PET/CT image obtained after chemotherapy shows decreased avidity of the chest wall mass, which indicates improvement, but also shows development of a metastasis to the spine.

Table 6: Role of Imaging for Vulvar Cancer

Pretherapy staging (in advanced tumors)
CT: local vulvar, vaginal, or pelvic extent; lymph node metastases; distant metastases
External beam radiation therapy planning
CT: delineation of tumor, lymph nodes, normal tissues, CTV, PTV
Brachytherapy planning
CT: delineation of brachytherapy applicator, vulva and vagina, normal tissues for image-guided brachytherapy
Response assessment
CT: tumor response, posttherapy

Table 7: Role of Imaging for Ovarian Cancer

Pretherapy staging
CT: abdominal tumor extent, lymph node metastases, pleural effusion, distant metastases
US: detection of ovarian cancer, staging (solid components or ascites)
External beam radiation therapy planning (palliative)
CT: delineation of tumor, lymph nodes, normal tissues, CTV, PTV
Response assessment
CT: tumor response to chemotherapy (in conjunction with tumor markers)

radiation therapy decreased groin recurrence (5% vs 24%) and improved the 2-year overall survival (68% vs 54%). An overview of vulvar cancer imaging is presented in Table 6.

Ovarian Cancer

Although ovarian cancer is primarily treated surgically and with chemotherapy, radiation therapy is useful in the palliation of regional focal disease (43). CT, as well as PET/CT (44), is the base for the delineation of recurrent ovarian cancer lesions for radiation therapy planning. In addition, administering low-dose radiation therapy to enhance the effectiveness of chemotherapy is being explored as a novel approach (5). The role of imaging is largely limited to CT, as detailed in Table 7.

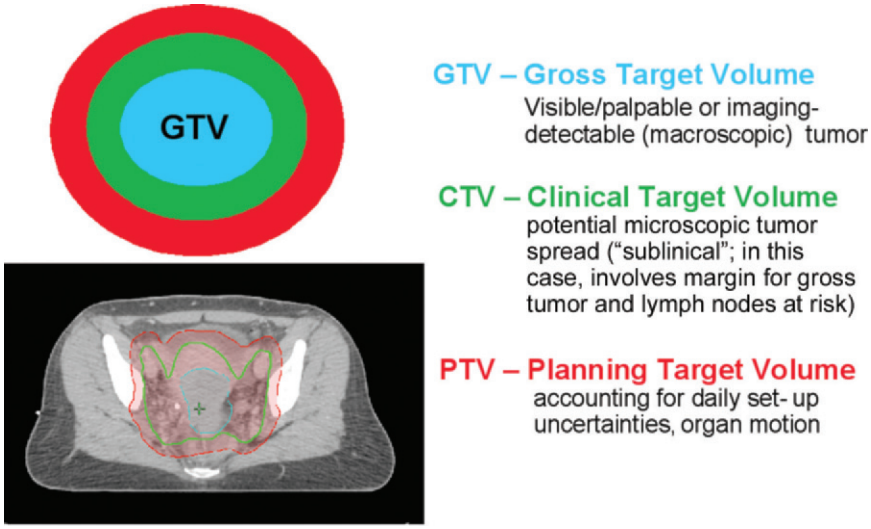


Figure 4. Principles of target definition in radiation therapy planning. Diagram (top) and axial CT image (bottom) illustrate the definitions of the GTV (blue), CTV (green), and PTV (red).

Principles of Radiation Therapy and the Role of Multimodality Imaging

Radiation oncologists rely on their radiology colleagues to help delineate tumor extension and the boundaries of tumor involvement, a task that can be challenging in pelvic tumors. Imaging information for the radiation oncologist (Tables 3–7) extends well beyond the diagnostic purpose. Imaging paradigms extend from diagnostic, diagnostic/targeting, theragnostic, and response assessment to the novel concept of predictive imaging. The diagnostic paradigm is used for staging and the assessment of disease extent and crosses into the targeting paradigm, in which precise delineation of the tumor volume and extensions is critical. Imaging-based response monitoring and response assessment allow adaptation of the treatment regimen to improve tumor control and survival.

Imaging for Tumor Targeting in Radiation Therapy Planning

Killing tumor cells with ionizing radiation is a function of the total radiation dose to the tumor target and the fraction size (the dose of each individual daily treatment in the course of radiation therapy). The dose required for tumor control (tumor control probability) is proportional to the logarithm of the number of clonogenic cells in the tumor. Therefore the dose required to control a palpable or visible tumor mass is higher than that required for subclinical extensions of tumor, such as microscopic involvement or disease below the level of clinical or imaging detection. The challenge is to deliver a maximal radiation dose to the tumor target while minimizing the dose received by normal radiosensitive tissues in the surrounding areas. To minimize radiation toxicity and complications, one must have as much information as possible with regard to the extent of tumor involvement and whether it has involved any neighboring organs.

Definition of Target Structures

One of the most important questions for a radiation oncologist in planning the treatment volumes for imaging-based and image-guided therapy in patients with gynecologic cancer is defining the target. The planning of treatment with radiation therapy has been revolutionized by the ability to delineate tumors and adjacent normal structures in three dimensions by using specialized CT scanners or MR imagers equipped with set-up lasers and software (45) to transfer the imaging and planning information to the planning software and subsequently to the linear accelerator for delivery of treatment. CT or MR imaging or both are performed in the treatment position with immobilization of the patient. Radiopaque fiducial marks are placed according to the lasers and are used as reference points on the patient's skin to ensure daily reproducible positioning for the delivery of treatment.

Local and regional tumor control (ie, the control of the tumor and its draining lymph node regions that are at risk for involvement) depends on the precise delineation, targeting, and delivery of the required radiation dose to grossly detectable (by palpation or imaging) tumor and microscopic (subclinical) tumor, respectively. Tumor control depends on accurate target delineation, which is based on the strict definition of tumor target volumes (Fig 4). Tumor target volumes are based on patterns of disease spread, correlative surgical and pathologic

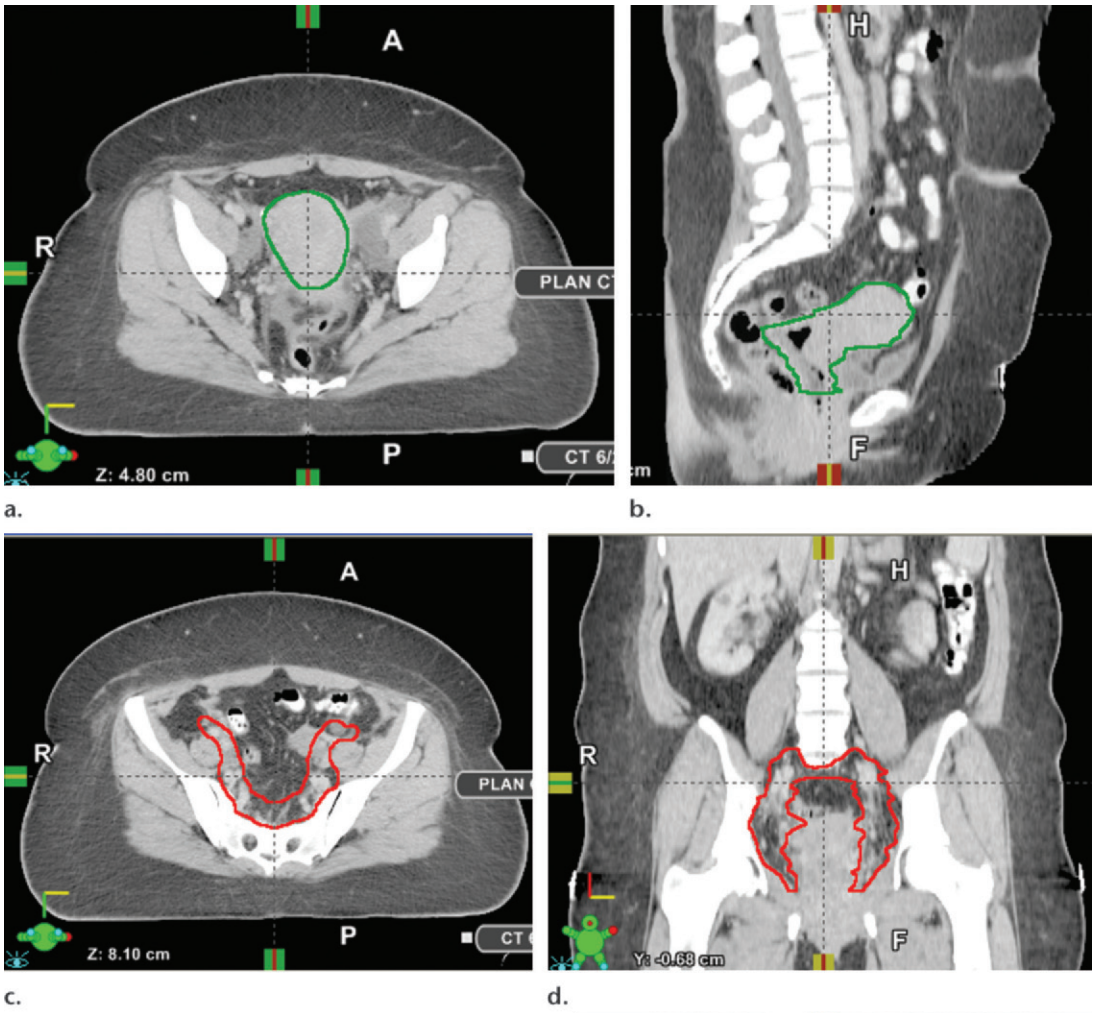


Figure 5. CT-based target delineation in a woman with gynecologic cancer, with color contouring of the target structures and the normal structures. **(a, b)** Axial **(a)** and sagittal **(b)** CT images show contouring of the target structure, the uterus (green contour). **(c–e)** Axial **(c)**, coronal **(d)**, and sagittal **(e)** CT images show contouring of the target regional lymph nodes (red contour) *(Fig 5 continues)*.

information, and the principles of radiation biology, which provides the basis for the radiation dose prescription in radiation therapy planning.

The *gross target volume* (GTV) denotes all demonstrable tumors (demonstrable with clinical or imaging-based detection). The GTV is often defined with multimodality imaging such as PET/CT fusion or MR imaging (or both). The *clinical target volume* (CTV) denotes the GTV and microscopic ("subclinical") tumor involvement. The GTV and CTV provide the basis for designing the *planning target volume* (PTV), which includes the CTV and margins for geometric uncertainties relating to patient motion and inherent set-up inaccuracy during the daily delivery of radiation therapy.

Target Delineation

On the basis of these principles, the GTV and CTV are contoured on each imaging section. Figure 5 illustrates the contouring of the uterus and tumor extensions in the pelvis (GTV) (Fig 5a, 5b; area within green contour) and the contouring of the external iliac and common iliac

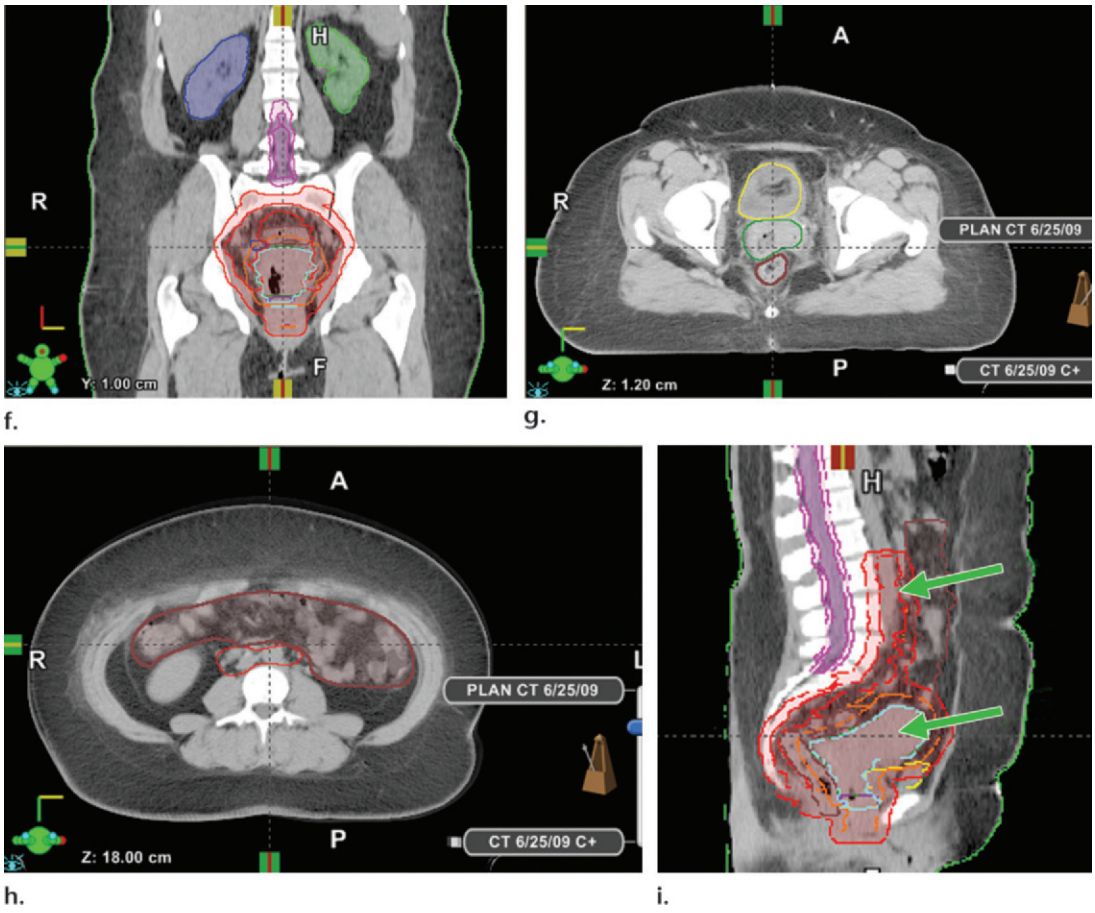


Figure 5. *(continued)*. **(f–i)** Coronal **(f)**, axial **(g, h)**, and sagittal **(i)** CT images show contouring of pertinent normal structures. Typical radiation dose requirements for the target structures and dose limits for the normal structures are 85 Gy or more for the tumor and uterus (aqua contour on **f**, lower arrow on **i**), 45–66 Gy for the lymph nodes (red contour, upper arrow on **i**), maximum dose of 25 Gy or less for each kidney (left kidney, green contour on **f**; right kidney, dark blue contour on **f**), maximum dose of 45 Gy or less for the spinal cord and cauda (hot pink contour on **f, i**), 45 Gy or less for the bladder (yellow contour on **g, i**), less than 40 Gy for the rectum (reddish brown contour on **g**), and 50 Gy or less for the bowel (reddish brown contour on **h**).

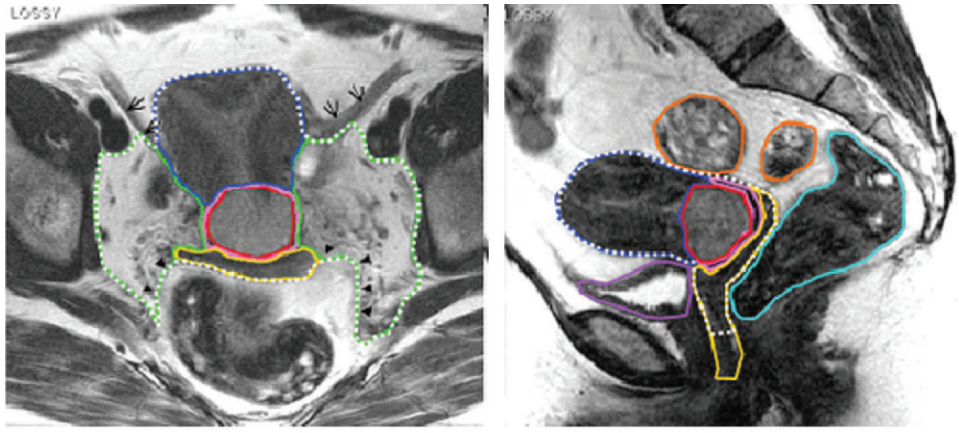
lymph nodes (Fig 5c–5e; red contour); together the two areas of contouring represent the CTV on the treatment planning CT in a patient with cervical cancer. The PTV (Fig 5f, 5i; area shaded with red) is then derived, which provides the basis for beam modeling and dosimetry.

Normal tissue structures are also contoured for the planning process because the radiation dose to these structures must be reduced as much as possible (Fig 5f–5i). The degree of radiation exposure to normal structures is directly correlated with complications in the normal tissue. Guidelines for target delineation of gynecologic pelvic tumors for CT- and MR imaging–based treatment planning have been published recently (46). Target delineation is generally performed on axial imaging sections; software allows real-time coronal and sagittal reconstructions to aid the contouring process.

Multimodality imaging has entered into the treatment planning process in patients with cervical cancer. In addition to the standard CT for radiation therapy planning, the GTV is frequently refined with MR imaging (Fig 6) (46) and PET/CT (Fig 7).

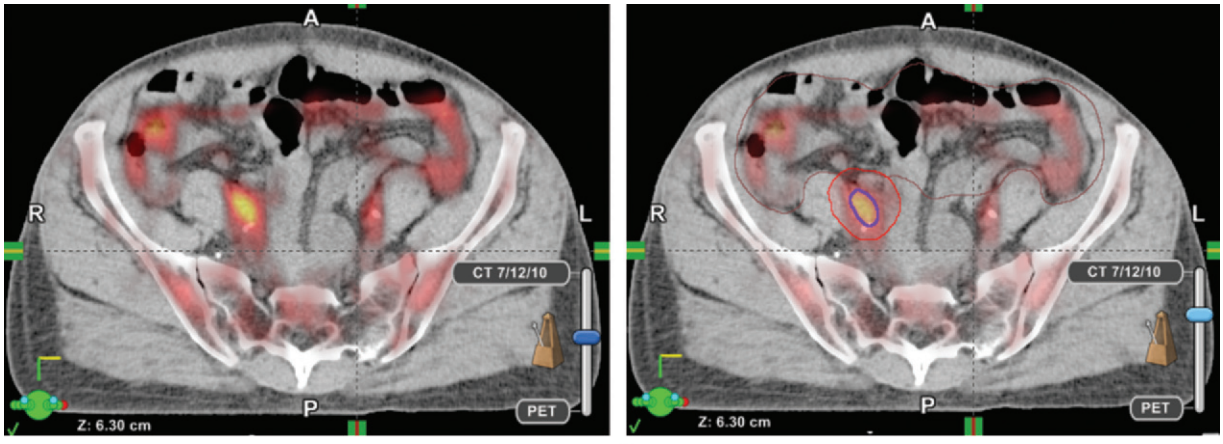
PET/CT-based delineation of involved pelvic lymph nodes has improved targeting and delivery of higher tumoricidal doses to these regions of tumor involvement. Figure 7 shows image coregistration between the treatment planning with CT and PET/CT. The metabolic activity of involved pelvic lymph nodes has been delineated on the PET/CT image and is projected onto the coregistered planning CT image. This process allows precise determination of the tumor-involved pelvic lymph node region and enables radiation dose intensification through the high-precision targeting of such involved structures.

Figure 5f–5i shows the complete process of delineation of the GTV, CTV (accounting for potential microscopic tumor spread), and PTV. The dose



a. b.

Figure 6. MR imaging–based target delineation in a woman with cervical cancer. Axial **(a)** and sagittal **(b)** MR images show that MR imaging–based planning allows contouring of the cervical tumor and GTV (red contour), cervix (pink contour), vagina (yellow contour), uterus (dark blue contour), parametria (green-dotted contour on **a**, aqua contour on **b**), bladder (purple contour on **b**), and large bowel (orange contour on **b**). Arrows on **a** point to the left and right broad ligaments, and arrowheads on **a** indicate the uterosacral ligaments and mesorectal fascia. (Reprinted, with permission, from reference 46.)



a. b.

Figure 7. Multimodality imaging-based target delineation in a woman with gynecologic cancer. Axial pelvic CT image acquired for treatment planning is coregistered with FDG PET images **(a)** to allow the delineation of a hypermetabolic external iliac lymph node, as shown on **b** (purple contour). This high-precision delineation allows targeting of the involved lymph nodes with a higher radiation dose.

constraints (imposed dose limits) to normal tissues are also represented. High doses to the uterus and tumor (≥85 Gy) and to tumor-involved lymph nodes (60–66 Gy) and moderate doses to the areas at risk for microscopic tumor involvement (45–50 Gy) are in stark contrast to the limitations posed for radiosensitive critical normal tissues, including the small bowel, kidneys, and spinal cord, and for moderately radiosensitive structures, including the rectum and bladder (Fig 5f–5i).

Beam Modeling and Dosimetry for Radiation Therapy Delivery

The fundamental challenge is how to deliver the required tumoricidal dose to the target structures and also protect sensitive normal tissues from dose exposure, thereby minimizing the risk of complications in normal tissue. Techniques such as 3D conformal radiation therapy, IMRT, and stereotactic body radiation therapy are used to achieve the dose distribution for the individual clinical situation.

Brachytherapy

Although traditionally prescribed on the basis of two-dimensional dose points (47), methods of refined imaging-based dose planning have only been introduced recently in gynecologic brachytherapy. A breakthrough has been achieved with the introduction of brachytherapy applicators that are compatible with CT and MR imaging, which now enable

Table 8: Sample Radiology Report for Pretreatment Studies (at the Time of Diagnosis)

Tumor size in three dimensions
3D tumor volume upon specific request
Tumor borders (specifically address the following)
Extension to adjacent structures such as parametria (extent of involvement helpful, especially in MR imaging report), vagina, uterus (lower uterine segment, body, fundus should be specified with MR imaging report), bladder, rectum, or ovaries
Thickness of uterine wall in endometrial cancer (at the midpoint of the corpus or at the location of abnormality; measure both anterior and posterior thickness)
Depth of myometrial invasion (MR imaging, in endometrial cancer)
Encasement of vessels
Obliteration of fat planes in cul-de-sac or between adjacent organs with any evidence of frank extension
Uterine findings
Fibroids
Presence of fluid within the cavity
Obstruction of endometrial canal
Uterine positioning (flexion and version)
Status of ovaries, such as presence of ovarian masses
Abnormal pelvic lymph nodes and their location
Define precise location within each lymph node station (ie, distal, proximal, medial, or lateral to a point of reference)
Morphology and size in two dimensions
Fixation (ie, obliteration of fat planes surrounding the abnormal lymph node)
Paraaortic lymph nodes: exact level or location by image numbers
Distant metastasis
Any parenchymal, soft-tissue, bone, or omental or peritoneal locations within the field of view
Presence of hydronephrosis and hydroureter, with exact level of obstruction if in the field of view
PET/CT additional items to report
Metabolic activity of the described lesions, with maximum standardized uptake value (SUV_{max}) for each

the use of image-guided brachytherapy (11,12). For image-guided brachytherapy, imaging is performed immediately after the insertion of the applicators with the applicators in place. High-precision delineation of the tumor target is thus feasible by using precise dose computation that allows the individualized target-based 3D conformal treatment planning and delivery necessary for brachytherapy.

For the delineation of the actual tumor extent within the cervix at the time of brachytherapy, MR imaging is the only modality that differentiates tumor from the normal uterus and surrounding pelvic structures (17,18,20). Figure 8 illustrates the delineation of the target at the time of brachytherapy in a patient with endometrial cancer. A sample radiology report is proposed here as a reference for pretreatment studies (at the time of diagnosis) (Table 8).

Morphologic and Functional Imaging for Response Assessment and Early Outcome Prediction

For personalized care in patients with gynecologic cancer, the monitoring of response and the prediction of treatment outcome are paramount. If treatment failure is not detected until months or years after therapy, the salvage treatment options will be severely limited. Assessing treatment response with imaging during the course of radiation treatment may provide a means for early prediction of treatment failure, thus opening an early window of opportunity to modify the treatment strategy for better outcome. Even though this image-based approach to the evaluation of treatment response has not been adopted routinely, it has been studied extensively (48).

Role of Anatomic or Morphologic Early Response Assessment during Therapy

In addition to tumor pretreatment staging for triaging treatment options, morphologic imaging during therapy has an important role for radiation oncologists for *(a)* tumor delineation and measurement of volume regression for response assessment, *(b)* tumor delineation for treatment planning and adaptation, *(c)* tumor delineation for treatment planning for brachytherapy, and *(d)* early outcome prediction and potential for adaptive therapy.

Tumor Delineation and Measurement of Volume Regression for Response Assessment.—Assessment of the tumor volume and volume regression rate of gynecologic cancers poses major challenges. The diameter-based measurements of the RECIST (Response Evaluation Criteria in Solid Tumors) guidelines assume elliptical tumor shape and linear tumor regression. Although valuable, these measurements cannot allow the appreciation of subtle changes in irregular tumor volumes during early treatment (49). Advanced 3D quantitative imaging overcomes such challenges. With 3D contouring of the tumor (Fig 6), which is commonly performed during radiation therapy planning, precise 3D tumor volume can be derived (17–20). On the basis of the reported 98% correlation between the 3D MR imaging–derived tumor volume and the 3D-reconstructed histo-

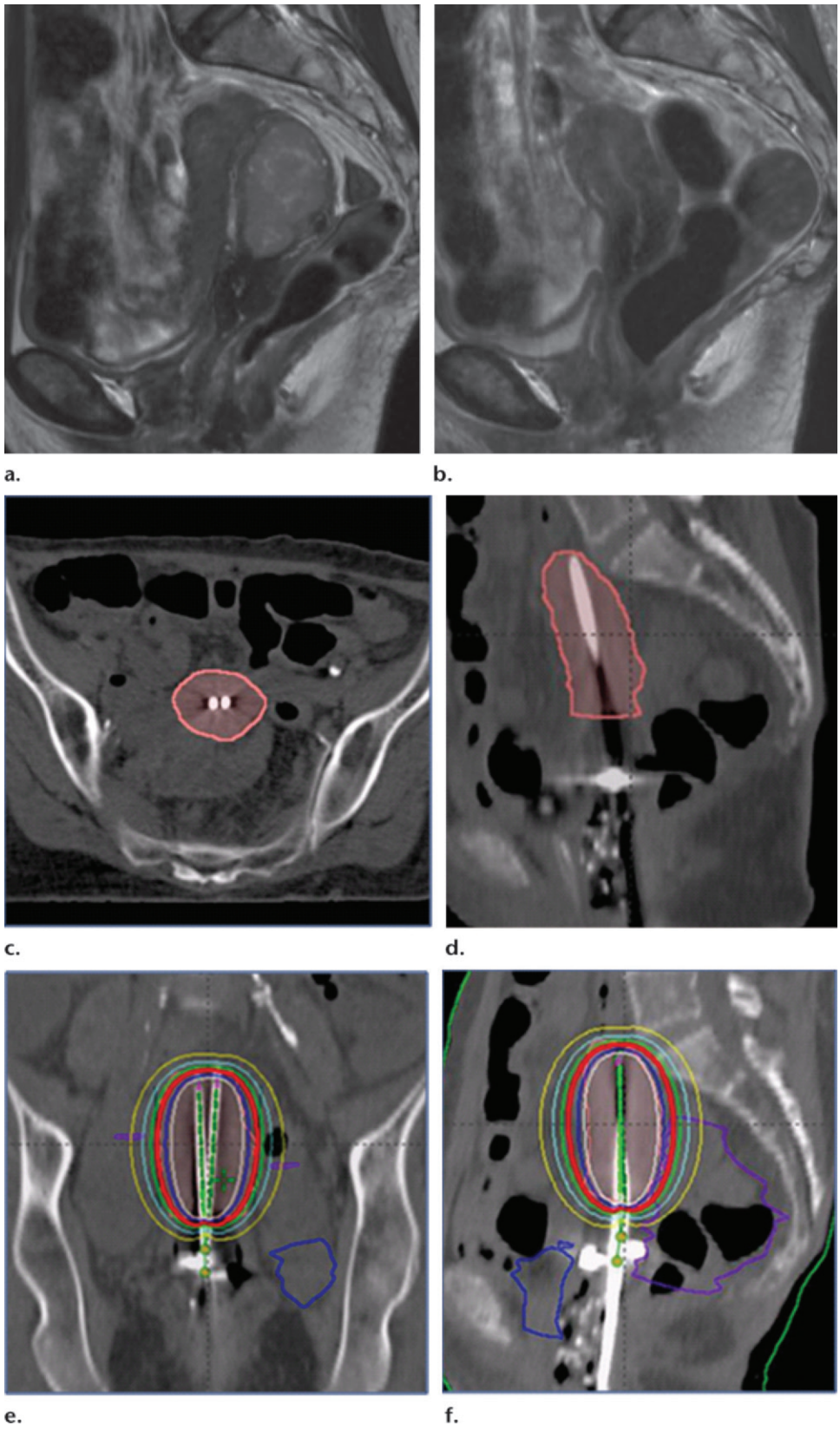


Figure 8. Role of multimodality imaging in the primary radiation therapy for a woman with stage IB endometrial cancer. **(a)** Pretherapy sagittal T2-weighted MR image shows a large tumor filling the endometrial cavity. **(b)** Repeat sagittal T2-weighted MR image obtained for brachytherapy planning at the completion of the external beam radiation therapy shows excellent response to a dose level of 45 Gy in 5 weeks of pelvic radiation therapy and also shows a change of the uterine position from retroversion **(a)** to mid position **(b)**, which is essential information for the placement of the intrauterine Y-tandem brachytherapy applicator. The Y-tandem applicator is placed with US guidance. **(c, d)** Treatment planning axial **(c)** and sagittal **(d)** CT images show the Y-tandem applicator within the contoured uterus (pink contour). **(e, f)** Treatment planning coronal **(e)** and sagittal **(f)** CT images show the brachytherapy dose distribution by various colored isodose lines (yellow, light blue, green, red, dark blue, and pink, with the area within the yellow line receiving the lowest dose and the area within the pink line with the pink shading receiving the highest dose).

logic tumor volume (18), the tumor regression can therefore be precisely measured, and the temporal response dynamics of the tumor with time can be determined in individual patients. Diagnostic radiologists play an essential role in implementing high-resolution imaging protocols to achieve high lesion-to-background contrast ratios in lesion delineation, radiation therapy planning, response assessment, and hence the potential early prediction of treatment outcome.

Table 9: Sample Radiology Report for Intratreatment Studies

Treatment response (regression or progression compared with the pretreatment examination)
Extension to adjacent structures (parametria, vagina, uterus, bladder, rectum, ovary, cul-de-sac, peritoneum)
In endometrial cancer: depth of tumor invasion (including changes) and thickness of uterine wall (at midpoint of the corpus or at a location of abnormality; measure both anterior and posterior thickness)
Thickness of residual tumor (especially in vaginal tumors)
3D tumor volume upon specific request
RECIST evaluation upon specific request
Presence of tumor necrosis
Uterine findings
Fibroids
Intrauterine fluid
Patency of endocervical canal
Uterine positioning (flexion and version)
Lymph node response compared with pretreatment examination
Define precise location within each lymph node station (ie, distal, proximal, medial, or lateral to a point of reference)
Morphology and size in two dimensions
Fixation (ie, obliteration of fat planes surrounding the abnormal lymph node)
Complications: fistula, fluid collections, hydronephrosis, hydroureter, new metastasis
PET/CT additional item to report
Metabolic activity of the described lesions with SUV_{max} for each, as compared with the pretreatment examination, is helpful (eg, SUV_{max} of tumor was two times that of the liver, compared with five times before treatment)

Tumor Delineation for Treatment Planning and Adaptation.—Tumor delineation (Fig 6) is critical for intratreatment planning and intratreatment adaptation of the PTVs. Changes in tumor volume and the configuration of pelvic organs have been shown to profoundly alter and shift the PTV and consequently the dose coverage for focused radiation therapy techniques, such as IMRT. If the PTV can be adapted to both of these changes, the tumor targeting may be improved by reducing the chance of a geometric miss, and better protection of normal tissues may be achieved. The optimal frequency for intratreatment imaging and planning is an active area of research.

Tumor Delineation for Treatment Planning for Brachytherapy.—Evaluation of tumor regression comes to the forefront in intratreatment planning for brachytherapy. Approximately half of the therapeutic radiation dose is given with brachytherapy, accentuating the importance of optimizing the brachytherapy. Only relatively limited centralized tumors are ideal for intracavitary brachytherapy, whereas larger tumors with more lateral extension require an interstitial component. Refined MR imaging–based tumor delineation and treatment response assessment have been critical for the paradigm change in image-guided brachytherapy (Fig 8).

A proposed sample radiology report for intratreatment imaging studies is provided (Table 9). In addition, a sample radiology report for posttreatment follow-up studies, which are commonly performed to evaluate for clinically suspected recurrence, is provided (Table 10).

Outcome Prediction.—At the posttherapy follow-up MR imaging, the complete disappearance of a tumor mass 3–6 months after therapy is associated with better outcome (17,50). However, such critical information is available relatively late, which does not allow early therapy adaptation. During treatment, the rate of tumor regression, quantified with high precision by using 3D tumor volumetry, has been found to be predictive of treatment outcome in cervical cancer patients treated with radiation therapy and chemotherapy (50–52). Patients with tumor regression to less than 20% of the original 3D volume at a radiation dose level of 40–50 Gy (4–5 weeks of radiation therapy) had 97% tumor control and a 72% disease-specific survival rate, compared with 53% and 50%, respectively, with slower tumor regression (50). Similarly, in another study, no tumor recurrences were found in patients with less than 30% of the original volume at a dose level of 30 Gy in approximately 3–3½ weeks (51).

Functional Imaging for Early Outcome Prediction: Predictive Imaging for Therapy Adaptation—Future Directions

Dynamic Contrast-enhanced MR Imaging for Assessment of Cervical Cancer.—Dynamic contrast-enhanced MR imaging provides an in vivo imaging biomarker that, through its assessment of tumor perfusion, reflects the delivery of oxygen and therapeutic agents to the tumor (53,54). Both of these factors are critical for the success of therapy in patients with cervical cancer (55–57). Dynamic contrast-enhanced imaging sequences are easy and fast to use within a routine MR imaging examination before, during, and after radiation therapy and therefore can be easily incorporated into routine practice. Low levels of tissue enhance-

ment at dynamic contrast-enhanced imaging (Fig 9) (58), which signal poor tumor perfusion and hypoxia, have been shown to correlate with unfavorable tumor control and survival in patients with cervical cancer (59–61). This predictive information can be acquired as early as 2 weeks after the start of radiation therapy in patients with cervical cancer (60,61). Low perfusion during radiation therapy predicts significantly unfavorable tumor control and survival (73% vs 100%, $P = .006$; and 47% vs 79%, $P = .001$, respectively). Assessment at the 2-week intratreatment time thus may be more sensitive than the pretherapy evaluation (61).

Diffusion-weighted MR Imaging.—The indirect assessment of tumor cellularity (62,63) with diffusion-weighted MR imaging provides another physiologic-radiologic correlate to serve as an imaging biomarker during radiation therapy. The apparent diffusion coefficient from diffusion-weighted MR imaging is a measure of the magnitude of diffusion (of water molecules) within tissues. A low value for the apparent diffusion coefficient indicates that the tissue is cellular. Apparent diffusion coefficient values in tumors typically increase with successful treatment (64), which can be assessed earlier than morphologic tumor changes. In recent early clinical experience, investigators have shown that an intratreatment increase in the apparent diffusion coefficient is associated with improved tumor response after chemoradiotherapy for cervical cancer (65,66).

The findings of these early studies suggest that both dynamic contrast-enhanced MR imaging and diffusion-weighted MR imaging show promise as functional imaging biomarkers for response monitoring and outcome prediction in patients with cervical cancer. Dynamic contrast-enhanced MR imaging provides the ability to assess tumor perfusion, which is reflective of oxygenation and chemotherapy delivery; and diffusion-weighted MR imaging allows the assessment of tumor cellularity.

Table 10: Sample Radiology Report for Posttreatment Follow-up Studies (Commonly Performed to Evaluate for Clinically Suspected Recurrence)

Answer the pertinent questions asked by clinicians because some may be dictated by the clinical trial in which the patient is enrolled
Presence of recurrence or progression (or both) compared with the most recent examination
Extension of suspected tumor to adjacent structures (parametria, fixation to pelvic wall, vagina, bladder, rectum, ovaries, cul-de-sac, peritoneum)
In endometrial cancer: depth of tumor invasion and thickness of uterine wall (at the midpoint of the corpus or at a location of abnormality; measure both anterior and posterior thickness)
Size of tumor in three dimensions
3D tumor volume upon specific request
RECIST evaluation upon specific request
Please be specific and objective with regard to imaging interpretation pertaining to tumor progression (eg, patient may have decreased tumor size with new enlarged right external iliac lymph node)
Presence of tumor necrosis
Uterine findings
Intrauterine fluid
Patency of endocervical canal
Abnormal lymph nodes
Morphology and size in two dimensions
Fixation (ie, obliteration of fat planes surrounding the abnormal lymph node)
Complications: fistula, fluid collections, hydronephrosis, hydroureter, new metastasis
PET/CT additional item to report
Metabolic activity of the described lesions with SUV_{max} for each, as compared with the most recent examination (eg, SUV_{max} of the tumor is two times that of the liver, which is stable compared with the previous examination)

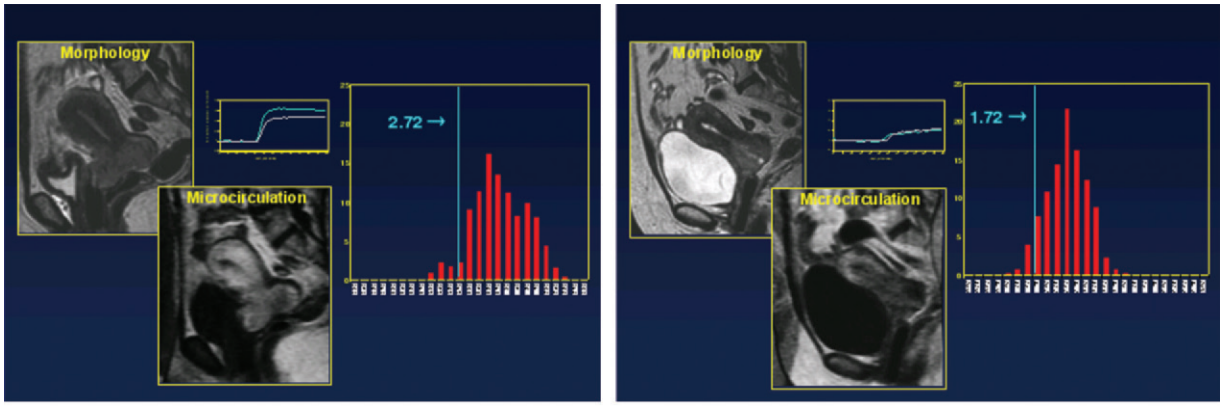
Early Outcome Prediction for Adaptive Therapy

With the early identification of the subgroup of patients at high risk for failure of standard therapy, more intensified therapy can be targeted to this population. Such risk-tailored personalization of care is a stark departure from the currently practiced evidence-based approach or current clinical trial designs that use therapy intensification indiscriminately for all patients with stage IB2–IVA cervical cancer.

Further clinical trials are under way to validate the outcome-predictive power of functional MR imaging in patients with gynecologic tumors and to determine the best method and timing of the imaging, so that imaging biomarker–based personalization of care can be built into the course of radiation therapy and chemotherapy by adapting the regimens of both the radiation therapy and the chemotherapy.

Conclusion

To optimize multidisciplinary care for patients with gynecologic cancer, radiologists should collaborate closely with their radiation oncology and gynecologic oncology colleagues and should tailor their radiology reports to the needs of the treating physicians because high-quality imaging has become essential not only for the staging of gynecologic malignancies but also for the delin-



a. b.

Figure 9. Dynamic contrast-enhanced MR imaging and tumor control in two women with stage IIB squamous cell carcinoma of the cervix. Dynamic contrast-enhanced MR images (left, center on **a, b**) and dynamic contrast enhancement distribution voxel histograms (right on **a, b**) of the two women show different heterogeneous dynamic contrast-enhanced patterns: intense dynamic contrast enhancement of the tumor region (high signal intensity, 10%) in one patient **(a)** and low dynamic contrast enhancement (low signal intensity, 10%) in the other patient **(b)**. The patient in **a** was alive and well 8 years after therapy and had experienced continued tumor control throughout the 8-year follow-up period, a finding consistent with cure of the cervical cancer. The tumor of the patient in **b** recurred in the cervix 2 months after therapy, and she died 6 months after therapy completion. (Adapted, with permission, from reference 58.)

eation of tumor extent for treatment planning and delivery, as well as for monitoring of the response to therapy.

***Disclosures of Conflicts of Interest.*—J.R.F.:** *Financial activities not related to the present article:* provided expert testimony; royalties from Morphometrics. **K.J.M.:** *Financial activities not related to the present article:* research grant from Siemens AG. **M.M.:** *Financial activities not related to the present article:* consultant for Amirsys.

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Imaging across the Life Span: Innovations in Imaging and Therapy for Gynecologic Cancer

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RadioGraphics 2014; 34:1062–1081 • **Published online** 10.1148/rg.344130099 • **Content Codes:** CT MR OB OI

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Advanced imaging is essential to radiation therapy for *(a)* the evaluation of the extent of tumor involvement for pretherapy staging and prognostic assessment, *(b)* tumor delineation for targeting in radiation therapy planning, *(c)* the evaluation of therapy response after or during the course of treatment, and *(d)* the prediction of early response and outcome, an emerging role that enables potential adaptive treatment.

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IMRT advances one step beyond 3D conformal radiation therapy by using inverse treatment planning by modulating the beam's intensity. The intensity of the radiation dose is elevated in the areas of the target and is decreased in the neighboring normal tissues. Inverse treatment planning is performed by first determining the dose objectives for the tumor target, as well as the normal tissues (normal tissue constraints). With the use of iterative algorithms and cost functions, inverse planning can be used to create a set of fluence maps for each beam angle, which result in a dose distribution that conforms to the predetermined dose objectives for target and normal tissues (3).

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Stereotactic body radiation therapy refers to stereotactically delivered radiation treatments within extracranial body sites. Because stereotactic body radiation therapy delivers only a few high-dose treatments (hypofractions) and applies highly focused radiation dose distributions to a relatively small and well-defined tumor target, stereotactic body radiation therapy requires extremely detailed imaging studies, real-time monitoring of imaging, rigid immobilization devices, and, in some cases, respiratory motion control.

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The actual tumor size, a well-established prognostic criterion in cervical cancer (10,14), is best assessed with MR imaging (15,16). With its superior soft-tissue contrast, MR imaging has been shown to be an excellent imaging modality to delineate the intrauterine tumor involvement in cervical and uterine cancer.

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Imaging, including CT, MR imaging, and PET/CT, plays an important role in *(a)* refining the tumor staging and target delineation, *(b)* monitoring therapy response, and *(c)* providing an early prediction of ultimate treatment failure, as well as a basis for adaptive therapy (Table 3).