At the end of the 19th century, following the discovery of x-rays by Roentgen and radium by the Curies, the first patient was treated with therapeutic x-rays. During the first few decades of the 20th century, the use of radiation increased significantly. The earliest uses of therapeutic radiation often involved treating gynecologic malignancies. Over the next one hundred years, radiation therapy became one of the integral treatment approaches for many cancers. Currently, it is an important therapeutic component in the management of many gynecologic malignancies, including cancers of the uterine cervix, uterine corpus, vulva and vagina.

Therapeutic radiation can be used by itself or in conjunction with surgery and/or chemotherapy to treat cancer. Radiation treatments are successful in killing tumors because cells of normal tissues in the body are better at repairing the damage caused by radiation than are tumor cells. The repair by normal tissues is not perfect; however, and so radiation oncologists design treatment plans that exclude as much normal tissue as possible while fully encompassing the tumor or target tissues.

Until recently, radiation treatments almost always delivered nearly the same dose to normal tissues adjacent to the tumor as to the tumor itself despite attempts to “block out,” or exclude, normal tissues. It is only recently, with technical advances in the planning and delivery of radiation, that treatments have become much more conformal, meaning that the tumor can receive a relatively high dose of radiation while nearby normal tissues receive lower doses. One such technique to achieve this reduction in dose to normal structures is with intensity-modulated radiation therapy (IMRT), a highly specialized type of radiation. IMRT has the potential to safely escalate radiation tumor doses and minimize normal tissue doses for a variety of malignancies, including gynecologic cancers. At the University of Wisconsin, the Radiation Oncology department thrives on exceptionally strong physics support, which is crucial for the implementation of new radiation techniques such as IMRT. Currently, we commonly use IMRT to treat prostate cancer, cancers of the head and neck, and some types of brain tumors. Although the national use of IMRT for gynecologic cancers is not as common as for other cancer types, it does hold some promise. At UW, we are participating in a multi-institutional study investigating the use of IMRT for select patients with cervical and endometrial cancer.

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The UW Gynecologic Oncology Program of the UW Comprehensive Cancer Center officially welcomes Stephen L. Rose, MD, and A.C. Evans, MD, PhD, to our clinical staff.
The decision to add radiation therapy after surgery for cervical or endometrial cancer is based upon intra-operative and pathologic findings that predict for a higher risk tumor recurrence, such as positive surgical margins, lymph node and large deeply invasive tumors. Studies have shown a reduction in the local recurrence rates following the addition of radiation therapy to the abdomen and/or pelvis for cervical and endometrial cancers with high risk features. Radiation used in conjunction with surgery for endometrial and cervical cancers, increases risk of treatment-related toxicities compared to either treatment modality used alone. In particular, the risk for long-term bowel complications is increased. This risk is mainly due to the increased doses of radiation that the small intestine receives following hysterectomy. When the uterus is in place, the majority of the small bowel is more superiorly located, and outside of the radiation field. After a hysterectomy, the small bowel falls inferiorly and is contained within standard pelvic radiation fields.

A few years ago, most patients receiving radiation therapy were treated using “conventional” planning. In this process, a patient undergoes a “simulation” in which fluoroscopic x-rays are obtained, and then the physician draws treatment fields that encompass the tumor and exclude some normal tissue that does not need to be irradiated. Although this technique is sometimes still used in palliative treatments, most treatments are now delivered with three-dimensional conformal radiation therapy (3-D CRT). In 3-D CRT, a patient undergoes a planning CT scan and the CT images are transferred to a computer with radiation planning software. This process provides visualization of all anatomic structures in much greater detail than fluoroscopic x-rays. The physician then contours the tumor and critical normal structures, and develops a treatment plan that best covers the tumor and delivers the least radiation dose to adjacent normal tissues.

Intensity-modulated radiation therapy (IMRT) is a highly specialized type of 3-D CRT designed to be even more conformal in the targeting of tumor and avoidance of nearby normal tissues. Like 3-D CRT, a CT is performed and the treating physician defines the tumor (target) dose and establishes dose constraints, or limits, for normal structures, such as kidneys, bowel, lungs, etc. Unlike standard 3-D CRT, an optimal treatment plan is generated via computer algorithms that modulate the intensity of the radiation by creating many “sub-beams” with varying radiation intensity. IMRT radiation plans have steep dose gradients between the tumor and the tissues that lie nearby, meaning that the targeted tumor can receive a high dose and adjacent normal tissues can receive much lower doses.

Because of its potential for widening the therapeutic window, either by dose escalation with higher tumor control rates, or by improved conformal avoidance with subsequent reduction of treatment-related complications, IMRT has become an increasingly popular radiation technique for treatment of prostate cancer and cancers of the head and neck region. Its use for gynecologic cancers, however, is still under investigation. The main potential advantage of IMRT in the treatment of gynecologic malignancies is its ability to develop a highly conformal radiation plan that delivers a lower dose to normal pelvic tissues, such as small bowel, than current standard radiation techniques. Initial studies, carried out at individual centers, have shown approximately a 50% reduction in the volume of small bowel irradiated to the prescribed treatment dose.

However, before IMRT can be employed more frequently for gynecologic cancers, it must be proven that the results achieved at single institutions can be duplicated in a multiinstitutional trial, and that IMRT for cervical and endometrial cancer can be widely implemented in a safe and reproducible manner. The University of Wisconsin Radiation Oncology and Gynecologic Oncology departments are participating in a Radiation Therapy Oncology Group (RTOG) study investigating the use of IMRT for patients with cervical and endometrial cancer in whom adjuvant radiation therapy is recommended. This is a national study evaluating the implementation of IMRT in a multiinstitutional setting. The study will also help determine whether post-operative IMRT for cervical and endometrial cancer reduces treatment-related toxicities compared to current radiation techniques.

**Protocol Eligibility***

- Endometrial cancer patients who have undergone total hysterectomy and bilateral salpingo-oophorectomy and require adjuvant radiation therapy

OR

- Cervical cancer patients who have undergone radical or simple hysterectomy and require postoperative chemoradiation therapy

- No para-aortic nodal disease

- 18 years or older

*Select eligibility requirements

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Our Current Protocols

Ovarian

GOG 199  Prospective Study of Risk-Reducing Salpingo-Oophorectomy and Longitudinal CA-125 Screening among Women at Increased Genetic Risk of Ovarian Cancer

GOG 212  A Randomized Phase II Trial of Maintenance Chemotherapy Comparing Single Agent Paclitaxel or Xyotax versus No Treatment until Relapse in Women with Advanced Ovarian or Primary Peritoneal Cancer

GOG 218  Phase III Trial of Carboplatin and Paclitaxel Plus Placebo Versus Carboplatin and Paclitaxel Plus Concurrent Bevacizumab in Women with Newly Diagnosed, Suboptimal, Advanced Stage Epithelial Ovarian and Peritoneal Cancer

GOG 220  Pelvic Mass Study to Develop Serum Proteomic Profiles (Signatures) for Epithelial Ovarian Cancer Diagnosis and Prognosis

Uterine

GOG 130-E  Phase II Evaluation of Gemcitabine and Docetaxel in the Treatment of Recurrent or Persistent Carcinomasarcoma of the Uterus

GOG 299  Randomized Phase III Trial of Doxorubicin/Cisplatin/Paclitaxel and G-CSF versus Carboplatin/Paclitaxel in Patients with Stage III & IV or Recurrent Endometrial Cancer

GOG 210  A Molecular Staging Study of Endometrial Carcinoma

GOG 230-B  Phase II Evaluation of Thalidomide in the Treatment of Recurrent or Persistent Carcinomasarcoma of the Uterus

Cervical

GOG 204  Randomized Phase III Trial of Paclitaxel/Cisplatin versus Vinorelbine/Cisplatin versus Gemcitabine/Cisplatin versus Topotecan/Cisplatin in Stage I/II, Recurrent or Persistent Carcinoma of the Cervix

GOG 206  Lymphatic Mapping and Sentinel Node Identification in Patients with Stage IB1 Cervical Carcinoma

GOG 9918  Phase I Trial of Tailored Radiation Therapy with Concomitant Celecoxib and Cisplatin in the Treatment of Patients with Cervical Cancer

Vulvar

GOG 173  Intraoperative Lymphatic Mapping and Sentinel Node Identification in Patients with Squamous Cell Carcinoma of the Vulva

Multiple Sites

CO 04702  Phase I Dose-Escalation Study of EMD 372066 Administered with Low-Dose Cyclophosphamide to Subjects with Epithelial Cell Adhesion Molecule (EpCAM) Positive Advanced Cancers

RT0G 0418  A Phase II Study of Intensity Modulated Radiation Therapy (IMRT) to the Pelvis +/- Chemotherapy for Post-operative Patients with either Endometrial or Cervical Carcinoma

For more information about these clinical trials at the UW Comprehensive Cancer Center, contact Cancer Connect, (800) 622-8922 or (608) 262-5225 in the Madison area.

A complete listing of all clinical trials at the UW Comprehensive Cancer Center is also available on our website, www.cancer.wisc.edu.
The UW Comprehensive Cancer Center has recently been renamed the UW Paul P. Carbone Comprehensive Cancer Center.

Tomotherapy, an innovative radiation treatment was discovered, developed and patented by UW Comprehensive Cancer Center researchers.

Radiation therapy is administered to roughly half of all cancer patients.

Both the UW Gyn-oncology and Radiation Oncology Clinics were named Star Clinics with scores above the 90th percentile in the Press Ganey customer satisfaction survey.

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