Int. J. Radiation Oncology Biol. Phys., Vol. 71, No. 2, pp. 428–434, 2008

0360-3016/08/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2007.09.042

CLINICAL INVESTIGATION **Uterus**

CONSENSUS GUIDELINES FOR DELINEATION OF CLINICAL TARGET VOLUME FOR INTENSITY-MODULATED PELVIC RADIOTHERAPY IN POSTOPERATIVE TREATMENT OF ENDOMETRIAL AND CERVICAL CANCER

William Small, Jr., M.D.,* Loren K. Mell, M.D.,† Penny Anderson, M.D.,‡ Carien Creutzberg, M.D.,§ Jennifer De Los Santos, M.D.,¶ David Gaffney, M.D., Ph.D.,‖ Anuja Jhingran, M.D.,# Lorraine Portelance, M.D.,** Tracey Schefter, M.D.,†† Revathy Iyer, M.D.,‡‡ Mahesh Varia, M.D.,§§ Kathryn Winter, M.S.,¶¶ and Arno J. Mundt, M.D.‖‖

*Department of Radiation Oncology, Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL; †Department of Radiation and Cellular Oncology, University of Chicago Pritzker School of Medicine, Chicago, IL; ‡Department of Radiation Oncology, Fox Chase Cancer Center, Philadelphia, PA; §Department of Clinical Oncology, Leiden University Medical Center, Leiden, The Netherlands; ¶Department of Radiation Oncology, University of Alabama at Birmingham, Birmingham, AL; ‖Department of Radiation Oncology, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; #Department of Radiation Oncology, M.D. Anderson Cancer Center, Houston, TX; **Department of Radiation Oncology, McGill University Health Center, Quebec, ON, Canada; ††Department of Radiation Oncology, University of Colorado, Aurora, CO; ‡‡Department of Radiology, M.D. Anderson Cancer Center, Houston, TX; §§Department of Radiation Oncology, University of North Carolina, Chapel Hill, NC; ¶¶Statistical Section, Radiation Therapy Oncology Group, Philadelphia, PA; and ‖‖Department of Radiation Oncology, University of California, San Diego, School of Medicine, La Jolla, CA

Purpose: To develop an atlas of the clinical target volume (CTV) definitions for postoperative radiotherapy of endometrial and cervical cancer to be used for planning pelvic intensity-modulated radiotherapy.

Methods and Materials: The Radiation Therapy Oncology Group led an international collaberation of cooperative groups in the development of the atlas. The groups included the Radiation Therapy Oncology Group, Gynecologic Oncology Group, National Cancer Institute of Canada, European Society of Therapeutic Radiology and Oncology, and American College of Radiology Imaging Network. The members of the group were asked by questionnaire to define the areas that were to be included in the CTV and to outline theses areas on individual computed tomography images. The initial formulation of the group began in late 2004 and culminated with a formal consensus conference in June 2005.

Results: The committee achieved a consensus CTV definition for postoperative therapy for endometrial and cervical cancer. The CTV should include the common, external, and internal iliac lymph node regions. The upper 3.0 cm of the vagina and paravaginal soft tissue lateral to the vagina should also be included. For patients with cervical cancer, or endometrial cancer with cervical stromal invasion, it is also recommended that the CTV include the presacral lymph node region.

Conclusion: This report serves as an international template for the definition of the CTV for postoperative intensity-modulated radiotherapy for endometrial and cervical cancer.

Intensity-modulated radiotherapy, Adjuvant therapy, Pelvic radiotherapy, Endometrial cancer, Cervical cancer.

INTRODUCTION

Intensity-modulated radiotherapy (IMRT) enables the delivery of complex RT plans that previously could not be accomplished with conventional techniques, including the most sophisticated three-dimensional (3D) conformal RT (3D-CRT). Conventional 3D-CRT is accomplished with a set of fixed radiation beams that are shaped using the projection of the target volume and normally have a uniform intensity across the field. When appropriate, conventional fields can be modified by simple devices such as compensating filters or wedges. IMRT delivers optimized, nonuniform, radiation beam intensities to deliver highly conformal therapies, especially to targets that have complex shapes and/or concave regions.

The advantage IMRT has over 3D-CRT is also the greatest challenge facing the radiation oncology community—that is,

Reprint requests to: William Small, Jr., M.D., Robert H. Lurie Comprehensive Cancer Center, Northwestern University, 251 E. Huron St., LC-178, Chicago, IL 60611. Tel: (312) 925-6819; Fax: (312) 926-6374; E-mail: wsmall@nmff.org

Conflict of interest: none.

Received Aug 21, 2007, and in revised form Sept 20, 2007. Accepted for publication Sept 20, 2007.

defining the targets that need to be irradiated to accomplish the goals of therapy. This is particularly challenging in whole pelvic RT for gynecologic malignancies. Traditional conformal postoperative RT has delivered RT in a ''four-field box'' technique. The anteroposterior–posteroanterior portions of the field's lateral extents tend to be defined by the bony pelvis. The lateral fields often include the presacral space posteriorly, especially in cervical cancer; anteriorly, the field is defined by the external iliac lymph nodes. This traditional treatment volume has provided excellent tumor control with what is traditionally considered acceptable toxicity. However, these techniques, based on generic bony landmarks as surrogates for the clinical target volume (CTV), do not lend themselves to customized treatment planning using an individual patient's CTV and results in substantial irradiation of normal organs such as the small bowel, rectum, and bone marrow.

The use of IMRT provides the ability to confine the high-dose portions of the radiation fields to nontraditional shapes. It is generally considered that the CTV to be irradiated postoperatively for endometrial cancer and cervical cancer includes the draining lymphatics, parametrium, and upper vagina. The middle of the pelvis, in the postoperative situation, is often occupied by relatively radiosensitive small intestine. In addition, the rectum and bone marrow are not thought to be at risk of recurrence and hence are unnecessary to irradiate. IMRT has been shown to reduce normal tissue irradiation (1–6) and has been associated with reduced acute (7, 8) and chronic (9) toxicity compared with conventional 3D-CRT.

Critical to the use of IMRT as a standard option for postoperative therapy for endometrial and cervical cancer is a clear understanding of the CTV definitions. In preparation for a prospective clinical trial (Radiation Therapy Oncology Group [RTOG] trial 0418), the RTOG led an international collaboration to define an atlas of target definitions for postoperative pelvic RT for endometrial and cervical cancer. This report provides the conclusions of this collaboration.

METHODS AND MATERIALS

The RTOG elected to proceed with a prospective trial evaluating the role of IMRT in postoperative RT for endometrial and cervical cancer (RTOG 0418). The primary objective of the trial was to determine the transportability of IMRT to a multi-institutional setting. Secondary objectives included toxicity and disease control endpoints. In preparation for the activation of the trial, it was believed that an atlas would improve the ability to obtain the trial's primary objective. The RTOG gynecologic working group thought that, to be successful, the atlas would need to be a consensus document with inclusion of multiple national and international cooperative groups.

The groups included in the atlas development were the RTOG (W.S., L.M., J.D., D.G., K.W., and A.M.), Gynecologic Oncology Group (P.A., M.V.), National Cancer Institute of Canada (L.P.), European Society of Therapeutic Radiology and Oncology (C.C.), and the American College of Radiology Imaging Network (R.I.). The representatives of the groups were asked to obtain formal endorsement of the final atlas before publication.

The initial formulation of the group began in late 2004. The final representatives were formalized early in 2005. During the ensuing months, multiple informal discussions were held by both electronic mail and telephone. Ultimately, a sample set of computed tomography (CT) images were distributed to the members of the group, along with a questionnaire. The questionnaire asked which sites should be considered target volumes for postoperative therapy, and the members of the group were asked to contour the CTV for postoperative therapy for endometrial and cervical cancer on each individual CT image. A formal consensus conference was sponsored by the RTOG and held in Philadelphia June 23, 2005. The members reviewed the sites and the contoured CTV data. Atlases of pelvic anatomy (10), pelvic surgery textbooks (11), surgical atlases (12), pelvic imaging textbooks (13–15), published pelvic IMRT experience (1–9, 16–20), imaging studies (21–28), and experience were used for this purpose. At this meeting, a general consensus regarding the CTVs was obtained. During the ensuing months, the chairs of the guideline (W.S., A.M.) worked out the remaining inconsistencies and presented the group with a final product. This CTV guideline atlas was approved and formally placed on the RTOG Website February 17, 2006 (29). The RTOG 0418 trial was activated March 20, 2006.

To allow for feedback and address any problems during the initiation of the RTOG 0418 protocol, formal publication of this atlas awaited the first amendment to the protocol in case of changes needed in the atlas. Amendment 1 occurred on September 20, 2006 without the need for any changes in the current atlas.

RESULTS

The committee achieved a consensus CTV definition. The CTV should include the common, external, and internal iliac lymph node regions (Table 1). The upper 3.0 cm of the vagina and paravaginal soft tissue lateral to the vagina should also be included. For patients with cervical cancer, or endometrial cancer with cervical stromal invasion, it was also recommended that the CTV include the presacral lymph node region. Specific recommendations have been given for a bladder integrated target volume (ITV) to take into account bladder filling variations on a day-to-day basis [see ''Inferior CTV (below and including vaginal cuff)'' below]. No consensus opinion was reached regarding the variation in rectal filling other than if excessive rectal distension was observed on the planning CT scan, repeat treatment planning should be considered. The superior border of the CTV should begin 7 mm below the L4–L5 interspace. A uniform, 3D planning target volume expansion (typically 7 mm) will mimic a block edge at the L4–L5 interspace, such as would customarily be used in a conventional four-field box. The inferior border should extend to 3.0 cm below the upper extent of the vagina (as defined by the vaginal marker) or to 1.0 cm above the inferior extent of the obturator foramen, whichever is lower, to mimic a lower block edge. A more detailed description of the CTV design follows (see also Figs. 1–8).

Superior CTV (above bifurcation of common iliac vessels)

The superior portion of the CTV should be defined initially by adding a 7-mm margin around the common iliac vessels seen on the axial CT slice (Fig. 1). The CTV should be