SUMMARY OF CHANGES
Amendment 3: August 17, 2011
(Broadcast: August 25, 2011)

RTOG 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”

Study Chair: Anuja Jhingran, M.D., (713)563-2347; Ajhingra@mdanderson.org

RTOG 0418 has been amended as follows:

As mandated by CTEP, this study will utilize CTCAE version 4.0 for AdEERS reporting of adverse events beginning October 1, 2011. Related changes were made to Section 7.5.

All AE reporting on the study case report forms will continue to use CTCAE version 3.0.

Note: References to CTCAE, version 3.0, may remain in the protocol. These are appropriate, as treatment decision for patients enrolled on this study were based on that version.

Other Changes
Global: All weblinks and related descriptions to sub-pages of the RTOG website were updated.

Title Page: The contact information for Brigitte E. Miller, MD has been revised; The Document Version History table was added per current RTOG standard
SUMMARY OF CHANGES
Amendment #2, Version Date: May 15, 2007

RTOG 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”

Study Chair: Anuja Jhingran, M.D., (713)563-2347; Ajhingra@mdanderson.org

RTOG 0418 has been amended as follows:

Eligibility checklist, question 2, page 1: “Within” was added before “7 weeks” for consistency with Section 3.1.1

Section 3.1.7
- 5th bullet: “mg%” was corrected to “mg/dl”
- 6th and 7th bullets: “AST” and “ALT” were moved from the last bullet and were given maximum values of ≤ 2 X ULN because these parameters were inadvertently omitted
- The hemoglobin requirement was moved to the beginning of the bulleted list, and all requirements except for hemoglobin were made mandatory for cervix patients only. Since endometrial patients are not receiving chemotherapy, there is no need to have these minimum counts in this population; radiation therapy alone does not affect these counts.

Section 6.1.1.1: 1st sentence: “ITV with 5 mm margin” was corrected to “ITV with 7.0 mm margin”

Section 6.4.3: 1st sentence: The definition of CTV was corrected from “GTV plus areas considered to contain potential microscopic disease” to “areas considered to contain potential microscopic disease”

Section 6.4.12: 2nd sentence: “Anteriorly” was added because it was inadvertently omitted

Section 7.1.7: Dose column: “Weekly” was added to “max total dose” for increased clarity and accuracy

Section 7.2.1
- Parameters column, 1st row: “mg%” was corrected to “mg/dl”; “50” was corrected to “50”
- Parameters column, 2nd row: “mg/m” was corrected to “mm³”
- Parameters column, 3rd row: “mm³” was added for increased clarity
- Parameters column, 4th row: “mg/dl” was added for increased clarity
- Parameters column, 6th row: “grade” was added for increased clarity
- Parameters column, 7th row: “grade” was added for increased clarity
- Toxicity column, 5th row: “ALT” was corrected to “AST”

Section 11.1
- Per the modifications described in Section 3.1.7, a row for hemoglobin was added, with a corresponding footnote k (“cervix and endometrial patients”)
- Per the modifications described in Section 3.1.7, footnote l was added ("cervix patients only") for CBC/platelets; AST, bilirubin, alkaline phosphatase, serum creatinine; creatinine clearance; and BUN, Lytes, Mg
- In footnote g, “mg%” was corrected to “mg/dl”

Appendix III: Staging for Endometrial Cancer: The 6th edition of the staging system has replaced the former text. The former text was inadvertently from the 5th edition
SUMMARY OF CHANGES
Amendment #1, Version Date: September 20, 2006

RTOG 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”

Study Chair: Anuja Jhingran, M.D., (713)563-2347; Ajhingra@mdanderson.org

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RTOG 0418 has been amended as follows:

**Schema:** “5 cycles” was changed to “5 weeks” for increased clarity and accuracy.

**Sections 3.1.7:** The Cockroft-Gault formula was modified to use ideal weight for creatinine clearance due to safety considerations. Patients with gynecologic malignancies, especially endometrial patients, tend to be heavier; therefore, using ideal weight in this formula is safer.

**Section 3.1.9:** The timeframe for chest x-ray was corrected from “8 weeks prior to registration” to “within 8 weeks prior to registration.”

**Section 6.4.11:** The second-to-last sentence, “the lateral margin of the vaginal PTV should be to the obturator muscle,” was added to provide better coverage to the parametrial space.

**Section 6.4.12:** The last sentence was modified from “The vaginal PTV will be 7.0 mm around the vaginal ITV superiorly, inferiorly and laterally; however, only 5 mm posteriorly around the rectum” to “The vaginal PTV will be 7.0 mm around the vaginal ITV superiorly, inferiorly, laterally, and posteriorly” to provide better coverage to the vagina.

**Section 6.5.5.1:** Specifications for a minor deviation were added for increased clarity and accuracy and to better clarify doses to specific organs in order to help physicians and physicists to better address coverage to the vagina and nodes while keeping the organs at risk to a minimum.

**Section 6.5.5.2:**
- Limits were changed from “< 30% to receive ≥ 40 Gy” to “< 60% to receive ≥ 30 Gy” because the original doses were too restrictive and not easily achieved.
- Specifications for a minor deviation were added for increased clarity and accuracy and to better clarify doses to specific organs in order to help physicians and physicists to better address coverage to the vagina and nodes while keeping the organs at risk to a minimum.

**Section 6.5.5.3:** Specifications for a minor deviation were added for increased clarity and accuracy and to better clarify doses to specific organs in order to help physicians and physicists to better address coverage to the vagina and nodes while keeping the organs at risk to a minimum.

**Section 6.5.5.4:** Specifications for a minor deviation were added for increased clarity and accuracy and to better clarify doses to specific organs in order to help physicians and physicists to better address coverage to the vagina and nodes while keeping the organs at risk to a minimum.

**Section 7.1.6**
- 1st sentence: “5 cycles” was changed to “5 weeks” for increased clarity and accuracy.
- 2nd sentence: Prehydration instructions were modified to permit prehydration according to institutional guidelines/policy.
Section 7.1.7: In the cisplatin row/last column, the text was modified from “Beginning Monday or Tuesday; 5 cycles concurrent with IMRT” to “Weekly (on Monday or Tuesday) X 5 weeks” for increased clarity and accuracy.

Section 7.2.1: In footnote **, the Cockroft-Gault formula was modified to use ideal weight for creatinine clearance due to safety considerations. Patients with gynecologic malignancies, especially endometrial patients, tend to be heavier; therefore, using ideal weight in this formula is safer.

Section 10.1: In the 2nd paragraph, 1st sentence, central review of pathology was removed because it is not a component of this study.

Section 10.2.5: Contact information was updated for LDS Hospital.

Section 11.1/study parameter table: The timeframe for Pap smears was changed from “Four weeks post completion of IMRT and then every 3 months during the first two years; every 6 months during years 3-5; then annually” (footnote c) to “Every 3-6 months during the first two years; every 6 months during years 3-5; then annually” (footnote j) because 4 weeks post-treatment is usually too early and results in treatment effect on the Pap smear; by 3-6 months, the treatment effects have resolved so that the Pap smear will be more predictive.

Appendix I
- Why is this study being done?: The last sentence of the first paragraph was deleted because quality of life is not a component of this study.
- What will happen if I take part in this research study?/during follow-up: The timeframe for Pap smear was added for consistency with the modification made in Section 11.
- Risks and side effects related to radiation therapy/less likely, but serious: The last two bullets were combined and modified because the description of “vaginal vault destruction” in the previous version was unclear.

Appendix III: In the Staging for Cervical Cancer, all references to FIGO IVB were deleted per the AJCC 6th edition. Deletions were made to the last line of the Primary Tumor section and to the last line of the Stage Grouping section.
SUMMARY OF CHANGES
Update Date: April 21, 2006

RTOG 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"

Study Chair: Anuja Jhingran, M.D., (713)563-2347; Ajhingra@mdanderson.org

RTOG 0418 has been updated as follows:

Section 3.1.7: The creatinine clearance formula was corrected; and has been provided in a more user-friendly format.