Dose-escalated hypofractionated IMRT for localized prostate cancer has similar side effects when compared to conventional IMRT

Fairfax, Va., April 3, 2014—Dose-escalated intensity modulated radiation therapy (IMRT) with use of a moderate hypofractionation regimen (72 Gy in 2.4 Gy fractions) can safely treat patients with localized prostate cancer with limited grade 2 or 3 late toxicity, according to a study published in the April 1, 2014 edition of the *International Journal of Radiation Oncology ● Biology ● Physics* (Red Journal), the official scientific journal of the American Society for Radiation Oncology (ASTRO).

Previous randomized clinical trials have shown that dose-escalated radiation therapy improves prostate cancer control compared to lower-dose conventional radiation therapy. Conventional fractionation of dose-escalated radiation therapy (1.8 or 2 Gy fractions) can take up to nine weeks to complete, while hypofractionated radiation therapy can deliver a higher biologically effective dose over a shorter period of time (six weeks) and has the potential to increase prostate cancer control without increasing toxicity. However, there are limited data on the late toxicity of moderate hypofractionated regimens for prostate cancer. This randomized trial from the University of Texas MD Anderson Cancer Center compares the late toxicity outcomes of men with localized prostate cancer treated with either conventionally fractionated IMRT (CIMRT) or dose-escalated hypofractionated IMRT (HIMRT).

Men with organ-confined prostate cancer were enrolled in this institutional review board-approved trial from January 2001 to January 2010 and were randomized to receive either CIMRT or HIMRT.
(75.6 Gy in 1.8 Gy fractions over eight-and-a-half weeks) or HIMRT (72 Gy in 2.4 Gy fractions over six weeks). Eligible patients had biopsy-proven prostate adenocarcinoma; good performance status; stage T1b-T3b disease; a prostate-specific antigen (PSA) ≤20 ng/ml; a Gleason score <10; and no clinical, radiographic or pathologic evidence of nodal or bone metastasis. Patients with stage cT3c or cT4 disease, a history of prior pelvic radiation therapy, or who received more than four months of hormone ablation therapy with prior or planned radical prostate surgery and with concurrent active malignancy other than nonmetastatic skin cancer or early-stage chronic lymphocytic leukemia were not eligible for the trial. The median age of the patient cohort was 68. Of the 203 patients analyzed in the study, 72 percent had stage T1 disease (146) and 89 percent had a PSA <10 ng/ml (181). Thirty-four percent (70) had Gleason 6 disease, 65 percent (131) had Gleason 7 disease and 1 percent (2) had Gleason 8 disease. Patients were classified into low-risk (28 percent = 57), intermediate risk (71 percent = 144) and high-risk (1 percent = 2) disease using current National Comprehensive Cancer Network risk-group definitions.

All patients were treated with static-field IMRT. One hundred and one (101) men received CIMRT and 102 men received HIMRT. Physician-reported toxicity was evaluated for all patients during treatment and at each follow-up visit. After completion of radiation therapy, follow-up was conducted at least every six months for the first two years post-treatment, and annually thereafter. Median follow-up was six years.

Late gastrointestinal (GI) and genitourinary (GU) toxicity were analyzed in this study, starting 90 days post-treatment, using modified Radiation Therapy Oncology Group toxicity grading. In the CIMRT arm, 17 percent (17) experienced grade 1 GI toxicity, 4 percent (4) experienced grade 2 GI toxicity and 1 percent (1) experienced grade 3 GI toxicity. In the HIMRT arm, 26 percent (27) experienced grade 1 GI toxicity, 9 percent (9) experienced grade 2 GI toxicity and 2 percent (2) experienced grade 3 GI toxicity. There was a numeric increase in the absolute frequency of late GI toxicity for men treated with HIMRT, but the difference was not statistically significant. The five-year actuarial grade 2 or 3 late GI toxicity was 5.1 percent (95 percent Confidence Interval (CI)) for patients treated with CIMRT and 10 percent for patients treated with HIMRT. The increase in late GI toxicity
for men receiving HIMRT was the result of moderate and high radiation dose to a larger proportion of the rectum, which suggests that more stringent dose constraints for the rectum may result in lower late GI toxicity for those patients.

Additionally, there was not a statistically significant difference in the absolute frequency of late GU toxicity in men treated with CIMRT or HIMRT. In the CIMRT arm, 15 percent (15) experienced grade 1 GU toxicity, 14 percent (14) experienced grade 2 GU toxicity and 1 percent (1) experienced grade 3 GU toxicity. In the HIMRT arm, 10 percent (10) experienced grade 1 GU toxicity and 15 percent (15) experienced grade 2 GU toxicity; no patients reported grade 3 GU toxicity. The five-year actuarial grade 2 or 3 late GU toxicity was 16.5 percent (95 percent CI) for patients treated with CIMRT and 15.8 percent for patients treated with HIMRT.

“These results demonstrate that the length of radiation treatment for prostate cancer can be safely decreased to six weeks (from eight-and-a-half weeks) by delivering larger daily doses of radiation without increasing the urinary and bowel effects,” said Karen E. Hoffman, MD, a co-author of the study and assistant professor in the Division of Radiation Oncology at the University of Texas MD Anderson Cancer Center in Houston. “Decreasing the length of treatment decreases the cost and is more convenient for patients.”

For a copy of the manuscript of the study, contact Brittany Ashcroft at 703-839-7336, press@astro.org. For more information about the Red Journal, visit www.redjournal.org.

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an extensive patient website, www.rtanswers.org; and created the Radiation Oncology Institute (www.roinstitute.org), a non-profit foundation to support research and education efforts around the world that enhance and confirm the critical role of radiation therapy in improving cancer treatment. To learn more about ASTRO, visit www.astro.org.

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