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News Release

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Men with low- and intermediate-risk prostate cancer can safely benefit from fewer, higher-dose radiation treatments

Large, long-term study finds stereotactic body radiation therapy (SBRT) to be as safe and effective as longer-course treatment

SAN ANTONIO, October 22, 2018 — Stereotactic body radiation therapy (SBRT) is a safe and effective treatment for men with low- and intermediate-risk prostate cancer, according to a long-term, multi-institutional study. The study clears the way for patients who may wish to shorten their course of treatment without fear of increasing their risk for severe, adverse side effects. Findings will be presented today at the 60th Annual Meeting of the American Society for Radiation Oncology (ASTRO).

Stereotactic radiation is a form of external beam radiation therapy (EBRT) that delivers substantially larger doses of radiation per treatment session over a much shorter time period than traditional EBRT. It is also known as extreme hypofractionation, because it delivers higher levels of radiation per fraction, or dose.

The treatment has been studied since 2000 but has not been widely adopted because of concerns over long-term safety and efficacy. Guidelines issued by ASTRO and by the National Comprehensive Cancer Network (NCCN) have called for longer follow-up studies of stereotactic radiation for prostate cancer, including multi-institutional data, to address concerns about potentially worse late toxicities occurring from higher-dose treatments.

“This study should meet those criteria and put patients at ease when considering treatment options,” said lead author Amar U. Kishan, MD, an assistant professor in the department of radiation oncology at the David Geffen School of Medicine at the University of California, Los Angeles (UCLA).

“Radiation therapy is typically delivered in small daily doses over a multi-week period,” explained Dr. Kishan. “However, because prostate cancer cells appear to be unusually sensitive to higher daily doses of radiation, you can reduce the duration of treatment from as many as 8-9 weeks with 39-45 treatments down to about 1.5 weeks with 4-5 treatments. This study should allay the fears of those who prefer to undertake a shorter treatment course that they can do so safely and with the same, positive outcomes they would receive from a longer course of treatment.”

This multi-institutional consortium study — to date the largest analysis of long-term outcomes following SBRT for this patient population — includes data from 10 institutional trials and two large multi-institutional studies. It examines the long-term safety and efficacy of SBRT for low- and intermediate-risk prostate cancer in a cohort of 2,142 men enrolled in institutional phase II trials of SBRT from 2000 to 2012.

Of the 2,142 patients evaluated, slightly more than half (55.3 percent, n=1,185) had low-risk disease; about a third (32.3 percent, n=692) had favorable intermediate-risk disease; and 12.4 percent (n=265) had unfavorable intermediate risk disease, that is, they had multiple intermediate risk factors, primary Gleason pattern 4 disease or ≥50 percent positive cores. Median patient age was 67.9 years (range: 41-92).

Most patients were treated daily (47.3 percent) or every other day (47.4 percent), while a small percentage (5.3 percent) were treated once a week. Doses ranged from 33.5 to 40 Gray (Gy) and were given in four or five fractions (88 percent of patients received five fractions). A small percentage (5.4 percent, n=115) of patients received concurrent androgen deprivation therapy (ADT, also known as hormone therapy), with utilization rates ranging from 3.6 percent in low-risk patients to 9.4 percent in unfavorable intermediate-risk patients. The median duration of ADT was three months.

Patients were followed for a median period of 6.9 years (interquartile range (IQR): 4.9-8.1). Those who were low-risk were followed for 7.1 years (IQR 5.4-8.8); those with favorable intermediate-risk were followed for 6.2 years (IQR 4.1-7.9); and those in the unfavorable intermediate-risk group were followed for 5.9 years (IQR 3.3-7.1). A subset of 305 patients had a minimum follow-up of nine years, and a median follow-up of 9.8 years. These included 223 patients with low-risk disease, 65 patients with favorable intermediate-risk disease and 27 patients with unfavorable intermediate-risk disease.

Researchers measured the safety and efficacy of stereotactic radiation using the following criteria: a cumulative incidence of biochemical recurrence (BCR) marked by rising PSA levels following SBRT; cumulative incidence of distant metastases (DM), i.e., the cancer spreading from the tumor to distant organs or lymph nodes; biochemical recurrence-free survival (BCRFS); and overall survival. They also evaluated the occurrence short-term adverse events within 90 days following completion of SBRT.

None of the patients in the study died from prostate cancer. In all, 100 patients (6 percent) experienced recurrence and 10 experienced distant metastases (0.6 percent). In the low-risk group, 95.5 percent of patients were free from BCR at seven years. In the favorable intermediate-risk group, 91.4 percent of patients were BCR-free at seven years. In the unfavorable intermediate-risk group, 85.1 percent were BCR-free at seven years.

Overall survival rates for the low-risk and favorable intermediate-risk groups were 91.4 and 93.7 percent at seven years following treatment. In the unfavorable intermediate-risk group, the most aggressive form of cancer in this study, overall survival was 86.5 percent at seven years.

Severe toxicities were rare. Thirteen patients (0.6 percent) experienced grade 3 acute genitourinary (genital or urinary, or GU) toxicities and 42 patients (1.9 percent) experienced grade 3 late GU toxicity. There was just one late grade 4 GU toxicity (hemorrhagic urethritis) and one late grade 4 gastrointestinal toxicity (fistula-in-ano).

"These numbers are identical, if not superior, to other types of more commonly used radiation techniques," said Dr. Kishan. "There is no evidence of worse toxicity with SBRT. We have shown that this method is both safe and effective and should be a standard treatment option for patients with low- and intermediate-risk prostate cancer."

Each year, approximately 233,000 men are diagnosed with prostate cancer, the most common cancer in men in the United States. The majority of those are low-risk cancers, which are eligible for a wide range of treatments, including EBRT, radical prostatectomy, brachytherapy, ADT and active surveillance. Radiation is one of the most effective options for treatment, with an overall cure rate of 98 percent.

"Fewer treatments for patients would be more convenient as well as less costly," said Dr. Kishan. "It could also reduce missed days of work. The health care system will save money, and patients will save a lot of time and money as well. And, it can provide a significant psychological benefit, in that men can get on with their lives and put their treatment behind them."

The abstract, "Long-term outcomes of stereotactic body radiation therapy for low- and intermediate-risk prostate adenocarcinoma: A multi-institutional consortium study," will be presented in detail during a news briefing and an oral abstract session at ASTRO's 60th Annual Meeting in San Antonio. To schedule an interview with Dr. Kishan and/or outside experts in prostate cancer and/or stereotactic radiation, contact ASTRO's media relations team on-site at the Henry B. González Convention Center October 21 through 24, by phone at 703-286-1600 or by email at press@astro.org.

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Attribution to the American Society for Radiation Oncology (ASTRO) Annual Meeting requested in all coverage.

This news release contains additional and/or updated information from the study author(s).

Study Presentation Details

- News Briefing: Monday, October 22, 11:00 a.m. – 12:00 p.m. CT, Room 225-D, http://bit.ly/ASTRO18-2
- Scientific Session: Tuesday, October 23, 4:45 – 6:15 p.m. CT, Room 214 C/D
- Abstract available on the final page of this release.

Resources on Prostate Cancer and Radiation Therapy

- Digital brochure: Radiation Therapy for Prostate Cancer; (Spanish version)
- Videos: Radiation Therapy for Prostate Cancer; (Spanish version), An Introduction to Radiation Therapy; (Spanish version)
- ASTRO's clinical practice statements and guidelines
- Additional brochures, videos and information on radiation therapy from ASTRO's patient site, RTAnswers.org

ABOUT ASTRO

The American Society for Radiation Oncology (ASTRO) is the world's largest radiation oncology society, with more than 10,000 members who are physicians, nurses, biologists, physicists, radiation therapists, dosimetrists and other health care professionals who specialize in treating patients with radiation therapies. The Society is dedicated to improving patient care through professional education and training, support for clinical practice and health policy standards, advancement

of science and research, and advocacy. ASTRO publishes three medical journals, International Journal of Radiation Oncology • Biology • Physics, Practical Radiation Oncology and Advances in Radiation Oncology; developed and maintains an extensive patient website, RT Answers; and created the nonprofit foundation Radiation Oncology Institute. To learn more about ASTRO, visit astro.org or RTanswers.org, sign up to receive our news and follow us on our blog, Facebook and Twitter.

Abstract 217 – Long-Term Outcomes of Stereotactic Body Radiotherapy for Low- and Intermediate-Risk Prostate Adenocarcinoma: A Multi-Institutional Consortium Study

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Purpose/Objective(s): While a growing body of evidence supports the use of stereotactic body radiotherapy (SBRT) for the treatment of low- and intermediate-risk prostate adenocarcinoma (PCa), some trepidation exists regarding its long-term efficacy and safety.

Materials/Methods: Men with low- and intermediate-risk PCa, as defined per the National Comprehensive Cancer Network guidelines, who were enrolled on various institutional phase II trials of SBRT between 2000- 2012 were included in a multi-institutional consortium. Men with multiple intermediate-risk factors, primary Gleason pattern 4 disease, or ≥50% positive cores (if known) were further subclassified as having unfavorable intermediate-risk disease. Biochemical relapse (BCR) was defined as PSA > "nadir +2" or initiation of androgen deprivation therapy (ADT). Toxicity data were scored according to the CTCAE v 3.0 or Radiation Therapy Oncology Group scoring systems.

Results: A total of 1641 men were eligible for analysis, with a median follow-up of 7.1 years. 297 patients (18.1%) had at least 9 years of follow-up. Fractionation schemes ranged from 33.50-40 Gy in 4-5 fractions. 1034 patients (63.0%) had low-risk disease, 444 (27.0%) had favorable intermediate-risk disease, and 163 (9.9%) had unfavorable intermediate-risk disease. 58 patients (3.6%) received short-term ADT. 100 patients (6.0%) experienced BCR, 10 (0.6%) experienced distant metastases, and no patients died of PCa. By Kaplan-Meier analysis, 5- and 10-year freedom from BCR (FFBCR) rates were 97% and 91% in the low-risk group and 94% and 89% in the favorable intermediate-risk group; 5- and 8-year rates (as no 10-year follow-up was available) in the unfavorable intermediate-risk group were and 93% and 85% ($p < 0.05$ by log-rank test). Corresponding 5- and 10-year overall survival rates were 94% and 87% and 96.6% and 90.0% for the low and favorable-intermediate risk groups, and 5- and 8-year rates were and 90.5% and 88.4% in the unfavorable-intermediate risk group ($p < 0.05$ by log-rank test). Toxicity rates are displayed in table 1. Five patients (0.3%) experienced grade 3 acute genitourinary (GU) toxicities and 32 (2%) experienced grade 3 late GU toxicity. One late grade 4 GU toxicity (hemorrhagic urethritis) and one late grade 4 gastrointestinal toxicity (fistula-in-ano) were seen.

Conclusion: To the best of our knowledge, this is the largest analysis of long-term outcomes following SBRT for PCa, and suggest an efficacy and toxicity profile that compares favorably with other radiation modalities, such as conventionally-fractionated radiotherapy and brachytherapy. Offering SBRT in the context of a balanced discussion and shared decision making is appropriate for men with low and intermediate risk prostate cancer.

Table 1. Physician-Scored Toxicity (CTCAE or RTOG)

	Grade 1	Grade 2	Grade 3	Grade 4
Acute GU	344 (20.1%)	145 (8.8%)	5 (0.3%)	0
Acute GI	256 (15.6%)	52 (3.2%)	0 (0%)	0

Late GU	148 (9.0%)	129 (7.9%)	32 (2.0%)	1 (0.1%)
Late GI	86 (5.2%)	52 (3.2%)	2 (0.1%)	1 (0.1%)