Genomic classifier appears to predict metastasis in prostate cancer patients following prostatectomy

San Antonio, October 20, 2015—For men with prostate cancer who have had a prostatectomy and salvage radiation therapy (SRT), analyzing their tumor genome provides clues as to whether their cancer will metastasize, therefore enabling clinicians to better personalize treatment options, according to research presented today at the American Society for Radiation Oncology’s (ASTRO’s) 57th Annual Meeting.

Prostate cancer treatment varies based on the severity and stage of the disease, with some patients requiring prostatectomy, which is the surgical removal of the prostate. For those patients who develop elevated prostate-specific antigen (PSA) levels following a prostatectomy, indicating that cancer cells remain in the body, additional treatment with SRT is generally the next step in treatment. Depending on other clinical indicators, the cancer metastasizing may be of concern and patients might also receive, in addition to RT, aggressive hormone therapy, which can aid in treating the cancer by suppressing male hormones.
The recurrence of a high PSA level alone is not an ideal indicator of future metastatic disease; therefore, researchers in this study looked to determine if a genomic classifier (GC), known as a validated predictor of metastasis, could distinguish the patients for whom additional, aggressive therapy is beneficial from those for whom SRT on its own is likely sufficient.

The study evaluated 166 prostate cancer patients, 53 African-American men (32 percent) and 113 Caucasian-American men (68 percent) who received SRT between 1990 and 2010 at Thomas Jefferson University, Veteran Affairs Medical Center Durham, and Mayo Clinic. GC scores were calculated for each patient based on genomic analysis of their own tumor tissue. A post-surgical sample was used from each patient’s removed prostate (a tissue sample was removed from the prostatectomy specimen from the area containing the highest Gleason score) and compared to the patient’s Cancer of the Prostate Risk Assessment Postsurgical (CAPRA-S) scores using survival c-index, competing-risks and Cox regression analysis for the prediction of metastasis. A patient’s CAPRA-S scores are based on clinical risk factors such as pre-surgical PSA score; Gleason score (a grading system used to help evaluate the prognosis of men with prostate cancer using samples from a prostate biopsy); area around the prostate affected by cancer; and lymph node involvement.

Data indicated that a patient’s GC score was the most significant factor in predicting the development of metastases five years after salvage radiation therapy, with GC low-risk patients having a 2.8 percent incidence of metastases at five years, GC average-risk patients having 5.8 percent incidence and GC high-risk patients having 33.5 percent as compared to 17 percent, 2.3 percent and 15 percent incidence of metastases in patients with low, average and high CAPRA-S scores, respectively. For those patients who were determined to be at low-risk by GC, there was no difference in the incidence of metastases regardless of the PSA value at which salvage radiation was initiated. For men with high risk, there was a significantly higher incidence of metastases in men receiving salvage radiation therapy with a PSA greater than 1 ng/ml as compared to those with PSA between 0.2-1 ng/ml.

“Our findings are particularly intriguing and provide a unique, more individualized approach to managing men receiving SRT after radical prostatectomy (RP),” said lead study author Robert Den.
MD, assistant professor of radiation oncology at Sidney Kimmel Medical College at Thomas Jefferson University. “Indeed, the GC biomarker provides an insight regarding tumor aggressiveness in these individuals. Despite salvage local therapy for recurrent prostate cancer after RP, some patients continue to progress to metastases. Identifying these men may allow them to undergo systemic therapy, including testing novel therapies to reduce the risk of metastases. And, the men at low risk of progression can be spared treatment intensification, such as high dose hormone therapy, which may lead to permanent side effects.”

The abstract, “Validation of a Genomic Classifier for Prediction of Metastasis Following Postoperative Salvage Radiation Therapy” will be presented in detail during a scientific session at ASTRO’s 57th Annual Meeting at 1:15 p.m. Central time on Wednesday, October 21, 2015.

To speak with Dr. Den, please call Nancy Mayes on October 18-21, 2015, in the ASTRO Press Office at the Henry B. González Convention Center, in San Antonio at 210-258-8104 or 210-258-8105, or email press@astro.org.

ASTRO’s 57th Annual Meeting, to be held at the Henry B. González Convention Center in San Antonio, October 18-21, 2015, is the nation’s premier scientific meeting in radiation oncology. The 2015 Annual Meeting is expected to attract more than 11,000 attendees including oncologists from all disciplines, medical physicists, dosimetrists, radiation therapists, radiation oncology nurses and nurse practitioners, biologists, physician assistants, practice administrators, industry representatives and other health care professionals from around the world. Led by ASTRO President Bruce D. Minsky, MD, FASTRO, a radiation oncologist specializing in gastrointestinal cancers, Professor of Radiation Oncology, and the Frank T. McGraw Memorial Chair at The University of Texas MD Anderson Cancer Center, Houston, the theme of the 2015 Meeting is “Technology Meets Patient Care.” Dr. Minsky’s Presidential Symposium, “Multidisciplinary Management of Esophageal and Rectal Cancers,” will feature Leonard L. Gunderson, MD, MS, FASTRO, and Joel E. Tepper, MD, FASTRO, to highlight imaging, staging, genomics and data mining approaches, as well as the latest advances in esophageal and colorectal cancer treatment. ASTRO’s four-day scientific meeting includes presentation of more than 2,100 abstracts: up to four plenary papers, 351 oral presentations,
1,609 posters and 171 digital posters in more than 52 educational sessions and 26 scientific panels for 20 disease-site tracks. Three keynote speakers will address a range of topics including cancer biology in radiation oncology, the essential roles of a physician, and patient safety: Arul Chinnaiyan, MD, PhD, Professor and Director, Michigan Center for Translational Pathology; Francisco G. Cigarroa, MD, Past President and Chancellor, University of Texas; and Gerald B. Hickson, MD, Senior Vice President and Assistant Vice Chancellor, Vanderbilt University Medical Center.

ABOUT ASTRO

ASTRO is the premier radiation oncology society in the world, 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. As the leading organization in radiation oncology, 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 (www.redjournal.org), Practical Radiation Oncology (www.practicalradonc.org) and Advances in Radiation Oncology (www.advancesradonc.org); developed and maintains 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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Validation of a Genomic Classifier for Prediction of Metastasis Following Postoperative Salvage Radiation Therapy

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Purpose/Objective(s): Most men who develop elevated prostate-specific antigen (PSA) level recurrence postprostatectomy are treated with salvage radiation therapy (SRT). However, since PSA recurrence is a poor surrogate for metastatic disease, it is unclear which men may benefit from a more aggressive approach (ie, incorporation of hormonal therapy). We hypothesized that a genomic classifier (GC), a validated predictor of metastasis, would distinguish those patients for whom additional therapy is beneficial from those for whom SRT on its own is likely insufficient.

Materials/Methods: Genomic classifier (GC) scores were calculated from 166 prostate cancer patients who received SRT at Thomas Jefferson University, Veteran Affairs Medical Center Durham, and Mayo Clinic, between 1990 and 2010. SRT was defined as the administration of RT with pre-RT PSA levels >0.2 ng/mL. GC and Cancer of the Prostate Risk Assessment Postsurgical (CAPRA-S) scores were compared using survival c-index, competing-risks, and Cox regression analysis for the prediction of metastasis.

Results: Survival c-index for predicting metastasis 5 years post-SRT was 0.87 (95% CI: 0.73-0.90) for GC and 0.62 (95% CI: 0.48-0.77) for CAPRA-S. The cumulative incidence of metastasis at 5 years post-SRT was 2.8%, 5.8%, and 33.5% for low, average, and high GC scores (P<.0001) and 17%, 2.3%, and 15% for low, average, and high CAPRA-S scores (P=.19). In univariable analysis only GC, extraprostatic extension, and pre-RT PSA were significant predictors of metastasis. In multivariable analyses with clinical risk factors or the CAPRA-S nomogram, GC was the only independent predictor of metastasis with an HR of 1.59 (1.17-2.16, P=.0017) for a 10% unit increase in risk score.

Conclusion: In patients treated with postoperative SRT for PSA recurrence, GC is a powerful predictor of metastasis. Patients with low GC scores have an excellent prognosis with SRT and may avoid concurrent hormonal therapy. Patients with a high GC risk are at highest risk for metastatic disease and SRT failure and may benefit from intensified systemic therapy.