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News Release

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Embargoed until 11:00 a.m. Central, Monday, October 22, 2018

High-dose, high-precision radiation therapy safe and effective for kidney cancer patients with only one kidney

New treatment option for patients facing this high-risk management scenario

SAN ANTONIO, October 22, 2018 — Treatment of renal cell carcinoma with stereotactic radiation therapy is as safe and effective for patients with one kidney as it is for those who have two, according to an analysis of the largest-ever, international dataset of solitary kidney patients to receive this emerging treatment. The findings will be presented today at the 60th Annual Meeting of the American Society for Radiation Oncology (ASTRO).

Renal cell carcinoma (RCC), which has been rising in incidence for decades, is the most common form of kidney cancer in adults in the United States, with approximately 65,000 new cases diagnosed annually. It is responsible for nearly 15,000 deaths each year. It is typically treated surgically, with tumor ablation reserved for patients who are not able or willing to have surgery.

A specialized form of radiation treatment known as stereotactic ablative radiotherapy (SABR), also known as stereotactic body radiation therapy (SBRT), is emerging as a potential alternative for kidney cancer patients. SABR has been shown to be effective in treating cancers in the lung, liver and spine using substantially higher doses of radiation delivered in a single, or just a few, treatment sessions. Earlier this year, a study published in the journal *Cancer* showed that SABR was safe and effective in treating patients with RCC who had both kidneys remaining. This new study shows it is just as safe and effective for patients who have only one kidney.

"Although RCC historically has been considered resistant to conventional radiation therapy, the high doses and high precision achievable with SABR overcome this resistance," said lead author Rohann J. M. Correa, MD, PhD, a radiation oncology resident at London Health Sciences Center in London, Canada. "Kidney SABR is thus emerging as a versatile, non-invasive outpatient treatment requiring one visit or a few visits. Our analysis demonstrates SABR to be highly effective with minimal side effects for RCC patients with a single kidney."

Dr. Correa and his colleagues analyzed patient data from nine institutions across the United States, Germany, Australia, Canada and Japan within the International Radiosurgery Oncology Consortium for Kidney (IROCK) group. Of the 223 patients who underwent renal SABR, 81 had a solitary kidney. In the single-kidney cohort,

patients were an average of 67.5 years old at time of treatment, mostly male (69 percent) and of good performance status (ECOG 0-1 in 97.5 percent). The median biologically-effective dose of radiation therapy was 87.5 Gray (Gy) and was identical in the solitary and bilateral cohorts (p=0.103).

With a median follow-up of 2.6 years, SABR provided 98 percent two-year local control and 98 percent two-year cancer-specific survival for RCC patients with a solitary kidney. These rates were not significantly different from those for patients with two kidneys treated with SABR: 97.8 percent local control (hazard ratio (HR) 0.89, p=0.923) and 94.3 percent cancer-specific survival (HR 0.16, p=0.082). Overall survival also did not differ between the cohorts, at 81 percent for the solitary group and 82 percent for the bilateral group (HR 0.75, p=0.445).

Renal function was modestly impacted by SABR. The decline in estimated glomerular filtration rate (eGFR) was similar for both cohorts, with average decreases of -5.8 (±10.8 mL/min) in the solitary cohort and -5.3 (±14.3 mL/min) in the bilateral cohort (p=0.984). None of the solitary kidney patients required dialysis, while six (4.2 percent) in the bilateral cohort did.

“We were somewhat surprised that SABR could achieve such a high local control rate without more significantly impacting renal function in the solitary kidney setting,” said Dr. Correa. “While this is partly attributable to the technology of SABR — allowing very high radiation doses to be delivered with incredible precision, thus maximally sparing renal function — it is also important to acknowledge important differences in baseline characteristics between groups.”

Patients with a single kidney had smaller tumors on average than patients with two kidneys (mean 3.7 cm vs. 4.3 cm, p<0.001). They also exhibited slightly better baseline kidney function on average than those in the bilateral cohort (p=0.016).

The research team used Cox hazards regression analysis to look at factors predicting which patients had worse outcomes after SABR. Larger tumor size (>4.0 cm) correlated with more profound decreases in eGFR after SABR (hazard ratio (HR) 4.2, p=0.029). “From this, we concluded that proper patient selection will be important in optimizing outcomes for solitary kidney patients treated with SABR,” said Dr. Correa.

“Treatment of RCC in the solitary kidney setting poses a unique management challenge, since a careful balance of minimizing nephron loss and maximizing cancer control is essential,” concluded Dr. Correa. “Recognizing the challenges of randomized controlled trials in this unique and somewhat-rare population, we hope that our large, international dataset will significantly advance the paradigm of kidney SABR, increasing awareness and access for patients facing this challenging management scenario.”

The abstract, “Renal SABR in patients with a solitary kidney: An individual-patient pooled analysis from the International Radiosurgery Oncology Consortium for Kidney (IROCK),” 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. Correa and/or outside experts in kidney cancer, 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 Radiation Therapy and Cancer

- Video: An Introduction to Radiation Therapy; (Spanish version)
- ASTRO's clinical practice statements and guidelines
- Additional brochures, videos and information 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 222 – Renal SABR in patients with a solitary kidney: an individual-patient pooled analysis from the International Radiosurgery Oncology Consortium for Kidney (IROCK)

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Purpose/Objective(s): SABR is an emerging ablative modality for primary renal cell carcinoma (RCC). Taking a multi-institutional and multi-national approach, we sought to evaluate oncologic and renal function outcomes in patients with RCC in solitary kidneys versus bilateral kidneys.

Materials/Methods: Individual patient data from 9 institutions across Germany, Australia, USA, Canada and Japan within the IROCK group were pooled retrospectively. Toxicities were recorded using CTCAE v4.03. Demographics and treatment outcomes were compared between those patients with solitary vs. bilateral functional kidneys using chi-square test, fisher's exact test, two-sample T-test or Wilcoxon rank sum test as appropriate. K-M estimates and Cox proportional hazards regression were generated for survival outcomes.

Results: 81 patients (of 223 total) harboring a solitary kidney underwent renal SABR. Mean age in this cohort was 62.5 years, 69% of patients were male, and 97.5% had good performance status (ECOG 0-1). Twelve patients (14.8%) had metastatic disease. Pathological confirmation was obtained in 91.4% (all clear cell RCC) with a further 8.6% demonstrating tumor growth on serial imaging. Median [IQR] diameter of solitary kidney tumors was 3.7cm [2.5-4.3], which was smaller ($p<0.001$) than those in patients with bilateral kidneys (4.3cm [3.0-5.5]). The median (range) total dose and number of fractions were 25Gy (14-70) and 1 (1-10), respectively. While both total dose and number of fractions were significantly lower in the solitary cohort ($p\leq0.001$), median (range) BED_{10} was similar between cohorts: 87.5Gy (33.6-125) in the solitary and 87.5Gy (37.5-125) in the bilateral cohort ($p=0.103$). Solitary kidney patients had a higher mean ± SD eGFR at baseline (64.6±21.7 mL/min) than those with bilateral kidneys (57.2±21.6 mL/min; $p=0.016$). Post-SABR decline in eGFR was similar for solitary and bilateral cohorts with mean (±SD) decreases of -5.8 (±10.8) and -5.3 (±14.3) mL/min, respectively ($p=0.984$). No patients in the solitary cohort required dialysis vs. 6 (4.2%) in the bilateral cohort. With median follow-up of 2.57 years, local control (LC), progression free survival (PFS), cancer-specific survival (CSS), and overall survival (OS) at 2 years were 98.0%, 77.5%, 98.2% and 81.5%, respectively. No difference in local failure rate for solitary (n=1) versus bilateral (n=2) cohorts was observed ($p=1.00$). On univariable analysis, moderate chronic kidney disease (eGFR ≤ 60 mL/min) was associated with poorer PFS (HR 2.66, $p=0.043$) in the solitary cohort.

Conclusion: Renal SABR appears to be a safe and well-tolerated option for RCC tumors in patients with solitary kidneys and yields comparable local control, survival, and renal function outcomes to patients with bilateral kidneys. Pre-existing moderate chronic kidney disease in patients with a solitary kidney may be predictive of poorer oncologic outcomes in this group, thus careful patient selection will be essential to optimize outcomes in this population.