Post-operative stereotactic radiosurgery a new standard of care for patients with resected brain metastases

Multi-institutional trial finds comparable survival, less cognitive decline and better quality of life following SRS versus whole brain radiotherapy after resection

BOSTON, September 25, 2016 -- For patients who have cancer that has metastasized to the brain, stereotactic radiosurgery (SRS) results in statistically comparable survival rates, reduced cognitive decline and better quality of life (QOL), compared to whole brain radiotherapy (WBRT), according to research presented today at the 58th Annual Meeting of the American Society for Radiation Oncology (ASTRO).

Surgical resection of large symptomatic brain metastases is often indicated to confirm diagnosis, remove the lesion(s) or reduce pressure within the brain, but there is a high incidence of tumor recurrence after surgery alone. Although post-operative WBRT significantly reduces tumor recurrence in the brain and is the current standard of care for patients following resection, the treatment can negatively impact a patient’s cognitive function and quality of life. SRS targets escalated doses of radiation to the tumor with extreme precision; the advanced technique can eliminate cancerous cells in a single or very small number of sessions while limiting the impact on surrounding tissue.

“Stereotactic radiosurgery to the surgical cavity is widely used, despite the lack of clinical trials to substantiate its effectiveness,” said Paul D. Brown, MD, lead author of the study and a radiation oncologist at the Mayo Clinic in Rochester, Minnesota. “Our multi-institutional, randomized trial is the first to demonstrate clearly the efficacy of SRS compared to WBRT in a post-operative setting.”

The trial was conducted at cancer centers across the U.S. and Canada from 2011 to 2015. Participants included 194 patients, each with one to four brain metastases. Patients were randomized to receive either
SRS or WBRT after surgical resection of one lesion. The majority of patients (77 percent) had a single brain metastasis, and lung tumors were the primary site for most patients (59 percent). The average patient age was 61 years, and study arms were balanced on baseline patient and tumor characteristics.

Primary outcomes in the trial included overall survival (OS) and cognitive deterioration free survival (CDFS), which was defined as a decline greater than one standard deviation from the patient’s baseline in any of six cognitive tests. Major secondary endpoints included local control of the surgical bed, time to intracranial failure, and quality of life (QOL). Researchers computed Hazard Ratios (HR) to compare outcomes between treatment arms.

With a median follow up of 15.6 months, there was no statistically significant difference in overall survival rates between treatment groups, with a median OS of 11.5 months following SRS and 11.8 months following WBRT ($p=0.65$). Moreover, SRS patients experienced significantly longer survival without cognitive decline, with a median CDFS of 3.2 months for SRS and 2.8 months for WBRT (HR, 2.0; $p < 0.0001$).

The cognitive impact of WBRT persisted at six months following treatment. The rate of cognitive deterioration at six months was 85.7 percent after WBRT, compared to 53.8 percent after SRS ($p=0.0006$), with a higher percentage of WBRT patients experiencing worse immediate recall, memory and attention compared to those treated with SRS.

WBRT did provide higher overall intracranial tumor control; rates at six and 12 months were 90.0 and 78.6 percent with WBRT versus 74.0 and 54.7 percent with SRS ($p < 0.0001$). There was no clinically meaningful difference in median surgical bed relapse free survival between treatment arms, although long term follow-up showed better control with WBRT (7.7 months vs. 7.5 months, $p = 0.04$).

Patients treated with SRS experienced better quality of life than those who received WBRT. At three months following treatment, declines in QOL and physical wellbeing were significantly smaller after SRS than WBRT (mean QOL change from baseline: -1.5 vs. -7.0, $p = 0.03$; mean wellbeing change from baseline: -6.4 vs. -20.2, $p = 0.002$). At six months, physical wellbeing (decline of -3.2 vs. -15.1, $p = 0.016$) remained significantly better for SRS patients for.

“Our results confirm that radiosurgery to the surgical cavity is a viable treatment option to improve local control with less impact on cognitive function and quality of life compared to WBRT,” said Brown. “There is no significant difference in survival whether a patient receives post-operative radiosurgery or WBRT, and radiosurgery avoids the well-known toxicities of WBRT. Furthermore, due to less time commitment and a quicker recovery after SRS, patients can restart systemic therapies more rapidly.
Radiosurgery to the surgical cavity after resection of brain metastases, should be considered a standard of care and a less toxic alternative than the historic standard of care WBRT.”

The abstract, “N107C/CEC.3: A Phase III Trial of Post-Operative Stereotactic Radiosurgery (SRS) Compared with Whole Brain Radiotherapy (WBRT) for Resected Metastatic Brain Disease,” will be presented in detail during a scientific session at ASTRO’s 58th Annual Meeting at 3:15 p.m. Eastern time on Sunday, September 25, 2016. To speak with Dr. Brown, please contact ASTRO’s media relations team on-site at the Boston Convention and Exhibition Center September 25 through 28, by phone at 703-286-1600 or by email at press@astro.org.

ATTRIBUTION TO THE AMERICAN SOCIETY OF RADIATION ONCOLOGY (ASTRO) ANNUAL MEETING REQUESTED IN ALL COVERAGE.

This news release contains updated data from the study author(s). Full study abstract available on the final page of this release.

ABOUT ASTRO’S ANNUAL MEETING
ASTRO’s 58th Annual Meeting, the nation’s premier scientific meeting in radiation oncology, will be held September 25-28, 2016, at the Boston Convention and Exhibition Center in Boston. The 2016 Annual Meeting is expected to attract more than 11,000 attendees from across the globe, including oncologists from all disciplines and members of the entire radiation oncology team. Led by ASTRO president David C. Beyer, MD, FASTRO, the 2016 meeting will feature keynote addresses from Kathleen Sebelius, former U.S. Secretary of Health and Human Services; Thomas James Lynch Jr., MD, Chair and CEO, Massachusetts General Physicians Organization; and Jason Ragogna, general manager, SMS and Safety Alliances, Corporate Safety, Security, and Compliance, Delta Air Lines, Inc. The Presidential Symposium, “Prostate Cancer: Defining Value and Delivering It,” highlights the meeting’s theme of “Enhancing Value, Improving Outcomes” and will feature recent practice-changing studies and current developments in value-based care for prostate cancer. ASTRO’s four-day scientific meeting will feature a record number of abstracts, including 368 oral presentations, 1,760 posters and 180 digital posters in more than 50 educational sessions and 20 scientific panels for 20 disease-site tracks. For more information about ASTRO’s 58th Annual Meeting, visit www.astro.org/AnnualMeeting. For press registration and news briefing information for ASTRO’s 58th Annual Meeting, visit www.astro.org/AMPress.

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, RT Answers (www.rtanswers.org); and created the Radiation Oncology Institute (www.roinstitute.org), a nonprofit 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.
Purpose/Objective(s): WBRT is the standard of care to improve intracranial control following resection of brain metastasis. However, SRS to the surgical cavity is widely used in an attempt to reduce cognitive toxicity, despite the lack of high level comparative data substantiating efficacy in the post-op setting.

Materials/Methods: On this multi-institutional cooperative group trial patients with one to four brain metastases were randomized to either SRS or WBRT after resection of one lesion. The unresected metastases were treated with SRS in both study arms. The primary endpoints were cognitive deterioration free survival (CDFS) and overall survival. Cognitive deterioration was defined as decline >1 SD from baseline in any of the 6 cognitive tests. Major secondary endpoints included local control of the surgical bed, time to intracranial failure, and QOL.

Results: Between July 2011 and December 2015, 194 patients were enrolled with a median follow up of 15.6 months (range 0, 48.5 months). Baseline characteristics were well-balanced between study arms. The median age was 61, most had a single metastasis (77%), and lung was the most common primary tumor (59%). There was a shorter CDFS after WBRT vs. SRS to the surgical cavity (median 2.8 vs. 3.2 months, HR = 2.0, p<0.0001). Cognitive deterioration at 6 months was more frequent after WBRT vs. SRS (85.7% vs. 53.8%, p = 0.0006). At 6 months, there was more cognitive deterioration in the WBRT arm in immediate recall (47.9% vs. 17.3%, p<0.0001), delayed recall (62.5% vs. 27.5%, p<0.0001), and processing speed (37.5% vs. 17.3%, p=0.03). Overall intracranial tumor control at 6 and 12 months was 90.0% and 78.6% with WBRT vs. 74.0% and 54.7 % with SRS (p<0.0001). There was better QOL with SRS at 3 months including overall QOL (mean change from baseline -1.5 vs.-7.0; p= 0.03) and physical wellbeing (-6.4 vs. -20.2; p= 0.002). At 6 months, there was better QOL with SRS including brain-specific concerns (2.9 vs. -4.4; p= 0.045) and physical wellbeing (-3.2 vs. -15.1; p= 0.016).

Conclusion: Decline in cognitive function at 6 months was more frequent with WBRT. Despite worse intracranial control, better QOL was reported in the SRS arm. Overall survival and local control will be presented at the time of the meeting.