Stereotactic radiosurgery decreases rate of post-operative local recurrence for brain metastases

Alternative to whole brain radiation therapy improved local control but did not augment overall survival or rate of distant metastases

BOSTON, September 25, 2016 -- Stereotactic radiosurgery (SRS) for cancer patients who receive the treatment for brain metastases decreases the likelihood of local recurrence but shows no positive difference in terms of overall survival (OS) or distant brain metastases (DBMs) rates, when compared to observation alone following surgical resection of brain metastases, according to research presented today at the 58th Annual Meeting of the American Society for Radiation Oncology (ASTRO).

Brain metastases occur in a large number of patients with common cancers and are more prevalent than many primary tumors, including primary brain tumors, lymphoma and colon cancer. Rates of brain metastasis have risen in recent years, as well. When cancer spreads to the brain, surgical resection can be employed to confirm the diagnosis, remove the lesion(s) or to reduce pressure in the brain. After resection, whole brain radiation therapy (WBRT) to the surgical cavity limits the growth of new lesions in the brain, yet radiation to healthy brain tissue can lead to cognitive decline and other toxicities. With SRS, oncologists deliver a single fraction of precise, high-dose radiation while preserving surrounding brain tissue.

“Over the past several years, with advances in technology, radiation to only the surgical bed of the resected lesion has become of interest,” said Anita Mahajan, MD, professor of radiation oncology at MD Anderson Cancer Center in Houston and lead author of the study. “While oncology teams see the potential of radiosurgery, its novelty means that we have limited prospective evidence of its efficacy.”

Study participants included 132 patients (128 eventually analyzed) with one to three metastatic brain tumors who wished to avoid or delay WBRT following complete surgical resection of at least one
brain metastasis. The median patient age was 59, and there were no relevant demographic differences between the treatment groups. Patients were randomly assigned to one of two arms, either SRS to the surgical cavity (or cavities for patients with more than one lesion removed) (SRS-cav, n = 63) or observation alone (OBS, n = 65). Patients were stratified by number of brain metastases (1 vs. 2-3), primary cancer type (melanoma vs. other histology) and pre-operative tumor size (less than vs. greater than three centimeters). Researchers assigned radiation dose for the SRS-cav group (12, 14 or 16 Gy) based on cavity volume at time of radiosurgery.

Failure of local control (LC), the primary endpoint of the study, was assessed through follow-up magnetic resonance imaging (MRI) by the study neuro-radiologist to determine whether local tumors recurred in the area treated with SRS. Researchers also examined the rates of overall survival (OS), development of distant brain metastases (DBM), time to WBRT, and complications following SRS. Hazard ratios (HR) and corresponding confidence intervals (CI) were computed to compare treatment arms. The median follow-up time was 13 months, with a range of 0.3 to 71 months.

Radiosurgery to the surgical bed significantly reduced local recurrence of the resected tumor. At six months following treatment, LC rates were 83 percent for the SRS-cav group and 57 percent for the OBS group. At 12 months follow-up, the LC rates were 72 percent for the SRS-cav group, compared to 45 percent for the OBS group (HR, 0.46; p = 0.01).

Although SRS improved LC, there were no differences between treatment arms for regional recurrence, overall survival or time to WBRT. At 12 months after treatment, 58 percent of the SRS-cav patients had developed DBMs, compared to 67 percent in the OBS group, though the difference was statistically non-significant (HR, 0.79; p = 0.29). Median OS was 17 months for both groups (HR, 1.22; p = 0.37). WBRT was given to 24 of the 64 patients in the SRS-cav group within an average timeframe of 16.1 months, compared to 30 of 67 patients in the OBS group within an average timeframe of 15.2 months (HR, 0.8; p = 0.42). No significant complications were noted in the SRS-cav patients.

In terms of non-treatment factors, only tumor size impacted LC, as determined by multivariate Cox regression analysis. A pre-surgery tumor size of greater than three centimeters was associated with worse LC, but local recurrence was not significantly affected by the number of brain metastases or the patients’ histology or graded prognosis assessments.

“Our research shows that radiosurgery in this patient cohort does reduce the incidence of local recurrence, although the findings for overall brain control, overall survival and time until whole brain radiation therapy limit our ability to conclude an obvious clinical benefit,” said Dr. Mahajan. “In addition,
it appears that smaller tumors may not need post-operative radiosurgery after resection, since the local failure rate for tumors smaller than 2.5 centimeters was very low.

The abstract, “Post-operative Stereotactic Radiosurgery vs. Observation for Completely Resected Brain Metastases: Results of a Prospective Randomized Study,” will be presented in detail during a clinical trials session at ASTRO’s 58th Annual Meeting at 3:15 p.m. Eastern time on Sunday, September 25, 2016. To speak with Dr. Mahajan, please contact ASTRO’s media relations team on-site at the Boston Convention and Exhibition Center on September 25-28, 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.
Post-operative Stereotactic Radiosurgery vs. Observation for Completely Resected Brain Metastases: Results of a Prospective Randomized Study


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Purpose/Objective(s): Stereotactic radiosurgery to a surgical cavity (SRS-cav) to improve local control (LC) after resection of brain metastases (BM) is an alternative to adjuvant whole brain radiotherapy (WBRT), which is associated with toxicity, particularly cognitive decline. However, limited prospective data regarding the efficacy or complications of SRS-cav for LC is available. In addition, LC after SRS-cav has not been compared to observation (OBS) alone after BM resection with modern surgical techniques.

Materials/Methods: Patients with one to three BMs with complete resection of at least one metastasis were enrolled. Patients were randomized to either SRS-cav or observation (OBS) of the surgical cavity (or cavities if >1 lesion was resected). Stratification variables were: 1) 1 vs 2-3 BM, 2) melanoma vs other histology and 3) pre-operative tumor size <3cm vs >3cm. The remaining 1-2 unresected BMs in both groups were treated with SRS. Maximum eligible diameters of the cavity and an unresected BM were 4 cm and 3 cm, respectively. SRS dose (12-14-16 Gy) was assigned by cavity volume at time of SRS. The primary endpoint was failure of LC in the resection cavity as determined by the study neuro-radiologist on follow up MRIs. Major secondary endpoints included overall survival (OS), development of distant BM (DBM), complications and use of WBRT. The study was designed with an 80% power to detect a HR of 0.6 assuming a two-sided 5% alpha and 50% LC at 6 mo in the OBS arm.

Results: From 10/2009 to 10/2015, 131 eligible patients (61 female, 70 male, median age 58 y) with a total 140 resected BMs were randomized to SRS-cav (n=64) vs OBS (n=67). 34 and 28 additional BMs were present and received SRS in the SRS-cav and OBS arms, respectively. There were no differences between the groups based on relevant demographic factors. Median follow-up for all patients was 12.6 mo, (range 0.3-70.6 mo). LC rates were superior in the SRS-cav vs OBS group with a HR of 0.46: 95% CI 0.25, 0.85, p=0.011. LC rates for SRS-cav and OBS were 83% vs 57% at 6 mo and 72% vs 45% at 12 mo, respectively. No significant SRS-cav complications were noted. DBM rate at 12 mo was 43% vs 33% in the SRS-cav vs OBS groups, respectively, (HR 0.79, 95% CI 0.50, 1.24, p=0.29). WBRT was given in 24 SRS-cav and 30 OBS patients with a median time to WBRT of 16.1 and 15.2 mo, respectively (HR 0.8, 95%CI 0.5,1.4, p=0.42). Median OS was 17 mo in both arms (HR 1.22, 95% CI 0.79,1.87, p=0.37). On multivariate Cox regression analysis, histology, lesion number, systemic disease status or GPA did not affect LC. Use of SRS-cav (HR 0.4, 95% CI 0.2,0.8) was associated with better LC and pre-operative tumor > 3 cm (HR 2.4, 95% CI 1.2,4.9) was associated with worse LC.

Conclusion: This study confirms the benefit of SRS to a surgical cavity in improving LC compared to observation alone. Larger lesions may have a worse LC than smaller ones. OS and DBM were not affected by the use of SRS. Further study on failure patterns and cause of death is ongoing.