

Contact: Michelle Kirkwood
703-286-1600
michellek@astro.org

Brittany Ashcroft
703-839-7336
brittanya@astro.org

Improved survival for patients with brain metastases who are ≤50 years old and receive stereotactic radiosurgery (SRS) alone, without whole brain radiation therapy (WBRT)

Affirms ASTRO's 2014 Choosing Wisely[®] recommendation for SRS

Fairfax, Va., March 2, 2015—Cancer patients with limited brain metastases (one to four tumors) who are ≤50 years old should receive stereotactic radiosurgery (SRS) without whole brain radiation therapy (WBRT), according to a study available online, open-access, and published in the March 15, 2015 issue of the *International Journal of Radiation Oncology • Biology • Physics* (Red Journal), the official scientific journal of the American Society for Radiation Oncology (ASTRO). For patients ≤50 years old who received SRS alone, survival was improved by 13 percentage points when compared to those patients ≤50 who received both SRS and WBRT.

This study, “Phase 3 Trials of Stereotactic Radiation Surgery With or Without Whole-Brain Radiation Therapy For 1 to 4 Brain Metastases: Individual Patient Data Meta-Analysis,” analyzed patient data from the three largest randomized clinical trials (RCT) of SRS and WBRT conducted to-date: the Asian trial (JROSG99-1) by Aoyama et al.¹, published in 2006; the North American trial (MDACC NCT00548756) by Chang et al.², published in 2009; and the European trial (EORTC 22952-26001) by Kocher et al.³, published in 2011. A total of 364 patients from the three RCTs were

¹ Aoyama H, Shirato H, Tago M, et al. Stereotactic radiosurgery plus whole-brain radiation therapy vs stereotactic radiosurgery alone for treatment of brain metastases: A randomized controlled trial. *JAMA* 2006;295:2483-2491.

² Chang EL, Wefel JS, Hess KR, et al. Neurocognition in patients with brain metastases treated with radiosurgery or radiosurgery plus whole-brain irradiation: a randomised controlled trial. *Lancet Oncol* 2009;10:1037-1044.

³ Kocher M, Soffiatti R, Abacioglu U, et al. Adjuvant whole-brain radiotherapy versus observation after radiosurgery or surgical resection of one to three cerebral metastases: results of the EORTC 22952-26001 study. *J Clin Oncol* 2010;29:134-141.

evaluated for this meta-analysis. Of those 364 patients, 51 percent (186) were treated with SRS alone, and 49 percent (178) received both SRS and WBRT. Nineteen percent of patients (68) were ≤ 50 years of age, and 61 percent (19) of these patients had a single brain metastasis. Twenty percent of all patients (72) had local brain failure, which is the occurrence of progression of previously treated brain metastases; and 43 percent (156) experienced distant brain failure, which is the occurrence of new brain metastases in areas of the brain outside the primary tumor site(s).

The impact of age on treatment effectiveness revealed SRS alone yielded improved overall survival (OS) in patients 50 years old and younger. Patients ≤ 50 years old who received SRS alone had a median survival of 13.6 months after treatment, a 65 percent improvement, as opposed to 8.2 months for patients ≤ 50 who were treated with SRS plus WBRT. Patients > 50 years old had a median survival of 10.1 months when treated with SRS alone, and 8.6 months for those who received SRS plus WBRT.

“We expected to see a survival advantage favoring combined therapy of SRS and WBRT. However, these data clearly demonstrate the benefit for SRS alone to improve survival for our younger patients with limited brain metastases,” said lead author of the study Arjun Sahgal, MD, associate professor of radiation oncology and surgery at the University of Toronto, and a radiation oncologist at the Odette Cancer Centre of the Sunnybrook Health Sciences Centre in Toronto. “Furthermore, it was previously thought that the positive effect of whole brain radiation in reducing the risk of distant brain relapse was generalizable for all patients. However, we did not observe this effect in patients 50 years and younger with limited brain metastases. In these patients, the same rate of distant brain failure was observed despite treatment with whole brain radiation. This result, together with our survival result, gave rise to the hypothesis that if patients are treated with whole brain radiation without realizing the benefits of improving distant brain control, then survival may be adversely affected. Therefore, our sub-group meta-analysis has swung the pendulum in favor of SRS alone as the standard of care. These findings also reinforce

ASTRO's *Choosing Wisely*® recommendation⁴ that states that it may not be necessary to add WBRT to SRS, thus improving patients' quality of life and memory function."

In addition to being open-access (free to the public), Sahgal et al.'s paper is also available for SA-CME credit at www.astro.org/JournalCME.

Drs. Nils D. Arvold and Paul J. Catalano have reviewed Sahgal et al.'s research. Their editorial, "Local Therapies for Brain Metastases, Competing Risks, and Overall Survival," is also published in the March 15, 2015, issue of the Red Journal.

For a copy of the study manuscript and the editorial, contact ASTRO's Press Office at press@astro.org. For more information about the Red Journal, visit www.redjournal.org.

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⁴ ASTRO's *Choosing Wisely*® List. ABIM Foundation. <http://www.choosingwisely.org/doctor-patient-lists/american-society-for-radiation-oncology/>