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Contact: Michelle Kirkwood  
703-286-1600  
[michellek@astro.org](mailto:michellek@astro.org)

Nancy Mayes  
Mayes Communications  
703-772-2510  
[nancy@mavescommunications.com](mailto:nancy@mavescommunications.com)

Press Room in Atlanta  
September 22-25  
404-222-5303  
404-222-5304

## **Adult cancer patients younger than 50 presenting with a limited number of brain metastases have improved overall survival after stereotactic radiosurgery alone**

Atlanta, September 22, 2013—When treated with stereotactic radiosurgery (SRS), that is not combined with whole brain radiotherapy (WBRT), adult brain cancer patients who were 50 years old and younger were found to have improved survival, according to research presented today at the American Society for Radiation Oncology's (ASTRO's) 55th Annual Meeting. Younger patients (under 50 years old) were also found to be at no greater risk of new brain metastases developing despite omission of WBRT.

A highly advanced brain cancer treatment, stereotactic radiosurgery (SRS) utilizes precisely focused radiation beams to treat a tumor with a high dose while minimizing exposure to the surrounding healthy brain tissue. Another approach, often combined with SRS, is WBRT, which is radiation therapy applied to the entire brain. This individual patient data (IPD) meta-analysis was conducted on the patient data of three randomized clinical trials (RCTs) from North America [MDACC NCT00548756 (Chang, 2009)], Europe [EORTC 22952-26001 (Kocher, 2011)] and Asia [JRSOG99-1 (Aoyama, 2004)], with the aim to evaluate the results of stereotactic radiosurgery (SRS)

alone, compared to WBRT and SRS, for patients with one to four brain metastases. Patients in this study received one or both types of treatments.

A total of 364 patients from the three RCTs were evaluated. Of those, 51 percent had been treated with SRS alone, and 49 percent with both WBRT and SRS; 19 percent were 50 years old or younger and 60 percent had a single brain metastasis. Twenty-one percent of all patients had local brain failure, which is the occurrence of progression of previously treated brain metastases, and 44 percent had distant brain failure, the occurrence of new brain metastases in areas of the brain outside the primary tumor site(s). Eighty-six percent of the patients died during follow-up.

The analysis revealed that patients who received only SRS had a median of 10 months survival time after treatment, as opposed to 8.2 months survival time for patients who underwent WBRT in addition to SRS. Overall, local brain failure occurred earlier in patients who received only SRS (6.6 months post-treatment), as opposed to patients who underwent WBRT and SRS (7.4 months post-treatment). Distant brain failure was also earlier overall in patients who received only SRS, occurring at 4.5 months post-treatment, compared to 6.5 months post-treatment for patients who received both WBRT with SRS.

The impact of age on treatment effectiveness revealed SRS alone results in improved overall survival (OS) in patients 50 years old and younger. For patients age 35, 40, 45 and 50, the estimated hazard ratio and the corresponding 95 percent confidence intervals (CIs)s were 0.46 (95% CI 0.24, 0.90), 0.52 (95% CI 0.29, 0.92), 0.58 (95% CI 0.35, 0.95) and 0.64 (95% CI 0.42, 0.99), respectively. With respect to distant brain failure, a significant association with age was also observed. Patients 50 years and younger were at no significantly greater risk of developing new tumors despite being treated with SRS alone.

“We expected to see a survival advantage favoring combined therapy, given the additional benefits of whole brain radiation, particularly with respect to increasing local control and reducing the risk of new brain metastases,” said lead study author Arjun Sahgal, MD, an associate professor of radiation oncology at the University of Toronto and deputy chief of radiation oncology at Odette Cancer Centre, Sunnybrook Health Sciences Centre in Toronto. “Our study indicates, however, a

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8280 Willow Oaks Corporate Drive • Suite 500 • Fairfax • VA • 22031  
phone 703-502-1550 • fax 703-502-7852 • Web [www.astro.org](http://www.astro.org) Page**

survival advantage for SRS alone in younger patients who also interestingly were observed to have no greater risk of new brain metastases despite the omission of whole brain radiation. This implies that WBRT may not be required for all patients with brain metastases, particularly younger patients, and SRS alone should be considered as the favored first-line therapeutic option. The implications are significant as it has been shown in other studies that WBRT is detrimental to short term memory function and negatively impacts some aspects of patients' quality of life."

The abstract, "Individual Patient Data (IPD) Meta-Analysis of Randomized Controlled Trials (RCT) Comparing Stereotactic Radiosurgery Alone (SRS) to SRS plus Whole Brain Radiotherapy (WBRT) in Patients with Brain Metastasis," will be presented in detail today at ASTRO's Annual Meeting at 1:45 p.m. Eastern time on Sunday, September 22, 2013. To speak with Dr. Sahgal, contact Michelle Kirkwood on September 22 - 25, 2013, in the ASTRO Press Office at the Georgia World Congress Center in Atlanta at 404-222-5303 or 404-222-5304, or email michellek@astro.org.

ASTRO's 55<sup>th</sup> Annual Meeting, held in Atlanta, September 22-25, 2013, is the premier scientific meeting in radiation oncology and brings together 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. The theme of the 2013 meeting is "Patients: Hope • Guide • Heal" and will focus on patient-centered care and the importance of the physician's role in improving patient-reported outcomes and the quality and safety of patient care. The four-day scientific meeting includes presentation of four plenary papers, 363 oral presentations, 1,460 posters and 144 digital posters in 70 educational sessions and scientific panels for 19 disease sites/tracks. Keynote speakers include: William B. Munier, MD, director of the Center for Quality Improvement and Patient Safety at the Agency for Healthcare Research and Quality; Darrell G. Kirch, MD, President and CEO of the Association of American Medical Colleges; James Cosgrove, PhD, Director, the U.S. Government Accountability Office; Otis W. Brawley, MD, Chief Medical Officer of the American Cancer Society; and Peter Friedl, MD, PhD, of St. Radboud University Nijmegen Medical Centre at the University of Nijmegen and MD Anderson Cancer Center.

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## 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 that 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 two medical journals, International Journal of Radiation Oncology • Biology • Physics ([www.redjournal.org](http://www.redjournal.org)) and Practical Radiation Oncology ([www.practicalradonc.org](http://www.practicalradonc.org)); developed and maintains an extensive patient website, [www.rtanswers.org](http://www.rtanswers.org); and created the Radiation Oncology Institute ([www.roinstitute.org](http://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](http://www.astro.org).*

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**2013 American Society for Radiation Oncology (ASTRO) 55<sup>th</sup> Annual Meeting**  
**News Briefing, Tuesday, September 24, 2013, 2:45 p.m. Eastern time**

Clinical Trials Session: Sunday, September 22, 2013, 1:45 p.m. - 3:15 p.m. ET, Georgia World Congress Center

**LBA3 Individual Patient Data (IPD) Meta-Analysis of Randomized Controlled Trials (RCT)  
Comparing Stereotactic Radiosurgery Alone (SRS) to SRS Plus Whole Brain Radiotherapy  
(WBRT) in Patients with Brain Metastasis**

**A. Sahgal**<sup>1</sup>, **H. Aoyama**<sup>\*2</sup>, **M. Kocher**<sup>\*3</sup>, **B. Neupane**<sup>\*4</sup>, **S. Collette**<sup>\*5</sup>, **M. Tago**<sup>\*6</sup>, **P. Shaw**<sup>\*1</sup>, **J. Beyene**<sup>\*4</sup>, **E. L. Chang**<sup>\*7</sup>, <sup>1</sup>*University of Toronto, Toronto, ON, Canada*, <sup>2</sup>*Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan*, <sup>3</sup>*University of Cologne, Cologne, Germany*, <sup>4</sup>*McMaster University, Hamilton, ON, Canada*, <sup>5</sup>*European Organisation for Research and Treatment of Cancer - Headquarters (EORTC HQ), Brussels, Belgium*, <sup>6</sup>*Teikyo University Mizonokuchi Hospital, Kanagawa, Japan*, <sup>7</sup>*University of Southern California and MD Anderson Cancer Center, Los Angeles, CA*

**Purpose/Objective(s):** Three published RCTs comparing patients assigned to SRS alone with SRS plus WBRT for newly diagnosed 1 to 4 brain metastases were individually under-powered for overall survival (OS) comparisons. An IPD meta-analysis was performed to investigate the critical endpoint of OS.

**Materials/Methods:** The raw IPD from all patients receiving either SRS alone or SRS plus WBRT were obtained from the three published RCTs (EORTC 22952-26001, JRSOG99-1 and MDACC NCT00460395). Patient inclusion was limited to those with a recursive partitioning analysis (RPA) score of 1 or 2 and Karnofsky performance score (KPS)  $\geq 70$ . A one-stage time-to-event IPD meta-analysis was performed. A multivariable hierarchical Cox analysis controlled for covariates: age, RPA and number of brain metastases along with treatment assignment. We also investigated for an interaction effect (i.e., effect modification) between treatment and the other covariates.

**Results:** 364 of 389 patients from the 3 RCTs met the inclusion criteria. 51% had been treated with SRS alone; 19% were age  $\leq 50$  years, 41% were RPA class 1 and 60% had a single brain metastasis. In total, 21% had a local failure, 44% had distant brain failure, and 86% died during follow-up. The SRS alone vs. the SRS plus WBRT assignments resulted in median times to death of 10 months vs. 8.2 months, local failure 6.6 vs. 7.4 months, and distant brain failure 4.5 vs. 6.5 months, respectively. The only significant treatment effect modifier was age with a p-value of 0.04 for the interaction term. The impact of age on treatment effectiveness revealed SRS alone favoring better OS for patient's age  $\leq 50$ . For patients age 35, 40, 45 and 50, the estimated HR and the corresponding 95% CIs were 0.46 (95% CI 0.24, 0.90), 0.52 (95% CI 0.29, 0.92), 0.58 (95% CI 0.35, 0.95) and 0.64 (95% CI 0.42, 0.99), respectively. Patients with a single metastasis also had significantly better OS than those with 2 to 4. Distant brain control and local control significantly favored the addition of WBRT; however, multivariable analysis yielded significant increases in distant brain failures in the SRS alone cohort only in those patients age  $> 50$ . Those with  $> 1$  brain metastases also had a significantly greater risk of distant brain failure with a HR of 1.59 (95% CI 1.14-2.2).

**Conclusions:** There is a statistically significant favorable treatment effect on OS when SRS alone is used for patients age  $\leq 50$  years. Distant brain relapse rates in patients age  $\leq 50$  treated with SRS alone were not increased, despite omission of upfront WBRT. Therefore, based on our IPD of RCTs from three continents, we conclude that SRS alone is the preferred treatment for patients presenting with 1 to 4 brain metastases, RPA class 1 or 2 (KPS>70), and age  $\leq 50$  years.

**A. Sahgal:** None. **H. Aoyama:** None. **M. Kocher:** None. **B. Neupane:** None. **S. Collette:** None. **M. Tago:** None. **P. Shaw:** None. **J. Beyene:** None. **E.L. Chang:** None.