Stereotactic Radiosurgery Benefit for Brain Mets: Case Closed?

Study finds SRS alone results in less cognitive decline

The use of stereotactic radiosurgery (SRS) alone on patients with limited (one to three) brain metastases results in less cognitive deterioration than when combined with whole brain radiotherapy (WBRT), investigators have reported.

In a study led by Paul D. Brown, MD, director of the CNS stereotactic radiotherapy program at the University of Texas MD Anderson Cancer Center, researchers determined there was less cognitive deterioration in patients who underwent SRS alone after 3 months (64%), than in patients who underwent SRS plus WBRT (92%).

The results, published online in the Journal of the American Medical Association, showed a "significant difference" in the level of cognitive deterioration, particularly considering the controversy surrounding the role WBRT should play in the treatment of patients with brain metastases, the authors wrote.

The use of WBRT has been associated with cognitive decline, and while previous randomized clinical trials have demonstrated improved intracranial tumor control with the combined use of WBRT and SRS for brain metastases, none have showed any significant survival advantage with adjuvant WBRT.

"Central to this issue is whether tumor progression anywhere in the brain is more detrimental to a patient’s well-being than the potential deterioration of cognitive function and quality of life associated with WBRT," Brown and his colleagues wrote. "Because more than 200,000 individuals in the United States alone are estimated to receive WBRT each year, it is important that the potential benefits and risk of adjuvant WBRT be clearly defined."

The study involved 213 patients from 34 institutions in North America who had between one and three brain metastases (all less than 3 cm in diameter); participants were randomized to receive SRS or SRS plus WBRT.

After excluding patients who died, did not return for a 3-month or subsequent evaluation, or did not complete the required baseline tests, 111 patients were available for evaluation.
There was less cognitive deterioration at 3 months after use of SRS alone (40 of 63 patients, 63.5%) than with the SRS-plus-WBRT group (44 of 48 patients, 91.7%). This was a difference of 28.2%; 90% CI, -41.9% to -14.4%.

In addition, quality of life was higher at 3 months with SRS alone (mean change from baseline, −0.1 versus −12.0 points; mean difference, 11.9; 95% CI, 4.8-19.0 points).

The time to intracranial failure was shorter for those in the SRS-alone group compared with those in the SRS-plus-WBRT group (hazard ratio [HR], 3.6; 95% CI, 2.2-5.9), and there was no significant difference in functional independence between the two groups at three months.

Median overall survival was 10.4 months for patients receiving SRS alone and 7.4 months for those given the combined treatments (HR, 1.02; 95% CI, 0.75-1.38).

"In the absence of overall survival, these findings suggest that for patients with one to three brain metastases amenable to radiosurgery, SRS alone may be a preferred strategy," the team concluded.

Limitations to the study included the fact that a majority of the participants had lung cancer and the trial did not attempt to include other types of primary cancers. However, Brown and his colleagues noted that lung cancer is the predominant primary cancer reported in most brain metastases trials and that "there is no obvious biological basis to believe that the quality-of-life and cognitive effects of WBRT would vary between different primary cancers."

The authors also noted that there was significant patient dropout in their trial, mostly due to death, and that clinicians and trial participants were not blinded to treatment.

In an editorial accompanying the study, titled "Whole Brain Radiotherapy for Brain Metastases: Is the Debate Over?," Orit Kaidar-Person, MD, Carey K. Anders, MD, and Timothy M. Zagar, MD, wrote that the trial "confirms previous recommendations that WBRT should not be routinely added to SRS for patients with brain metastases of limited number or size."

But, while there may be little role for WBRT in the type of patient enrolled in this particular study, the editorial argued that based on the findings, and "until proven otherwise," WBRT could still have an important role to play in the treatment of patients not in that disease category.

"However, the study results cannot be extrapolated to infer that SRS is the standard for patients with four or more metastases or that WBRT no longer has a role in the treatment of brain metastases," Kaidar-Person and his colleagues wrote.

The authors report that there were no commercial sponsors for the study. One co-author reported relationships with Orbus Therapeutics and Bristol-Myers Squibb.