Is whole-brain radiation still best for brain metastases from small-cell lung cancer?
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Chad Rusthoven, MD

Lung cancer often metastasizes to the brain. Historically, brain metastases have been treated with whole-brain radiation therapy. However, whole-brain radiation is associated with cognitive side-effects and studies of non-small cell lung cancer patients have shown that a more targeted form of radiation, known as stereotactic radiosurgery, can improve cognitive outcomes and is highly effective for treating limited numbers of brain metastases. However, these studies have usually excluded patients with the related but different form of the disease known as small-cell lung cancer and, for patients with this tumor type, whole-brain radiation remains the standard of care for limited and even solitary brain metastases.

A recent study from investigators at the University of Colorado Cancer Center challenges the use of whole-brain radiation for all small-cell lung cancer patients with brain metastases. The study, recently published in the journal Lung Cancer, compared the outcomes of 5,752 small-cell lung cancer patients who received whole-brain radiation therapy (WBRT) with those of 200 patients who received stereotactic radiosurgery (SRS), finding that the median overall survival was actually longer with SRS (10.8 months with SRS versus 7.1 months with WBRT).

"One of the historic reservations regarding the use of SRS in small-cell lung cancer has been the concern that, by omitting WBRT, a patient could be at a higher risk of a diffuse progression of brain metastases, and that this could negatively affect prognosis. This study begins to address that concern by showing encouraging survival outcomes with SRS alone," says Chad Rusthoven, MD, assistant professor in Radiation Oncology at the University of Colorado Cancer Center, the paper's senior author.

The study used the largest cancer registry in the U.S., the National Cancer Database (NCDB), and analyzed cases of patients with brain metastases at time of diagnosis from 2010-2014. Because the standard of care was WBRT, the vast majority of patients were treated with this therapy. But a significant minority was treated with SRS, allowing the researchers to compare the outcomes of these two populations. Across age, gender, race, and health status, patients treated with SRS tended to have better overall survival than patients treated with WBRT.

"Even though we only identified 200 patients treated with SRS, to the best of our knowledge, it's the largest data set of patients treated this way and one of the first dedicated analyses of the approach in the U.S. The study offers preliminary evidence to support further research into the role of SRS for patients with small-cell lung cancer," says the study's lead author, Dr. Tyler Robin.

The authors point out that the study is limited by the fact that it retrospectively looks back at historical outcomes of patients treated with SRS and WBRT, rather than randomizing patients to SRS and WBRT groups and then tracking their outcomes prospectively. This makes the current study subject to the influence of selection bias, for example, if...
SRS patients happened to be healthier than WBRT patients to begin with. As such, the authors do not suggest that the observations from this study will change the standard of care, but they think that the results will encourage further investigation into SRS for small-cell lung cancer.

"We hope that this analysis will encourage other investigators to ask questions about the potential role of SRS for carefully-selected patients with small-cell lung cancer," says Rusthoven, "and we believe that as therapies improve and patients live longer, strategies designed to limit the negative neurocognitive and quality-of-life effects of WBRT are likely to gain increasing importance."


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