

Risks of whole brain radiation therapy outweigh benefits for patients with limited brain metastases

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Whole Brain Radiation Therapy (WBRT) is associated with significantly worse cognitive function than radiosurgery, and should no longer be used in the adjuvant setting after radiosurgery to treat cancer patients with brain metastases, according to a large study led by a researcher at The University of Texas MD Anderson Cancer Center.

MD Anderson's Paul Brown, M.D., professor, Radiation Oncology, presented the Phase III randomized trial findings from the Alliance cooperative research group on the plenary session of American Society for Clinical Oncology's 2015 Annual Meeting.

More than 200,000 [cancer patients](#) in the U.S. alone will be diagnosed and treated for brain metastasis this year. WBRT is currently used in a variety of settings as an adjuvant therapy after surgery or [radiosurgery](#) for patients with a few metastases, as a definitive treatment for patients with a greater number of metastases and in the palliative care setting.

Multiple randomized trials have shown adjuvant WBRT significantly improves tumor control. However, none of the studies have shown a survival benefit, Brown explains. WBRT's side effects include hair loss, skin redness, dry mouth and fatigue. It is associated with significant interruptions in systemic therapy. In contrast, side effects associated with radiosurgery are minimal, and it's generally not associated with significant interruptions in chemotherapy, says Brown.

"The question we were left with was understanding the toxicities associated with whole [brain radiation](#) therapy, specifically cognitive function," said Brown, the study's corresponding author. "We needed to understand what's worse - the cognitive

impact of the whole brain [radiation therapy](#), or, in other words, the therapy itself, or the recurrence of tumors.

"Our study gives us the clearest picture of the impact of WBRT on cognitive function. To date, we've really not had that," Brown continued.

The North American study enrolled 213 patients of different tumor histologies (the majority of whom had a lung primary diagnosis), from 2002-2013, all with one-to-three [brain metastases](#). Patients were randomized to receive either radiosurgery alone, or radiosurgery followed by WBRT, and underwent cognitive testing before and after treatment. The study's primary endpoint was cognitive progression (CP), defined as significant decline in any of the seven cognitive tests at three months.

At three months, CP was more frequent in the WBRT-radiosurgery arm, compared to those who received radiosurgery alone, 92 percent and 64 percent, respectively. Specifically, in patients those that underwent WBRT and radiosurgery compared to radiosurgery alone, there was more deterioration in immediate recall (30 percent and 8 percent, respectively); delayed recall (51 percent and 20 percent, respectively); and verbal fluency (19 percent vs. 2 percent).

Intracranial tumor control at three and six months were 75 and 65 percent, respectively, with radiosurgery alone, compared to 94 and 88 percent, respectively, with radiosurgery and WBRT. Although intracranial control was significantly better with the addition of WBRT, there was no difference in survival with a median overall survival of 10.7 months in the radiosurgery arm of the clinical trial versus 7.5 months in those who received radiosurgery and WBRT. In addition [patients](#) treated with WBRT and radiosurgery had a worse

quality of life compared to those treated with radiosurgery alone.

The definitive findings should serve as recognition that the deleterious impact on cognitive function outweighs any benefit associated with WBRT and tumor control, says Dr. Brown.

"Overtime there's been a general shift in moving away from using whole brain radiation, in favor of [stereotactic radiosurgery](#)," says Brown. "With these results and appropriate concerns for cognitive decline, it will likely will be pushed even further—reserving WBRT for later in a patient's disease course."

As a follow up, Brown and colleagues plan to analyze the cost effectiveness data associated with WBRT added to radiosurgery versus radiosurgery alone. Also, Brown is currently leading an Alliance trial studying WBRT use versus radiosurgery to the surgical cavity following surgical resection of a [brain metastasis](#). This ongoing trial will determine which treatment approach is better.

Provided by University of Texas M. D. Anderson Cancer Center

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