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Title

The Tippy Barstool of Prophylactic Cranial Irradiation

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<https://escholarship.org/uc/item/6rq4m731>

Journal

JCO Oncology Practice, 13(11)

ISSN

2688-1527

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Publication Date

2017-11-01

DOI

10.1200/jop.2017.027623

Peer reviewed

The Tippy Barstool of Prophylactic Cranial Irradiation

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ASSOCIATED CONTENT



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Use of radiotherapy to prophylactically treat the brain is a fascinating application of radiation treatments. As outlined in the review by Schild et al,¹ the rationale and clear efficacy of this treatment dates back nearly four decades. It is critical that we continue to re-evaluate the utility of our treatment paradigms. Schild et al highlight how prophylactic cranial irradiation (PCI) still should fit into our treatment regimen for small-cell lung cancer (SCLC); however, it is useful to raise a few additional points that require reflection.

Our continued use of PCI in the treatment of SCLC balances on a three-legged stool composed of the following: that systemic treatments are inadequate at controlling the brain disease; that the harm to the patient caused by untreated brain metastases is high; and that the risks of injury from radiotherapy are reasonable for patients. If any of these legs breaks, the stool tips. We do not prophylactically treat other sites of the body with radiotherapy because the legs of the stool are clearly inadequate for other disease sites. We assume that systemic treatments are adequately balanced against the harms of upfront radiation and our collective ability to provide palliative salvage treatments in an incurable patient population. Is this same assessment true for PCI?

It likely depends on the degree of bias toward the harms of PCI treatment versus intracranial progression and salvage treatment. Which is worse? If one wants to argue against PCI, one must simply point out that the imaging requirements of the trials included in the meta-analyses of Aupérin et al²

and Meert et al,³ as well as those of the Slotman trial,⁴ were inadequate and, thus, the results are no longer applicable. It seems inexcusable in 2017 to not complete staging with magnetic resonance imaging of the brain before treatment. It is conceivable that large proportions of patients had brain metastases at the outset on these trials. That only leaves the Takahashi phase III trial, which was closed early as a result of the futility of the PCI treatment.⁵ It included a robust imaging component and, as a result, the survival benefit of upfront treatment was likely quashed by better staging. If we follow a strategy of no PCI, the likelihood of brain failure is 64% at 18 months, of which 40% would have recurred in the brain despite treatment and 36% would have been overtreated, thus leaving only 24% of patients with benefit.

Is it worth overtreating more patients with PCI than those who would have benefited? The data to answer this question are not clearly informative. Quality-of-life data from the Slotman trial suggest that there was no decrement to the PCI arm, but this could also be interpreted as a lack of benefit.⁶ If survival is the same as in the Takahashi study, then it seems that the goal of treatment, in part, should be to help patients feel better. This is not the necessarily the case. The poor adherence to health-related quality of life submission in the Slotman study raises the question of reporting bias, which would likely favor the patients who are feeling and functioning better. In studies of whole-brain radiotherapy or radiosurgery, quality-of-life data clearly favors treating less brain



DOI: <https://doi.org/10.1200/JOP.2017.027623>

tissue.^{7,8} In addition, the long-held standard of treating brain metastases in SCLC is biased toward whole-brain radiotherapy. Perhaps this bias, too, should be challenged. Data such as that from the University of Pittsburgh suggests a role for stereotactic radiosurgery for a subset of these patients. Stereotactic radiosurgery could play a role in additionally limiting these patients' exposure to whole-brain radiotherapy and its neurocognitive risks.⁹ Given the specific focus on neurocognitive outcomes, the ongoing hippocampal-sparing trials, one hopes, will be informative in setting a baseline that is consistent with a 2017 treatment paradigm ([ClinicalTrials.gov: NCT02635009](https://clinicaltrials.gov/ct2/show/study/NCT02635009)).

Overall, the assessment by Schild et al is well reasoned. With the currently available data, our collective bias still favors the utility of PCI in SCLC and, specifically, in extensive-stage disease; however, the choice of treatment is not entirely straightforward, and it is important to raise questions about our underlying bias. It is possible that one of the legs of our stool will collapse soon. Wouldn't that actually be a good thing? **JOP**

Author's Disclosures of Potential Conflicts of Interest

Disclosures provided by the authors are available with this article at jop.ascopubs.org.

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References

- Schild SE, Sio T, Daniels T, et al: Prophylactic cranial irradiation for extensive small-cell lung cancer. *J Oncol Pract* 13:730-736, 2017
- Aupérin A, Arriagada R, Pignon JP, et al: Prophylactic cranial irradiation for patients with small-cell lung cancer in complete remission. Prophylactic Cranial Irradiation Overview Collaborative Group. *N Engl J Med* 341:476-484, 1999
- Meert AP, Paesmans M, Berghmans T, et al: Prophylactic cranial irradiation in small cell lung cancer: A systematic review of the literature with meta-analysis. *BMC Cancer* 1:5, 2001
- Slotman B, Faivre-Finn C, Kramer G, et al: Prophylactic cranial irradiation in extensive small-cell lung cancer. *N Engl J Med* 357:664-672, 2007
- Takahashi T, Yamanaka T, Seto T, et al: Prophylactic cranial irradiation versus observation in patients with extensive-disease small-cell lung cancer: A multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol* 18:663-671, 2017
- Slotman BJ, Mauer ME, Bottomley A, et al: Prophylactic cranial irradiation in extensive disease small-cell lung cancer: Short-term health-related quality of life and patient reported symptoms—Results of an international phase III randomized controlled trial by the EORTC Radiation Oncology and Lung Cancer Groups. *J Clin Oncol* 27:78-84, 2009
- Brown PD, Ballman KV, Cerhan JH, et al: Postoperative stereotactic radiosurgery compared with whole brain radiotherapy for resected metastatic brain disease (NCCTG N107C/CEC-3): A multicentre, randomised, controlled, phase 3 trial. *Lancet Oncol* 18:1049-1060, 2017
- Brown PD, Jaeckle K, Ballman KV, et al: Effect of radiosurgery alone vs radiotherapy with whole brain radiation therapy on cognitive function in patients with 1 to 3 brain metastases: A randomized clinical trial. *JAMA* 316:401-409, 2016
- Wegner RE, Olson AC, Kondziolka D, et al: Stereotactic radiosurgery for patients with brain metastases from small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 81:e21-e27, 2011

AUTHOR'S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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No relationship to disclose