

Controversies in radiation oncology

Prophylactic cranial irradiation: *con*



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Prophylactic cranial irradiation (PCI)

- Prophylactic strategies have been adopted to prevent (micro)brain metastases in high risk patients
- Weighing potential benefits and risks

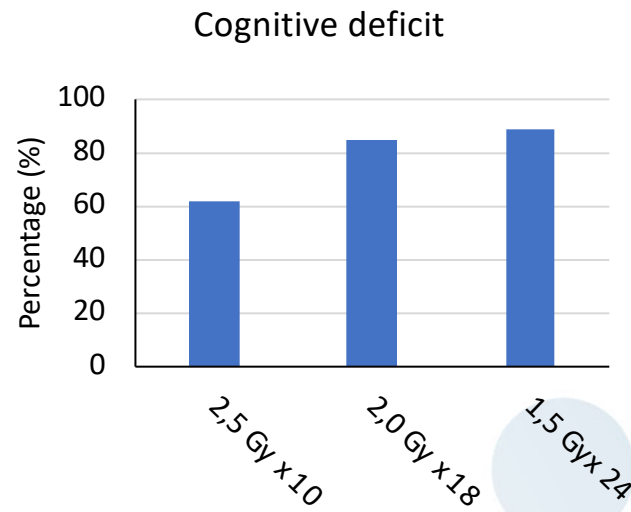
- Reduction in the risk of new brain metastases
- Prolonged PFS / OS



- Toxicity
 - Acute
 - Early-delayed
 - Late

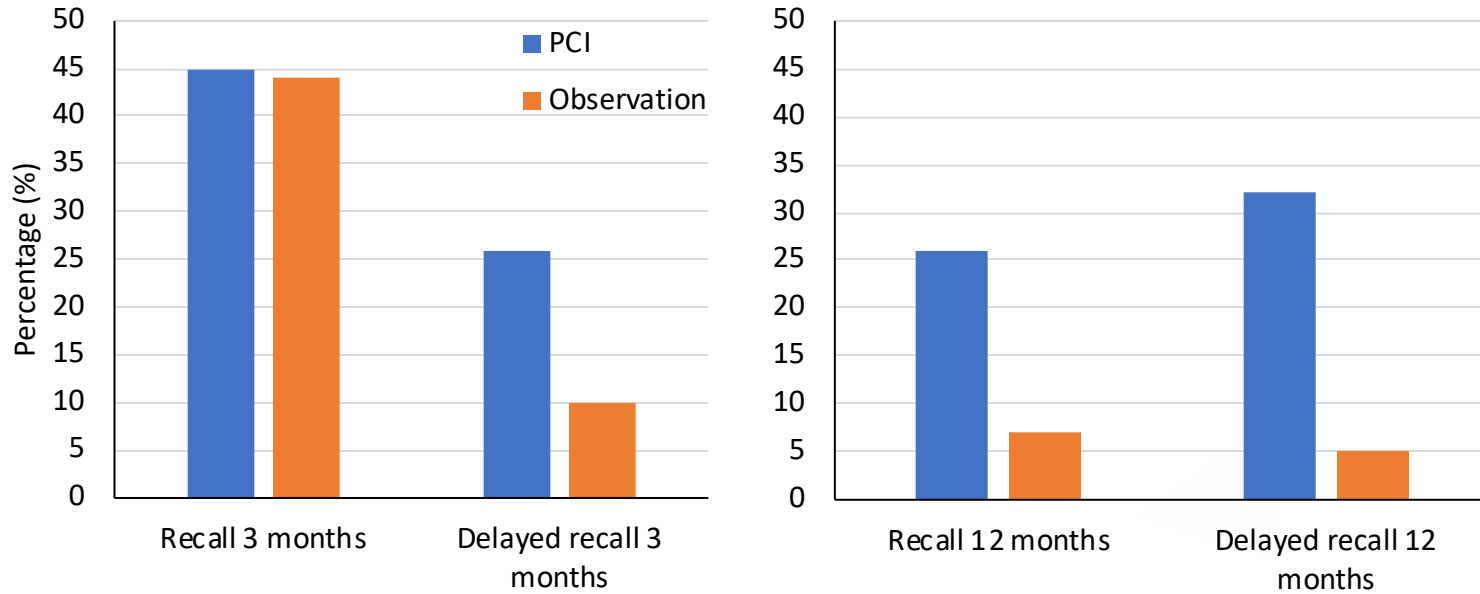
Neurocognitive deficits: SCLC

- LD-SCLC (n=22) had decreased cognition 3 months after PCI, with notable structural changes in gray and white matter¹
- LD-SCLC treated with hippocampal sparing PCI (n=22); reduction in brain volume was associated with a decline in cognition at 6 months²
- 52/64 (81%) of long-term SCLC survivors had impaired functioning on ≥ 1 cognitive test³
- Phase II RCT in LD-SCLC (n=265)⁴:



Neurocognitive deficits: NSCLC

- Phase III trial in locally advanced NSCLC, PCI (n=163) versus observation (n=177)⁵



⁵Sun et al. 2011 JCO

Alternative treatment strategies

- PCI: trade-off between higher rates of BM and worse cognition
- Other treatment options for subgroups of patients?
 - Hippocampal sparing PCI is **not** effective⁶





Hippocampal sparing PCI (NTC01780675)

- Phase III trial comparing HA-PCI versus PCI (n=168) in SCLC
 - Overall survival rate at 18 months: 54% versus 53% with HA-PCI
 - Cognitive failure rates: 28% vs 29% with HA-PCI after 4 months
 - No new brain metastases in the HA zone

Alternative treatment strategies

- PCI: trade-off between higher rates of BM and worse cognition
- Other treatment options for subgroups of patients?
 - Hippocampal sparing PCI is **not** effective⁶
 - Active surveillance with MRI
 - (Salvage) therapy
 - SRS as first-line treatment in selected patients?
 - Immunotherapy or targeted therapy
 - E.g. in EGFR positive advanced NSCLC, EGFR-tyrosine kinase inhibitors result in better CNS control than conventional therapy⁷





Conclusion

- PCI results in:
 - Lower rate of new brain metastases
 - Prolonged survival in a subgroup of patients
 - Worse cognitive functioning
- Alternative treatment options should be explored
 - Reducing late toxicity, without compromising intracranial tumor control