



A retrospective study on stereotactic radiotherapy or whole brain radiotherapy for brain metastases of small cell lung cancer

Chu Wu^{1,2,3}, Jingcong Pan^{1,2,3}, Sunjing Qiang^{1,2,3}, Zehua Sun^{1,2,3}, Xiao Hu^{1,2}

Zhejiang Cancer Hospital¹, Hangzhou Institute of Medical Sciences, Chinese Academy of Sciences², Graduate Training Base of Wenzhou Medical University³

Correspondence: Xiao Hu, Email: huxiao@zjcc.org.cn



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INTRODUCTION

- Small-cell lung cancer (SCLC)** is an aggressive lung malignancy, and brain metastasis is a leading cause of treatment failure and poor prognosis. Without treatment, median survival is less than 3 months.
- Whole-brain radiotherapy (WBRT)** is the traditional standard treatment for SCLC brain metastases, but it brings notable neurocognitive toxicities. **Stereotactic radiotherapy (SRT)** spares normal brain tissue with precise targeting. However, its role for SCLC, which is prone to multiple intracranial micrometastases, remains controversial.
- WBRT plus focal boost (WBRT+Boost)** combines whole-brain irradiation and local dose escalation. Real-world head-to-head comparisons of these three radiotherapy strategies in the immunotherapy era are scarce.
- This research conducted a comparative analysis of SRT, WBRT, and WBRT plus focal boost (WBRT+Boost) to inform clinical management strategies.

METHODS

Study Design & Patient Population

- Single-center retrospective cohort study.
- Enrolled 337 patients with pathologically confirmed SCLC and brain metastases, treated at Zhejiang Cancer Hospital (Jan 2019 – Jan 2026).
- Inclusion: Brain metastases verified by gadolinium-enhanced MRI; aged ≥ 18 years; received prior systemic therapy.
- Exclusion: Prior cranial radiotherapy; concurrent other active malignancies; hydrocephalus; leptomeningeal metastasis.

Treatment Modalities

- Patients were divided into 3 groups by cranial radiotherapy strategy.
- SRT (n=95): Stereotactic radiotherapy, mostly 15–35 Gy in 2–5 fractions.
- WBRT alone (n=181): Whole brain radiotherapy, standard 30 Gy in 10 fractions (80.5% of cases).
- WBRT+Boost (n=61): WBRT plus concurrent or sequential focal dose boost.

Endpoints

- Primary endpoint: Intracranial Progression-Free Survival (iPFS).
- Secondary endpoint: Overall Survival (OS).

Statistical Analysis

- Kaplan-Meier method with log-rank test for survival comparison.
- Univariate and multivariate Cox proportional hazards models for prognostic factor analysis.
- 1:1 Propensity Score Matching (PSM) to balance baseline confounders.
- Rosenbaum sensitivity analysis to validate result robustness.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- For SCLC patients with brain metastases, the choice of cranial radiotherapy modality (SRT / WBRT / WBRT+Boost) shows no significant impact on overall survival.
- WBRT plus focal boost achieves better intracranial disease control, and is preferred for patients with >3 brain lesions or high risk of diffuse micrometastasis.
- SRT remains a rational alternative for patients with 1–3 brain metastases, especially when neurocognitive preservation is a priority.
- Post-radiotherapy immunotherapy is an independent protective factor for survival and should be actively implemented in eligible patients.

Future Direction for Research

- Large-scale prospective clinical trials are needed to further define the optimal indications and patient selection criteria for SRT versus WBRT+Boost.
- Further studies are warranted to explore the optimal sequencing and synergistic mechanism of cranial radiotherapy combined with immunotherapy.
- Neurocognitive function and quality of life should be included as core endpoints to comprehensively evaluate the clinical value of different radiotherapy strategies.
- Biomarker-based research is required to identify subgroups of patients who derive the greatest benefit from specific intracranial radiotherapy regimens.

REFERENCES & ACKNOWLEDGEMENTS

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RESULTS

1. Overall Survival (OS)

Intergroup analysis:

Median OS: SRT 13.47m, WBRT 8.27m, WBRT+Boost 8.93m; overall **P=0.041**. 2-year OS: 26.5%, 22.8%, 23.6%

Pairwise analysis: SRT vs WBRT: HR 1.502, **P=0.013**

SRT vs WBRT+Boost: P=0.239

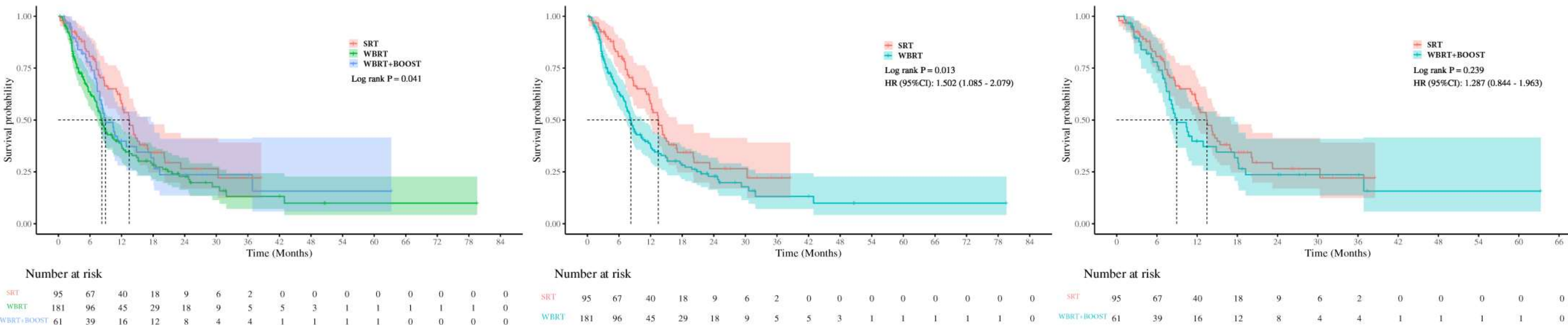


Figure 1 Shows the effects of different brain radiotherapy on the OS of patients with SCLC brain metastases.

2. Intracranial Progression-Free Survival (iPFS)

Intergroup analysis:

Median iPFS: SRT 6.13m, WBRT 6.10m, WBRT+Boost 7.87m; overall P=0.324. 2-year iPFS: 9.5%, 9.2%, 9.1%

Pairwise analysis: SRT vs WBRT: HR 1.018, P=0.903

SRT vs WBRT+Boost: HR 0.776, P=0.191

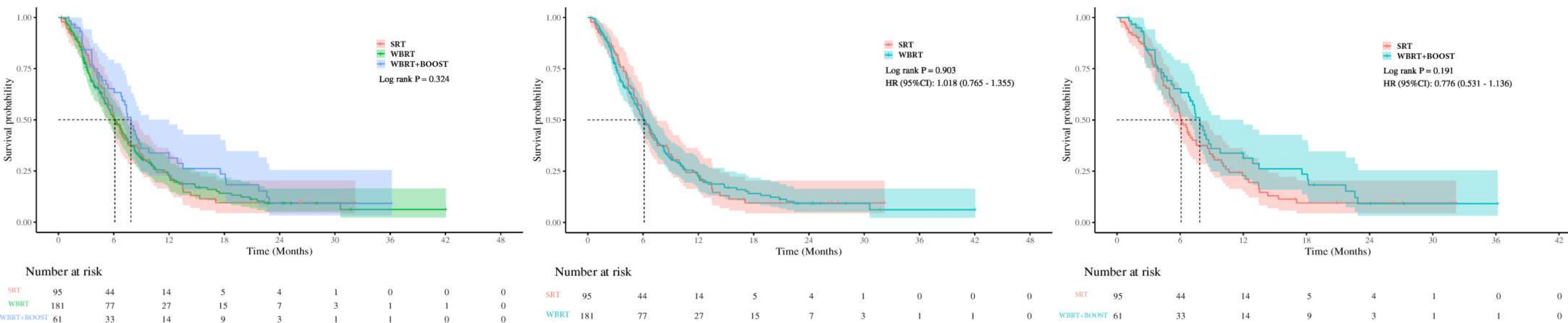


Figure 2 Shows the effects of different brain radiotherapy on iPFS in patients with SCLC brain metastases.

3. PSM Survival Analysis

OS : SRT vs WBRT (n=136): 11.77 vs 8.70 m, P=0.412; adj HR 0.70 (0.39–1.27), P=0.241 (Fig 3a)

SRT vs WBRT+Boost (n=90): 11.73 vs 12.90 m, P=0.387; adj HR 1.15 (0.55–2.43), P=0.706 (Fig 3b)

iPFS: SRT vs WBRT (n=136): 5.47 vs 6.30 m, P=0.582; adj HR 1.16 (0.68–1.98), P=0.587 (Fig 3c)

SRT vs WBRT+Boost (n=90): 5.87 vs 8.17 m, **P=0.021**; adj HR 1.27 (0.64–2.49), P=0.494 (Fig 3d)

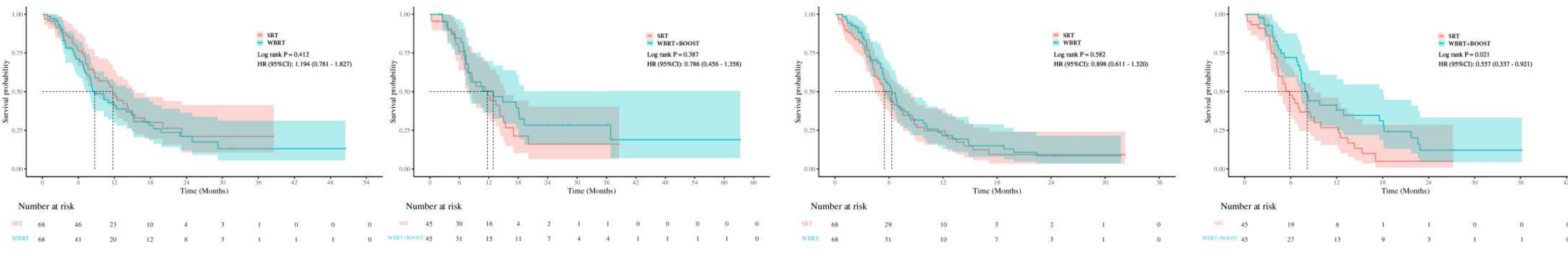


Figure3: Figures a and b show the OS survival analysis results after propensity score matching, while figures c and d show the iPFS survival analysis results after propensity score matching