

Intensity-Modulated Proton Postoperative Radiotherapy for Resected Non-Small Cell Lung Cancer in Lung Cancer in the Era of Contemporary Systemic Therapy

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INTRODUCTION

PORT improves locoregional control in high-risk resected resected NSCLC, but **Lung ART and PORT-C showed no no survival benefit alongside cardiopulmonary toxicity toxicity concerns.**

Both trials predate **contemporary perioperative systemic systemic therapy**, which preferentially reduces distant relapse — leaving locoregional recurrence a **proportionally greater competing risk**.

IMPT by pencil beam scanning spares heart and lung better than IMRT, but published proton PORT predate these modern techniques and systemic regimens.

The first PBS IMPT PORT outcomes in a contemporary, molecularly enriched cohort.

METHODS

DESIGN

IRB-approved retrospective review of consecutive patients at a single institution, **January 2019 – December 2024**, after curative-intent resection.

TREATMENT

Robustly optimized PBS IMPT from 4D simulation CT with motion-adaptive target delineation. Prescription **50.4 GyE / 28 fractions**. Comparison IMRT plans generated for 7 patients.

ENDPOINTS

Co-primary: cumulative incidence of **isolated locoregional failure** (no concurrent or subsequent distant failure) and **distant failure**, by Aalen-Johansen with death as a competing event.

Secondary: OS and PFS by Kaplan-Meier; toxicity per **CTCAE v5.0**; dose-volume metrics as median (IQR). Analyses in R 4.3.

RESULTS

n = 29 · median age 65 (35–82) · median follow-up 30 months (13–70)

93%
Overall survival at 36 months

68%
Progression-free survival at 36 months

3%
Isolated locoregional failure
1 event

28%
Distant failure
8 events (2 w/ concurrent LRF)

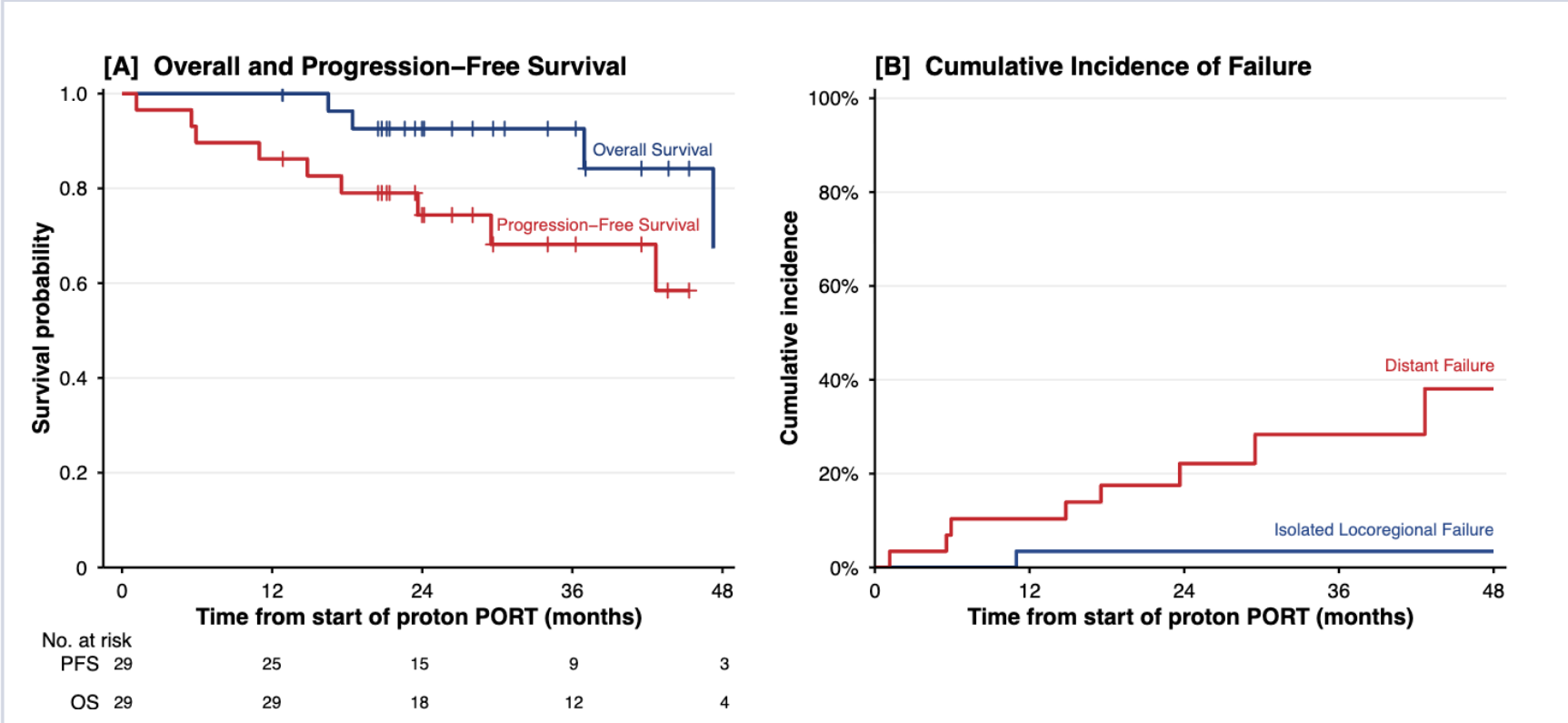
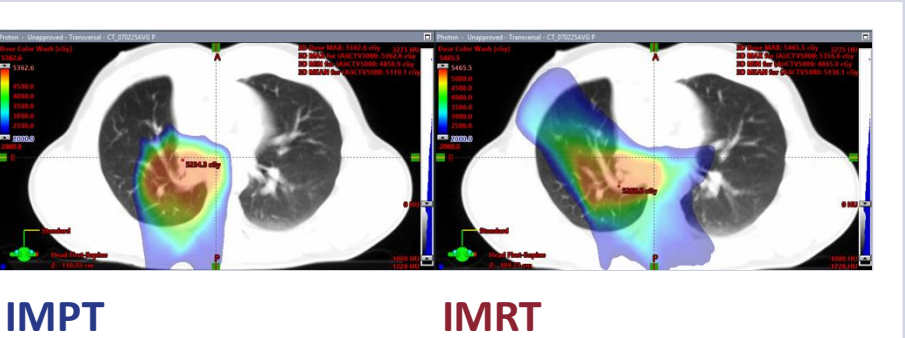


Figure 1. (A) Kaplan-Meier overall and progression-free survival with risk tables. **(B)** Cumulative incidence of isolated locoregional failure versus distant failure (Aalen-Johansen, death as a competing risk).



IMPT **IMRT**

Figure 2. Representative paired dose distributions in the same patient. The proton plan confines low-dose spread to the ipsilateral hemithorax; the photon plan deposits low dose across the heart and contralateral lung.

Delivered IMPT dosimetry

n = 29, median: mean lung **5.2 Gy**, mean heart **3.3 Gy**, lung V20 **11.2%**, contralateral lung 0.2 Gy; CTV D95 50.7 Gy.

Patient and treatment characteristics

Age, median (range), y	65 (35–82)
Histology	
Adenocarcinoma	22 (76)
Squamous cell carcinoma	4 (14)
NSCLC NOS	3 (10)
Molecular alteration	
EGFR	12 (41)
ALK	4 (14)
None identified	13 (45)
Pathologic nodal stage N2	24 (83)
Neoadjuvant systemic therapy	22 (76)
Adjuvant therapy post-PORT	15 (52)
TKI maintenance (EGFR 9, ALK 4)	13 (45)
Surgery-to-PORT, median (range), d	105 (44–205)

Toxicity

No grade ≥3 events.

No significant cardiac toxicity.

Radiation Pneumonitis

Grade 2	2 (7 %)
Grade 3+	0

Cardiac toxicity, any grade

Any grade ≥3 toxicity **0**

No treatment interruptions or hospitalizations.

Nine patients (31%) had cardiology follow-up, none with PORT-attributable events.

Paired IMPT vs IMRT plans

n = 7, median (IQR). IMRT was higher on every metric.

Metric	IMPT	IMRT	p
Contralateral lung V5, %	1.3	48.3	0.016
Contralateral lung D _{mean} , Gy	0.2	6.0	0.016
Total lung V5, %	17.9	52.4	0.016
Total lung D _{mean} , Gy	4.8	9.1	0.016
Heart D_{mean}, Gy	3.5	6.2	0.016
Heart V5, %	13.5	24.1	0.016

The IMPT advantage is largest in the **low-dose range** — the exposure implicated in photon-PORT cardiopulmonary morbidity. Prior photon PORT data identified **heart V8Gy ≥35.5%** as the strongest cardiac predictor of reduced survival.

DISCUSSION & CONCLUSION

Actionable Take Away Message

IMPT PORT delivered durable locoregional control with no grade ≥3 or significant cardiac toxicity in a contemporary, molecularly enriched cohort.

Where PORT has been avoided over toxicity concerns Proton PORT may allow for improved locoregional outcomes without excess toxicity.

These findings are increasingly relevant given that **contemporary perioperative systemic therapies preferentially reduce distant relapse.**

Future Direction for Research

Refining patient selection for PORT in this landscape is the open question. **Prospective evaluation incorporating patient-reported outcomes, cardiopulmonary functional assessment, and circulating tumor DNA-based minimal residual disease is warranted** to establish the role of proton PORT as a precision adjuvant strategy.

Limitations:

retrospective, single institution, n = 29, heterogeneous systemic therapy reflecting real-world practice, toxicity captured from documented clinical events only.

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Funding:

No specific external funding.