Upright Image-Guided Proton Therapy for Thoracic Re-Irradiation: Interim Results of a Prospective Clinical Trial

Philip Blumenfeld[1], Aviad Berger[1], Alexander Pryanichnikov[2,3], Daniel Levy[1], Yair Hillman[1], Marcel Fang[1], Sarit Appel[4], Jon Feldman[1], Aron Popovtzer[1]

[1]Sharett Institute of Oncology, Hadassah Medical Center, Hebrew University of Jerusalem, Jerusalem, Israel
[2]Institute of Biomedical Engineering, Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany
[3]Division of Biomedical Physics in Radiation Oncology, German Cancer Research Center (DKFZ), Heidelberg, Germany
[4]Department of Radiation Oncology, Sheba Medical Center, Tel Hashomer, Israel

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Introduction

Clinical problem. Thoracic re-irradiation is limited by cumulative dose to lung, heart, esophagus, spinal cord, and central airways.
Physics opportunity. IMPT can reduce exit dose; upright positioning may enlarge aerated lung, alter mediastinal geometry, and enable treatment on a fixed horizontal beamline.
Objective. Prospectively test the feasibility, setup reproducibility, dosimetry, early toxicity, response, and quality of life of upright image-guided IMPT versus supine IMPT and VMAT.

Population	Intervention	Comparators	Study Endpoints
10 patients	**Upright IMPT**	**Supine VMAT vs Upright PT**	**3-month LC and Adverse Events (CTCAE V5)**
Recurrent thoracic malignancy after prior definitive thoracic RT	Fixed horizontal beamline, robotic chair, daily image guidance	Comparable target coverage; OAR-focused planning comparison	Setup reproducibility, dosimetry comparison, QoL using FACT-L and QLQ-LC13

Study Design

1. **Prior RT review** — Dose reconstruction and cumulative OAR assessment
2. **Dual simulation** — Supine and upright CT; ITV-based motion management
3. **Comparative planning** — VMAT, supine IMPT, upright IMPT
4. **Treatment** — Upright IMPT with daily CT, adaptation if necessary and orthogonal kV verification
5. **Follow-up** — Weekly OTV; 1- and 3-month response, toxicity and QoL

Patient Cohort

Characteristic	Summary
Histology	8 NSCLC, 1 adenoid cystic carcinoma, 1 SCLC
Stage at recurrence	IIB 2 • IIIA /B: 2 • IV: 6 (Oligoprogression/Oligorecurrence)
Concurrent systemic therapy	4 received concurrent chemotherapy (Carbo/Taxol)
In-Field (within 80% IDL)	9 of 10
Time from Previous radiation	25.1 months; Range: 8.3–71.7 month
ITV (cc)	110.2 cc (range 31-236)
Location of Recurrence	6 Ultracentral; 4 Central: Mediastinum (5) hilar (2) upper-lobe (2): Upper lobe with Paravertebral (1)

Patient Cohort

10	71	80%	80%
prospectively treated patients	median age, years	male	NSCLC histology

Dose / fractionation	Patients	Clinical rationale
60 Gy(RBE) / 30 fx	4	conventional reRT ± chemotherapy
45–55 Gy(RBE) / 15–20 fx	6	hypofractionated IMPT alone

Methods and Materials

Design: Prospective single-institution interim analysis (NCT05549414); first 10 consecutive patients treated July 2024 - March 2025.
Delivery: Pencil-beam scanning IMPT on a fixed horizontal beamline with a 6-DoF robotic chair and vertical CT, P-Cure Proton Therapy System.
Comparison: Identical targets/OARs planned as upright IMPT, supine IMPT, and supine VMAT when feasible, including manual delineations for every patient positioning.
Endpoints: Setup shifts, lung volume, target/OAR dosimetry, CTCAE v5.0 toxicity, 3-month imaging response, EORTC QLQ-LC13, and FACT-L.
Analysis: Paired two-tailed t tests or Wilcoxon signed-rank tests, as appropriate; statistical significance p<0.05.

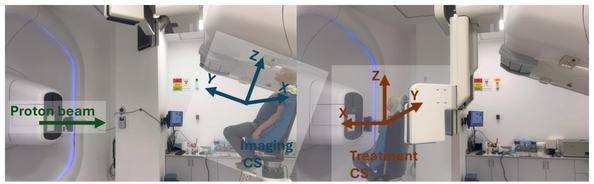

Figure 1. Imaging and treatment coordinate systems for gantry-less upright delivery

Figure 2. Imaging in upright position with arm up patient positioning

Results

15–20 min	0	0
daily positioning workflow	treatment interruptions	re-immobilizations

Table 1. Setup accuracy

Registration	Δx	Δy	Δz	Rotations
Pre-treatment 3D/3D	+0.6 mm	−0.4 mm	−1.1 mm	~0.6°
In-treatment 2D/3D	−0.7 mm	−1.3 mm	+0.5 mm	~0.5°

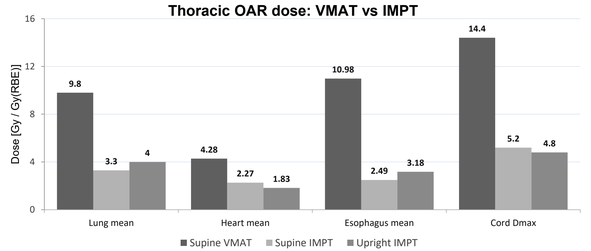

Figure 3. IMPT reduced mean lung, heart, and esophagus dose and spinal-cord Dmax versus VMAT

Table 2. Key dosimetric results

Metric	Supine VMAT	Supine IMPT	Upright IMPT	VMAT vs upright p	Supine vs upright IMPT p	Reduction
Lung V5	32.2%	12.9%	12.5%	0.007	NS	−61%
Lung V20	15.4%	7.6%	5.6%	0.004	NS	−64%
Mean lung dose	9.8 Gy	3.3 Gy(RBE)	4.0 Gy(RBE)	0.002	NS	−59%
Mean heart dose	4.28 Gy	2.27 (RBE)	1.83 Gy(RBE)	0.010	NS	−57%
Mean esophagus dose	10.98 Gy	2.49 Gy (RBE)	3.18 Gy(RBE)	0.023	NS	−71%
Esophagus Dmax	35.0 Gy	23.7 Gy(RBE)	23.3 Gy(RBE)	0.031*	NS	−33%
Spinal cord Dmax	14.4 Gy	5.2 Gy(RBE)	4.8 Gy(RBE)	0.008*	NS	−67%
Mean Prox Bronch Tree	24.8 Gy	18.1 Gy(RBE)	19.0 Gy(RBE)	0.02*	NS	−28%

Pulmonary sparing. Upright IMPT versus VMAT: lung V5 12.5% vs 32.2% (p=0.007), V20 5.6% vs 15.4% (p=0.004), and mean dose 4.0 vs 9.8 Gy/Gy(RBE) (p=0.002).
Central OAR sparing. Mean heart 1.83 vs 4.28 (p=0.010), mean esophagus 3.18 vs 10.98 (p=0.023), and spinal-cord Dmax 4.8 vs 14.4. No major OAR or target-coverage differences between upright and supine IMPT.

Early Outcomes: Local Control and AEs

100%	5 CR	3 PR	2 SD
local control within the re-irradiated volume at 3 months	complete metabolic responses on PET/CT using PERCIST criteria	partial metabolic responses on PET/CT using PERCIST criteria	stable disease on CT, PET not available

Table 3. CTCAE v5.0 AEs (n=10)

Finding	Any grade	Grade ≥3
Fatigue	30% (3)	0
Chest wall pain	20% (2)	0
Pneumonitis	20% (2)	0
Esophagitis	10% (2)	0
Vasovagal episode	10% (1)	0
Neutrophil count decrease	10% (1)	0
Lymphocyte count decrease	10% (1)	0
White blood cell count decrease	10% (1)	10% (1)

Cough: 33.3 → 44.4 (baseline to 3 months)
Dysphagia: 10.0 → 5.6 (improved by 3 months)
Dyspnea: 24.7 → 26.7 (minimal change)
FACT-L total: 101.4 → 95.9 (no meaningful decline)

Discussion

Primary finding. The dominant dosimetric benefit was proton modality: upright IMPT substantially spared thoracic OARs versus VMAT while preserving target coverage.
Posture effect. Upright positioning enlarged lung volume but did not further reduce major OAR metrics versus supine IMPT.
Implementation. Robotic chair positioning plus daily 3D/3D and intra-treatment 2D/3D image guidance enabled reproducible delivery on a fixed beamline without workflow failure.

Conclusions

Feasible and reproducible: 10/10 patients completed upright image-guided IMPT without interruption.
Dosimetrically favorable: clinically important OAR reductions versus VMAT with equivalent target coverage.
Physics-driven access: upright delivery supports fixed-beam, gantry-less proton therapy without compromising setup accuracy.
Posture insight: greater lung volume did not translate into additional OAR sparing versus supine IMPT in this ITV-based workflow.
Early clinical signal: 100% in-field control at 3 months, predominantly grade 1–2 toxicity, and preserved patient-reported QOL.
Take-home: Upright IMPT is a promising thoracic re-irradiation strategy; mature control and late-toxicity data are still required.

Contact

Correspondence: Philip Blumenfeld, MD
Sharett Institute of Oncology, Hadassah Medical Center, Hebrew University of Jerusalem, Jerusalem, Israel
Email: philipb@hadassah.org.il | Trial: NCT05549414
Website: https://www.hadassah.org/

References

1. Feldman J, Pryanichnikov A, Achkienasi A, et al. Commissioning of a novel gantry-less proton therapy system. Front Oncol. 2024;14:1417393. doi:10.3389/fonc.2024.1417393.
2. Feldman J, Pryanichnikov A, Shwartz D, et al. Study of upright patient positioning reproducibility in image-guided proton therapy for head and neck cancers. Radiother Oncol. 2024;201:110572. doi:10.1016/j.radonc.2024.110572
3. Blumenfeld P, Pryanichnikov A, Hillman Y, et al. Prospective clinical trial of upright image-guided proton therapy for locally recurrent head and neck and brain malignancies. Radiother Oncol. 2025;211:111097. doi:10.1016/j.radonc.2025.111097
4. Blumenfeld P, Pryanichnikov A, Tochner Z, et al. Pediatric CNS relapse of neuroblastoma treated with upright proton craniospinal irradiation. Clin Transl Radiat Oncol. 2025;56:101080. doi:10.1016/j.ctro.2025.101080