CBCT-Guided Online Adaptive Radiotherapy for Isotoxic Dose Escalation in Hypofractionated Treatment of Locally Advanced Lung Cancer

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2026 JULY 19–22 VANCOUVER, BC
JOINT AAPM | COMP MEETING

INTRODUCTION

Non-small cell lung cancer **(NSCLC)** patients that are ineligible for surgery often receive radiotherapy. However, efficacy (local/distant control) is limited in standard (e.g., 6000cGy in 30 fractions or BED_{10}=7200cGy) treatment regimens.

Hypofractionation can increase biological effectiveness, but tumor doses must be limited to ensure safe organ-at-risk **(OAR)** doses and avoid toxicities such as pneumonitis and esophagitis.

We have developed a novel approach that leverages CBCT-guided online adaptive radiotherapy **(oART)** to allow for a personalized isotoxic escalation of target doses for hypofractionated radiotherapy.

METHODS AND MATERIALS

4500 cGy in 15 fractions (300 cGy/fraction) - Ensures OAR sparing but has limited biological effectiveness *(BED_{10}=5850cGy)*

6000 cGy in 15 fractions (400 cGy/fraction) - Risks OAR toxicity but improves tumor control probability *(BED_{10}=8400cGy)*

Workflow for Isotoxic oART dose escalation is shown in **Fig. 1.**

Structure Definitions (Fig. 2):

- ITV/IGTV = Physician delineated target region accounting for internal breathing motion using 4DCT
- OARs are Esophagus & Proximal Bronchial Tree **(PBT)**
- PTV_4500 = ITV/IGTV + 5mm(radial) + 7mm(sup/inf)
- IGTV_6000 = ITV/IGTV – [OARs + 3mm]

Data Analysis:

- Retrospective data from 12 patients (180 oART sessions)
- Dosimetric comparison for daily adapted**(ADP)** vs. non-adapted/scheduled**(SCH)** plans
- Structure-guided rigid registrations across all 15 treatments estimates target/OAR cumulative doses:
  - IGTV-guided ➔ highlight the effect of daily hot-spot migration providing increased homogeneity
  - PBT-guided ➔ highlight the effect of pushing high dose away from OAR daily *(Note: to account for inherent contouring/fusion uncertainties, cumulative PBT dose was evaluated within a local 5 mm region)*

Structure	Objective	Goal	Reference	Scheduled	Adapted	Improvement (%)
IGTV	$V_{6000cGy}$	95%	95.2 ± 2.9	88.8 ± 8.3	95.4 ± 2.7	8.4 ± 12.0
	$D_{90\%}$	400cGy	402.3 ± 6.2	395.3 ± 14.8	404.3 ± 3.7	2.4 ± 4.0
Esophagus	$D_{0.03cc}$	342cGy	305.5 ± 48.9	328.8 ± 55.0	309.8 ± 40.2	4.9 ± 8.9
PBT	$D_{0.03cc}$	369cGy	360.0 ± 8.9	392.1 ± 28.5	359.4 ± 8.9	7.9 ± 6.2

Table 1. Average achieved dosimetry for initial reference, scheduled, and adapted plans as well as improvement with adaptive vs. scheduled.

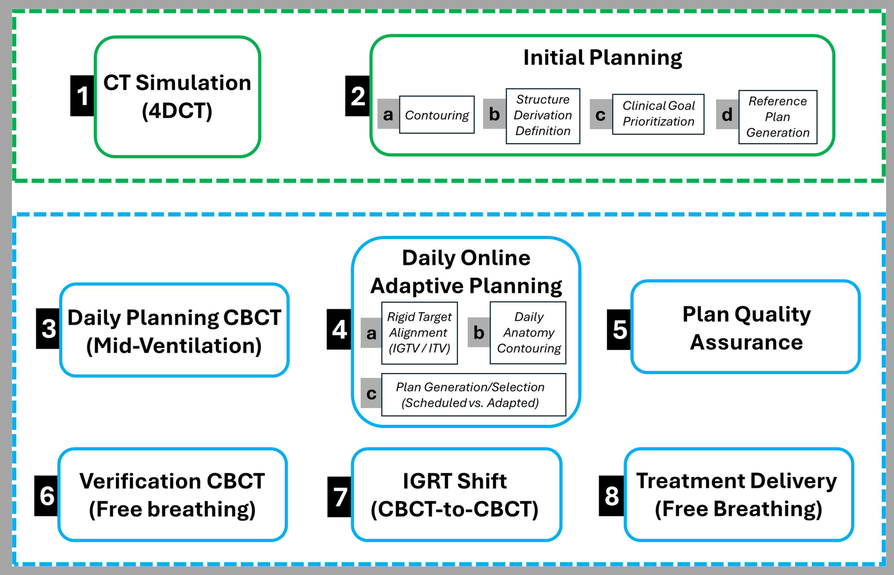

Fig 1. Workflow for isotoxic dose escalation with oART. Steps 1-2: initial planning/contouring. Steps 3-8: daily adaptive process repeated for each treatment fraction.

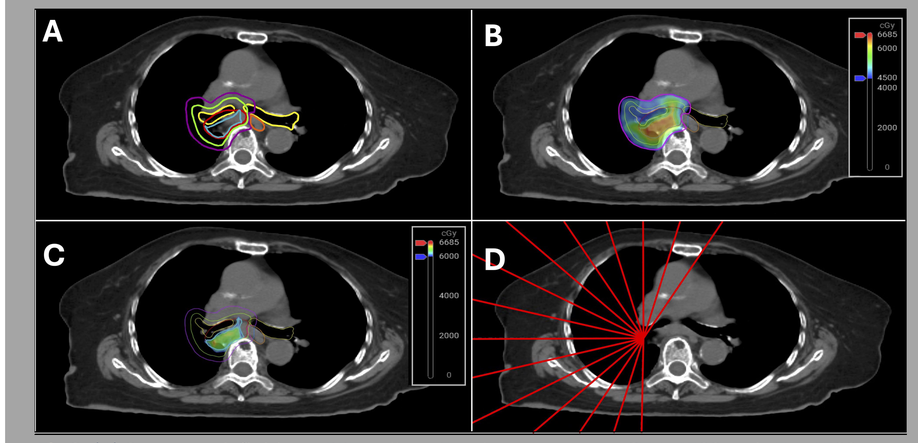

Fig 2. (A) Structure definitions: PBT-*yellow*, *Esophagus-orange*, IGTV_4500-*red*, ITV_4500-*green*, PTV_4500-*purple*, IGTV_6000-*cyan*. (B) 4500 cGy dose volume. (C) 6000 cGy dose escalated volume (D) Example beam geometry.

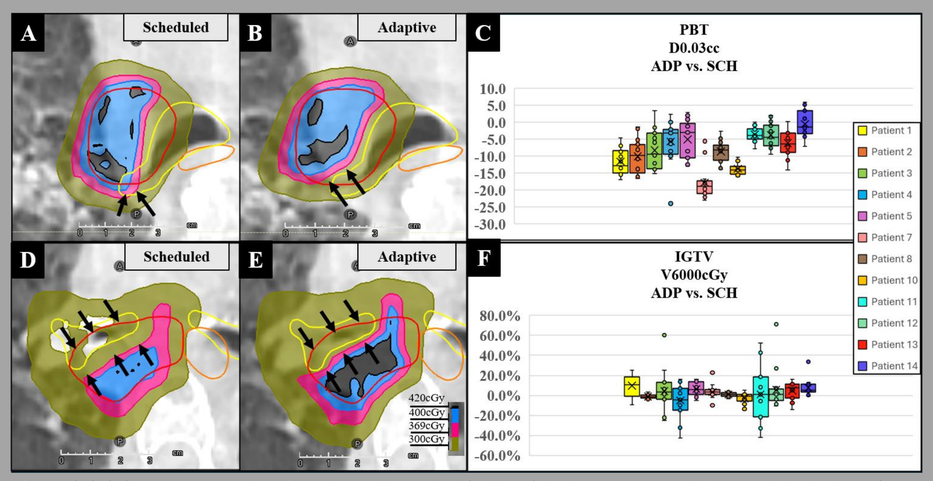

Fig 3. (A)-(B) Representative fraction where PBT(yellow) is better spared from critical dose (369 cGy/fraction) for ADP vs. SCH. (D)-(E) Representative fraction where IGTV(red) coverage improved for ADP vs. SCH. (C) Per-patient box plot of change in PBT max dose for ADP vs. SCH over all treatments (negative indicates improvement with adaptation). (F) Per-patient box plot of change in volume of IGTV receiving escalated dose for ADP vs. SCH over all treatments (positive indicates improvement with adaptation).

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RESULTS

Average oART session time was 31.2 ± 6.9 minutes (from planning CBCT acquisition to treatment completion)

Average dosimetric improvement with daily adaptation is given in **Table 1.** Representative changes in dose distribution resulting in better OAR sparing and improved target coverage as well as per-patient dosimetric gains are shown in **Fig. 3.**

Cumulative dose analysis highlighted decreased target dose heterogeneity due to hotspot migration in ADP vs. SCH plans (**Fig. 4)** and a small (1.4%) decrease in $D_{0.03cc}$ within the local (5mm) PBT region.

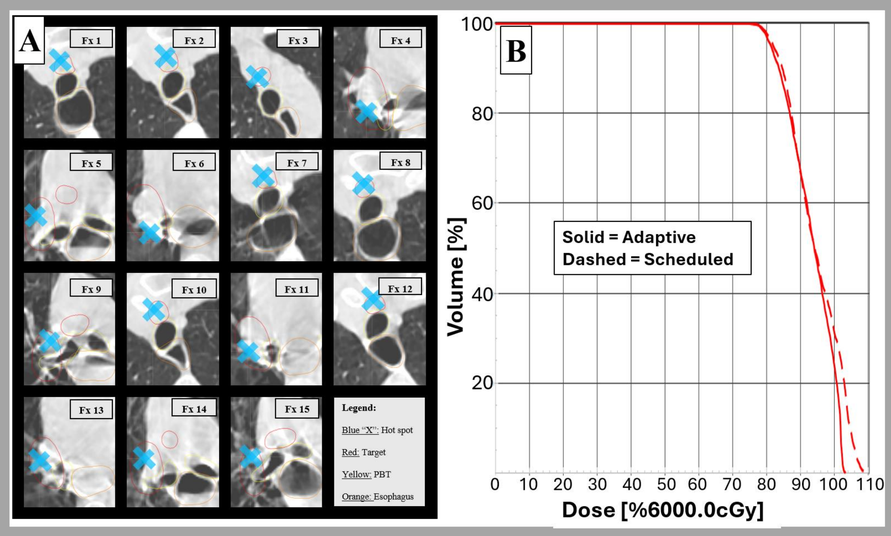

Fig 4. (A) Zoomed in axial slice on daily CBCT with individual adaptive fraction hot spots depicted with blue "X" demonstrating a different anatomical location daily. (B) DVH for a single patient's cumulative dose for the IGTV based on IGTV-guided rigid registrations. V6000cGy is relatively similar, whereas the maximum dose is reduced with adaptive plans, providing decreased heterogeneity.

DISCUSSION/CONCLUSION

Dose escalation and hypofractionation are promising options for locally advanced lung cancer patients that are ineligible for surgery. However, these approaches historically have come with high rates of Grade 3 esophagitis and pneumonitis (rates of ~24% and ~12%, respectively). These toxicities may be due to consistent hot spot placement and interfractional OAR variability with respect to high-dose regions.

We have developed a methodology leveraging daily CBCT-guided online adaptive radiotherapy to ensure consistent target coverage with at least 300 cGy/fraction (using more traditional motion encompassing targets rigidly aligned daily) while incorporating an isotoxic simultaneous integrated boost to 400 cGy/fraction to a dynamic tumor sub-volume accounting for daily OAR variations.

Analysis of daily doses with oART demonstrates appreciable OAR dose reduction while maintaining comparable target coverage. Analysis of cumulative dose reveals improved target homogeneity and reduced maximum doses near organs as a result of hot-spot migration and consistent OAR sparing with daily CBCT-guided oART.

While additional follow up is required to determine the clinical benefit from these dosimetric improvements, this may be a promising treatment option for locally advanced lung cancer patients.

REFERENCES

Polce SA, Nasser N, Chiodo C, et al., *Leveraging CT-based online adaptive radiotherapy for dose escalation in hypofractionated radiotherapy for locally advanced unresectable lung cancer*, Front. Oncol. 16:1777077 (2026).