From Segmentation to Modeling Tumor Evolution: Trajectory-Aware Time-Series Learning (TRASE) for Adaptive Radiotherapy

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ABSTRACT

Purpose
Accurate delineation of the gross tumor volume of the primary lesion (GTVp) during radiotherapy is essential for ART, particularly in head-and-neck cancer where tumor regression and anatomical deformation occur during treatment. However, mid-treatment contouring remains challenging due to limited soft-tissue contrast in CBCT and the inability of conventional methods to model tumor evolution. This study proposes Trajectory-Aware Time-Series Learning (TRASE), a framework that formulates mid-treatment GTVp delineation as tumor evolution modeling rather than static segmentation.

Methods
A total of 101 patients with planning CT at week-0 and weekly CBCT during treatment were split into 65/15/20% training, validation, and test cohorts. TRASE models temporal tumor morphology evolution by integrating deformation-based shape propagation with longitudinal image-driven feature learning. Baseline GTVp geometry is propagated toward the target week to establish a warp-first morphological evolution backbone. Longitudinal CBCT image patches from weeks 1–3 are stacked as input channels and temporally integrated through patch-based convolutional representations to extract features capturing tumor shape and appearance changes, with inter-week intensity differences encoding evolution. Region-of-interest annotations at weeks 1–3 were used only during training. Performance was evaluated using the Dice similarity coefficient (DSC) and average surface distance (ASD) and compared with DIR, U-Net, and nnU-Net.

Results
At mid-treatment (week-4), TRASE achieved a DSC of 0.73 ± 0.03 and an ASD of 0.94 ± 0.08 mm, significantly outperforming DIR (DSC 0.44 ± 0.03, ASD 2.38 ± 0.11 mm), U-Net (DSC 0.34 ± 0.05, ASD 5.39 ± 0.68 mm), and nnU-Net (DSC 0.47 ± 0.03, ASD 5.75 ± 0.51 mm). Qualitative evaluation showed that TRASE produced evolution-consistent contours with stable boundaries, whereas conventional methods showed boundary degradation.

Conclusion
By explicitly modeling tumor evolution as a temporal trajectory, TRASE enables accurate and robust mid-treatment GTVp prediction without additional contouring workload, providing a physics-consistent and clinically practical foundation for ART.

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INTRODUCTION

Adaptive radiotherapy requires accurate identification of the gross tumor volume of the primary lesion (GTVp) during treatment, particularly in head-and-neck cancer where tumor regression, anatomical deformation, and patient-specific response patterns occur over the course of fractionated radiotherapy. Although cone-beam CT (CBCT) provides valuable on-treatment imaging, mid-treatment GTVp delineation remains challenging because CBCT has limited soft-tissue contrast and tumor boundaries may become less distinct as treatment progresses. Repeated manual contouring can also increase clinical workload and may introduce observer variability.Conventional approaches, including deformable image registration (DIR) and single-timepoint deep learning segmentation, generally treat target delineation as either geometric propagation or independent image segmentation. However, these methods do not explicitly model the continuous temporal evolution of tumor morphology and appearance during radiotherapy. This limitation is especially important in adaptive treatment settings, where clinically useful target prediction should reflect both baseline tumor geometry and longitudinal changes observed on serial CBCT images.To address this issue, we developed Trajectory-Aware Time-Series Learning (TRASE), a framework that reformulates mid-treatment GTVp delineation as tumor evolution modeling rather than static segmentation. TRASE integrates deformation-based shape propagation from the planning CT with longitudinal CBCT-derived temporal features from early treatment weeks, enabling evolution-consistent prediction of week-4 GTVp without requiring additional manual contouring at deployment.

METHODS AND MATERIALS

Study cohort
This study included 101 patients with head-and-neck cancer who underwent planning CT at week 0 and weekly on-treatment CBCT during radiotherapy. Patients were divided into training, validation, and test cohorts using a 65%/15%/20% split.

Input data
The baseline GTVp contour on planning CT was used as the initial tumor geometry. Longitudinal CBCT images acquired during early treatment weeks 1–3 were used to capture temporal changes in tumor morphology and appearance.

TRASE framework
Trajectory-Aware Time-Series Learning (TRASE) was designed to predict the week-4 GTVp by modeling tumor evolution rather than performing static segmentation. First, the baseline GTVp was propagated toward the target week using deformation-based shape propagation to provide a warp-first morphological backbone. Then, CBCT patches from weeks 1–3 were stacked as longitudinal input channels and processed using patch-based convolutional representations to extract temporal image features.

Comparison model settings
DIR was used as a deformation-based reference method, in which the baseline week-0 GTVp was propagated to week 4 using registration between planning CT and week-4 CBCT. U-Net was trained as a single-timepoint segmentation model using week-4 CBCT as input. nnU-Net was evaluated as a self-configuring segmentation model under the same week-4 CBCT input condition. These comparison models therefore represented conventional geometric propagation and single-timepoint segmentation approaches without explicit longitudinal tumor evolution modeling.

Training and deployment
GTVp annotations from weeks 1–3 were used only during model training to enforce temporal consistency. During clinical deployment, TRASE predicts the week-4 GTVp without requiring additional manual contouring from weeks 1–3.

Evaluation
Performance was evaluated on the test cohort using the Dice similarity coefficient and average surface distance. TRASE was compared with deformable image registration, U-Net, and nnU-Net as reference methods.

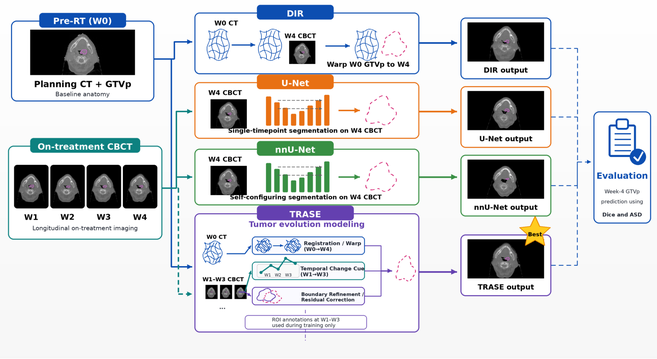

Fig 1. Overall workflow of TRASE and comparison models

RESULTS&DISCUSSION

Quantitative performance
At week 4, TRASE achieved the highest segmentation accuracy among all evaluated methods, with a Dice coefficient of **0.73 ± 0.03** and an average surface distance of **0.94 ± 0.08 mm**. TRASE outperformed DIR, which achieved a Dice coefficient of **0.44 ± 0.03** and an ASD of **2.38 ± 0.11 mm**, as well as U-Net and nnU-Net, which achieved Dice coefficients of **0.34 ± 0.05** and **0.47 ± 0.03**, respectively. Surface distance was also substantially lower with TRASE than with U-Net and nnU-Net, which showed ASDs of **5.39 ± 0.68 mm** and **5.75 ± 0.51 mm**, respectively.

Comparison with baseline and single-timepoint segmentation
Baseline segmentation at week 0 showed moderate performance for U-Net and nnU-Net; however, performance decreased when these models were applied to week-4 CBCT. This indicates that direct single-timepoint segmentation on mid-treatment CBCT is limited by anatomical deformation, tumor regression, and reduced target conspicuity.

Qualitative evaluation
Qualitative comparison demonstrated that TRASE produced evolution-consistent GTVp contours that were closely aligned with the ground truth at week 4. In contrast, DIR showed limited correction of local tumor boundary changes, while U-Net and nnU-Net demonstrated boundary degradation with over- or under-segmentation.

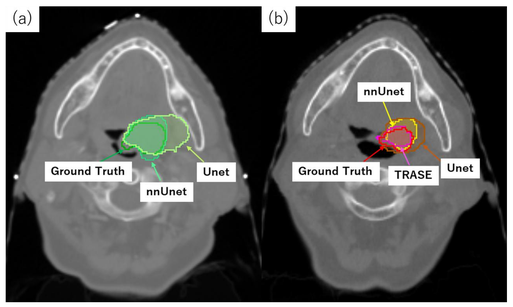

Figure 2. Representative GTVp contours at week 0 and week 4. TRASE produced more evolution-consistent boundaries than the comparison models.

TRASE showed superior mid-treatment GTVp prediction compared with conventional geometric propagation and single-timepoint segmentation approaches. The improved Dice coefficient and markedly reduced surface distance suggest that explicitly modeling tumor evolution provides a more stable and anatomically consistent representation of the week-4 target volume than relying on either deformation alone or direct segmentation from CBCT alone. DIR preserved baseline tumor geometry through deformation-based propagation, but it was limited in capturing treatment-related changes in tumor shape and appearance. U-Net and nnU-Net directly segmented week-4 CBCT, but their lower performance suggests that static segmentation is vulnerable to reduced soft-tissue contrast and evolving tumor boundaries during treatment. In contrast, TRASE combined a warp-first morphological backbone from planning CT with temporal change cues derived from longitudinal CBCT images from weeks 1–3. This design allowed the model to incorporate both structural continuity and image-driven evolution, leading to more accurate and boundary-consistent GTVp prediction. These findings support the concept that mid-treatment target delineation should be treated not simply as a static segmentation task, but as a tumor evolution modeling problem. By using week 1–3 annotations only during training and not requiring additional manual contours during deployment, TRASE may provide a clinically practical framework for adaptive radiotherapy in head-and-neck cancer.

Table 1. Quantitative comparison of GTVp segmentation performance. Baseline week-0 segmentation performance.

		Unet	nnUnet
Dice	Average	0.43	0.56
	SD	0.02	0.02
IoU	Average	0.30	0.40
	SD	0.01	0.02
ASD	Average	6.75	6.76
	SD	0.61	0.51

Table 2. Quantitative comparison of GTVp segmentation performance. Week-4 mid-treatment prediction performance. Values are shown as mean ± SD; best results are highlighted in bold.

		DIR	Unet	nnUnet	TRASE
Dice	Average	0.44	0.34	0.47	**0.73**
	SD	0.03	0.05	0.03	0.03
IoU	Average	0.30	0.23	0.33	**0.58**
	SD	0.03	0.04	0.02	0.03
ASD	Average	2.38	5.39	5.75	**0.94**
	SD	0.11	0.68	0.51	0.08

CONCLUSIONS

TRASE improved week-4 GTVp prediction by explicitly modeling tumor evolution from baseline anatomy and early-treatment CBCT changes, providing a clinically practical approach for adaptive radiotherapy.

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