

Evaluating prognostic impact of time-series circulating tumour DNA and tumour volume in oropharyngeal cancer

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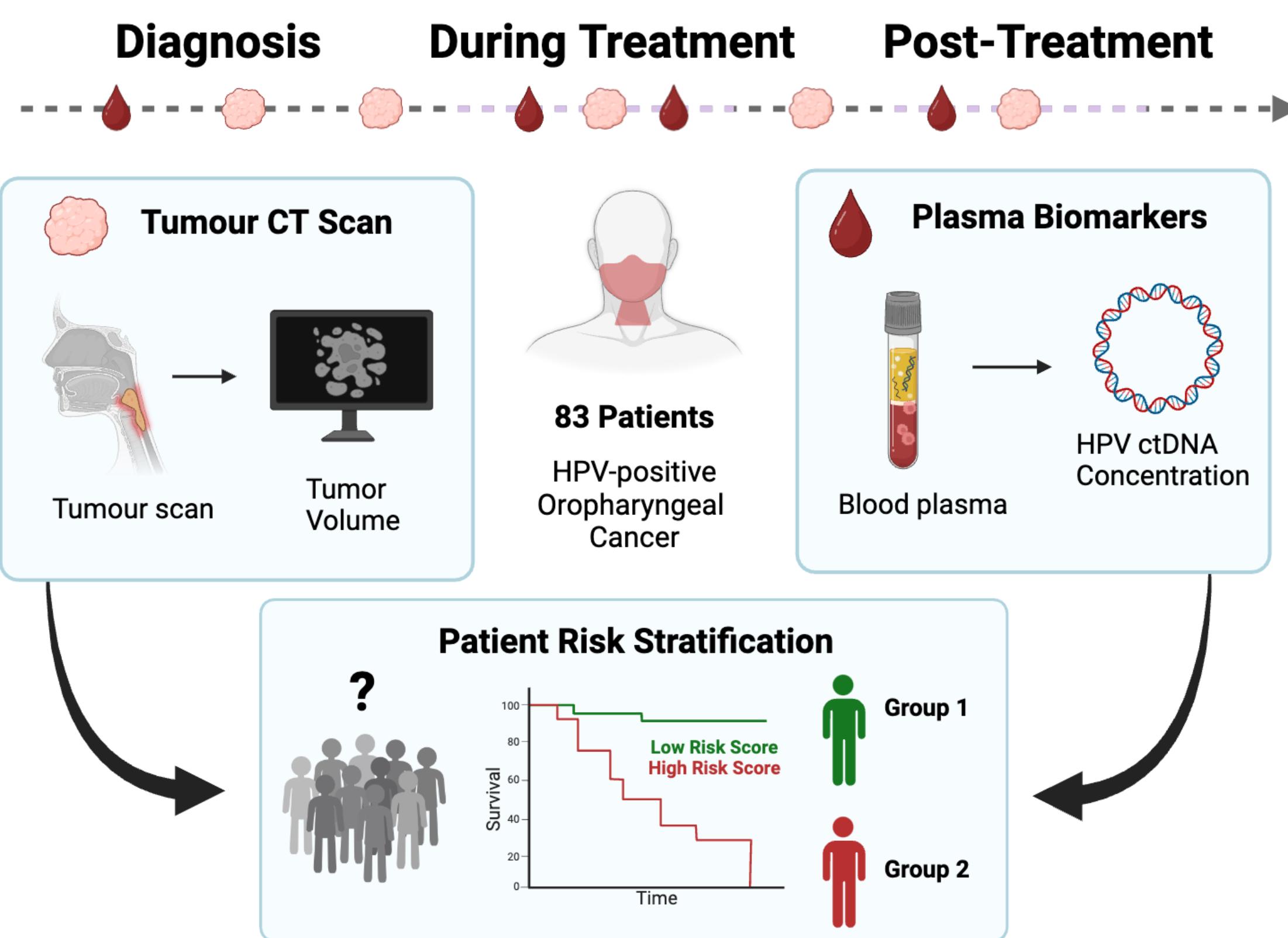
ABSTRACT

Introduction

- Oropharyngeal cancer (OPC), often associated with HPV, requires effective biomarkers for prognostication and treatment monitoring.

Methods

- Tumour volume was quantified through serial CT imaging at multiple treatment stages.
- Circulating tumour DNA (ctDNA) levels were measured from blood plasma samples using advanced molecular techniques.



Results

- Longitudinal analysis revealed significant changes in tumour volume and ctDNA levels during radiotherapy.
- Complementary metrics highlight that tumour volume correlates with tumour stage, while ctDNA levels correlate with nodal stage.
- The combined analysis of tumour volume and ctDNA across treatment stages showed enhanced prognostic value.

Conclusion

- Continuous monitoring of tumour volume and HPV ctDNA has the potential to improve prognostic accuracy for HPV-positive oropharyngeal cancer patients.

INTRODUCTION

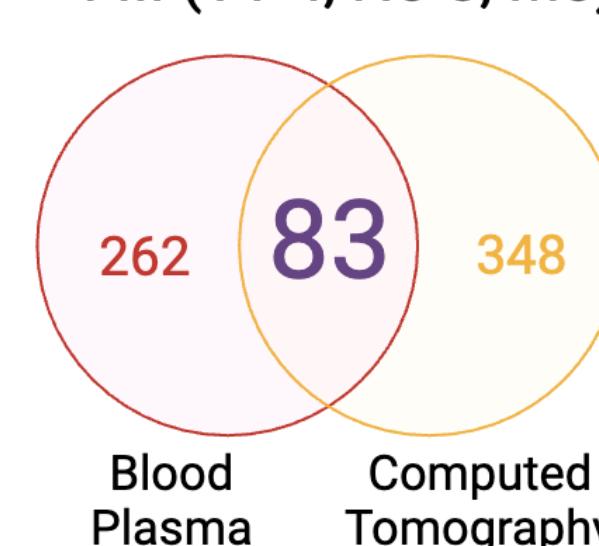
- Oropharyngeal cancer (OPC) cases have significantly increased, largely due to human papillomavirus (HPV). [1]
- Despite advancements in definitive radiotherapy (RT), predicting treatment response remains difficult. [2]
- Primary Gross Tumour volume (GTVp), assessed through computed tomography (CT) imaging, is commonly used to characterize tumour burden in OPC patients. [2]
- Circulating tumour DNA (ctDNA) from blood plasma samples offers a non-invasive biomarker for patient stratification and have shown promise in predicting patient outcomes. [3]
- Previous studies have focused on baseline data for prognostication. [3]
- We hypothesize that longitudinal analysis of GTVp and ctDNA will improve prognostication and risk stratification for OPC patients.

METHODS

Patient Cohort



- Patients with HPV-positive oropharyngeal cancer (OPC)
- TNM-8 clinical stage I-III (T1-4, N0-3, M0)



Process of Data Collection

Quantification of HPV ctDNA in Blood Plasma

- Collected at:

 - Baseline (before radiotherapy)
 - Early RT (week 1-2)
 - Mid RT (week 4-6)
 - Follow-up (3 months post-radiotherapy)

- Whole viral genome sequencing with a custom HPV-targeted capture panel for 38 HPV genotypes
- HPV circulating tumour DNA (ctDNA) quantified

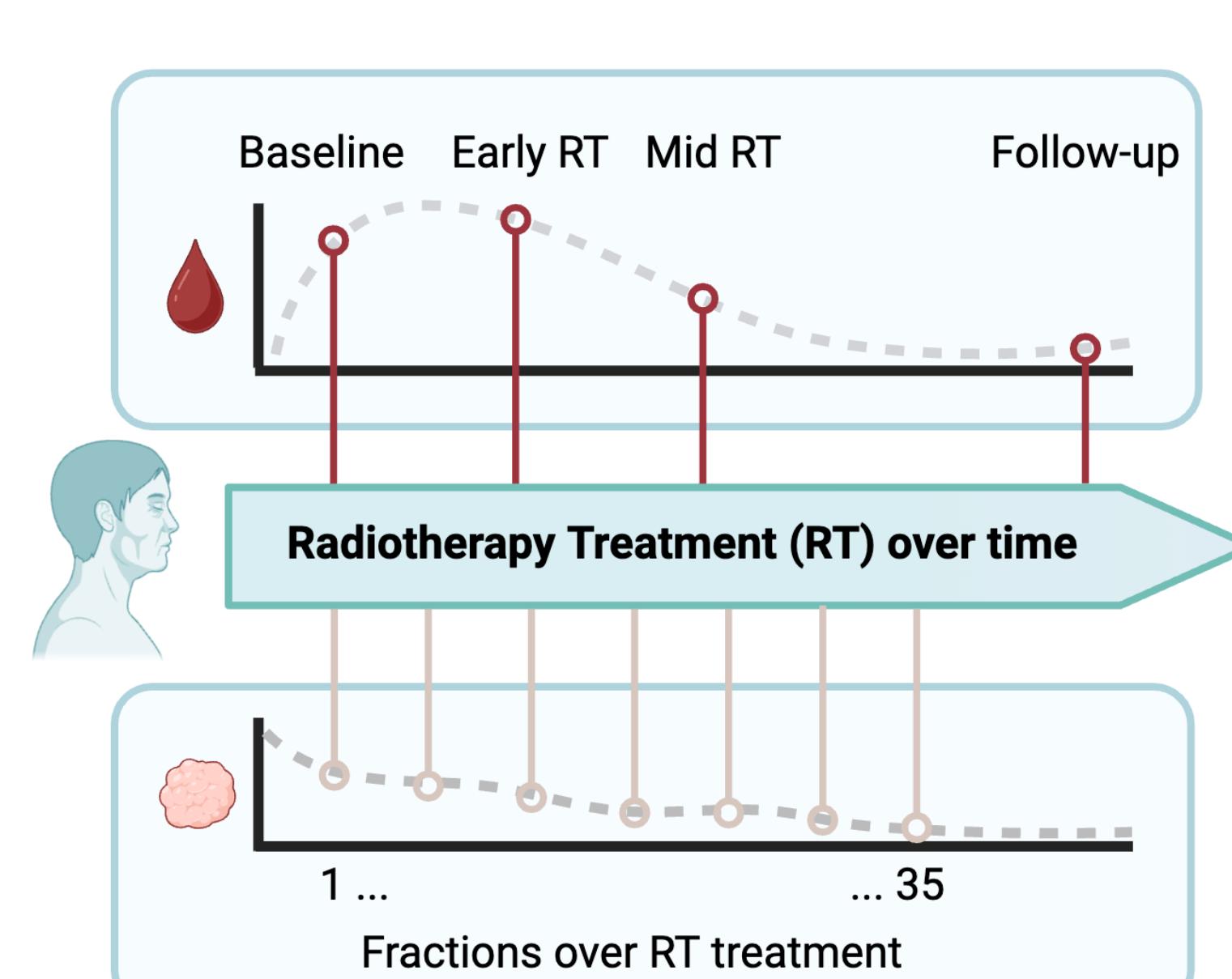
Radiologic Measurement of Gross Tumour Volume

- Collected at:

 - Fraction 1 to 35, covering the entire course of radiotherapy, around 7 weeks

- CT scans of the head and neck
- Gross tumour volume (GTV) contours generated
- Primary tumour volume (GTVp) measured in cubic centimeters

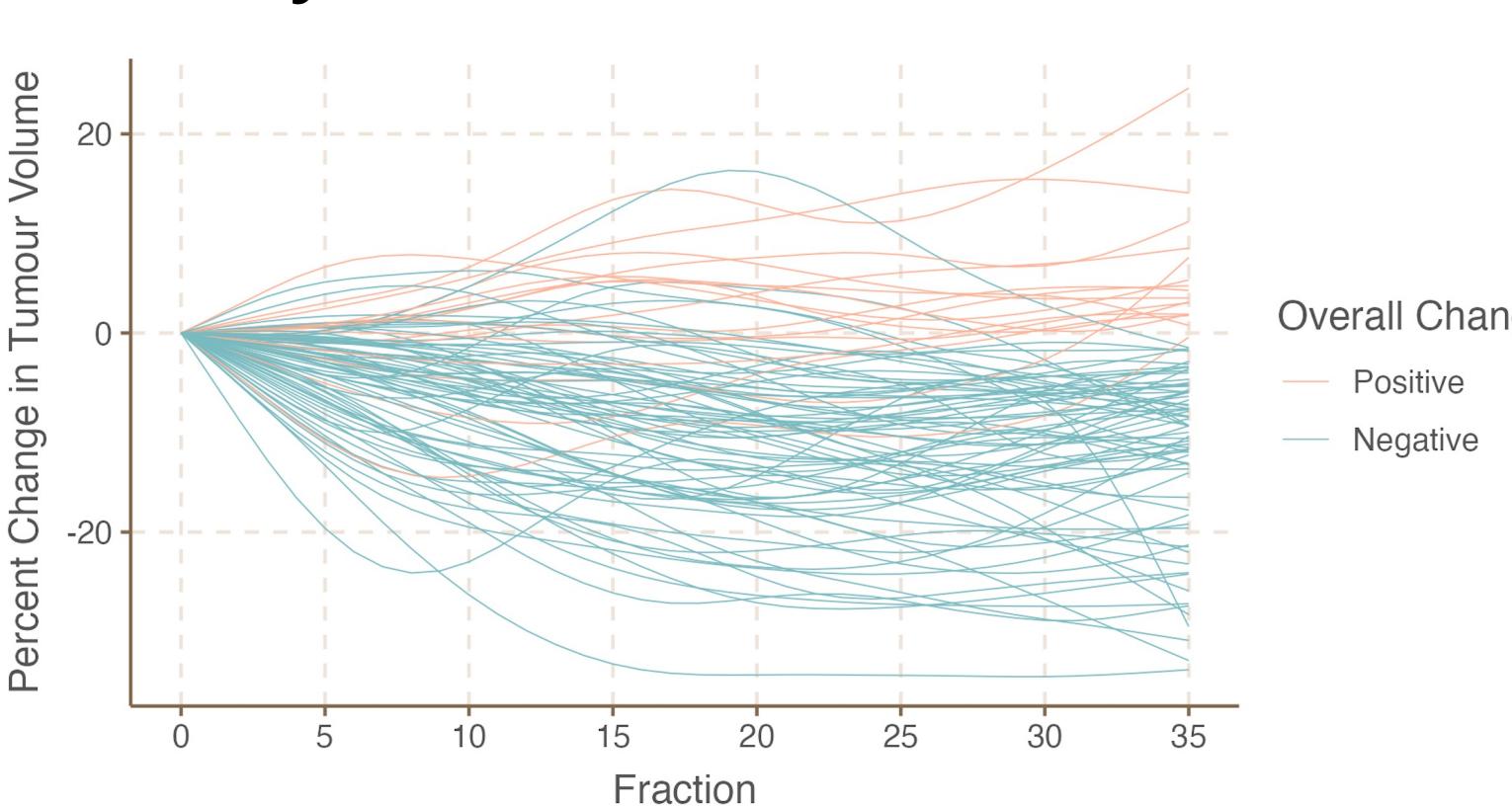
Timeline of Data Collection



RESULTS

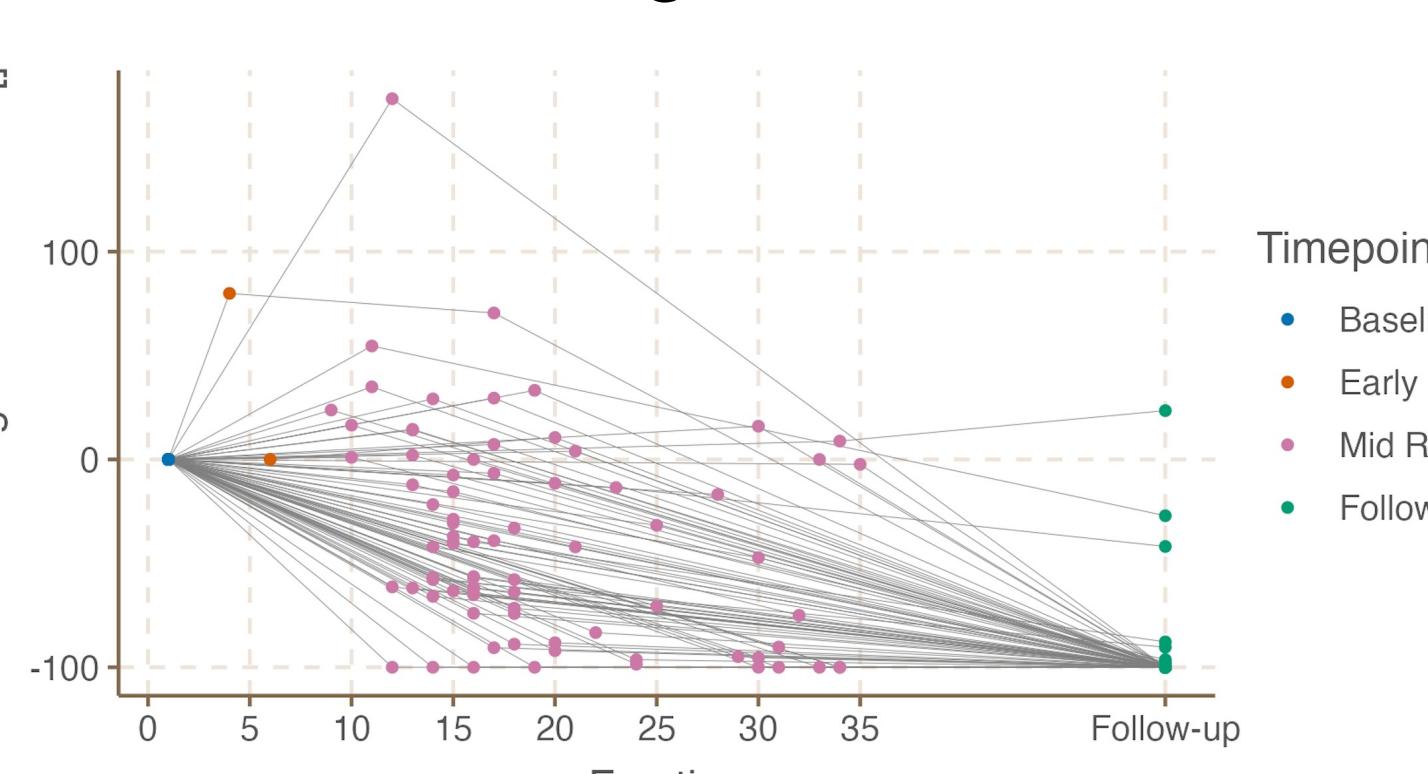
Dynamic Time-series Changes in Tumour Volume and HPV ctDNA During Treatment

Primary Gross Tumour Volume



Percent change in tumour volume over 35 fractions of radiotherapy. The average tumour volume trajectory has a decreasing trend across the cohort. Positive and negative changes highlight variability in patient responses.

HPV Circulating Tumour DNA



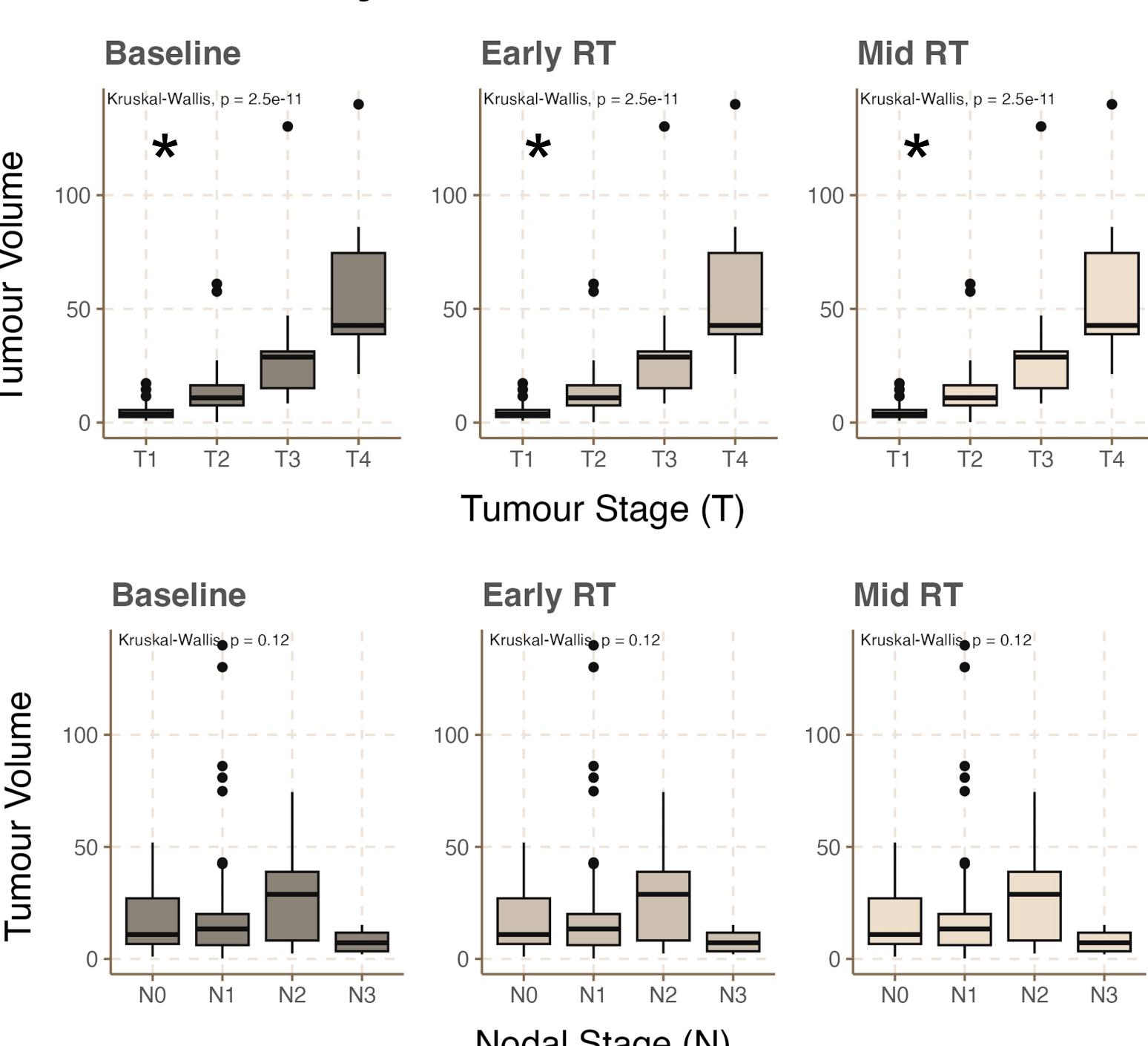
Percent change in HPV ctDNA levels at Baseline, Early RT, Mid RT, and Follow-up. The decrease in ctDNA levels throughout treatment suggests its potential as a biomarker for monitoring tumour burden and response.

Complementary Insights from Tumour Volume and HPV ctDNA Across Treatment Stages

This section demonstrates the correlation between primary gross tumour volume (GTVp) and tumour (T) stage, as well as the correlation between HPV circulating tumour DNA (ctDNA) concentrations and nodal (N) stage, based on the AJCC 8th edition cancer staging system. The graphs show data at baseline, early radiotherapy (RT), and mid RT.

Asterisk (*) indicates statistical significance ($p < 0.05$).

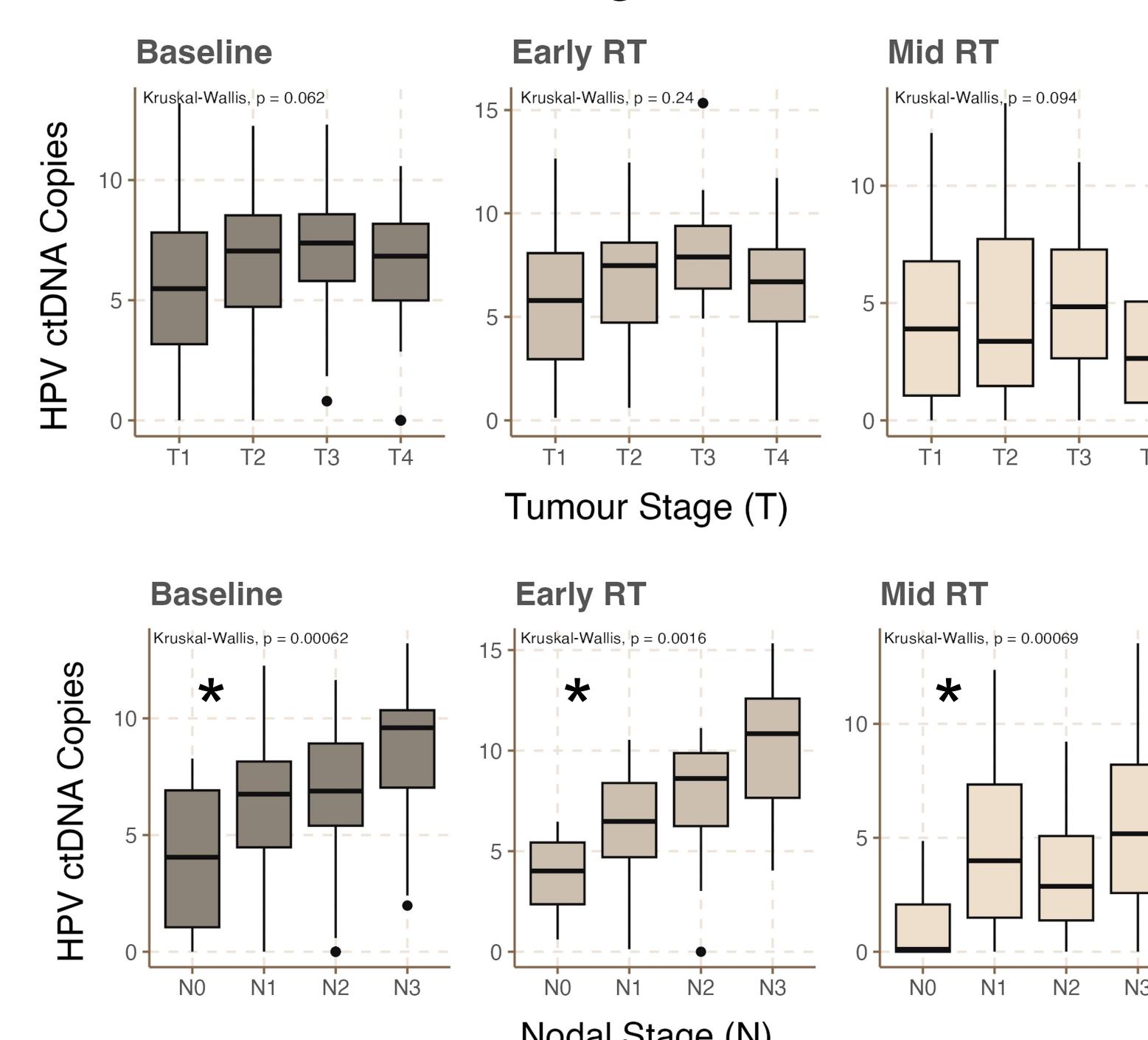
Primary Gross Tumour Volume



Tumour Stage

Nodal Stage

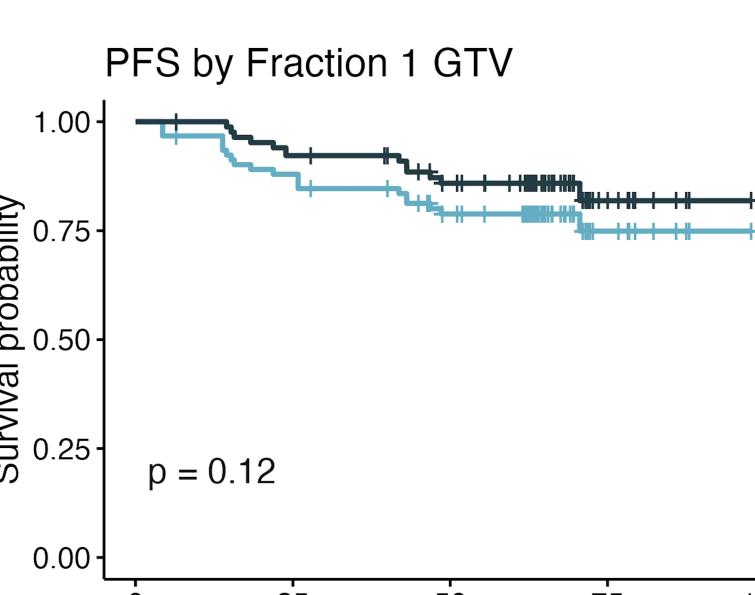
HPV Circulating Tumour DNA



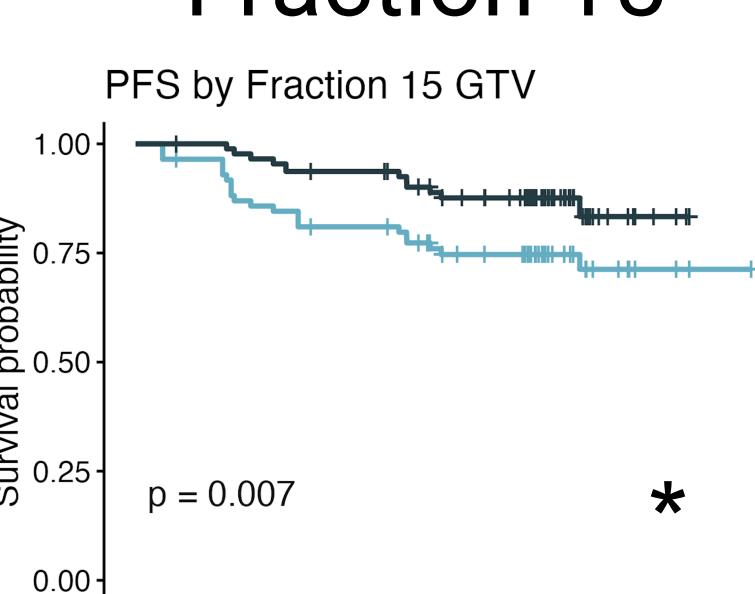
Enhanced Prognostic Value from Longitudinal Analysis of Tumour Volume and HPV ctDNA

Primary Gross Tumour Volume

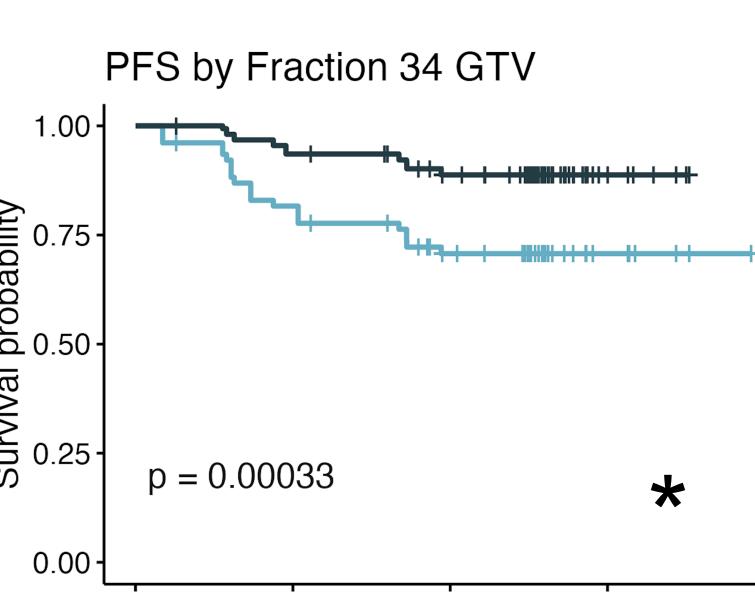
Fraction 1



Fraction 15



Fraction 34



Kaplan-Meier survival curves stratified by median primary gross tumour volume and HPV ctDNA concentration, showing progression-free survival (PFS) for patients at each timepoint.

Asterisk (*) indicates statistical significance ($p < 0.05$).

DISCUSSION

- Longitudinal analysis of primary gross tumour volume and HPV circulating tumour DNA (ctDNA) revealed significant prognostic value.
- Future research will integrate longitudinal nodal tumour volume measurements with ctDNA levels, given the correlation between ctDNA and nodal staging.

CONCLUSION

Continuous monitoring of tumour volume and HPV circulating tumour DNA (ctDNA) significantly enhances prognostic accuracy and personalized treatment planning for HPV-positive oropharyngeal cancer patients.

ACKNOWLEDGEMENTS

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