Time-Aware Dosimetric Assessment of PEG-Defined Swallowing Toxicity in Head and Neck Re-Irradiation

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ABSTRACT

Purpose: PEG dependence is widely considered a consequence of head and neck re-irradiation (HN reRT), yet peri-treatment PEG use may be misclassified as durable swallowing toxicity. We introduce a time-anchored definition of PEG-defined persistent feeding-tube dependence (FTD) and evaluate whether integrating physiologic reserve improves risk discrimination beyond dosimetric injury alone.

Methods: We retrospectively analyzed 72 patients treated with curative-intent HN reRT. The primary endpoint was persistent FTD, defined as PEG/tube dependence ≥3 months after reRT completion. Cumulative mean dose to swallowing-related organs at risk, including the pharyngeal constrictors and submandibular glands, was extracted using dose summation. Physiologic reserve was assessed using weight, albumin, absolute lymphocyte count, and prognostic nutritional index collected at baseline, end of reRT, and early post-reRT recovery. Group comparisons were performed using Mann–Whitney U tests. Logistic regression was used for prediction modeling, and discrimination was assessed using apparent and bootstrap-corrected area under the ROC curve (AUC).

Results: Persistent PEG dependence occurred in 21/72 patients (29%) and was associated with higher cumulative swallowing-OAR dose (pharyngeal constrictors 86 vs 54 Gy, p=0.02; left submandibular gland 98 vs 58 Gy, p=0.008) and poorer nutritional reserve/trajectory (baseline albumin 3.6 vs 4.0 g/dL, p=0.07; late % weight change −0.3% vs −2%, p=0.4). In logistic regression, post-reRT weight loss alone showed poor discrimination (AUC 0.53), which improved with the addition of cumulative dose (AUC 0.82); and further improved with baseline albumin (AUC 0.89).

Conclusion: PEG-defined persistent FTD at ≥3 months post-reRT better reflects durable swallowing dysfunction than peri-treatment PEG use alone. These findings support a time-aware dose–reserve framework in which cumulative dose captures treatment-related injury, while physiologic reserve captures recovery capacity. Integrating dosimetric and reserve information may improve individualized risk assessment for persistent FTD after HN reRT, pending prospective validation.

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INTRODUCTION

Head and neck re-irradiation (reRT) offers a potentially curative option for locoregional recurrence but carries a high risk of persistent swallowing dysfunction. Although cumulative dose to swallowing-related organs at risk is a major determinant of toxicity, patients receiving similar doses often experience different recovery trajectories[1,2].

We hypothesized that persistent feeding-tube dependence (FTD) is better characterized by a time-aware dose–reserve framework integrating cumulative swallowing-organ dose with baseline nutritional reserve and early physiologic change.

METHODS AND MATERIALS

Patients:	• **72 HN re-RT patients** treated from 2011-2026 • FTD0 = 51, FTD1 = 21
Endpoint:	• Persistent feeding tube dependence (FTD) • ≥ 3 months after reRT
Dose:	Cumulative EQD_2 mean dose to pharyngeal constrictors and submandibular glands (α/β = 3Gy)
Physiologic reserve:	Weight, Albumin, ALC, NLR and PNI at three timepoints: • T0 ≤ 50 days pre-reRT • T1 end of reRT • T2 20-50 days post-reRT
Analysis:	• Group comparisons: Mann–Whitney U • Prediction modeling: **logistic regression** • Model discrimination: ROC/AUC • Internal validation: bootstrap-corrected AUC

Neutrophil-to-lymphocyte ratio:

$$NLR = \frac{ANC}{ALC}$$

Prognostic nutritional index:

$$PNI = 10 \times albumin + 5 \times ALC$$

Where, ANC = absolute neutrophil count; ALC = absolute lymphocyte count

STUDY TIMELINE

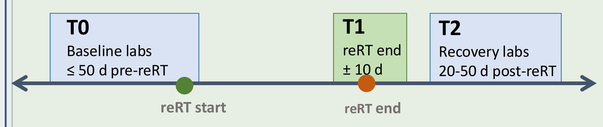
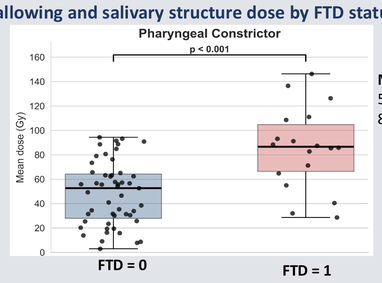


Figure 1. Time-anchored dose–reserve workflow. Laboratory reserve was assessed at T0, T1, and T2 around reRT, capturing baseline reserve, end-of-treatment change, and early recovery. Cumulative swallowing-organ dose and physiologic reserve trajectories were evaluated in relation to persistent FTD.

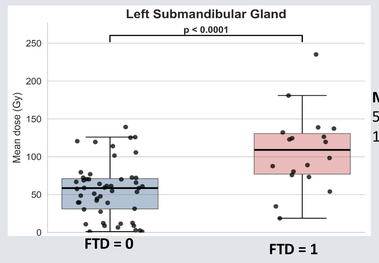
RESULTS

RADIATION INJURY

Figure 2. Swallowing and salivary structure dose by FTD status.



Mean (IQR)
52.6(27.9-64.2) Gy vs
86.6 (66.4-104.7) Gy

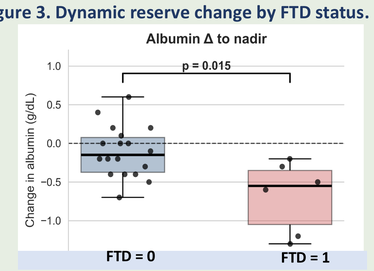


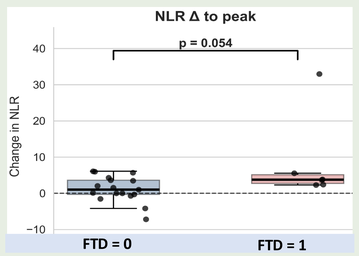
Mean (IQR)
58.6 (30.9-71.2) Gy vs
109.0 (76.4-130.7) Gy

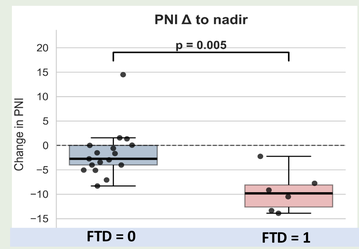
Persistent FTD was associated with significantly higher cumulative dose to key swallowing structures

PHYSIOLOGIC RESERVE

Figure 3. Dynamic reserve change by FTD status.



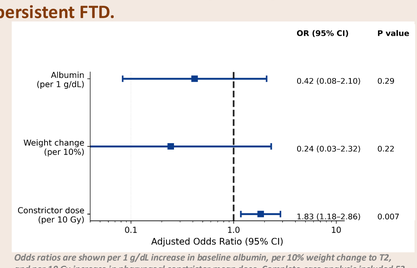




Persistent FTD was associated with greater deterioration in physiologic reserve markers

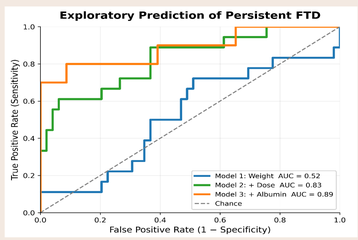
MODEL DISCRIMINATION

Figure 4a. Multivariable logistic regression for persistent FTD.



Odds ratios are shown per 1 g/dL increase in baseline albumin, per 10% weight change to T2, and per 10 Gy increase in pharyngeal constrictor mean dose. Complete-case analysis included 53 patients (10 events).

Figure 4b. Bootstrap-corrected ROC curves.



Model	n/events	Apparent AUC	Bootstrap corrected AUC
Model1 Weight	71/21	0.52	0.47
Model 2 +Dose	71/21	0.83	0.81
Model3 +Albumin	53/18	0.89	0.86

Complete case analysis because baseline albumin was unavailable for some patients

Integrating the dose and physiologic reserve improved the discrimination

KEY TAKEAWAY

Radiation dose explains the injury; physiologic reserve explains recovery.

Together, they improve risk stratification for persistent FTD after re-irradiation.

DISCUSSION & CONCLUSION

- Dose remained the dominant predictor of persistent feeding tube dependence.
- Physiologic reserve markers reflected recovery capacity beyond dosimetric injury.
- Combining dosimetric and physiologic information improved model discrimination in exploratory analyses.
- A biologically informed dose–reserve framework may guide individualized re-irradiation planning, pending prospective validation.

REFERENCES

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2. Wopken, K., H.P. Bijl, and J.A. Langendijk, Prognostic factors for tube feeding dependence after curative (chemo-) radiation in head and neck cancer: a systematic review of literature. Radiotherapy and Oncology, 2018. 126(1): p. 56-67