Oncospace™ Risk Prediction Model for Radiation Toxicities: Novel Insights to Reduce the Risk of Radiation-Induced Xerostomia in Head and Neck Cancer Patients

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Purpose/Objectives

Background

- Radiotherapy is a **major** component of the management strategy for local or regionally advanced head and neck cancer

- Irradiation of surrounding normal tissues commonly occurs, leading to radiation-induced xerostomia
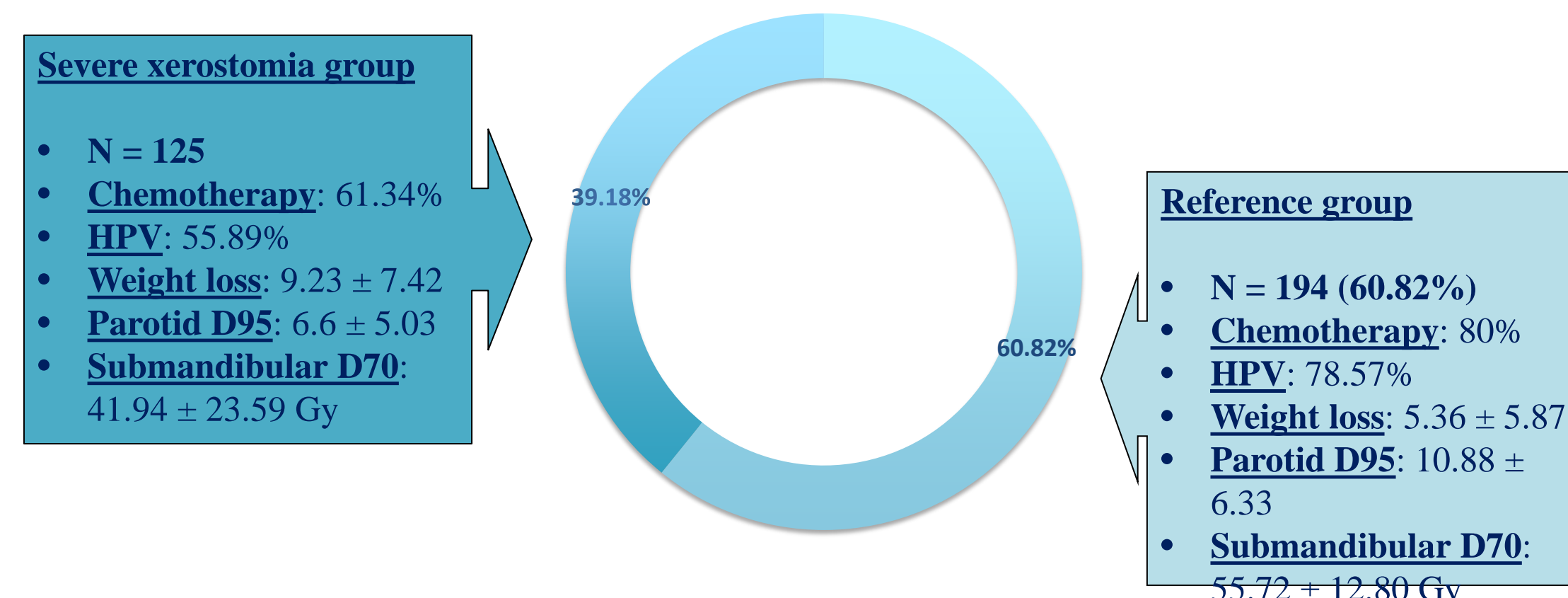
Objectives

- To develop a comprehensive prediction model for the development of radiation-induced xerostomia, forecast the risk of xerostomia among different patients

- To enhance treatment decisions and provide a foundation for a personalized xerostomia learning health system
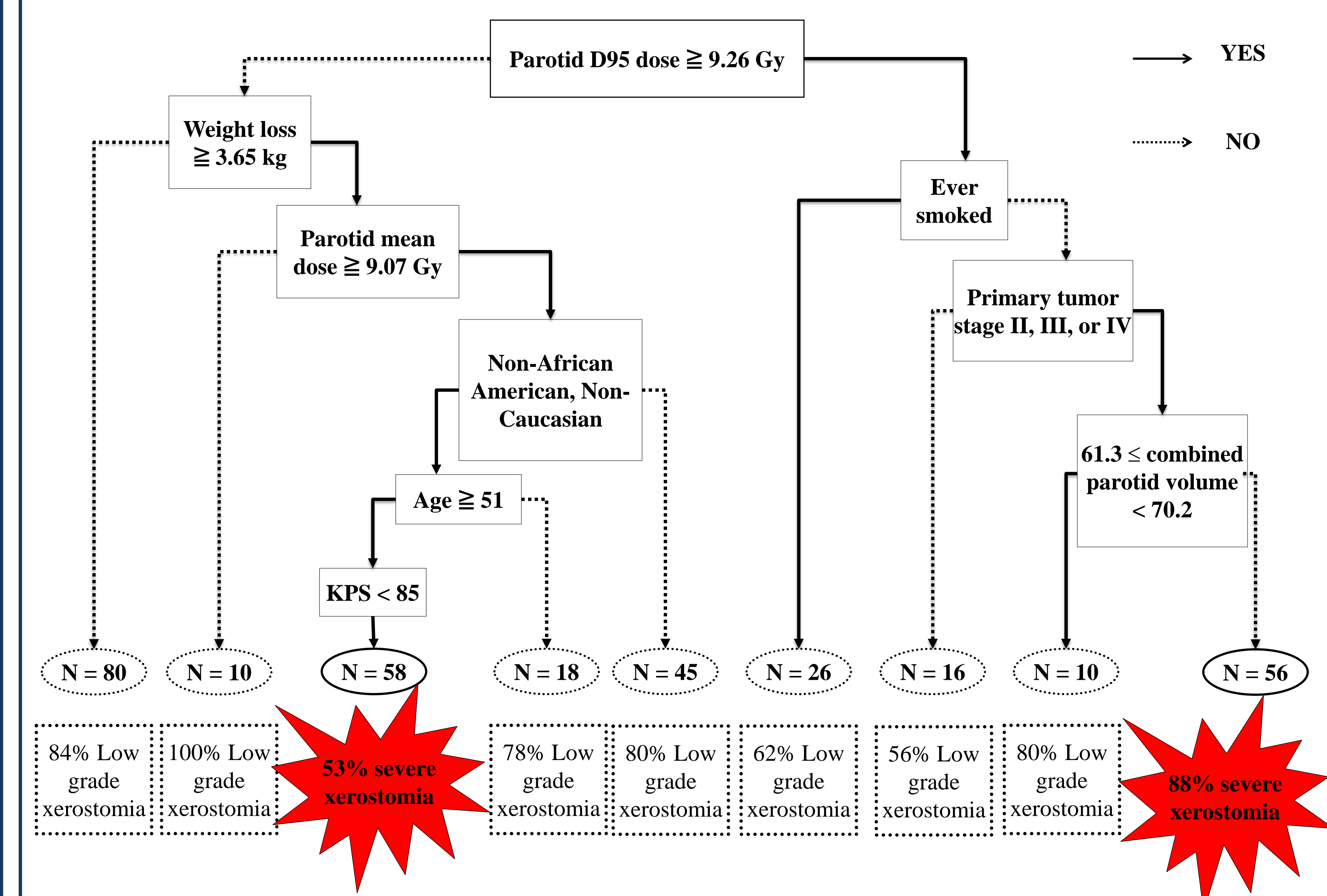
Materials/Methods

Data collection and study design

- Study design: Case-control study
- Primary outcome: xerostomia grade (CTCAE v4.0) at 90 - 150 days after RT
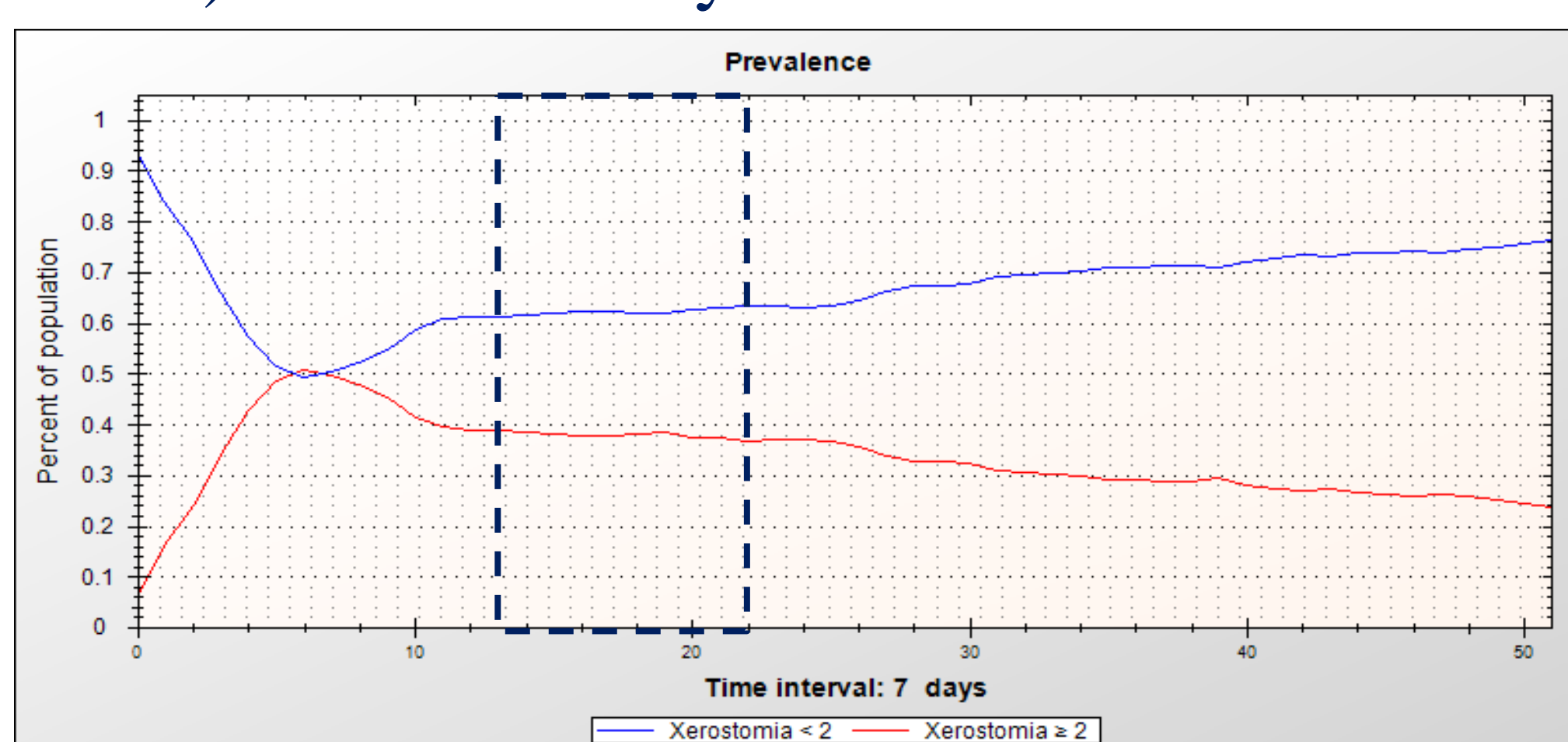
- Risk factors: demographic factors, clinical assessments, medical history, volumetric factors, dosimetric factors
- Statistical analysis: Logistic regression; Classification and Regression Tree (CART)

Results

Table 1. Baseline Characteristics

❖ Baseline **imbalanced** characteristics

Severe xerostomia group
- **N = 125**
- **Chemotherapy**: 61.34%
- **HPV**: 55.89%
- **Weight loss**: 9.23 ± 7.42
- **Parotid D95**: 6.6 ± 5.03
- **Submandibular D70**: 41.94 ± 23.59 Gy

Reference group
- **N = 194 (60.82%)**
- **Chemotherapy**: 80%
- **HPV**: 78.57%
- **Weight loss**: 5.36 ± 5.87
- **Parotid D95**: 10.88 ± 6.33
- **Submandibular D70**: 55.72 ± 12.80 Gy

❖ Baseline **balanced** characteristics
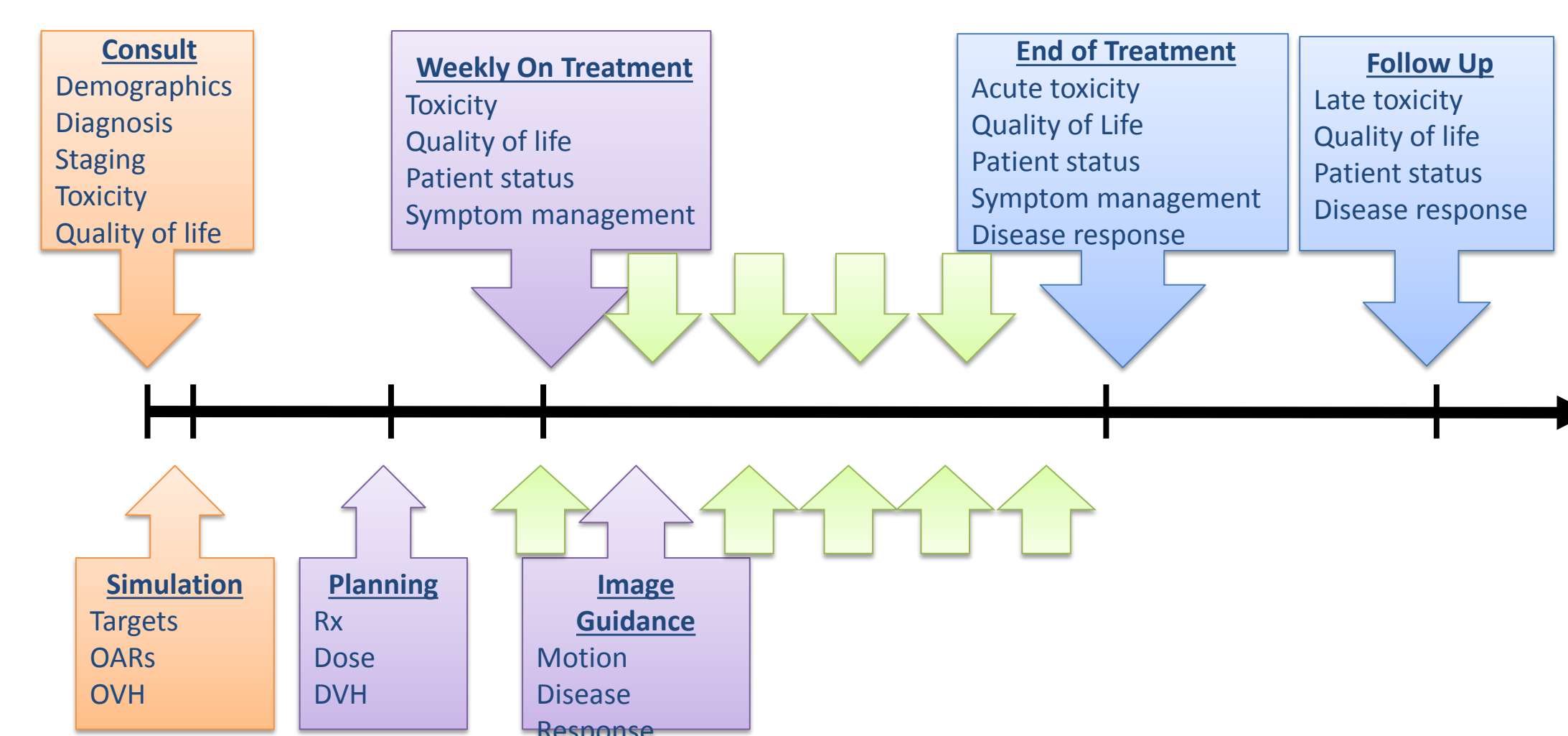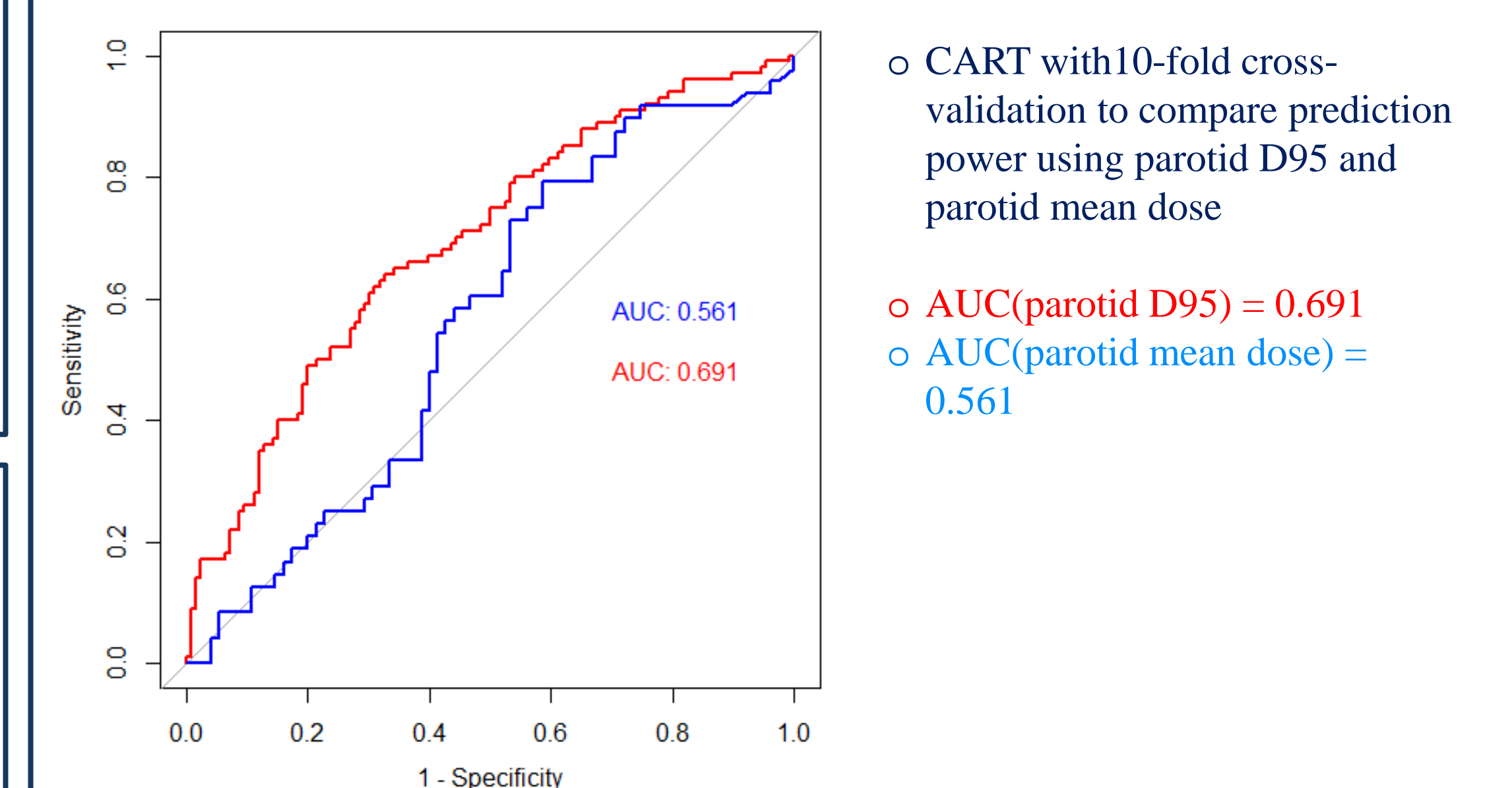
- **Age:** 57.82 ± 11.10 (yo)
- **Male**: 76.8%
- **Caucasian**: 75.69%
- **Smoking**: 49.47%
- **Alcohol use**: 50.68%
- **Tumor site:**
  - Oral cavity: 1.28%
  - Nasopharynx: 4.49%
  - Hypopharynx: 1.6%
  - Larynx: 14.42%
  - Others: 54.49%
- **Primary tumor stage:**
  - 0: 4.58%
  - 1: 22.08%
  - 2: 32.92%
  - 3: 18.33%
  - 4: 22.08
- **Regional lymph nodes stage:**
  - 0: 24.79%
  - 1: 15.55%
  - 2: 56.72%
  - 3: 2.94%
- **Distant metastasis:** 0.91%
- **Taste change:** 37.57 ± 32.36
- **KPS:**
  - < 80: 11.39%
  - ≧ 80: 88.61%
- **Combined parotid volume:** 58.13 ± 20.72 (cc)
- **Combined submandibular volume:** 17.81 ± 11.84 (cc)

Figure 1. Non-parametric Modeling - CART

Table 2. Backward Stepwise Elimination

	OR	p-value	95% Confidence Interval
alpha = 0.05			
Parotid D95	1.15	<0.001	[1.09, 1.21]
Submandibular D70	1.04	<0.001	[1.01, 1.05]
Submandibular D60	1.05	0.036	[1.02, 1.07]
alpha = 0.01			
Parotid D95	1.15	<0.001	[1.09, 1.21]
Submandibular D70	1.04	<0.001	[1.01, 1.05]

Table 3. Parametric Modeling – Univariate Analyses

Parameters	OR	p-value	95% Confidence Interval
Chemotherapy			
No	ref.		
Yes	2.52	**0.001**	[1.49, 4.26]
HPV			
No	ref.		
Yes	2.67	**<0.001**	[1.32, 5.38]
Weight loss at 1st visit			
≤ 5 kg	ref.		
loss > 5 kg	2.58	**<0.001**	[1.62, 4.09]
Parotid D95	1.15	**<0.001**	[1.09, 1.21]
Submandibular D70	1.04	**<0.001**	[1.02, 1.06]
Parotid mean dose	1.04	**0.023**	[1.01, 1.08]

Figure 2. ROC curves of prediction using parotid D95 and parotid mean dose

- CART with10-fold cross-validation to compare prediction power using parotid D95 and parotid mean dose
- AUC(parotid D95) = 0.691
- AUC(parotid mean dose) = 0.561

	AUC	Accuracy*	Sensitivity	Specificity
Parotid D95	0.691	0.659	0.640	0.674
Parotid mean dose	0.561	0.561	0.792	0.413

*Accuracy: the weighted average of a test's sensitivity and specificity

Conclusions

- The **low dose bath (at 9.26 Gy)** - a potentially important treatment-modifying parameter to reduce the risk of severe xerostomia.
- **A better accuracy** for parotid D95 than the conventional parotid mean dose.
- A risk prediction model to be incorporated into **learning health system**.