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Dose-Response Relationships for Early Toxicities in Head & Neck Cancer Patients Undergoing Radiotherapy

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1. Background-Aim

- Estimation of dose-response relations from Attikon Hospital patient's data that underwent Head & Neck radiotherapy treatment.

- We will determine which organs doses are most strongly related with the occurrence of early and late toxicities in patients.

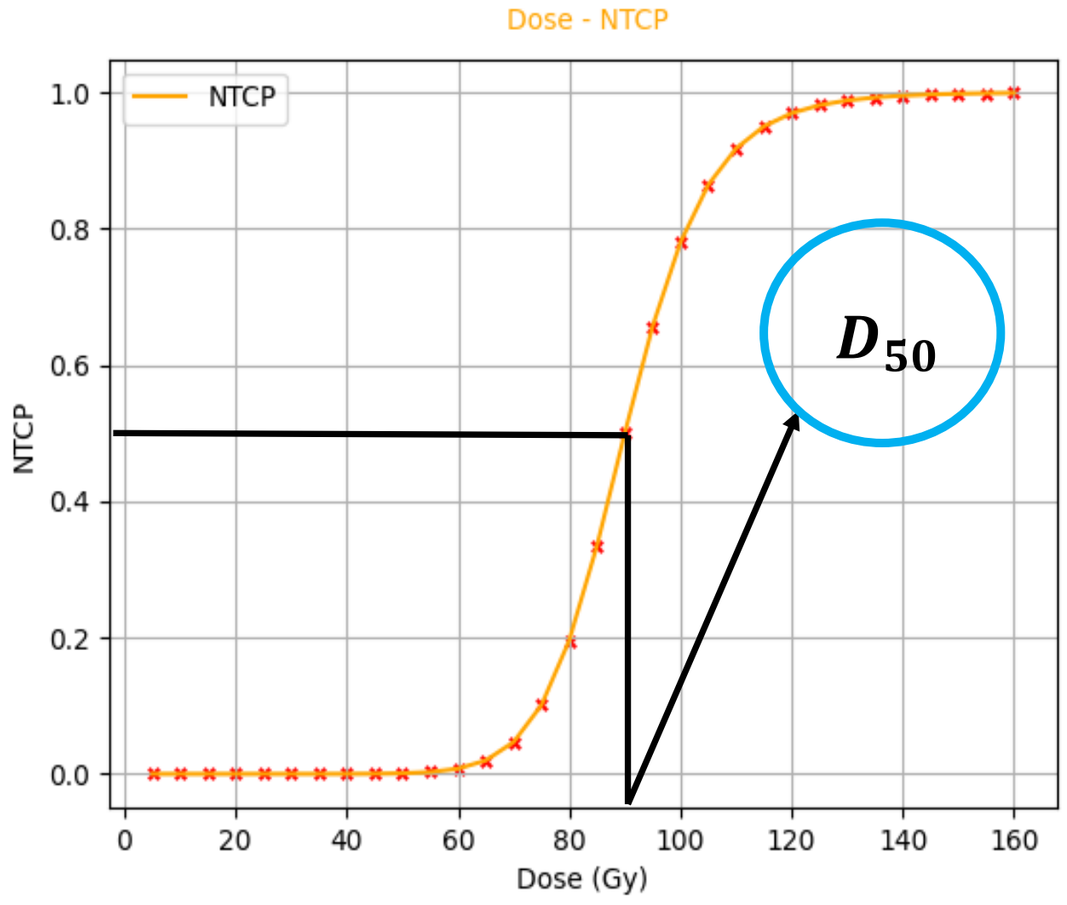
- How can we avoid these symptoms in the future?

Normal Tissue Complication Probability (NTCP)

- *Probit Model*

$$\boldsymbol{NTCP(D) = \frac{1}{2} * \left[1 - Erf\left(\gamma_{50} * \sqrt{\pi} * \left(1 - \frac{D}{D_{50}}\right)\right)\right]}$$

where,
the prescription dose.
$\boldsymbol{D_{50}}$ is the dose that corresponds to 50% complication probability.
$\boldsymbol{\gamma_{50}}$ is related to the steepness of the curve.



$\boldsymbol{D_{50}}$ and $\boldsymbol{\gamma_{50}}$ are estimated trough Maximum Likelihood Method.
Their Confidence Intervals (68% - 1SD) are estimated through Profile Likelihood Method.

Collection of Patient Data

1) We used the after-treatment questionnaires EORTC – QLQ - H&N35 that patients answered immediately after their treatment.

2) Out of the initial 84 patients, we excluded 24 patients due to stopping the radiotherapy treatment, leaving the study, were outliers or did not have the total Dose Volume Histogram and mean dose due to replanning

3) For each patient of our filtered sample we extracted the cumulative Dose Volume Histogram (DVH), mean doses to the organs of interest (pharyngeal constrictors, oral cavity, left and right parotids).

4) For every patient we collected the demographic/clinical characteristics:

- Age
- Smoking habits
- Alcohol habits
- Gender
- If they underwent also surgery with the radiotherapy treatment
- If they underwent also chemotherapy with the radiotherapy treatment

Data analysis

1) Division of the sample into two groups: symptomatic and symptom-free

2) Mean doses comparison between the two groups with SPSS tests.

3) Conduction of a *Power analysis* to find out our level of confidence in the SPSS tests. **(G*Power software)**

4) Calculation of the Area Under the ROC Curve (AUC), by using *ROC curve analysis* to estimate the goodness of the separation between of patients with and without the symptom. **(SPSS software)**

5) Calculation/Comparison of the mean cumulative DVHs of the two groups. This way we will further prove the difference of dose deliverance between the two groups.

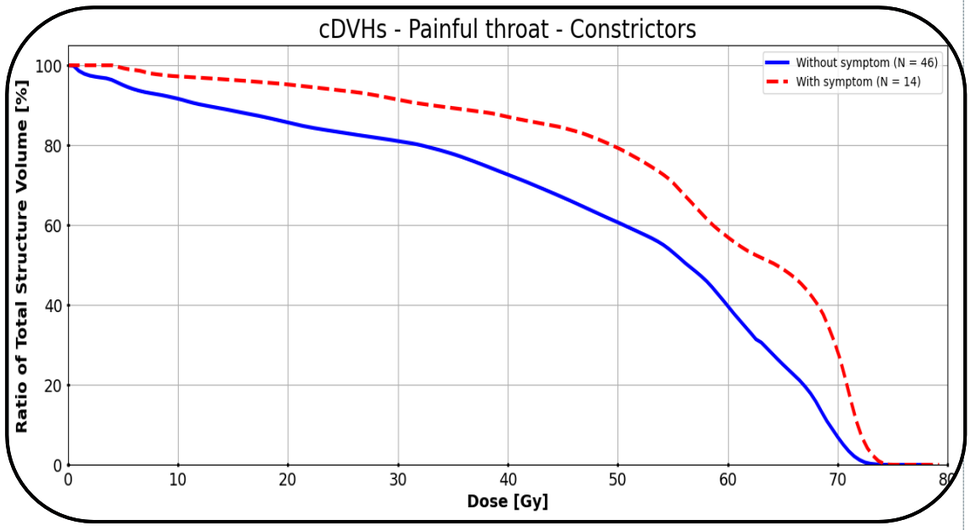
6) After we identified the organs which have the best dose-response relation we conducted a Univariate analysis in SPSS to investigate for possible:

- Dependence between the occurrence of the symptom and the demographic data (age, gender, surgery, chemotherapy, smoking and alcohol)
- Dependence in appearance between two different symptoms.

Indicators for the dose-response relationships

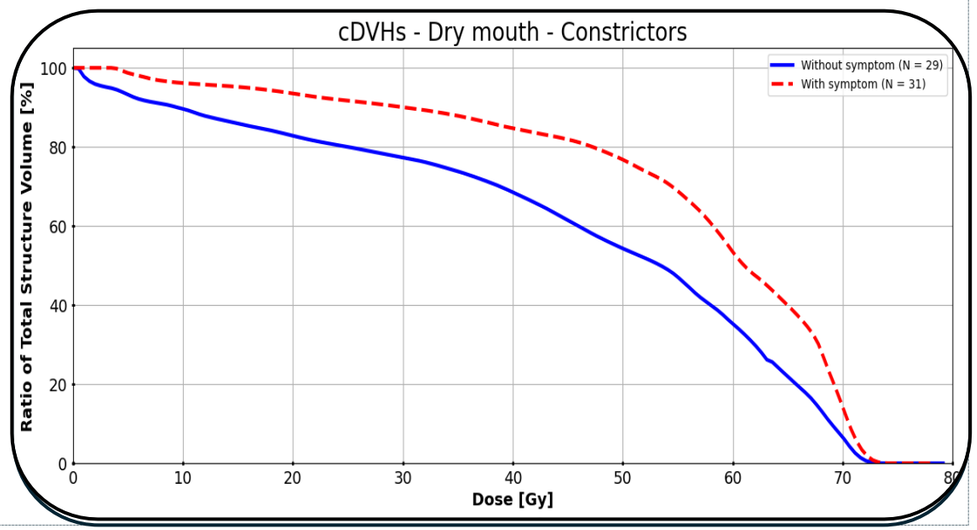
Relation of dose in pharyngeal constrictors with painful throat

- 14 patients with painful throat and 46 without
- Pass mean comparison test with p-value = 0.016
- AUC = 0.714 & Power = 0.695



Relation of dose in pharyngeal constrictors with dry mouth

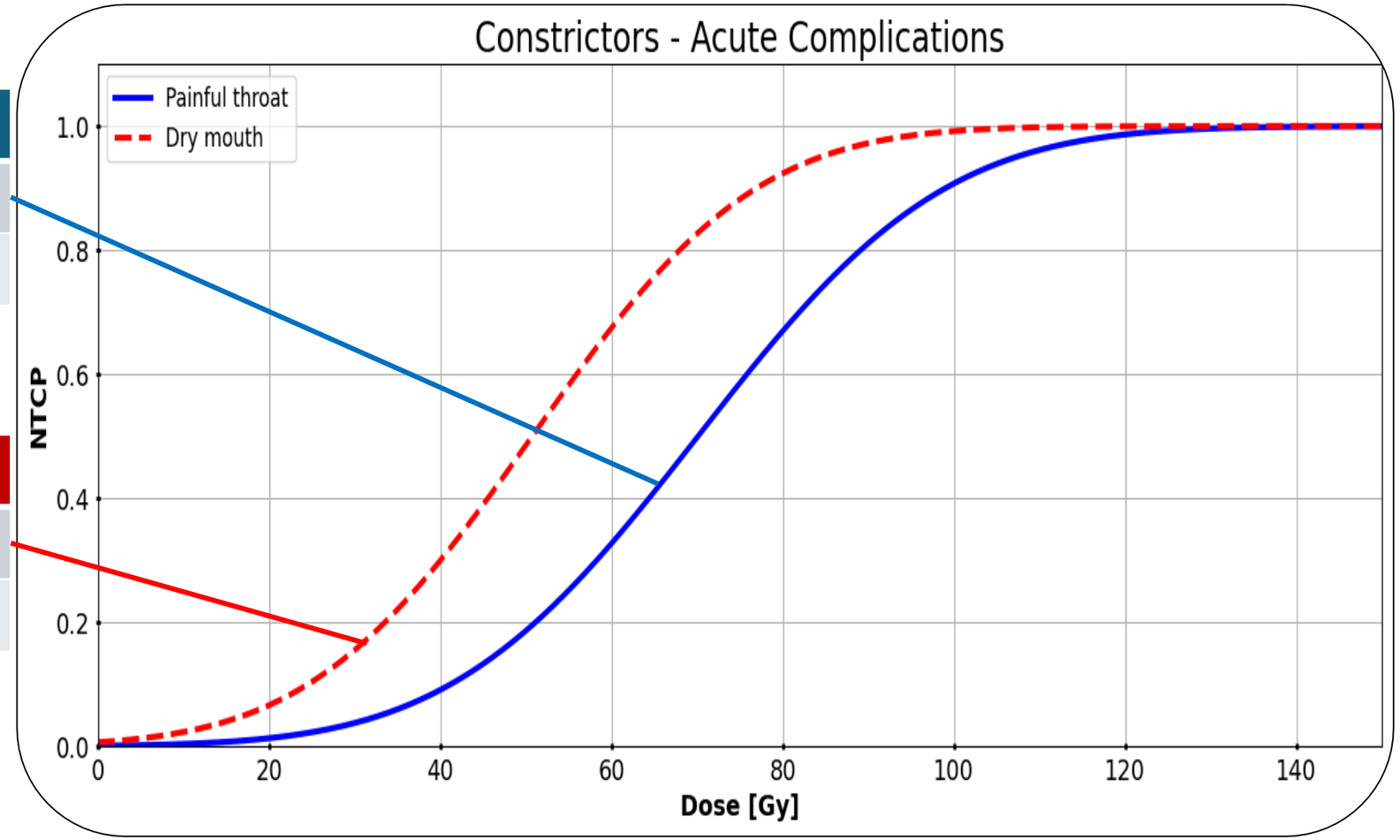
- 31 patients with painful throat and 29 without
- Pass mean comparison test with p-value = 0.001
- AUC = 0.742 & Power = 0.904



NTCP modeling of Acute symptoms

Symptoms	Painful Throat
γ_{50}	1.24 (0.95, 1.55)
D_{50} (Gy)	70.1 (65.21, 75.88)

Symptoms	Dry mouth
γ_{50}	0.99 (0.67, 1.33)
D_{50} (Gy)	50.74 (47.58, 54.31)



Correlations between Symptoms – Demographic/Clinical Characteristics

	Painful Throat	Dry mouth
Age	p = 0.891	p = 0.331
Gender	p = 0.122	p = 0.114
Smoking	p = 0.781	p = 0.657
Alcohol	p = 0.102	p = 0.029
Surgery	p = 1.000	p = 0.358
Chemotherapy	p = 0.712	p = 0.225

Indication for alcohol – dry mouth dependence but cannot further prove it because of our lack of data

4. Conclusions

- Dose to the pharyngeal constrictors best predicted the symptoms painful throat and dry mouth
- Indication for alcohol – dry mouth dependence
- 50% probability of experiencing dry mouth with 50.74 Gy at the pharyngeal constrictors
- 50% probability of experiencing a painful throat with 70.1 Gy at the pharyngeal constrictors
- Bigger sample size would reduce uncertainties and further prove the findings from the univariate analyses
- The exact time of the symptom’s appearance was unknown
- Our NTCP curves could be taken into consideration during treatment plan design to minimize the likelihood of occurrence of the found symptoms

5. References

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