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PALAZZO DEI CONGRESSI

Radioterapia Oncologica: l'evoluzione al servizio dei pazienti

INDEPENDENT EXTERNAL VALIDATION OF FOUR NTCP MODELS FOR HEAD AND NECK CANCER PATIENTS

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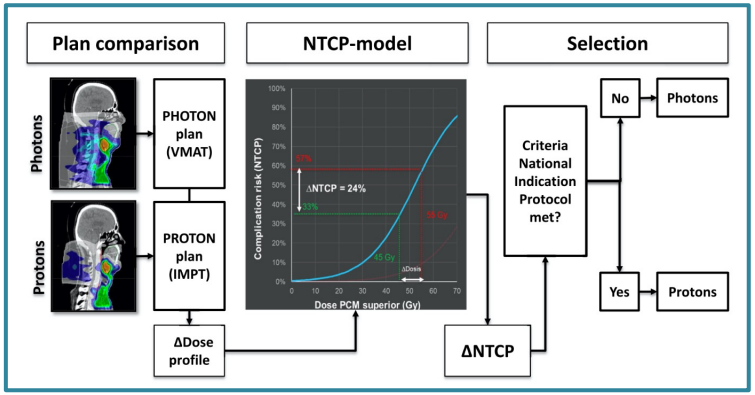
Radioterapia e Oncologia clinica

Introduction

Normal Tissue Complication Probability (NTCP) models provide radiation-induced toxicities probability.

Applicability to external patients cohort need to be tested before clinical use.



Delta NTCP: Netherlands

Modelli NTCP

- ✓ Pochi
- ✓ Poco validati

According to National Indication Protocol for PT (NIPP) patients qualify for proton therapy if:

- Δ NTCP ≥ 10% for grade ≥ II side effects
- ≥ 5% for grade ≥ III side effects
- the summed risk reduction (ΣΔNTCP) for grade ≥ II side effects ≥ 15%

Aim

External validation of 4 NTCP models for head & neck cancer patients

Multivariable logistic regression: $\mathbf{NTCP} = \frac{1}{e^{-s}}$

1) Predictive modelling for swallowing dysfunction after primary (chemo)radiation: Results of a prospective observational study

Miranda E.M.C. Christianen [a], Cornelis Schilstra [a], Ivo Beetz [a], Christina T. Muijs [a], Olga Chouvalova [a], Fred R. Burlage [a], Patricia Doornaert [b], Phil W. Koken [b], C. René Leemans [c], Rico N.P.M. Rinkel [c], Marieke J. de Bruijn [c], G.H. de Bock [d], Jan L.N. Roodenburg [e], Bernard F.A.M. van der Laan [f], Ben J. Slotman [b], Irma M. Verdonck-de Leeuw [c], Hendrik P. Bijl [a], Johannes A. Langendijk [a,*]

$s=a_1+a_2*D_{mean}(PMC_{sup})+a_3*D_{mean}(SL)$

PMC_{sup}: superior pharyngeal constrictor muscle; SL: supraglottic larynx

2) Development of a multivariable normal tissue complication probability (NTCP) model for tube feeding dependence after curative radiotherapy/ chemo-radiotherapy in head and neck cancer

Kim Wopken [a,*], Hendrik P. Bijl [a], Arjen van der Schaaf [a], Hans Paul van der Laan [a], Olga Chouvalova [a], Roel J.H.M. Steenbakkers [a], Patricia Doornaert [b], Ben J. Slotman [b], Sjoukje F. Oosting [c], Miranda E.M.C. Christianen [a], Bernard F.A.M. van der Laan [d], Jan L.N. Roodenburg [e], C. René Leemans [f], Irma M. Verdonck-de Leeuw [f], Johannes A. Langendijk [a]

$s=a_1+a_2*AdT+a_3*MWL+a_4*SWL+a_5*AR+a_6*ChR+a_7*RadCet+a_8*D_{mean}(PMC_{sup})+a_9*D_{mean}(PMC_{inf})+a_{10}*D_{mean}(ContrP)+a_{11}*D_{mean}(CriPM)$

AdT: Advanced T-stage; MWL: Moderate Weight Loss; SWL: Severe Weight Loss; AR: Accelerated Radiotherapy; ChR: ChemoRadiation; RadCet: Radiotherapy plus Cetuximab; PMC_{sup}: superior pharyngeal constrictor muscle; PMC_{inf}: inferior pharyngeal constrictor muscle; ContrP: Contralateral Parotid; CriPM: CricoPharyngeal Muscle.

3) Multivariable model for predicting acute oral mucositis during combined IMRT and chemotherapy for locally advanced nasopharyngeal cancer patients

Ester Orlandi[a,b,*], Nicola Alessandro Iacovelli[a], Tiziana Rancati[c], Alessandro Cicchetti[c], Paolo Bossi[d], Emanuele Pignoli[e], Cristiana Bergamini[d], Lisa Licitra[d,f], Carlo Fallai[a], Riccardo Valdagni[b,c,f], Anna Cavallo[e]

Multivariable logistic regression: $\mathbf{NTCP} = \frac{1}{e^{-s}}$

$s=a_1+a_2*D_{mean}(OC)$ (mean G ≥ 1.5)

$s=a_1+a_2*EUD(OC)_{n=0.05}+a_3*D_{mean}(cPG)+a_4*(BMI>30)$ (G>3)

cPG: parotid glands (r+l); OC: oral cavity

4) NTCP MODELING OF SUBACUTE/LATE LARYNGEAL EDEMA SCORED BY FIBEROPTIC EXAMINATION

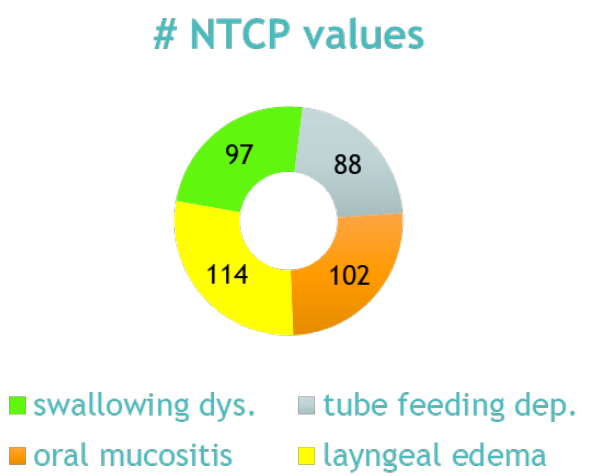
TIZIANA RANCATI, PH.D.,* CLAUDIO FIORINO, PH.D.,† AND GIUSEPPE SANGUINETI, M.D.‡

Logit-EUD: $\mathbf{NTCP} = \frac{1}{1+\left(\frac{D_{50}}{EUD}\right)^{k}}$

$$EUD = EU(EQD_2)\ {}_{\alpha/\beta=3Gy}(larynx)$$

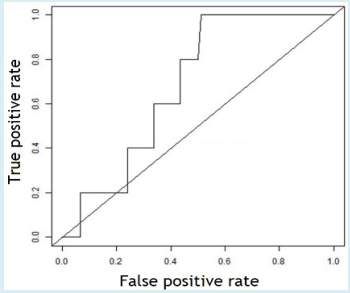
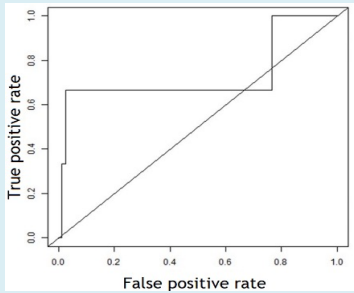
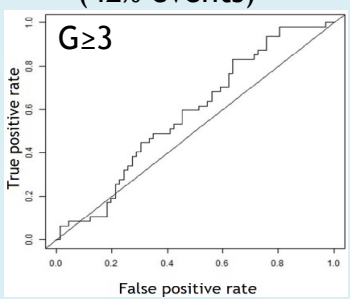
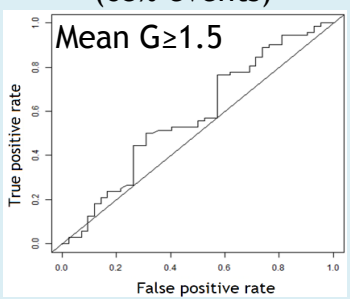
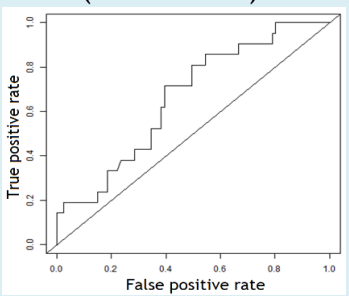
Materials & Methods

- Retrospective analysis on 150 patients treated with VMAT;
- 401 computable NTCP values;
- Toxicities from electronic medical charts;
- Organs at risk contoured by a single radiation oncologist;
- Dosimetric parameters from treatment plans on TPS.



Validation included:

- **DISCRIMINATION ABILITY** using area under receiver operating characteristic curve (AUROC);
- **GOODNESS-OF-FIT** using Hosmer-Lemeshow test and Brier Score;
- **CALIBRATION** measurements using slope and intercept

Swallowing dys. (5% events)	Tube feeding dep. (3% events)	Oral and oropharyngeal mucositis (42% events) G≥3	Oral and oropharyngeal mucositis (63% events) Mean G≥1.5	Laryngeal edema (21% events)
				
AUROC (95% CI)				
0.684 (0.515,0.852)	0.733 (0.244,1.223)	0.581 (0.475,0.686)	0.578 (0.465,0.691)	0.662 (0.54,0.785)
Hosmer-Lemeshow p-value				
0.886	0.06	0.338	0.109	0.239
Brier score (non-informative cutoff)				
0.04894 (0.04889)	0.02712 (0.0393)	0.24 (0.243)	0.229 (0.233)	0.15467 (0.16349)
Intercept (p-value)				
-2.9643 (0.0000)	-3.3799 (0.0000)	-0.7556 (0.0001)	-0.0921 (0.6354)	-1.5587 (0.0000)
Slope (p-value)				
6.2731 (0.5483)	15.5779 (0.0055)	3.9862 (0.2850)	4.4570 (0.1705)	5.7173 (0.0224)

Results

Models for laryngeal edema showed best validation performances.

Results for late swallowing dysfunction and for late tube feeding dependence models suggest poor fit capabilities (low incidence: 5% and 3% respectively).

Models for acute mucositis performed poor discrimination ability (clinical differences with the original cohort).

Miscalibration is probably an effect of differences in patients' characteristics, that were not included in the models.

Conclusions

Our results suggest that validation tests lead to **better results** when:

- ☑ validation cohort have almost the **same clinical characteristics** to the one used to build the model;
- ☑ test population and the original one have **similar incidence** of radiation-induced complications.

THANK YOU FOR YOUR ATTENTION