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**A COMPUTER APPLICATION FOR THE PREDICTION OF
RISK OF DYSPHAGIA IN THE IRRADIATION
OF HEAD AND NECK CANCER**

BY

**CĂLIN GHEORGHE BUZEA^{1,*}, CAMIL CIPRIAN MIREȘTEAN¹ and
DRAGOȘ TEODOR IANCU^{1,2}**

¹Regional Institute of Oncology Iași

²“Grigore T. Popa” University of Medicine and Pharmacy, Iași

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Abstract. Dysphagia is a severe late complication in radiotherapy of head and neck cancer. Aspiration associated risk, weight loss and affecting the quality of life are just a few of the consequences. Dose limitation at the pharyngeal constrictors and larynx for the radio-treated patients with locally advanced head and neck cancers decreases the risk of late dysphagia.

Radiobiological model proposed by Christianen *et al.* for evaluation of late dysphagia can provide a good prognostic by calculation of NTCP (normal tissue complication probability) values, using the median dose received by the supraglottic larynx and superior pharyngeal constrictor muscles contoured as OARs (organs at risk). We designed a simple Microsoft Windows computer application for calculation in a simple way the risk of post radiotherapy dysphagia in neoplasms of the head and neck.

Keywords: dysphagia; radiobiological model; NTCP; computer application; head and neck cancer.

*Corresponding author; *e-mail*: calinb2003@yahoo.com

1. Introduction

Radiotherapy-induced dysphagia became a common complication in patients receiving high-dose radiotherapy as a part of the multimodal treatment of head and neck cancers. Nearly 50% report this distressing symptom a year after treatment completion (Roe *et al.*, 2014). Dose limitation at the pharyngeal constrictors and larynx for the radio-treated patients with locally advanced head and neck cancers decreases the risk of late dysphagia.

Treatments intensifications in head and neck cancers had led to improvement the prognostic but also to a high rate of mucosal and pharyngeal toxicity. The resulting impaired swallowing can lead to severe complications like aspiration pneumonia. For clinicians it is important to identify patients with the potential risk of dysphagia to prevent related complications (malnutrition, aspiration) and to provide supportive treatment for this purpose (Denaro *et al.*, 2013).

Radiobiological model proposed by Christianen *et al.* for evaluation of late dysphagia can provide a good prognostic by calculation NTCP (normal tissue complication probability) values using the median dose received by the supraglottic larynx and superior pharyngeal constrictor muscles contoured as OARs (organs at risk)

$$NTCP = (1 + e^{-S})^{-1}$$

where $S = -6.09 + (D_{\text{mean constrictor faringian superior}} * 0.057 + D_{\text{mean laringe supraglottic}} * 0.037)$.

2. Materials and Methods

For 3 patients with locally advanced oropharyngeal cancer treated with the VMAT technique the upper pharyngeal constrictor and the supraglottic larynx were subsequently contoured (Fig. 1) and Dmean (mean dose) was evaluated. All patients were treated with 3 cycles of Carboplatin-Paclitaxel induction chemotherapy. The treatment plan was performed on a CT-Simulator Siemens Somatom Definition As with 3 mm slices from the vertex to the emerging aorta cross.

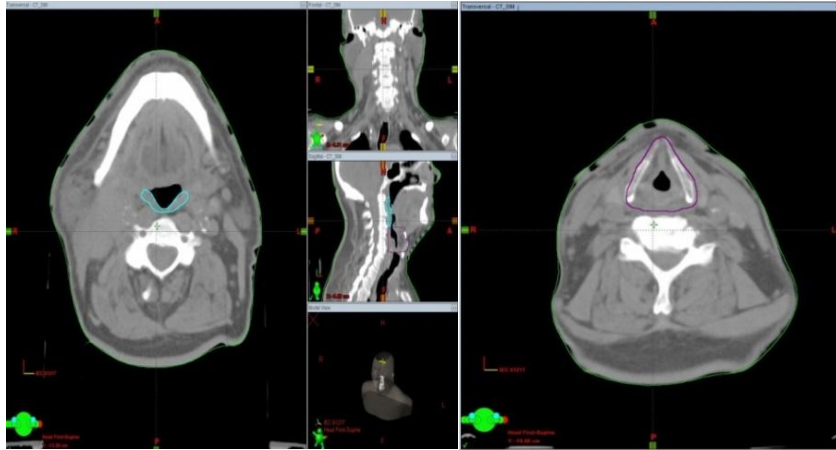


Fig. 1 – Upper pharyngeal constrictor (left) and supraglottic larynx (right) contoured as OAR.

The treatment plan was performed using Eclipse™ Treatment Planning System (Fig. 2) based on the CT simulation images. Image fusion and rigid registration with diagnostic i.v. contrast CT/MRI scan for a more precise target volume delimitation. Irradiation was performed in 3 sequential phases up to a maximum dose of 70Gy/35 fractions on the macroscopic volume of the primary tumor. High risk lymph nodes areas and macroscopically involved nodes received the maximum total dose of 66Gy/33 fractions, and the low-risk nodes levels were prophylactically irradiated with a total dose of 50Gy/25 fractions.

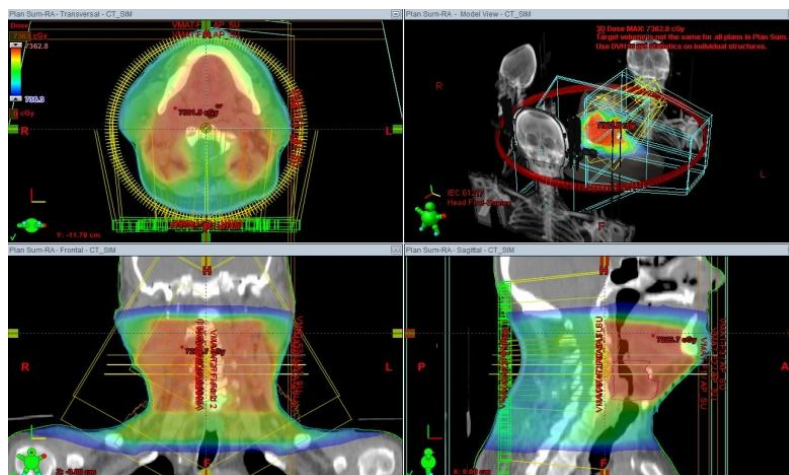


Fig. 2 – Dose distribution - “colorwash” representation in radiotherapy in VMAT for a case of neoplasm of oropharynx.

The treatment plans were done using RapidArc with single arc and implemented on the Varian Clinac iX linear accelerator, after being verified on ArcCHECK® phantom.

Christianen equation for NTCP values was used. A JAVA application has been created with a friendly interface (depicted in Fig. 3) that provides the NTCP value by introducing Dmean for supraglottic larynx and superior pharyngeal constrictor.

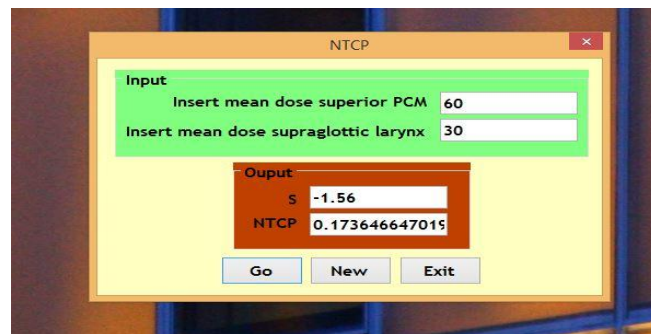


Fig. 3 – The graphical interface of the application that calculates NTCP with endpoint dysphagia.

3. Results and Discussion

Introducing Dmean obtained from the TPS in the computer application, NTCP values were generated.

Table 1
Dmean Values for the Superior Pharyngeal Constrictor and the Supraglottic Larynx; NTCP Calculated Values

	Case 1		Case2		Case3	
	Dmean (cGy)	NTCP (%)	Dmean (cGy)	NTCP (%)	Dmean (cGy)	NTCP (%)
superior pharyngeal constrictor	6907.4	47	6971.5	56.62	6443.9	53.75
supraglottic larynx	5547.1		5289.4		6940.3	

The most common late complications that affect the quality of life of radio-treated patients for head and neck cancers are dysphagia and xerostomia. Considering the complexity of structures involved in swallowing, it is difficult to assess the contribution of each of them to the occurrence of dysphagia (Narayanasamy *et al.*, 2015).

Lyman normal tissue complication probability (NTCP) model is based on DVH of the OARs.

Luxton *et al.* presented the values of the main parameters of the model: TD50/5, slope parameter (m), and the volume parameter (n) (Luxton *et al.*, 2008).

The study of Christianen includes 238 head and neck cancer patients treated with radiotherapy or chemo-radiotherapy. It appears that severe persistent and progressive swallowing dysfunction is associated with high doses received by the structures of upper pharyngeal region. Severe dysphagia is defined as swallowing dysfunction of grade 2 or higher at 6 months after RT or CH-RT which remained up to two year after the treatment. For long-term follow up, the importance of the dose to the supraglottic larynx appears to decline, while the effect of the dose to the superior PCM remains stable. The authors suggests that swallowing dysfunction can be prevented by maintaining the dose to the superior PCM as low as possible (Christianen, 2015).

On prospective cohort of 124 survivors included in the artscan study, Söderström and collaborators have tried to identify the dosimetric predictors of late dysphagia and the effect of elective lymph node irradiation. The main aim of the study was to identify in a multivariate ntcp model the prognostic factors of late dysphagia. They found that the mean dose to the superior pharyngeal constrictor and swallowing complaints at baseline were associated to patient reported choking and dose to the middle pharyngeal constrictor and post-radiotherapy neck dissection were predictors for late dysphagia (Söderström *et al.*, 2017).

From a dosimetric point of view the sparing of glottic larynx, oral cavity and superior pharyngeal constrictor is associated with preserved long-term swallowing function. These constraints are currently undergoing prospective validation. Beam-split IMRT techniques offer protection of the glottic larynx reducing the risk of aspiration. Dosimetric constraints: $V_{30} < 65\%$ and $V_{35} < 35\%$ for anterior oral cavity and $V_{55} < 80\%$ and $V_{65} < 30\%$ for high superior pharyngeal constrictors have been associated with a decrease in the risk of severe dysphagia (Schwartz *et al.*, 2010).

4. Conclusions

Radiobiological models - used more and more frequently as a predictor of toxicity and tumor control in IMRT and VMAT radiotherapy. The NTCP model for dysphagia can help the clinician to guide the post-radiotherapy supportive care treatment in order to reduce the effects of severe dysphagia and to prevent its complications. The application provides user friendly and easy calculation using a complex mathematical equation.

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O APLICAȚIE PE CALCULATOR PENTRU
PREDICȚIA RISCULUI DE DISFAGIE ÎN RADIOTERAPIA CANCERULUI
CAPULUI ȘI GĂTULUI

(Rezumat)

Disfagia este o complicație severă tardivă în radioterapia cancerului capului și gâtului. Riscul asociat aspirației, pierderea în greutate și afectarea calității vieții sunt doar câteva dintre consecințe. Limitarea dozei la nivelul mușchilor constrictori faringieni și a laringelui, scade riscul de disfagie tardivă pentru pacienții iradiați pentru cancer de cap și gât local avansat

Modelul radiobiologic propus de Christianen și colab. pentru evaluarea disfagiei tardive poate oferi un prognostic bun prin calcularea valorilor NTCP (probabilitatea de complicație a țesutului normal) utilizând doza mediană primită de laringele supraglotic și constrictorul faringian superior, conturați ca OAR (organe cu risc). Am proiectat o aplicație simplă Microsoft Windows pentru calculul simplu al riscului de disfagie post-radioterapie în neoplasmale capului și gâtului.