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ORIGINAL PAPER

Enhancing treatment precision through radiobiological modeling for evaluating complex VMAT plans in prostate and head-and-neck cancers

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Abstract

Background and objectives Regarding the importance of radiation therapy treatment planning in treatment outcomes, this study aimed to evaluate the quality of treatment plans for external radiotherapy of prostate and head-and-neck cancer patients using radiobiological modeling.

Methods Treatment plans of five prostate and five head-and-neck cancer patients treated with volumetric modulated arc therapy were evaluated. The RADBIOMOD software tool was used to calculate tumor control probability (TCP) and normal tissue complications probability (NTCP). TCPs were calculated based on Poisson, Zaider-Minerbo, and equivalent uniform dose (EUD) models. Lyman-Kutcher-Burman (LKB) and EUD models were used to calculate NTCPs. Uncomplicated tumor control probability (UTCP) was also calculated.

Results For the evaluated prostate cancer treatment plans, the Zaider-Minerbo model achieved the highest TCP of 99.34%, while the Poisson model had the highest TCP of 97.78% for head-and-neck cases. The LKB model was effective in determining NTCP for cancer treatment plans being studied. Although acceptable values of calculated UTCP for both prostate and head-and-neck cancer cases were observed, the NTCP values obtained using the EUD model exceeded the permitted range for evaluated head-and-neck cases.

Conclusions The acceptable quality of evaluated treatment plans was proved using calculated values of TCP, NTCP, and UTCP. These indices, along with the conventional dosimetric indicators obtained from dose volume histograms (DVHs), can help to assess the quality of treatment plans and to identify the optimal treatment plans. The observed varied TCP results across models, highlighting the importance of evaluating treatment plans with multiple models to ensure biologically guaranteed quality.

Keywords RADBIOMOD · Radiobiological modeling · Tumor control probability (TCP) · Normal tissue complications probability (NTCP) · Uncomplicated tumor control probability (UTCP)

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1 Introduction

Advanced radiation therapy techniques precisely deliver complex dose distributions to tumors while sparing organs at risk (OARs) [1]. Treatment machines administer intricate doses calculated using treatment planning systems (TPS). TPSs use various algorithms to estimate dose in patient CT voxels, evaluating dose distributions in target volumes and OARs with statistical dose volume histograms (DVHs) to assess treatment plan quality. The effectiveness of a TPS relies on its ability to generate optimal treatment plans using dose calculation algorithms and adjustable parameters that enhance plans via objective functions [2–4].

In modern radiotherapy, plan complexity from machine parameter modulation strains treatment machines and TPSs, increasing dose calculation and delivery uncertainties due to interactions of parameters such as aperture modulation and beam aperture size [5]. Complex treatment plans require thorough evaluation and patient-specific quality control for optimization and treatment alignment verification [6]. Clinicians commonly use DVHs to ensure plans meet clinical goals, relying on dose and dose-volume parameters to assess quality. Incorporating biological indices directly reflects clinical goals, enhancing quality assessment. Integrating biology into treatment planning improves understanding of dose-response models. Biologically based treatment planning systems (BBTPSs) utilize biologically related cost functions to optimize radiotherapy treatment plans, improving treatment outcomes [7, 8].

Assessing treatment outcomes requires considering biological effects on both target volumes and OARs [9]. Radiotherapy effectiveness is typically evaluated using tumor control probability (TCP) and adjacent normal tissue complication probability (NTCP) indices, integrated into an objective function to optimize treatment plans [1]. TCP and NTCP models enhance plan quality by gauging treatment success rates and mitigating tissue toxicity risks [10, 11]. These models have been utilized across various radiotherapy techniques, including intensity-modulated radiation therapy (IMRT) for head-and-neck cancer, stereotactic body radiotherapy (SBRT) for lung cancer, volumetric modulated arc therapy (VMAT) for prostate cancer, and 3D-conformal radiation therapy (3D-CRT) [12–15]. Moreover, Chaikh et al. [16] explored TCP scores of treatment plans with varied radiobiological parameter settings, highlighting the importance of combining relevant parameters for each cancer type to enhance plan quality.

Advanced mathematical algorithms for TCP and NTCP calculation, integrated into treatment planning systems, are crucial for achieving greater accuracy in complex plans. Various software tools facilitate TCP and NTCP computation, such as IsoBED, Radiation Outcome Explorer (ROE), DVH metrics, RadioBio data, pyRadioBiology, BioSuite, BIOPLAN, and RADBIOMOD [17–21]. These tools offer multiple mathematical models for calculating TCP and NTCP indices and the biological evaluation of radiation therapy treatment plans.

User-friendly software for physicists is crucial to promote the adoption of biologically based optimization and evaluation in complex treatment plans [20] .Warkentin et al. [22] introduced a MATLAB-based TCP-NTCP-CALC module for plan evaluation, while Singh et al. [23] developed a MATLAB-based program for radiobiological evaluation, generating biological effective dose (BED) and 2 Gy equivalent dose (EQD2)-based DVHs using tissue-specific radiobiological parameters. Tsougos et al. [24] created DORES software for NTCP estimation, and Naqa et al. [1] utilized Monte Carlo simulation for plan quality assurance based on TCP/NTCP models. These advancements enhance the assessment of complex radiotherapy treatment plans.

Biological-based treatment planning systems may not be available in all radiotherapy centers. Physicists should integrate radiobiological evaluation into treatment plans and assess quality using accessible software. This study evaluates complex radiotherapy plans for prostate and head-and-neck cancers, utilizing various radiobiological models provided in RADBIOMOD. The findings emphasize the significance of radiobiological evaluation, even with simple tools like RADBIOMOD, to improve plan quality and minimize uncertainties in complex VMAT treatments.

2 Materials and methods

This study was conducted at National Institute of Oncology in Morocco, utilizing treatment plans from the TPS archive of previously treated patients. Approval for the study protocol was obtained from the institutional ethics committee, and ethics guidelines were adhered to throughout all study procedures. Patients' data and plans were anonymized before utilization.

2.1 Study population and treatment protocol

The study population consisted of 10 adult cancer patients with complex treatment plans (five prostate and five head-and-neck) receiving external radiotherapy using Versa HD (Elekta) linear accelerator. A Monaco TPS version 5.5 had been used to calculate treatment plans for the VMAT technique. VMAT was prominently utilized, employing a comprehensive full double arc technique for optimal efficacy. Due to the complexity of such tumors and the difficult localization encompassing several critical organs, radiobiological validation is a must.

For prostate cases, the target volume included lymph nodes (PTV 46 Gy) and prostate (PTV 76 Gy). The rectum, bladder, right and left femoral heads and small intestine had been considered as the OARs. Based on the treatment protocol prescribed dose was 76 Gy in 38 fractions. The PTVs for the five evaluated patients were 170.5, 58.8, 111.4, 136.4, and 152.3 cm^3. Treatments lasted 56, 57, 61, 59, and 61 days, respectively.

For head-and-neck cases, the target volume comprised of PTV (70 Gy), and the OARs were cerebellum, brain optic chiasm, optic nerves, larynx, right and left parotids, lens, cornea, right and left cochlea and temporomandibular joint (TMJ). The treatment protocol comprised of delivering 70 Gy in 35 fractions. The PTVs for the five evaluated patients were 151, 101.7, 80.5, 236.9, and 308.8 cm^3, respectively. Treatments lasted 52, 57, 55, 53, and 61 days, respectively.

2.2 Analyzing the radiobiological quality of treatment plans

To analyze the radiobiological quality of treatment plans, DVH values for PTVs and OARs, along with their volumes, were extracted from the TPS in Excel format. RADBIOMOD software (https://sites.google.com/site/radbiomod) was utilized for analyzing DVHs and assessing TCP and NTCP parameters, offering a standardized platform independent of TPS.

RADBIOMOD employs various radiobiological models, including Poisson/ Linear quadratic (LQ), Zaider-Minerbo, and equivalent uniform dose (EUD) for TCP calculation, and Lyman-Kutcher-Burman (LKB) and EUD for NTCP calculation. This software was used because it is user-friendly and facilitates DVH data processing from the TPS. Detailed mathematical relationships, equations, and parameters for each model are provided in references [21, 25]. The used parameters in our study for each model are documented in the supplementary file (Tables S1 to S5).

2.3 Statistical analysis

Statistical analysis was conducted using SPSS software version 26 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). The Kruskal-Wallis test was used to compare TCPs calculated using different radiobiological models for studied treatment plans.

Table 1 The calculated TCPs using different radiobiological models presented in RADBIOMOD for five prostate cancer patients

	TCP %		
Patient ID	Poisson Model	Zaider Minerbo Model	EUD Model
Patient 1	78.03	99.59	78.13
Patient 2	80.39	99.46	63.05
Patient 3	74.34	99.03	63.14
Patient 4	77.97	99.36	71.4
Patient 5	76.23	99.28	71.01
Mean TCP	77.40	99.34	69.35

Table 2 Kruskal-Wallis test result for comparing TCP% for prostate cases calculated using different models

Pairwise Comparisons of Models	*P*-Value
EUD Model-Poisson Model	0.229
EUD Model-Zaider Minerbo Model	0.001*
Poisson Model-Zaider Minerbo Model	0.040*
Note: * shows statistically significant differences.	

3 Results

3.1 Prostate cancer treatment plans

Calculated TCP values using RADBIOMOD software based on the applied radiobiological models (the Poisson, Zaider-Minerbo, and EUD) provided in RADBIOMOD for the five studied prostate cases are presented in Table 1. The p-values for comparing TCPs calculated using different models are presented in Table 2.

Figure 1A and B illustrate calculated TCPs using RADBIOMOD software for prostate cancer patient 5, based on the Poisson and Zaider-Minerbo models, respectively. These data serve as criteria for evaluating treatment plan quality.

Figure 2A represents cumulative DVHs of the treated volumes and OARs for prostate cancer patient 5, providing another essential tool for quality estimation. As detailed in the methods, this patient received a total radiation dose of 76 Gy over 38 fractions with VMAT, employing a full double arc strategy to ensure comprehensive PTV coverage at 46 and 76 Gy levels while limiting OAR doses. Figure 2B and C display dose map distributions calculated using Monaco TPS for this patient in axial and sagittal views, respectively.

Table 3 presents NTCPs calculated using the LKB model from RADBIOMOD software and uncomplicated tumor control probabilities (UTCPs) for prostate cancer cases.

The percentage of calculated NTCP using the LKB model as dose functions (Gy) for the rectum and bladder of prostate patient 5 are presented as an instance, in Fig 3A and B, respectively. As seen for this patient, for the prescribed dose of 76 Gy, the dose received by 5% of the rectum volume does not exceed the dose of 74 Gy. Moreover, 25 and 30% of the rectum volume receive doses less than 70 and 60 Gy, respectively. These results indicate the accuracy

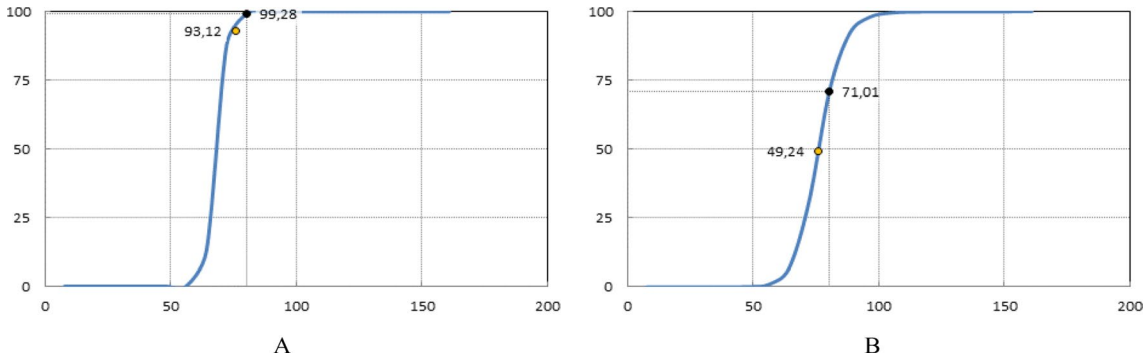

Fig. 1 Calculated TCP (%) for prostate patient 5 as a function of applied dose (Gy), **A**) using the Poisson model, **B**) using the Zaider Minerbo model. *Note* The horizontal axis shows the dose in Gy and the vertical one represents the percentage of the probability for tumor control (TCP%)

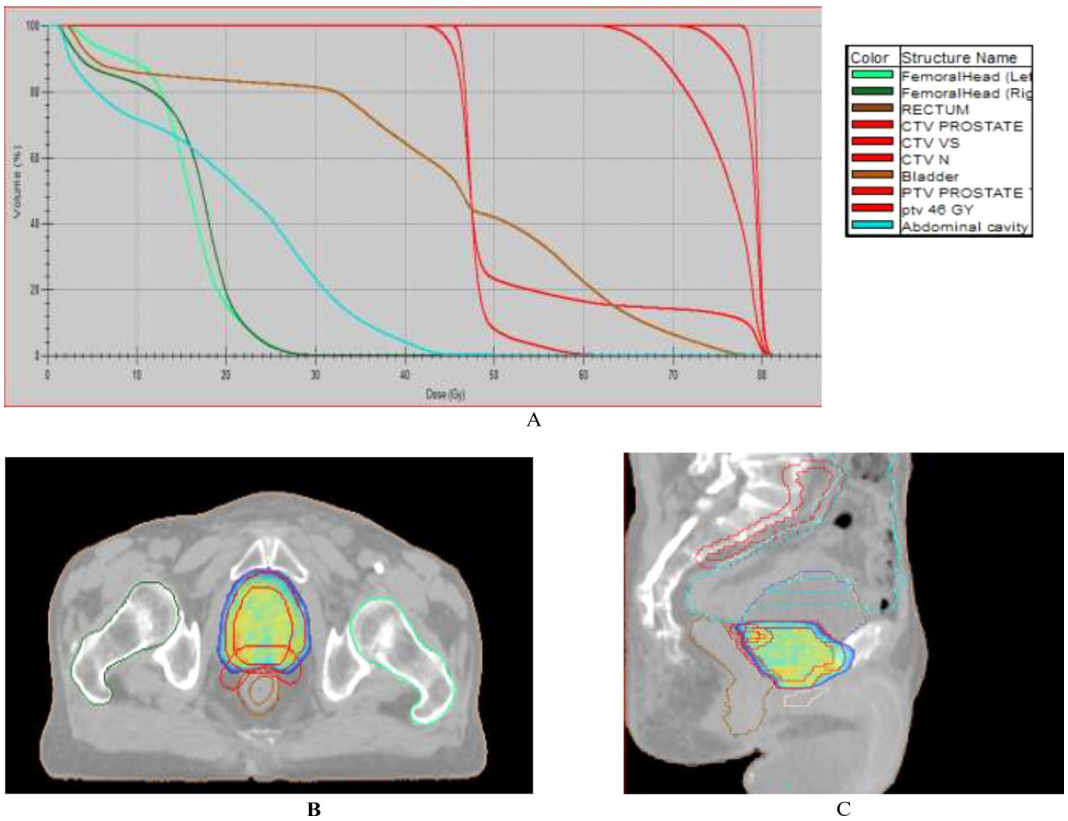

Fig. 2 The Monaco TPS-calculated cumulative DVHs for all structures, including treated volumes and OARs, for prostate patient 5, treated with 76 Gy in 38 fractions (**A**), Transverse image (**B**), and Sagittal image (**C**)

Table 3 The calculated NTCPs and UTCPs using RADBIOMOD (LKB model) for studied prostate cancer cases

	LKB-NTCP %				
Patient ID	Bladder	Rectum	Small Intestine	Total NTCP	UTCP
Patient 1	0.00	1.43	21.64	23.07	76.61
Patient 2	0.00	1.93	19.31	21.24	78.33
Patient 3	0.00	1.46	19.53	20.99	78.24
Patient 4	0.00	0.89	15.18	16.07	83.29
Patient 5	0.19	1.34	12.98	14.51	84.87
Mean	0.04	1.41	17.73	19.18	80.27

of the evaluated treatment plan for the VMAT technique, which depends on the optimization algorithms and the target functions. Furthermore, 25 and 50% of the bladder volume in patient 5 receive doses less than 70 and 60 Gy, respectively. The same trend was seen for the rest of the OARs for this patient. Also, acceptable values of UTCP were seen in the reviewed plans.

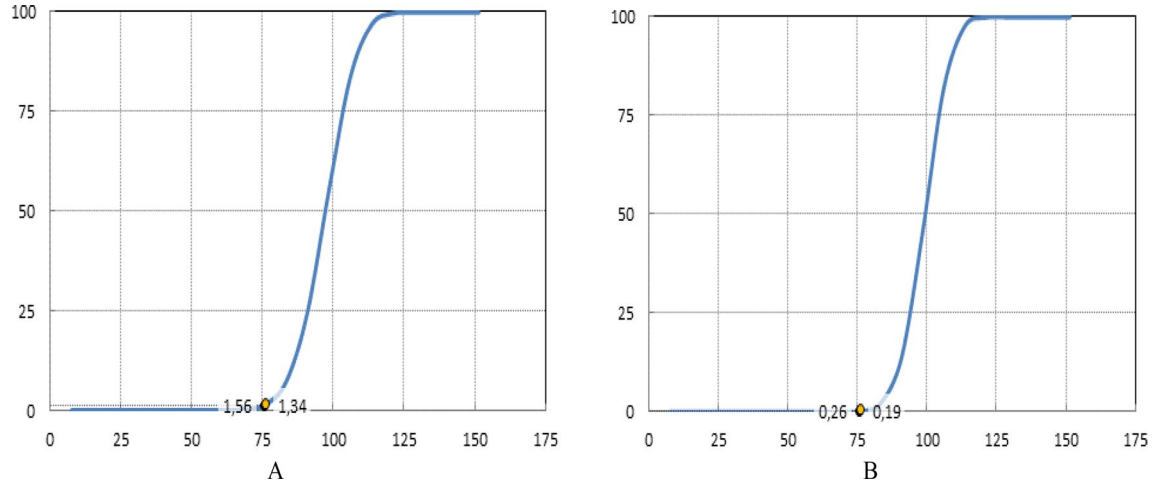

Fig. 3 LKB-NTCP curve as a function of dose (Gy), for the rectum of patient 5 (**A**) and for the bladder of patient 5 (**B**). *Note* The horizontal axis shows the dose in Gy, and the vertical axis shows the percentage of OAR complication probability

Table 4 The calculated TCPs using different models of RADBIOMOD for studied head-and-neck cancer patients

	TCP%		
Patient ID	Poisson Model	Zaider - Minerbo Model	EUD-TCP Model
Patient 1	93.39	100.00	91.80
Patient 2	99.00	100.00	99.85
Patient 3	99.48	97.25	99.85
Patient 4	80.37	99.67	71.16
Patient 5	80.01	74.16	52.73
Mean TCP	90.45	94.22	83.08

3.2 Cases of head-and-neck cancer

Table 4 illustrates RADBIOMOD calculated TCPs using Poisson, Zaider-Minerbo, and EUD models for the five head-and-neck cancer patients.

Figure 4A displays cumulative DVHs for PTV and OARs of a larynx cancer case treated with a specialized regimen of 70 Gy in 35 fractions. This approach aimed to precisely target PTVs while limiting radiation exposure to surrounding OARs within safe thresholds. Figure 4B and C further depict dose distributions in PTV and OARs in transverse and sagittal views for this case.

Tables 5 and 6 summarize calculated NTCPs for OARs of head-and-neck cancer cases using LKB and EUD models, respectively.

Figure 5A to E depict the plotted cumulative DVHs using RADIOBIOMOD software for the contralateral parotid as an organ at risk for the evaluated treatment plans.

4 Discussion

Unlike traditional dose-based indices, which primarily quantify the physical aspects of radiation delivery, biological models incorporate factors such as TCP and NTCP to provide a more comprehensive evaluation of treatment plan efficacy and toxicity [8, 26, 27]. Biological models offer several advantages, including the ability to compare treatment plans across different cancer types and fractionation schemes, and to account for the effects of treatment interruptions [8, 27, 28]. However, it is crucial to acknowledge and address the uncertainties associated with these models, including variability in biological parameters, modeling assumptions, and inter-patient heterogeneity [29]. To facilitate the integration of biological models into clinical practice, it is imperative to benchmark the current treatment plan evaluation approach based on dose indices against these models [30, 31]. This entails comparing the outcomes predicted by dose indices with those predicted by biological models to ensure consistency and reliability in treatment plan assessment. Incorporating biological models into clinical decision-making processes can enhance treatment precision and individualize radiotherapy plans to optimize patient outcomes [30]. By understanding and mitigating the uncertainties associated with these models, clinicians can make more informed treatment decisions tailored to the specific needs and characteristics of each patient [32].

Based on the findings, the mean TCP values of 77.4, 99.34, and 69.35% were calculated for the evaluated prostate cancer treatment plans using the Poisson, Zaider-Minerbo, and Gay and Niemierko (EUD) models, respectively (Table 1). Literature suggests TCP values for prostate cancer treated with 76 Gy in external radiotherapy are 80–90% for the Poisson model and 85–90% for the Zaider-Minerbo

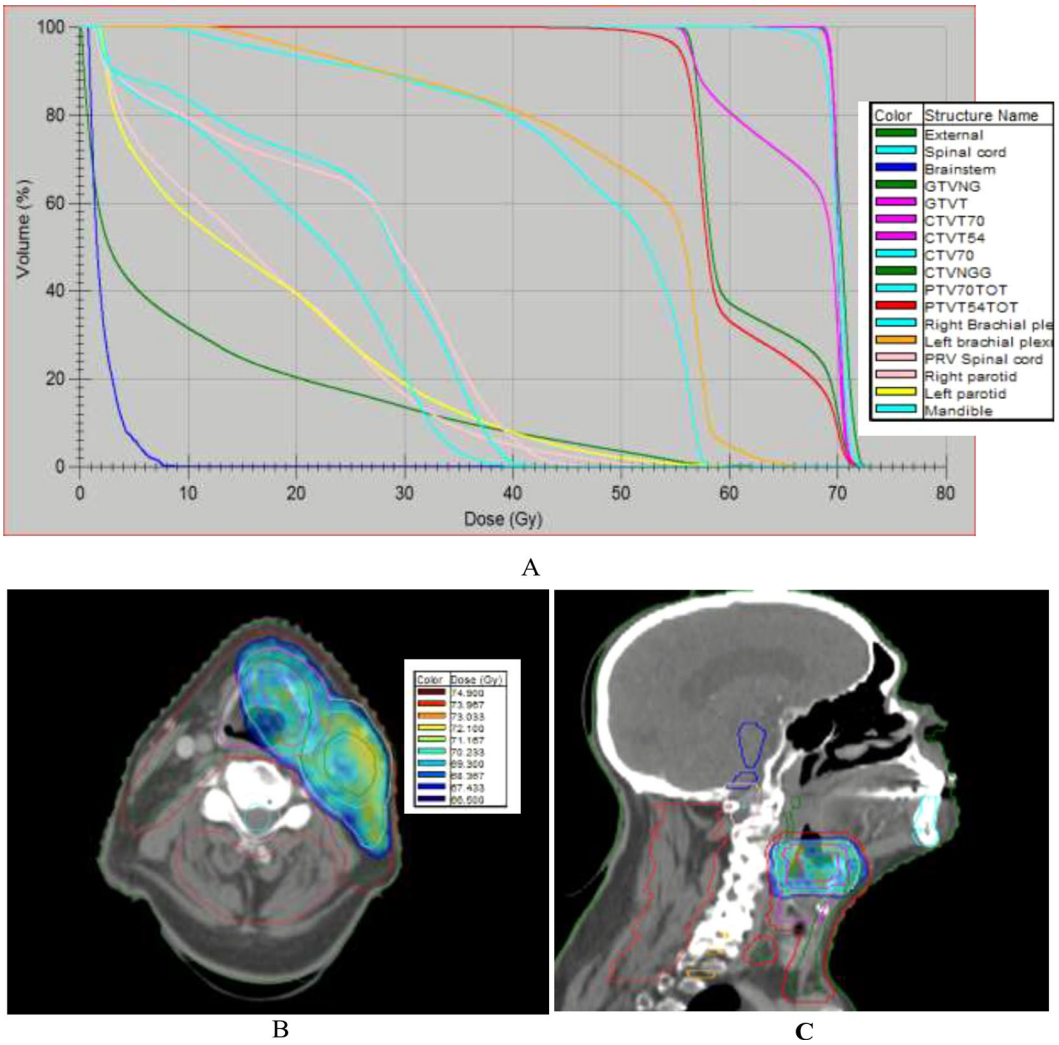

Fig. 4 Cumulative DVHs of PTV and OARs for one of the evaluated head-and-neck (larynx cancer) treatment plans (**A**), the calculated dose distributions using the Monaco treatment planning system for this plan treated with 70 Gy in 35 fractions, in transverse view (**B**) and sagittal view (**C**)

Table 5 The calculated NTCPs by RADBIOMOD using the LKB model for studied head-and-neck cancer patients

	LKB model-Based NTCP %							
Patient ID	Brainstem	Brain	Optic chiasma	Optic nerves	Larynx	Parotids	TMJ	TOTAL NTCP
Patient 1	0.30	0.18	0.10	0.02	0.3	18.58	0.25	19.51
Patient 2	0.07	0.05	0.10	0.08	0.08	17.74	0.02	18.07
Patient 3	0.08	0.07	0.11	0.09	0.09	18.4	0.02	18.77
Patient 4	0.31	0.25	0.66	0.55	0.5	24.6	0.12	26.39
Patient 5	0.30	0.30	0.81	0.68	0.68	18.38	0.50	21.02
Mean NTCP	0.21	0.17	0.36	0.28	0.33	19.54	0.18	20.75

Table 6 The calculated NTCPs by RADBIOMOD using the EUD model for studied head-and-neck cancer patients

	EUD model Based-NTCP%					
Patient ID	Brainstem	Brain	Optic chiasma	Optic nerves	Parotids	TOTAL NTCP
Patient 1	0.47	0.60	20.21	20.21	40.57	62.57
Patient 2	0.31	0.08	54.00	75.75	25.38	91.71
Patient 3	0.15	0.09	73.87	51.56	28.04	90.91
Patient 4	1.00	0.35	13.93	13.58	59.55	70.32
Patient 5	0.42	0.40	52.93	51.33	28.77	83.82
Mean NTCP	0.47	0.30	42.99	42.49	36.46	79.87

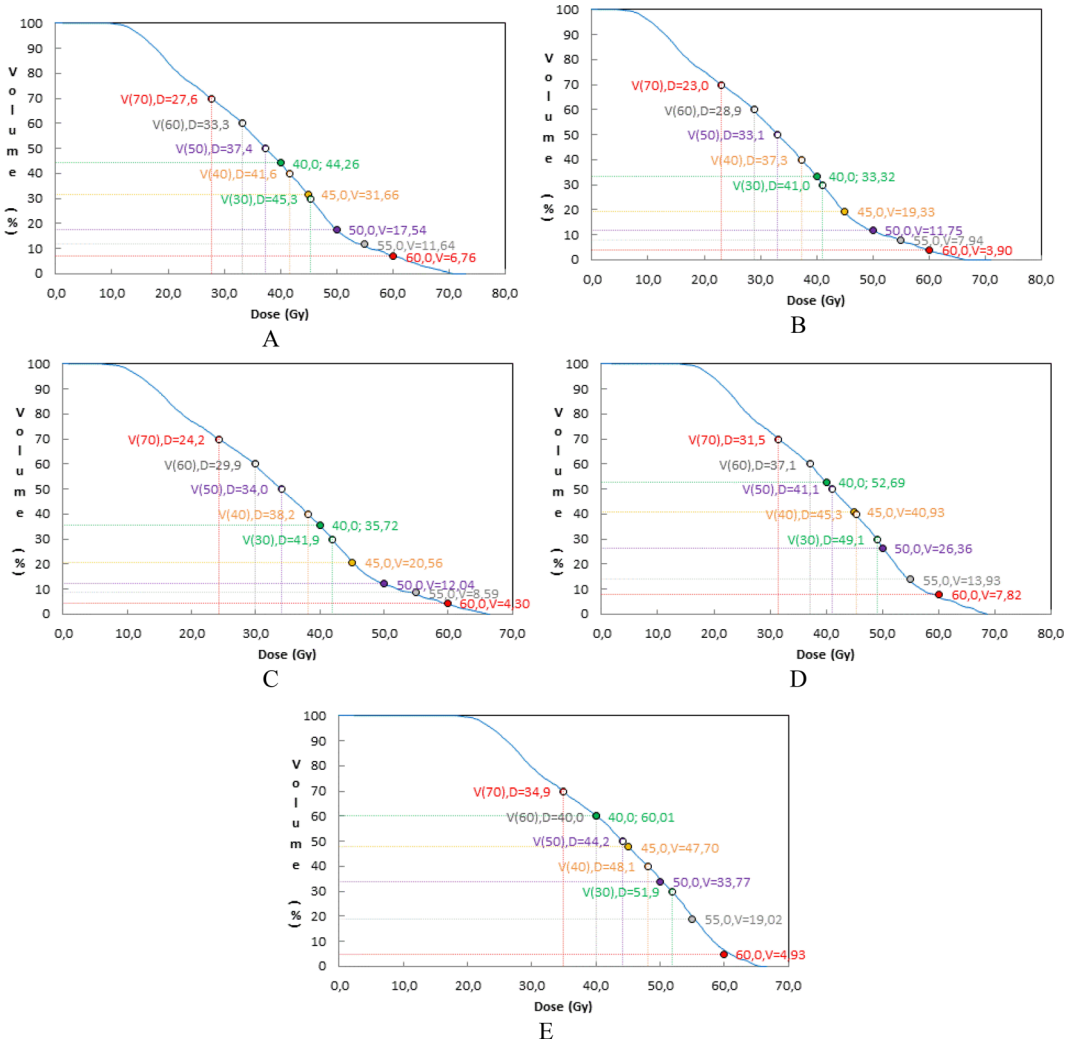

Fig. 5 Cumulative DVHs for contralateral parotid as an organ at risk for evaluated head-and-neck treatment plans, (**A**) Patient 1, (**B**) Patient 2, (**C**) Patient 3, (**D**) Patient 4, (**E**) Patient 5. The horizontal axis shows the dose in Gy, and the vertical axis represents the percentage of the OAR volume irradiated

and EUD models. These values vary based on patient factors, planning techniques, dose per fraction, schedules, and other variables [15, 33].

Our results align with Mesbahi et al. [15] showing that TCP calculated using the Poisson model varies significantly with $\frac{\alpha}{\beta}$ parameter while EUD-based TCP for prostate cancer is less dependent on this parameter. They also noted different models yield different TCP outcomes. Wang et al. [33] reported median TCP values of 85.1% (56.4–90.9%), 81.2% (56.1–88.7%), and 62.5% (28.2–75.9%) for prostate plans using the Poisson, Niemierko, and Marsden models, respectively.

Our findings show statistically significant differences ($P < 0.05$) in TCPs calculated using the EUD, Zaider-Minerbo, and Poisson models for prostate plans. TCP values from the Zaider-Minerbo model were higher than those from the Poisson and EUD models. TCP reflects treatment plan quality and the effectiveness of irradiation using radiobiology models. Differences in TCP values arise from varying biological effects considered in each model [9].

Rana and Cheng [34] evaluated technique effectiveness by calculating EUD-based TCP and NTCP for single and double-arc treatments of low-risk prostate cancer. They reported average prostate TCPs of 98.30% for single-arc and 98.27% for double-arc, with NTCP values below 0.1% for bladder and femoral heads, and rectum NTCPs of 2.21 and 1.88% for single and double-arc, respectively. NTCP are influenced by the biological response, dose constraints, calculation model, patient characteristics, tumor volume, total dose, and fractionation. Literature suggests approximate NTCP values of 5–20% for the bladder, 10–30% for the rectum, and 5–10% for the small intestine [35, 36]. Our study found LKB model NTCP values for prostate cancer OARs ranging from 14.51 to 23.07%, with bladder and

rectum NTCPs within accepted ranges. Sparing the small intestine may require additional attention. NTCP is largely influenced by organ structure [9]. ASTRO guidelines recommend personalized plans based on risk, advanced techniques, and balancing tumor control with minimizing side effects, with moderate hypofractionation as a safe option for localized prostate cancer [37, 38].

Jang et al. [39] evaluated NTCPs of half-field VMAT (VMAT-HF) and full-field VMAT (VMAT-FF) techniques using LKB and logistic models for the small bowel and colon in whole pelvic radiation therapy. For the small bowel, NTCPs in VMAT-FF were 11.74 ± 5.52% (LKB) and 10.98 ± 5.49% (logistic), while in VMAT-HF, they were 8.61 ± 3.69% (LKB) and 7.80 ± 3.57% (logistic). For the colon, NTCPs in VMAT-FF were 3.01 ± 2.36% (LKB) and 3.08 ± 2.32% (logistic), and in VMAT-HF, they were 1.69 ± 1.64% (LKB) and 1.78 ± 1.62% (logistic).

Our results show Uncomplicated TCP (UTCP) for prostate cancer cases ranged from 76.61 to 84.87%, indicating high overall tumor control probability. UTCP serves as a therapeutic gain index, predicting tumor control probability without adverse effects by calculating the maximum difference between TCP and NTCP [8, 40]. El-Mesidy et al. [41] calculated UTCP by subtracting the sum of NTCPs for OARs from the TCP. Higher UTCP values indicate better outcomes. The peak of the UTCP curve shows the dose range that balances tumor control and normal tissue complications. Literature suggests UTCP values of 10–20% for prostate cancer patients treated with 76 Gy using the LKB multi-OAR model, varying based on patient characteristics and treatment planning techniques [42].

The mean TCP values for evaluated head-and-neck plans were 90.45% (Poisson model), 94.22% (Zaider-Minerbo model), and 83.08% (EUD model). Statistical analysis showed no significant differences in TCP values among these models ($P = 0.40$) (Fig. 6), although variations in TCP calculations reflect model differences. Approximate TCP values for head-and-neck cancer in external radiotherapy vary from 60 to 80% for the Poisson model, 70–85% for the Zaider-Minerbo model, and 65–80% for the EUD model [9, 28, 40]. These values depend on patient specifics, treatment techniques, and biological considerations in the models. Smaller PTV sizes generally correspond to higher TCP values. LKB-based NTCPs for OARs in head-and-neck plans ranged from 0.02 to 26.39%, while EUD-based NTCPs ranged from 0.08 to 91.71% (Tables 5 and 6). Mean NTCPs were 3.01% (LKB) and 24.54% (EUD) for OARs, reflecting model differences.

Nuraini and Widita [9] calculated Poisson TCP and NTCP values for 10 head-and-neck patients, considering cell biological effects, and compared the results with other models. They observed mean TCPs of 91.33% (biologically modified Poisson), 81.81% (EUD), and 90.58% (Zaider-Minerbo). Average NTCPs were 11.65% (Poisson), 11.56% (EUD), and 11.44% (LKB). The Poisson model, accounting for cell repair, showed an average NTCP of 3.5%. Also, Kan et al. [40]. evaluated IMRT plans for 20 nasopharyngeal carcinoma patients, comparing biologically based (BBTP) and dose/dose volume-based (DVTP) approaches. Poisson-LQ-based TCP values exceeded 98% for both methods: 98.91 ± 1.50% (BBTP) and 98.64 ± 1.73% (DVTP) in early-stage NPC, and 88.95 ± 9.61% (BBTP) and 86.19 ± 11.00%

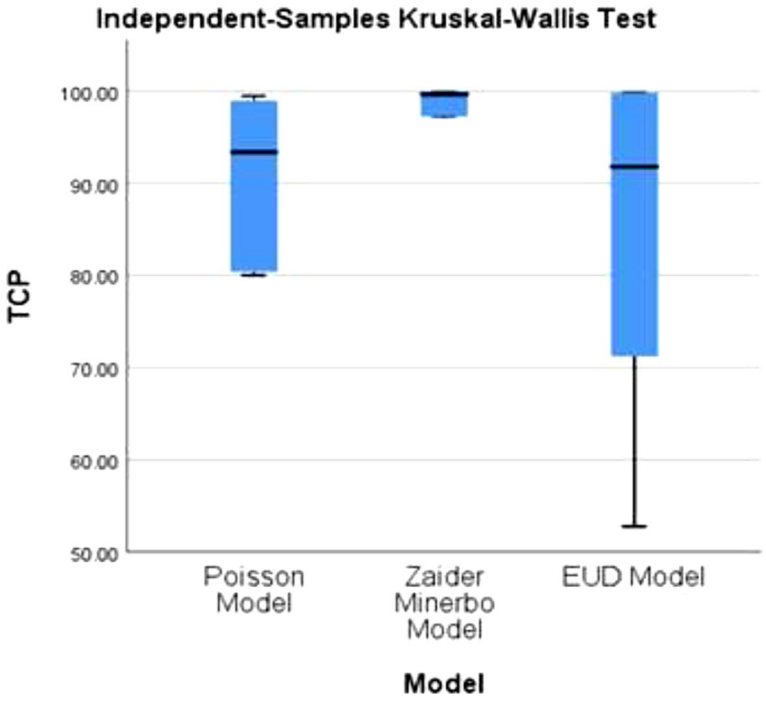

Fig. 6 Kruskal-Wallis test result for comparing TCP% for head-and-neck cases calculated using different models. The calculated values showed no significance differences ($P = 0.40$)

(DVTP) in advanced-stage NPC. Poisson-LQ-based NTCP values for the parotid glands were 8.0 ± 5.8% (early) and 7.9 ± 8.7% (advanced) with BBTP, versus 21.3 ± 8.3% (early) and 24.4 ± 12.8% (advanced) with DVTP.

Our findings show significant differences in NTCPs calculated using LKB and EUD models for the contralateral parotid in evaluated treatment plans. These differences reflect the capability of each model to assess cell repair effects and tissue radiation tolerance. Sequential organs may see increased NTCP with radiation exposure, while parallel organs correlate increased complication risk with increased exposed volume. Common endpoints in head-and-neck cancer radiotherapy planning include xerostomia, dysphagia, mucositis, radiation-induced fibrosis, and dermatitis [43]. NTCP values for optic chiasm, optic nerves, and parotids in external radiotherapy vary based on patient characteristics, treatment planning techniques, radiation dose, and fractionation. In the LKB model, approximate NTCP values are Optic chiasm < 10%, Optic nerves < 5%, and Parotids < 30% [40]. Comparing our results to these benchmarks, NTCP values using the LKB model generally fell within acceptable ranges for most evaluated head-and-neck treatment plans. However, the EUD model yielded higher values due to its parameter setup and limitations, such as not considering biological effects like cell repair [9]. Moreover, in the study of Narayanasamy et al. [44] for 33 head-and-neck patients, the mean Poisson-based TCP value of 0.8 ± 0.03% was recorded, while the LKB-based NTCP values of the parotids, esophagus, and larynx were 0.4 ± 0.1, 0.2 ± 0.1, and 0.1 ± 0.1%, respectively. Also, Mosleh-Shirazi et al. [45] showed that the NTCP for acute esophagitis in head-and-neck treatment plans is only moderately sensitive to the type of applied dose calculation algorithm. Based on their results, the simpler algorithm underestimates the LKB-based NTCP for acute esophagitis.

According to our findings, UTCP values of 80, 81.11, 81.81, 59.16, and 63.19% were obtained for the five studied head-and-neck cancer cases, indicating a relatively high therapeutic gain. The results show TCP variations across different radiobiological models for each head-and-neck treatment plan. For instance, in case 4, TCPs calculated using Poisson, Zaider Minerbo, and EUD models were 80.37, 99.67, and 71.16%, respectively. The observed varied TCP results across models, highlighting the importance of evaluating treatment plans with multiple models to ensure biologically guaranteed quality. Poisson and EUD models yield relatively low TCP values compared to Zaider Minerbo due to considering different characteristics and parameters in each model, emphasizing the need for a comprehensive assessment. Additionally, the average dose calculated by the EUD model closely matched the given dose of 75.75 Gy. Furthermore, NTCP values for OARs using the LKB model align well with previous studies [15], particularly for IMRT plans.

Despite the lower TCP from the EUD model, these plans remain acceptable, given their complexity. Generally, the EUD model yields lower TCP values due to its exclusion of biological effects and reliance on tissue-specific parameters like the alpha parameter. On average, head-and-neck cancer cases exhibit higher TCP values across all models compared to prostate cases. Adherence to ICRU 83 recommendations [46] is essential for head-and-neck cancer patients receiving a 70 Gy dose. NTCP values calculated with the EUD model for these plans surpassed permissible ranges, indicating potential brain and brain stem complications despite minor model variations. NTCP values for the optic chiasm and optic nerve also exceeded expected levels, suggesting limitations in the EUD model for these regions.

While physical indices support treatment plans, radiobiological assessment may not fully endorse them due to model limitations. For instance, the prostate cancer TCP model may overlook subclinical disease, and the rectum NTCP model assumes a linear dose-response relation unsuitable for high-dose radiotherapy. UTCP models include uncertainties in radiobiological parameters. In head-and-neck cancer, the TCP model assumes a homogeneous dose distribution, while the salivary glands NTCP model may overlook late effects. Additionally, the head-and-neck cancer UTCP model might assume equal radiation sensitivity for all tumor cells, which may not apply universally [47].

Studies indicate tissue structure strongly influences radiotherapy planning, affecting TCP and NTCP values. Variations in density, composition, and oxygenation within tissues impact dose distribution. Chaikh et al. [48] emphsize the significant influence of tissue heterogeneity on TCP and NTCP values in prostate and head-and-neck cancers. Accurate modeling of tissue heterogeneity is vital for optimizing treatment plans and improving radiobiological outcomes.

Selecting appropriate radiobiological models is crucial for calculating TCP, NTCP, and UTCP values in radiotherapy planning. Factors such as patient data, cancer type, and treatment approach influence model choice. The Poisson model is commonly used for TCP, and the LKB model is preferred for NTCP. Complex models like gEUD and logit require more patient-specific data. There is no consensus on the best UTCP model for prostate cancer, highlighting the need to combine models and clinical judgment for optimal care [49, 50].

VMAT and IMRT techniques enhance treatment outcomes by precisely targeting tumors and minimizing damage to healthy tissues, resulting in higher TCP and lower NTCP levels than traditional 3D radiotherapy. Predicting TCP and NTCP is challenging due to interpatient and intratumor heterogeneity, changes in tumor biology during

treatment, and patient setup variations. Recommendations include developing specialized protocols, refining TCP and NTCP algorithms, and considering tumor size. Biological treatment volume (BTV) is crucial for improving TCP and NTCP values [51–53].

5 Conclusion

The effectiveness of radiobiological modeling in prostate and head-and-neck cancer treatment plans using RADIOBIOMOD software was evaluated by comparing TCP and NTCP values from various models with conventional DVH metrics. For prostate cancer, the Zaider-Minerbo models showed high accuracy with a mean TCP of 99.34%. NTCP values for OARs varied significantly with the LKB model, reflecting differences in radiobiological parameters and organ anatomy. In head-and-neck cancer plans, the LKB model indicated lower NTCP values, while the EUD model showed higher NTCP values. The Poisson model yielded an average TCP of 97.78% for head-and-neck cancers. The calculated TCP, NTCP, and UTCP values, along with conventional DVH indicators, can assess treatment plan quality and identify optimal plans. The varied TCP results across models highlight the importance of using multiple models for evaluation. This study demonstrates the potential of radiobiological models to enhance treatment plan evaluations, advocating for further clinical validation and algorithmic advancements.

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