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Radiobiological Impact of Calculation Slice Thickness on Head and Neck IMRT Plans Using MATLAB

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Abstract:

In radiotherapy there are many evaluation tools available to achieve the best treatment plan. One of them is equivalent uniform dose (EUD) based model. It use to estimate the tumor control probability (TCP) and normal tissue complication probability (NTCP). While the current generation of radiobiological models has low predictive power that prevents it from being used as a primary evaluation tool, projections from radiobiological model may still be a helpful supplement to clinical experience. The perfect treatment plan provides the highest tumor control and lowest normal tissue complications. The purpose of this study is to use different grid sizes (2, 3, 4, 5) and different algorithms (Monte Carlo and Pencil Beam) when calculating TCP and NTCP. Eleven patients with head and neck (H&N) cancer cases were included in this study. Comparison achieved for each patient with the variation of grid size and algorithm. A total of 88 plans were generated in MONACO treatment planning system (TPS). Treatment plans were designed using Intensity modulated radiation therapy (IMRT) technique. Dose and volume parameters were derived from the dose volume histograms (DVHs) for target and critical structures. The average value of TCP was 94.13 ±12.80% for the 2 mm grid size and 95.16 ±10.05% for 5 mm with Monte Carlo (MC) algorithm. Statistically there was significance difference between two plans ($p < 0.05$). For Pencil Beam (PB) algorithm, the average TCP value was 91.78 ±19.54% and 93.04 ±17.13% for 2 mm and 5 mm respectively with $p < 0.05$. In comparison between MC and PB plans, the NTCP of PB algorithm plans were greater for brainstem, spinal cord, and chiasm compared to

MC algorithm plans. It could be concluded that the smallest available grid size (2 or 3 mm) is the favorable. The MC algorithm is recommended for improved plan accuracy.

Keywords: *grid size, Monte Carlo, Pencil Beam, radiobiological evaluation.*

1. Introduction

Head and neck (H&N) cancer type was the third most common cancer globally. It estimated about 7.6% of all cases diagnosed with cancer worldwide [1]. Around 50% of these cases dead from cancer of H&N [2].

Radiotherapy become an important type of therapy to kill cancer cells. More than half of all cancer cases will get radiation as part of their cancer treatment [3]. The aim of radiotherapy is to obtain the highest probability of tumor control, or cure, with the lowest morbidity and toxicity to normal tissues [4]. Achieving that using advanced techniques with high accuracy and precise dose delivery.

One of the most common used of these techniques in H&N cancer is intensity-modulated radiation therapy (IMRT) [5, 6]. IMRT is an advanced form of external radiotherapy. It has a revolution in the treatment of H&N cancer [7]. The accuracy of IMRT plans relies heavily on the precise calculation of dose distributions, which is influenced by the grid size and algorithm used in the treatment planning system (TPS) [8]. The mainly tool used in evaluating treatment plan is dose-volume histogram (DVH) which generated for each plan to get volume and dose parameters for the planning target volume (PTV) and organs at risk (OARs) [2].

Based on the predicted dose distribution and data obtained from DVH, radiobiological models are able to estimate the tumor control probability (TCP) and normal tissue complication probability (NTCP). TCP is a parameter used to calculate the percentage of tumor killing. NTCP is the response of normal tissue damage in the surrounding tumor area. Both TCP and NTCP depend on fractionation and cell biological effects such as repopulation, repair, redistribution and re-oxygenation [9, 10].

To get the optimal plan it should be maximize the TCP of tumor volume and minimize the NTCP of the surrounding normal tissues. Despite the importance of these factors, there is a lack of comprehensive studies evaluating the radiobiological impact of different grid sizes and algorithms on head and neck IMRT plans [11]. This knowledge gap can lead to suboptimal treatment plans, compromising treatment outcomes and patient safety.

Several authors, Shiv P. Srivastava et al. studied the dosimetric and radiobiological parameters with different grid size in head and neck IMRT plans [11]. Duong Thanh Tai et al. evaluated the dosimetric and radiobiological comparison in head and neck radiotherapy using JO-IMRT and 3D-CRT [12]. G. Narayanasamy et al. assessed the possibility of a correlation between OAR-related toxicities and its radiobiologically calculated parameters (NTCP) in SIB-IMRT plans at two different institutions for patients with head and neck cancers [13]. Anoop Kumar Srivastava et al. investigated the radiobiological impact of linear accelerators (Linac) using 6 MV X-rays and cobalt-60 (Co-60) gamma photons for the treatment plans of head and neck cancer cases [14]. Guadalupe Martin-Martin et al. estimated the improvement of dose accuracy and impact of using AXB and AAA algorithms in head and neck cancer using FFF-VMAT planning [15].

This study aims to investigate the radiobiological effects of varying grid sizes and algorithms on head and neck IMRT plans, providing valuable insights for clinicians and physicists to optimize treatment planning and improve patient outcomes.

2. Materials and Methods

2.1. Patient data

Eleven patients with H&N cancer were selected randomly for this retrospective study. Tumor sites for them are between nasopharynx and tongue. The planning target volumes (PTVs) ranged from 259.0 to 848.9 cc. The CT images were acquired with slice thickness of 3 mm on light speed® GE® CT simulator.

IMRT Planning

IMRT plans were generated using MONACO 5.1®TPS. Utilizing 9 fields started from Gantry 180° and rotate equally spaced around the patients using SYNERGY ELEKTA® linear accelerator. The delivery technique used was Step and shoot IMRT to deliver 60 Gy at 30 fractions to PTV (2 Gy / f).

Monaco® uses two different dose calculation algorithms Monte Carlo (MC) and Pencil Beam (PB). In order to balance between computational time and dose calculation accuracy, MONACO® typically uses grid sizes between 2.5 and 5.0 mm [8].

When the IMRT plans were completed for each patient, the plans were recalculated with different calculation grid sizes of 2, 3, 4, and 5 mm using each algorithm separately (MC and PB). This results in having eight plans generated for each patient in this study.

The dose-volume histograms (DVHs) were acquired for all PTVs and OARs with respect to the variation of grid size and algorithm. Radiobiological parameters were recalculated for each plan and compared based on the grid size and algorithm variation.

3. Radiobiological Analysis

3.1. Equivalent Uniform Dose (EUD) Based Models

Equivalent uniform dose represents the uniform dose causing the same injury probability as the non-uniform dose distribution for normal tissues. For tumors EUD represents the uniform dose achieving the same local control probability as the non-uniform dose distribution. According to Niemierko’s model, EUD is defined as:

$$\text{EUD} = \left(\sum_{i=1}(V_i\, D_i^{a})\right)^{\frac{1}{a}}$$

where V_i: fractional volume receiving dose D_i (unitless), D_i: dose received by the fractional volume V_i (Gy), a: model parameter specific to the normal structure or tumor of interest (unitless). This equation is applicable to both tumors and normal tissues. The required D_i and v_i data are obtained from the differential DVH of a given treatment plan.

3.2. Calculating TCP

To calculate TCP using the EUD-based model, substitute EUD into the following equation:

$$\text{TCP} = \frac{1}{1+\left(\frac{TCD_{50}}{EUD}\right)^{4\gamma_{50}}}$$

where: TCD_{50}: the tumor dose to control 50% of the tumors when the tumor is homogeneously irradiated, γ_{50}: unitless parameter describing the slope of the dose response curve for the specific tissue.

3.3. Calculating NTCP:

Niemierko proposed a model using the logistic function to parameterize the dose response characteristics for NTCP calculations:

$$\text{NTCP} = \frac{1}{1+\left(\frac{TD_{50}}{EUD}\right)^{4\gamma_{50}}}$$

where TD_{50}: the tolerance dose for a 50% complication rate at a specific time interval.

3.4. MATLAB Program

This study proposes using the MATLAB programming language to investigate the differences between Intensity-Modulated Radiation Therapy (IMRT) plans for head and neck (H&N)

cancers with various biological models. MATLAB stands as a high-level technical computing environment equipped with interactive features. The investigation will leverage two radiobiological models, TCP and NTCP, and their associated biological variables. We aim to explore their applicability in daily clinical hypofractionated radiotherapy, aiming to predict treatment plans that maximize tumor control probability while minimizing normal tissue damage.

```
%Save this file in Matlab as eudmodel.m
%EUDMODEL(DVH), where DVH is a 2 column matrix corresponding to the cumulative, not
%differential, dose volume histogram. The 1st column corresponds to increasing absolute dose or
%percentage dose values, and the 2nd column to the corresponding absolute or relative volume value.
%The matrix must have a minimum of two rows, and both columns must be of equal length.
%by Hiram A. Gay, MD
%Revised July 8 2007
function probability = eudmodel(dvh)
%user input section
clc; disp('Welcome to the Equivalent Uniform Dose (EUD)-Based Model Program'); disp(' ');
disp('Please note that: 1) the variable dvh should be a CUMULATIVE, not differential, DVH');
disp('                  2) the program assumes that all treatment fractions are equal');
disp(' '); disp(' ');
%end of user input section
%verifying that the cumulative DVH has at least 2 rows and columns
 [nb,N]=size(dvh);
if (nb < 2)
    disp('Error: Cumulative dvh must have at least 2 rows.'); return;
end
if (N < 2)
    disp('Error: Cumulative dvh must have at least 2 columns.'); return;
end
%verifying that the cumulative DVH has no negative numbers in the dose or volume columns
for i=1:nb
    if (dvh(i,1) < 0)
        message = sprintf('Error: Dose data error. dvh column 1, row %g is negative',i);
        disp(message); return;
    end
    if (dvh(i,2) < 0)
        message = sprintf('Error: Volume data error. dvh column 2, row %g is negative',i);
```

Figure 1: EUD model code for calculating TCP & NTCP in MATLAB

Table 1: Radiobiological parameters for NTCP and TCP calculations.

Type	**Organ**	A	γ_{50}	**TCD50|TD50**	α/β
Tumor	Microscopic Squamous cell	-13	2.6	35.4	10
Critical organ	Brain stem	7	3	65	2.1
	Spinal cord	13	4	66.5	3.0
	Optic chiasm	25	3	65	3.0
	Parotid gland	0.5	4	46	3.0

3.5. Statistical Analysis

The statistical analysis was carried out using two-way ANOVA using SPSS®25(IBM Corp. Released 2013). Data were treated as a complete randomization design according to Steel *et al.* (1997). Multiple comparisons were carried out applying Duncun test. The significance level was set at < 0.05.

4. Results and Discussion

TCP indicates how effectively the treatment plan is killing cancer cells. So the high values of TCP are desirable. Unless the critical normal cells suffer significant harm.

Mean and standard deviation of TCP and NTCP for parotid glans and chiasm with respect to algorithm and grid size variation are detailed in table 2.

The average value of TCP was 94.13 ±12.80% for the 2 mm grid size and 95.16 ±10.05% for 5 mm with MC algorithm. Statistically there was significance difference between two plans ($p < 0.05$). For PB algorithm, the average TCP value was 91.78 ±19.54% and 93.04 ±17.13% for 2 mm and 5 mm respectively with $p < 0.05$.

The largest TCP of PTV60 was 95.2% for MC and 3 mm. The lowest value was 91.8% for PB and 2 mm. On the other hand, NTCP indicates how much the damage caused by the treatment plan occurs in critical healthy cells. The lower NTCP values is favorable if the acceptable target coverage has been achieved.

In comparison between MC and PB plans, the NTCP of PB algorithm plans were greater for brainstem, spinal cord, and chiasm compared to MC algorithm plans.

The largest NTCP of the right and left parotid glands were 0.493% and 1.04% for MC, 5 mm. The lowest values were 0.41% and 0.76% for MC, 2 mm respectively.

The largest NTCP of chiasm was 0.17% for PB, 2 mm. The lowest value was 0.06 for MC, 4 mm.

All NTCP values of the spinal cord and brainstem were less than 0.1%, in all cases.

The TCP and NTCP values for spinal cord and brainstem represented in figures 2, 3, and 4 for eleven patients and the average values respectively. From figures it was found that TCP slightly increased with increasing grid size. This contradicts to the studies Shiv P. Srivastava et al., 2016 and James C.L. Chow et al., 2017 [11, 16]. Which found that the TCP decreased with increasing grid size and NTCP increased. In this study the NTCP of both parotids increased with MC and it changed with PB. Also, it is found that the NTCP values of chiasm decreased with increasing grid.

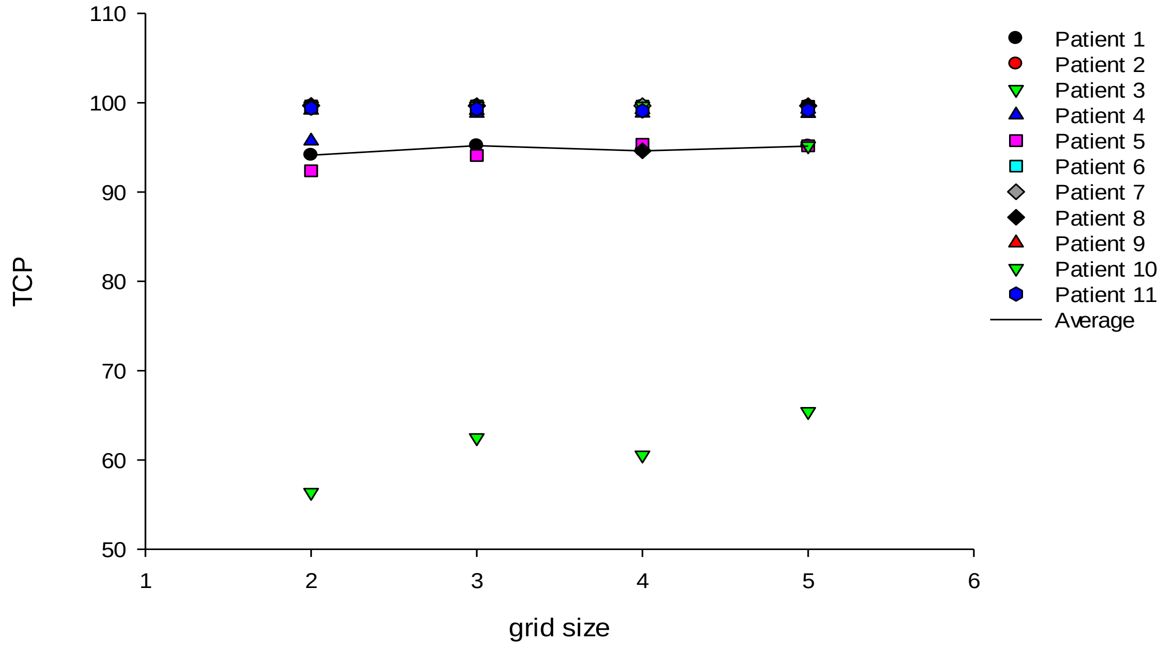
Table 2: Mean and standard deviation of TCP and NTCP.

TCP/ NTCP	Algorithm	Grid Size (mm)			
		2	3	4	5
		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
TCP	Monte Carlo	94.13 ± 12.80^{aB}	95.20 ± 11.02^{aA}	94.62 ± 11.49^{aB}	95.16 ± 10.05^{aA}
	Pencil Beam	91.78 ± 19.54^{bC}	92.30 ± 18.31^{bB}	92.91 ± 18.10^{bA}	93.04 ± 17.13^{bA}
Parotid RT	Monte Carlo	0.4061 ± 1.2182^{bC}	0.4283 ± 1.2848^{aB}	0.4913 ± 1.3181^{aA}	0.4938 ± 1.3248^{aA}
	Pencil Beam	0.4549 ± 1.3646^{aA}	0.4457 ± 1.3370^{aA}	0.4868 ± 1.4603^{aA}	0.4703 ± 1.4108^{bA}
Parotid LT	Monte Carlo	0.7594 ± 2.1462^{bB}	0.8043 ± 2.2733^{aB}	0.9411 ± 2.3455^{aA}	1.0386 ± 2.5889^{aA}
	Pencil Beam	0.8439 ± 2.3853^{aA}	0.8267 ± 2.3366^{aA}	0.9319 ± 2.6340^{aA}	0.9144 ± 2.5841^{bA}
Chiasm	Monte Carlo	0.1460 ± 0.2167^{bA}	0.1228 ± 0.1821^{bAC}	0.0651 ± 0.1079^{bD}	0.1194 ± 0.1791^{bB}
	Pencil Beam	0.1716 ± 0.2472^{aA}	0.1562 ± 0.2360^{aAB}	0.1420 ± 0.2098^{aB}	0.1474 ± 0.2217^{aB}

SD: standard deviation, RT: right, LT: left.

- a, b, c: there is no significant difference (P>0.05) between any two means, within the same column have the same superscript letter.
- A, B, C: There is no significant difference (P>0.05) between any two means for the same attribute, within the same row have the same superscript letter.

a



b

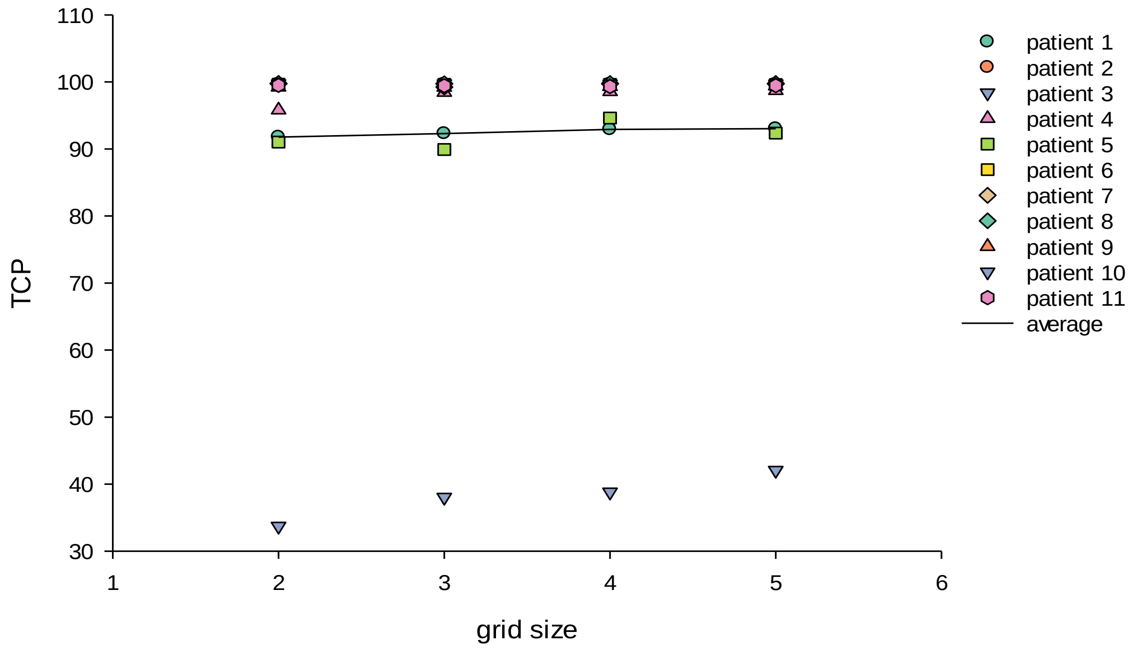


Figure 2: TCP for PTV60 for eleven patients and the average value, a represents values with Monte Carlo algorithm, b represents values with Pencil Beam algorithm.

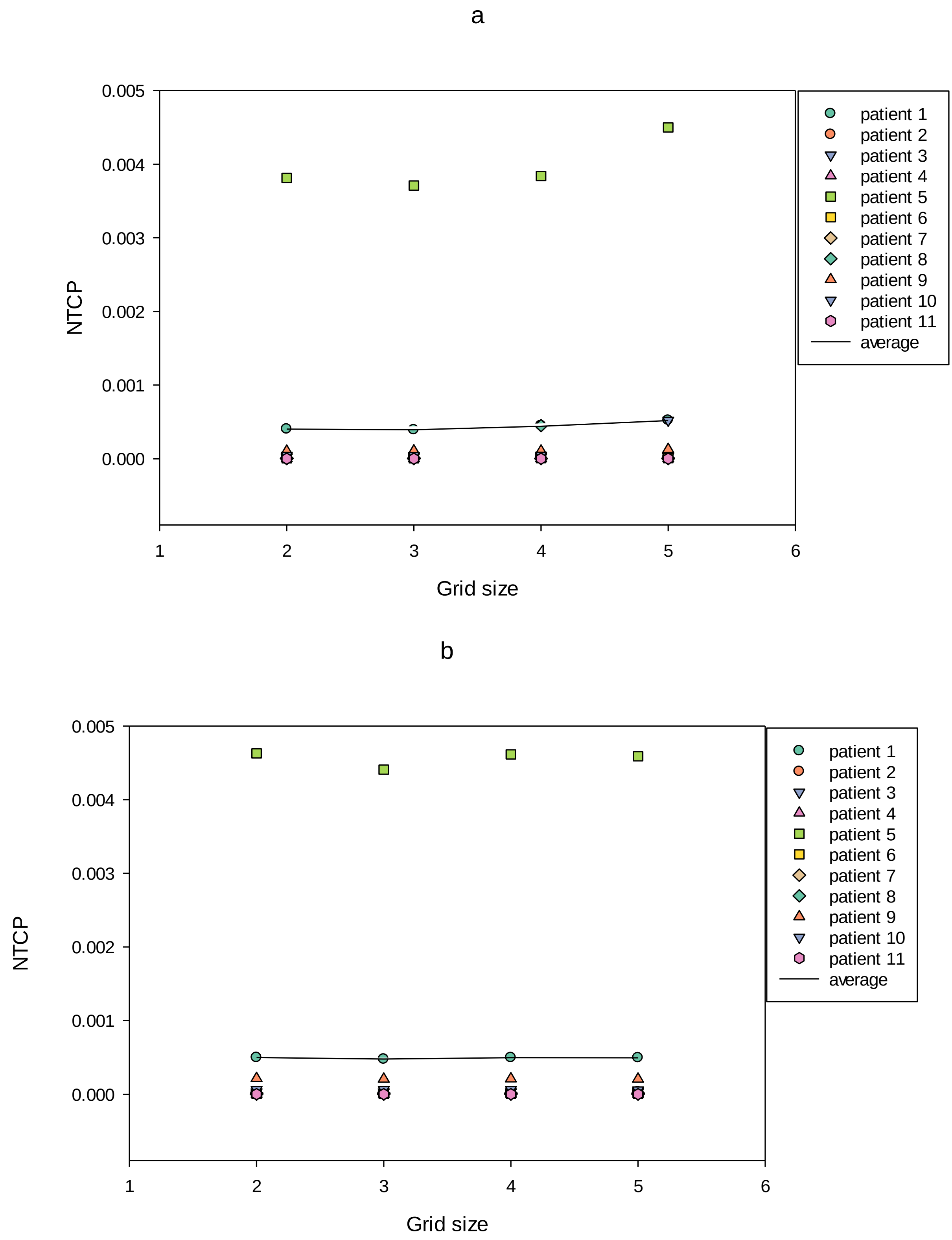


Figure 3: NTCP for spinal cord for eleven patients and the average value, a represents values with Monte Carlo algorithm, b represents values with Pencil Beam algorithm.

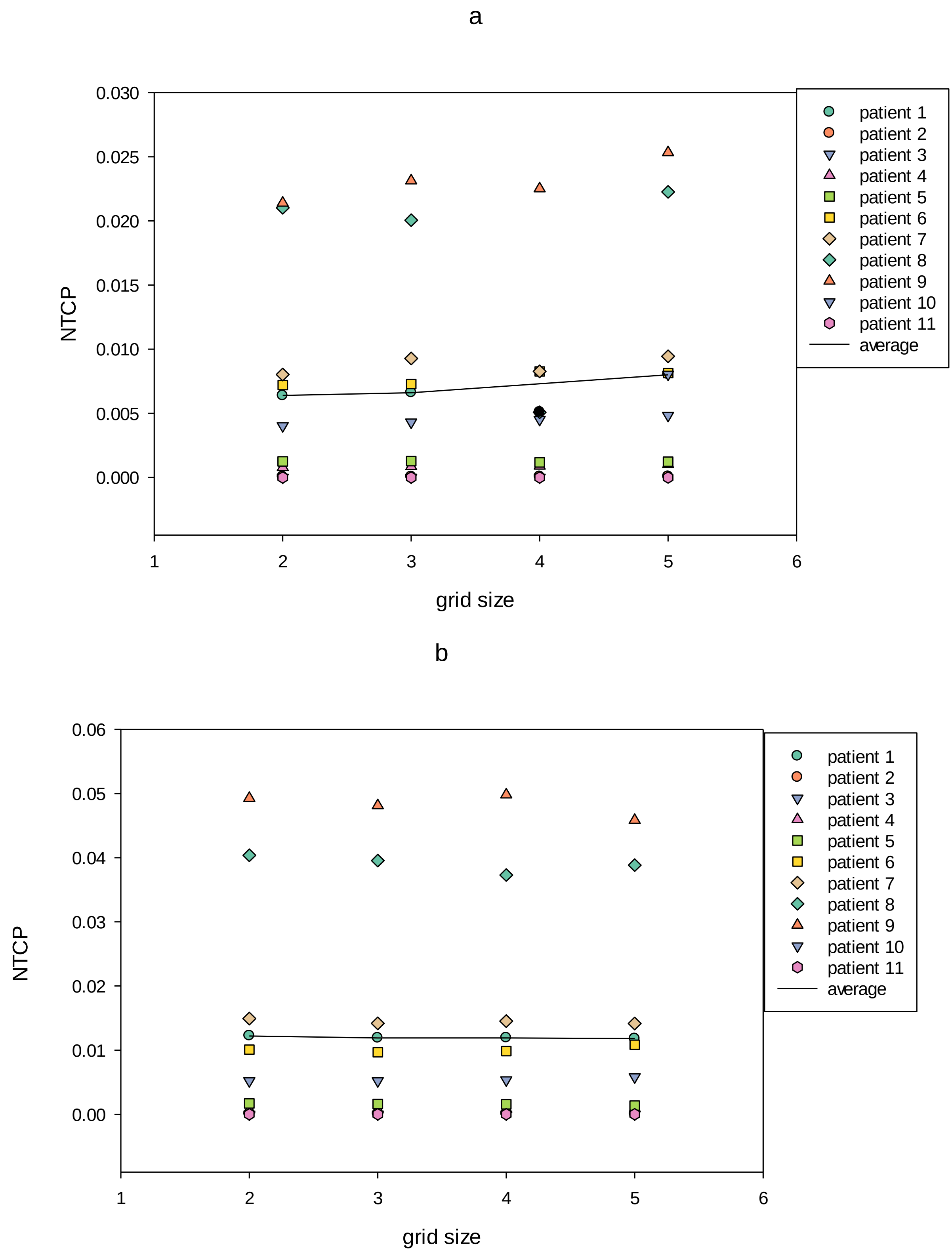


Figure 4: NTCP for brainstem for eleven patients and the average value, a represents values with Monte Carlo algorithm, b represents values with Pencil beam algorithm.

Table 3: P values for TCP and NTCP of PTV and critical structures.

TCP/ NTCP	P- value	
	algorithm	Grid size
TCP	0.000	0.000
Brainstem	0.000	0.08
Spinal cord	0.01	0.09
Parotid gland RT	0.5	0.04
Parotid gland LT	0.8	0.01
Chiasm	0.001	0.01

From the previous studies it is found that smaller grid sizes can provide more accurate dose calculations, but it can also increase the computational time. Furthermore, different algorithms employed in IMRT planning, such as Pencil Beam or Monte Carlo, can also impact the accuracy and efficiency of dose calculations.

The results of this study demonstrate that the choice of grid size and algorithm can significantly affect the radiobiological outcomes of IMRT plans. The study indicate that decreasing grid size can improve the accuracy of dose calculations, particularly in regions with complex anatomy such as the head and neck area. The use of smaller grid sizes resulted in improved target coverage and reduced doses to organs at risk. However, this improvement in accuracy came at the cost of increased computational time. These results are consistent with previous studies that have demonstrated the importance of grid size in IMRT planning [17, 8]. The Monte Carlo algorithm was found to provide more accurate dose calculations compared to the pencil beam algorithm, particularly in regions with high-density heterogeneities. These results are in agreement with previous studies that have demonstrated the superiority of Monte Carlo algorithms in simulating complex radiation transport [18, 19].

5. Conclusion

In conclusion, this study provides a comprehensive radiobiological evaluation of the impact of different grid sizes and algorithms on head and neck IMRT plans. The results of this study demonstrate that the choice of grid size and algorithm can significantly affect the radiobiological outcomes of IMRT plans, including target coverage and doses to organs at risk.

The study's findings highlight the importance of considering the interplay between grid size and algorithm in IMRT planning, and provide valuable insights for clinicians and physicists to optimize treatment planning and improve patient outcomes. The results of this study suggest that the use of smaller grid sizes and Monte Carlo algorithms can improve the accuracy of IMRT plans, leading to better treatment outcomes and reduced toxicity to normal tissues.

However, the study's findings also underscore the need for careful consideration of the computational time and resources required for these approaches, as well as the potential limitations and uncertainties associated with IMRT planning. Further studies are needed to validate these findings in larger patient populations and to investigate the impact of other factors that can influence IMRT planning.

6. References

[1] T. Zhou, W. Huang, X. Wang, J. Zhang, E. Zhou, Y. Tu, J. Zou, K. Su, H. Yi and S. Yin, "Global burden of head and neck cancers from 1990 to 2019," *iScience,* 2024.

[2] A. Ali, M. Rshbek, A. Mohamed, M. Meselhy, E. M. Attalla and S. M. Sallam, "Impact of Different Grid Sizes and Different Dose Calculation Algorithms on Dosimetric Parameters for Head and Neck IMRT.," *Egypt. J. Biophys. Biomed. Eng,* vol. 25, 2024.

[3] H. Niko, X. Dafina, K. Theodhor and T. Ervis, "calculation Methods in Radiotherapy Using MATLAB," *J. Int. Environmental Application & Science,* 2014.

[4] A. Chaikh, J. Ojala, C. Khamphan, R. Garcia, J. Y. Giraud, J. Thariat and J. Balosso, "Dosimetrical and radiobiological approach to manage the dosimetric shift in the transition of dose calculation algorithm in radiation oncology: how to improve high quality treatment and avoid unexpected outcomes.," *Radiation Oncology,* 2018.

[5] Y. Kim and W. A. Tome, "On the radiobiological impact of metal artifacts in head-and-neck IMRT in terms of tumor control probability (TCP) and normal tissue complication probability (NTCP)," *Med Bio Eng Comput,* vol. 45, 2007.

[6] J. v. d. Veen and S. Nuyts, "Intensity modulated radiotherapy for head-and-neck cancer: discussing

safety of modern radiation techniques," *Transl Cancer Res,* vol. 6, 2017.

[7] N. Y. Lee and Q.-T. Le, "NEW DEVELOPMENTS IN RADIATION THERAPY FOR HEAD AND NECK CANCER: INTENSITY MODULATED RADIATION THERAPY AND HYPOXIA TARGETING," *Semin Oncol,* vol. 35, 2008.

[8] S. P. Srivastava, C.-W. Cheng and I. J. Das, "The dosimetric and radiobiological impact of calculation grid size on head and neck IMRT," *Practical Radiation Oncology,* vol. 16, 2016.

[9] R. Nuraini and R. Widita, "Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP) with Consideration of Cell Biological Effect," *Journal of Physics,* 2019.

[10] M. Zaider and G. N. Minerbo, "Tumour control probability: a formulation applicable to any temporal protocol of dose delivery," *Phys. Med. Biol.,* 2000.

[11] S. p. Srivastava, C.-W. Cheng and I. J. Das, "The dosimetric and radiobiological impact of calculation grid size on head and neck IMRT," *Practical Radiation Oncology,* vol. 7, 2016.

[12] D. T. Tai, L. T. Oanh, P. H. Phuong, A. Sulieman, F. A. Abolaban, H. Omer and J. C. Chow, "Dosimetric and radiobiological comparison in head-and-neck radiotherapy using JO-IMRT and 3D-CRT," *Saudi Journal of Biological Sciences,* vol. 29, 2022.

[13] G. Narayanasamy, A. Pyakuryal, S. Pandit, J. Vincent, C. Lee, P. Mavroidis, N. Papanikolaou, M. Kudrimoti and T. sio, "Radiobiological Evaluation of Intensity Modulated Radiation Therapy Treatments of Patients with Head and Neck Cancer: A

Dual-Institutional Study," *Medical Physics,* vol. 40, 2015.

[14] A. K. Srivastava, M. Rastogi and S. Mishra, "Evaluation of Tumor Control and Normal Tissue Complication Probability in Head and Neck Cancers with Different Sources of Radiation: A Comparative Study," *Iran J Med Phys,* vol. 14, 2017.

[15] G. Martin-Martin, . S. Walter and E. Guibelalde, "Dose accuracy improvement on head and neck VMAT treatments by using the Acuros algorithm and accurate FFF beam calibration," *Reports of Practical Oncology and Radiotherapy,* vol. 26, 2021.

[16] J. C. Chow and R. Jiang, "Dose-volume and radiobiological dependence on the calculation grid size in prostate VMAT planning," *American Association of Medical Dosimetrists,* 2017.

[17] H. Chung, J. Palta, H. Jin, T. Suh, C. Liu and S. Kim, "TH-C-T-6E-10: The Impact of Calculation Grid Size On the Accuracy of IMRT Dose Distribution," *Medical physics,* vol. 32, 2005.

[18] Y. Elcim, B. Dirican and O. Yavas, "Dosimetric comparison of pencil beam and Monte Carlo algorithms in conformal lung radiotherapy," *J Appl Clin Med Phys,* 2018.

[19] S. . J. Kim, S. K. Kim and D. H. Kim, "Comparison of Pencil-beam, Collapsed-cone and Monte-Carlo Algorithms in Radiotherapy Treatment Planning for 6-MV photons," *Journal of the Korean Physical Society,* vol. 67, 2015.