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Dosimetric Impact on IMRT Plans of Altering Per Control Point Statistical Uncertainty in Monaco TPS

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ABSTRACT

Intensity-Modulated Radiation Therapy (IMRT) uses computer-controlled linear accelerators to deliver precise radiation doses to benign or malignant tumors or specific areas within tumors while minimizing exposure to healthy tissues and organs at risk. The purpose of this study is to evaluate the dosimetric impact on IMRT plans of changing the per control point Statistical Uncertainty (SU) from 1% to 6% in 1% increments using the Monaco Treatment Planning System (TPS) for three different diagnoses: Larynx, Oesophagus, and Prostate. The per control point SU is a key factor in determining dose calculation accuracy and calculation time. In this study, 54 IMRT plans were generated by varying the per control point SU as 1%, 2%, 3%, 4%, 5%, and 6%, using nine patients for each diagnosis. Dosimetric indices, including Conformity Index, Heterogeneity Index, Target Dose (PTV), Organ At Risk doses, Dose Calculation Time, Treatment Delivery results, and Dose Volume Histogram, were used to evaluate the generated plans. No significant differences were observed across all dosimetric indices, and an exponential relationship was found between Dose Calculation Time and the per control point SU. For IMRT plans, a 3% per Control Point SU is acceptable, providing shorter and adequately accurate dose calculation times without compromising plan quality or deliverability.

Keywords: Radiotherapy, IMRT, dosimetric impact, Per Control Point, Statistical Uncertainty

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INTRODUCTION

Radiotherapy is a medical treatment that uses high doses of radiation (gamma rays, high-energy X-rays, and Electrons) to kill or damage benign and malignant tumors (Hall & Giaccia, 2019). It is a crucial component of cancer treatment and is employed either as radiotherapy itself or in combination with surgery, chemotherapy, or immunotherapy (Delaney, Jacob, Featherstone, & Barton, 2005). Radiotherapy can be given inside or outside of our bodies. The most common kind is External Beam Radiation Therapy (EBRT). It uses a large machine called a Linear Accelerator (Linac) to treat cancer patients using high-energy X-rays and electrons. At present, there are other advanced types of machines used for radiotherapy treatment too. Such as Tomotherapy machine, Cyberknife machine, MR-Lianc, PET-Linac, ProBeam machine, GammaKnife machine, and ZAP-X machine (Palta & Mackie, 2011). There are ordinary and advanced treatment techniques currently used in the oncology field using those advanced machines. Such as three-dimensional conformal Radiotherapy (3DCRT), Intensity-Modulated Radiation Therapy (IMRT), Image-Guided Radiation Therapy (IGRT), Volumetric Modulated Arc Therapy (VMAT), Stereotactic Body Radiation Therapy (SBRT), Proton Therapy, and Adaptive Radiation Therapy (ART) (Khan & Gibbons, 2014). Apart from those machines, the cobalt 60 machine is used to treat cancer patients using Gamma-rays, and it is an older version of a raditherapy treatment machine (Podgorsak, 2005).

Intensity-Modulated Radiation Therapy, also called IMRT, is an advanced type of radiation therapy technique, and it is an inverse planning technique (Bortfeld, 2006). Inverse planning is a technique that uses a computer program to automatically achieve a treatment plan that has an optimal merit. Here, it is less dependent on the geometric parameters but more on the specification of volumes of tumor targets and organs at risk, as well as their dose constraints. IMRT uses computer-controlled linear accelerators to deliver precise radiation doses to a benign or malignant tumor or specific areas within the tumor. IMRT allows for the radiation dose to conform more precisely to the three-dimensional (3-D) shape of the tumor by modulating or controlling the intensity of the radiation beam in multiple small segments. Also, IMRT allows higher radiation doses to be focused on the tumor while minimizing the dose to surrounding normal critical structures. Because the ratio of normal tissue dose to tumor dose is reduced to a minimum with the IMRT approach, higher and more effective radiation doses can safely be delivered to tumors with fewer side effects compared with conventional radiotherapy techniques. IMRT also has the potential to reduce treatment toxicity, even when doses are not increased. Due to its complexity, IMRT does require slightly longer daily treatment times, additional planning, and safety checks before starting the patient treatment (IMRT Patient Specific Quality Assurance) when compared with conventional radiotherapy (Gupta, Agarwal, Ghosh-Laskar, & Shrivastava, 2009).

IMRT was first conceptualised in the 1960s (Intensity Modulated Radiation Therapy Collaborative Working Group, 2001). Although the concept of IMRT and early algorithms for planning were developed in Sweden, clinical application did not begin until a fully integrated IMRT planning and delivery system, namely, the NOMOS Peacock system, was invented and commissioned in 1993 by the collaborated effort between NOMOS and Baylor College of Medicine/the Methodist Hospital (Houston, TX, USA) (Mohan, 2005). After obtaining investigational device exemptions and protocol approval by Baylor's Investigational Review Board, the first patient with brain metastases was to have three brain tumors treated simultaneously using IMRT in September 1993 (Lawrence & Cox, 1995). In 1994, the NOMOS Peacock system was introduced as the first commercial IMRT delivery unit. The Peacock system required the use of a beam modulation device known as a dynamic multivane intensity-

modulating collimator (MIMiC). This particular form of IMRT, called serial tomotherapy, could be treated by a continuously rotating gantry (Carol, 1995). Step and shoot IMRT represents another commonly used technique whereby multiple static beams are subdivided into 'segments' (LoSasso, Chui, & Ling, 1998). In the sliding window technique (dynamic Multileaf Collimator- dMLC), a window defined by the MLC leaves sweeps across the treatment field at variable speed, while the monitor units are delivered continuously (Zhang et al., 2007).

Dose calculation accuracy in IMRT is an important and crucial factor to prevent mistreatment of radiation treatment delivery using linear accelerator machines (Papiez & Langer, 2006). Among the commercially available dose calculation algorithms, Monte Carlo (MC) is considered to be potentially more accurate and complex than others. Although MC dose calculation algorithms are recognized as the most accurate dose computation algorithms for treatment planning, their inherent Statistical Uncertainty (SU) determines the accuracy of the dose calculation and the time span of the dose calculation (Taleei & Tabrizi, 2019). The SU decreases inversely with the square root of the time span of the dose calculation. By decreasing the SU, one can increase the dose calculation accuracy. But the SU decreases, resulting in a significant increase in the time span of the dose calculation. Therefore, it should be a compromise between the SU and the dose calculation accuracy, with a suitable time span for the dose calculation in IMRT planning. Therefore, by studying this, it is possible to get an idea about how to optimize the accuracy of the dose calculation and the SU with a suitable time span of the dose calculation in IMRT planning (Chetty et al., 2007).

There are many Treatment Planning Systems (TPSs) that can be used to develop IMRT plans, utilizing their own dose calculation algorithm (Vassiliev et al., 2010). The Elekta's Monaco TPS is one of the most powerful tool that bring increased automation, intelligent workflows, and high-quality treatment planning to a wide range of radiotherapy treatment delivery systems.

The Monaco TPS combines the MC dose calculation algorithm with robust optimization tools to provide high-quality radiotherapy treatment plans for IMRT, VMAT, and SBRT (Goodall & Ebert, 2020). The Monaco 5.11.02 TPS used two kinds of SUs. Such as per control point SU and per calculation SU, and the planner can manually select one of them. In this research, we used a per control point SU to generate IMRT plans. Also, the Monaco 5.11.02 TPS has an option to choose different percentage values between 0.1% - 10 % (Kry et al., 2019). In the per control point SU, the percentage uncertainty is based on the per voxel on a per segment. Also, the uncertainty was not the same in all voxels. The low-dose voxels in the peripheral regions of the patient had a higher uncertainty of dose than the voxels in the region of the maximum dose (PTV) (Keall, Siebers, Jeraj, & Mohan, 2000). The dose uncertainty in the target volume (PTV) for the final plan was calculated and appeared in the TPS console window after the second stage dose calculation.

There are a few other studies that have previously evaluated the overall effect of SU on dose calculation. But not about altering the per control point SU in IMRT plans. In 2000, Keall, Siebers, Jeraj, and Mohan (2000) found that the dose in Monte Carlo (MC) calculation does not significantly affect isodose lines and Dose Volume Histogram (DVH) for SU of 2% or lesser values. In 2004, Cheong, Suh, and Cho (2004) investigated the effect of SU on photon dose calculation using BEAMnrc and DOXXYZnrc MC simulation systems and evaluated SU based on DVH, isodose comparison, and root mean-square. In 2005, Ma et al. (2005) studied the issues related to the statistical analysis of MC dose calculations for realistic clinical beams using various variance reduction or time-saving techniques. Also, they discussed the effect of statistical uncertainties on dose prescription and monitor unit calculation for conventional treatment and IMRT based on MC simulations.

In 2016, Sarkar et al. (2016) investigated the interplay between Monte Carlo Variance (MCV) and Fluence Smoothing Factor (FSF) in VMAT for carcinoma of esophagus patients using a CMS-Monaco^{TM} Treatment Planning System (TPS). They reported that variation in FSF causes a difference in dosimetric and physical parameters for the treatment plan. In 2019, Palanisamy et al. (2019) explored the dosimetric impact of varying SU when calculating the dose of VMAT plans, and in 2021, Rembish et al. (2021) determined the severity of the effects on VMAT dose calculations caused by varying per control point SU in an MC-based TPS. Also, they assessed the impact of the uncertainty during DVH evaluation.

The goal of IMRT planning is to shape the radiation dose to avoid or reduce exposure of healthy tissue and limit the side effects of treatment while delivering a therapeutic dose to the cancer. According to the best of our knowledge, no precise data are available for the optimal acceptance level of SU% % per control point for different diagnoses in IMRT.

Also, no one studied the Dosimetric Impact on IMRT Plans of altering the per control point SU in Monaco TPS. Therefore, the purpose of this study is to evaluate the dosimetric impact on IMRT plans of altering the per control point SU (1% - 6%) using Elekta's Monaco TPS for three different diagnoses (Larynx, Esophagus, and Prostate).

METHODOLOGY

CT Simulation and Radiotherapy Treatment Machine

In this research work, three different diagnoses, which have high diversity, such as the Larynx, Oesophagus, and Prostate, were planned using the IMRT technique. A total of nine patients, three from each diagnosis, were selected for this study. The necessary CT image sets of all nine patients were obtained using a CT simulator (Siemens Healthineers, SOMATOM Confidence). The CT slice thickness of 5 mm was obtained for each clinical case for treatment planning. All generated IMRT plans were delivered using a 6 MV photon beam of Elekta Synergy Platform linear accelerator and its having a 1 cm multi-leaf collimator (MLC) at the iso-center.

Contouring and Dose Prescription

The tumor volume (Planning Target Volume - PTV) and Organs At Risk (OARs) volumes were contoured, and the doses prescribed to the Larynx, Oesophagus, and Prostate were 66 Gy/30 fractions, 50.4 Gy/28 fractions, and 78 Gy/39 fractions, respectively.

Treatment Planning System (TPS)

In this research work, the Monaco 5.11.02 TPS (IMPAC Medical System, Inc., Maryland Heights, MU, USA) was used to generate IMRT plans. It has a two-stage process of optimizing dose distribution. At the first stage, the ideal fluence distribution of a beam is optimized to meet a user-defined prescription for a single set of beams. At the second stage, the ideal distribution is transmitted into a set of segments where the shapes and weights are optimized based on the same prescription. For this research work, the Monte Carlo (MC) algorithm was used for dose calculation to generate an IMRT plan.

The Dosimetric Parameters used in Monaco TPS

All the 54 IMRT plans were generated using the dosimetric parameters, which are given in Table 1 below. By keeping these parameters constant, IMRT plans were generated using MC dose calculation algorithm only by varying per control point SU 1%, 2%, 3%, 4%, 5%, and 6%. To analyze IMRT plans, different dosimetry indices were used as mentioned below.

Table 1. The Dosimetric Parameters used in Monaco TPS

Parameter	Value
Delivery Mode	dMLC
CT Slice Thickness	0.5 cm
Grid Size	0.3 cm
Beamlet Width	0.3 cm
Control Points	40
Segment Width	0.5 cm
Auto Flash Margin	0.2 cm
Surface Margin	0.3 cm
Target Margin	0.8 cm
Fluence Smoothing	Medium

Dosimetric Indices used for IMRT Plan Evaluation

In this study, we used several dosimetric indices for IMRT Plan evaluation. Such as, Conformity Index (CI), Heterogeneity Index (HI), Target Dose and Critical Organ Doses, Dose Calculation Time (DCT), Treatment Delivery Results (IMRT Patient Specific QA and Gamma Indices), and Dose Volume Histogram (DVH).

- Conformity Index (CI)

The Conformity Index (CI) describes the degree to which the prescribed isodose volume conforms to the shape and size of the target volume. This value is only reported for Monaco plans (Elekta, 2017). The CI formula is given in equation 1:

$$CI = \frac{V_{Rx}^2}{(TV * V_{RI})} \quad (1)$$

where, TV = Structure Volume, V_{Rx} = is the structure volume covered by the Dose of Interest and V_{RI} is the total volume of the Dose of Interest.

- Heterogeneity Index (HI)

The Heterogeneity Index (HI) describes the uniformity of dose within a target volume and is directly calculated from the statistics of the DVH. This value is only reported for Monaco plans (Elekta, 2017). The HI formula is is given in equation 2:

$$HI = \frac{D_{5\%}}{D_{95\%}} \tag{2}$$

where, D_5% is the dose delivered to the hottest 5% of the tissue volume. D_{95}% is the minimum dose received by 95% of the tissue volume.

- Target Dose and Organ At Risk (OAR) Doses

The target dose (Dose to PTV) was analyzed as D95% (the dose received by 95% of the volume of PTV and V95% (the volume received 95% of the prescribed dose). Moreover, the maximum dose (Dmax) and mean dose (Dmean) for PTV and Organ at Risk (OAR) were analyzed for all three clinical cases. The OAR dose constraints (Table 2) were taken from the Practical Radiotherapy Planning book (5th Edition) (Morris, Roques, Ahmad, & Loo, 2023).

Table 2: Organ at Risk (OAR) Dose Constraints

Organ	Constraint	Optimal	Mandatory
Brainstem	Dmax whole organ		54 Gy (60 Gy if PRV used)
Spinal Cord	Dmax to PRV (cord +5 mm or spinal canal)		50 Gy (48 Gy if concomitant chemotherapy)
Parotid Gland	Mean Dose	24 Gy	
Lens	Dmax	10 Gy	
Heart	Mean Dose	25 Gy	30 Gy
Heart	V30 Gy	45 %	
Heart	V40	30 %	
Lungs	V20 Gy	35 % (25 % if risk factors)	
Lungs	Mean Dose	18 Gy	
Bladder	V50 Gy	50 %	
Bladder	V60 Gy	25 %	50 %
Femoral Heads	V50 Gy	5 %	50 %
Kidney (each)	V20 Gy	25 %	30 %
Kidney (both)	V20 Gy	30 %	35 %
Rectum	V30 Gy	70 %	80 %
Rectum	V40 Gy	51 %	65 %
Rectum	V50 Gy	38 %	50 %
Rectum	V60 Gy	27 %	35 %
Rectum	V70 Gy	15%	20 %

- Dose Calculation Time (DCT)

The dose calculation time was measured from the Monaco TPS optimization console window, which could give the dose calculation start and end time for all IMRT plans with different per control point SU values ranging from 1% to 6%. The total calculation time was defined as the time difference between the start and finish time of the MC dose calculation. For this research work, HP Z840 workstations, 128 GB RAM, Intel(R) Xeon(R) CPU E5-2697 v3 @ 2.60GHz (2 processors), and the 64-bit Operating system were used.

- Treatment Delivery Results (IMRT Patient Specific QA and Gamma Indices

The MatriXXEvolution (IBA) instrument and myQA software (Version 2019-002 (2.12.15.0), IBA Dosimetry GmbH, Germany) were used for the IMRT patient-specific QA with Elekta Synergy Platform Linear Accelerator. The MatriXX Evolution has 1020 air vented pixel ionization chambers arranged in a 32 x 32 grid (except for the four corner positions where chambers are missing) that cover an active field of 24.4 cm x 24.4 cm at 100 cm Source to Detector Distance (SDD). The distance between the individual chambers is 7.62 mm center to center. The diameter is 4.5
mm. Also, this MatriXXEvolution includes a temperature and pressure sensor to perform an automated k (t, p) correction of the chamber signal. The effective point of measurement is 3 mm below the MartiXXEvolution housing surface. The measured data is then transmitted to a PC or laptop via a standard Ethernet interface in the PC or laptop. The two-dimensional (2D) Gamma indices were compared at the isocenter between measured dose and TPS planned dose based on the dose to distance agreement (3%, 3mm) with 5% threshold value.

- Dose Volume Histogram

A Dose Volume Histogram (DVH) is a histogram that represents radiation dose (cGy or %) in the x-axis and volume (%) in the y-axis in radiation therapy planning. DVHs are most commonly used as a plan evaluation tool. Also, it is used to compare doses from different plans or to different structures. DVHs were introduced by Michael Goitein and Verhey in 1979 (Shipley et al., 1979). The ”volume” referred to in DVH analysis is a target of radiation treatment, a healthy organ near a target, or an arbitrary structure, and DVH summarizes 3D dose distributions in a graphical 2D format. In present radiation therapy, 3D dose distributions are typically created in a computerized TPS based on a 3D reconstruction of a CT scan.

STATISTICLE ANAYLISYS

The Statistical analysis was performed for all three diagnoses (for 54 IMRT Plans) using the percentage variation technique. Also, the comparison results were represented using tables, figures, and charts with the aid of OriginPro and overleaf softwares.

RESULTS & DISCUSSION

The dosimetric parameters were evaluated using the results of dosimetric indices. Some similarities and differences were observed due to the impact of Monte Carlo (MC) dose calculation uncertainty (per control point). The comparison results were analyzed using descriptive and inferential statistics. For the comparison process, we used several statistical terms in Monaco 5.11.02 Treatment Planning System (TPS), like mean dose, and max dose. The mean dose (cGy or Gy) is the averaged sampled dose within the total volume of the structure that is within the calculation volume, and the max dose (cGy or Gy) is the largest sampled dose within the total volume of the structure that is within the calculation volume (ICRU, 2010).

According to the measured average results shown in Table 3-5, the PTV dose coverage slightly changed as the per control point Statistical Uncertainty (SU) increased from 1% - 6% for PTV Dmean, PTV D95% (dose received by 95% volume of PTV), and V95% (the volume received 95% of the prescribed dose). This is primarily due to the **nature of the MC dose calculation algorithm** used in the Monaco Treatment Planning System. The MC algorithm simulates particle interactions to calculate dose. A **higher SU** allows **fewer particle histories** (simulations), which **speeds up the calculation** but introduces **greater stochastic noise**. With higher SU, random dose fluctuations can slightly raise or lower the average depending on spatial variation of statistical noise (**Miften et al., 2018).**

However, the maximum dose to PTV (PTV Dmax) increased as the per control point SU increased from 1% to 6% with a significant dose difference. This is a well-known and expected behavior of **MC-based dose calculation** systems. Unlike D95% or Dmean (which are averages), **Dmax is based on one or a few voxels**. When SU increases, **even a single voxel with a random high dose** due to low sampling is enough to **raise Dmax** significantly. This makes Dmax particularly **unstable** at high SU values (Low, Moran, Dempsey, Dong, & Oldham, 2011).

The Global Max of the plan slightly increased with per control point SU. This is also a characteristic effect of **MC dose calculation noise.** The **Global Maximum Dose** is usually defined as the **dose in the single highest-dose voxel** in the entire 3D dose matrix. With higher SU, **random fluctuations** (positive outliers) in individual voxels are more likely. Therefore, one or a few voxels may report **artificially high dose values**, raising the Global Max (Low, Moran, Dempsey, Dong, & Oldham, 2011).

According to the measured average results given in Table 3, the mean dose to Organs at Risk (OARs) such as the left parotid and right parotid showed a small variation. The max dose to brain stem, spinal cord, left lens, and right lens also showed small dose differences. But no clinically and statistically significant dose differences were observed.

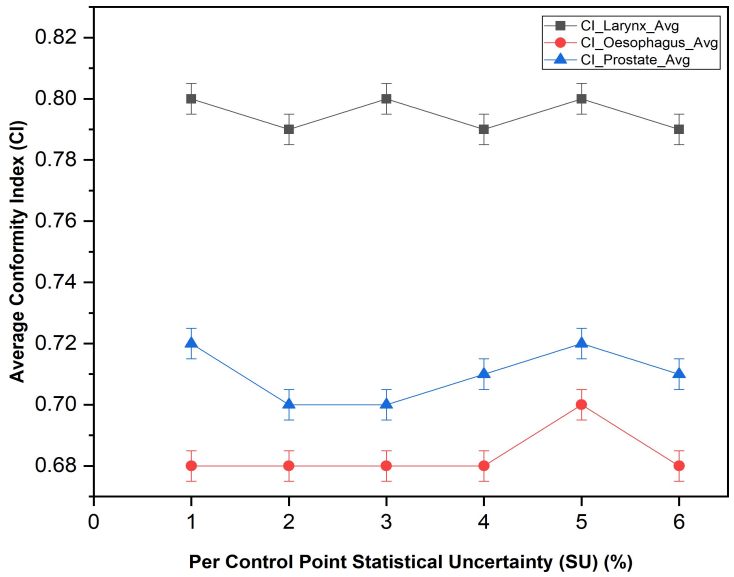

Figure 1. Average Conformity Index (CI) Vs. Per Control Point Statistical Uncertainty (SU) (%)

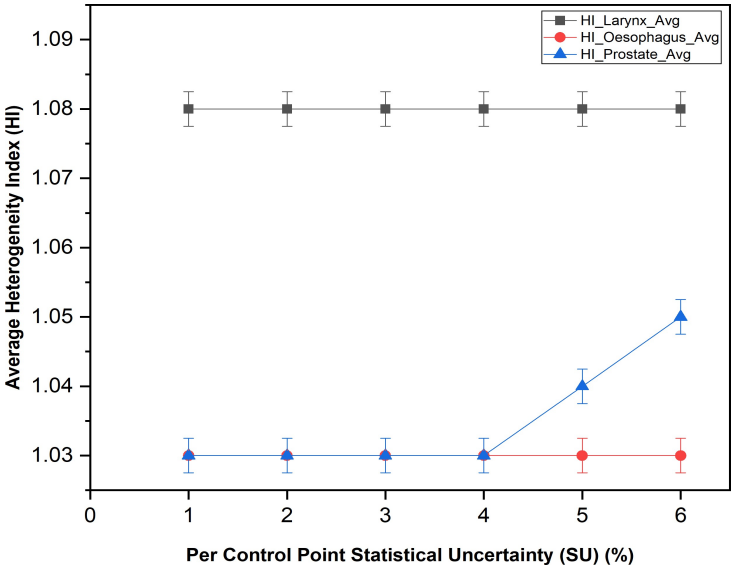

Figure 2. Average Heterogeneity Index (HI) Vs. Per Control Point Statistical Uncertainty (SU) (%)

According to the measured average results given in Table 4, the mean dose to OARs such as the heart, left lung and right lung, left kidney, and right kidney showed a small difference. The max dose to spinal code also showed a small dose difference. But no clinically and statistically significant dose differences were observed. According to the measured results given in Table 5, the mean dose to OARs such as the rectum, bladder, left pelvic bone, and right pelvic bone showed a small difference. But no clinically and statistically significant dose differences were observed.

According to the measured average results shown in Figure 1, no significant variation was observed between the Conformity Index (CI) values with per control point SU for Larynx, Oesophagus, and Prostate. A CI value of 1 indicates perfect conformity, but in clinical practice, values between 0.7 and 0.9 are considered acceptable, depending on the complexity of the case and treatment site (Feuvret et al., 2006).

There is a significant variation observed between Heterogeneity Index (HI) values with per control point SU for Prostate (Figure 2). This observation in **Monaco TPS** is indeed supported by studies focused on the **Monte Carlo-based dose calculation** used in Monaco. This behavior is particularly evident in **prostate IMRT/VMAT plans,** where the precision of dose gradients is affected by SU levels**.** The **higher per control point SU values can cause statistical noise,** leading to elevated **D5%** and suppressed **D95%** values—hence increasing the **HI** (Elekta AB, 2017).

According to the measured average results shown in Table 3-5, the gamma index (pass rate) (Miften et al., 2018), (Low et al., 2011) results showed a good pass rate of 97.5 % - 98.8 % for 3%, 3 mm dose to distance agreement with 5% threshold value for the per control point SU from 1% to 6% and no significant variation was observed by the influence of the per control point SU.

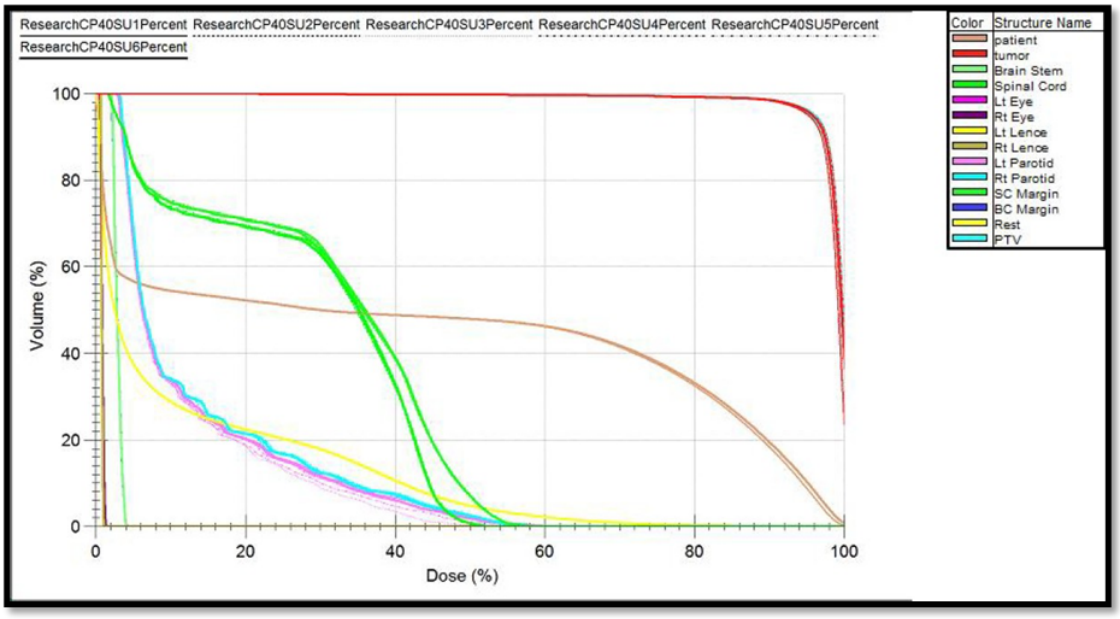

Figure 3. Average Dose Volume Histogram for Larynx

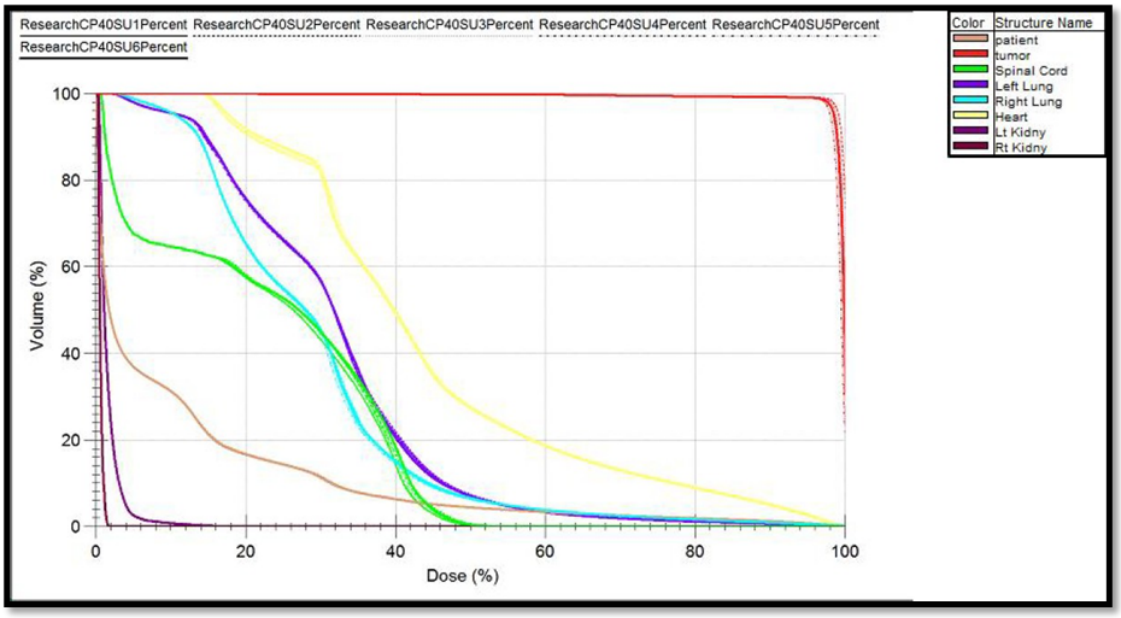

Figure 4. Average Dose Volume Histogram for Oesophagus

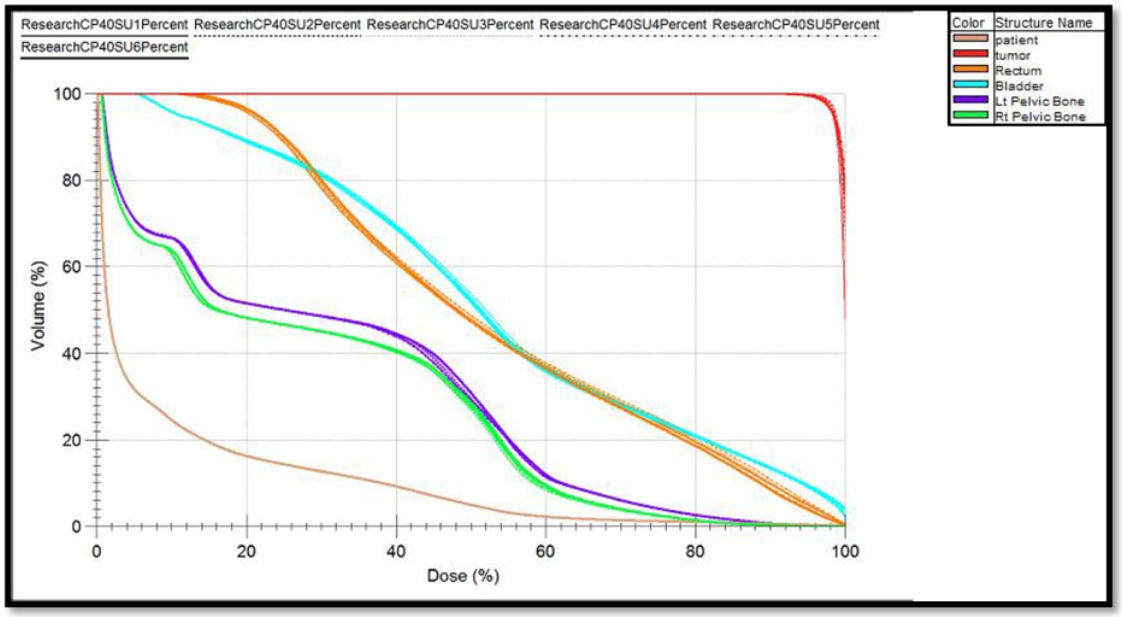

Figure 5. Average Dose Volume Histogram for Prostate

Figures 3-5 show the average Dose Volume Histogram (DVH) for Larynx, Oesophagus, and Prostate, respectively, for six different per control point SUs (Such as 1%, 2%, 3%, 4%, 5%, 6%). The measured average DVH results showed a very small dose difference between the per control point SU 1% - 6% and no significant dose differences were observed. According to the measured average results shown in Figure 6, there is an exponential relationship between dose calculation time and the per control point SU. The increase of per control point SU leads to a decrease in MC dose calculation time with a significant difference. Approximately reducing the per control point SU by a factor of two requires a four times increase in Central Processing Unit (CPU) time (Palanisamy, David, Durai, Bhalla, & Puri, 2019). Figure 7 indicates a linear relationship between average final dose uncertainty and the per control point SU values from 1% to 6%. The important fact is that the final dose uncertainty should be approximately 1% for the entire plan, and it shouldn't be greater than 1% for the entire plan (Elekta AB, 2017).

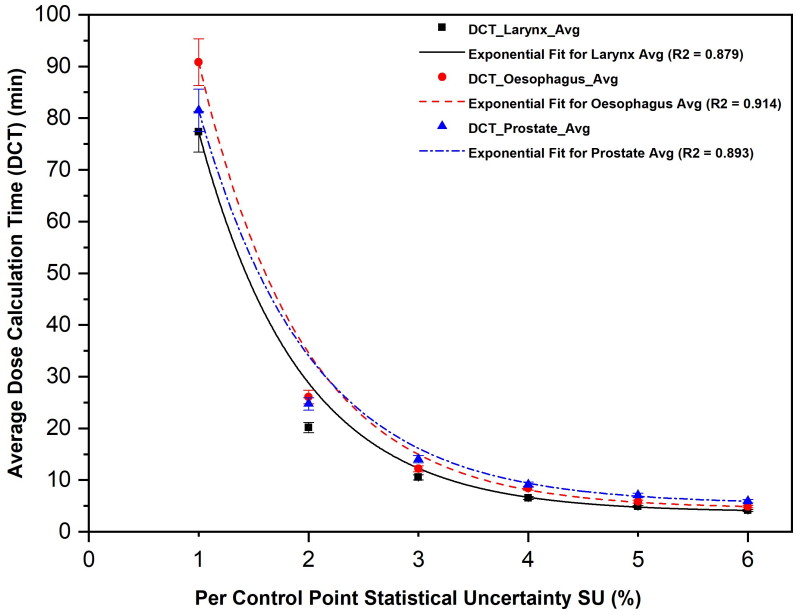

Figure 6. Average Dose Calculation Time (DCT) (min) Vs. Per Control Point Statistical Uncertainty (SU) (%)

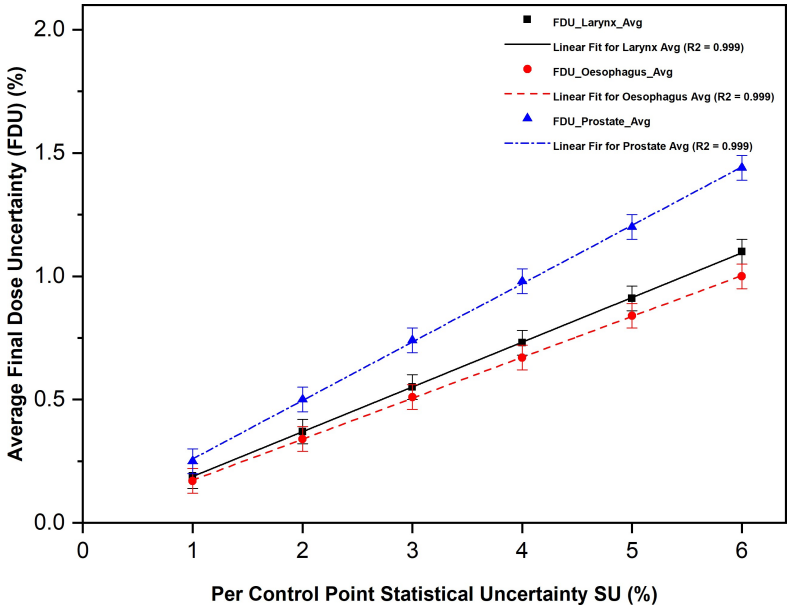

Figure 7: Average Final Dose Uncertainty (%) Vs. Per Control Point Statistical Uncertainty (SU) (%)

Table 3: Average Comparison Results of Dosimetric Indices for Different Per Control Point Statistical Uncertainty (SU) Levels for Larynx

Target and OARs Larynx	SU 1%	SU_2%	SU_3%	SU_4%	SU_5%	SU_6%
PTV 66 D95% (cGy)	6208.60 ±11.60	6238.73 ±23.11	6209.03 ±33.96	6219.47 ±45.65	6213.13 ±56.78	6224.47 ±68.31
PTV 66 Dmax (cGy)	6908.70 ±12.90	6924.47 ±25.63	6925.10 ±37.86	6932.83 ±50.85	6961.60 ±63.59	6982.30 ±76.58
PTV 66 Dmean (cGy)	6487.07 ±12.12	6511.67 ±24.11	6490.13 ±35.48	6501.53 ±47.69	6496.07 ±59.35	6512.03 ±71.43
PTV 66 V95% (%)	93.81 ±0.19	94.38 ±0.37	93.73 ±0.55	93.78 ±0.73	93.78 ±0.91	94.16 ±1.10
PTV 66 Heterogeneity Index	1.08 ±0.002	1.08 ±0.004	1.08 ±0.006	1.08 ±0.008	1.08 ±0.009	1.08 ±0.012
PTV 66 Conformity Index	0.80 ±0.001	0.79 ±0.003	0.80 ±0.004	0.79 ±0.006	0.80 ±0.007	0.79 ±0.009
Brain Stem Dmax (cGy)	1072.60 ±2.68	1202.47 ±6.08	1152.77 ±8.75	1136.80 ±11.36	1102.43 ±13.59	1164.63 ±17.52
Spinal Cord Dmax (cGy)	3680.90 ±6.89	3679.20 ±13.66	3678.57 ±20.14	3687.30 ±27.08	3712.33 ±33.93	3676.87 ±40.34
Lt Parotid Dmean (cGy)	1841.53 ±3.66	1794.90 ±7.13	1785.67 ±10.54	1819.60 ±14.29	1797.97 ±17.57	1792.87 ±20.91
Rt Parotid Dmean (cGy)	1775.77 ±3.50	1836.20 ±7.27	1824.23 ±10.63	1810.53 ±14.14	1790.10 ±17.29	1784.20 ±20.72
Lt Lens Dmax (cGy)	60.77 ±0.12	62.33 ±0.23	61.77 ±0.35	63.83 ±0.48	61.17 ±0.57	64.07 ±0.72
Rt Lens Dmax (cGy)	61.53 ±0.12	62.30 ±0.24	61.63 ±0.35	63.17 ±0.47	61.87 ±0.58	64.10 ±0.72
Global Max of the Plan (%)	104.68 ±0.19	104.92 ±0.37	104.92 ±0.55	105.11 ±0.73	105.48 ±0.91	105.96 ±1.10
Dose Calculation Time (mins)	77.32 ±3.91	20.14 ±1.02	10.54 ±0.53	6.55 ±0.33	4.90 ±0.25	4.14 ±0.22
Gamma Pass Rate 3%, 3 mm	98.1 ±2.94	98.5 ±2.95	98.3 ±2.95	98.6 ±2.96	98.4 ±2.95	98.8 ±2.96

Table 4. Average Comparison Results of Dosimetric Indices for Different Per Control Point Statistical Uncertainty (SU) Levels for Oesophagus

Target and OARs Larynx	SU 1%	SU_2%	SU_3%	SU_4%	SU_5%	SU_6%
PTV 50.4 D95% (cGy)	4950.47 ± 8.43	4963.87 ± 16.73	4952.93 ± 25.12	4955.83 ± 33.41	4939.50 ± 38.88	4949.03 ± 49.71
PTV 50.4 Dmax (cGy)	5189.47 ± 8.83	5209.37 ± 17.56	5210.03 ± 26.44	5212.10 ± 35.14	5226.63 ± 44.16	5261.10 ± 52.85
PTV 50.4 Dmean (cGy)	4997.70 ± 8.50	5013.07 ± 16.90	5002.13 ± 25.37	5010.37 ± 33.79	4999.80 ± 42.23	5011.73 ± 50.34
PTV 50.4 V95%	98.67 ± 0.17	98.71 ± 0.34	98.68 ± 0.51	98.73 ± 0.67	98.70 ± 0.84	98.71 ± 1.00
PTV 50.4 Heterogeneity Index	1.03 ± 0.002	1.03 ± 0.004	1.03 ± 0.005	1.03 ± 0.007	1.03 ± 0.009	1.03 ± 0.010
PTV 50.4 Conformity Index	0.68 ± 0.001	0.68 ± 0.002	0.68 ± 0.003	0.68 ± 0.005	0.70 ± 0.006	0.68 ± 0.007
Heart Dmean (cGy)	2303.07 ± 3.93	2278.23 ± 7.70	2285.87 ± 11.64	2276.40 ± 15.38	2273.73 ± 19.26	2290.83 ± 23.09
Spinal Cord Dmax (cGy)	3560.20 ± 6.23	3584.77 ± 12.43	3576.33 ± 18.70	3558.87 ± 24.73	3572.70 ± 31.15	3547.00 ± 36.66
Rt Lung Dmean (cGy)	1523.03 ± 2.61	1516.70 ± 5.11	1522.23 ± 7.74	1522.50 ± 10.28	1511.73 ± 12.79	1518.63 ± 15.28
Lt Lung Dmean (cGy)	1458.57 ± 2.49	1456.60 ± 4.92	1455.77 ± 740	1455.80 ± 9.83	1448.57 ± 12.26	1456.53 ± 14.65
Lt Kidney Dmean (cGy)	168.80 ± 0.38	167.77 ± 0.78	164.23 ± 1.12	162.93 ± 1.50	165.97 ± 1.91	162.77 ± 2.22
Rt Kidney Dmean (cGy)	40.70 ± 0.07	40.73 ± 0.15	40.80 ± 0.22	40.67 ± 0.29	40.57 ± 0.36	40.60 ± 0.43
Global Max of the Plan (%)	102.97 ± 0.17	103.36 ± 0.34	103.38 ± 0.51	103.42 ± 0.67	103.70 ± 0.84	104.39 ± 1.00
Dose Calculation Time (mins)	90.8 ± 4.66	26.06 ± 1.32	12.18 ± 0.62	8.42 ± 0.43	5.85 ± 0.30	4.89 ± 0.25
Gamma Pass Rate 3%, 3 mm	97.5 ± 2.93	98.3 ± 2.95	97.9 ± 2.94	98.1 ± 2.94	97.7 ± 2.93	98.4 ± 2.95

Table 5. Average Comparison Results of Dosimetric Indices for Different Per Control Point Statistical Uncertainty (SU) Levels for Prostate

Target and OARs_Larynx	**SU_1%**	**SU_2%**	**SU_3%**	**SU_4%**	**SU_5%**	**SU_6%**
PTV 78_D95% (cGy)	7657.57 ± 18.89	7672.97 ± 38.12	7681.73 ± 56.61	7662.20 ± 75.37	7633.23 ± 91.90	7615.20 ± 109.41
PTV 78_Dmax (cGy)	8046.73 ± 19.85	8075.70 ± 40.12	8118.27 ± 59.83	8139.67 ± 80.06	8132.50 ± 97.93	8202.93 ± 117.88
PTV 78 Dmean (cGy)	7793.60 ± 19.23	7811.20 ± 38.80	7822.13 ± 57.65	7810.90 ± 76.83	7813.40 ± 94.07	7827.07 ± 112.47
PTV 78_V95% (cm3)	99.43 ± 0.2	99.54 ± 0.50	99.53 ± 0.74	99.39 ± 0.98	99 ± 1.20	98.77 ± 1.44
PTV 78 Heterogeneity Index	1.03 ± 0.003	1.03 ± 0.005	1.03 ± 0.008	1.03 ± 0.010	1.04 ± 0.012	1.05 ± 0.014
PTV 78 Conformity Index	0.72 ± 0.002	0.70 ± 0.004	0.70 ± 0.005	0.71 ± 0.007	0.72 ± 0.009	0.71 ± 0.011
Rectum_Dmean (cGy)	4109.13 ± 9.89	4164.23 ± 20.69	4144.10 ± 30.53	4132.20 ± 40.63	4098.40 ± 49.35	4083.50 ± 58.68
Bladder_Dmean (cGy)	3778.87 ± 9.40	3811.00 ± 19.09	3801.77 ± 28.27	3768.13 ± 37.42	3741.43 ± 45.53	3741.30 ± 54.08
Lt Pelvic Bone_Dmean (cGy)	2168.93 ± 5.39	2180.77 ± 10.92	2170.37 ± 16.11	2159.70 ± 21.40	2181.27 ± 26.47	2193.07 ± 31.65
Rt Pelvic Bone_Dmean (cGy)	2189.97 ± 5.46	2189.70 ± 11.02	2199.67 ± 16.41	2187.13 ± 21.80	2200.87 ± 26.84	2223.80 ± 32.26
Global Max of the Plan (%)	103.21 ± 0.25	103.73 ± 0.50	104.08 ± 0.74	104.45 ± 0.98	104.37 ± 1.20	105.16 ± 1.44
Dose Calculation Time (mins)	81.5 ± 4.11	24.74 ± 1.24	14.03 ± 0.71	9.12 ± 0.47	7.06 ± 0.36	5.92 ± 0.30
Gamma Pass Rate_3%, 3 mm	97.1 ± 2.91	97.7 ± 2.93	97.5 ± 2.93	97.6 ± 2.93	97.2 ± 2.92	97.6 ± 2.93

DISCUSSION

The Monte Carlo (MC) methods are mainly used in three distinct problem classes: optimization, numerical integration, and generating draws from a probability distribution. In Monaco 5.11.02 TPS, MC was used for optimization, and the MC method has been identified as the gold standard for dose calculation (Clements, Schupp, Tattersall, Brown, & Larson, 2018). At present, MC simulation calculates the dose very closely to reality, taking into account the contribution of secondary photons and electrons scattering and dose absorption, especially in homogeneous environments (Tugrul, 2021). The per control point SU is the percentage (%) SU per voxel, on a per-segment basis, that is willing to accept for the final dose calculation. So, the mean, per voxel, uncertainty in a central region of the dose of a segment is equal to the user-specified SU at the end of the dose calculation. A voxel is a measurement of volume in a structure that is to be imaged. Each voxel represents a defined volume and can be localized by coordinates on a three-dimensional (3D) grid. Here, the very important fact is that the smaller the per control point SU, the longer the dose calculation time. Also, when we used per control point SU values between 0.1% - 10%, the results should be a final dose uncertainty of approximately 1% for the plan in the central region of the target volume.

The main difference between Per Calculation SU and Per Control Point SU is based on the number of histories (Uyar & Günekbay, 2023) and the voxel. In other words, Per Calculation SU is fast because it estimates the number of histories for the entire plan (recommended value 1%). Per control Point SU gives better resolution because it uses percentage uncertainty per voxel on a per-segment basis. So it should vary for the number of control points. In this work, we used 40 control points to generate each IMRT plan. The MC dose calculation without any SU is the most worthwhile in an IMRT plan from the accuracy point of view. However, it would take infinite time to calculate. So the planner should accept a certain range for this calculation uncertainty. The SU of MC is inversely proportional to the volume of the dose voxel (Mohan, Antolak, & Hendee, 2001). For example, when decreasing the voxel size from 5 mm to 3 mm, it caused to increase in the Monte Carlo calculation time of approximately fivefold. Also, when reducing the SU by a factor of two, it caused the MC calculation time to be fourfold (Figure 6). So it was very crucial in decreasing/ increasing voxel size or SU in both ways.

Overall analysis of this study suggests that there were no diagnosis-specific dosimetric variations. As reported by Jiang et al. (Jiang, Pawlicki, & Ma, 2000), large Statistical Uncertainties (SUs) are expected to blur the Dose Volume Histogram (DVH) curves and may become unreliable. The statistical noise should have practically no effect on inverse treatment planning (as IMRT) because the intensity along a ray is affected by the average of dose values over a large number of voxels lying along the ray and not by the dose in any one voxel (Mohan, Antolak, & Hendee, 2001).

It was suggested that large SU can be used for large tumors and OARs such as parallel organs (Palanisamy, David, Durai, Bhalla, & Puri, 2019). The effect of the per control point SU in this study showed no significant dose differences on the mean dose to the target and OAR volumes. So, it is suggested that SU can be used up to 5% for parallel organs. For the structures with small volumes (such as small tumors, lens), Monaco does not recommend using per control point SU higher than 5%. If we use a higher value (higher than 5%), it causes the system to underestimate the cost function value assigned to that structure (Elekta, 2017).

Significant variation was observed in average dose calculation time and the per control point SU. There is an exponential relationship observed between average dose

calculation time and the per control point SU (Figure 6). The dose calculation time may not be too long. Also, the gamma index showed a good pass rate for all three different diagnoses (such as Larynx, Oesophagus, and Prostate), and there are no significant variations were observed in the gamma pass rate for all three diagnoses. The final dose uncertainty should be approximately 1% for the entire plan (Elekta, 2017), and it shouldn't be greater than 1% for the entire plan (Figure 7).

Finally, based on all the measured average results, as well as considering other important factors and constraints, we recommend maintaining a control point SU value of 3% without compromising the quality or delivery of the plan. Additionally, we analyzed the percentage variations concerning the 3% per control point SU for the Larynx, Oesophagus, and Prostate (refer to Tables 6-8).

Table 6. Percentage Variation values with respect to 3% for Larynx

Target and OARs___Larynx (wrt.3%)	SU_1%	SU_2%	SU_4%	SU_5%	SU_6%
PTV_66_D95% (cGy)	0.01	0.48	0.17	0.07	0.25
PTV_66_Dmax (cGy)	0.24	0.01	0.11	0.53	0.83
PTV 66_Dmean (cGy)	0.05	0.33	0.18	0.09	0.34
PTV_66_V95% (%)	0.09	0.69	0.05	0.05	0.46
PTV 66 Heterogeneity Index	0	0	0	0	0
PTV_66_Conformity Index	0	1.25	1.25	0	1.25
Brain Stem_Dmax (cGy)	6.95	4.31	1.39	4.37	1.03
Spinal Cord_Dmax (cGy)	0.06	0.02	0.24	0.92	0.05
Lt Parotid_Dmean (cGy)	3.13	0.52	1.9	0.69	0.4
Rt Parotid_Dmean (cGy)	2.66	0.66	0.75	1.87	2.19
Lt Lens_Dmax (cGy)	1.62	0.91	3.33	0.97	3.72
Rt Lens_Dmax (cGy)	0.16	1.09	2.5	0.39	4.01
Global Max of the Plan (%)	0.23	0	0.18	0.53	0.99
Gamma Pass Rate_3%, 3 mm	0.20	0.20	0.31	0.10	0.51

Table 7: Percentage Variation values with respect to 3% for Oesophagus

Target and OARs Oesophagus (wrt.3%)	SU_1%	SU_2%	SU_4%	SU_5%	SU_6%
PTV 50.4 D95% (cGy)	0.05	0.22	0.06	0.27	0.08
PTV 50.4 Dmax (cGy)	0.39	0.01	0.04	0.32	0.98
PTV 50.4 Dmean (cGy)	0.09	0.22	0.16	0.05	0.19
PTV 50.4 V95%	0.01	0.03	0.05	0.02	0.03
PTV 50.4 Heterogeneity Index	0.00	0.00	0.00	0.00	0.00
PTV 50.4 Conformity Index	0.00	0.00	0.00	2.94	0.00
Heart Dmean (cGy)	0.75	0.33	0.41	0.53	0.22
Spinal Cord Dmax (cGy)	0.45	0.24	0.49	0.10	0.82
Rt Lung Dmean (cGy)	0.05	0.36	0.02	0.69	0.24
Lt Lung Dmean (cGy)	0.19	0.06	0.00	0.49	0.05
Lt Kidney Dmean (cGy)	2.78	2.16	0.79	1.06	0.89
Rt Kidney Dmean (cGy)	0.25	0.17	0.32	0.56	0.49
Global Max of the Plan (%)	0.40	0.02	0.04	0.31	0.98
Gamma Pass Rate 3%, 3 mm	0.41	0.41	0.20	0.20	0.51

Table 8. Percentage Variation values with respect to 3% for Prostate

Target and OARs Prostate (wrt.3%)	SU_1%	SU_2%	SU_4%	SU_5%	SU_6%
PTV 78 D95% (cGy)	0.31	0.11	0.25	0.63	0.87
PTV 78 Dmax (cGy)	0.88	0.52	0.26	0.18	1.04
PTV 78 Dmean (cGy)	0.36	0.14	0.14	0.11	0.06
PTV 78 V95% (cm3)	0.1	0.01	0.14	0.53	0.76
PTV 78 Heterogeneity Index	0	0	0	0.97	1.94
PTV 78 Conformity Index	2.86	0	1.43	2.86	1.43
Rectum Dmean (cGy)	0.84	0.49	0.29	1.1	1.46
Bladder Dmean (cGy)	0.6	0.24	0.88	1.59	1.59
Lt Pelvic Bone Dmean (cGy)	0.07	0.48	0.49	0.5	1.05
Rt Pelvic Bone Dmean (cGy)	0.44	0.45	0.57	0.05	1.1
Global Max of the Plan (%)	0.84	0.34	0.36	0.28	1.04
Gamma Pass Rate 3%, 3 mm	0.41	0.21	0.10	0.31	0.10

According to the calculated percentage variation values (Table 6-8) with respect to a 3% per control point SU, showed no any significant variation between the dosimetric indices and the per control point SU (%) values for all three diagnoses (Larynx, Oesophagus, and Prostate).

CONCLUTION

This study proposed an optimal acceptable range for the per Control Point Statistical Uncertainty (SU) in Monte Carlo Dose calculations during IMRT planning in Monaco 5.11.02 Treatment Planning System (TPS). Based on the measured average results, a 3% per control point SU is acceptable for all three diagnoses (Larynx, Oesophagus, and Prostate) in IMRT planning, allowing for reduced calculation time without compromising target coverage, Organ at Risk (OAR) doses, or plan delivery.

Conflict of Interest

None declared.

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