Original Article

An institutional study on determining the optimal minimum segment width for Intensity Modulated Radiation Therapy plans in base-of-tongue cancer

Priya Saini, Mary Joan, Anirudh Pradhan

Abstract

Purpose: The aim of this study was to determine the optimal minimum segment width (MSW) for intensity-modulated radiotherapy (IMRT) planning in base-of-tongue (BOT) cancer, with a focus on balancing dosimetric quality and delivery efficiency.

Materials and Methods: A retrospective analysis was performed on 30 BOT cancer patients treated with IMRT. For every patient, four distinct treatment plans were created, corresponding to MSW settings of 0.5 cm, 1.0 cm, 1.5 cm, and 2.0 cm, while all other optimization and constraint parameters remained constant throughout. Dosimetric evaluation included target coverage metrics (D95, Dmean, Dmax), conformity index (CI), homogeneity index (HI), and doses to organs at risk (OARs). Delivery efficiency was assessed using monitor units (MUs) and treatment time. Statistical differences across MSW settings were analyzed using the Wilcoxon signed-rank test.

Results: Increasing MSW was associated with a progressive reduction in CI and decreased PTV dose coverage (D95) for both PTV70 and PTV56. Plans generated with MSW values of 1.5 cm and 2.0 cm failed to meet the clinical D95 requirement for PTV70, while the 2.0 cm MSW also did not satisfy requirements for PTV56. HI increased with larger MSW, whereas Dmean and Dmax remained statistically unchanged across the four plan groups ($p > 0.05$). The MSW 0.5 cm plans produced significantly higher D95 values ($p < 0.02$). All OAR doses remained within recommended tolerance limits. Monitor units and treatment time decreased as MSW increased; however, the MSW 0.5 cm plans required the highest MU (1016) and demonstrated reduced delivery efficiency.

Conclusion: Although larger MSWs improved delivery efficiency, smaller MSWs yielded superior dosimetric quality. An MSW of 1.0 cm provided the optimal balance between target coverage, plan conformity, and delivery efficiency, making it the most suitable setting for BOT cancer IMRT planning.

JK-Practitioner 2026-31(2):----

Introduction

Base-of-tongue (BOT) cancer is a subtype of oropharyngeal squamous cell carcinoma and is increasingly associated with human papillomavirus (HPV) infection.[1,2] Owing to the complex anatomy of the tongue base, its deep position , and its close adjacency to several normal structures, the management of BOT cancer demands highly precise and advanced radiotherapy approaches. Intensity-Modulated Radiation Therapy (IMRT) has become a preferred technique in this setting, as it allows the delivery of radiation with modulated beam intensities, enabling improved dose conformity to the tumor while minimizing radiation exposure to surrounding OARs. [3] In the Monaco Treatment Planning System (TPS), the MSW specifies the smallest permissible width of segments formed by the multi-leaf collimator (MLC). Within this system, MSW values typically range from 0.5 cm to 2.0 cm, and this parameter plays a key role in influencing both the quality of the treatment plan and its deliverability. [4-10] Despite its significance, there is a lack of published research specifically examining how MSW variations affect IMRT plans for patients with base-of-tongue (BOT) cancer. Therefore, the objective of this study is to evaluate the influence of different MSW settings on the dosimetric quality and deliverability of BOT cancer IMRT plans.

Author Affiliations

Priya Saini, Department of Radiological Physics, S.M.S Medical College & Hospitals, Jaipur-302004 (Rajasthan) India and Department of Physics, Institute of Applied Science and Humanities, GLA University, Mathura-281406(U.P), India. **Mary Joan,** Department of Radiation Oncology, Christian Medical College, Ludhiana, Punjab, India. **Anirudh Pradhan,** Centre for Cosmology, Astrophysics and Space Science, GLA University, University, Mathura-281406(U.P), India.

Correspondence

Priya Saini,
Department of Radiological Physics, S.M.S Medical College & Hospitals, Jaipur-302004 (Rajasthan) India and Department of Physics, Institute of Applied Science and Humanities, GLA University, Mathura-281406(U.P), India.
Email:
Phone no.

Indexed

EMBASE, SCOPUS, IndMED , ESBCO, Google Scholar besides other national and international databases.

Cite this article as

Saini P, Joan M, Pradhan A.An institutional study on determining the optimal minimum segment width for Intensity Modulated Radiation Therapy plans in base-of-tongue cancer. JK-Pract2026;31(1):----

Full length article available at **jkpractitioner.com** one month after publication

Keywords

Intensity modulated radiation therapy, dose volume histogram, BOT cancer, minimum segment width

Material and Methods

Simulation and Preparation of Patients

This study included thirty patients with BOT cancer who received IMRT at our institution from March 2022 to March 2023. For each patient, CT simulation was performed in a stable and reproducible supine position using a four-clamp, customized thermoplastic immobilization mask mounted on an acrylic base plate with an appropriate headrest. A slice thickness of 2.5 mm was used to acquire images on a GE Discovery 16-slice spiral CT scanner. The resulting CT datasets were then transferred to the Monaco Treatment Planning System in DICOM format via the local area network for further treatment planning.

Structures Delineation and Radiation Dose Prescription

Gross tumor volume (GTV), clinical target volume (CTV), and the surrounding normal structures were delineated by a skilled oncologist in accordance with RTOG guidelines. A uniform margin of 10 mm was expanded around the GTV, including involved lymph nodes, and a 3–5 mm margin was added around the CTV to generate the planning target volumes (PTVs). These were prescribed doses of 70 Gy (PTV70) and 56 Gy (PTV56), respectively. Critical organs such as the spinal cord, parotid glands, lips, brainstem, and thyroid were contoured as OARs.

Treatment Plan Development Using the Monaco TPS

For each patient, four IMRT plans were developed in the Monaco TPS (version 6.1.2.0) using MSW settings of 0.5 cm, 1.0 cm, 1.5 cm, and 2.0 cm. They were named MSW 0.5, MSW 1.0, MSW 1.5 , and MSW 2.0 respectively. Only MSW value was varied in all plans. Cost functions and remaining parameters were kept constant. Dose calculation grid size was used 3mm and maximum dose rate was used 600 MU/min. Treatment plans were delivered with 6MV X-ray photon beam using elekta versa HD linear accelerator. Nine fields with gantry angles 200º, 250º, 300º, 0º, 50, 100º and 150º were used to designed IMRT plan.

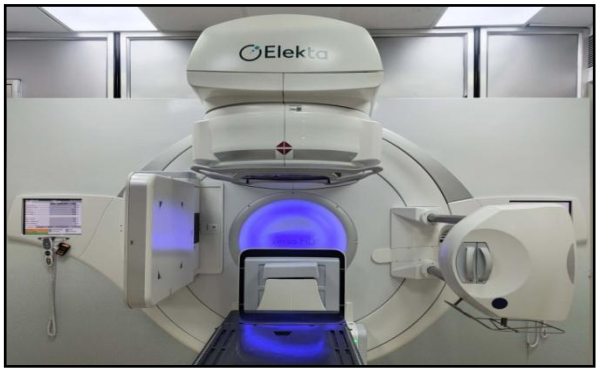


Figure 1: Elekta versa HD linear accelerator

Analysis of Treatment Plan Quality

The dosimetric quality of IMRT plans designed with different MSW was evaluated using a range of quantitative parameters. These included the median dose (D50%), maximum dose (D2%), minimum dose (D98%), dose homogeneity index (HI), conformity index (CI), the percentage of the PTV covered by 95% of the prescription dose, and dose–volume histogram (DVH) metrics for all relevant organs at risk (OARs). Plan complexity was assessed through the total number of monitor units (MUs), while plan delivery efficiency was determined using the plan delivery time (PDT) and the gamma passing rate (GPR) from patient-specific quality assurance.

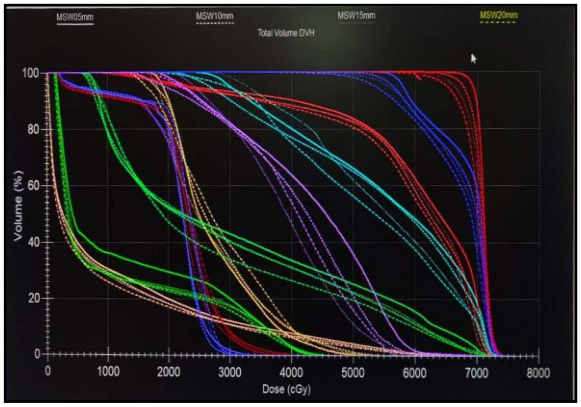
The CI and HI values for the target volumes were calculated according to the recommendations of the ICRU Report 83 using equations (1) and (2): [6]

$$HI=(D_{2\%}-D_{98\%})/D_{50\%} \quad (1)$$

$$CI = (TV_{RI})^2 / (TV * V_{RI}) \quad (2)$$

In these equations, $D_{x\%}$ denotes the minimum dose received by (x %) of the PTV; (TV) represents the total target volume; TV_{RI} indicates the target volume encompassed by the prescription isodose; and V_{RI} refers to the overall volume covered by the prescription dose.

Figure 2: The Dose volume histogram of four different IMRT plans with different MSW for a typical BOT cancer patient



Verification of Treatment Plan

Octavius II system was used for dosimetric verification of the plan. The criterion for GPR was dose to distance agreement 3%, 3mm. MU, GPR, and PDT were noted.

Statistical Analysis

Statistical evaluations were performed using Primer software. The Wilcoxon signed-rank test was applied to compare the dosimetric and delivery metrics among

the different MSW groups. The MSW 0.5 cm group served as the reference for all comparisons. p-values were calculated for each parameter, with a value of $p < 0.05$ considered indicative of a statistically significant difference.

Result:

Target Dose Analysis

Target Dosimetric parameters of four different MSW IMRT plan group were listed in Table 1and Table 2. CI values [Figure 3and 4] and PTV coverage (D_{95}) of both PTVs are decreased as the MSW value increased. For PTV 70, MSW1.5 and MSW2.0 IMRT plans group failed to satisfy clinical criteria, i.e., for MSW 2.0 group $D_{95\%}$=65.31 Gy (93.3 % of 70 Gy) and for MSW 1.5 group $D_{95\%}$ = 65.06 (92.94% of 70Gy). For PTV 56 IMRT plan group MSW 2.0 failed to satisfy clinical criteria, i.e, D95% = 50.31 (71.87% of 70 Gy). HI values for both PTVs are increased as MSW value increased [Figure 5 and 6]. The mean and maximum dose of PTV70 and PTV56 were not markedly different among the all four plans ($p>0.05$). In term of dose coverage $D_{95\%}$ MSW 0.5 plan group had significant difference from another three group for both PTVs ($p<0.02$).

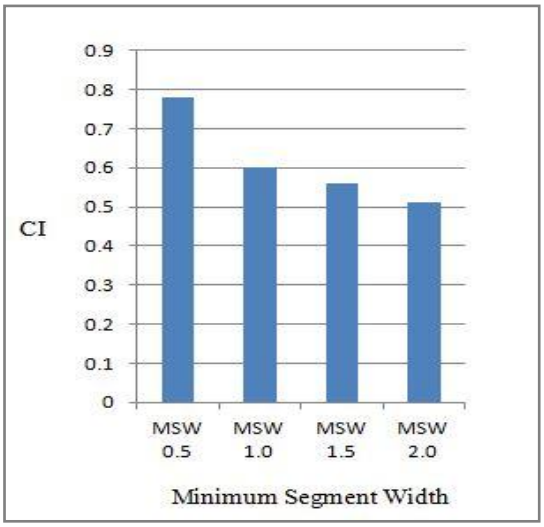


Figure 3: Graphical representation of CI for PTV70 of four different MSW settings
CI: Conformity Index

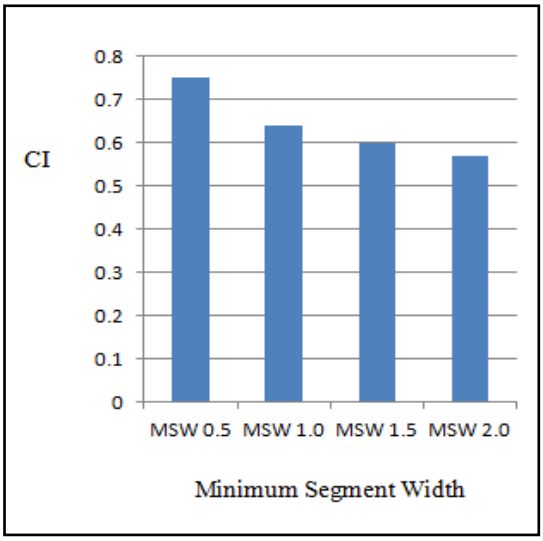


Figure 4: Graphical representation of CI for PTV56 of four different MSW setting
CI: Conformity Index

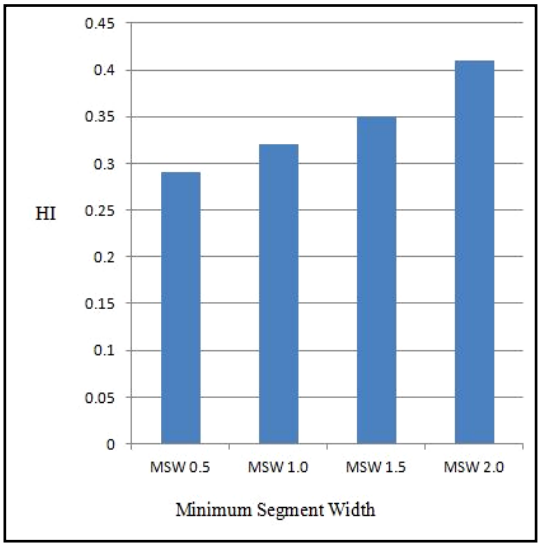


Figure 5: Graphical representation of HI for PTV56 of four different MSW settings
HI: Homogenity Index

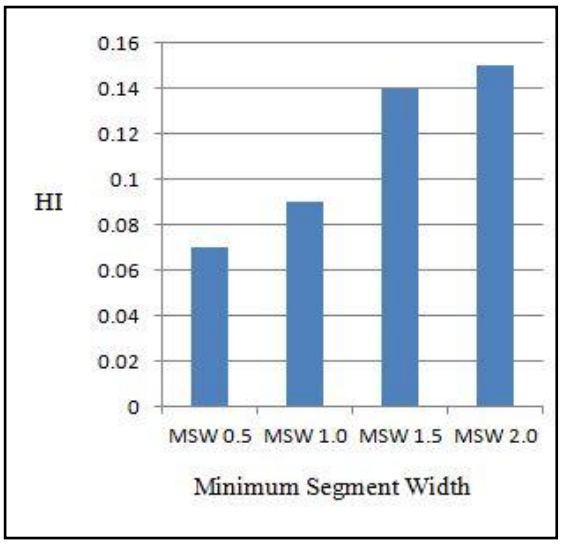


Figure 6: Graphical representation of HI for PTV70 of four different MSW settings
HI: Homogenity Index

Table 1. Dosimetric comparison of PTV56 for four MSW settings of BOT Cancer plans

Structure	Parameter	MSW 0.5	MSW 1.0	MSW 1.5	MSW 2.0	P1	P2	P3	P4
PTV56	PTV Coverage 95% (Gy)	55.2 ± 0.47	53.4 ± 0.52	53.38 ± 0.42	50.31 ± 0.42	<0.02	<0.02	<0.02	>0.05
	Mean Dose (Gy)	57.22 ± 0.25	57.19 ± 0.43	56.31 ± 0.30	56.10 ± 0.30	>0.05	>0.05	>0.05	>0.05
	Maximum Dose (Gy)	61.8 ± 0.30	60.91 ± 0.54	61.47 ± 0.54	61.31 ± 0.54	>0.05	>0.05	>0.05	>0.05
	HI	0.29 ± 0.03	0.32 ± 0.02	0.35 ± 0.01	0.41 ± 0.01	>0.05	>0.05	>0.05	>0.05
	CI	0.75 ± 0.10	0.64 ± 0.18	0.60 ± 0.17	0.57 ± 0.16	>0.05	>0.05	>0.05	>0.05

P1: p-value of comparison between MSW 0.5 and MSW 1.0, **P2:** p-value of comparison between MSW 0.5and MSW 1.5, **P3:** p-value of comparison between MSW 0.5and MSW 2.0, **P4:** p-value of comparison between MSW1.0 and MSW 1.5, HI: Homogeneity index, CI: Conformity Index

Table2. Dosimetric comparison of PTV70 for four MSW settings of BOT Cancer plans

Structure	Parameter	MSW 0.5	MSW 1.0	MSW 1.5	MSW 2.0	P1	P2	P3	P4
PTV70	PTV Coverage 95% (Gy)	68.72 ± 0.17	67.09 ± 0.27	65.00 ± 0.35	65.31 ± 0.30	< 0.02	< 0.02	< 0.02	> 0.05
	Mean Dose (Gy)	70.98 ± 0.45	69.20 ± 0.35	69.38 ± 0.41	69.59 ± 0.32	> 0.05	> 0.05	> 0.05	> 0.05
	Maximum Dose (Gy)	75.86 ± 0.30	74.91 ± 0.54	75.35 ± 0.72	75.47 ± 0.72	> 0.05	> 0.05	> 0.05	> 0.05
	HI	0.07 ± 0.01	0.09 ± 0.01	0.14 ± 0.01	0.15 ± 0.01	< 0.02	< 0.02	< 0.02	> 0.05
	CI	0.78 ± 0.08	0.60 ± 0.06	0.56 ± 0.12	0.51 ± 0.12	< 0.02	< 0.02	< 0.02	> 0.05

P1: p-value of comparison between MSW 0.5 and MSW 1.0, **P2:** p-value of comparison between MSW 0.5and MSW 1.5, **P3:** p-value of comparison between MSW 0.5and MSW 2.0, **P4:** p-value of comparison between MSW1.0 and MSW 1.5, HI: Homogeneity index, CI: Conformity Index

OARs Dose Analysis

OARs doses of all four groups were shown in Table 3. All OARs doses were within tolerance, although they were not directly comparable for all four group plans

Dosimetric verification, MU and plan delivery time

GPR, PDT and MUs for all four groups were shown in Table 4. Dosimetric plan evaluation was done using a comparison between measured planer dose and calculated dose by TPS studying the gamma passing criteria of a 3% dose difference (DD) and a 3mm distance to agreement (DTA). MSW2.0 group plan had highest GPR value and MSW0.5 group plan had lowest GPR value. MUs of the IMRT plans decreased as the MSW increased (Table 4).The MSW0.5 group had the highest MUs (1016MUs).The PDT decreased with increasing MSW ($p < 0.05$). However plans with 0.5 cm MSW had worse delivery accuracy and efficiency than other groups. There were no significant difference between MSW 1.5 and MSW1.0 group in term of MUs (p4>0.05).

.

Table3. Dosimetric comparison of OAR doses across four MSW settings of BOT Cancer plans

OARs	Parameter	MSW 0.5	MSW 1.0	MSW 1.5	MSW 2.0	P1	P2	P3	P4
Brainstem	Dmax (Gy)	32 ± 2.33	34.9 ± 2.25	36.5 ± 2.50	37.9 ± 2.56	P>0.05	P>0.05	P>0.05	P>0.05
Spine	Dmax (Gy)	36 ± 2.00	34.9 ± 3.80	35.9 ± 2.96	36.6 ± 3.15	P>0.05	P>0.05	P>0.05	P>0.05
Thyroid	Dmean (Gy)	41.2 ± 4.13	42.7 ± 5.46	42.5 ± 4.40	42.5 ± 6.00	P>0.05	P>0.05	P>0.05	P>0.05
Lip	Dmean (Gy)	26.4 ± 13.3	27.1 ± 8.36	26.6 ± 12.8	27.2 ± 4.56	P>0.05	P>0.05	P>0.05	P>0.05
Right Parotid	Dmean (Gy)	22.7 ± 3.20	21.7 ± 3.25	21.3 ± 2.15	21.3 ± 2.50	P>0.05	P>0.05	P>0.05	P>0.05
Left Parotid	Dmean (Gy)	23.6 ± 2.0	22.9 ± 3.27	23.8 ± 1.50	22.4 ± 1.23	P>0.05	P>0.05	P>0.05	P>0.05

Dmax: maximum dose, Dmean ; Mean Dose

Table4. Monitor units and plan delivery time comparison of four MSW settings of BOT Cancer plans

Parameter	MSW 0.5	MSW 1.0	MSW1.5	MSW 2.0
MUs	1016.76±54.414	716.32± 46.23	667.55±53.11	693.12±109.64
PDT(mint)	5.00 ± 0.50	4.43 ± 0.32	4.20±0.30	4.02±0.40
GPR	95.5± 1.32	96.37±1.30	96.40±1.45	97.2±1.5

MSW: Minimum segment width, MUs: Monitor units, PDT: Plan delivery time
IMRT: Intensity modulated radiation therapy, MSW: Minimum Segment Width

Discussion

The sequencing parameters in a treatment planning system can influence both plan quality and clinical deliverability to a degree comparable to that of dosimetric constraints.[11-19] In the Monaco TPS, MSW is a key sequencing parameter that specifies the smallest allowable width of multileaf collimator (MLC) segments.[20] Designing IMRT plans for base-of-tongue (BOT) cancer often results in numerous small, narrow, and irregular apertures. Because MSW directly influences the shape and size of these apertures, it plays a critical role in generating optimized segments. When MSW values are not selected appropriately, plans may contain excessively small or elongated segments, which can compromise verification results and even cause interruptions during clinical delivery. [20-26] In this study, four IMRT optimization schemes were compared; each created using a different MSW value. The findings indicate that MSW not only affects target dose distribution and sparing of organs at risk (OARs) but also has a notable impact on PDT and MU. The plan generated with MSW 0.5 cm served as the reference group. This group achieved the highest PTV coverage at the 95% dose level, whereas MSW 2.0 cm produced the lowest coverage. For PTV70, the MSW 1.5 cm and MSW 2.0 cm groups failed to meet clinical criteria, and for PTV56, the MSW 2.0 cm group also did not satisfy requirements. Doses to OARs across all four MSW groups remained within acceptable tolerance levels.

As MSW increased, both MUs and PDT decreased, while gamma passing rate (GPR) increased. The MSW 1.0 cm plans exhibited the highest MU and PDT values but showed the lowest GPR. Conversely, although the MSW 0.5 cm group demonstrated superior dose conformity, homogeneity, and overall dose distribution, its treatment efficiency and delivery

accuracy were inferior to those of the other groups. No statistically significant differences were observed between the MSW 1.0 cm and MSW 1.5 cm groups regarding PTV95% coverage, mean dose, maximum dose, or OAR doses ($p > 0.05$) for both target volumes.

Plans created with MSW 2.0 cm and MSW 1.5 cm showed poorer dose distribution and failed to meet clinical target coverage criteria; however, they achieved better treatment efficiency and higher delivery accuracy. Overall, increasing MSW values resulted in fewer MUs, shorter PDT, and higher GPR. The MSW 0.5 cm group required the greatest number of MUs and longest PDT but produced the lowest GPR (>95%) among all groups. Reductions in MU and PDT achieved with larger MSW settings may help minimize patient movement during treatment, enhance treatment efficiency, and potentially improve biological treatment effectiveness**.**

Conclusion

Based on a comprehensive assessment of all dosimetric and delivery parameters—including PTV95% coverage, OAR sparing, homogeneity index (HI), conformity index (CI), maximum and mean doses, monitor units (MUs), planning delivery time (PDT), and gamma passing rate (GPR)—we observed that the MSW 1.5 cm and MSW 2.0 cm groups did not fulfill the clinical requirements for acceptable IMRT plan quality. Although the MSW 0.5 cm group achieved strong dose conformity and homogeneity, it demonstrated poorer delivery accuracy and lower efficiency compared with the other groups. Overall, our findings indicate that an MSW value of 1.0 cm provides the most favorable balance between dosimetric quality and delivery efficiency for IMRT planning in base-of-tongue cancer. Therefore, an MSW of 1.0 cm may be considered the optimal setting for BOT patients undergoing IMRT technique.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References:

1. Ang KK, Harris J, Wheeler R, Weber R, Rosenthal DI, Nguyen-Tân PF, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med 2010; 363(1):24–35.
2. Yom SS, Torres-Saavedra P, Caudell JJ, Waldron JN, Gillison ML, Xia P, et al. Reduced-dose radiation therapy for HPV-associated or pharyngeal cancer. J clin oncol 2021; 39(9):956-965.
3. Nutting CM , Morden JP, Harrington Kj, Harrington TG, Bhide SA, Clark C, et al. (2011). Parotid-sparing IMRT versus conventional RT in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. Lancet Oncol 2011; 12(2):127–136.
4. Sun H, Wang N, Wang X, Huang G, Chang Y, Liu Y. A study of different minimum segment area parameters on automatic IMRT plans for cervical cancer using Pinnacle3 910 TPS. Medicine (Baltimore) 2022; 101:29290.
5. Clements M, Schupp N, Tattersall M, Brown A, Larson R. Monaco treatment planning system tools and optimization processes. Med Dosim 2018;43:106–17.
6. International Commission on Radiation Units and Measurements. ICRU Report 83: Prescribing, Recording, and Reporting IMRT.Bethesda (MD): ICRU 2010.
7. Sun X, Xia P, Yu N. Effects of the intensity levels and beam map resolutions on static IMRT plans. Med Phy 2004; 31:2402–11.
8. Sun X, Xia P. A new smoothing procedure to reduce delivery segments for static MLC-based IMRT planning. Med Phys 2004; 31:1158–65.
9. Wang N, Chen L, Huang G, Sun H. Influence of minimum segment width on intensity-modulated radiotherapy plan for left sided breast after breast conversing surgery. Medicine (Baltimore) 2023; 102(46):e36064.
10. Jiménez-Puertas S, González Rodríguez A, Lozares Cordero S, González González T, Díez Chamarro J, Hernández Hernández M, et al. Evaluation of the Minimum Segment Width and Fluence Smoothing Tools for Intensity-modulated techniques in Monaco Treatment Planning System. J Med Phys 2024; 49(2):250-260.
11. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA cancer J clin 2021; 71:209-49.
12. Coselmon MM, Moran JM, Radawski JD, Fraass BA. Improving IMRT delivery efficiency using

intensity limits during inverse planning. Med phys 2005; 32: 1234-45.
13. Ur Rehman J, Ahmad N, Khalid M, Gilani ZA, Ullah I, Nasar G, et al. Intensity modulated radiation therapy: A review of current practice and future outlooks. J Radiat Res Appl Sci 2018; 11: 361-7.
14. Baba MH, Singh BK, Wani SUQ: Skin sparing in intensity modulated radiation therapy of nasopharyngeal carcinoma. J Med Phys 47(3): 243-249, 2022. DOI: 10.4103/jmp.jmp_27_22
15. Guowei Z, Ziping J, Shepard D, Earl M, Yu C. Effect of beamlet step-size on IMRT plan quality. Med phys 2005; 32: 3448-54.
16. Sutterley C, Gautier Q, Graves Y, Li N, Jia X, Jiang S. SU-E-T-570: Optimizing Dose Calculation Parameters for GPU-Based Treatment Planning. Med Phys 2013; 40:336.
17. Hong J, Han JH, Luo HL, Song YQ. Optimization of Minimum Segment Width Parameter in the Intensity-Modulated Radiotherapy Plan for Esophageal Cancer. Int J Gen Med 2021; 16: 9913-21.
18. Wang Y, Chen L, Zhu F, Guo W, Zhang D, Sun W. A study of minimum segment width parameter on VMAT plan quality, delivery accuracy, and efficiency for cervical cancer using Monaco TPS. J Appl Clin Med Phys 2018; 19: 609-15.
19. Nguyen D, O'Connor D, Yu VY, Ruan D, Cao M, Low DA, et al. Dose domain regularization of MLC leaf patterns for highly complex IMRT plans. Med Phys 2015; 42: 1858-70.
20. Wu M, Jin J, Li Z, Kong F, He Y, Liu L, et al. Influence of beamlet width on dynamic IMRT plan quality in nasopharyngeal carcinoma. Peer J 2022; 10: 13748.
21. Coselmon MM, Moran JM, Radawski JD, Fraass BA. Improving IMRT delivery efficiency using intensity limits during inverse planning. Med phys 2005; 2: 1234-45.
22. Yoosuf AM, Ahmad MB, AlShehri S, Alhadab A, Alqathami M. Investigation of optimum minimum segment width on VMAT plan quality and deliverability: A comprehensive dosimetric and clinical evaluation using DVH analysis. J Appl Clin Med Phys 2021; 22: 29-40.
23. Jain N, Alok K, Ashok K. Investigating the influence of minimum segment width in volumetric-modulated arc planning of prostate cancer. Turk J Oncol 2024;39:84–91.
24. Nithiyanantham K, Kadirampatti Mani G, Subramani V, Karukkupalayam Palaniappan K, Uthiran M, Vellengiri S, et al. Influence of segment width on plan quality for volumetric modulated arc based stereotactic body radiotherapy. Rep Pract Oncol Radiother 2014; 19:287–95.
25. Moon YM, Bae SI, Choi CW, Jeon WW, Kim JY, Lee MW, et al. Effect of minimum segment width on gamma passing rate considering MLC position error for volumetric modulated arc therapy. J Korean Phys Soc 2019; 74:724–30.
26. Baba MH, Singh BK. In-vivo skin dose measurement using gafchromic EBT3 film dosimetry in the radiation therapy of Head and Neck cancers: 2DRT versus IMRT. J Radiat Res Appl Sci. 2022;15(2):170–174, ISSN 1687–8507. https:// doi. org/ 10. 1016/j. jrras. 2022. 05. 019. https:// www. scien cedir ect. com/ scien ce/ artic le/ pii/ S1687 85072 20718 01.