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Nasopharyngeal cancer radiotherapy in resource-limited setting: Optimizing Cobalt-60 for forward planning field-in-field intensity modulation technique. A case series in Tugurejo Hospital.

Elia Aditya Bani Kuncoro[1,3,4], Piryadi[2,3], William Alfred Lapian Pandeirot[5], Yunarti[6], Anita Zakiyah[3], Galih Puspa Sekarsari[4]
[1]Radiation Oncologist, [2]Physicist, [3]Department of Radiation Oncology Tugurejo Hospital, [4]Department of Radiation Oncology Ken Saras Hospital, [5]Department of Surgical Oncology Ken Saras Hospital, [6]Department of Otolaryngology, Head, and Neck Tugurejo Hospital

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Correspondence:
Elia Aditya Bani Kuncoro
E-mail:
elia3714@gmail.com

Abstract

Introduction. Cobalt-60 remains a mainstay modality in some areas in developing countries. Several modifications can be made in order to optimize the machine's capability to treat nasopharyngeal cancer cases.
Methods. Authors developed a Cobalt-60 based forward planning field-in-field intensity modulation technique for radiotherapy. Some challenges and limitations were addressed by modifying the dose, isocentre placement, tray, collimator, and blocks. The standard beam configuration consisted of 12-15 beamlets, within 7-9 blocks, within 3-5 trays.
Result. This technique managed to achieve the approval criteria for patient treatment. Nine patients treated using this technique showed 71% complete response rate with acceptable acute side-effects.
Conclusion. The use of Cobalt-60 to treat nasopharyngeal cancer can potentially be improved by modifying treatment planning. Forward planning field-in-field intensity modulation technique may cope with some limitations of Cobalt-60 physical profile and results showed promising outcome.

Keywords: Cobalt-60, field-in-field, intensity modulation, nasopharyngeal cancer

Introduction

Cobalt-60 is one of the oldest teletherapy modalities. Its existence in the modern world is mostly being replaced by newer models of linear accelerator (LINAC). However, the Cobalt-60 machine is still a mainstay modality to treat cancer patients in many centres in developing countries. In a resource-limited setting, or a remotely located centre, or one without a good supply of electricity, one must adapt with the provided situation despite the limitations and disadvantages of the Cobalt-60 machine.

The demands to provide high curability with lesser late-adverse effects have recently become the focus of interest. The efforts to meet these demands, especially in head and neck cancers, have encouraged centres with Cobalt-60 teletherapy to push to their limits to produce the best achievable planning. On the other hand, from the practical perspective, better dose distribution using Cobalt-60 machine is associated with more planning complexity; resulting in more gantry angle, blocks, and beamlets.[1] Therefore it may become difficult to implement in the clinical situation.

In this paper, we describe several modifications made in order to optimize Cobalt-60 machine's capability for the treatment planning. The discussion will be focused on nasopharyngeal cancer radiotherapy as this is one of the most complex and challenging areas to obtain satisfactory dose distribution.

Methods

Authors carried out several trials in order to develop a method to devise a deliverable forward-planning intensity modulation plan using the Cobalt-60 machine. During the process, authors aimed to achieve two objectives: a good dose distribution and to create a method that simplifies the planning. Specifically, a method to reduce the frequency of which a radiographer has to go in and out of the treatment room. This objective was achieved by using multiple blocks per tray. Some challenges and limitations during the development of this technique are addressed below, along with some adaptation made on the dose, isocentre placement, tray, collimator, and blocks.

Acknowledgement of theoretical disadvantages

Cobalt-60 teletherapy machine has been used for more than 60 years to treat cancer patients. For generations, changes have been made to upgrade the functionalities of Cobalt-60 teletherapy, but the main physical profile of the source still remained. By the late 1960s, there were approximately 1700 external beam devices in the world and about 90% of them were cobalt therapy units. Over the following years, major advances were made in the production of electron beams using LINACs, technical improvement like MLC, and digital readout gave the LINAC many advantageous aspects, and in the 1990s cobalt therapy units essentially vanished in the US.[1]

The physical advantages of a Cobalt-60 are its relative stability and constancy of output, uniform energy, and dose-rate stability. The disadvantages of Cobalt-60 machines include the need for source replacement around every 5 years, poor field flatness for large fields, large penumbra, having d1/2 in tissue of about 10 cm (lower depth dose compared with high energy LINAC) and round shape isodose curves. These disadvantages might not be objectively measured as neither volumetric calculation nor organ at risk definition were needed when using 2D technique. However, 3D-CRT approach using Cobalt-60 to achieve conformality, coverage of target volume and avoiding dose to the serial (or sometimes parallel) organ at risk is often challenging and sometimes frustrating. Further details on physical factors are listed on **Table 1**.[2]

Details of Cobalt-60 machine specification

Nasopharyngeal cancer cases were treated with 100cm SSD telecobalt machine at our hospital. Dose rate was recorded at 185 cGy min-1, and the advantages as well as the limitation of the physical system are listed below on the **Table 2**.

The Cobalt machine parameters were considered standard, and some specifications could be attributable to less beam profile quality (the 100 cm SID and 2 cm source size corresponded to the large penumbra, rounded shape of isodose profile especially for large collimator opening).

In clinical practice, we tried to use mono-isocentric technique whenever possible for the reason of practicality. The consequence of this approach is that we tend to use large beam opening, and therefore obtained a rounded shape isodose profile that will affect the dose distribution in distal areas e.g., the supraclavicular area. Further modifications and tricks that we used to manage the situation are explained below.

Planning Parameters and Configuration for Nasopharyngeal cancer

Applying 3D-conformal technique using Cobalt-60 for cervical, rectal, or endometrial rectal cancer is generally not complex. In these groups of cases, good dose distributions for OAR and target are generally achievable through several expected planning configuration. In head and neck cancer, CTV encompasses several areas nearby critical structures and are usually irradiated with high curative dose. Therefore, achieving good dose distribution in the head and neck area could be challenging.

Patient Preparation.

The standard positional patient set-up in

Table 1. Physical factors differences between Cobalt and Linac machines (Page et. al)

	Cobalt	**Linac**
Buildup	Equivalent in 4MV, build-up 5mm	6MV build-up 15mm, 15-18MV build-up 28-35mm
Skin dose	40-50%	6MV 25%, 15MV 15-25%
Penetration	54% (10cm depth)	6MV 67% (10cm depth), 18MV 77%.
Penumbra	1.5cm field definition	Sharp beam field definition
Shape of isodose curves	Rounded (correctable)	Flattened by filter
Irregular fields	Achievable with blocks and MLCs being adapted	MLC
Dose rate	2.5Gy/min, factors of 4 longer than LINAC	4-25 Gy/min
Energy	Lower; greater effect on tissue density and air gap	Higher: less superficial dose and dose bath.

Source: Reference no. 2

nasopharyngeal cases was supine position with neck extension and depressed shoulder. Specific pillow for extension, 4 or 5 points head & neck thermoplastic masks, and shoulder retractor were used. As we used half-beam and multiple fields opening, the positioning of the patient in a symmetric position with chin lifted was important in order to easily achieve good dose distribution and to minimize unnecessary blocks.

Target and OAR definition.
Target delineation followed standard nasopharyngeal cancer CTV contouring as per the modification of delineation guideline by Lee et. al and RTOG 0225, with 3-5mm isotropic margin to create PTV1 (gross disease), PTV2 (high risk subclinical disease), PTV3 (elective nodal coverage).[3,4]
If there is involvement of lateral retropharyngeal nodes with the cancer, then we modified the CTV definition to include lateral retropharyngeal nodes and the medial retropharyngeal space. The inferior level of the retropharyngeal nodes was based off the caudal border of C2, instead of the caudal border of hyoid bone.
To simplify our work, organ at risk dose constraints were categorized into two groups: higher and lower priority, with the clinical goals as shown in the **Table 3**.

Table 2. Details for machine profile measurements.

	Advantages	Disadvantages
Source size		~ 2cm
Source-isocentre distance	100 cm	
Gantry clearance		43cm
Rotating collimator	Yes	
Asymmetric collimator	Yes	
Minimum collimator distance		1cm
Collimator close at 0cm	Yes	
Overtravel collimator		No
MLC		No
Individual block	Yes	
Penumbra 10x10 at SSD 100		16mm
Beam Symmetry in/cross 10x10	<3%	
Beam Flatness in/cross 10x10		>3%
3D dose calculation / Treatment planning algorithm	Collapsed cone convolution	
Wedge		Physical
Dose-rate*	185 cGy min-1	
Penumbra trimmer		No

In practice, we prioritized upon PTV target coverage, but not to exceed the absolute constraints for higher organ at risk priority. The lower priority organ at risk may be utterly sacrificed if PTV coverage was inadequate and was required expanding. Re-planning was scheduled if there were significant changes for patient's masses, symptoms, or head/neck contours.

Field-in-field beam configuration and modification.
The beam configuration of this cobalt field-in-field RT in our technique took into account several physical aspects: the beam penumbra for cobalt, no over travel jaw, and rounded flatness of the isodose curve especially when the collimator opening was larger than 15cm.
The standard fields were grouped into: superior and inferior fields, main fields and field-in-fields, gantry directions (as explained in **Table 4**).
In our practice, most cases required only four trays with, on average, twelve to thirteen fields. This could be achieved if the optimization of each block was designed to be used in multiple fields, and collimator rotation. The beam configuration example is shown in **Figure 1**. The last beam on the lower right (**Fig.1**) was

Table 3. Clinical goals criteria for optimization and planning.

	Goals (relative)	Goals (absolute)
Target		
PTV1 gross disease (70Gy/35)	V66.5>95%, V74.9<2%	V63>95%, V74.9<2%
PTV2 hi-risk (60Gy/30)	V57>95%	V54>95%, V74.9<2%
PTV3 elective (52.5/30)		V49.86>95%, V64.2<2%
Organ at risk (higher priority)		
Brainstem	D0.01<56Gy	D0.01<62Gy
Optic chiasm & nerves	D0.01<56Gy	D0.01<62Gy
Oral cavity	Mean < 35Gy	Mean<45Gy
Spinal cord	D0.01<46Gy	D0.01<50Gy
Lens	D0.01<12Gy	D0.01<12Gy
Organ at risk (lower priority)		
Parotid glands	Mean<40Gy	
Mandible (TMJ)	D0.01<70Gy	
Inner ears	Mean<50Gy	
Larynx	Mean<45Gy	
Eyes	Mean<35Gy	

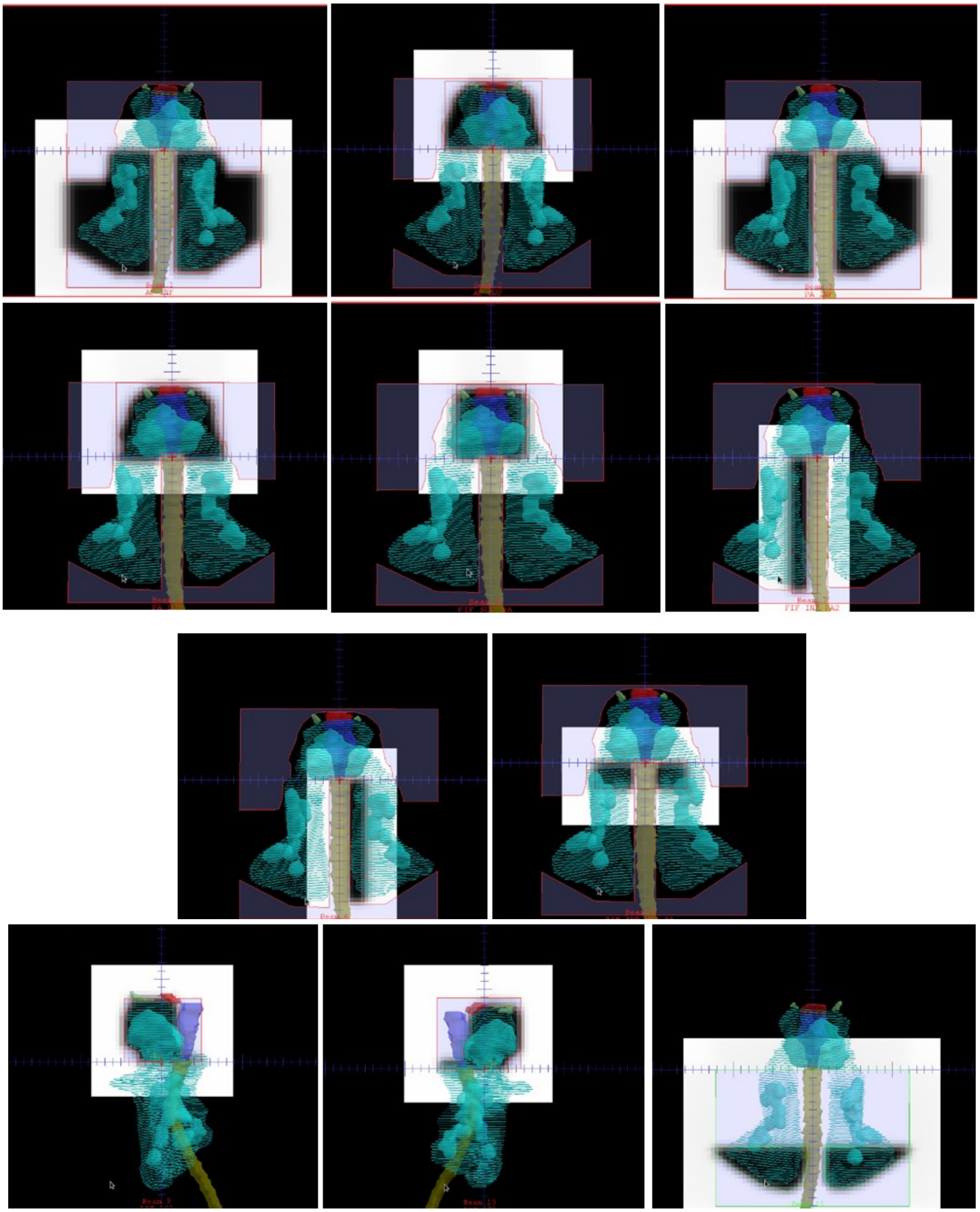

Figure 1. Example of beam and field configuration. Field 1 to 11: the intensity map (black shadow) of a patient with nasopharyngeal cancer treated by field-in-field Co-60 teletherapy. This planning used 3 trays for 5 blocks for 11 fields. Tray 1: contains a block for the first eight fields (first eight pictures from top left to down right). Tray 2 contains two blocks, each for 90° gantry (collimator 0°) and 270° gantry (collimator 180); and the last one was for supraclavicular area (could be delivered using 2nd isocentre).

optional in N1-2 cases. It was needed when using 2 Gy/fraction for supraclavicular area (for elective up to 50Gy/25fx), but was omitted when using 1.8Gy/fx and deliver 52.5Gy/30fx altogether with the high-risk dose of 60Gy/30fx. In these cases, we tried to “utilize” the disadvantageous physical aspect arising from the energy profile of Cobalt-60 generated beam in which the beam flatness decreases the further the distance is from the isocentre.

The last beam on the lower right (**Fig.1**) was optional in N1-2 cases. It was needed when using 2 Gy/fraction for supraclavicular area (for elective up to 50Gy/25fx), but was omitted when using 1.8Gy/fraction and deliver 52.5Gy/30fx altogether with the high-risk dose of

Table 4. Beam configurations. The standard template of the beams for nasopharyngeal cancer irradiation. Not all of the configurations below were needed, in a few cases we required only 3 trays using single isocentre, but most cases need 4 trays with up to 12 number of beams. The less the number of trays, the more practical the treatment flows are.

Tray	Sup/Inf	Block	Gantry	Field	Beamlet Number
1	Inf	SPC_MS	AP	Main field	1
			PA	Main field	2
			AP or PA	Fif medial-jugular Right	3
			AP or PA	Fif medial-jugular Left	4
			AP or PA	Fif Retropharynx bilateral	5
	Sup	Parotis	AP	Main field	6
			PA	Main field	7
			AP or PA	Fif	8
2	Sup	90 Main	90	Main 90	9
		270 Main	270	Main 270	10
3	Sup	90 Fif	90	Fif 90	11
		270 Fif	270	Fif 270	12
4	Sup	Axial Fif	140-170	Fif 140-170	13
		Axial Fif	190-220	Fif 190-22	14
5	(Optional)	SPCLV	AP or PA	FIF SPCLV	15

60Gy/30fx. In these cases, we tried to "utilize" the disadvantageous physical aspect arising from the energy profile of Cobalt-60 generated beam in which the beam flatness decreases the further the distance is from the isocentre.

Results

Nine patients were treated using the field-in-field optimization for Cobalt-60. The follow-up duration was relatively short (<6 months). The evaluation of the planning statistics and results are described on **Table 5**,

Table 5. Clinical-goals results for nine treated patients (A to I).

Abbreviations: R(relative criteria achieved), A(absolute criteria achieved), LD (Lowering prescription dose), - (not achieved)

Target	A T3N2	B *T4N2*	C T3N3	D *T4N2*	E *T4N1*	F *T2N1*	G *T3N2*	H *T4N2*	I *T3N2*
PTV1 gross disease (70Gy/35)	R	LD*	A	R	R	R	R	A	R
PTV2 hi-risk (60Gy/30)	R	R	A	R	R	R	R	R	R
PTV3 elective (52.5/30)	A	A	A	A	A	A	A	A	A
Organ at risk (higher priority)									
Brainstem	R	A	R	R	R	R	R	A	R
Optic chiasm & nerves	R	A (LD)	R	R	A	R	R	A	R
Oral cavity	R	A	A	R	R	R	R	R	R
Spinal cord	R	A	A	R	R	R	R	A	R
Lens	R	A	R	R	R	R	R	R	R
Organ at risk (lower priority)									
Parotid glands	R	-	-	-	-	-	-	-	-
Mandible (TMJ)	R	-	R	R	-	R	R	-	R
Inner ears	R	-	R	R	R	R	-	-	R
Larynx	R	R	-	R	R	R	R	R	R
Eyes	R	-	R	R	R	R	R	R	R

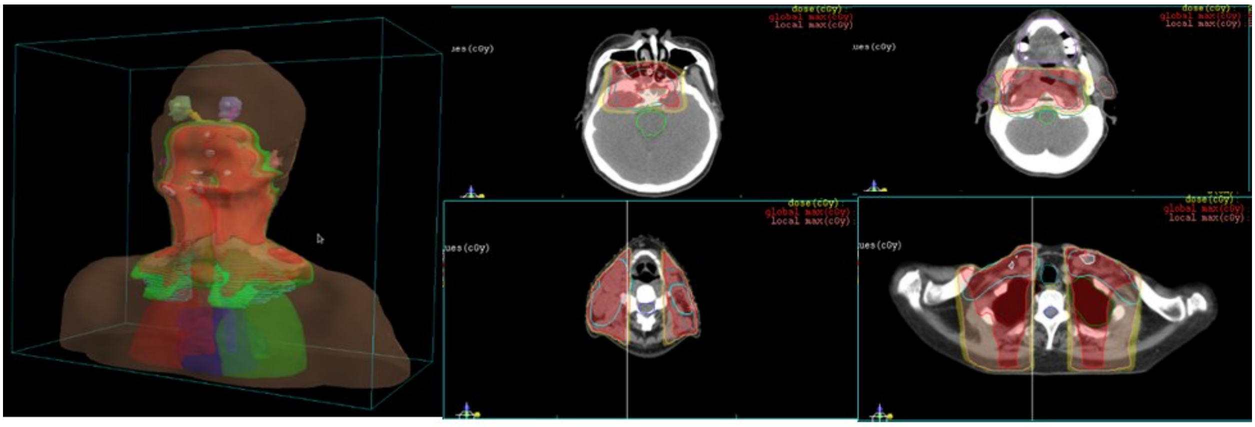

Figure 2. Treatment planning calculation. Left: the 3D dose distribution. Colors white: isodose 7490, red: isodose 7000, orange isodose 6650, pink: 6300, green: isodose 5985.

and the planning illustrations are shown in **Figure 2**.

Dose distribution for the targets must achieve at least an absolute criterion. In the majority of cases, the relative clinical goals were fulfilled. Pushing to the limits took some time and effort to obtain the best forward-optimization result.

High priority organ at risk became the first priority for the planning, and the absolute tolerance criterion were always achieved. If the tumor is T4 and the absolute criterion for target and organ at risk were not possibly achieved, then lowering the total dose became the next alternative decision policy (PTV1 to 66Gy).

Among nine patients treated, 71% patients showed complete response on contrast CT evaluation as per 2.5 months after treatment. The significant acute effects were severe dysphagia with weight loss >15% (44%), and confluent moist skin desquamation (22%). Data on late effects were limited due to the relatively short duration of follow-up. The brief clinical results are descripted below.

Discussion

This technique attempted to reckon the strength and advantages of the Cobalt-60 system, as well as to modify the disadvantages of the system to become beneficial for the purpose of treatment planning. The characteristic of 1.25MeV energy caused the beam flatness of the Cobalt-60 systems to be rounded as the jaws opening were larger. Flatness is measured by finding the maximum Dmax and minimum Dmin dose point values on the beam profile within the central 80% of the beam width.[5]

Table 6. Clinical results and patient follow-up. ORR: Overall Response Rate, CR: Complete response, PR: Partial response, CCRT: Concurrent Chemo-RT, >Gr3 percentage of receiving grade 3 toxicity. (-) patient was treated less than the evaluation period (for response at 10 weeks, and for late effects is more than at least 12 weeks).

	A **T3N2**	**B** ***T4N2***	**C** **T3N3**	**D** ***T4N2***	**E** ***T4N1***	**F** ***T2N1***	**G** ***T3N2***	**H** ***T4N2***	**I** ***T3N2***	
Response	CR	PR	PR	CR	CR	CR	CR	-	-	ORR:100% CR:71%
CCRT	Y	Y	N	Y	Y	Y	Y	N	Y	
Treatment completion	Y	Y	Y	Y	Y	Y	Y	Y	Y	100%
				Acute effects (RTOG)						≥Gr3
Skin	3	2	3	2	2	2	2	2	2	22%
Mucous membrane	2	1	2	1	1	1	1	2	2	0
Esophagus & Pharynx	3	2	3	3	2	2	3	2	2	44%
Larynx	2	1	2	2	1	1	1	2	1	0
				Late effects (RTOG) < 6mo f.u.						>Gr3
Skin	1	1	2	1	1	1	-	-	-	0
Salivary glands	3	3	3	3	3	3	-	-	-	100%
Spinal cord	0	0	0	0	0	0	-	-	-	0
Mucous membrane	0	0	1	0	0	0	-	-	-	0
Eye	0	0	0	0	0	0	-	-	-	0

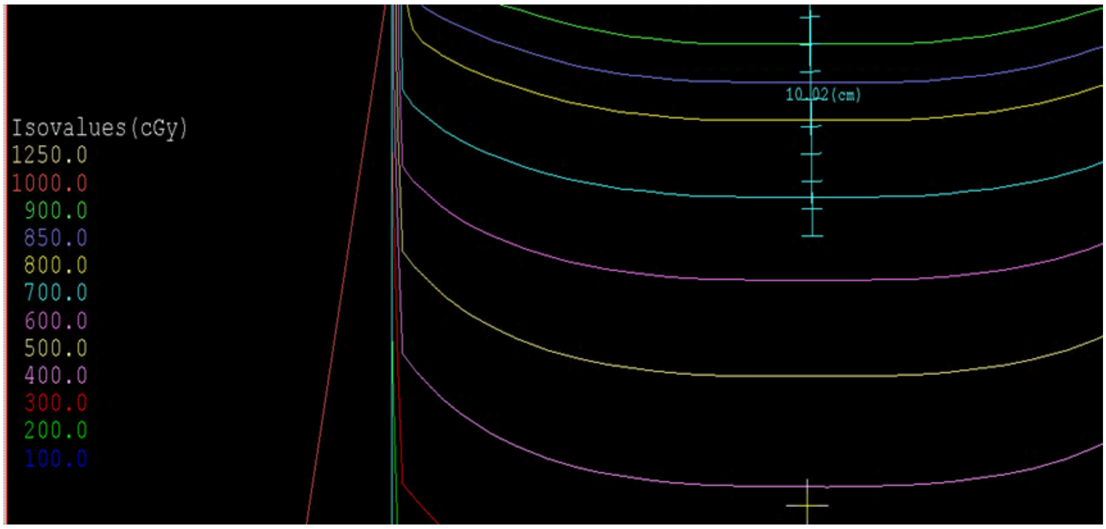

Figure 3. Isodose profile on the virtual phantom, 20cm jaw Y1 opening. Note that on the depth of 4cm, the dose at 0 to 10 cm away from the isocentre is relatively flat (yellow box), and beyond 10cm, the dose are decreasing, up to 12% from the dose at the center (green box), these profile that is considered as disadvantage, can be used to treat elective nodal area on the supraclavicular region.

As previously mentioned, we could use different dose-fractionation in the supraclavicular region (elective nodes level) by utilizing the drop-down dose at the peripheral regions at a distant area from the isocentre. It should be noticed that in this elective nodal area we were lenient to more inhomogeneous distribution, as such we accepted the dose of 64.2Gy<2% for PTV52.5Gy. **Figure 3** shows the beam flatness of the Cobalt-60 on the virtual phantom.

When using this forward planning Cobalt-60 field-in-field technique, we were aware of small fields utilization, defined as the one having smaller dimension than the lateral range of the charged particles that contribute to the deposited dose at a point along the central axis of the beam.[6] We use beam apertures larger than 4x4 cm2 (or equivalent) whenever possible, but it is not an absolute prerequisite.

All of the patients treated with this forward planning Cobalt-60 field-in-field responded to the treatment, and 71% of them had excellent remission. This is slightly lower than the result from Hu et. al that showed complete response rate in 85% of locally advanced nasopharyngeal patient treated with paclitaxel CCRT.[7] Another result from Bossi et. al stated similar results with complete response rate in 78% of patients and partial response rate in 20% of patients. In this study, 76% patients was treated with IMRT.[8] A study by Kim et.al showed administration of concurrent weekly cisplatin (30mg/m2) with radiotherapy achieved the complete response rate of 72.7% and partial response rate 9.2%.[9]

Another important aspect corresponds to the utilization of half-beam block and multiple collimator rotation. Usage of half beam blocks along with putting several blocks in the same tray, the gantry, collimator, and block has made the set-up robust. The daily QA of the treatment machine includes: collimator axis of rotation, collimator motion, light and radiation field congruence, gantry axis of rotation, radiation isocentre, optical distance indicator, gantry angle indicators and collimator field size indicators. These parameters should be routinely checked and measured to ensure the mechanical aspects of the machine are good in performance. The beam delivery is controlled by the oncology information system with treatment data sent directly from the TPS, which ensures that the setup for gantry, collimator, wedge, and prescribed dose are set correctly. The limitations of this study were that it was neither prepared nor powered for statistical analysis, and the number of subjects needs to be increased for the evaluation of treatment effectiveness and quality of life.

Based on the article published by IAEA in 2014, the utilization of Cobalt-60 in Asia-Pacific low-income country, low-middle income country, and upper-middle income country ranged from 59%, 46%, and 19% respectively. Nevertheless, the number of teletherapy machines can only cover for 34-45% of the needs.[10]

In India, the disparity between capacity and demand is high and there is also a huge gap in terms of radiotherapy technology availability. In 2019, there were 545 existing teletherapy machines in the whole country, compared to an estimated number of 4550 machines shortage.[11] Among 545 teletherapy machines, around 180 units of Cobalt-60 machines were operational and contributed in covering 30% of radiotherapy needs, meanwhile there were 3 proton facilities that were recently built and were being prepared.[11] The role of Cobalt-60 to provide radiotherapy accessibility in the resource-limited areas is still essiential, and further improvement to meet the demand of good quality radiotherapy is required.

Conclusion

In resource-limited settings, the utilisation of Cobalt-60 to treat nasopharyngeal cancer can potentially be improved through modifications made to the treatment planning. Forward planning field-in-field intensity modulation technique may be implemented with some disadvantages of Cobalt-60 dose distribution profile or it's physical limitation and shows promising outcome.

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