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Quality assurance and dosimetric analysis of intensity modulation radiotherapy using compensators for head and neck cancers

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In this study we describe our experience in implementing compensator based intensity modulated radiotherapy (cIMRT) for head and neck cancer with regard to pre treatment quality assurance (QA), dosimetric parameters and other technical detail.

This study represents the analysis of initial 48 patients who underwent cIMRT for head and neck cancers. All patients were treated with pre treatment QA in terms of point dose with ion chamber and spatial dose comparison with film dosimetry.

In our study for all 48 patients, compensators revealed a deviation in central axis dose of 2% $\pm$ 1.8% in terms of cumulative calculated versus measured dose. Target coverage for high dose volume (70 Gy) was adequate in terms of volume receiving 93% and 95% of the prescription dose, which was 98.5% and 97.5% respectively. Parotid and other critical organs were spared adequately. Contralateral parotid (CLP) was spared. V30 Gy and V35 Gy was 55.9% and 36.8% for CLP and average dose was 31.7 Gy. Median variation in cumulative measured dose versus cumulative calculated dose was 1.8% (SD + 1.8) and mean variation was 2.5% (95%CI 1.5, 2.6). Range was 0 to 7%.

cIMRT is practically feasible. Our QA tests revealed high degree of concordance between cumulative measured doses versus cumulative calculated doses. All dosimetric parameters were within acceptable limits. The manufacturing of compensator is cumbersome but it is a one time job followed by easy treatment delivery and simple QA procedure, high monitor unit (MU) efficiency and

less treatment time. cIMRT is easy to implement and now can be applied to larger number of patients with different type of tumor.

Key words: Compensator, IMRT, Quality Assurance, Dosimetry, Head and neck.

Introduction

Intensity modulated radiotherapy (IMRT) is a novel way of achieving desired dose distribution. Several IMRT treatment delivery techniques are commercially available namely Multileaf Collimator (MLC) based, Serial/Helical Tomotherapy and compensator based [9]. We are using compensator for IMRT (cIMRT) treatment delivery. Initially, compensators were used to deliver homogenous dose within the body by compensating the effect of missing tissues, internal tissue inhomogeneities and beam obliquity [8]. Designs of variable compensators in the multibeam situation have been discussed by Djordievich et al. [5]. Computerized tomography (CT) based compensator design for three dimensional treatment planning is reported by Megeras et al. [12]. There are various established methods to calculate and fabricate compensators [2]. Delivering an optimized fluence map produced by an inverse treatment planning algorithm is possible with compensators. Compensators for IMRT are designed in such a way that they produce optimized primary fluence profile over the patient's surface [12]. Head and neck cancers are the best suited site for IMRT as there are many critical organs adjacent to tumor which needs to be spared for better quality of life while at the same time delivering adequate dose to the tumor and thus prolonging the disease free life. We have been treating head and neck cancers patients with cIMRT since October 2003. In this paper we have discussed the technical details with regard to inverse treatment planning, manufacturing of compensators, their quality assurance and dosimetric results with regard to tumor coverage and normal tissue sparing.

Materials and methods

Study Overview

This study represents the QA and dosimetric analysis of the initial 48 patients who underwent cIMRT for head and neck cancers at Batra Hospital and Medical Research Centre, New Delhi, India. Prior permission to start cIMRT program was taken from the

institutional review board and ethics committee. Our cIMRT program started clinically from October 2003 and we have treated 48 patients till January 2006. QA for all the patients was done as a routine practice before their first treatment. In this paper we have discussed the results of pre treatment QA procedures as well as the results of dosimetric analysis.

Treatment Preparation

All patients were immobilized with the help of five point thermoplastic cast (Orfit industries, Belgium) in supine position. Simulation was done on Verasim simulator (GE Medical Systems, France). The probable isocentre was marked with radiopaque CT markers. Treatment planning helical CT with contrast was done on Prospeed SX Advantage (GE Medical Systems, Wisconsin, USA). CT scan with 2.5 mm slice thickness were obtained from head down through the clavicle and transferred to our planning system. Detail of target delineation has been discussed in our previous publication [13].

Optimization and treatment planning

Three dimensional treatment planning system Plato RTS version 2.5.2 (Nucletron Corporation, Veenendaal, The Netherlands) was used for treatment planning and dose calculation. Optimized fluence was generated with KonRad inverse treatment planning module (ITP) using gradient search algorithm and it is integrated into Plato RTS [16]. Inbuilt sequencer within ITP converts the optimized fluence to the deliverable compensator thickness. Sequencer is on during optimization. The ITP calculation algorithm is a three dimensional single pencil beam convolution [14]. The dosimetric accuracy of the ITP has been tested and found accurate for IMRT [14]. Once the optimization is done in the ITP module, the monitor units per beam and the compensator shape is sent to the RTS module where it computes the final dose using the three dimensional pencil beam algorithm [1]. A grid size resolution of 0.2 cm was used for all dose calculations. An optimized fluence map generated by ITP is shown in Figure 1. All patients were treated with simultaneous integrated boost (SIB). In most of the cases dosimetric parameters were achieved by using 5 equally spaced beams while in few cases 6 or 7 beams were used. Beam angle, collimator angle and couch angle optimization is not done by the treatment planning system; we place the beam as per the geometric shape of the target volume.

Figure 1. Optimized fluence map generated by ITP.

Compensator Detail

Choice of compensator material is very crucial. Different types of compensator material have been used for IMRT treatment delivery [3, 10, 17]. We have been using a high density alloy and its composition had a mixture of bismuth 52%, lead 30% and tin 18%. The generated optimized fluence is transferred to AUTIOMO 2.5D milling machine (BEBIG Isotopen, Medizintechnik GmbH, Germany) via network (Figure 2). This machine has a position accuracy of 0.005 mm and repeat accuracy ± 0.05 mm [7]. Milling machine has maximum milling speed of 8 mm/sec. Milling machine is connected to computer via RS232 interface. Drill bit size was 0.6 cm which has a projection of 1.0526 cm at isocentre and this is equal to the most widely used MLC. Smaller drill bit size was also available. Milling machine is customized for the clinical purpose. It drills four deep holes at the four corner of the necuper block, and five other holes for reference as it helps to maintain the proper orientation of the compensator (Figure 3). Once the compensator is milled it is filled upside down to avoid any air bubbles with high density alloy. Once the compensators are fabricated, they are endorsed with respective patient's name and his registration number along with beam angle, and it was checked every time prior to treatment.

Figure 2. AUTIMO milling machine.

Figure 3. Milled Compensator with reference holes.

Figure 4a. DRR from treatment planning system.

Figure 4b. Simulator film.

Treatment Delivery

Treatment was delivered on Siemens Mevatron MD2 linear accelerator (Siemens Medical Systems, Concord, USA). cIMRT treatment delivery is similar to physical wedge and blocks, which is well known in clinic. The compensators are checked for accuracy with regard to beam angle, patient name and registration number prior to placement in the collimator of linear accelerator. Radiation therapist technologist (RTT) had to enter the treatment room as many times as the number of beams used. We use one compensator per beam for our cIMRT.

Quality Assurance

Solid water phantom (Nuclear Associate, USA) was scanned in CT machine with a 0.6 cc ion chamber FC65G, (Scanditronix Welhoffer AG, Upsalla, Sweden) placed in the grove at a depth of 10 cm. These CT slices were 2.5 mm thick and were transferred to our treatment planning system. Digitally reconstructed radiographs (DRR) were generated and checked against simulator or port films taken using the treatment isocentre (Figure 4a and b). For quality assurance a new ready pack film known as EDR-2 Dosimetric films with enhanced dynamic range (Eastman Kodak Co., Rochester, New York, USA) were used. Dosimetric characteristic of EDR-2 films has been investigated [6, 15]. The EDR-2 film has an AgBr grain size of 1/10 and is more uniform in shape than those used for XV2 film. In addition the silver content of EDR-2 is about half that of the XV2 film [15]. It has been reported that this new film has a larger dynamic range from 0 up to 700 cGy. Problem of energy dependence in EDR-2 film is reported to be less due to the reduced silver content and smaller grain size. EDR-2 film can be used to measure the same daily fraction dose as delivered to the patient without saturation because of its large dynamic range. It is also reported that the EDR-2 film when compared with XV2 film is more resistant to the changes in film processor condition [15].

Results

Forty eight patients of head and neck cancer were treated with cIMRT technique from October 2003 to January 2006 at Batra Hospital and Medical Research Centre, New Delhi, India. There were 41 male patients and 7 female patients. Mean age was 59.5 (SD $\pm$ 11.2). Twenty four (50%) patients were of stage IV disease and patients with stage II and

III disease were 9 (18.8%) and 15 (31.3%) respectively. Five patients were treated in postoperative settings and 43 patients were treated definitively. All the patients were histologically proven cases of squamous cell carcinoma. Site was distribution was as follows: Larynx 22 (45.8%), Oropharynx 14 (28.2%), Nasopharynx 3 (6.3%), Oral Cavity 3 (6.3%), Hypopharynx 5 (10.4%) and secondary neck with primary unknown 1 (2.1%).

Average High dose (70 Gy) prescription volume was 190.8 cc (SD $\pm$ 116.7), range was 10 cc to 467.7 cc. Prescription was 70 Gy as GTVPTV in 16 patients and as CTV1PTV in 27 patients while prescription was 66 Gy as CTV1PTV in 17 patients. Target

Table 1. Dosimetric parotid and tumor coverage parameters.

TARGET COVERAGE PARAMETER

	Average Dose	*V _{95%}	*V _{93%}
Ideal Coverage	± 3 Gy of prescribed dose	$\geq 98\%$	$\geq 99\%$
Acceptable	± 5 Gy of prescribed dose	$\geq 95\%$	$\geq 98\%$

PAROTID VOLUME SPARING PARAMETER

	Average Dose	$\ddagger$ V _{30 Gy}	$\S$ D _{20 cc}
Ideal Sparing	≤ 30	50.00%	≤ 20 Gy
Acceptable	≤ 32	50.00%	≤ 25 Gy

CRITICAL STRUCTURE PARAMETER

	Spine ($\ddagger$ V _{45 Gy})	Mandible ($\ddagger$ V _{60 Gy})	Brainstem ($\ddagger$ V _{54 Gy})
Ideal Sparing	$\leq 1\%$	$\leq 10\%$	0.00%
Acceptable	$\leq 5\%$	$\leq 15\%$	$\leq 1\%$

*V_{X%} – Percentage volume of target receiving X% of prescribed dose

$\dagger$ D2/D98 – Ratio of dose received by 2% of target and 98% of target

$\ddagger$ V_{X Gy} – Percentage volume of organ receiving more then or equal to X Gy of dose

$\S$ D_{20 cc} – Dose received by 20cc combined volume of both parotids.

delineation and dose prescription has been discussed earlier [13]. Low dose prescription was 56 Gy as target in 43 patients who were treated definitively (excluding patients with postoperative settings). The 70 Gy prescription volume had 0.5% of the volume which was under dosed for dosimetric parameter of V93 and V95 both. Target Volume which was prescribed 66 Gy had 4.3% and 3.9% of volume which was under dosed for dosimetric parameter of V93 and V95. Prescription for target was 56 Gy and under dosed volume 2.8% and 1.9% for V93 and V95. Percentage of high dose volume receiving 110% of the 70 Gy prescription dose was 26.4% (95% CI 20.2, 32.5).

Dosimetric parameters for parotid sparing and there results are detailed in Table 1. In majority of cases contralateral parotid (CLP) was spared. V30 Gy and V35 Gy was 55.9% and 36.8% for CLP and average dose was 31.7 Gy. In 26 (54%) patients, criteria for V30 Gy was fulfilled and in 41 (85.4%) patients criteria for V35 Gy was achieved. Dosimetric parameters for these two groups of patients were significantly different in terms of V28 Gy, V30 Gy, V35 Gy, D2/3V and Average dose for CLP. When this was analyzed for patients who had minimum of 6 months of follow up ($n = 42$) only V35 Gy, D2/3V and average dose to CLP retained their significance (Table 2). Dose volume data for serial and parallel structures are described in Table 3.

Figure 5. Scatter plot showing individual values.

Table 2. DVH analysis for target coverage and parotid sparing for patients treated definitively

TARGET PRESCRIPTION VOLUMES			
Parameters representing coverage or sparing	70 Gy volume GTVPTV (n = 16) CTV1PTV (n = 27)	66 Gy volume CTV1PTV (n = 17)	56 Gy volume Target (n = 43)
Average dose [Gy]	74.3 (95% CI 73.7, 74.9)	Not relevant	Not relevant
Minimum dose	54.2 (95% CI 52.1, 56.3)	47.6 (95% CI 43.9, 51.2)	30.2 (95% CI 27.5, 32.8)
V93 [%]	98.5 (95% CI 97.9, 99.0)	95.7 (95% CI 93.2, 98.3)	97.2 (95% CI 96.4, 97.9)
V95 [%]	97.5 (95% CI 96.8, 98.1)	94.1 (95% CI 90.8, 97.4)	96.1 (95% CI 95.1, 97.1)
V100 [%]	90.1 (95% CI 88.3, 91.9)	86.1 (95% CI 80.4, 91.9)	93.0 (95% CI 91.4, 94.6)
V110 [%]	26.4 (95% CI 20.2, 32.5)	Not relevant	Not relevant

DVH ANALYSIS FOR PAROTID			
Parameters representing coverage or sparing	Ipsilateral Parotid	Contralateral Parotid	Both Parotid
Volume [cc]	23.9 (95% CI 20.6, 27.2)	23.8 (95% CI 21.1, 26.4)	47.2 (95% CI 41.5, 52.9)
V20Gy [%]	91.1 (95% CI 86.5, 95.6)	83.6 (95% CI 77.8, 89.3)	NA
V28Gy [%]	82.5 (95% CI 75.5, 89.4)	63.3 (95% CI 56.6, 70.1)	NA
V30Gy [%]	79.7 (95% CI 72.3, 87.2)	55.9 (95% CI 48.9, 62.8)	NA
V35Gy [%]	71.2 (95% CI 62.4, 79.9)	36.8 (95% CI 30.5, 43.0)	NA
V20Gy [cc]	02.4 (95% CI 00.9, 03.9)	04.0 (95% CI 02.4, 05.6)	06.4 (95% CI 03.5, 09.3)
Average Dose [Gy]	44.3 (95% CI 40.2, 48.5)	31.7 (95% CI 29.5, 33.9)	NA
D1/3V	51.2 (95% CI 47.0, 55.3)	36.6 (95% CI 33.9, 39.4)	NA
D1/2V	44.1 (95% CI 39.7, 48.6)	29.8 (95% CI 26.5, 33.1)	NA
D2/3V	41.3 (95% CI 36.2, 46.5)	26.5 (95% CI 23.3, 29.6)	NA
Maximum Dose [Gy]	75.1 (95% CI 72.6, 77.6)	65.9 (95% CI 63.0, 68.9)	NA
Minimum Dose [Gy]	19.8 (95% CI 15.4, 24.2)	10.7 (95% CI 08.4, 13.0)	NA

Table 3: Dose volume data for critical structures.

Serial structures		Parallel structures	
Structures	Maximum dose (±SD)	Structures	Average dose (±SD)
Spinal Cord	52.4 ± 3.5	Ipsilateral Parotid	43.9 ± 13.6
Mandible	79.0 ± 6.7	Contralateral Parotid	31.4 ± 7.1
Optic Chiasma (n = 3)	42.9 ± 33.2	Larynx	56.3 ± 6.2
Brain Stem (n = 3)	61.9 ± 7.7	Oral Cavity	47.7 ± 6.7
Brain Stem (n = 45)	46.2 ± 14.1		

Table 4. Average variation between calculated and measured, cumulative doses and individual beam doses.

Beams	N	Average variation [%]	*SD	5% minus variation	†P value
Beam 0	39	5.27	±4.2	−0.27	0.69
Beam 72	39	5.14	±5.46	−0.14	0.87
Beam 144	39	6.26	±6.12	−1.26	0.26
Beam 216	39	6.86	±7.17	−1.86	0.11
Beam 288	39	5.91	±5.84	−0.91	0.34
Beam 300	14	4.8	±5.31	+0.2	0.89
Beam 308	12	5.06	±3.94	−0.06	0.96
Cumulative	44	2.08	±1.82	+2.08	0

*SD = Standard Deviation, †Significance was calculated using One Sample T-test and 5% was taken as test value as this was our acceptable limit for dose variation.

Measurement at a depth of 10 cm of an IMRT treatment plan were performed in a phantom with a 0.6 cm³ Farmer chamber. Ideally ion chamber measurements in high dose, low gradient regions should agree with the planned dose and variation within 3% to 5% was acceptable. Median variation in cumulative measured dose versus cumulative calculated dose was 1.8% (SD +1.8) and mean variation was 2.1% (95% CI 1.5, 2.6). Range was 0% to 7%. Considering a 5% variation acceptable, T-test was conducted and our mean value of 2.1% was far below the 5% mark and this difference was statistically significant ($p = 0.001$). Cumulative dose variation above 5% was present in 5 patients (Figure 5) with individual value of 6%, 7%, 5.4%, 5.2% and 5.1%. In these 5 patients, off axis dose was measured and variation was within acceptable limit. Average variation in terms of calculated versus measured dose for individual beam were also recorded. Average values were marginally above the acceptable limit for beam 0, beam 72, beam 144, beam 216, beam 288 and beam 308 while for beam 300 it was below the acceptable and this difference was statistically not significant.

Discussion

The cIMRT can achieve the dosimetric parameters with regard to target coverage and organ sparing. There is enough data on compensator based IMRT with regard to design, fabrication, choice of material and implementation. Data regarding dosimetric details of clinical significance are scanty. We have tried to incorporate all dosimetric data achieved by our cIMRT technique which is also relevant to MLC based IMRT as there is lot of data which confirms correlation between dosimetric parameters and clinical outcome for this latter approach. In our earlier publication we have reported our outcome in terms of dosimetric parameters and their correlation with clinical results [4, 13]. In our knowledge this is the first study focusing on quality assurance and dosimetric data with largest number of patient dataset reported till date with cIMRT.

Jiang et al. [10] have used Lipowitz metal as a compensator material for IMRT, composed of 13.3% tin, 50% bismuth, 27.7% lead and 10% cadmium by weight with a density of 9.76 gm/cm³, though it provides a high degree of intensity modulation, but it is hazardous to health as it contains cadmium.

Chang et al. [3] have used tin granules as compensator material for IMRT treatment delivery but it is a medium density material and modulation range always does not meet the clinical needs.

Salz et al. [17] have used compensator consists of tin granules embedded in wax, with 6 MV photon beam for head and neck tumors and switch to MCP96 alloy to get superior tumor coverage and better sparing of normal tissue. Alloy used by us in this study is a high density material and does not contain cadmium so it is not hazardous and provide higher degree of modulation.

Salz et al. [17] have reported their experience for 24 patients using IMRT with compensators for head neck cancer. Salz et al. [17] reported deviation of central axis dose of less than equal to 1.5% and they found less than 2% of the target dose deviation because of inhomogeneities. In our studies for all 48 patients, compensators revealed a deviation in central axis dose of $2\% \pm 1.8\%$ in terms of cumulative calculated versus measured dose (Table 4). Their prescription for high dose volume was 60-70 Gy and low dose volume was 48-54 Gy. They recalculated seven patients and compared the target coverage and parotid sparing. With tin granules plus wax compensator, 95% and 90% of the prescribed dose was covering 87% and 96% of the high dose volume respectively while with MCP96 alloy compensator coverage was 93% and 99% respectively. Similarly parotid sparing in terms of median dose improved from 26.3 Gy to 23.8 Gy. Overall their results revealed high dose volume coverage by 95% and 90% of the prescription dose was 88% and 96% and similarly low dose volume coverage was 90% and 96%. In 21 patients contralateral parotid received dose < 30 Gy. In our study 100% and 95% of the prescription dose was covering 90.1% and 97.5% of the GTVPTV and CTV1PTV, 86.1 and 94.1% of the CTV1PTV and 93% and 96.1% of the target respectively.

Nancy Lee et al. [11] used MLC based IMRT and reported their experience for head neck cancers. The prescribed dose was 70 Gy to the GTV and positive neck nodes, 60 Gy to the CTV which included the GTV plus a margin of potential microscopic disease, and 50 to 60 Gy to the clinically negative nodal regions. The average maximum, mean, and minimum doses (in Gy) delivered were 80, 74 and 56 to the GTV and 80, 69 and 33 to the CTV. An average of only 3% of the GTV and 3% of the CTV received less then 95% of the prescribed dose. Mean left and right parotid volume doses were both 29 Gy.

In our series target coverage was achieved in all the patients within the defined dosimetric limits and all the dosimetric parameters are comparable with the above mentioned studies using either compensator based or MLC based IMRT [11]. Target coverage in terms of average mean and minimum dose (in Gy) delivered were 74.3 (± 3.4), and 54.2 (± 8.9) to the GTVPTV, 71.3 (± 3.2), and 48.4 (± 9.3) to the CTV1PTV and 67.6 (± 4.1), and 32.4 (± 11.2) to the Target. Average dose for CTV1PTV and Target seems

to be very high and the reason for this is that our planning software does not have the option of subtracting overlapping volumes. While calculating the average dose to CTV1 and CTV2 the system also incorporates the dose to GTV and thus increasing the overall average dose. Considering 95% of the prescription dose, under dosage of 0.5% for GTVPTV, 3.9% for CTV1PTV and 1.9% for Target was within acceptable limit and was comparable with reviewed literature.

Our median average dose for contralateral parotid (CLP) was 31.3 Gy. In 25 (52.1%) patients it was less than or equal to 30 Gy. Median parotid volume receiving 30 Gy or more dose was 51.4% and in 28 patients it was below or equal to 30 Gy. As in our earlier report we emphasized the importance of 35 Gy volume for parotid with respect to xerostomia and same was evident in these studies [4, 13]. Our average dose was far below the 35 Gy mark and median parotid volume receiving 35 Gy or more dose was 33.3%. Only 7 patients had more than 50% of their CLP volume receiving more than 35 Gy dose.

Salz et al [17] used two asymmetric fields in one compensator for small tumors so that RTT had to enter the treatment room after every two fields while we had majority of our patients with locally advanced head neck patients, and we delivered one compensator per field. RTT had to enter the treatment room as per the number of beams used. On an average total treatment time on machine with compensators was 18 minutes $\pm$ 5 minutes. It includes patient's entry into the treatment room, setup, treatment on machine and exit from the treatment room. Factors influencing the total treatment time were monitor units per field, number of fields, single field IMRT or split field for lower supraclavicular fossa and general condition of the patient (initial part of the treatment i.e first three weeks setup quick and easy but later on with intense radiation reaction setup slow and difficult thus taking more time to complete treatment). Overall treatment delivery using compensators is easy and practically feasible even in centers with high patient load. Yoda has described a multiportal compensator system for IMRT delivery [18]. This will further reduce the human intervention and overall treatment time

Conclusion

Our growing clinical experience with cIMRT clearly indicates its usefulness in terms of target coverage and organ at risk sparing. Not only our results were comparable to other studies using compensator, but also they were comparable to studies using MLC based

IMRT in terms of achieving dosimetric parameters [11]. Though with limitation of intensity modulation because of limited thickness and density of compensator blocks, our results were within acceptable limits with slightly higher parotid doses. The manufacturing of compensator is cumbersome but it is a one time job followed by easy treatment delivery and simple QA program high monitor unit efficiency, less beam on time. This technology to deliver IMRT with compensators is quite mature, at least in our experience and now can be applied to larger number of patient population with different type of tumor.

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