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Dosimetric Comparison between Three Dimensional Conformal Radiation Therapy (3DCRT) & Intensity Modulated Radiation Therapy (IMRT) in Mid-Lower Oesophageal Carcinoma

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Abstract

Purpose: To investigate if intensity modulated radiation therapy (IMRT) offers a better planning target volume (PTV) coverage and/or lower dose to normal thoracic structures in comparison to three dimensional conformal radiation therapy (3DCRT) in the treatment of mid and lower oesophageal carcinoma patients. **Materials and Methods:** A prospective study in the period from 2014 till 2015 was held in the radiation therapy department of the National Cancer Institute, Cairo University, in which 20 locally advanced or inoperable mid and lower oesophageal cancer patients were treated by chemo-radiation using 3DCRT technique. IMRT plans were generated for those 20 patients. The 3DCRT and IMRT plans were compared as regards PTV coverage and doses to critical organs at risk. **Results:** All plans had produced satisfactory PTV coverage with no significant differences noted. The lung V20 for both lungs in 3DCRT was 16.94% ± 4.2% which was increased to 21.42% ± 3.6% in IMRT ($p = 0.017$). The mean dose to the heart and V30 were higher in IMRT plans while the mean dose to the spinal cord was higher with 3DCRT plans, yet that didn't reach a statistically significant level ($p = 0.156$). The dose delivered to the liver didn't pose any difference between both techniques. **Conclusion:** 3DCRT remains to be a feasible cost effective treatment delivery option for mid and lower oesophageal cancer cases with a lower optimization and delivery time than that for IMRT. Moreover, that calls for further dosimetric studies and clinical trials to assess IMRT technique. In our study, IMRT using nine fields didn't prove to be superior to 3DCRT.

Keywords

Oesophageal Carcinoma, 3DCRT, IMRT, Dosimetric

1. Introduction

Oesophageal cancer continues to rank as one of the highly aggressive and lethal gastrointestinal diseases globally [1]. Poor treatment outcomes continue to challenge the multidisciplinary array of surgeons, medical and radiation oncologists.

Most patients are present in an advanced or an unresectable stage [2]. This fact has led to the establishment of concurrent chemo radiotherapy (CCRT) as the staple treatment policy for such cases [3]. Moreover, local failure remains to be the commonest failure pattern coupled by local persistence of the tumor [4].

The technique of radiation therapy delivery has evolved along the years starting with the basic antero-posterior/postero-anterior (AP/PA) field arrangement, then the 4 fields box technique reducing the lateral fields' weight to decrease dose to lungs, as well as the 3-field technique; anteroposterior field and 2 posterior oblique fields. Up until the era of the 3D conformal radiation therapy (3DCRT) has become the technique of choice for many years now in various centers [5].

Since locoregional failure or persistence after treatment reaches 50% [4] [6] that raised the flag for delivering higher radiation dose to increase local control. Meanwhile, critical surrounding normal tissue tolerance must be respected, namingly the lungs, spinal cord and heart specially that the planning target volume (PTV) is central. Various studies reported good dosimetry and patient outcome by IMRT [7] [8]. The main disadvantages of IMRT despite its being effective in dose conformity to tumor are increased treatment delivery time and monitor units (MU).

We conducted this prospective study in our department to compare the dose distribution for the PTV and organs at risk (OAR) using the 3DCRT and those were compared with the IMRT generated plans.

2. Materials and Methods

Patients Data and Simulation

This is a prospective dosimetric study conducted in the radiation therapy department of the National Cancer Institute, Cairo University, Egypt. 20 patients with locally advanced histopathologically proven mid and lower oesophageal carcinoma, not reaching gastro-esophageal junction were treated with chemoradiation from the period of April 2014 till July 2015.

Patients were aged from 48 to 70 years, they all had histopathologically proven oesophageal Squamous cell carcinoma.

Patients were simulated with a General Electric Lightspeed RT 16 computed tomography simulator with 2.5 mm slices. Patients were asked to lie in a supine position with both arms raised over their heads.

Treatment planning was done on XIO (CMS) treatment planning system version 5.1

A gross tumor volume (GTV) covering the gross oesophageal tumor and positive regional lymph nodes was contoured. The clinical target volume (CTV) encompassed a proximal and distal margin of 5 cm and a radial margin of 15 mm added to the GTV. The planning target volume (PTV) varied from case to case yet usually averaged 10 mm all around the CTV to account for organ movement. OAR included the heart, lungs, spinal cord and liver. Figure 1 shows dose distribution for one of our mid oesophageal cancer cases for both the 3DCRT and IMRT plans.

3DCRT plan were created using XIO treatment planning system 6 MV photons. 3 - 5 fields were shaped at the beam's eye view to encompass the PTV shape using MLC at gantry angles of 0˚, 90˚, 270˚ or 0˚, 45˚, 90˚, 270˚ and 315˚ The treatment target volume included PTV and an additional 0·7 cm margin for beam penumbra in all directions. Physical and virtual wedges were used to modify the dose in the treatment plan and to perform dose homogeneity in PTV. The prescribed dose was 1.8 Gy × 28 fractions for a total dose of 50.4 Gy.

IMRT plan was performed using Monaco treatment planning system 6 MV photons with 9 equally spaced coplanar beams using commercial inverse planning software and avoid opposing fields. For inverse-planned 9F-IMRT, the gantry angles were 0˚, 40˚, 80˚, 120˚, 160˚, 200˚, 240˚, 280˚ and 320˚.

The organs at risk dose constraints given for lungs, heart, spinal cord and liver for planning and optimization are shown in Table 1 [9].

A 9 beam IMRT plan was generated for all patients considering same contouring. All plans aimed to achieve a min. dose > 95% and max. dose < 107%

Statistical analysis was performed using SPSS version 22.0 software (Chicago, IL, USA) and SAS version 9.4. Significance level was set at $p \leq 0.05$ (Figure 1).

3. Results

The 3DCRT and IMRT plans were dosimetrically evaluated, dose coverage to PTVs all techniques achieved the constraint that 95% of the volume is covered by more than 95% of the prescribed dose. Dose homogeneity within the various PTVs was comparable with no statistically significant difference between both techniques (Table 2).

As for the organs at risk (OAR) the mean dose to the heart and the V30 were both higher in the IMRT plans without reflecting any statistically significant difference and not exceeding the dose constraints where the mean dose for 3DCRT was 12.6 Gy vs. 13.9 Gy for IMRT ($p = 0.324$), and the Heart V30 was 14.5 Gy for 3DCRT vs. 19.6 Gy for IMRT technique plans ($p = 0.116$).

Despite the fact that the mean dose to the spinal cord delivered by IMRT was 34.5 Gy vs. 37.5 Gy with 3DCRT yet that didn't amount to a statistically significant difference ($p = 0.156$).

Table 1. Dose constraints for organs at Risk (OAR).

Structure	Constraint
Lungs	V20 ≤ 35%
Heart	Mean dose < 26 Gy V30 < 46%
Spinal Cord	Dmax < 45 Gy 45 Gy to whole SC with not more than 2% of SC > 50 Gy
Whole Liver	Mean dose < 32 - 30 Gy

Table 2. Average Dose-Volume Statistics for PTV for Both 3DCRT and IMRT Techniques.

	3DCRT (Gy)	IMRT (Gy)	p-Value
Min. Dose	40.7	39.8	0.47
Max Dose	52.8	56.2	0.06
Mean Dose	49.9	51.0	0.182

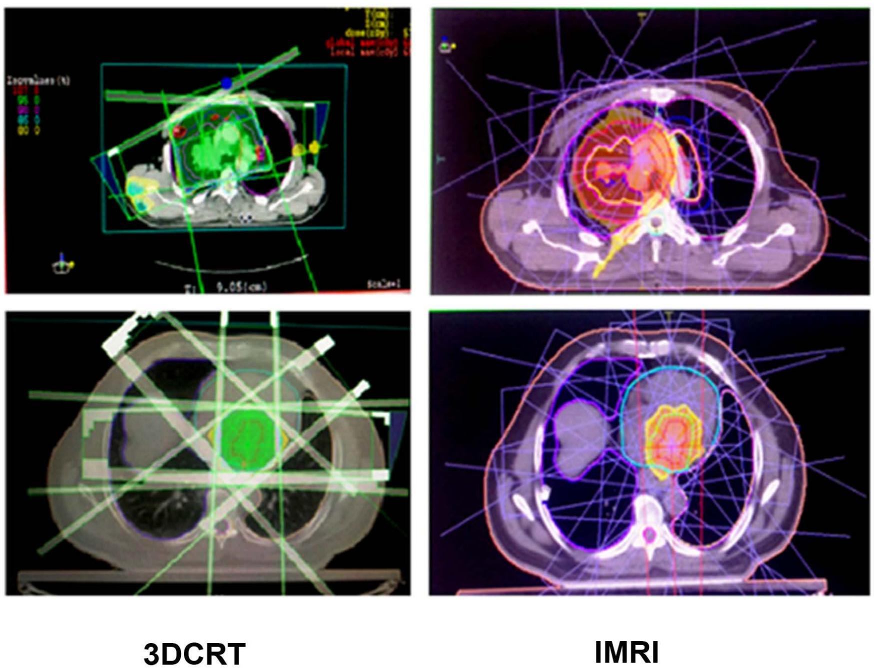

Figure 1. Dose distributions of 3DCRT plan were created using XIO treatment planning system 6 MV photons. 3 - 5 fields were shaped at the beam's eye view to encompass the PTV shape using MLC (left) and IMRT plan was performed using Monaco treatment planning system 6 MV photons with 9 equally spaced coplanar beams (right) for a middle third oesophageal cancer in axial view.

The V20 for the 3DCRT plans delivered lesser lung volume irradiation; 16.9% when compared to IMRT plans; 21.4% with a p-value of 0.017 denoting a statistically significant value in favor of the 3DCRT plans.

The mean dose delivered to the liver was 4.3 Gy for 3DCRT vs. 5.1 Gy for IMRT plans and that did not show any statistically significant difference between

3DCRT and IMRT arms (p = 0.192).

4. Discussion

In order to tackle the pitfall of low survival rates and after various randomized trials, concomitant chemoradiation has become a standard treatment in oesophageal cancer patients producing up to 25% - 30% 5 year survival rates [10] [11]. Yet again studies showed that chemoradiation can come with a high price tag of severe complications [4] [6].

Thus we designed current study to address the question of dosimetric differences between IMRT and 3DCRT for mid and lower esophageal cancers, and to evaluate if IMRT can be implemented for dose escalation to the target volume without increasing the dose to various organs at risk specially the lungs.

Current study didn't show any significant improvement in the PTV coverage by IMRT compared to 3DCRT and this finding matches the results from the study published by Ghosh *et al.* [12] where the dose homogeneity was comparable for both 3DCRT and IMRT techniques. Similarly the study by Wu *et al.* [13] reported no significant superiority of IMRT or even Volumetric Modulated Arc Therapy (VMAT) plans over 3DCRT in middle oesophageal cancer cases. Our findings differ from the results of the study by Fenkell *et al.* [5]; where they compared IMRT with 3DCRT in the treatment of the cervical esophageal cancer, the median coverage of various PTVs even 50 and 70 were all improved with IMRT. This discrepancy could be explained by the relatively simpler shape of the target for our middle and lower esophageal cancers versus that of cancers located in the cervical oesophagus in Fenkell's study. On the other hand Nutting *et al.* [14] concluded that the dose conformity of IMRT and VMAT was improved for middle esophageal cancer when compared to 3DCRT. The study of Vivekanandan *et al.* [15] again showed superiority of IMRT and VMAT in target dose conformity versus 3DCRT in esophageal cancer. Though they didn't specify which segment of the oesophagus did they study.

As early as 1999, Khoo *et al.* [16] reported that the superiority of IMRT with its dose painting ability was more established for complex targets; as with the more complicated target coverage of head and neck cancers compared to 3DCRT, in oesophageal cases the greatest benefit was seen when the tumor was concave, thus in most cases of oesophageal carcinoma cases where the PTV is mostly cylindrical that minimizes the benefit from IMRT. The dose deliver for patient in 3DCRT technique is easier than IMRT. It is also lower in cost and less time-consuming compared with IMRT [17] [18].

The results of this study match these algorithms where there was a small benefit as regards sparing of spinal cord yet none seen as regards the heart or lungs; where IMRT shows superior conformality to treatment volume thus delivering higher doses yet at the expense of increased number of beams delivering small radiation doses to greater normal tissue volume [5]. This fact had a clear impact on our results since our patients had advanced oesophageal tumors producing a large PTV alongside large volume of surrounding organs at risk specially lungs and spinal cord. We generated 9 beam IMRT plans and compared them to the original 3DCRT treatment plans, in our case the 9 beams were equispaced as in the study by Nutting *et al.* [19], who concluded no benefit in dose reduction to the lungs in their IMRT plans, still we shared same conclusion and our lungs V20 was statistically significantly higher with the IMRT plans. Moreover, Ghosh *et al.* [12] reported statistically significant higher lung V20 with IMRT which is in accordance with our results. As for Chandra *et al.* [7] they compared 4, 7 & 9 IMRT beem plans to 3DCRT in lower oesophageal cancer patients and they reported a 5% reduction in lung V20 with IMRT plans which is different than our findings. Similarly, Wu *et al.* [13] reported a lower lung V20 with IMRT yet not reaching a statistically significant value. Nutting *et al.* [19] reported a reduction in mean lung dose upon using a 4 field IMRT when compared to the 9 fields IMRT and the 3DCRT plans.

On the other hand, in current study IMRT delivered lower mean dose to the spinal cord but not reaching a statistically significant level, this was also reported by Ghosh *et al.* [12] and also consistent with the results reported by Vivekeanandan *et al.* [15].

Current study results showed lower mean dose to the heart with 3DCRT when compared with IMRT and the V30 was also lower with 3DCRT still neither of those values reached a statistically significant value. Similar results were published by Candra *et al.* [7]. Chen *et al.* [20] also published a study on a dosimetric analysis of 10 mid-distal esophageal carcinoma cases comparing helical tomotherapy, step-and-shoot IMRT and 3DCRT, the IMRT plans resulted in decreased heart V30 and V45. Our findings are also consistent with Wu *et al.* [13] regarding the V30 heart sparing effect with 3DCRT that reached a statistically significant value. Mayo *et al.* [21] supported the same findings as well. The study by Ghosh *et al.* [12] stands to differ with our findings as they reported higher mean heart dose with 3DCRT yet not exceeding the dose constraints.

Another organ at risk is the liver that surrounds part of the oeosophageal circumference distally thus the more coplanar beams implemented the more the dose that will reach the liver as our results showed higher mean dose delivered with the IMRT plans (**Table 3**). Our results are consistent with the findings published by Chandra *et al.* [7]. Also Ghosh *et al.* [12] reported that IMRT delivered a higher mean dose to the liver than with the 3DCRT in their lower oesophageal cancer cases though not of statistical significance same as our cases.

5. Conclusion

3DCRT can be reliably applied in the treatment of in Mid-Lower Oesophageal carcinoma, as it is easy to deliver, low in cost and time-saving compared to IMRT. It provides homogenous doses to the target and good sparing of OARs. IMRT did not produce any dosimetric advantage over the 3DCRT technique, apart from the decreased mean dose to the spinal cord. On the contrary, IMRT

Table 3. Dose statistics extracted from the DVHs of Organs at Risk (OAR) for 3DCRT and IMRT techniques.

	3DCRT	IMRT	p-value
Heart mean dose V30	12.6 Gy	13.9 Gy	0.324
	14.5 %	19.6 %	0.116
Spinal Cord	37.5 Gy	34.5 Gy	0.156
Both lungs V20	16.9 %	21.4 %	0.017
Liver	4.3 Gy	5.1 Gy	0.192

technique poses a higher chance of lung toxicity compared to 3DCRT which is so far a better choice in combined chemo-radiation therapy in oesophageal cancer cases by virtue of decreasing lung dose as well as being cost effective in a busy radiation therapy department. In order to consider implementing IMRT with or without escalated dose for the treatment of oesophageal cancer further clinical trials and dosimetric studies are called for.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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