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Dosimetric Comparison between Intensity Modulated Radiation Therapy (IMRT) and Three-Dimensional Conformal Radiation Therapy (3DCRT) in Mid Lower esophageal Carcinoma: An Analytical Observational Study

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Abstract

Esophageal cancer (EC) is a common cancer with high mortality because of its rapid progression and poor prognosis. One of the most successful therapies for EC is radiotherapy. Two recently created radiation methods are intensity-modulated radiotherapy (IMRT) and three-dimensional conformal radiotherapy (3D-CRT). In terms of target coverage, dose homogeneity, and lowering toxicity to healthy organs, IMRT is thought to be superior to 3D-CRT. These benefits haven't been proven in the treatment of EC, though. This study was performed to investigate if intensity modulated radiation therapy (IMRT) offers a better planning target volume (PTV) coverage and/or lower dose to organs at risk in comparison to three-dimensional conformal radiation therapy (3DCRT). 30 patients with locally advanced histo-pathologically proven mid and lower oesophageal carcinoma, not reaching gastro-esophageal junction were treated with chemoradiation using IMRT technique. 3DCRT plans were generated for those 30 patients. The IMRT and 3DCRT plans were compared in terms of PTV coverage and doses to organs at risk. Our results revealed that IMRT is better than 3DCRT comparing PTV coverage and doses to organs at risk having statistically significant difference between both techniques (p<0.001). As for the organs at risk (OAR), the V20 for the IMRT plans delivered lesser lung volume irradiation also the mean dose to the heart and the V30 were both higher in the 3DCRT plans.

Keywords: *esophageal cancers (ECs), Organs at risk (OAR), Intensity modulated radiation therapy (IMRT), Three-dimensional conformal radiation therapy (3DCRT), Planned target volume (PTV).*

INTRODUCTION

Esophageal cancer continues to rank as one of the highly aggressive and lethal gastrointestinal diseases globally (Jemal, *et al*., 2008). Poor

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treatment outcomes continue to challenge the multidisciplinary array of surgeons, medical and radiation oncologists. Moreover, EC at earlier stages does not present typical clinical symptoms; thus, it is always diagnosed at later stages and the 5-year survival rate of patients with ES is only 15% to 25% (Pennathur, *et al*., 2013, Domper Arnal, *et al*., 2015, Liang, *et al*., 2017). Radiotherapy is one of the most effective treatments for cancer and plays an important role in the treatment of both resectable and unresectable ECs (Hu, *et al.*, 2016, Kole, *et al*., 2012). However, it is a great challenge to deliver radiation dose accurately with minimal toxicity (Wang, *et al*., 2011, Ling, *et al*., 2014). In the past few decades, several advanced radiotherapy techniques, including three-dimensional conformal radiotherapy (3DCRT), intensity-modulated radiotherapy (IMRT), image-guided radiotherapy, tomotherapy, intensity-modulated arc therapy, and volumetric modulated arc therapy, have been developed to increase the conformal degree of target areas as well as the radiation dose, and to decrease the toxicity to normal organs (Hu, *et al*., 2016, Ling, *et al*., 2014, Ghosh, *et al*., 2012).

Esophageal cancer is a malignant parenchymal tumor in the human esophagus, whose incidence rate has gradually increased in recent years and mortality rate is among the worst in human malignant tumors. The major clinical manifestations of esophageal cancer are cough, chest pain, chest distress, hemoptysis and difficulty in swallowing, and even dyspnea in severe cases. Esophageal cancer develops rapidly and can metastasize to adjacent organs or distant organs, leading to organ failure and seriously threatening the life of patients. Radical resection of esophageal cancer is a major therapeutic method for esophageal cancer. However, the surgical incision is large, and the chest cavity is exposed for a long-time during surgery, so the lungs are prone to infection and compression, and the lung function is affected easily, producing an unsatisfactory surgical effect.

3DCRT is developed and proven in the late 1990s as a preferred treatment for cancer for its better target coverage and significantly decreased toxicity to normal organs compared to 2DCRT. Later, the IMRT technique is proven to be more effective than 3DCRT in target coverage, dose homogeneity, and reducing toxicity to normal organs (Chandra, *et al*., 2005). The esophagus is an organ close to spinal cord, heart, and is surrounded by the lung. When radiotherapy is applied for treating EC, these organs of lung, heart and spinal cord are the main 3 organs at risks (OARs) (Ghosh, *et al*., 2012). Thus, the advantages of IMRT are important for these OARs. It has been reported that IMRT is superior to 3DCRT in the treatment of non-small cell lung cancer and gynaecologic malignancies in terms of treatment toxicity (Hu, *et al.*, 2016, Yang, *et al*., 2012). Several studies have compared IMRT and 3DCRT in the treatment of EC. However, whether IMRT is superior to 3DCRT in the treatment of EC remains controversial. We conducted this study in our department to compare the dose distribution for the PTV and organs at risk (OAR) like lung, heart, spinal cord and liver using the IMRT and those were compared with the 3DCRT generated plans. Target coverage, dosage uniformity, and toxicity to healthy organs are thought to be improved by IMRT over 3D-CRT. And the results of this study revealed similar results.

METHOD AND MATERIALS

This is an analytical observational study related to dosimetry of mid-lower esophageal carcinoma, conducted in our hospital. From January 2017 through December 2021, a total of 30 patients with locally advanced histo-pathologically proven mid and lower oesophageal carcinoma that had not reached the gastro-esophageal junction were treated with chemo radiation using the IMRT technique. Of these patients, 17 (56.66%) men and 13 (43.34%) women. 3DCRT plans were generated for those

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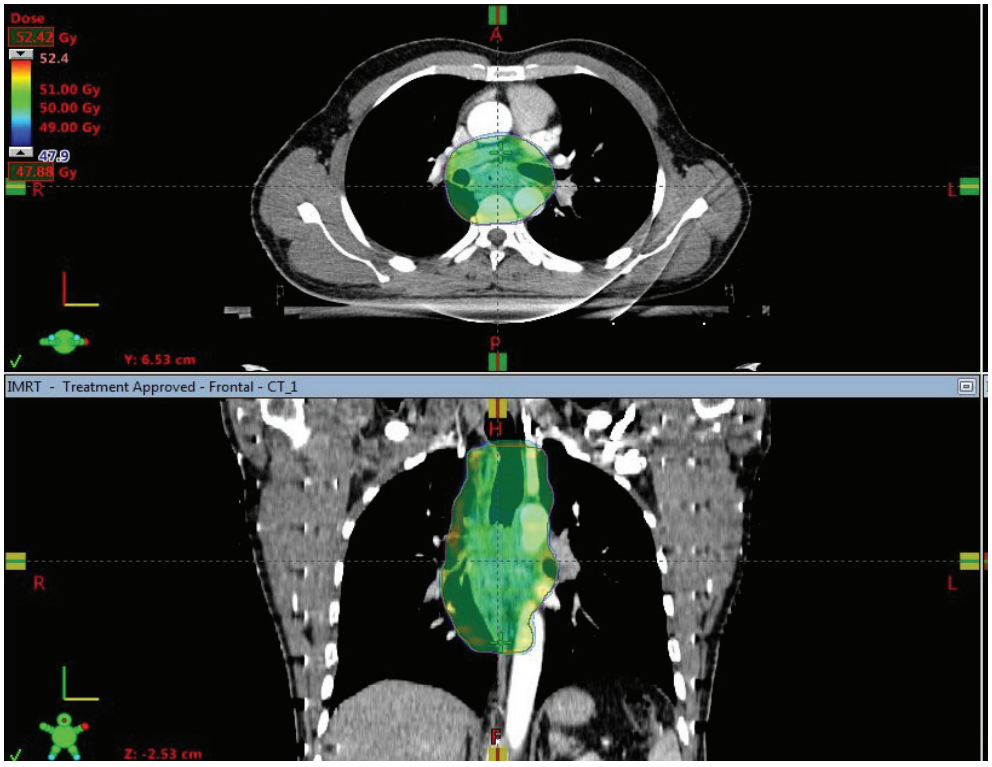

Figure 1. Dose colour wash of 47.9 Gy (95% of prescribed dose) to the PTV high for 7F-IMRT in axial and coronal view for middle third esophageal cancer.

30 patients. The IMRT and 3DCRT plans were compared in terms of PTV coverage and doses to organs at risk (OAR).

Patients were aged from 40 to 75 years, they all had histo-pathologically proven esophageal Squamous cell carcinoma. Patients were simulated with 16 slice helical siemens somatom sensation computed tomography simulator with 3mm slices. Patients were asked to lie in a supine position with both arms lying on sides of body. 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, liver and spinal cord.

Two types of treatment plans were generated for each patient case: 7F-IMRT equally spaced, and 5F-3DCRT using MLC at gantry angels of 00, 450,900,2700,3150 degrees. Treatment planning was done on eclipse treatment planning system version 13.2 using AAA (anisotropic analytical algorithm). The target dose was 50.4 Gy delivered in 28 fractions prescribed to 95% coverage of the PTV with concurrent chemotherapy. A 5-field 3DCRT plan was generated for all patients considering same contouring. All plans aimed to achieve a min. dose >95% and max. dose <107%

Statistical Analysis

Statistical analysis was done by using SPSS software v22.0 (Chicago, IL, USA). All results was discussed at 5% level of significance (*i.e.* $p<0.05$).

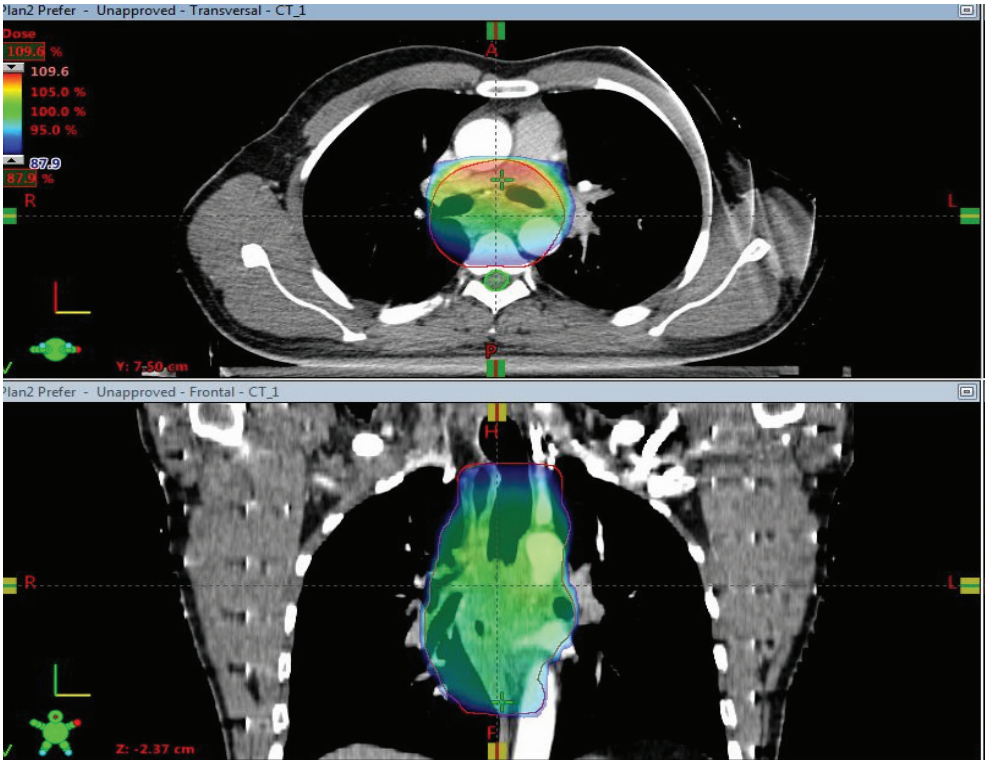

Figure 2. Dose colour wash of 47.9 Gy (95% of prescribed dose) to the PTV high for 5F-3DCRT in axial and coronal view for middle third esophageal cancer.

RESULTS

The IMRT and 3DCRT 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 PTV's was compared. There was a statistically significant difference between both techniques in average dose volume (p<0.001), proving IMRT to be better with respect to 3DCRT as the doses in IMRT are closer to the mean dose of 50.4 Gy.

The V20 for the IMRT plans delivered lesser lung volume irradiation; 22.56% when compared to 3DCRT plans 24.63% with a p-value of (0.001) denoting a statistically significant value in favour of the IMRT plans. As for the organs at risk (OAR) the mean dose to the heart and the V30 were both higher in the 3DCRT plans where the mean dose for IMRT was 20.06 Gy vs. 21.10 Gy for 3DCRT (p=0.001), and the Heart V30 was 13.60 Gy for IMRT vs. 14.21 Gy for 3DCRT technique plans (p=0.001). The mean dose to the spinal cord delivered by IMRT was 14.83Gy vs.

Table 1. Average dose-volume statistics for PTV for both IMRT and 3DCRT techniques.

PTV	IMRT (Gy)	3DCRT (Gy)	*p*-Value
Min. Dose	48.33	46.37	0.001
Max Dose	52.61	54.38	0.001
Mean Dose	50.40	50.70	0.001

16.44 Gy with 3DCRT showing a statistically significant difference (p=0.001). The mean dose to the liver delivered by IMRT was 1.00 Gy vs. 1.22 Gy with 3DCRT showing a statistically significant difference (p=0.001).

DISCUSSION

We designed current study to address the question of dosimetric differences between IMRT and 3DCRT for mid and lower esophageal cancers. Concomitant chemoradiation has become a standard treatment in esophageal cancer patients producing up to 25%-30% 5 year survival rates (Bosset, *et al*., 1997; Al-Sarraf, *et al*., 1997). Current study shows significant improvement in the PTV coverage by IMRT compared to 3DCRT and this finding matches the results from the study published by Fenkell, *et al*., 2008, 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. Nutting, *et al.* 2000, concluded that the dose conformity of IMRT and VMAT (volumetric modulated arc therapy) was improved for middle esophageal cancer when compared to 3DCRT. The study of Vivekanandan, *et al*., 2012, again showed superiority of IMRT and VMAT in target dose conformity versus 3DCRT in oesophageal cancer. Though they didn't specify which segment of the esophagus did they study.

Radiation-induced pulmonary injury and radiation esophagitis are major factors limiting the radiotherapy dose of thoracic tumors. The overall survival of patients with esophageal cancer is significantly prolonged with the application of multiple therapeutic methods, but radiation-induced pulmonary injury and radiation esophagitis are important reasons affecting the quality of life of patients, which can offset the benefits of radiotherapy (RT). As for Chandra, *et al*., 2005, they compared 4, 7, and 9 IMRT beam plans to 3DCRT in lower esophageal cancer patients and they reported a 5% reduction in lung V20 with IMRT plans which is similar as our findings *i.e* V20 for the IMRT plans delivered lesser lung volume irradiation; 22.56% when compared to 3DCRT plans 24.63% with a p-value of (0.001) denoting a statistically significant value in favour of the IMRT plans. Similarly, Wu, *et al*., 2014, reported a lower lung V20 with IMRT. Nutting, *et al.*, 2001, reported a reduction in mean lung dose upon using a 4 field IMRT when compared to the 9 fields IMRT and the 3DCRT plans. Chen, *et al*., 2007, also published a study on a dosimetric analysis of 10 mid distal oesophageal carcinoma cases comparing helical tomotherapy, step-and-shoot IMRT and 3DCRT, the IMRT plans resulted in decreased heart V30 and V45. The study by Ghosh, *et al*., 2012, reported higher mean heart dose with 3DCRT which stands similar to with our findings *i.e* the mean dose to the heart and the V30 were both higher in the 3DCRT plans where the mean dose for IMRT was 20.06 Gy vs. 21.10 Gy for 3DCRT (p=0.001), and the Heart V30 was 13.60 Gy for IMRT vs. 14.21 Gy for 3DCRT technique plans (p=0.001). In current study IMRT delivered lower mean dose to the spinal cord, this was also reported by Ghosh, *et al.*, 2012, and also consistent with the results reported by Vivekeanandan, *et al*., 2012. In our study the mean dose to the spinal cord delivered by IMRT was 14.83Gy vs. 16.44 Gy with 3DCRT showing a statistically significant difference (p=0.001). The mean dose to the liver delivered by IMRT was 1.00 Gy vs. 1.22 Gy with 3DCRT showing a statistically significant difference (p=0.001).

CONCLUSION

The current study indicates that IMRT is better than 3DCRT with respect to target coverage and normal tissue sparing in the cancer of mid lower esophagus. It provides homogenous doses to the target and lower radiation dose to organs at risk (OAR). 3DCRT did not produce any dosimetric advantage over the IMRT technique.

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