Original Article

Dosimetric comparison of modern radiotherapy techniques for gastric cancer after total gastrectomy

ABSTRACT

Purpose: The purpose of this study is to investigate the optimal radiotherapy technique for postoperative irradiation of gastric cancer treated with total gastrectomy.

Materials and Methods: The database of ten patients was used for this study. Three-dimensional (3D) conformal radiotherapy, intensity-modulated therapy (IMRT), volumetric modulated arc therapy (VMAT), and helical tomotherapy (HT) plans were created for each dataset. The prescription dose was 45 Gy in 25 fractions. Comparative analyses of the target volume coverage and the doses of organs at risk were performed.

Results: HT was significantly provided more homogeneity. The best conformal plans were achieved with VMAT. Both kidneys were better preserved with HT and VMAT. HT significantly lowered the V13 of the left kidney and VMAT significantly lowered V20. However, the mean left kidney doses were not statistically different. The lowest liver V30 was obtained with VMAT but not with statistically different than IMRT and HT. Mean liver doses were statistically inferior with 3D. The worst spinal cord doses were seen with 3D. The integral dose of the body did not differ among the techniques.

Conclusion: In comparison of the four techniques, 3D seems to be the most unsuitable method regarding sparing the normal tissues. According to availability, HT and VMAT should be primarily preferred. IMRT can also be used with carefully paying attention to the clinical condition of the patient.

KEY WORDS: Gastric cancer, helical tomotherapy, intensity-modulated therapy, three-dimensional conformal radiotherapy, volumetric modulated arc therapy

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INTRODUCTION

Gastric cancer is still one of the common cause of cancer-related deaths worldwide.[1,2] Adjuvant chemoradiation became the standard of care for high-risk patients after INT-0116 trial.[3] Although this approach prolongs survival and reduces the local recurrence rates, toxicity due to the therapy is a remaining issue.

Regarding radiotherapy technique, three-dimensional (3D) radiotherapy was found to be superior to two-dimensional (2-D) treatment planning.[4] Further studies showed that intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) have better coverage of planning target volume (PTV) and also a better normal tissue sparing.[5-8]

We investigated the best compatible radiotherapy technique comparing 3D, IMRT, VMAT, and helical tomotherapy (HT) for adjuvant treatment of gastric cancer with this study.

MATERIALS AND METHODS

Patients and volume definition

Institutional Ethics Board approval was obtained. Ten patients were selected for this study. All patients had total gastrectomy for fundus-corpus-antrum-located tumors. All had negative surgical margins with T4aN2-3 disease. This selection was made to achieve the possible largest treatment fields. Computed tomography (CT) scans which were generated for radiotherapy planning were used. After fasting for 3–4 h, the

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patients were immobilized in a supine position on a T-board with arms raised above the head. No intravenous contrast was administered if the patient had a CT with contrast before the surgery. The slice thickness was 3 mm. Free breathing was performed.

The target volumes and organs at risk (OAR) were contoured on axial slices by the same radiation oncologist. To define the volumes, individual patient data of presurgical CT (with a generated deformable fusion on treatment planning system [TPS]), endoscopic, and pathological findings were used. The clinical target volume (CTV) included the tumor bed, anastomoses, and the draining lymph node stations (perigastric, celiac, splenic, peripancreatic, paraaortic, and hepatoduodenal). For the delineation of lymph node stations, the gastric lymph node atlases of Massachusetts General Hospital[9] and Zhongnan Hospital of Wuhan University[10] and recommendations of Gunderson and Tepper[11] as well as International Commission on Radiation Units and Measurements reports 50 and 62 were taken into account. PTV was constructed by a 1-cm margin to the CTV. Kidneys, liver, and spinal cord were defined as OAR.

Treatment planning

For 3D and IMRT plans and VMAT plans, Varian Clinac DHX linear accelerator and Varian Truebeam linear accelerator were used (Varian Medical Systems, Palo Alto, CA, USA), respectively. The plans were generated on Eclipse TPS.

Field-in-field (FIF) technique was applied for the 3D plans. There were five FIF fields at the angles 0, 90 and 270. The photon beam energy was 18 MV. IMRT had inversely planned seven coplanar fields at the angles of 150°, 100°, 50°, 0°, 310°, 260°, and 210° with 6 MV photon beams. VMAT plans were generated with two full coplanar arcs at 179°–181° and reversed with a collimator angle at 30°. The photon beam energy was 10 MV.

HT plans were created with the superposition-convolution system method on the VoLO TPS (Accuray Incorporated, Sunnyvale, CA, USA). Helical IMRT technique was applied with HT-HDA with a photon beam energy of 6 MV.

The prescribed dose was 45 Gy in 25 fractions. The main aim of all the plans was to cover the PTV. The optimization of the plans was done as the PTV coverage to be between 98% and 108% of the prescribed dose. Inhomogeneity corrections were applied during treatment planning. Dose constraints for OAR were as follows: maximum spinal cord dose (D_{max}) <45 Gy, mean liver dose (D_{mean}) <32 Gy, and liver volume receiving 30 Gy (V30) <30%. Mean kidney dose <18 Gy, V13, and V20 for the kidneys <50% and <70%, respectively. Body volumes receiving doses 5 Gy (V5) and 20 Gy (V20) were reviewed as integral doses but were not taken into account as constraints.

Plan evaluation

Dose-volume histograms were generated for all plans. Conformity indexes (CIs) and homogeneity indexes (HIs) were calculated for each plan. $CI = (PTV \cap 95\%)^2/(PTV_v \times 95\%_v)$.[12] This ratio is preferred to take into account the volume of overlap between the structures. The ideal value for perfect conformity is 1. $HI = (D_2\% - D_{98}\%/D_{50}\%)$ where D98 and D2 were the dose values covering 98% and 2% of the PTV, respectively, and D50 was the median dose. The smaller values closer to 0 indicate superior homogeneity. The planning parameters of OARs for each patient were also analyzed as follows: D_{max} to the spinal cord, mean liver and kidney doses, V30 of the liver, and V13 and V20 for the kidneys [Figure 1].

Statistical analysis

Data were analyzed using SPSS software version 20 (SPSS, Inc., Chicago, IL, USA). ANOVA and Tukey's multiple comparison tests were performed. However, as HI found to be nonnormalized on One-sample Kolmogorov–Smirnov test, nonparametric Kruskal–Wallis test was applied for HI to search a significant difference, if any. The statistical significance level was considered as $P < 0.05$.

RESULTS

The plans of VMAT had the best conformity ($P < 0.001$); however, HT and IMRT also provided sufficient results (mean CI was 0.89 ± 0.02 for IMRT and 0.72 ± 0.23 for HT). HT was significantly better than both IMRT and VMAT regarding homogeneity ($P = 0.005$). Median HI for HT was 0.06 whereas it was 0.1 for IMRT and 0.07 for VMAT. Less suitable results of CI and HI were seen with 3D plans (CI Mean 0.57 ± 0.04 and HI median 0.1).

Spinal cord doses were significantly higher in 3D plans where the doses of other techniques were similar ($P = 0.04$).

The right kidney was significantly better preserved with HT and VMAT. Both mean, V13, and V20 values were lower than 3D and IMRT (mean dose $P = 0.02$, V13 $P < 0.001$ and V20 $P < 0.001$).

HT and VMAT were significantly lowered the V13 and V20 doses of the left kidney ($P = 0.001$ and $P = 0.04$, respectively). Lowest V13 doses were seen with HT (mean 31.78 ± 11.94), and lowest V20 doses were obtained with VMAT (mean 17.95 ± 5.05). However, the mean doses were similar among the four methods.

Mean liver doses were significantly lower with both IMRT, HT and VMAT ($P < 0.001$). The same significance was achieved for V30 of the liver ($P < 0.001$). VMAT plans assured the lowest V30 dose (mean 21.82 ± 4.31).

The integral doses of the body which could be defined with V5 and V20 did not significantly differ among the techniques ($P = 0.7$ and $P = 0.06$, respectively).

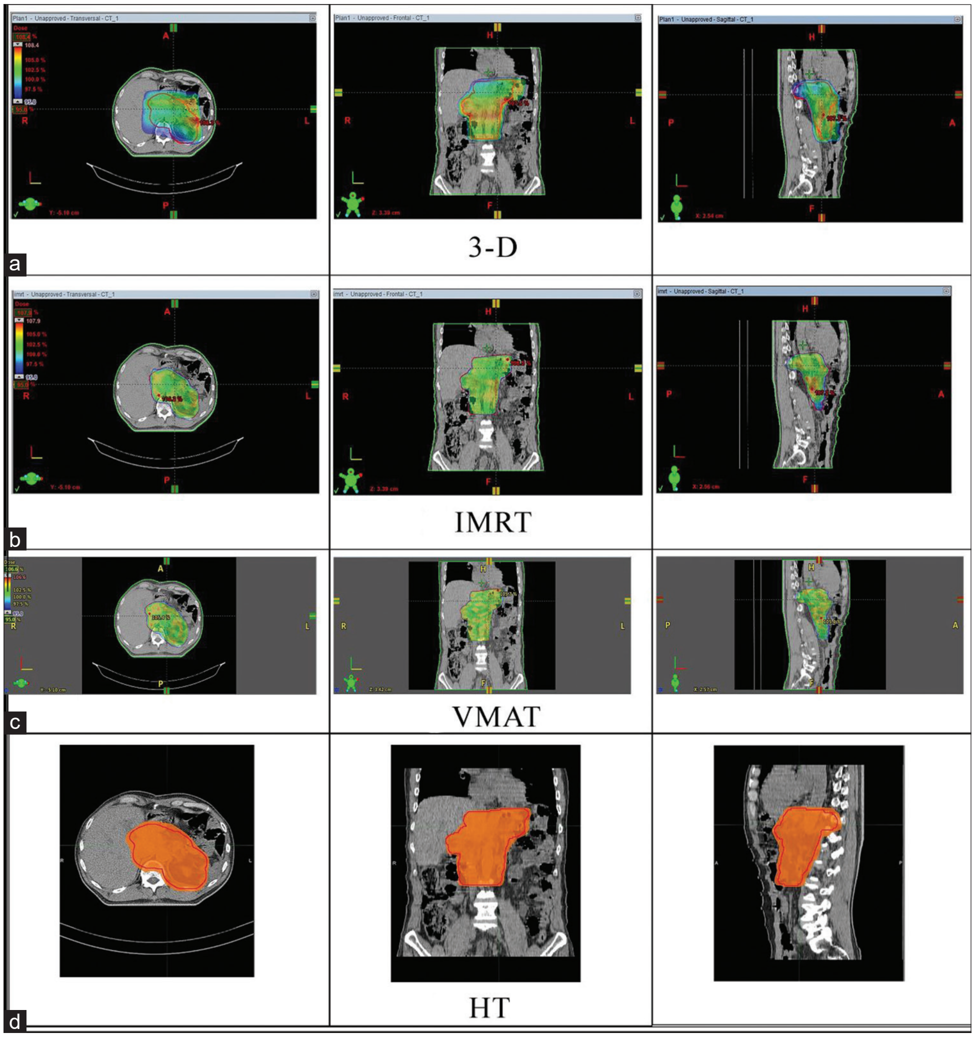

Figure 1: Dose distributions of the same patient in axial, coronal, and sagittal views with three-dimensional (a), intensity-modulated radiation therapy (b), volumetric modulated arc therapy (c), and helical tomotherapy (d) plans 95% coverage of the prescribed dose of each plan is presented

The results and the value of significance are summarized in Table 1.

DISCUSSION

Central location in the abdomen and extensive lymphatic drainage of the stomach cause a relatively wide irradiation field. This handicaps the effective protection of the surrounding normal tissues, especially the liver and the kidneys. The most appropriate technique for postgastrectomy radiotherapy is still under research.

Early studies comparing traditional 2D approach with 3D showed some conflicting results regarding sparing OAR.[13] High liver and left kidney doses enforced the researchers to find better solutions with the newer irradiation techniques such as IMRT, VMAT, and HT.

Lohr *et al*. compared 8-field step-and-shoot IMRT and 3D and found that the liver and the left kidney were significantly better preserved with IMRT.[14] Spinal cord doses were higher but not statistically significant. Milano *et al*. produced similar results for the liver and the kidneys.[15] Murthy *et al*. evaluated if there is any difference between IMRT and the two arrangements of 3D plans.[16] The 3-field and 4-field 3D plans did not differ from each other and IMRT was significantly better just regarding mean liver doses. From the opposite point of view, Ma *et al*. compared two different IMRT plans with 3D.[17] Particularly, maximum spinal cord and mean liver doses were improved with IMRT. However, the mean doses of the kidneys in both 5- and 7-field IMRT plans were higher. As a contrary result, Serarslan *et al*. found significantly better kidney doses using both FIF and dynamic IMRT techniques comparable to 3D.[18] The mean doses and V30 of the liver were also better with IMRT; however, dynamic IMRT was the worst technique to spare the spinal cord. Yet, Alani *et al*. stated higher liver doses with 9-field IMRT whereas significantly better kidney and marginally better spinal cord doses.[5] Apart from the dosimetric studies, Minn *et al*. presented their clinical data showing that in long-term follow-up, the reduced V20 doses

Table 1: Mean values and significance levels of the comparisons

	Mean±SD				*P*
	3-D	IMRT	HT	VMAT	
Spinal cord	41.56±6.29	38.97±1.68	36.35±3.88	38.08±2.35	0.043
Right kidney D_{mean}	14.91±4.27	13.77±2.36	10.84±2.63	12.59±1.26	0.019
Right kidney V13	47.82±15.75	48.46±8.10	23.23±10.45	30.40±4.99	<0.001
Right kidney V20	26.96±11.64	18.01±8.45	10.12±6.47	13.83±2.82	<0.001
Left kidney D_{mean}	15.51±3.79	15.04±1.69	15.12±4.61	15.14±1.57	0.988
Left kidney V13	43.57±11.66	50.30±8.42	31.78±11.94	37.56±4.24	0.001
Left kidney V20	29.94±10.81	20.79±6.84	23.70±12.39	17.95±5.05	0.04
Liver D_{mean}	30.89±1.57	22.38±2.08	22.00±2.52	21.98±2.24	<0.001
Liver V30	64.49±5.73	24.75±6.31	24.49±5.18	21.82±4.31	<0.001
Body V5	48.95±9.19	50.55±9.99	54.01±9.86	52.56±9.94	0.671
Body V20	28.78±5.87	25.62±4.73	27.54±5.04	22.79±4.36	0.061
CI	0.57±0.04	0.89±0.02	0.72±0.23	1.00±0.01	<0.001
	Mean±SD/median				
HI	0.10±0.01/0.097	0.10±0.01/0.099	0.17±0.24/0.059	0.07±0.02/0.070	0.005

IMRT=Intensity-modulated radiation therapy, HT=Helical tomotherapy, VMAT=Volumetric modulated arc therapy, 3-D=Three-dimensional, HI=Homogenity indexes, CI=Conformity indexes, D_{mean}=Mean dose, SD=Standard deviation

of the kidneys reflected better creatinine levels with IMRT rather than 3D plans.[6] In the current study, comparing 3D and IMRT, CI was statistically better with IMRT plans. HI was not different. Highest spinal cord doses were seen with 3D but not statistically different than IMRT. This can be explained by that both plans did not use a posterior field. Furthermore, the spinal cord was covered with a FIF technique in 3D plans. Liver mean and V30 doses were statistically better with IMRT. Both kidney means, V13 and V20 doses, did not demonstrated a significance, yet right kidney V20 was slightly better in IMRT plans. As we used a 7-field IMRT, this may resulted in a lower spinal cord but higher kidney doses.

VMAT both with single-arc (SA) and double-arc (DA) was also questioned in several studies. Wang *et al*. showed no significant difference between SA-VMAT and IMRT other than liver V20, which was better with SA-VMAT.[19] The 3D technique was only better for the spinal cord. By utilizing DA-VMAT plans, Zang *et al*. obtained significantly lower spinal cord, liver V30, and kidney V20 doses.[20] There was no difference between the mean doses. Li *et al*. investigated for the best method using two different IMRT and VMAT techniques.[8] Among these four (5-field IMRT, 7-field IMRT, SA-VMAT, and DA-VMAT), DA-VMAT achieved the best CI, HI, and also significantly lower kidney mean, V13, and V18 doses. Mean liver doses were lowest with 5-field IMRT, and liver V30 was higher with SA-VMAT. In this study, VMAT did not provide better spinal cord protection than IMRT. Although mean kidney doses were not statistically different among 3D, VMAT, and IMRT, the significance was observed in favor of VMAT for the right kidney V13 (better than both) and V20 (better than 3D). Furthermore, the left kidney V13 was better than IMRT and V20 was better than 3D and were statistically significant. The liver mean and V30 were significantly better than 3D but similar to IMRT. Regarding lowering the V20 of both kidneys, VMAT and IMRT provided similar results.

In an early study conducted by Dahele *et al*., HT had superior HI but gave the same results with IMRT regarding OAR.[7] More recent studies worked on comparing newer HT equipment. Wang *et al*. found that HT had significantly better CI and HI than IMRT and SA-VMAT.[21] Liver V5 and V40 doses were significantly better with HT plans; however, SA-VMAT was superior for V20 of the left kidney. In a newer study, Önal *et al*. compared HT with DA-VMAT and 3D.[22] HT was found to be significantly better for CI, mean liver, and kidney doses, as well as liver V20 and V30. HT and DA-VMAT were similar and significantly better than 3D for V20 of the kidney. In the current study, HT plans had significantly better HI than IMRT and VMAT plans. However, we did not reach any significant level between HT and VMAT regarding kidney and liver sparing. Probably, the wide treatment fields used in this study are the reason for these results.

Although all treatment plans have been optimized to a clinical treatment standard, current is a dosimetric study and cannot reflect the real clinical impacts completely and also has limitations with smaller sample size.

CONCLUSION

As a summary of the studies which are perplexing ever and anon, it is obviously clear that the actual techniques achieve better PTV coverage and preserve OAR better than 3D. In most studies, in comparison with IMRT, liver and kidneys are better protected with HT and VMAT. Further dosimetric studies are expected to include respiratory motion parameters. This approach will probably lower the doses of both kidneys and the liver.

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Conflicts of interest

There are no conflicts of interest.

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