Fewer beams and segments result in a shorter delivery time and a better quality intensity-modulated radiotherapy plan in gastric cancer

Y. Shen [1#], X. Li [2#], L. Liang[3], Y. Zhao[1], S. Bai[2], F. Xu[1*]

[1] *Department of Abdominal Oncology, Cancer Center, West China Hospital, Sichuan University, Chengdu, Sichuan Province, P.R. China*

[2] *Radiation Physics Center, Cancer Center, West China Hospital, Sichuan University, Chengdu, Sichuan Province, P.R. China*

[3] *Department of Oncology, Sichuan Province People's Hospital, Chengdu, Sichuan Province, P.R. China*

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Corresponding authors:
Dr. Feng Xu,
Fax: *+ 860 288 5423609*
E-mail: *XF5780@163.com*

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[#] *These authors contributed equally to this work.*

ABSTRACT

Background*:** This study evaluated whether IMRT using fewer beams and segments could reduce delivery time without compromising plan quality in gastric cancer adjuvant radiotherapy. ***Materials and Methods*:** Fifteen patients with advanced gastric cancer who underwent D2, R0 surgery were included in this study. IMRT plans for each patient were designed as 7 equal beams with 40 segments, 5 beams with 25 segments and 4 beams with 20 segments. The dosimetric parameters were compared for the planned target volume (PTV). The dose of normal organs at risk (OARs) was also assessed. The monitor units and treatment times of the different IMRT plans were calculated. ***Results: The 20-segment IMRT plan significantly reduced the PTV maximum dose compared to the 40-segment IMRT plan. The 20-segment IMRT plan improved left kidney and liver dose sparing in V20 and V30 as well as the 40-segment IMRT plan did and provided better protection for the V20 (13.86±7.78) of the right kidney, the V30 (9.25±4.04) of the left kidney, the D mean (19.68±2.47) of liver and D max (38.79±3.57) of the spinal cord. Irradiation times in the 20-segment and 25-segment plans decreased by 2.5 and 1.9 min, respectively, compared to the 40-segment IMRT plan. ***Conclusion:*** IMRT using fewer beams and segments reduced delivery time without compromising plan quality in gastric cancer adjuvant radiotherapy. Fewer segments IMRT plans lowered the monitor units and the treatment time.

Keywords: *Beams and segments, intensity-modulated radiotherapy; plan quality; delivery time; gastric cancer.*

INTRODUCTION

Gastric cancer (GC) is the second most common cause of cancer-related death worldwide [(1)] . Surgery is the primary therapy for GC in Japan and Western countries [(2)]. However, the local recurrence rate and distal metastasis incidence are high after surgical resection with curative intent in GC [(3,4)]. The publication of Gastric Surgical Adjuvant Trial Intergroup 0116 (INT 0116) established chemo-radiotherapy as the standard adjuvant treatment for local advanced GC after surgery [(5)]. However, only 10% of patients received D2 lymph node dissection in the Intergroup 0116 trial, and the results are controversial for suboptimal surgery. The Adjuvant Chemo-radiotherapy in Stomach Tumors (ARTIST) trial was unique because it included patients with D2 -resected GC. The results of the ARTIST trial suggested a significant DFS effect of chemo-radiotherapy in subsets of patients with node-positive, D2-resected GC [(6)].

The radiotherapy range for GC is wide, the

target area is irregular, and multiple organs may be involved. The conventional radiation field is too large in the standard 2D or 3D radiotherapy, which results in radiotherapy-related toxicity. In the INT0116 study, 41% and 32% of patients developed 3rd to 4th degree side effects, including hematological and gastrointestinal toxic effects. Moreover, abdominal radiation can induce damage of residual stomach epithelium and affect its function [7]. IMRT may result in a more conformal dose distribution than three-dimensional conformal radiotherapy (3D-CRT). Furthermore, IMRT tended to increase the total delivery time and the cost compared to 3D-CRT. IMRT provides better target uniformity and conformity than four-field 3DCRT [8,9]. However, conventional 7-field IMRT often requires a high number of fields or subfields, which increases treatment time. Irradiation times longer than a few minutes are uncomfortable for the patients, and carry an increased risk of intrafraction motion [10]. Conventional 7 equal fields IMRT plans do not exhibit an absolute dosimetric advantage to reduce the dose that is applied to normal organs at risk (OARs) [8]. A reduction in treatment time can be achieved using fewer fields or subfields in an IMRT plan or modern treatment techniques, such as volume modulated arc therapy (VMAT) [11]. However, not all hospitals are equipped with linacs that are capable of VMAT delivery. Therefore, lower delivery time and better plan quality using fewer fields or subfields in IMRT plans are of great interest.

Previous studies indicated that increasing IMRT segments may be beneficial for the protection of normal tissues, such as parotid gland, bladder and rectum, for head, neck and pelvic tumors [12-14]. However, whether increasing IMRT segments in GC was beneficial for normal tissues is not clear. This study evaluated whether IMRT using fewer beams and segments reduced delivery time without compromising plan quality in gastric cancer adjuvant radiotherapy. We started with an IMRT plan (7 equal beams with 40 segments) that was the standard approach at our institution. We created new IMRT plans with fewer beams and segments (4 beams with 20 segments and 5 beams with 25 segments) and compared the dosimetric parameters, monitor units and treatment time with the conventional 7 equal beams IMRT plan. We try to create a better IMRT plan to balance the accepted dose results and efficient delivery.

MATERIALS AND METHODS

Clinical population

This study was conducted between February and August 2013. Fifteen patients with confirmed locally advanced gastric cancer were randomly selected for the study. All patients had undergone D2 R0 surgery in our cancer center and were staged according to the 2010 American Joint Committee on Cancer staging system [15] (table 1). All patients received postoperative chemo-radiotherapy. Concurrent chemotherapy was capecitabine (n =7) and S-1 (Tegafur, Gimeracil and Oteracil potassium capsules) (n =8). The Research Ethics Board of West China Hospital approved this study, and informed consent was obtained from all of the patients.

Table 1. Clinical characteristics of the patient population (n=15).

Variables	
Total No. of patients	15
Age(y)	
Median	60
Range	72-35
Sex	
Male	10
Female	5
Lesion location	
Upper third	5
Middle third	5
Lower third	5
Disease stage	
IIIA	7
IIIB	6
IV(M0)	2
Extent of node dissection	
D1	2
D2	13
ECOG Performance	
0	12
1	3
2	0

Target delineation and dose prescription

All patients underwent CT-based treatment planning and were immobilized by a custom immobilization device to minimize setup variability. The distance between the CT images was 3 mm. CT data were transferred into the treatment planning system pinnacle 9.2 via DICOM. The same clinical doctor on the planning CT scan team contoured the target and normal adjacent structures. Targets and normal tissues were defined according to the Radiation Therapy Oncology Group 50 and 62 reports [16,17]. The clinical target volume (CTV) included the original tumor volume, surgical bed including the operative note, pathologic findings and surgical clips, which followed published guidelines [18, 19]. The CTV to PTV expansion was isotropically 10 mm to account for daily setup error and organ motion. The organs at risk (OARs) were also contoured, included kidneys, liver, spinal cord and bowel. A single physician was assigned for the entire contouring task to avoid inconstancies between different physicians.

PTV prescriptions were 50.4 Gy in 28 fractions for all plans. All plans were generated for the Elekta Synergy accelerator (Elekta Oncology Systems, Crawley, UK) using 6-MV photons. The tolerated doses for the OARs were settled as follows: the volume of accepted 20 Gy for each kidney should be less than 50%, the volume of accepted 30 Gy should be less than 20%, and the mean dose should be less than 15 Gy. The volume of accepted 30 Gy for the liver less than 30%, and the mean dose should be less than 15 Gy. The max dose should be less than 40 Gy for the spinal cord. The volume of accepted 40 Gy and 50 Gy should be less than 20% and 5%, respectively, for the small intestine.

The monitor units (MU) and radiotherapy times were compared in different IMRT plans. We randomly selected and transferred one patient's schemes to the accelerator. We recorded the time from the first beam to completion of the treatment as the radiotherapy time during simulated radiotherapy. The irradiation time difference was tiny in clinical applications, when the number of segments, gantry angles, and MU mean times are relatively constant. Therefore, one case of irradiation time was measured in this study.

Treatment plan designs

Every patient had three IMRT plans with 4 beams (20 segments), 5 beams (25 segments) and 7 beams (40 segments) respectively, which were designed by a single physicist. Twenty segments for each plan were used based on 4 coplanar beams (with angles were 20°, 90°, 180°, and 310°, separately). Twenty-five segments were used based on 5 coplanar beams (with angles of 20°, 60°, 100°, 180°, and 340°). Forty segments were used based on 7 coplanar beams (with angles of 204°, 256°, 308°, 0°, 52°, 104°, and 156°). Unified scripts were used for every patient in our study, including tumor and organ name, beam parameters and optimization parameters, to maintain the consistency of the treatment plans. A 6MV-X ray was used, and the beams were coplanar in all plans. DMPO was selected as the optimization type. The minimum segment area was 5 cm^2, and the minimum segment MUs was 5. The maximum number of iterations was 80, and the convolution dose iterations were 35. Three different treatment plans were obtained by changing the maximum number of segments to 20, 25 or 40 and the beam orientation while keeping optimization parameters consistent. The second circle optimization was performed through the creation of automatically assistant regions of interest (ROI) for the unsatisfied regions and adding the same objectives after the first circle optimization as described previously to achieve a preferable PTV dose objective. All IMRT plans were performed in the pinnacle 9.2 system.

Evaluation of the DVH-based parameters

The conformal index (CI) was defined as $CI=(V_{Tref}/V_T) \times (V_{Tref}/V_{ref})$, where V_{Tref} is the PTV volume irradiated by the reference dose. The reference dose was 95% of the prescription dose in our cases. V_T indicates the PTV volume. V_{ref} is the whole volume irradiated by the reference dose. The CI number ranged from 0 to 1, and conformability was better when the CI was close to 1. Homogeneity index (HI) was defined as $HI=D_5/D_{95}$. D_5 and D_{95} indicate the irradiation

doses of 5 and 95% of PTV, respectively. HI becomes larger when it is farther from 1, and the dose homogeneity becomes worse. The evaluated parameters were collected from the DVH of these generated plans and compared, including: 1. The maximum, mean, and minimum doses of the PTV; and 2. V 20/30 (the percentage volumes that accepted 20 Gy and 30 Gy) and mean dose of each kidney, V30 (the percentage volumes that accepted 30 Gy) and mean dose of the liver, V 40/50 (the percentage volumes that accepted 40 Gy and 50 Gy) of the intestine, and D max (the maximum dose accepted) of the spinal cord.

Data processing

Data were analyzed using SPSS software (version 19.0). Non-parametric Wilcoxon test was performed to compare groups. A p-value less than 0.05 was considered statistically significant.

RESULTS

A total of 15 patients were chosen in this study. A total of 45 IMRT plans with different beams and segments were evaluated.

DVH-Based parameters of the PTV

Three plans fulfilled the dose requirement based on PTV evaluations, and there were no significant differences in the D minimum dose, D mean dose and the homogeneous indexes between these evaluations. However, the 20-segment IMRT plan significantly reduced the PTV maximum dose compared to the 40-segment IMRT plan. The 20- and 25-segment IMRT plan was similar in conformability (0.72±0.04 and 0.76±0.16), which was lower than the 40-segment IMRT plan (0.81±0.03) (table 2).

Table 2. DVH-Based Parameters of the PTV (n=15).

	IMRT_20 mean ± SD	IMRT_25 mean ± SD	p value[a]	IMRT_40 mean ± SD	p value[a]	p value[b]
D_{min}(Gy)[c]	2.97±37.41	2.51±40.73	0.599	2.41±40.03	0.457	0.779
D_{mean}(Gy)[c]	0.64±51.58	0.11±53.07	0.956	0.30±53.06	0.763	0.872
D_{max}(Gy)[c]	0.51±53.20	0.82±55.58	0.001	0.63±57.69	0.001>	0.005
CI[d]	0.04±0.72	0.16±0.76	0.129	0.03±0.81	0.001	0.003
HI[e]	0.006±1.061	0.010±1.064	0.811	0.01±1.089	0.792	0.774

SD = standard deviation.
a Compared to the parameters of the 20-segment IMRT plan.
b Compared to the parameters of the 25-segment IMRT plan.
c The minimum, maximum, and mean irradiation doses of the PTV, respectively.
d Conformity index, calculated using the formula described previously.
e Homogeneous index, calculated using the formula: HI= D5/D95.

Organs at risk

The 20- and 40-segment IMRT plans improved the left kidney and liver dose sparing in V 20 and V 30 and provided somewhat better protection for the spinal cord compared with the 25-segment IMRT plan. The V 20 and V 30 of the left kidney in the 20-segment (24.80±6.03 and 10.58±5.01) and 40-segment IMRT plans (24.74±7.03 and 9.25±4.04) were significantly lower. The 20-segment and 40-segment IMRT plans did not reduce dose sparing of other evaluated OARs, such as the V 20 and V 30 of the intestine. Between the 20-segment and 40-segment IMRT plans, the 20-segment IMRT plan improved dose sparing in the V 20 (13.86±7.78) of the right kidney, the V 30 (9.25±4.04) of the left kidney, the D mean (19.68±2.47) of liver and D max (38.79±3.57) of the spinal cord ($p<0.05$) (table 3).

The MU and radiotherapy time decreased with the reductions in segment number. There were significant differences in MU between the

IMRT plans with 20 segments (498±59), 25 segments (557±61) and 40 segments (615±84) (table 4). Three schemes were selected: 470, 550 and 670 MUs in 20-segment, 25-segment and 40-segment IMRT plans, respectively. The irradiation times were 3.8, 4.4 and 6.3 min when the actual beam dose rate was 600 MU/min. Results demonstrated that the irradiation time decreased with the decrease in segment number. The irradiation time in the 20-segment and 25-segment plans decreased by 2.5 and 1.9 min, respectively, compared to the 40- segment IMRT plan. The 20-segment and 25-segment IMRT plans improved efficiency by 39.7% and 30.0%, respectively, compared to the 40-segment IMRT plan.

Table 3. Comparisons of the DVH-based parameters of the OARs (n=15, $\bar{x} \pm s$) Monitor units and irradiation time.

		IMRT_20	IMRT_25		IMRT_40		
OAR[a]		mean±SD	mean±SD	P value[b]	mean±SD	p value[b]	p value[c]
Right kidney							
V_{20}[d](%)	7.78±13.86	8.32±18.58	0.039	8.41±18.71	0.043	0.790	
V_{30}[d] (%)	4.14±4.03	4.57±5.06	0.01>	3.30±4.06	0.089	0.01>	
D_{mean}[e](Gy)	3.01±11.72	3.00±14.93	0.01>	3.63±11.69	0.092	0.01>	
Left kidney							
V_{20}[d] (%)	7.03±24.74	6.30±29.57	0.01>	6.03±24.80	0.086	0.01>	
V_{30}[d] (%)	4.04±9.25	4.33±11.47	0.01>	5.01±10.58	0.041	0.254	
D_{mean}[e] (Gy)	2.07±15.63	2.29±16.64	0.01>	2.30±14.79	0.001>	0.01>	
Liver							
V_{30}[d] (%)	6.05±21.84	6.31±22.80	0.051	6.35±23.60	0.041	0.089	
D_{mean}[e](Gy)	2.47±19.68	2.51±21.41	0.030	2.46±23.33	0.010	0.079	
Spinal cord							
D_{max}[f] (Gy)	3.57±38.79	2.14±39.00	0.018	1.92±39.75	0.009	0.078	
Intestine							
V_{40}[d] (%)	5.71±42.58	6.80±43.88	0.501	5.87±42.45	0.884	0.610	
V_{50}[d] (%)	2.51±24.62	2.36±24.67	0.061	2.32±25.12	0.031	0.035	

a Organs at risk.
b Compared to the parameters of the 20-segment IMRT plan.
c Compared to the parameters of the 25-segment IMRT plan.
d The volume of the OAR that received the 20, 30, 40, and 50 Gy irradiation dose, respectively.
e The mean irradiation dose that the kidneys and liver received.
f The maximum irradiation dose that the spinal cord received.

Table 4. MU and a single treatment time analysis.

	Segments No. <=25		**Segments No. > 25**				
	IMRT_20		IMRT_25	p[a]	IMRT_40	p[a]	p[b]
	No.	mean±SD	mean±SD		mean±SD		
Monitor units (MU)	15	59±498	61±557	0.01>	84±615	0.01>	0.01>
Radiotherapy time (min)	1	3.8	4.4		6.3		

a Compared to the parameters of the 20-segment IMRT plan.
b Compared to the parameters of the 25-segment IMRT plan.

DISCUSSION

Postoperative chemo-radiation is one of the main treatments for patients with advanced gastric cancer. This study compared plan quality and treatment time in IMRT plans with different beams or segments in gastric cancer adjuvant radiotherapy. We found that 20- and 25-segment IMRT achieved favorable PTV coverage compared to 40-segment IMRT. Fewer segment IMRT plans provided better protection for the kidneys, liver, and spinal cord, and lowered the treatment time.

Increasing IMRT segments may be beneficial for the protection of normal tissues, such as the parotid gland, for head and neck tumors. However, the conventional seven equal beams IMRT plan does not exhibit an absolute dosimetric advantage in GC IMRT [20]. The different segments IMRT plans in this study basically achieved the target prescription and OARs requirements. However, there were some statistically significant differences in the quality measures considered. The 20-segment IMRT plan significantly reduced the PTV maximum dose compared to the 40-segment IMRT plan. The kidney is one of the most important organs to protect in GC adjuvant radiation. The 20-segment IMRT plan exhibited a similar sparing of the left and right kidneys compared to the 40-segment IMRT plan. The doses of the liver mean and spinal cord max were lowest in the 20- segment IMRT plan. Therefore, fewer beams and segments reduced delivery time without compromising IMRT plan quality in GC. IMRT plan quality was also affected by the choice of gantry angles, patient and ray energy, except beams and segments [21]. A previous study found that a limited number of IMRT beams could be used, and the segments could be re-distributed over a certain range of gantry angles for further optimization [22].We optimized IMRT plans following this method. The 20-segment IMRT plan was different from the conventional seven equal beams plan because it was designed using four unequal beams with gantries of 310°, 20°, 90° and 180°. The horizontal-field of 90°and the back-field of 180° provided superior protection of the kidneys. Only the 310° field directly irradiated through the liver. The choice of gantry angles favored the OAR results in the 20-segment IMRT plan. The conformity index in this study decreased with lower segment number. The CI of the 40-segment IMRT plan (mean 0.81) was better than the 20- (mean 0.72) and 25-segment (mean 0.76) IMRT plans ($p<0.05$). However, the loss in conformity did not appear to worsen the ability of the 20- and 25-segment IMRT plan to spare critical structures. It is not clear whether a small loss of conformity between two plans is relevant to the overall clinical picture [23].

Irradiation times longer than a few minutes are uncomfortable for the patients, and carry an increased risk of intrafraction motion [10]. The impact of treatment time on biological effects and organ motion in tumor treatment cannot be ignored [24]. Short delivery time in GC is desirable for several reasons, such as the effect on biological properties of tumors, reduction of problems related to patient movement, and because more patients can be treated with the same linear accelerator. Theoretically, the delivery time depends on several factors, including the number of equidistant gantry angles, number of segments, gantry rotation time between beams, segment shaping time, monitor units and the data handling time per beam. Clinical applications found that the factors that influenced the irradiation time primarily include the beam numbers and segment numbers of the plan [25]. The 20-segment and 25 -segment plans in this study used lower monitor units and shorter treatment time. The irradiation times for the 20-segment and 25-segment plans decreased by 66% and 43%, respectively, for one case compared to the 40-segment IMRT plan. The decrease in treatment time was inevitable with the reduction of segment number, beam number and MU, which significantly improved the work efficiency.

Chemotherapy is the standard treatment for advanced gastric cancer. Moreover recent studies showed that neoadjuvent chemotherapy can lead to tumor downstaging in locally advanced gastric cancer [26,27]. To further improve the local control and survival rate,

radiation combined fluorouracil based chemotherapy is an effective combination treatment strategy.

It is important to consider the limitations of our study. The present study had a small sample size and emphasized comparisons of dosimetry of different IMRT plans. This study also did not evaluate clinical efficacy. Future prospectively studies of a larger study group are needed to confirm the technical feasibility of these plans and evaluate clinical efficacy and toxicity.

CONCLUSION

IMRT using fewer beams and segments reduced delivery time without compromising plan quality in gastric cancer adjuvant radiotherapy. The 20- and 25-segment IMRT plans achieved favorable PTV coverage compared to the 40-segment IMRT plan. Fewer segments IMRT achieved better dosimetry and provided better protection for the kidneys, liver, and spinal cord. Fewer segments IMRT plans lowered the treatment time. These results need long-term follow-up studies in a larger study group for further confirmation.

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