

## RapidArc versus intensity modulated radiation therapy in adjuvant gastric cancer irradiation: Any dosimetric advantage?

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**Abstract: Background:** The purpose was to compare dosimetrically intensity modulated radiation therapy (IMRT) and RapidArc (RA) techniques for gastric carcinoma patients. **Methods:** For IMRT, a coplanar seven-field plan was performed. Regarding the RA, plans were done using a double arc plan consisting of 2 co-planar arcs of 360° in clockwise & counter clockwise direction. The PTV dose coverage criteria was at least 95% of PTV received 45Gy. **Results:** The mean V95 was 94.7% and 94.8% for the IMRT and RA, respectively ( $p = 0.32$ ). The CI for IMRT and RA were  $0.93 \pm 0.01$  &  $0.94 \pm 0.01$ , respectively; while the HI was  $1.153 \pm 0.01$  for IMRT &  $1.142 \pm 0.02$  for RA (both  $p > 0.04$ ). The maximum spinal cord dose for IMRT and RapidArc was 37.87 Gy vs 36.42 Gy ( $p = 0.34$ ). For the right kidney, IMRT had significantly lower mean V20 compared to RA (22.2 vs. 24.3Gy,  $p = 0.01$ ). The mean V20 to the left kidney were 24.4 and 23.4 Gy in the IMRT and RA ( $p = 0.01$ ). The treatment time was  $193.5 \pm 25.0$ s in IMRT and  $66.0 \pm 8.7$  s in RA ( $p = 0.002$ ). The total monitor units (MU) for RA and IMRT were  $343.0 \pm 94.0$  &  $363.0 \pm 44.0$  ( $p = 0.07$ ), respectively. **Conclusions:** RA obtained similar dosimetric outcomes to IMRT plans regarding target coverage & organs at risk (OAR) sparing with an advantage of shorter delivery time & lower number of MU.

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**Keywords:** dosimetric, double arc, IMRT, MUs

### Important Information:

Few articles, addressed the superiority of volumetric modulated radiation therapy (VMAT) over intensity modulated radiation therapy (IMRT) in the adjuvant treatment of gastric cancers and usually the studies were on a small number of patients.

The current study was conducted to dosimetrically compare RapidArc and IMRT in the treatment of gastric cancers, evaluating both techniques as regards target volume coverage and doses received by organs at risk.

All authors contributed significantly and are in agreement with the content of the manuscript.

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### Introduction

Adenocarcinoma of the stomach is a significant public health problem with a poor general outcome.<sup>1</sup> Surgery is considered the cornerstone of treatment for gastric cancer, yet adjuvant treatment is also important to lower loco-regional recurrences.<sup>2</sup> In the management of a resectable localized gastric cancer, two adjuvant approaches are currently used nowadays.<sup>3</sup> Cunningham and his colleagues reported that

administering chemotherapy peri-operatively using epirubicin, fluorouracil and cisplatin improved both the progression-free and overall survival rates.<sup>4</sup> On the contrary, Macdonald et al. observed that adjuvant chemo-radiotherapy (external-beam radiotherapy to the operative bed and draining lymphatics plus fluorouracil and leucovorin) used in the postoperative setting, had significantly improved the disease-free and overall survival rates. In the latter trial (Intergroup Trial 0116), more than one-sixth of the patients had terminated their therapy due to a high incidence of acute radiation toxicity and this was related to the use of anteroposterior-posteroanterior (AP-PA) beam orientation (two-dimensional planning).<sup>5</sup>

Although radiation therapy is very important in the treatment of gastric cancer, yet adequate doses of radiation delivery is usually limited by the presence of sensitive normal structures in the abdomen i.e. the liver, kidneys, small intestine and spinal cord. Intensity modulated radiotherapy (IMRT) usually offers a more precise dose distribution, when compared to three-dimensional conformal radiotherapy (3DCRT), allowing a better normal tissue sparing which has the potential to decrease the toxicity without compromising the local control.<sup>6-8</sup>

RapidArc (RA) is a novel form of IMRT in which radiotherapy delivery is achieved by

dynamically altering the speed of the gantry, shape of the multi-leaf collimator (MLC) and the dose rate resulting in superior dose distribution and shorter treatment time.<sup>9</sup> RA can dosimetrically produce equivalent plans to conventional IMRT for cancers of the head and neck, cervix and prostate.<sup>10-12</sup> On the other hand, few studies for the application of RA in gastric cancer have been reported.<sup>13</sup>

The objective of this study was to investigate a possible dosimetric benefit of RA compared to IMRT techniques with respect to target coverage and doses received by the organs at risk (OAR) in the adjuvant treatment of gastric cancers. RA and IMRT plans were done for each patient and dose distribution parameters were compared.

## Methods And Materials

### Patient selection

This retrospective study was accepted by the scientific and ethical committee at Kasr El-Ainy medical University hospital. A written informed consent for all participants was mandatory before inclusion in this study. Between November 2015 and August 2016, twenty gastric cancer patients who had a radical gastrectomy with D2 dissection at our hospital were eligible for this study and were staged based on the 2010 AJCC manual.<sup>14</sup> All patients had T2–4 and/or node positive disease. The patient and tumor characteristics are summarized in Table 1.

### Patient preparation and target volume delineation

A planning computed tomography (CT) scan starting from the neck till mid-pelvic region was obtained for each patient immobilized in supine position with a support for the arms above their heads. Oral and intravenous contrasts were used and the CT sections were set to be taken every 3mm for more accurate target volume delineation. The scan was then transferred to the Aria Network (Varian system) and reconstructed in three dimensional view using the Eclipse treatment planning system (Version 8.6, Varian Medical System, Palo Alto, CA, USA). Based on the ICRU (International Commission on Radiation Units and Measurements) Report 62,<sup>15</sup> the clinical target volume (CTV) included the gastric operative bed, regional lymph nodes and the anastomotic site with 2 cm proximal/distal margins. Delineation of the CTV was based on the information obtained from the pre-operative and pathological data. The planning target volume (PTV) consisted of CTV plus a uniform margin of 10 mm all around. The OAR included the spinal cord, liver, heart and both kidneys.

### Treatment planning, dose prescription and plan evaluation

For IMRT, a coplanar seven-field plan was performed using equidistantly spaced gantry angles which are adjusted and modified when an OAR could be avoided for better target coverage. Regarding the RapidArc, plans were done using a double arc plan consisting of 2 co-planar arcs of 360° in clockwise & counter clockwise direction. Dose prescribed was 45 Gy to the PTV in 25 fractions using 6MV photons. The plans were normalized to 100% (45Gy) dose and were created in the Eclipse treatment planning system (v8.6, Varian Medical System, Palo Alto, USA).

The PTV dose coverage criteria were at least 95% of PTV received 45Gy. Other criteria used to assess PTV coverage were V107% (volume receiving 107% of dose),  $D_{min}$  (minimum dose within the PTV). The homogeneity index (HI) was calculated similar to the ICRU 83 using the equation  $(D2\% - D98\%) / D50\%$  where the D2% is the maximum dose within the PTV, D98% is the minimum dose within the PTV and the D50% or  $D_{median}$  is the absorbed dose received by 50 % of the volume. Conformity index (CI) was calculated using the following equation:  $TV/PTV$  where the TV is the treated volume receiving 98% of dose and PTV is planning target volume receiving 98% of dose. With respect to the OAR, dose constraints used in radiotherapy planning are outlined in table 2. The dose-volume histogram (DVH) for target coverage and doses received by the OAR were generated. Calculation of the treatment delivery time and the total number of monitor units (MUs) for each plan was also recorded.

### Statistical methods:

Data analysis was done using SPSS (version 17.0, SPSS Inc., Chicago, IL, USA). Comparison between the study plans was done using Mann Whitney *U* test for independent samples. *p*- values less than 0.05 was considered statistically significant.

### Results

Between November 2015 and August 2016, 20 patients with a pathological diagnosis of gastric adenocarcinoma were enrolled in our study. For each patient, two plans were done on the Eclipse planning system (version 8.6); one with doublearc RA and a second plan with IMRT i.e a total of 40 plans were done.

Target coverage was similar for both techniques. The mean V95 was found to be  $94.7\% \pm 4.5$  and  $94.8\% \pm 4.75$  for the IMRT and RA respectively ( $p = 0.32$ ). The CI for IMRT and RA were  $0.93 \pm 0.01$  &  $0.94 \pm 0.01$ , respectively; while the HI was  $1.153 \pm 0.01$  for IMRT &  $1.142 \pm 0.02$  for RA (both  $p > 0.04$ ). Table 3 summarizes the dosimetric parameters for PTV coverage.

All plans met the required dose limitations. The maximum spinal cord dose for IMRT and RapidArc was  $37.87 \text{ Gy} \pm 16.9$  vs  $36.42 \text{ Gy} \pm 18.1$  ( $p = 0.34$ ). For the right kidney, IMRT had significantly lower mean V20 (volume receiving 20 Gy) compared to RA ( $22.2\% \pm 11.6$  vs.  $24.3\% \pm 8.8$ ,  $p = 0.01$ ). The mean V20 to the left kidney were  $24.4\% \pm 15.1$  and  $23.4\% \pm 13.2$  in the IMRT and RA plans, respectively ( $p = 0.01$ ). The IMRT produced a similar liver mean V30 (volume receiving 30 Gy) ( $24.3\% \pm 13.4$  vs.  $23.1\% \pm 9.1$ ,  $p = 0.52$ ) to RA. Similarly, the mean V40 (volume

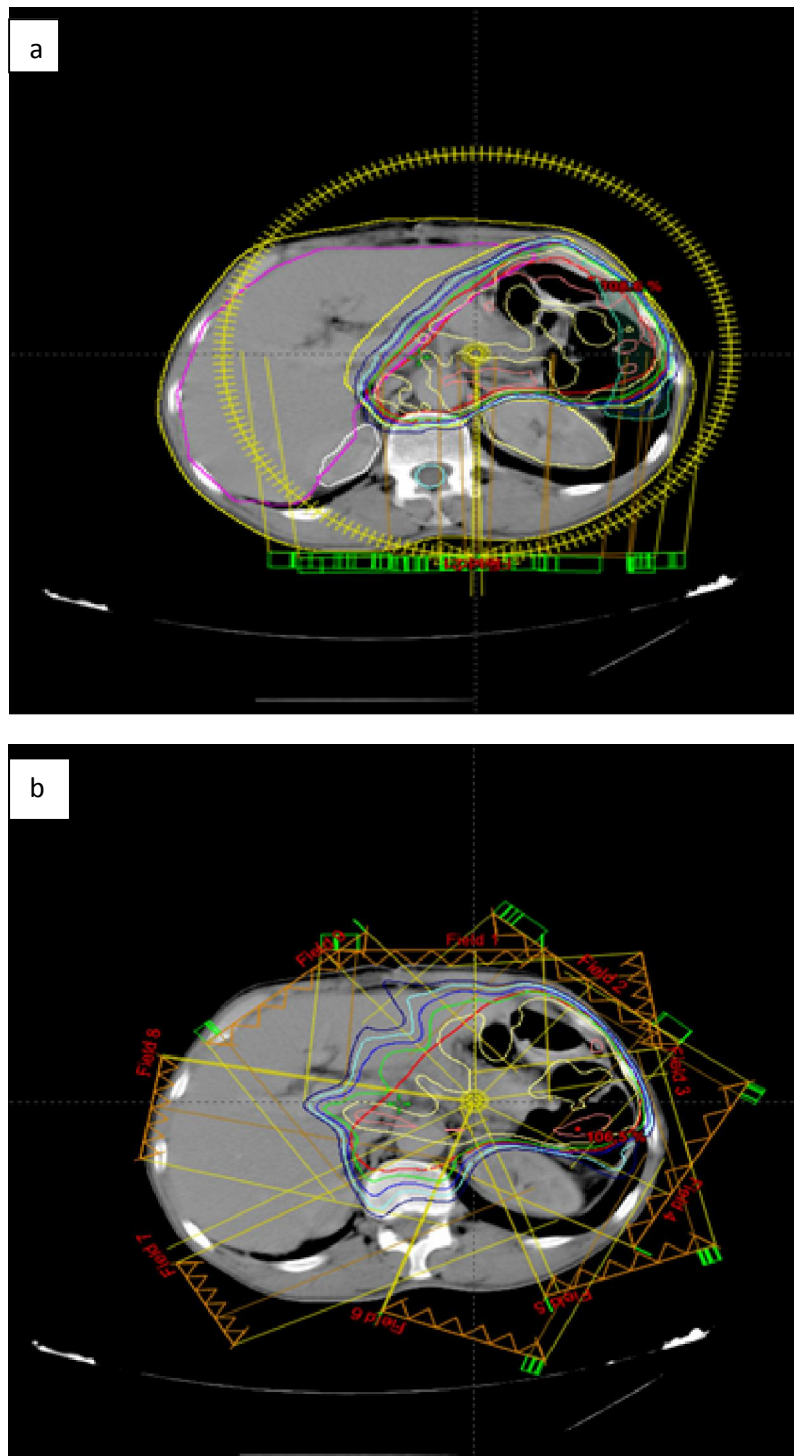
receiving 40 Gy) to the heart was kept within tolerance in both plans ( $p=0.245$ ). Table 4 illustrates the dosimetric endpoints for the OAR. Figure 1 shows the dose distribution in an axial view illustrating both techniques for the same patient and figure 2 shows the DVH for PTV and OARs comparing the two plans.

The treatment delivery time was  $193.5 \pm 25.0$  s (range 157–230 s) to IMRT and  $66.0 \pm 8.7$  s (range 55–77 s) to RapidArc ( $p = 0.002$ ). The total monitor units (MU) for RA and IMRT were  $343.0 \pm 94.0$  &  $363.0 \pm 44.6$  ( $p = 0.071$ ), respectively.

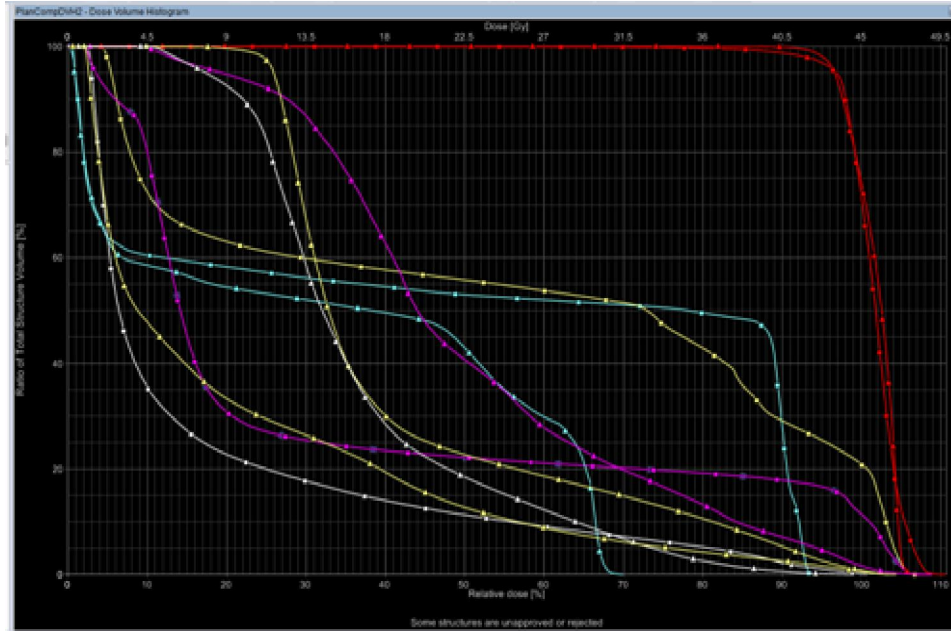
**Table 1: Patients and tumor characteristics**

	No	%
<b>Age (years)</b>		
≤ 40	4	20
41-50	6	30
51-60	9	45
> 60	1	5
<b>Sex</b>		
Male	12	60
Female	8	40
<b>Performance status</b>		
0	4	20
1	12	60
2	4	20
<b>T-stage</b>		
T1	0	0
T2	5	25
T3	9	45
T4a	6	30
T4b	0	0
<b>N-stage</b>		
N0	0	0
N1	3	15
N2	11	55
N3a	4	20
N3b	2	10
<b>Pathological grade (WHO)</b>		
II	8	40
III	12	60
<b>Disease stage</b>		
I	0	0
II	6	30
III	9	45
IV	5	25

†: WHO= World Health Organization



**Figure 1:** Dose distribution in an axial view created by doublearc RA plan ( **a** ) and similar CT cut planned by IMRT ( **b** )



**Figure 2:** A Comparative DVHs for PTV coverage and doses to OAR for IMRT (squares) and double arc RA (triangles).

**Table 2: Dose constraints for radiotherapy planning**

Structure	Constraint	Priority
<i>Spinal cord</i>	Max. < 45 Gy	High
<i>Right kidney</i>	Mean < 20Gy or V20 <25 %	Intermediate
<i>Left kidney</i>	Mean < 20Gy or V20 <25 %	Intermediate
<i>Liver</i>	mean < 30 Gy or V30 < 60%	Intermediate
<i>Heart</i>	Mean < 26 Gy or V40 < 30%	Intermediate

**Table 3 – Dosimetric outcomes for the PTV**

Parameter	IMRT plan	RapidArc plan	P-value
<i>V95%</i>	94.7 ± 4.5	94.8 ± 4.75	0.320
<i>V107%</i>	1.31 ± 1.63	1.08 ± 0.11	0.326
<i>Dmin (Gy)</i>	43.98 ± 0.39	43.54 ± 1.21	0.104
<i>CI95%</i>	0.93 ± 0.01	0.94 ± 0.01	0.040
<i>HI</i>	0.153 ± 0.01	0.142 ± 0.01	0.040
<i>MU</i>	363 ± 44.6	343 ± 94.4	0.071

**Table 4 – Dosimetric outcomes for the organs at risk**

Organ	Parameter	IMRT plan	RapidArc plan	P-value
<i>Spinal cord</i>	Max.dose (Gy)	37.87 ± 16.9	36.42 ± 18.1	0.340
<i>Right kidney</i>	V20 (%)	22.2 ± 11.6	24.3 ± 8.8	0.010
<i>Left kidney</i>	V20 (%)	24.4 ± 15.1	23.4 ± 13.2	0.010
<i>Liver</i>	V30 (%)	24.3 ± 13.4	23.1 ± 9.1	0.521
<i>Heart</i>	V40 (%)	14.4 ± 21.1	13.3 ± 15.9	0.245

## Discussion

In this study, we compared two different radiation treatment planning approaches for the management of gastric cancer. After reviewing the

data published in many studies addressing the dosimetric superiority of IMRT compared to 3D-CRT in the treatment of gastric carcinoma,<sup>16, 17</sup> our center became interested in adopting IMRT/VMAT into our



routine clinical practice. Though our initial clinical experience was mainly in treating head and neck and prostate cancers, yet we intend to expand the applications of IMRT and RA in different tumor subsites. The initial problem that we faced was how to precisely delineate the CTV and how to adopt a suitable radiation therapy technique that would provide adequate coverage of this volume while reducing the dose to the adjacent risk structures. Defining the high-risk sites that should be adequately included in the radiation fields (tumor bed, anastomoses and regional lymph nodes) in relation to the OAR (spinal cord, kidneys and liver) was the most important issue in most of the reports published addressing postoperative radiotherapy for gastric cancer.<sup>18,19</sup>

IMRT has potential disadvantages that should be taken in consideration. An IMRT plan increases the low dose areas outside the treatment volume due to higher scattered dose of radiation, raising the risk of secondary malignancies to occur with a suggested increase from 1% to 1.75%.<sup>20,21</sup> However, further data is needed to accurately estimate the incidence of IMRT induced secondary malignancies compared to other techniques. Other limitations of IMRT are the longer delivery time and higher number of MUs which might have an impact on the outcome of treatment, especially for tumors with a low alpha/beta ratio.<sup>22</sup>

Planning studies of RA technology in a wide variety of tumors has suggested that the quality of plans were comparable to conventional IMRT with a shorter delivery time and lower number of MU.<sup>23-26</sup> An improvement of dose uniformity to the target and lowering the exposure to OAR was observed in these studies. Moreover, double arc plans dosimetrically had additional advantages when compared to IMRT and single arc plans.<sup>27,28</sup> A possible explanation for this finding is that summing the two arcs can reduce the hot spots in the target volume and suboptimal dosing by the first arc is compensated by the second one. For gastric cancers irradiation, irregularity of the target volumes and low tolerance for the surrounding risk structures raises the question whether volumetric modulated radiation therapy (VMAT) would be of real benefit for adjuvant radiotherapy. To our own knowledge, few studies in literature investigated the potential benefit of applying VMAT in the treatment of gastric cancers in the adjuvant setting.<sup>29</sup>

In a study by Weigang Hu and his colleagues comparing RA to IMRT based on a novel beam angle and multicriteria optimization technique (BAMCO). They concluded that BAMCO IMRT provided an equivalent OAR sparing and target volume coverage when compared to RA. However, delivery time with the BAMCO technique was longer than RA (189.3 ± 26.0 s vs 65.0 ± 9.7 s), respectively.<sup>30</sup> Similarly,

Zhiping Li et al investigated four different techniques in the adjuvant treatment of gastric cancer (five and seven fields IMRT in addition to single and double arc VMAT plans). Their results showed faster treatment delivery with the VMAT plans with the double arc VMAT showing a better HI (0.10±0.01) and CI (0.87±0.03) when compared to other techniques. Regarding the OAR sparing, IMRT plans were marginally better than VMAT.<sup>31</sup> Tao Zhang and his colleagues compared double arc VMAT to static IMRT and 3D-CRT techniques. They reported that a better PTV coverage was achieved by both the RA and IMRT plans when compared to 3D-CRT. Moreover, the VMAT plans provided lower doses to OAR and better dosimetric endpoints than 3D-CRT and IMRT plans.<sup>32</sup>

In treating upper abdominal malignancies, there are many challenges to improve the radiotherapy delivery including patient immobilization, advances in diagnostic imaging, as well as image-guided radiotherapy and organ motion management. More and above, a better knowledge of the normal tissues tolerance is mandatory to optimize the radiotherapy treatment planning.<sup>33-35</sup> However, limitations of our study should be addressed and considered as well. First of all, the study did not evaluate clinical toxicity and was performed on a small number of patients. Moreover, respiratory gating was not used in our study which might influence the accuracy of the dose distribution. Therefore, more studies are needed to evaluate and confirm the feasibility of RA in the management of gastric cancers.

## Conclusion

At our institution with early arc delivery experience, RapidArc obtained similar dosimetric outcomes to IMRT plans regarding target coverage & OAR sparing with an advantage of shorter delivery time & lower number of MU.

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## Disclosure:

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Paper is submitted as our experience

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#### Author Contribution:

K. Mashhour was the principle radiation oncologist involved in delineation and plan acceptance.

W. Hashem was involved in contouring of cases in addition to manuscript writing

H. Abdelghany was the medical radiation physicist who generated all plans in this research study

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