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RESEARCH ARTICLE

Intensity Modulated Radiation Therapy vs. Volumetric Modulated Arc Therapy in Locally Advanced Unresectable Pancreatic Cancer: Dosimetric Study

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Abstract

Pancreatic carcinoma is considered one of the most complicated cancers in treatment. VMAT technique is a novel IMRT form. Pancreatic motion is an essential problem in its radiotherapy planning, VMAT can lessen this risk of motion by shortening the time of treatment therefore it can minimize radiotherapy toxicity.

Our study aim was to define if VMAT achieves a high dose distribution and more dose homogeneity with shorter overall treatment time in comparison to IMRT.

Patients and methods: The medical records of five patients of locally advanced unresectable pancreatic cancer treated by conventional fractionation using VMAT were reviewed and re-planned by IMRT techniques at International Medical Center, Cairo, Egypt.

Results: Both techniques have comparable PTV54 target coverage. PTV50.4 is statistically significant and better in VMAT than IMRT.

Both techniques have comparable sparing in case of liver, RT kidney and bowel. Sparing of left kidney and stomach is more significant and better in VMAT than IMRT. However, the spinal cord is relatively better spared in IMRT than VMAT.

Lower Integral dose is attained in IMRT than VMAT so IMRT can achieve further reduction of complication rates in pancreatic cancer.

VMAT has shorter treatment time beam on than IMRT and more conformity and homogeneity index.

Conclusions: VMAT provided a higher dose distribution regarding to organs at risk as all OAR have statistically significant better sparing in case of VMAT than IMRT except the spinal cord without compromising CTV coverage. Moreover VMAT can achieve more dose homogeneity in shorter treatment time.

Abbreviations

VMAT: The Volumetric Modulated Arc Therapy; IMRT: Intensity-Modulated Radiation Therapy; MLC: Multileaf Collimator; OARs: Organs at Risk; 4DCRT: 4 Dimensional Conformal Radiotherapy; 3DCRT: 3 Dimensional Conformal Radiotherapy; CT: Computed Tomography; GTV: Gross Target Volume; CTV: Clinical Target Volume; PTV: Planning Target Volume

Introduction

Pancreatic carcinoma is one of the most complicated cancers in treatment. There are 2 approaches in its treatment such as “chemoradiotherapy followed by chemotherapy” and “chemotherapy alone” [1]. This difference is due to pancreas site since it is placed in the middle of many critical structures [2].

IMRT is a superior mode of high-precision radiotherapy [3]. VMAT technique is a novel IMRT form [4,5]. As in pancreatic radiotherapy planning, its motion is an essential problem, VMAT can lessen this risk of motion by shortening the time of treatment therefore it

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has a hopeful effect on minimizing radiotherapy toxicity [6-8].

Aim of Our Study

Our study aim was to define if VMAT achieves a high dose distribution and more dose homogeneity with shorter overall treatment time in comparison to IMRT depended on 4D-CT target volume coverage and organs at risk doses in definitive treatment by concurrant chemoradiotherapy in locally advanced unresectable pancreatic cancer.

Patients and Methods

Study design

The medical records of five patients of locally advanced unresectable pancreatic cancer treated by conventional fractionation using VMAT were reviewed and re-planned by IMRT techniques at International Medical Center, Cairo, Egypt. PTV50.4 is contoured and covering 5 mm around CTV that encompasses all relevant nodal regions including the porta hepatis, celiac/SMA and PA/RP lymph nodes in all techniques delivering 28 fractions with 1.8 Gy per fraction. PTV54 is contoured and covering 5 mm margin around GTV that consists of hypodense area "a biopsy proven disease in the pancreas and any positive lymph nodes visualized on diagnostic pancreatic protocol CT". The same objectives were determined for both IMRT and VMAT plans. Contouring of OAR was done according to RTOG guidelines [9].

Dose limitations

Conventional fractionation

Organ at risk	Tolerance dose
Spinal cord	Maximum point dose is less than 45 Gy.
Bowel	Dmax is less than 55 Gy Keep bowel volumes receiving 45-55 GY < 30%
Kidney	Mean total kidney dose is < 18 Gy. If only one kidney is functional limit radiotherapy dose delivered < 10-15% over 18 Gy and less 30% over 14 Gy
Liver	Mean dose < 25-30 Gy to prevent radiation hepatitis.

Adapted from RTOG 1102(IMRT, 2.2-54Gy).

Adapted from RTOG 0848(3D or IMRT) [10].

Planning system

IMRT technique: Six to eight fields were calculated using the dynamic IMRT technique, 10 Mv energy and Monte Carlo Algorithm at different angles.

VMAT technique: Plans were generated using dynamic VMAT and Monte Carlo Algorithm and 2-3 arcs of 6-10 Mv in clockwise and counterclockwise.

Plan evaluation: We compared target volumes coverage, critical organs sparing, integral dose, Homogeneity index, Conformity index and beam on treatment time between two plans.

Statistical analysis

Using Microsoft Office Excel 2010 for windows for data collection, tabulation and statistically analysis and SPSS 22.0 for windows. Expression of Continuous Quantitative variables were done as the mean ± SD & median (range). Check of continuous data for normality was done by using Shapiro Walk test. Using of Wilcoxon singed ranks test was done for two dependent groups of non-normally distributed data. All tests were two sided. P-value < 0.05 was considered statistically significant.

Results

Table 1 and Table 2.

Target volumes

Both IMRT and VMAT techniques have comparable PTV54 target coverage. PTV50.4 is statistically significant and better in VMAT than IMRT so it is in favor of VMAT than IMRT.

Organ at risk sparing

IMRT & VMAT techniques have comparable sparing in case of liver, RT kidney and bowel. Sparing of left kidney and stomach is more significant and better in VMAT than IMRT so it is more in favor of VMAT than IMRT. However, the spinal cord is relatively better spared in IMRT than VMAT.

Integral dose (Normal tissue outside PTV)

The integral dose represents the total energy deposited by ionizing radiation within a body. Lower Integral dose is attained in IMRT than VMAT so IMRT can achieve further reduction of complication rates in pancreatic cancer and this is in favor of IMRT than VMAT technique. (P value 0.038).

Beam on treatment time and dose homogeneity

VMAT has shorter treatment time beam on (median 0.7600) than IMRT (median 1.6700) (P value 0.042) and more conformity (P value 0.025) and homogeneity index (P value 0.042) so it can achieve more dose homogeneity.

IMRT & VMAT techniques have comparable sparing in case of liver, RT kidney and bowel. Sparing of left kidney and stomach is more significant and better in VMAT than IMRT so it is more in favor of VMAT than IMRT. However, the spinal cord is relatively better spared in IMRT than VMAT.

Discussion

Pancreatic cancer radiotherapy is a complex area due to its site and movement factor due to organ

Table 1: All patients' characteristics and statistics are showed.

	Patient 1		Patient 2		Patient 3		Patient 4		Patient 5	
	VMAT	**IMRT**	**VMAT**	**IMRT**	**VMAT**	**IMRT**	**VMAT**	**IMRT**	**VMAT**	**IMRT**
PTV54%										
Mx	107.4	102.5	106	103	105.2	103.5	104.8	104	103.7	103.8
Mn	101.6	99.3	100	100.2	101	99.8	102	101	101.5	101
Mm	90.5	91.2	91	92	91.5	92.4	90	91.2	91.5	91
PTV50.4%										
Mx	107	102	106	104	106.5	102	107.2	103	105.8	103.5
Mn	94.3	92.8	95	94	95.6	94	95.4	94.2	95.8	94.3
Mm	73.7	69.4	75.5	60.4	74	70.2	76.2	71.6	73.8	70.6
Bowel										
Mx	95.6	101.6	94	100	96	102	97	101	95	102
Mn	48.5	42.4	50	44.2	47	40.8	49	43.2	51	44.8
RK										
Mx	91	92.9	88	90	87	88	85	86.5	90	91.5
Mn	28	28.3	27	28	26	26.8	25.5	25	27.8	27.4
LK										
Mx	103.8	100.5	101.2	100	101	97	102	99	102.5	98.5
Mn	28.6	32.6	27	30.5	26.2	29.8	29	32.4	25	29.2
SC										
Mx	74.9	68.1	77	71	78	72.2	72	67.4	70	64.5
Mn	47	37	45	36	48	39	50	41	46.8	37.2
Liver										
Mx	104.3	99.7	101	98	100	97.2	103	99	102.4	98.3
Mn	26.2	26.9	24	24.5	27.4	28	25.8	26.1	28	28.3
Stomach										
Mx	99.5	100.2	100	100.2	99.2	99.4	98	99.1	97.4	98.1
Mn	57.7	64.2	50.4	56	52.5	59.1	54.6	61.1	55.3	62
ID										
V5	6194	5750	7210	6760	5780	5336	6820	6370	4980	4536
V10	4782	4560	5798	5572	4370	4145	5405	5180	3568	3345
V15	3725	3612	4740	4622	3311	3202	4350	4230	2511	2398
TT	0.76	1.67	0.8	1.6	0.74	1.7	0.81	1.65	0.73	1.78
CI	0.79	0.37	0.8	0.38	0.75	0.33	0.74	0.32	0.77	0.35
HI	0.09	0.06	0.085	0.065	0.095	0.065	0.09	0.065	0.092	0.061

Mx: Maximum; Mn: Mean; Mm: Minimum; PTV: Planning Target Volume; RK: Right Kidney; LK: Left Kidney; SC: Spinal Cord; ID: Integral Dose; V5: Volume of Body in C.C, TT beam on treatment time, CI: Conformity Index; HI: Homogeneity Index

Table 2: Comparison between VMAT plan and IMRT plan regarding dosimetric parameters.

	VMAT plan (N = 5)	IMRT plan (N = 5)	Test[a]	p-value
PTV54				
Maximum (%)				
Mean ± SD	105.40 ± 1.14	103.40 ± 0.89	-1.841	0.066
Median (Range)	105 (104-107)	104 (102-104)		
Minimum (%)				
Mean ± SD	101.40 ± 0.89	100.20 ± 0.83	-1.890	0.059
Median (Range)	102 (100-102)	100 (99-101)		
Mean (%)				

Mean ± SD	91 ± 1	91.40 ± 0.54	-1.000	0.317
Median (Range)	91 (90-92)	91 (91-92)		
PTV50.4				
Maximum (%)				
Mean ± SD	106.40 ± 0.54	103 ± 1	-2.041	0.041
Median (Range)	106 (106-107)	103 (102-104)		
Minimum (%)				
Mean ± SD	76.64 ± 1.13	68.44 ± 4.56	-2.023	0.043
Median (Range)	74 (73.70-76.20)	70.20 (60.40-71.60)		
Mean (%)				
Mean ± SD	95.20 ± 0.83	93.80 ± 0.44	-2.070	0.038
Median (Range)	95 (94-96)	94 (93-94)		
Bowel				
Maximum (%)				
Mean ± SD	95.60 ± 1.14	101.40 ± 0.89	-2.060	0.039
Median (Range)	96 (94-97)	102 (100-102)		
Mean (%)				
Mean ± SD	49 ± 1.58	43 ± 1.58	-2.236	0.025
Median (Range)	43 (41-45)	43 (41-45)		
Right kidney				
Maximum (%)				
Mean ± SD	88.20 ± 2.38	89.80 ± 2.86	-2.070	0.038
Median (Range)	88 (85-91)	90 (86-93)		
Mean (%)				
Mean ± SD	27 ± 1	27 ± 1.22	0.000	1.000
Median (Range)	27 (26-28)	27 (25-28)		
Left kidney				
Maximum (%)				
Mean ± SD	102 ± 1.22	98.80 ± 1.30	-2.060	0.039
Median (Range)	102 (101-104)	99 (97-100)		
Mean (%)				
Mean ± SD	27.20 ± 1.78	30.80 ± 1.64	-2.070	0.038
Median (Range)	27 (25-29)	30 (29-33)		
Cord				
Maximum (%)				
Mean ± SD	74.40 ± 3.36	68.40 ± 3.20	-2.060	0.039
Median (Range)	75 (70-78)	68 (64-72)		
Mean (%)				
Mean ± SD	47.40 ± 1.81	38 ± 2	-2.070	0.038
Median (Range)	47 (45-50)	37 (36-41)		
Liver				
Maximum (%)				
Mean ± SD	102 ± 1.58	98.40 ± 1.14	-2.070	0.038
Median (Range)	102 (100-104)	98 (97-100)		
Mean (%)				
Mean ± SD	26.20 ± 1.48	26.60 ±1.67	-1.414	0.157
Median (Range)	26 (24-28)	27 (24-28)		
Stomach				
Maximum (%)				
Mean ± SD	98.80 ± 1.30	99.20 ± 0.83	-1.414	0.157

Median (Range)	99 (97-100)	99 (98-100)		
Mean (%)				
Mean ± SD	54 ± 3.08	60.40 ± 3.04	-2.070	0.038
Median (Range)	55 (50-58)	61 (56-64)		
ID				
V5 (cGy)				
Mean ± SD	6196.80 ± 875.96	5750.40 ± 873.16	-2.070	0.038
Median (Range)	6194 (4980-7210)	5750 (4536-6760)		
V10 (cGy)				
Mean ± SD	4784.60 ± 875.19	4560.40 ± 874.21	-2.032	0.042
Median (Range)	4782 (3568-5798)	4560 (3345-5572)		
V15 (cGy)				
Mean ± SD	3727.40 ± 875.50	3612.80 ± 872.34	-2.032	0.042
Median (Range)	3725 (2511-4740)	3612 (2398-4622)		
Dose homogeneity				
TT				
Mean ± SD	0.76 ± 0.03	1.68 ± 0.06	-2.032	0.042
Median (Range)	0.76 (0.73-0.81)	1.67 (1.60-1.78)		
CI				
Mean ± SD	0.77 ± 0.02	0.35 ± 0.02	02.236	0.025
Median (Range)	0.77 (0.74-0.80)	0.35 (0.32-0.38)		
HI				
Mean ± SD	0.090 ± 0.003	0.063 ± 0.001	-2.032	0.042
Median (Range)	0.090 (0.085-0.095)	0.065 (0.060-0.065)		

Continuous variables were expressed as mean ± SD & median (range); a: Wilcoxon singed ranks test; p-value < 0.05 is significant

motion and respiration. IMRT has been proved to improve dosimetric parameters and minimize the doses delivered to normal critical tissues. The first significant problem of radiotherapy is the high recurrence rate of acute adverse of gastrointestinal tract via concurrent chemo radiotherapy. The second problem was intra-fraction motion in pancreas cancer. Using VMAT could achieve more effective dose distribution and more target coverage and more dose homogeneity. In our study IMRT & VMAT techniques have comparable sparing in case of liver, RT kidney and bowel. Sparing of left kidney and stomach is more significant and better in VMAT than IMRT so it is more in favor of VMAT than IMRT in accordance with **SEZEN, et al. study at 2017** [11].

As our study, Ali, et al., analyzed the dosimetric data of 10 patients and the conclusion of this study that using VMAT in patients with pancreatic cancer either for curative or adjuvant radiotherapy intent, achieved lower mean doses of both kidney in comparison to IMRT, however similar other organ doses of both techniques were detected [12].

One of the essential acute adverse effects was caused by the dose that delivered to the small bowel during therapy. It is revealed that radiotherapy toxicity can be achieved with even large volume of low dose areas (5-15 Gy) [13]. This is a great care for using of recent technologies as IMRT and VMAT. **Landry, et al.**, GTV and microscopic disease received 45 Gy, and in comparison with 3DCRTand IMRT, the dose that delivered to 1/3 of the small bowel reduced to 38.5 Gy vs. 30.2 Gy [14,15].

In our study spinal cord max dose is less in IMRT (p value 0.039) than VMAT in contrast to **Jethwa, et al. study 2018** [16].

In pancreatic cancer radiotherapy planning, to overcome the motion factor, using new radiotherapy technologies for reduction normal organ doses [17]. **Sangalli, et al.,** studied 4DCT planning impact for unresectable pancreatic cancer patients. Via using this planning system, target volumes lessened by 37% in comparison to standard target delineation [14]. In our study, 4DCT simulation was done as a standard approach for radiotherapy planning of pancreas cancer patients.

Lower Integral dose is attained in IMRT than VMAT so IMRT can achieve further reduction of complication rates in pancreatic cancer and this is in favor of IMRT than VMAT technique. This finding is in agree with many previous dosimetric studies as **Chen, et al.,** [18].

VMAT has shorter treatment time beam on than IMRT and more conformity and homogeneity index so it can achieve more dose homogeneity as reported in previous dosimetric studies [19].

Conclusions

In the dosimetric comparison of ssIMRT and VMAT techniques based on 4D CT scans in the cases of locally advanced irresectable pancreatic cancer patients, both plans achieve dosimetric organ goals, however VMAT provided a higher dose distribution regarding to organs at risk as all OAR have statistically significant better sparing in case of VMAT than IMRT except the spinal cord without compromising CTV coverage. Moreover VMAT can achieve more dose homogeneity in shorter treatment time. This study is restricted by a quite small number of patients but these results could be hopeful for more and more usage of VMAT for pancreatic cancer as routine as the other sites for example cancers of head and neck.

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Not applicable.

Conflict of Interest

Declare.

Financial Support

Not applicable.

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