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Dosimetric comparison of constant dose rate volumetric modulated arc therapy (CDR-VMAT) and intensity-modulated radiation therapy (IMRT) for gallbladder cancer

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Original Article

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Abstract

Aim: To study the feasibility of constant dose rate volumetric modulated arc therapy (CDR-VMAT) in radiotherapy for gallbladder cancer by comparing dosimetric parameter suggested by International Commission on Radiation Units and Measurements-83 (ICRU-83) with step and shoot intensity-modulated radiation therapy (SS IMRT).

Methods: For this study, we selected 21 post-operative gallbladder cancer patients, which were treated with the IMRT technique from 2016 to 2019. For each patient, we generated SS IMRT plan and CDR-VMAT plan and were dosimetrically compared by parameters suggested by ICRU-83 for PTV. Homogeneity Index (HI) and Conformity Index (CI) were also calculated. For evaluation of Organ at Risk (OAR), we compared the mean doses, volume doses to the right kidney, left kidney, both kidneys combined, liver and max dose to the spinal cord. Monitor units (MUs) and treatment delivery time were also compared.

Results: On comparing, we found that CDR-VMAT plans were highly conformed as CI and PCI (CI define by Paddick) were found more (0·98 ± 0·01 vs. 0·97 ± 0·03 and 0·86 ± 0·05 vs. 0·85 ± 0·05) than IMRT plans but not statistically significant. Better dose HI was found for IMRT plans with statistical significant difference ($p < 0·001$). The tumour coverage was found similar 98·24% and 97·83% for SS IMRT and CDR-VMAT, respectively. For D2%, the maximum dose to PTV was significantly lower in IMRT ($p = 0·001$). D50% and mean dose to PTV were also comparable to IMRT with no statistically significant difference. The OAR parameters were comparable in both the techniques. The mean doses and volume doses V10, V20 and V30 to the right kidney, left kidney and liver were also comparable with no significant difference ($p > 0·05$) was noted among them. However, the maximum dose to the spinal cord was significantly less in CDR-VMAT (21·1 Gy vs. 25·1Gy) than SS IMRT with $p = 0·006$. More MUs were associated with the CDR-VMAT technique, but shorter treatment delivery time than the IMRT technique.

Conclusions: On dosimetric comparison of two treatment techniques, we conclude that CDR-VMAT can be a valid option in radiotherapy as it achieved highly conformed dose distribution, comparable tumour coverage and OAR sparing as IMRT technique for gallbladder cancer.

Introduction

Gall bladder carcinoma (GBC) is the fifth most common cancer[1] and one of the most aggressive gastrointestinal tract malignancies worldwide,[2] which has a poor prognosis.[3,4] GBC is more common in females than in males. The standard treatment for GBC is surgery. More recently, adjuvant chemotherapy plus radiotherapy has been an effective treatment for gallbladder cancer. Many authors have studied the role of adjuvant therapy, chemotherapy plus radiation and their impact on survival rate improvement.[5–9] In our institute, the standard treatment for gall bladder cancer is surgery then adjuvant chemo plus radiation therapy. If the tumour size is large and surgery is not possible, then chemotherapy is administered to reduce the tumour size and then surgery and radiotherapy are performed.

Xiao-nan San et al. suggested that IMRT is a better treatment modality than conventional 3DCRT for gall bladder cancer.[10] There are many developments in radiotherapy in terms of planning and delivery like intensity-modulated radiation therapy (IMRT), image-guided radiation therapy, volumetric modulated arc therapy (VMAT), stereotactic radiosurgery, stereotactic radiation therapy, stereotactic body radiation therapy, etc. However, these techniques require advance technology. The IMRT is mostly used to treat complex, conical shape tumours, multiple tumour targets, and where more organs at risk (OARs) are optimised to reduce the dose to OAR and increase tumour coverage. To achieve this goal, we use many IMRT techniques like step and shoot IMRT, dynamic IMRT and sliding window IMRT which require static gantry and deliver

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dose to the tumour from fixed gantry angles. IMRT techniques have disadvantages too such as longer treatment time, more number of monitor units (MU) and inhomogeneous dose distribution in tumour than the conventional three-dimensional radiation therapy (3DCRT) technique.[11,12] To overcome the demerit of longer treatment time, VMAT was proposed by Otto[13] in 1998.

The rotational IMRT technique (VMAT or Rapid arc) is being popular because its variable gantry speed, gantry rotation, variable dose rates and variable leaf speed give similar or a better quality plan than static IMRT with the shortest delivery time. The original form of rotation therapy by solving the integral equation was given in 1982 by Brahame et al.[14] The VMAT from Elekta (Elekta AB, Sweden) and Rapid Arc from Varian (Varian medical system, Polo Alto, CA) are the two examples of this technique which are becoming more popular. Many researchers compare these rotational IMRT techniques with static IMRT techniques by comparing many dosimetric parameters and found rotational IMRT (VMAT or Rapid arc) better due to its better tumour coverage, in sparing OAR, more conformed dose distribution, less MUs and shortest treatment delivery time among all treatment techniques.[15,16] But this technique needs advanced technologies or upgrading in software and hardware in existing Linac, but constant dose rate VMAT (CDR-VMAT) technique does not require advanced technologies like variable dose rate VMAT (VDR-VMAT) and can be done with conventional Linac, so it is cost-effective.

In our present study, we used the CDR-VMAT technique for planning gall bladder cancer to see the feasibility of CDR-VMAT in modern-day radiotherapy by comparing the dosimetric parameters suggested by International Commission on Radiation Units and Measurements-83 (ICRU-83)[17] and OAR comparison with Step and Shoot IMRT (SS IMRT). Therefore, the objective of the present study was to find the feasibility of CDR-VMAT compared to SS IMRT by using dosimetric parameters suggested by ICRU-83 for the treatment of gallbladder cancer.

Material and Method

Patient selection

In this prospective study, we included 21 post-operative gallbladder cancer patients. Average age of patients was 48·3 years (28 years–66 years). The patients were treated with the IMRT technique from 2016 to 2019 at our institute. Due to unavailability of previous trials with similar treatment technique, a convenient sampling of 21 patients was selected for this study.

CT simulation and contouring

Each patient was simulated on a CT simulator (SOMATOM, SIEMENS, Germany) in a supine position and used a thermoplastic cast for immobilisation. CT images were acquired at a slice thickness of 5 mm, and data were transferred to the monacosim contouring station (ELEKTA, Crawley, UK) using DICOM protocol. The radiation Oncologist contoured tumour and OAR like liver, kidneys, spinal cord, etc. These data were then transferred to the Monaco Treatment Planning System (TPS).

Treatment planning

We created a total of 42 plans for 21 patients, two plans for each patient (one SS IMRT and one CDR-VMAT). SS IMRT plan consists of 5 or 6 fields, and the CDR-VMAT plan consists of 2 partial arcs, one clockwise (220^0-100^0) and another one anti-clockwise (100^0-220^0) by using the Monte Carlo algorithm on Monaco TPS version 5.11.01 for 6 MV photon energy. The angle selection in IMRT and arc selection in CDR-VMAT were optimum avoiding OAR as much as possible. The isocentre was selected at the centre of PTV. The prescription dose was 50·4 Gy in 28 fractions (1·8 Gy per fraction). The plans were optimised to get a 95% prescription dose to 95% volume of PTV. SS IMRT plan and CDR-VMAT plan were dosimetrically compared by parameters suggested by ICRU-83 for PTV by DVH evaluation tools – maximum dose to PTV (D2%), minimum dose to PTV (D98%), mean dose to PTV, median dose to PTV (D50). HI and CI were also calculated. The Conformity Index (CI) was calculated by using Radiation Therapy Oncology Group (RTOG) formula[18] and formula given by Paddick.[19]

Homogeneity Index (HI): The HI was calculated by using formula:

$$HI = D2 - D98/D50$$

where D50 is dose in 50% of PTV, D2 refers to dose in 2% of PTV, indicating the maximum dose and D98 refers to the dose in 98% of PTV, indicating the minimum dose.

The ideal value of HI is zero. HI equal to zero means more homogeneous dose distribution across tumour.

Conformity Index (CI): The plan conformity has been evaluated by calculating the RTOG CI:

$$CI = V_{RI}/TV$$

where,
VRI denotes reference isodose volume
TV signifies tumour volume

The conformity of the plan was also calculated by using the formula given by Paddick

$$PCI = (TV_{RI}/TV) \times (TV_{RI}/V_{RI})$$

where,
TV – tumour volume,
RI – reference isodose,
TV_{RI} – tumour volume covered by reference isodose and
V_{RI} – the volume of the reference isodose

This formula was used because it taking into account the irradiation of tumour volume as well as normal tissue. The ideal value of CI is one which indicates that dose distribution is more conformed to the tumour.

For evaluation of OAR, we compared mean doses, V10, V20, V30 to right kidney, left kidney, liver and max dose to the spinal cord, and volume doses of both kidney combined V12, V20, V23, V28 suggested by Quantec. The dose constraints used for OAR are presented in Table 1. MUs and treatment delivery time were also compared.

Statistical analysis

We used IBM SPSS software (version 20, IBM Corporation) for statistical analysis. For statistical comparison of two techniques, we used paired samples *t*-test and a *p*-value< 0·05 considered statistically significant.

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Table 1. Dose constraints for Organ at Risk (OAR)

OAR	Dose constraints
Liver	Mean dose < 28 Gy
Spinal cord	Max dose < 45 Gy
Bilateral whole kidney	V12 < 55%
	V20 < 32%
	V23 < 30%
	V28 < 20%

Vx (%) means x Gy dose covered the percentage of volume.

Table 2. Dosimetric comparison of tumour volume parameters

PTV Parameters	SS IMRT (mean ± SD)	CDR-VMAT (mean ± SD)	*p*-Value
PTV95 (%)	98·24 ± 0·9	97·83 ± 1·0	0·88
PTV max (D2 Gy)	52·43 ± 0·35	52·84 ± 0·36	**0·001**
PTV min (D98 Gy)	48·21 ± 0·67	47·89 ± 0·42	**0·016**
PTV median (Gy)	50·91 ± 0·42	50·75 ± 0·37	0·179
PTV mean (Gy)	50·80 ± 0·42	50·70 ± 0·36	0·372
HI	0·083 ± 0·01	0·098 ± 0·009	**<0·001**
CI	0·97 ± 0·03	0·98 ± 0·01	0·385
PCI	0·85 ± 0·05	0·86 ± 0·05	0·938

SS IMRT, step and shoot IMRT; CDR-VMAT, constant dose rate volumetric modulated arc therapy; PTV95, volume of PTV covered by the 95% isodose line; HI, homogeneity index; CI, conformity index; PCI, conformity index define by Paddick; SD, standard deviation.

Results

PTV evaluation

A total of 42 plans were created for comparison. The average volume of PTV was 562·088 cc, and the median volume was 483·303 cc (range: 293·856 cc to 965·395 cc). PTV coverage V95 was 98·24% and 97·83% for SS IMRT and CDR-VMAT, respectively, with no statistical significant difference ($p = 0·88$) was noted. The CDR-VMAT plans were highly conformed as CI and PCI were found more (0·98 ± 0·01 vs. 0·97 ± 0·03 and 0·86 ± 0·05 vs. 0·85 ± 0·05) than IMRT plans. However, no statistically significant difference between them was found. Better dose HI was found for IMRT plans with statistical significance ($p < 0·001$). D2 the maximum dose to PTV was significantly less in IMRT with mean value 52·43 ± 0·35 Gy vs. 52·84 ± 0·36 Gy ($p = 0·001$). The average PTV minimum dose (D98) was 48·21 ± 0·67 Gy and 47·89 ± 0·42 Gy for IMRT and CDR-VMAT plan, respectively ($p = 0·016$). The average PTV median dose was 50·91 ± 0·41 Gy and 50·75 ± 0·37 Gy for IMRT and CDR-VMAT plan, respectively ($p = 0·179$). Moreover, the average PTV mean dose was 50·80 ± 0·42 Gy and 50·70 ± 0·36 Gy for IMRT and CDR-VMAT plan, respectively ($p = 0·372$). The dosimetric comparison of tumour volume parameters is shown in Table 2. All values displayed were mean value plus standard deviations.

Figure 1 shows the dose distribution on axial slice, and Figure 2 shows the DVH comparison for tumour volumes and OAR for IMRT and CDR-VMAT

The dosimetric comparisons for OAR are given in Table 3. The mean doses, V10, V20, V30 to the right kidney, left kidney and liver were compared, and no statistical significance ($p > 0·05$) between them was found. However, the average maximum dose to the spinal cord was significantly less in CDR-VMAT than IMRT (21·1 Gy vs. 25·1 Gy) with a statistical significant difference ($p = 0·006$). Liver mean dose was 21·43 Gy (± 6·5 SD) and 21·31 Gy (± 5·9 SD) for IMRT and CDR-VMAT plan, respectively, with a *p*-value difference 0·765. All parameters for the bilateral whole kidney were lower than their constraint. Moreover, the V12 was 44·03 % (± 16·87 SD) and 46·94 % (± 17·33 SD) for IMRT and CDR-VMAT, respectively ($p = 0·145$), which was much less than constraint 55%. The V20 is 26·43 % (± 13·9 SD) and 26·86 % (± 15·02 SD) for IMRT and CDR-VMAT, respectively ($p = 0·833$), which was much <32%. Furthermore, the V23 is 20·92% (± 12·8 SD) and 19·54% (± 12·68 SD) for IMRT and CDR-VMAT, respectively ($p = 0·389$), which was much less than constraint 30%. The V28 is 15·02 % (± 10·1 SD) and 13·31% (± 9·23 SD) for IMRT and CDR-VMAT, respectively ($p = 0·150$), which was much less than constraint 20%.

The treatment delivery parameters MU and treatment delivery time were also compared and are showed in Table 4. The average MU was 473·11 ± 73·15 for IMRT, and the MU for CDR-VMAT was 838·97 ± 176·75 which was 1·77 times more than IMRT. The average treatment time was 3·9 minutes for CDR-VMAT which was 3·12 times less than IMRT (12·2 minutes) with a difference of *p*-value <0·001. MUs were higher for the CDR-VMAT technique, but treatment delivery time was significantly shorter than IMRT.

Discussion

In this study, the CDR-VMAT plan is compared with the IMRT plan for 21 post-operative gallbladder cancer patients by using ICRU-83 parameters like DVH parameters for PTV evaluation and OAR comparison. On comparing these two techniques, we found that the CDR-VMAT technique gives comparable or even better clinically acceptable plan than IMRT in terms of PTV coverage and OAR sparing.

Similarly, many studies found that the CDR-VMAT technique achieved comparable plan as VDR-VMAT and IMRT plan in terms of PTV coverage and OAR sparing.[10,20–27] But there is a limited demand for VDR-VMAT technique due to higher cost associated with it to purchase new advanced Linac or for upgrading hardware and software in the existing Linac. So, we studied the CDR-VMAT technique which is cost-effective and can be done with conventional Linac to see the feasibility of this technique in radiotherapy for gallbladder carcinoma, and found that it also generates a similar plan as IMRT for gallbladder cancer in terms of PTV coverage and OAR sparing.

In our study, we found that the CDR-VMAT plans were highly conformed as, CI and PCI were found more (0·98 ± 0·01 vs. 0·97 ± 0·03 and 0·86 ± 0·05 vs. 0·85 ± 0·05) than IMRT plans but not statistically significant. Better dose HI was found for IMRT plans with a significant difference. However, the tumour coverage was similar for both the techniques with no statistical significant difference. For D2%, the maximum dose to PTV was significantly lower in IMRT. The OAR parameters are comparable in both the techniques; the mean doses, volume doses V10, V20, V30 to the right kidney, left kidney and liver were also comparable with no significant difference was noted among them. However, the maximum dose to the spinal cord was significantly less in CDR-VMAT (21·1 Gy vs. 25·1 Gy) than SS IMRT. All Quantec parameters for the bilateral whole kidney were much lower than their constraint. More MUs were associated with the CDR-VMAT technique, but shorter treatment delivery time than the IMRT technique.

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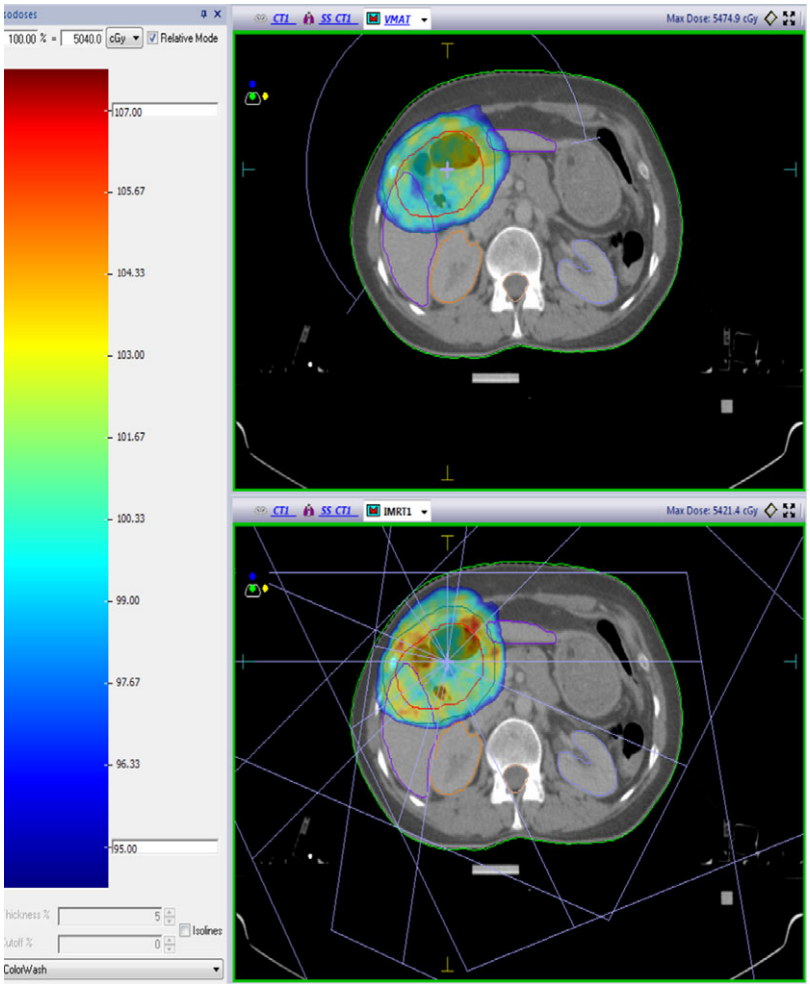

Figure 1. Dose distribution on axial slice.

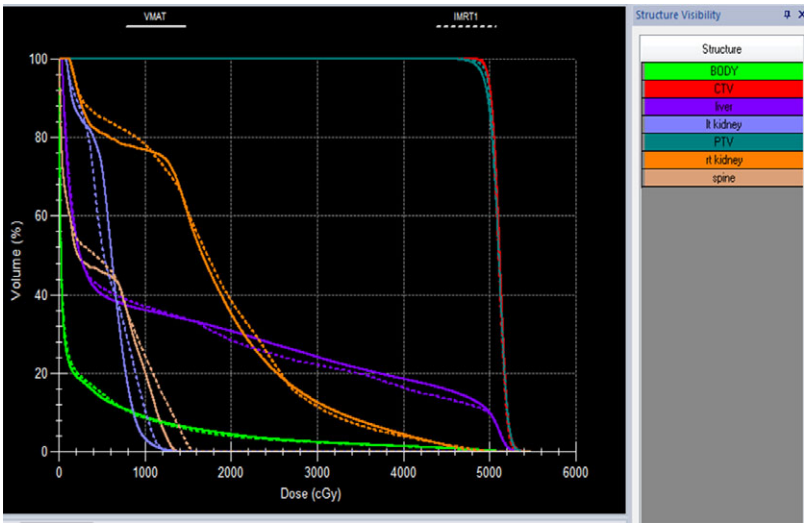

Figure 2. DVH comparison for tumour volumes and organs at risk (OAR) for intensity-modulated radiation therapy (IMRT) and constant dose rate volumetric modulated arc therapy (CDR-VMAT).

The intrafraction motion is reduced due to shorter treatment delivery time, hence reduced intrafractional positional error compared with IMRT. Low-cost CDR-VMAT also improved the patients' throughput, hence beneficial for patients and to the institute.

Similar findings were found in the past literatures.[10,20–27] Hatanaka et al.[20] studied CDR-VMAT, VDR-VMAT and IMRT in 28 prostate cases and found that the dose distribution and DVH of the CDR, f-IMRT and VMAT methods were clinically equivalent. CDR can reduce the total number of MUs and the patient irradiation time compared to f-IMRT, resulting in a lower initial cost compared to that of VMAT. In our study, MU is more but treatment time is shorter in CDR-VMAT.

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Table 3. Dosimetric comparison of Organ at Risk

Organ at Risk	Parameters	SS IMRT (mean ± SD)	CDR-VMAT (mean ± SD)	*p*-Value
Lt Kidney	Mean dose (Gy)	8·63 ± 3·82	8·65 ± 4·7	0·965
	V10 (%)	28·57 ± 21·6	28·49 ± 25·31	0·981
	V20 (%)	3·34 ± 5·4	4·98 ± 9·3	0·372
	V30 (%)	1·9 ± 3·42	2·1 ± 5·3	0·798
Rt Kidney	Mean dose (Gy)	19·02 ± 5·1	19·77 ± 5·5	0·340
	V10 (%)	69·64 ± 14·77	72·94 ± 16·72	0·061
	V20 (%)	45·11 ± 16·4	46·95 ± 20·69	0·619
	V30 (%)	23·77 ± 16·36	21·42 ± 13·97	0·342
BL whole kidney	V12 (%)	44·03 ± 16·87	46·94 ± 17·33	0·145
	V20 (%)	26·43 ± 13·9	26·86 ± 15·02	0·833
	V23 (%)	20·92 ± 12·8	19·54 ± 12·68	0·389
	V28 (%)	15·02 ± 10·1	13·31 ± 9·23	0·150
Liver	Mean dose (Gy)	21·43 ± 6·5	21·31 ± 5·9	0·765
	V10 (%)	53·3 ± 14·70	54·56 ± 14·72	0·095
	V20 (%)	44·95 ± 13·78	46·77 ± 14·5	0·143
	V30 (%)	35·56 ± 12·49	36·91 ± 12·96	0·170
Spinal cord	Max dose (Gy)	25·1 ± 8·85	21·1 ± 5·9	**0·006**

Vx (%) means x Gy dose covered the percentage of volume, CDR-VMAT, constant dose rate volumetric modulated arc therapy; SS IMRT, step and shoot intensity-modulated radiation therapy; SD, standard deviation.

Table 4. Treatment delivery parameters

Parameters	SS IMRT (mean ± SD)	CDR-VMAT (mean ± SD)	*p*-Value
MU	473·11 ± 73·15	838·97 ± 176·75	<**0·001**
Treatment delivery Time(minutes)	12·2 ± 0·73	3·9 ± 0·52	<**0·001**

CDR-VMAT, constant dose rate volumetric modulated arc therapy; SS IMRT, step and shoot intensity-modulated radiation therapy; MU, monitor units; SD, standard deviation.

Wenliang Yu et al.[21] showed that CDR-VMAT generates a similar plan as VDR-VMAT and MCO VMAT for nasopharyngeal cancer in terms of PTV coverage and OAR sparing. They found that CDR-VMAT showed a better dose HI ($p = 0·01$) in PTV-CTV and no significant difference in other target coverage parameters was observed. There was no significant difference in OAR sparing among these three planning schemes except for a higher maximum dose (Dmax) on the brainstem for CDR-VMAT. Our study showed similar results in terms of PTV coverage and OAR sparing, but HI is less for CDR-VMAT than IMRT.

Xiao-Nan Sun et al.[10] compared dosimetric parameters of 3DCRT and IMRT in 20 patients with gallbladder cancer and found that IMRT offered better sparing of the right kidney compared to CRT planning, with a significantly lower mean dose and volume above the constraint. They also mentioned that compared to CRT planning, IMRT significantly reduced the volume of right kidney receiving > 20 Gy and the volume of liver receiving > 30 Gy. Apart from it, IMRT has a negligible impact on the volume of left kidney receiving > 20 Gy and 95% of prescribed dose for a planning tumour volume using either 3D CRT or IMRT planning were 84·0% ± 6·7% and 82·9% ± 6·1%, respectively ($p > 0·05$).

Palma et al.[22] performed a planning comparison in 10 patient data sets between standard three-dimensional (3D)-CRT, fixed-field IMRT using 5 coplanar fields (SW), CDR-VMAT and VDR-VMAT. The results reported significantly improved OAR sparing with both IMRT and VMAT plans compared with 3D-CRT, with acceptable planning target volume (PTV) coverage. The lowest doses to the OARs were achieved in the VDR-VMAT plans, which required 42% fewer MU compared to the fixed-field IMRT plans. Both VDR-VMAT and CDR-VMAT plans required fewer MU than IMRT plans (relative reductions of 42% and 38%, respectively; $p = 0·005$), but more than 3D-CRT ($p = 0·005$). Treatment times for both CDR-VMAT and VDR-VMAT were significantly less than IMRT plans. So, VMAT plans may allow for more patient throughput than IMRT plans. In our study, more MU associated with CDR-VMAT technique but significantly shorter treatment delivery time than IMRT.

Annamaria Didona et al.[23] created SS IMRT, CDR-VMAT and VDR-VMAT plans for 15 Head and neck cancer patients and found that compared with SS IMRT and VDR-VMAT, CDR-VMAT was associated with higher average MU values and significantly shorter average delivery time. Similar results were found in our study in terms of higher MU.

Yang et al.[24] studied nine-field IMRT, VDR-VMAT and CDR-VMAT plans were created for 9 patients with endometrial cancer undergoing whole pelvic radiation therapy and found that compared to IMRT, the CDR-VMAT plans delivered a slightly greater V20 of bowel, bladder, pelvis bone and normal tissue, but significantly decreased the dose to the high dose region of rectum and pelvis bone. They found very similar dose distribution in the VDR-VMAT and CDR-VMAT plans. The average gamma pass rate was 95·6 % at the 3%-3 mm criteria with pre-treatment verification for nine patients. The MUs decreased from 1105 with IMRT to 628 with CDR-VMAT. The delivery time also decreased from 9·5 min to 3·2 min. Similarly, in our study, the treatment time was reduced from 12·2 min for IMRT to 3·9 min for CDR-VMAT.

On comparing these two techniques, we found that the CDR-VMAT technique gives comparable or even better quality plan than IMRT in terms of PTV coverage and OAR sparing. The intra-fraction motion is reduced due to shorter treatment delivery time, hence reduced intrafractional positional error compared with IMRT. The CDR-VMAT also improved patients throughput hence benefited to patients and institutes. The low-cost CDR-VMAT technique may help low and middle socio-economic countries, which could not afford expensive VDR-VMAT advance technology and wants to adapt VMAT technique.

In this study, we attempted to validate the CDR-VMAT technique in radiotherapy practice to increase the patient throughput with quality treatment for a better clinical result and this can be done with conventional Linac. In India, to date, many radiotherapy centres have Co-60 units and conventional Linac due to financial constraints. Centres which have conventional Linac may get benefited from this study and can increase patient throughput with quality treatment for a better clinical result because of its cost-effectiveness. CDR-VMAT can be a valid option for the treatment of gall bladder cancer where the dedicated linear accelerator is not available for VDR-VMAT.

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Limitation of Study

There were several limitations to this study. First of all, the number of patients was small. Second, all patients were female in nature. Finally, the contour in all patients was not drawn by the same oncologist.

Conclusion

On dosimetric comparison of two treatment techniques, we found that CDR-VMAT can be a valid option in radiotherapy as it achieved highly conformed dose distribution, comparable tumour coverage and OAR sparing as IMRT technique for gallbladder cancer. The main advantage of CDR-VMAT is that it significantly reduced treatment delivery time in comparison to IMRT, thus may increase patient throughput on conventional Linac. Moreover, because VDR-VMAT is an expensive technique, it is more reasonable to consider the use of CDR-VMAT for irradiation of gall bladder cancer as a feasible and cost-effective technique.

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Conflict of Interest. None

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