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Dosimetric comparison of 3-D Conformal Radiotherapy (3DCRT) and Intensity Modulated Radiotherapy (IMRT) for patients with hepatocellular carcinoma (HCC).

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Abstract

Introduction
The use of radiotherapy in treating HCC is rapidly increasing. IMRT is more suitable for treating complex target volumes as it creates complex dose distributions that conform to the target volume than those allowed using 3DCRT.
Purpose
To compare dose distribution and dosimetric parameters of 3DCRT and IMRT for patients with hepatocellular carcinoma.
Methods
Ten patients with HCC (average volume 336cc) planned using 3DCRT and IMRT. The PTV, spinal cord, kidneys and normal liver were outlined. 40Gy was prescribed. Dose volume histogram parameters (DVPs) for both plans were compared and analyzed statistically using SPSS Wilcoxon Signed Ranks test.
Results
3DCRT and IMRT achieved adequate and comparable target coverage as assessed by PTV $D_{95\%}$ (39.24Gy and 39.44 Gy, *P*= 0.493) and dose homogeneity index (1.07 and 1.07, *P*= 0.257). For sparing of adjacent normal organs: IMRT resulted in significantly lower irradiated normal liver volume at 5Gy-30Gy; it showed a significant reduction of 2.5%, 5%, 6% and 15% of normal liver V_{5Gy}, V_{10Gy}, V_{20Gy} and V_{30Gy} compared to 3DCRT (*P*= 0.041, 0.010, 0.048 and 0.013 respectively). IMRT also achieved better sparing of spinal cord and kidneys with a non significant reduction of 9%, 12% and 2% of spinal cord maximum dose, right and left kidney mean doses compared to 3DCRT (*P* =0.203, 0.205 and 0.498 respectively).
Conclusion
Comparing the dose distribution of 3DCRT and IMRT of HCC; IMRT provides adequate comparable target coverage with significant sparing of normal liver at 5Gy-30Gy and less exposure of spinal cord and kidneys compared to 3DCRT.

I declare that there is no conflict of interest with any financial organization regarding the material in this manuscript.

Introduction

Hepatocellular carcinoma (HCC) is the third cause of cancer related death following lung and stomach cancer.[1] The use of radiotherapy in treating unresectable HCC is rapidly increasing.[2,-3] Various techniques are available for liver irradiation such as three-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT). [4]

While 3DCRT can irradiate the target volume accurately while minimizing the dose to normal liver with a chance of long survival for some patients, IMRT is more suitable for treating complex target volumes. [4] IMRT can improve radiation plan quality by using an inverse planning algorithm which generates complex spatial dose distributions that conform more closely to the target volume than those allowed using 3DCRT. [5]

There is no accepted standard strategy for liver irradiation. Although some previous studies have shown that IMRT achieved acceptable target coverage for HCC, but had a negative dosimetric effect on the liver, with a significant increase in mean dose compared with 3DCRT. [6] Others suggested that IMRT improved planning target volume (PTV) coverage while maintaining normal tissue tolerance in most

3DCRT liver plans. [7] Because the optimal irradiation technique depends on the location of the liver lesion and the presence of multiple critical structures including the normal liver, kidneys, and spinal cord so it is important to compare dose distribution of 3DCRT and IMRT and to investigate cases in which IMRT might offer benefit compared with 3DCRT. [8, 9, 10]

Purpose

To compare dose distribution and dosimetric parameters of 3DCRT and IMRT for patients with hepatocellular carcinoma.

Methods

From September 2013 to November 2014 ten patients with locally advanced non metastatic HCC were planned retrospectively in the Alexandria Clinical Oncology Department using 3DCRT and IMRT. CT simulation was performed in supine position with 3mm slice thickness. Then the CT data were transferred to treatment planning system (Precise Elekta) where required structures were contoured. They include GTV (high CT value area in early phase contrast-enhanced CT image), CTV (1cm margin around the GTV) and PTV (0.5cm and 1.5cm margin to the CTV in axial and craniocaudal axes) respectively to account for errors caused by the daily setup process and internal organ motion. [11] Whole liver, normal liver (total liver volume minus PTV), kidneys and spinal cord were also contoured.

For each patient, 3DCRT optimum plan was carried out with 6MV photon beam using different number and directions of photon fields according to the position of the PTV and the relationship of the PTVs and OARs. 5-7 fields shaped using MLCs were used to encompass the PTV and to well spare nearby OARs (Figure 1).

Inverse planned IMRT was carried out using step and shoot technique. The same treatment parameters for 3DCRT were optimized with five segments per beam distributed according to the position of the target volume. After defining planning parameters many trials were carried out to choose the best dose volume constrains (DVC). (Table 1)

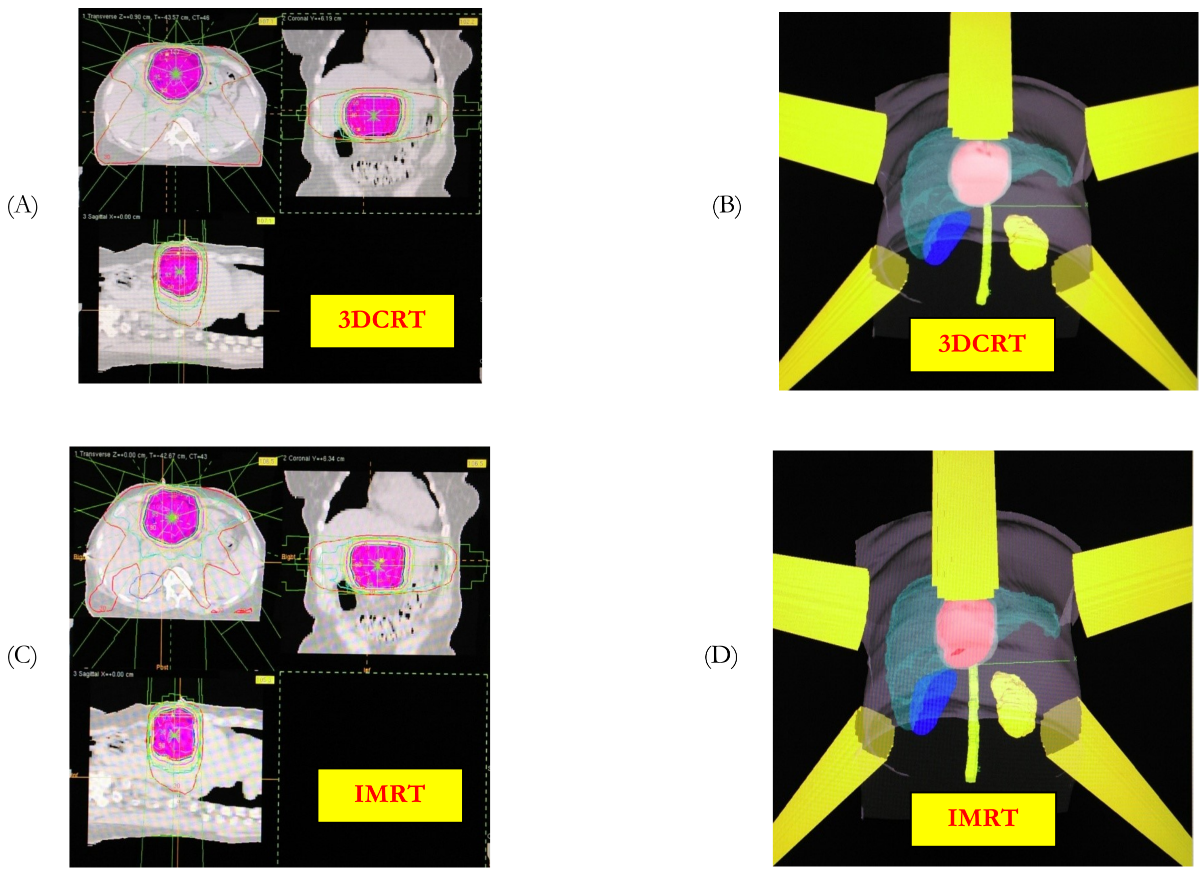


Figure 1. Typical dose distribution displayed in axial, coronal and sagittal views for 3DCRT and IMRT plans using 5 fields for a patient with HCC (A and C) and the room eye views of the same patient (B and D). Both show the colour wash of 95% of the dose (pink in A and C and white in B and D) match well the PTV shape.

Structure	Type	Priority	Rx (cGy)	Mean dose (cGy)	Under dose (cGy)	Under dose volume (%)	Over dose (cGy)	Over dose volume (%)
PTV	Target	100	4000		4000	95	4500	5
Spinal cord	OAR	30					3500	
Rt. Kidney	OAR	20		1000				

Table 1. Optimization setup table

Dose prescribed was 40Gy in 20 fractions. For all plans, isodose distributions and DVHs were generated. The optimum plan was evaluated by PTV dose coverage and homogeneity within PTV and sparing of OARs. PTV dose coverage assessed by $D_{95\%}$ and $D_{max\%}$. Homogeneity within PTV HI calculated as $D_{5\%}/D_{95\%}$. Sparing of OARs assessed using the mean dose of normal liver (23-26 Gy), V_{5Gy}, $V_{10\ Gy}$ (<5%, V_{20Gy}) and V_{30Gy} (<10%), the mean dose to the kidneys (23Gy for at least one kidney) and the maximum point dose of spinal cord (≤45 Gy). [12,13]

3DCRT and IMRT plans for the ten patients were compared using dose distribution, DVHs and DVPs for PTV, normal liver, spinal cord, and kidneys.

This study had approval of Institutional Review Board as a retrospective one in which confidentially of records was considered.

Statistical analysis

DVPs of PTV and OARs for 3DCRT and IMRT plans for ten patients were listed, compared and statistically analyzed using Wilcoxon Signed-Ranks test of SPSS (version 18). A P-value of less than 0.05 was taken as statistically significant.

Results

3DCRT and inverse plan IMRT for HCC were produced for 40 Gy and compared for ten patients. By reviewing the treatment planning, DVHs, and DVPs the followings were the results as regard dose distribution of PTV and OARs (normal liver, spinal cord, right, and left kidneys).

Dose distribution within PTV

Table. 2 gives the statistical analysis for PTV DVPs comparing 3DCRT and IMRT plans. It shows that PTV $D_{95\%}$ ranged from 38Gy to 40Gy (average 39.24 Gy) for 3DCRT plans compared to 39.2Gy to 39.6 Gy (average 39.44 Gy) for IMRT plans. The maximum dose ranged from 42.4 Gy to 44.4 Gy (average 43.24 Gy) for 3DCRT plans compared to 42.8 Gy to 44 Gy (average 43.28 Gy) for IMRT plans. So PTV coverage was adequate and comparable in both plans as the differences in PTV $D_{95\%}$ and maximum dose between both plans were not statistically significant (*P*=0.493and 0.792 respectively). (Figures 1 and 2A). Dose homogeneity index HI ranged from 1.05 to 1.1 (average 1.073) for 3DCRT plans compared to 1.04 to 1.09 (average 1.07) for IMRT plans. So IMRT doesn't show any significant difference in HI compared to 3DCRT (*P*=0.257).

Dose distribution within organs at risk

Table 3 gives the statistical analysis for normal liver DVPs, spinal cord maximum dose and right and left kidney mean dose for 3DCRT and IMRT plans. It shows that; the average of normal liver mean dose 12 Gy for 3DCRT plans compared to 12.3 Gy for IMRT plans; there is no significant difference between 3DCRT and IMRT (*P*=0.414). The average of normal liver V_{5Gy}, V_{10Gy}, V_{20Gy} & V_{30Gy} was 56.5%, 48.6%, 28.1% & 14.4% for 3DCRT plans compared to 54.4%, 45.8%, 26.4% & 12.4% for IMRT plans; IMRT showed a significant reduction of 2.5%, 5%, 6% & 15% of normal liver V_{5Gy}, V_{10Gy}, V_{20Gy} & V_{30Gy} compared to 3DCRT (*P*= 0.041, 0.010 , 0.048 & 0.013). (Figure 2 B)

Table 2. Relevant dose volume parameters of PTV comparing 3DCRT & IMRT plans.

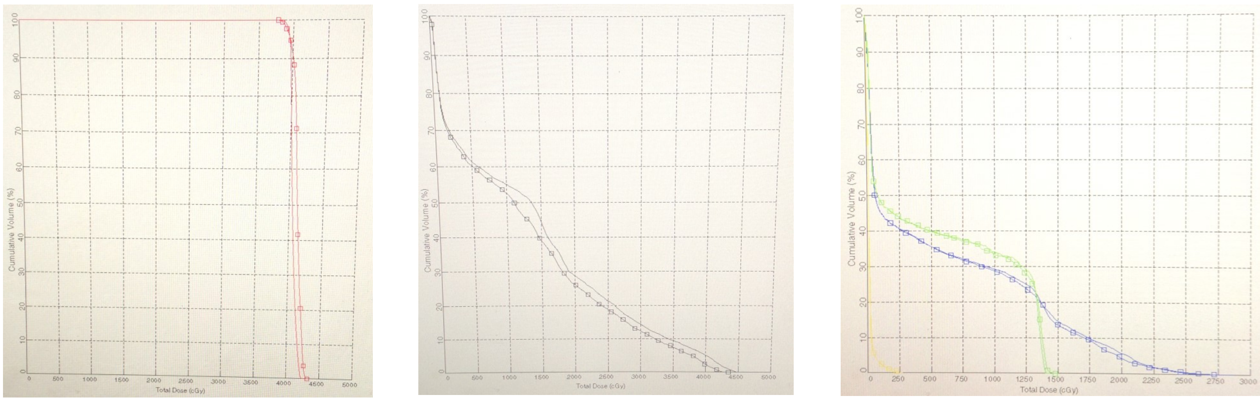
PTV DVPs	Min	Max	Average	P value
$D_{95\%}$ (CR)	38.0	40.0	39.24	0.493
$D_{95\%}$ (IMRT)	39.2	39.6	39.44	
D_{max} (CR)	42.4	44.4	43.24	0.792
D_{max} (IMRT)	42.8	44.0	43.28	
HI (CR)	1.05	1.10	1.073	0.257
HI (IMRT)	1.04	1.09	1.07	

CR, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy. The dose is in Gy

Regarding spinal cord and kidneys sparing; the average of spinal cord maximum dose, right and left kidney mean doses was 13Gy. 6.63 Gy and 1.13 Gy for 3DCRT plans compared to 11.6 Gy. 6.13 Gy & 0.862 Gy for IMRT plans; IMRT showed a non significant reduction of 9%, 12% & 2% of spinal cord maximum dose, right and left kidney mean doses compared to 3DCRT (*P* =0.203, 0.205 & 0.498). (Figure 2C).

Table 3 Relevant dose volume parameters of OARs comparing 3DCRT & IMRT plans

DVPs	Min	Max	Average	P-value	Reduction%
Normal liver (Gy)				0.414	1.35
Mean (CR)	5	18	12		
Mean (IMRT)	5	21	12.3		
V_{5Gy} (CR)	24	90	56.5	0.041	2.5
V_{5Gy} (IMRT)	25	80	54.4		
V_{10Gy} (CR)	18	80	48.6	0.010	5
V_{10G} (IMRT)	17	75	45.8		
V_{20Gy} (CR)	12	55	28.1	0.048	6
V_{20Gy} (IMRT)	11	53	26.4		
V_{30Gy} (CR)	9	27	14.4	0.013	15
V_{30Gy} (IMRT)	7	25	12.4		
Spinal cord (Gy)					
Max (CR)	4	24	13	0.203	9
Max (IMRT)	0	21	11.6		
Right Kidney (Gy)					
Mean (CR)	0.13	15	6.63	0.205	12
Mean (IMRT)	0.13	20	6.13		
Left Kidney (Gy)					
Mean (CR)	0	9	1.13	0.498	2
Mean (IMRT)	0	6	0.862		



(A) (B) (C)

Figure 2. DVH for PTV (A), normal liver (B), spinal cord in green & right kidney in blue, left one in yellow (C) comparing 3DCRT (solid line) and IMRT plans**.**

Discussion

Although 3DCRT is commonly used for treatment of HCC, dosimetric analysis of other plans using different techniques such as IMRT is required to compare target coverage and normal tissue sparing.

In the current study; 3DCRT and IMRT plans for 10 patients with HCC were compared. As regard target coverage; current study showed that the **PTV** coverage was adequate and comparable in both plans as the differences between the plans were not statistically significant. This is in accordance with the results of Chen D et al [14]. The findings of the current study were also supported by Kuo Y et al [15] who compared 3DCRT and IMRT for primary HCC; they reported that the homogeneity & target coverage were comparable in 3DCRT & IMRT plans.

Regarding to **spinal cord**; current study indicates that IMRT plans achieved non significant spinal cord sparing compared to 3DCRT plans. This is in accordance with Chen D et al, [14] and Li Z et al study [16]; they achieved non significant spinal cord sparing in IMRT plans compared to 3DCRT plans.

Regarding to **Kidneys**; current study indicated that IMRT plans achieved non significant right and left Kidneys sparing compared to 3DCRT plans. The findings of the current study were supported by Yuanyuan Z et al [17] who compared 3DCRT and IMRT in terms of their advantages and disadvantages in the treatment of primary HCC with portal vein tumor thrombus; they found that there were no significant differences in kidneys D_{max}, and kidney $V_{20\,Gy}$ between IMRT and 3DCRT. The findings of the current study were also supported by Li Z et al [16] study who found comparable sparing of normal tissues including kidneys in both plans.

Regarding to **normal liver;** in the current study; the mean of normal liver showed no significant difference between 3DCRT and IMRT. This agrees with Li Z et al [16]; they found that the mean dose to normal liver 20.5Gy for 3DCRT Vs 20.9 Gy for IMRT. On the other hand; in the current study IMRT plans achieved significantly normal liver sparing compared to 3DCRT plans at the low-dose region i.e at volume received 5Gy -30Gy (V_{5Gy}, V_{10Gy}, V_{20Gy}, and V_{30Gy}). The findings of the current study are supported by Yuanyuan Z et al study [17]; they reported that the liver V_{30Gy} and V_{20Gy} were significantly better with IMRT plans than with 3DCRT plans. On the other hand, there was no significant difference in liver V_{10Gy} & V_{5Gy}. Kuo Y et al [15] also demonstrated that IMRT provided better dose distribution, with significantly better mean dose, $V_{10\,Gy}$, $V_{20\,Gy}$ $V_{30\,Gy}$ and $V_{40\,Gy}$ compared with 3DCRT. In Kim Th et al.[18] study and Liang SX et al study[19] V_{30Gy} & V_{20Gy} were demonstrated as significant parameters for Radiation-induced liver disease (RILD) in patients treated with conventional fractionated radiotherapy. As IMRT shows lower $V_{20\,Gy}$ and $V_{30\,Gy}$ compared to 3DCRT therefore, IMRT is superior to 3DCRT at decreasing the risk of Radiation-induced liver disease (RILD) which is the most severe radiation-induced complication that may result in hepatic failure and death [14]

Conclusion

Comparing the dose distribution of 3DCRT and IMRT plans of HCC; IMRT provides adequate comparable target coverage with significant sparing of normal liver at 5Gy-30Gy and less exposure of spinal cord and kidneys compared to 3DCRT.

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