Dose Distributions of Three-Dimensional Conformal Radiotherapy for hepatocellular carcinoma: Dosimetric Analysis

Mohamed Medhat Abo Salama, Ihab Mohamed Hassanin, Maha Lotfy Zamzam, Sharehan Hassan Soliman, Fifi Mostafa Elsayed

Clinical Oncology Department, Faculty of Medicine, Suez Canal University, Ismailia, Egypt.

*** Corresponding author**: **Mohamed Medhat Abo Salama**

Abstract

Background: Background: In adults, hepatocellular carcinoma (HCC) is among the most prevalent cancers. With the development of three-dimensional conformal radiotherapy (3D-CRT), a number of reports have recently shown increased safety and encouraging outcomes in patients with unresectable intrahepatic malignancies treated with radiation to a portion of the liver. Several modalities have been used in the treatment of HCC. **Purpose:** To analyze the correlation of radiation-induced liver disease (RILD) with patient-related and treatment-related dose-volume factors for patients with hepatocellular carcinoma (HCC) treated with three-dimensional conformal radiotherapy (3D-CRT). **Methods:** Between June 2022 and May 2024, 14 patients were diagnosed with locally advanced hepatocellular carcinoma and were assigned to receive palliative 3D conformal radiotherapy 50 Gy over 25 fractions. **Results:** there were 11 patients who completed their radiotherapy course 50 Gy over 25 fractions while 3 patients didn't complete their sessions due to adverse events such as fatigue and GIT symptoms. The coverage of 95% of the planning target volume (PTV) mean was 94.5% (90%-97%),the mean dose of liver was 26.5 Gy (21 Gy -30 Gy), while the mean dose of liver minus gross tumor volume (GTV) was 23 Gy (18 Gy -27 Gy). The mean dose of both kidneys was 12.7 Gy (3.7Gy-18Gy), the spinal cord maximum dose ranging between (5 Gy-32 Gy). While the absolute volume of bowel that received 45 Gy was ranging (105 cc- 200cc) meant 159cc. **Conclusion:** Dose-volume histogram analysis can be effectively used to quantify the tolerance of the liver to RT. Patients with radiation induced liver disease had received a significantly higher mean dose to the liver.

Key words: Hepatocellular Carcinoma, radiotherapy.

Background

In adults, hepatocellular carcinoma (HCC) is among the most prevalent cancers. The tumor's stage determines how individuals with HCC are treated (1). HCC has been treated using a variety of techniques, such as radiation, liver transplantation, percutaneous ethanol injection therapy, microwave coagulation therapy, transcatheter arterial chemoembolization (TACE), and surgery (2). Due to the liver's low radiation tolerance, radiotherapy's usage was restricted (3). Recent studies have shown improved safety and encouraging outcomes for patients with incurable intrahepatic cancers treated with radiation to a section of the liver because to advancements in three-dimensional conformal radiotherapy (3D-CRT).The development of three-dimensional (3D) planning tools has made it possible to gather comprehensive data on the distribution of dosage and volume in structures of interest (4). Numerous researchers have assessed the dose-volumetric factors that predict RIHT in individuals with HCC after RT (5). These studies discovered that a number of dose-volumetric parameters, such as the mean dose to the normal liver (Mean), the percentage of the normal liver volume that received ≥30 Gy (V30Gy), the percentage of the total liver volume that received ≥30 Gy (V30Gy), and the normal tissue complication probability (NTCP) estimates, were linked to the risk of radiation-induced hepatic toxicity (RIHT). Which dose-volumetric characteristics best predict RIHT risk is yet unknown, however (6,7).

Methods

Study design and conduct

From June 2022 to May 2024, a thorough investigation was carried out in the Clinical Oncology Department at Suez Canal University Hospital in the Ismailia Governorate, Egypt. The study's objective was to examine the relationship between radiation-induced liver disease (RILD) and treatment-related and patient-related dose-volume variables in patients receiving three-dimensional conformal radiation therapy (3D-CRT) for hepatocellular carcinoma (HCC). All patients gave written informed permission prior to research participation, and the institute's Research Ethics Committee approved the study procedure. The correctness, data confidentiality, and protocol compliance are entirely the authors' responsibility.

Patients

The sample size was 14 patients who were diagnosed with locally advanced hepatocellular carcinoma and were assigned to receive palliative 3D conformal radiotherapy 50 Gy over 25 fractions.

Eligible patients were pathological or radiological proven HCC patients , Patients with unresectable disease, or who were medically inoperable due to comorbidity and unfit for surgery, patients who had comorbidities interfere with usage of Targeted and Immunotherapy and a performance status of 0–2 according to the Eastern Cooperative Oncology Group performance scale and fall within the Child-Pugh A or B classification. Patients with Tumor size totally do not exceed 10 cm.

We excluded patients who had small sized lesion eligible for Surgery, or who received definitive targeted therapy and Immunotherapy, or Patients with Performance Status > 2.

Intervention

All patients were assigned to receive 3D conformal radiotherapy with a dose 50Gy over 25 sessions on Liver mass. We used multiple fields during treatment to do forward IMRT plans to achieve best coverage and give more protection to the Organ at Risk (OAR).

Technique of External Beam Radiotherapy:

CT Simulation and patient set up:

CT simulation is performed with 3 mm slice thickness. Bowel prepared night prior by rectal voiding and low residue diet after treatment is advised to avoid diarrhea. IV contrast may aid in delineation of Hepatic lesion. Planning CT is obtained in treatment position, Patient is positioned supine and fixed with arms under his head. Skin reference tattoos are placed to prevent lateral rotation. Radio-opaque markers are placed on skin to locate the tattoos on CT scans. Scan from chest to pelvis to allow for delineation of Heart, Spinal cord, both Kidneys and relevant small bowel areas adjacent to high dose distributions. Image guided verification and adjustment will be done 3 times in the first week then one weekly for the remaining course.

Target Volume Delineation and Treatment planning:

A. GTV: gross tumor shown on the on the arterial-phase CT scan.

B. CTV: An additional margin of 1 cm around the GTV, confined to the liver to form a clinical target volume (CTV) to account for microscopic extensions and internal movement as (ITV).

C. PTV: expanded from CTV to three-dimensional, typically with margins of 5 mm, accounting for Set up error. Planning systems: (Eclipse, Varian, Palo Alto, USA).

Dose prescription: 50 Gy over 25 Fractions, 2 Gy per Fraction.

Data collection was systematically conducted, and all data were anonymized for analysis. The statistical analysis was performed using SPSS version 25.

Results

We enrolled 14 patients with Locally advanced Hepatocellular Carcinoma who were unfit for resection or radiofrequency ablation, and unavailability of targeted therapy or Immunotherapy attending Department of Clinical Oncology in Suez Canal University Hospital at the time from June 2022 till May 2024. Patients received external beam radiotherapy localized to the hepatic mass with dose 50 Gy.

Table 1: Baseline data of patients.

		Radiotherapy	
		N:14	**%**
Age		Median 63 (52 – 74)	
Gender			
	Male	10	71.4
	Female	4	28.6
Stage			
	T4N1	8	57.1
	T4N0	2	14.3
	T3N1	2	14.3
	T3N0	2	14.3
Size			
	< 5 cm	0	0
	≥ 5-10 cm	14	100
ECOG			
	0	2	14.3
	1	7	50
	2	5	35.7
Child Pugh scale			
	A	5	35.7
	B	9	64.3

Table 2: Details of treatment with radiotherapy dose.

Treatment Course	N	%	Median (min-max)
RT dose			
• Complete course 50 GY	11	78.6	48 (45 – 50)
• Incomplete course 30-40 GY	3	21.4	34 (30 – 40)

Table 3: Treatment adverse events in two arms of study.

	Radiotherapy N:14	Percentage
Nausea		
GI-II	12	85.7
GIII	2	14.3
Vomiting		
GI-II	12	85.7
GIII	2	14.3
Fatigue		
GI-II	10	71.4
GIII	4	28.6
GI-II	14	100
GIII	0	0
GIT bleeding		
Yes	0	0
No	14	100

Table 4: Comparison of treatment adverse events in patients treated with RT and their impact on treatment omission.

	Radiotherapy		Omission treatment		P-value
	N:14	%			
Nausea					
GI-II	12	85.8	1	8.3	**0.003***
GIII	2	22.2	2	100	
Vomiting					
GI-II	12	85.8	1	8.3	**0.003***
GIII	2	22.2	2	100	
Fatigue					
GI-II	10	71.4	2	20	0.837
GIII	4	28.6	1	25	
Abdominal pain					
GI-II	14	100	3	25	-
GIII	0	0	0		
GIT bleeding					
No	14	100	3	25	-
Yes	0	0	0		

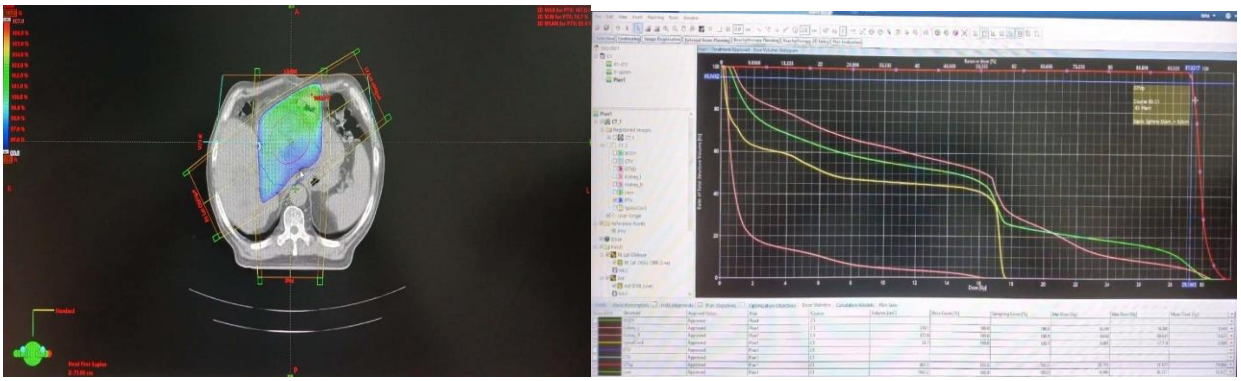

Figure 1: Contouring and Dose colour wash 95% of 50 Gy to liver mass covered by 4 Fields with Dose Volume Histogram showing the coverage of PTV, and dose delivered to OAR.

Table 5: This table showed that the PTV coverage, and the dose constrains of organ at risk, and all parameters were in the accepted records.

	Median (min-max)
PTV dose (covered with 95% of Volume)	94.5 (90 – 97) %
Mean Liver dose (Gy)	26.5 (21 – 30) (Gy)
Liver minus GTV mean dose (Gy)	23 (18 – 27) (Gy)
Mean Kidney dose (Gy)	12.5 (3.7 – 18.5) (Gy)
Max Spinal cord dose (Gy)	8 (5 – 32) (Gy)
Intestinal bowel dose (V45)/ cc	159 (105 – 200) cc

Table 6: The relation of number of RT fields.

	Number of RT fields						
	4		5		6		**P-value**
	N:5	**%**	**N:5**	**%**	**N:4**	**%**	
Site of lesion							
Lt lobe	1	20	4	80	1	25	0.495
Rt lobe	3	60	1	20	3	75	
Both lobes	1	20	0	0	0	0	
	Mean						
Number of lesions	2.2 ± 1.3		1.4 ± 0.54		2.5 ± 0.57		0.742
Tumor size (cm)	8.9 ± 1.7		8.4 ± 1.3		8.5 ± 2.8		0.739
PTV$_{95}$	94.1 ± 2.9		93.8 ± 1.09		94.6 ± 2.2		0.747
Mean liver dose	26.9 ± 3.6		26.6 ± 2.8		24.4 ±3.7		0.289
Mean Liver minus GTV dose	23.9 ± 3.7		22.6 ± 2.8		21.3 ± 2.7		0.216
Mean kidneys dose	9.3 ± 4.6		10.3 ± 3.7		13.8 ± 6.9		0.206
Max spinal cord dose	17.99 ± 15.5		13.5 ± 11.02		11.37 ± 9.8		0.422

The results of the research, which are compiled in a number of tables and figures, provide light on how effective the therapy is. The patient variables shown in Table 1 include the participant's age, gender, tumor size, stage, and performance status profile as determined by the Child Pugh scale and ECOG score prior to beginning treatment. The study included 14 patients in all, with a median age of 63 years, 10 males and 4 females, with tumor sizes ranging from 5 to 10 cm in diameter. Of these, 2 had an ECOG score of 0, 7 had a score of 1, and 5 had a score of 2.

Every patient had less severe liver disease, as shown by their Child-Pugh A or B stage. Eleven patients finished their 50 Gy radiation treatment over 25 fractions, according to Table 2, whereas three patients did not finish their sessions because of side effects such exhaustion and GIT symptoms, which are detailed in Tables 3 and 4. The dosage Volume Histogram (DVH) and dosage color wash parameters were shown in Table 5. The mean liver dose was 26.5 Gy (21 Gy-30 Gy), the mean liver dose minus gross tumor volume (GTV) was 23 Gy (18 Gy-27 Gy), and the coverage of 95% of the planned target volume (PTV) mean was 94.5% (90%-97%). The maximal dosage for the spinal cord ranged from 5 Gy to 32 Gy, whereas the mean dose for both kidneys was 12.7 Gy (3.7 Gy-18 Gy). 159cc was the absolute volume of bowel that got 45 Gy, which ranged from 105cc to 200cc.

Table 6 displayed the relationships between the use of many fields (4-6) that resembled the use of IMRT plans, the liver tumor location, the DVH coverage, and the Organ at Risk.

Discussion

In the study, patients with locally advanced hepatocellular carcinoma (HCC) who were not suitable for resection, radiofrequency ablation, or the availability of targeted therapy or immunotherapy were given external radiation therapy (ERT). Eleven patients finished the course of radiation therapy, while three patients did not. According to our research, three patients reported experiencing Grade III nausea and vomiting following radiation treatments, whereas eleven patients reported experiencing Grade I–II nausea and vomiting. No one reported experiencing esophageal hemorrhage, however all of our patients had grade I–II stomach discomfort (8,9).

In order to achieve good coverage of the PTV by 95% of the dose prescription (50 Gy) and to provide good protection of the OAR below the limit of acceptable doses in QUANTEC dose constraints, we employ multiple fields, ranging from (4-6) fields in 3DCRT plans and multiple fields in field (segments) as a forward IMRT. Therefore, the PTV coverage of 95% of volume

received is 94.1 ± 2.9% of the recommended dosage when using 4 fields, 93.8 ± 1.09% of the prescribed dose when using 5 fields, and 94.6 ± 2.2% of the prescribed dose when using 6 fields (10).

Conclusion

The liver's tolerance to RT may be measured with the use of dose-volume histogram analysis. Both the mean dose to the liver and the NTCP were considerably greater in patients with radiation-induced liver disease. Forward IMRT designs considerably decreased the radiation to non-liver OARs and normal liver tissues, including the kidneys, colon, and spinal cord.

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