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Accurate Tracking of Position and Dose during Abdominal Cancer Treatment based on IMRT and VMAT Techniques

Rania Abdelrahman^{1,*}, Khaled. M. El-Shahat², Mostafa Abdelwanis³, Hany El-Gamal⁴, Wafaa Rashed⁵

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Abstract: The treatment planning process is the core of radiotherapy for malignancy treatment, it is an essential tool for optimal beam arrangements, energies, field sizes, and ultimately fluence pattern to produce a safe and effective dose distribution for achieving therapeutic goal which maximize the dose covered the planning tumor volume PTV and minimize the dose delivered to the surrounding normal tissue. This study evaluates real-time tumor tracking (RTRT) in SBRT-VMAT for hepatocellular carcinoma (HCC) to address tumor motion challenges in conventional IMRT. Twenty HCC patients treated with IMRT were replanned using SBRT-VMAT with RTRT to compare dosimetric outcomes, focusing on PTV coverage and OAR sparing. RTRT enabled reduced PTV margins by mitigating setup errors and organ motion, enhancing targeting precision. SBRT-VMAT plans achieved superior dose conformity (CI) and homogeneity (HI) compared to IMRT, with improved tumor coverage (CO). Normal liver tissue receiving >15 Gy was significantly reduced using SBRT-VMAT, preserving liver function in patients with compromised hepatic health. Critical OARs (spinal cord,

esophagus, stomach, and small intestine) showed reduced radiation exposure with SBRT-VMAT.RTRT integration ensured accurate tumor localization without additional radiation dose during tracking. Shorter treatment delivery times and higher dose conformity make SBRT-VMAT clinically efficient for mobile upper abdominal tumors. The study demonstrates SBRT-VMAT with RTRT as a safer, more precise option for HCC, particularly in patients with limited liver reserve. Findings support adopting RTRT-guided SBRT-VMAT to optimize therapeutic ratios by sparing healthy tissues while maintaining tumor control.

Keywords: VMAT, IMRT, SBRT, Real-Time Tumor Tracking, Hepatocellular carcinoma.

1 Introduction

Hepatocellular carcinoma (HCC) is the most frequent type of primary liver malignancy and is a serious and aggressive cancer disease that can be fatal if not treated on time. It originates from the hepatocytes, the main cells in the liver responsible for its normal functioning. It often develops in people with pre-existing liver diseases, such as cirrhosis or chronic infections with hepatitis B virus (HBV) or hepatitis C virus (HCV) [1].

Hepatocellular carcinoma treatment options depend on several factors such as the cancer stage, the extent of fibrosis/cirrhosis, overall liver function, and the patient's overall health condition. These may include tumors curative

resection, liver transplantation, ablation therapy, targeted drug therapies, chemotherapy, or radiation therapy. Many patients are unable to undergo surgical resection because of advanced underlying liver disease, which is classified typically based on the Child-Pugh classification (Table 1) [2]. In addition, many hepatocellular carcinoma patients are not candidates for transplantation due to advanced malignancy that is outside the Milan criteria (e.g., solitary tumor ≤ 5 cm or up to three tumors all ≤ 3 cm) on presentation. If surgery isn't an option for HCC treatment, radiation therapy may be recommended as a treatment option. However, there was a historical bias against liver malignancies radiotherapy because of the low tolerance of whole liver radiation. To avoid the risk of Radiationinduced liver disease (RILD), the

¹Assiut Military Center for Radiotherapy, Assiut, Egypt.

²Department of Medical Physics, Al Azhar University, Cairo, Egypt.

³Radition Oncology Department, South Egypt Cancer Instuite, Assuit University, 172526 Assuit,

⁴Technology of Radiology and Medical Imaging Department, Faculty of Applied Health Sciences Technology, Menoufia University, 32951, Menoufia, Egypt.

⁵Physics Department, Faculty of Science, New Valley University, 72511, El-Kharga, Egypt.



whole liver radiation should be limited to less than 33 Gy. Modern radiation therapy techniques were based on the maximum tolerated dose calculated from the Lyman Normal Tissue Complication Probability (NTCP) model to be ≤10%−15% risk of developing Radiation-Induced Liver Disease (RILD) [3]. So, HCC can be safely treated with high doses of conformal radiation therapy that can allow for focused partial liver irradiation (Grade B) [2]. Child-Pugh class A liver function is treated with a specialized type of radiation therapy, called stereotactic body radiotherapy (SBRT).

Table 1: Child-Pugh classification of severity of liver disease. [2]

parameter	Point assigned		
	1	2	3
Ascites	Absent	Slight	Moderate
Bilirubin, mg/dl	≤ 2	2-3	> 3
Albumin, g/dl	> 3.5	2.8-3.5	< 2.8
Prothrombin time	1-3	4-6	> 6
Seconds over control or INR	< 1.8	1.8 -2.3	>2.3
Encephalopathy	None	Grade1-2	Grade 3-4

Grade	Points	1-year patient survival (%)	2-year patient survival (%)
A:well-compensated disease	5-6	100	85
B:significant functional compromise	7-9	80	60
C:decompensated disease	10-15	45	35

Stereotactic Body Radiotherapy (SBRT):

For hepatocellular carcinoma patients, conformal radiation therapy is a practical treatment option for whom Trans-Arterial Chemo-Embolization TACE is ineffective or unsuitable. Stereotactic body radiation therapy (SBRT) is hypo-fractionated multi-beam conformal radiotherapy delivering high radiation doses in a small number of fractions [4]. SBRT can deliver a highly focused ablative dose to the target volume, leading to high biological effectiveness and hence increased cell kill, with sharp dose gradients outside the tumor which can accordingly achieve

effective tumor control while minimizing the radiation-induced toxicity to normal tissue maintaining adequate organ function and also result in a smaller volume of normal liver irradiation and a lower risk of RILD. In patients with good liver function (Child-Pugh Class A) and small tumors, SBRT appears tolerable (Grade B) [2].

SBRT is used successfully to treat sites involving breathing movement like the lung and upper abdomen [5-8] when surgery is not an option. SBRT is unique because it is the only potentially non-invasive ablative therapy for the treatment of unresectable hepatocellular carcinoma. It may be used as a sole treatment or in combination with other local therapies as well as a bridging strategy for patients awaiting transplants and results in excellent local control rates with low toxicity.

SBRT treatment is either isocentric (Linac-based) [9] or non-isocentric (CyberKnife) [10]. Motion secondary to breathing can be controlled by breathing exercises, the Active Breathing Control (ABC) device (Linac-based), or a robotic arm (CyberKnife) which moves to track the motion of the tumor (fiducial placed in the tumor) or an external surrogate of breathing motion placed on the patient's chest [2].

Among various radiotherapy techniques, volumetric modulated arc therapy (VMAT) is considered the best way to deliver SBRT because of its short treatment time [11-12]. Kida *et al.* [13] developed a 4D version of volumetric modulated arc therapy computed tomography (VMAT-CT) following the concept of VMAT-CT proposed by Poludniowski *et al.* (2010)[14].

Volumetric Modulated Arc Therapy (VMAT):

It is also called RapidArc, it is one of the cutting-edge radiotherapy technologies for cancer treatment [15], and can be used to treat head and neck cancer, whole brain cancer, esophagus cancer, lung cancer, pancreatic cancer, prostate cancer, and a wide variety of other cancerous tumor sites [11][16-21]. Two main vendors manufacture linear accelerators (Linacs) that can deliver VMAT: Elekta (Elekta Oncology Systems, Crawley, UK) and Varian (Varian Oncology Systems, Palo Alto, CA).

VMAT is an advanced form of Intensity-modulated radiation therapy (IMRT) while the gantry is rotating, the beam aperture is changed continuously; also, dose rate, gantry speed, and multi-leaf collimator (MLC) positions will dynamically vary with a 360-degree rotation of the gantry in a single or multi-arc treatment [22] during VMAT plan delivery, as opposed to the original IMRT technique where the dose rate and the gantry speed values are fixed within each single arc. VMAT can provide single or multiple arc delivery, coplanar or non-coplanar delivery along with the collimator rotation.

There has been increasing use of VMAT because it is a dynamic, highly conformal dose to the tumor region and spares the healthy organ around it with a short treatment time (usually within two minutes). This fast treatment is very useful for avoiding patient movement during sessions as possible. Also, due to its short treatment time, VMAT is considered the best way to deliver Stereotactic body radiation therapy (SBRT) which is one of the most significant advances for treating localized diseases like non-small cell lung cancer and it is also used in other tumor sites, including liver, pelvis and head and neck and upper abdomen cancers [23].

SBRT VMAT is a complex treatment and any dosimetric errors that occur in one fraction can have a significant impact. The dosimetric errors will occur due to many factors such as (i) Patient breathing in which his breathing pattern during planning CT acquisition can differ from the respiratory one during beam delivery; (ii) anatomical change including weight loss and tumor shrinkage that may occur through the treatment period that can last up to two weeks or more. So we need effective monitoring and tracking methods that can track the tumor location after patient setup or during dose delivery, the Real Time Tumor Tracking system is requisite to be used within this type of treatment.

Intensity-modulated radiation therapy:

IMRT is a type of 3D conformal radiation therapy (3DCRT) but IMRT uses many smaller radiation beams aimed at the tumor from several directions and it also differs from the treatment field in which the field is as a bundle of beamlets, the beamlet's intensity can be adjusted individually to give higher doses to certain parts of the tumor. By adjusting the intensities of individual beamlets, IMRT can give greater conformity [24-26].

Three types of IMRT delivery systems can provide high precision and an exquisitely conformal dose distribution using multiple non-uniform intensity beams: (i) step-andshoot IMRT; in which small MLC-generated segments are used and the beam is turned off when MLC leaves switching from a segment to the next one, (ii) sliding window IMRT; in which modulated MLC velocity in multiple static radiation fields is used and the beam is on as the collimator leaves are moving continuously, and More recently, techniques, (iii) volumetric modulated arc therapy (VMAT); which is a rotational form of IMRT whereby the MLC leaf positions and dose delivery rates vary during beam rotation. [17] [27]. IMRT is increasingly being used in the planning of patients with HCC due to it can improve the coverage of the target tissues and reduce the dose to the nearby normal tissues. Many dosimetric studies recommended IMRT for unresectable or inoperable hepatocellular carcinoma and simultaneously allow for focused partial liver irradiation (Grade B) [2] as in (figure 1).

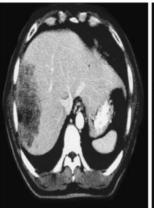




Fig. 1. Radiographic response of hepatocellular carcinoma after radiation. The left image is a CT scan taken before radiation therapy; while the right one is 6 months after the completion of radiation therapy (Courtesy of Dr. Theodore Lawrence) [2]

2 Experimental Section

2.1 Study Design and Patient Populations:

The study included twenty patients with unresectable Child-Pugh (CP) class (A:9 & B:11) hepatocellular carcinoma received and treated with IMRT, then planned and calculated with SBRT using RapidArc with the aid of the RTRT system. Data collection occurred over a time frame from February 2024 to August 2024. Individuals were immobilized in a supine position with arms overhead as the same position in the treatment session in case treated by IMRT and with stereotactic body immobilization system (BodyFIX: Medical Intelligence, Schwabmuenchen, Germany), in case treated by SBRT, that is a negative "vacuum cast" molded individually for each patient to provide the required patient setup accuracy. For each patient, a free-breathing treatment planning (FB CT) (Sensation Open, Siemens Healthineers, Germany) was used for four-dimensional computed tomography (4D CT) image acquisition with 3 to 5 mm thick CT slices from the level of the carina to L5-S1. 4D CT scan can be used to reduce motion artifact, estimate motion range, reconstruct tumor motion trajectory, and design Internal Target Volume (ITV) [28] with breathing before treatment planning [29]. Oral and Intravenous (IV) contrast should be administered to better define the tumor and any adjacent lymph nodes and visualize the stomach and bowel very easily.

All the images were transferred from the CT workstation to the treatment planning system (TPS, Eclipse version 15.6.03, Varian Medical Systems, Palo Alto, CA) for delineation. The tumor volume is defined by a thin sliced CT scan. In general, treatment volumes should encompass primary tumors as well as regional lymph nodes. Gross target volumes (GTV) and Planning target volumes (PTV), including (Internal Target Volume (ITV) which is clinical



target volume (CTV) plus the internal margin (IM), and setup margin (SM)) to account for daily setup error and motion, were designed according to the recommendation of the International Committee for Radiological Units (ICRU) Report 83 [30]. For radiation planning of primary liverhepatocellular carcinoma, the CTV was not used and the planning target volume (PTV) was calculated by adding a 0 to 7 mm margin to the GTV in all directions for set-up uncertainty and an additional margin for breathing motion.

The fluoroscopic RTRT system has been shown to reduce translational set-up error and internal error with an accuracy of \pm 1.5 mm for moving objects. Fluoroscopy should be considered at the time of simulation, verification, or 4D treatment planning to evaluate organ movement during respiration. Using 4D data; Organs at risk (OARs) such as bilateral kidneys, normal and diseased liver, esophagus, spinal cord, stomach, and small bowel were contoured. The irradiated dose must be calculated. Dose-volume histograms should be used to outline the dose to these structures.

According to the functional subunits; usually, the single point high dose irradiation doesn't have enough power to destroy the structure and function of the parallel organs as thoroughly as the serial organs [31]. As the liver parenchyma is arranged with a functionally parallel architecture, the liver is regarded to be one of the organs at risk in HCC treatment. The normal liver volume that must be delineated as OAR should exclude the gross tumor volume [32].

2.2 Planning techniques and dose constraints:

The compared technique used in this study is treated Intensity Modulated Radiotherapy plans and retrospective SBRT VMAT plans with the RTRT system. To optimize the SBRT VMAT & IMRT plans, a progressive resolution optimizer (PRO, Version13.7.16) and a dose volume optimizer (DVO, Version 13.7.16) was utilized respectively. Anisotropic Analytical Algorithm (AAA, version 15.6.03), in Eclipse considering the heterogeneity correction, was used for dose calculation. The two compared types of plans using the same defined tumor volumes, OAR volumes, and optimization constraints but differ in dose prescription and fractionation for the total 20 patients' hepatocellular carcinoma. In general, all treatment plans aimed to reduce the irradiation to OARs as much as possible while encompassing at least 95% of PTV by 95% of the prescribed dose. A statistical comparison between those two planning techniques using the real-time tumortracking system, concerning the best dose coverage to the target volume and the best sparing to the irradiated normal structures, is performed to obtain the best radiotherapy planning techniques as appropriate for HCC treatment.

Treated IMRT plans:

IMRT plans, a 10 MV-FFF photon beam, allowed delivery of the desired target dose of 45-50.4 Gy to the tumor bed with a standard fractionation consisting of 1.8 Gy/fx in 25-28 fractions [33]. To avoid the risk of RILD, the mean dose delivered to the liver should be limited to less than 30 Gy. The mean irradiated dose to the esophagus is 34 Gy. Radiation-induced gastric injury (RIGI), which manifests acutely as radiation gastritis and gastric ulcers, is a common complication of radiotherapy (RT) for thoracic and abdominal tumors such as esophageal and hepatocellular cancers, to avoid ulceration of the whole stomach shouldn't receive more than the threshold cumulative dose (50 Gy). 120 cm³ of the bowel should receive less than 15 Gy. To lower the risk of radiation myelopathy (RM), the maximum spinal cord dose must be less than 45 Gy. These tolerance doses are summarized in table (2).

Table 2: Normal Tissue Tolerance for Standard Fractionation [34].

OAR	Dose constraint
Normal Liver	$D_{mean} \le 30 \text{ Gy}$
Esophagus	D _{mean} ≤ 34 Gy
Stomach	D ₁₀₀ <50 Gy
Small Bowel	$V_{15Gy} \le 120 \text{ ccm}$
Spinal cord	$D_{max} \le 45 \text{ Gy}$

In which: D_{mean} mean dose, D_x minimum dose received by x% of the organ, V_{xGy} volume of the organ receiving \geq x Gy, D_{max} maximum dose.

Retrospective SBRT-VMAT plans:

SBRT using RapidArc plans had a 6 MV-FFF photon beam applied with a biologically effective dose (BED) of 36-60 Gy to the tumor bed which is the standard prescription for SBRT HCC cases with a hypofractionation consisting of 12 Gy/fx in 3-5 fractions delivered at 48-hour intervals [33]. The OARs dose constraints were defined, for HCC SBRT due to hypofractionation, as the following as in table (3). The delivery of conformal partial liver RT allows for safe dose escalation as the liver is regarded as a paralleled organ [35]. To deal with RILD for SBRT administration, several liver constraints were recommended; the minimum normal liver volume that must be spared from receiving 15 Gy is 700 cm³ and the mean dose allowed to this critical volume was estimated to be limited to less than 13 Gy. The minimum dose absorbed in 2 cm³ of the esophagus, stomach, and small intestine should be less than 21 Gy, 18 Gy, and 18 Gy respectively. The maximum tolerable dose (MTD) to the spinal cord must be less than 18 Gy.



Table 3: Normal tissue tolerance due to hypofractionation SBRT for HCC [36].

OAR	Dose constraints
Normal Liver	$V_{d<15 \text{ Gy}} > 700cc$
	D _{mean} < 13 Gy
Esophagus	D _{2cc} < 21 Gy
Stomach	D _{2cc} < 18 Gy
Small Bowel	D _{2cc} < 18 Gy
Spinal cord	$D_{\text{max}} < 18 \text{ Gy}$

In which: D_{mean} mean dose, D_x minimum dose received by x% of the organ, V_{xGy} volume of the organ receiving $\geq x$ Gy, D_{max} maximum dose.

2.3 Real-time Tumor-tracking System:

In the current study, we investigated the safety and early tumor response of real-time tumor-tracking radiation therapy (RTRT) for 20 patients with HCC with the aid of insertion of a fiducial marker. The real-time tumor-tracking system of linear accelerator (LINAC) is used to reduce uncertainty, which results due to setup error and organ motion, as possible as it can during thoracic and abdominal radiotherapy.

The real-time tumor-tracking system used in this study is (Mitsubishi Electronics Co., Ltd., Tokyo, Japan) [37]. RTRT consists of four sets of diagnostic X-ray television (TV) systems, an image processor unit, and a gating control unit that are mounted in the treatment room. Two of the Xray TV systems offer an unobstructed view of the patient at any time while the others display the position of a fiducial marker. An image processor unit consists of two image acquisition units, two image recognition units, and a central processor unit (CPU). The system can gate and track the real position of the tumor by gating fiducial marker, a 2.0mm gold cylindrical seed implanted in or near the tumor using image-guided implantation, which assists in positional verification during radiotherapy. fluoroscopic tracking system recognizes the position of the marker in the patient 30 times per second. The linear accelerator is gated to irradiate the tumor only when the marker is within a given tolerance region from its planned coordinates relative to the isocenter as illustrated in Figure (2).

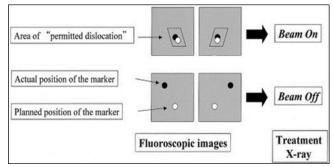


Fig. 2. The concept behind fluoroscopic real-time tumor-tracking radiotherapy. [38]

2.4 Plan comparison and evaluation: [39]

The two compared plans were evaluated by the dose constraints which are previously mentioned and the dose distribution on PTV using parameters such as homogeneity index (HI) and conformity index (CI).

❖ The HI (formula 1) [40-41] was described as an objective tool that describes the degree of uniformity of dose within the target. The most commonly used formula of the homogeneous index (HI) of dose distribution is:

$$HI = (D_{2\%}-D_{98\%})/D_p \times 100$$
 formula 1

In which; $D_{2\%}$ meant the dose delivered to 2% of the target volume indicating the "maximum dose", $D_{98\%}$ meant the dose absorbed by the 98% of the target volume, indicating the "minimum dose" and D_p is the prescribed dose of the PTV. The ideal value is zero indicates that D_2 and D_{98} are equal and increase as homogeneity decreases.

❖ The <u>CI (formula 2)</u> was defined as the quotient of the volume of the reference isodose and the treated volume as described by Radiation Therapy Oncology Group (RTOG) [42].

$$CI_{RTOG} = V_{RI}/TV \qquad \text{formula 2}$$

In which, the V_{RI} and TV are reference isodose volume and target volume, respectively.

The CI ranges from 0 to 1, the better conformity the closer the value of CI was to 1, and 1 suggested the best value.

Also, the treatment time and the number of monitor units MU were recorded and compared in both plans for every HCC patient.



3 Results and Discussion

3.1 Comparison of dosimetric parameters and Results:

The dosimetric comparison in our study showed that the PTV coverage, also dose gradient, and sharpness in the SBRT plan were better than those of the IMRT plan, as was obvious in Figures (3 & 4). Also, from the DVH (figure 4); we can extract CI, HI, and OAR dose constraints. Statistically; in the SBRT VMAT plan, all PTV volume ranges showed better conformity than that of the IMRT plan in which CI is (1.05 ± 0.02) in the SBRT plan while in the IMRT plan it was (1.15 ± 0.10) as in figure (5; A).

Figure (5; B) shows that all HIs values were consistently higher in the SBRT plan(0.25 \pm 0.02) than that of the IMRT plan (0.1 \pm 0.02).In other words, IMRT has an advantage in the tumor region in achieving homogeneous dose distributions that aren't considered an advantage for SBRT. In addition, the D_{max} of the spinal cord using SBRT technique is in the range of approximately (5.4 \pm 1.2) Gy, while by IMRT ranged in (8.1 \pm 1.8) Gy as shown in figure (6).

It is obvious from the figure (7) that in the IMRT technique, the mean esophagus dose is ≤ 6.5 Gy, while in the SBRT technique $D_{mean} \leq 5.9$ Gy in addition to it conserves the Tolerance Dose (TD) under the accepted value as $D_{2cc} < 7$ Gy. V_{15} of the bowel by using IMRT plans is in the range (22-30) cc, while by using VMAT plans is in the range (15-20) cc beside that $D_{2cc} < 15Gy$, which is illustrated in figure (8). In figure (9), D₁₀₀ of the stomach due to IMRT plans is less than 3.5 Gy while its value slightly decreases with SBRT plans in which D₁₀₀≤ 2.5Gy plus D_{2cm3}also is less than the tolerance dose that it is equal to 4.5 Gy. It was very clear that the doses to the spinal cord, esophagus, small bowel, and stomach were comparable between the IMRT and SBRT plans. However, the SBRT plans demonstrated a statistically significant reduction in the mean dose to the normal liver in which $D_{mean} \le 9.8$ Gy vs. $D_{mean} \leq 11$ Gy in the IMRT plans as shown in figure (10), and this is expected as a result of the hypo-fraction of the stereotactic body radiotherapy technique that gives more dose in one fraction than standard one (IMRT), however, it is still under the accepted tolerance dose as $V_{15} < 20.5$ % and $V_{S10} \ge 601.8$ mL; in which V_{15} is the volume receiving less than 15 Gy; V_{S10} is the absolute normal liver volume spared from at least 10 Gy.

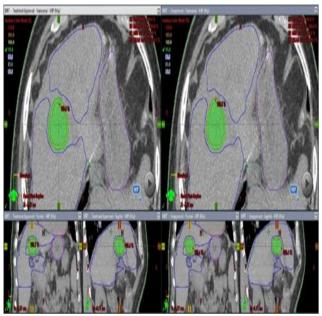


Fig. 3. Show the PTV coverage in the three different views (Axial, Coronal, & Sagittal) according to SBRT (on the left) and IMRT (on the right).

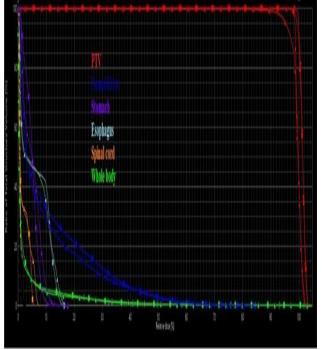
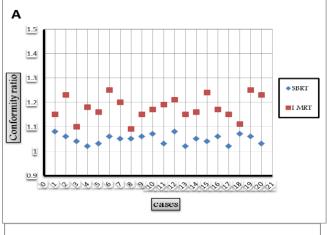


Fig. 4. The Dose Volume Histogram (DVH) of SBRT plan (■) & IMRT plan (▲) dosimetric comparison.



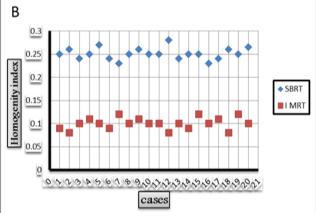


Fig.5. Comparison of the (A) conformity index and (B) homogeneity index for planning target volume (PTV) in SBRT and IMRT plans.

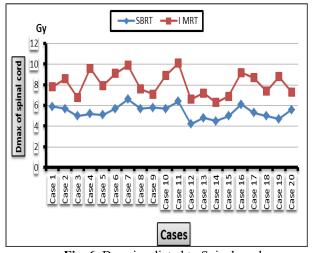


Fig. 6. Dose irradiated to Spinal cord.

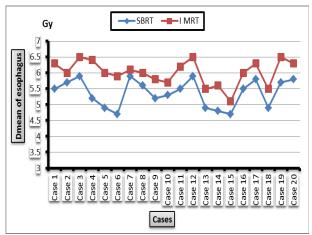


Fig.7. Dose delivered in esophagus.

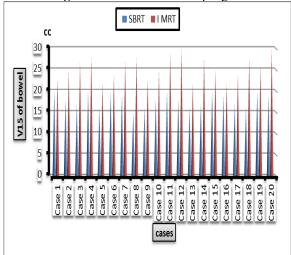


Fig. 8. Bowel volume receiving TD.

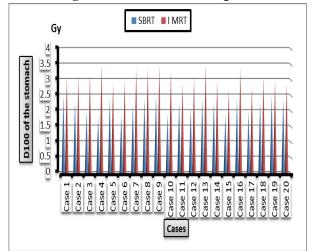


Fig. 9. Delivered dose in whole stomach.



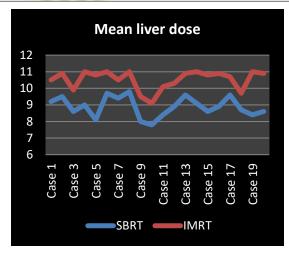


Fig.10. Absorbed dose in residual normal liver.

3.2 Discussion:

Target coverage:

The result, due to dosimetric comparison, shows the differences in CI and HI between the SBRT RapidArc plans and the IMRT plans with the aid of the RTRT system. CI has a smaller value in the SBRT plan than that of IMRT plans which means that PTV conformity of SBRT is more than that of IMRT. While the HI of PTV was higher in the SBRT plan than in the IMRT plan; in other words, IMRT has an advantage in achieving homogeneous dose distributions in the tumor region than SBRT. However, there was negligible further dose benefit for a heterogeneous target, as loosening or abandoning homogeneity can improve dose falloff around the target as well as the dose sparing of normal tissue. According to the study of Widder et al. [43] on the prescription strategy of SBRT plans, it is not necessary to obtain a higher homogeneous target dose level. The advantage of the target dose heterogeneity has been demonstrated in the SBRT plans for abdominal malignancies [44] that the lower the percentage of the prescription isodose level to the isocenter dose, the faster the dose falloff would be, which was beneficial to reduce the normal tissue dose. Our study was indirectly confirmed and was consistent with their findings.

Furthermore, D_{max} has greater value in the SBRT than in the IMRT, due to the highly absorbed prescribed dose applied in the SBRT plans. In addition to that, D_{min} in SBRT is approximately the same value as the D_{max} in IMRT which indicates that the cancer cell will be well killed rapidly, without cell reproduction, in SBRT greater than in IMRT. Moreover, SBRT specifically provided reduced monitor units and faster treatment time.

The delivered doses to the OARs:

By analyzing dosimetric parameters, we observed the distinct dosimetric advantage of the SBRT plan over the IMRT plan at high-dose regions with the aid of the RTRT system in normal tissues sparing, as the following:

For spinal cord toxicities, it was very clear that SBRT can lower the risk of radiation myelopathy injury compared to IMRT. For esophagus toxicities, it was observed that SBRT exhibited superiority in protecting the esophagus from the probability of injury compared to IMRT. For bowel toxicities, it is apparent that VMAT significantly reduced the irradiated dose to the intestine as well as decreased the bowel toxicity in the treatment of hepatocellular carcinoma patients compared to IMRT. For stomach toxicities, it is obvious that SBRT dose reduction is more dramatic in the volumes of the stomach and may decrease the gastric ulcer than IMRT. For liver toxicities, the risk of developing RILD is about 5–10% when the whole liver is irradiated up to 30-35 Gy. However, the radiation dose to control most of the solid malignancies is around 50-70 Gy [45]. However; it is very clear that SBRT, despite its higher prescribed dose, exhibited superiority in protecting the residual normal liver from the risk of Radiation-Induced Liver Disease (RILD) occurrence after conformal radiation therapy in patients with HCC cancer compared with IMRT. Therefore, SBRT provides a reduced tolerance dose to the normal liver during radiotherapy for HCC compared to IMRT, which is an ongoing goal to be a protective effect from liver metastasis. Further multi-institutional prospective studies may be warranted to validate the optimal dose of SBRT for HCC.

Unlike conventional radiotherapy, the PTV in SBRT plans mainly involves tumor tissue with its necessary margins arising from tumor motion. SBRT delivers high-dose radiation in a few fractions and requires accurate target delineation, highly conformal treatment planning, and high-precision treatment delivery, including strict attention to motion control and setup reproducibility. RTRT provides effective focal high doses to liver tumors adjacent to the critical organs or to tumors that are located too deep for other treatments. Because the fiducial markers for RTRT need not be implanted into the tumor itself, RTRT can be applied to HCC in patients who are not candidates for other surgical or nonsurgical treatments [46].

SBRT is an emerging promising technique, showing good local control in carefully selected patients. An international survey on radiotherapy for liver metastases has recently been conducted [47]. SBRT is a safe, effective, noninvasive option for patients with HCC \leq 6 cm. As such, SBRT should be considered when bridging to transplant or as definitive therapy for that ineligible transplant [48].



4 Conclusions

SBRT with real-time tumor tracking (RTRT) demonstrates superior dose conformity, homogeneity, and normal tissue sparing compared to IMRT in hepatocellular carcinoma (HCC) treatment. Reduced PTV margins via RTRT minimize setup errors and organ motion uncertainties, enhancing precision for mobile liver tumors. Critical OARs (spinal cord, esophagus, bowel, stomach, normal liver) receive significantly lower doses with SBRT, enabling safer dose escalation to tumors. Normal liver sparing is markedly improved, with SBRT reducing volumes receiving >15 Gy, critical for patients with compromised liver function. Treatment efficiency increases with SBRT: shorter delivery times and fewer monitor units (MUs) compared to IMRT. Local control rates with SBRT-RTRT are excellent (e.g., 98% in 2 years), rivaling surgical/resection outcomes for small HCCs.4D motion management in SBRT addresses respiratory tumor movement, ensuring accurate targeting without extra margins. Clinical feasibility is proven for HCC patient's ineligible for surgery/ablation, offering survival benefits and bridging to transplantation. Toxicity profiles favor SBRT, with fewer grade ≥3 adverse events compared to conventional radiotherapy or TACE combinations. Despite small sample sizes, findings advocate SBRT-RTRT as a standard option for HCC, warranting larger trials to validate long-term efficacy and safety.

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