Original Article

Stereotactic body radiotherapy using helical tomotherapy for hepatocellular carcinoma: clinical outcome and dosimetric comparison of Hi-ART *vs.* Radixact

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Background: Helical tomotherapy (HT), a unique rotational dose delivery machine, has been updated from Hi-ART to Radixact. We retrospectively evaluated the treatment outcomes of stereotactic body radiotherapy (SBRT) using HT for hepatocellular carcinoma (HCC) and compared the dosimetric details of Hi-ART and Radixact.

Methods: Between April 2014 and November 2020, 28 patients with HCC were treated with SBRT using HT for a cure at Soonchunhyang University College of Medicine, Bucheon. According to the Barcelona Clinic Liver Cancer classification, 9 patients had stage 0 disease, 12 had stage A, 4 had stage B, and 3 had stage C. The tumor size ranged from 1 cm to 8 cm (median, 2 cm). The SBRT dose ranged from 40 to 60 Gy (median, 48 Gy) with 4 fractions. Twenty-three patients were treated with Hi-ART and 5 patients were treated with Radixact. To compare the dosimetric parameters between Hi-ART and Radixact, we created treatment plans with the same constraints, pitch, modulation factor, and field width for the same patient in pairs.

Results: The median follow-up time from the date of SBRT administration was 24 months (range, 3–67 months). The local failure-free survival and intrahepatic failure-free survival rates were 96% and 58% at 1 year, 84% and 36% at 2 years, and 76% and 18% at 3 years, respectively. The overall survival rate was 93% at 1 year, 93% at 2 years, and 53% at 3 years, respectively. When the paired treatment plans were reviewed, the beam-on time and intermediate dose-spillage were found to be significantly reduced in Radixact than Hi-ART ($P<0.001$). With regard to normal organ sparing, the irradiated dose to the total liver, normal liver, heart, and kidney was significantly lower with Radixact ($P<0.001$).

Conclusions: SBRT using HT for HCC showed favorable treatment outcomes. Radixact, the latest version, physically improved treatment efficiency by reducing treatment time and provided better organ sparing than Hi-ART.

Keywords: Hepatocellular carcinoma; helical tomotherapy (HT); Hi-ART system; Radixact; stereotactic body radiotherapy (SBRT)

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Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver cancer (1). In the early 1960s, several studies showed that radiotherapy (RT) with 2-dimensional planning system to the whole liver could be treated safely only up to 30–35 Gy in conventional fractionation (2). Such doses could produce only short-term palliation of solid cancer, and RT led to an extremely limited role in the treatment of HCC for the last 30 years (3). However, the development of 3-dimensional conformal RT in the 1990s has allowed the safe delivery of high dose to tumor with normal liver sparing. Subsequently, the introduction of more advanced technologies, such as intensity-modulated radiotherapy (IMRT) and stereotactic body radiotherapy (SBRT), has expanded the indication from palliation to a cure. Several retrospective and prospective studies of SBRT for HCC have reported local control rates ranging from 68% to 97% at 3 years and overall survival (OS) rates of 39% to 84% at 3 years, which are comparable with the current standards of care (4).

Helical tomotherapy (HT; Accuray Inc., Sunnyvale, CA, USA) is a unique rotational IMRT machine. There have been three major system upgrades including several hardware and software innovations since its clinical inception in 2002: The first delivery system was named Hi-ART; the second generation system was called TomoHDA, which was equipped with both helical and discrete gantry dose delivery with dynamic jaw movement; the newest version is Radixact, in which the major dosimetric change is a higher dose rate of 1,000 cGy/min as contrary to the 850 cGy/min on the previous system (5,6). Our institution installed Hi-ART in December 2009 and additionally Radixact X9 in March 2020. Previously, we reported that IMRT or SBRT using HT with Hi-ART system for HCC tends to increase intermediate-dose spillage (IDS) but is not related to an increase in hepatic toxicity (7). Until now, there is no study to compare the dosimetric parameters of Hi-ART and Radixact in HCC.

Therefore, the current study evaluated the treatment outcomes of SBRT using HT for HCC and compared the dosimetric details of Hi-ART and Radixact. We present the following article in accordance with the STROBE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-1565/rc).

Methods

Patient selection

From medical records, we retrospectively identified 40 patients with HCC who received SBRT using HT between April 2014 and November 2020 at Soonchunhyang University College of Medicine, Bucheon. We excluded 10 patients who received SBRT to the tumor outside the liver, 1 patient who refused the planned 4 fraction treatment after receiving 2 fractions, and 1 patient who received 30 Gy in 3 fractions with palliative aim. The remaining 28 patients with HCC who were treated with SBRT for the liver tumor with curative intent were included in this study. Until February 2020, 23 patients underwent SBRT using Hi-ART system. After the installation of Radixact in March 2020, we treated patients with HCC using Radixact, considering the higher dose rate and dynamic jaw planning capability of Radixact. Therefore, 5 patients underwent SBRT using Radixact system. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Institutional Review Board of Soonchunhyang University College of Medicine, Bucheon (IRB No. 2021-04-004-001) and individual consent for this retrospective analysis was waived.

Simulation and SBRT planning

Each patient underwent contrast-enhanced computed tomography (CT) simulation with free-breathing conditions and were immobilized by a posterior vacuum-lock body fixation device. To decrease the respiratory liver motion, the patients were asked to keep the minimal breathing movement and were immobilized with an anterior vacuum-sealed cover sheet or belt. Two CT scans (rotation time, 1 s; rotation time, 1.5 s) were acquired in a 3 mm slice thickness. Reconstructed image data was inserted into a MIM workstation (MIM software Inc., Cleveland, OH, USA). Gross tumor volume (GTV) was contoured along with lesion enhancement on axial CT images and could be modified at the discretion of the physician when determining the boundaries of the tumor on 2 simulation CT images. The internal target volume (ITV) was equivalent to GTV. planning target volume (PTV) margins to ITV added asymmetrically 3–5 mm in all directions to

decrease the RT dose to the esophagus, stomach, or heart. When the tumor was located at the dome of the liver, we cephalocaudally added an extra 2–5 mm margin, considering uncertainties resulting from respiratory liver motion.

All contouring structures were moved to a Tomotherapy Hi ART II Planning System (Accuray Inc., Sunnyvale, CA, USA) for inverse treatment planning. All SBRT plans were made using the helical IMRT technique. For 23 patients treated with Hi-ART, plans were made with a modulating factor of 2 or 2.4 and a longitudinal aperture size of 1 cm or 2.5 cm with fixed-jaw mode. For 5 patients treated with Radixact, plans were made with a modulating factor of 2.4, and a longitudinal aperture size of 2.5 cm with dynamic jaw mode. The total dose was prescribed to the 90% isodose line. At least 700 mL of the normal liver volume [NLV; total liver volume (TLV) minus PTV] did not receive a total dose >17 Gy [reverse V_{17Gy} (rV_{17Gy}), ≥700 mL]. The maximal point dose (D_{max}) for the esophagus, stomach, and bowel was ≤30 Gy. Other normal organ constraints were restricted to the lowest possible levels.

Creation of paired plans

To compare the dosimetric details of Hi-ART and Radixact, paired plans were retrospectively created. Because a 1 cm opening at the beginning and end of RT is essential to get dosimetric accuracy of the dynamic jaw, there is no difference in the longitudinal penumbra of the 1 cm field width between the fixed and dynamic jaws (8). Moreover, a field width of 2.5 or 5 cm is commonly used in the clinical setting; in this study, a field width of 1 cm was applied for only 4 patients. Therefore, we fixed the field size with at 2.5 cm for all patients. Optimization was initiated with an intensity modulation factor of 2.4. Except for changes in the jaw mode, all other planning parameters, such as pitch, prescription point of PTV, and normal organ constraints, were the same in the paired plans of the same patient. Four Hi-ART plans with a field width of 2.5 cm from 4 patients treated with a field width of 1 cm in Hi-ART were created. Additionally, 5 Hi-ART plans from 5 patients treated with Radixact was created. Twenty-three Radixact plans from 23 patients treated with Hi-ART was created.

Dose-volume histogram (DVH) analysis was used to compare the dosimetric quality of the paired plans. To assess the target coverage, D_{max}, $D_{95\%}$ (dose at 95% of the PTV), D_{min} (minimum point dose of the PTV) were obtained. The homogeneity index was indicated as $D_{2\%}$ of the PTV minus $D_{98\%}$ of the PTV divided by the prescription dose. The conformity index (CI) was calculated by the ratio of the prescription isodose volume to the PTV. A CI of 1 corresponds to an ideal conformation (9). To assess high-dose spillage (HDS), the percentage ratio of the cumulative volume of all tissues outside the PTV receiving a dose >105% of the prescription dose to the PTV was estimated. To assess IDS, $R_{50\%}$ (the ratio of the volume of 50% of the prescription dose isodose to the volume of the PTV) and D_{2cm} (the percent ratio of the maximum dose at 2 cm from the PTV to the prescription dose) were calculated. The CI, HDS, and IDS were analyzed by the RTOG 0915 recommendation as the reference point. To estimate the risk of hepatic toxicity, the mean dose of the TL, $V_{30\ Gy}$ (percentage of TLV receiving ≥30 Gy) of the TL, the mean dose of the NL, $rV_{17\ Gy}$ of the NL, V_{5Gy} of the NL, and V_{1Gy} of the NL were derived from DVHs. Normal organ sparing was assessed using D_{max} or D_{mean} (mean dose).

Follow-up after SBRT

Patients were followed up 1–2 months after the end of HT and then every 3 months using diagnostic CT or magnetic resonance imaging. Local failure (LF) was defined as progressive disease according to the Modified Response Evaluation Criteria in Solid Tumors of the treated lesions. Local failure-free survival (LFFS) was estimated from the date of the start of HT to LF or last follow-up. Intrahepatic failure-free survival (IHFFS) and OS were defined as the time from HT to the date of tumor progression recorded within the liver and the date of death from any cause or the last follow-up. Hepatic toxicity was defined as classic radiation-induced liver disease (RILD; i.e., anicteric hepatomegaly, ascites, or elevated alkaline phosphatase level more than twice the upper limit of the normal value) and non-classic RILD (i.e., elevation of liver transaminases more than 5 times the upper limit of the normal level or a worsening of the Child-Pugh (CP) score ≥2 points), which occurred within 4 months after HT. Other toxicities were assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0, and treatment-related severe toxicity was defined as grade ≥3 adverse events or classic/non-classic RILD.

Statistical analysis

The Kaplan-Meier method was used to analyze survivals. A two-sided paired *t*-test was used to compare the dosimetric

Table 1 Patients' characteristics

Parameter	No. of patients	Parameter	No. of patients
Median age, years	61 (range, 50–82)	Baseline CP class	
Sex		A [5]	15
Male	24	A [6]	11
Female	4	B [7]	2
ECOG 1	28	mUICC_T	
Hepatitis		1	10
No	3	2	12
Alcohol	5	3	4
HBV/HCV	17/3	4	2
LC		mUICC_N	
No	4	0	28
Yes	24	PVTT	
Previous treatment		No	25
No	1	Yes	3
Surgery	8	Median tumor size, cm	2 (range, 1–8)
RFA	4 (cycles of 1–3)	SBRT target	
TACE	24 (cycles of 1–16)	All	24
Systemic treatment	1 (3 regimen)	Partial[†]	4
BCLC stage		RT machine	
0/A	9/12	Hi-ART	23
B/C	4/3	Radixact	5

[†], these patients had 2 lesions: SBRT was applied for 1 lesion and TACE was followed for another lesion. ECOG, Eastern Cooperative Oncology Group; HBV, hepatitis B virus; HCV, hepatitis C virus; LC, liver cirrhosis; RFA, radiofrequency ablation; TACE, transarterial chemoembolization; BCLC, Barcelona Clinic Liver Cancer; CP, Child-Pugh; mUICC, the modified International Union Against Cancer Stage; T, tumor; N, lymph nodes; PVTT, portal vein tumor thrombosis; SBRT, stereotactic body radiotherapy; RT, radiotherapy.

details. All statistical analyses were performed using Statistical Package for the Social Sciences software (version 27.0; SPSS Inc., Chicago, IL, USA), and a value of $P<0.05$ was considered statistically significant.

Results

Patient characteristics

The median age of the patients was 61 years (range, 50–82 years). Of the 28 patients, 24 were male and 4 were female. Hepatitis B virus infection was the predominant cause of liver disease (61%), and liver cirrhosis was present in 24 patients (86%). Twenty-seven patients underwent diverse courses of previous treatment (range, 1–16 courses), including surgery, radiofrequency ablation, transarterial chemoembolization (TACE), or systemic treatment. According to the Barcelona Clinic Liver Cancer classification, 9 patients had stage 0 disease, 12 patients had stage A, 4 patients had stage B, and 3 patients had stage C. Most patients had CP class A disease (93%), and the median tumor size was 2.0 cm. Four patients had 2 lesions: SBRT was applied for 1 lesion, and TACE was followed for another lesion. SBRT doses ranged from 40 to 60 Gy (median, 48 Gy) in 4 fractions. Patient characteristics are summarized in *Table 1*.

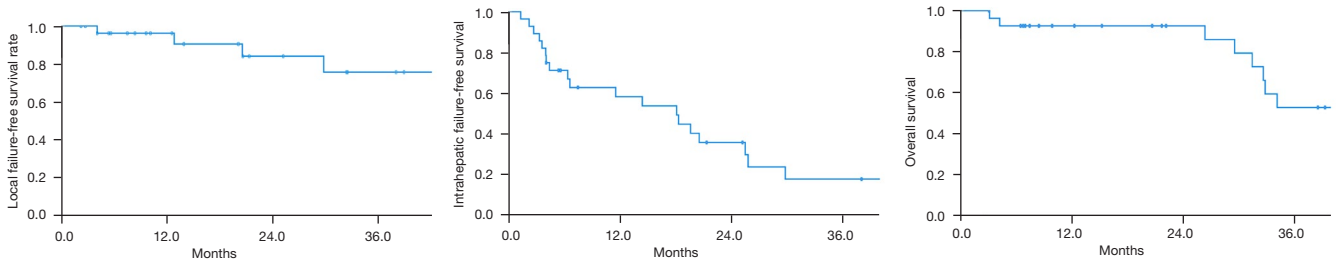

Figure 1 Survival curves after stereotactic body radiotherapy using helical tomotherapy for hepatocellular carcinoma.

Table 2 Patients who experienced severe toxicity after stereotactic body radiotherapy

No	Age	Sex	Tumor size (cm)	Baseline CP score	BCLC stage	mUICC_T	PTV (mL)	NLV (mL)	SBRT dose (Gy)	NL_mean dose (Gy)	NL_rV$_{17Gy}$ (mL)	Toxicity
1	70	F	2.6	5	A	2	72	1,197	52	11.2	948	Classic RILD
2	58	M	6.7	6	C	4	308	965	44	13.5	742	Nonclassic RILD
3	76	M	2.8	6	A	2	74	902	48	12.1	724	Nonclassic RILD
4	57	M	3.7	7	A	2	87	1,204	48	11.6	927	Nonclassic RILD
5	68	M	3.1	5	A	2	53	810	46	7.3	686	Nonclassic RILD
6	65	M	2.2	5	A	2	52	1,693	48	5.8	1,588	Grade 3 radiation pneumonitis

CP, Child-Pugh; BCLC, Barcelona Clinic Liver Cancer; mUICC, the modified International Union Against Cancer Stage; T, tumor; PTV, planning target volume; NLV, normal liver volume, SBRT, stereotactic body radiotherapy; RILD, radiation-induced liver disease.

Treatment outcome

The median follow-up duration was 24 months (range, 3–67 months). The LFFS and IHFFS rates were 96% and 58% at 1 year, 84% and 36% at 2 years, and 76% and 18% at 3 years, respectively. The median OS was not reached, and the 1-, 2-, and 3-year OS rates were 93%, 93%, and 53%, respectively. Survival curves are shown in *Figure 1*. Classic RILD was developed in 1 patient at 3 months after SBRT and immediately recovered. Four patients experienced non-classic RILD by the increase of CP score above 2 points: among these, the CP score of 2 patients worsened due to liver abscess (patient No. 2 in *Table 2*) or biliary obstruction of the anastomotic site of the previous surgery (patient No. 4 in *Table 2*), which are located on the opposite segment to the SBRT site and was improved. One patient who was treated with SBRT for HCC located at the liver dome had emphysema in both lungs, experienced repeated pneumonia even after TACE, and experienced grade 3 radiation pneumonitis. The characteristics of the 6 patients with severe toxicity are summarized in *Table 2*.

Dosimetric details of paired plans

Representative dose distributions of plans of Hi-ART and Radixact are presented in *Figure 2*. Treatment parameters are listed in *Table 3*. Beam-on time was significantly reduced in Radixact system than in Hi-ART system (3,660.59±574.57 *vs.* 4,203.60±1,034.42 s, P<0.001). The dosimetric details of PTV coverage and normal organ sparing are described in *Table 4*. The $D_{95\%}$ of the PTV was better covered in Radixact. Although D_{max} and D_{min} tended to increase in Radixact, HDS was not significantly different. The CI was significantly better in Hi-ART, however, the proportion of minor deviation according to RTOG 0915 was the same in the 2 systems and there was no major deviation (*Table 5*). With regard to IDS, R50% was significantly improved in Radixact: compliance with RTOG 0915 was 4% in Hi-ART *vs.* 21% in Radixact; minor and major deviations were 71% and 25% in Hi-ART *vs.* 68% and 11% in Radixact, respectively. The irradiated doses to normal organs were decreased in Radixact: doses to the liver, heart, and kidney were significantly reduced.

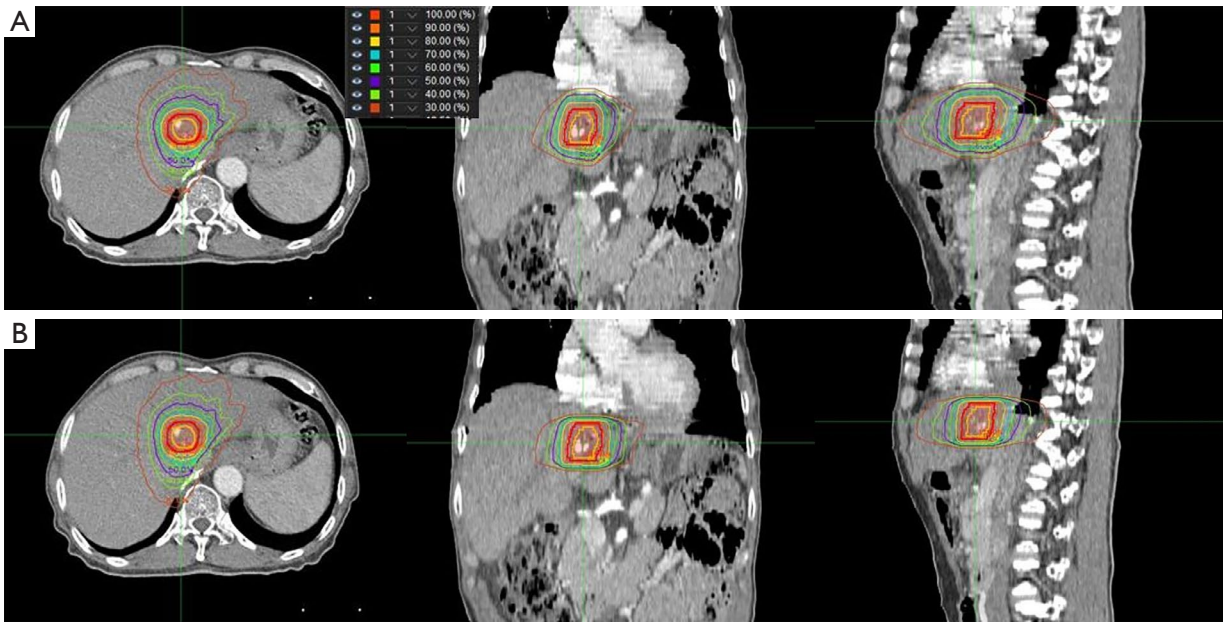

Figure 2 Representative dose distributions of plans of Hi-ART (A) and Radixact (B).

Table 3 Comparison of treatment parameters between Hi-ART and Radixact

Parameters	Hi-ART	Radixact	P value
PTV (mL)	14.6–345.1 (median 57.2)		–
SBRT dose (Gy)	40–60 (median 48)		–
Pitch	0.143–0.287		–
Modulation factor	2.4		–
Jaw size	2.5 cm_fixed	2.5 cm_dynamic	–
Gantry period (s), mean ± SD	33.97±7.08	29.64±5.73	<0.001
Total MU, mean ± SD	60,547.26±15,127.83	63,633.73±13,117.94	<0.001
Beam on time (s), mean ± SD	4,203.60±1,034.42	3,660.59±574.57	<0.001

PTV, planning target volume; SBRT, stereotactic body radiotherapy; MU, monitor units; SD, standard deviation.

Discussion

Multiple prospective and retrospective studies of SBRT using 3–10 fractions for HCC have reported LFFS rates ranging from 68% to 97% at 3 years and OS rates of 39% to 84% at 3 years (4,10-12). Although the optimal fractionation regimen remains uncertain, the most reported treatment regimen is 4–6 fractions with various doses ranging from 24 to 60 Gy (13). The total dose depends not only on liver function based on CP class, but also on the restrictions of the dose delivered to the NL and the dose delivered to normal organs (14). Additionally, the study populations were heterogeneous with large tumors, previously treated with several modalities, and various stage. These factors affect a diverse range of survival outcomes after SBRT for HCC. Our study also included various sizes and stages including portal vein tumor thrombosis, and showed a LFFS rate of 76% and an OS rate of 53% at 3 years, comparable with published data. Regarding safety, the reported rates of hepatic toxicity have been highly variable, generally ranging from 0% to 38% in patients with HCC with well-compensated liver function (15). Classic RILD rarely occurs after SBRT. On the other hand, non-

Table 4 Comparison of dose-volume parameters between Hi-ART and Radixact

Structure	Parameters	Hi-ART	Radixact	P value
Planning target volume	D_{max} (%)	107.94±2.92	108.03±3.21	0.786
	$D_{95\%}$ (%)	99.96±1.23	100.18±1.16	0.015
	D_{min} (%)	91.96±6.24	92.51±7.41	0.512
	HI	0.06±0.03	0.06±0.03	0.115
	CI	1.06±0.09	1.10±0.10	0.002
	HDS	0.06±0.09	0.11±0.40	0.451
	R50%	4.66±0.91	4.32±0.72	<0.001
	D_{2cm} (%)	64.06±11.62	63.46±10.81	0.419
Total liver volume	D_{mean} (Gy)	12.09±3.89	11.32±4.04	<0.001
	V_{30Gy} (%)	11.22±6.74	10.91±6.75	<0.001
Normal liver volume	D_{mean} (Gy)	10.14±2.73	9.34±2.82	<0.001
	rV_{17Gy} (mL)	1,028.02±351.89	1,046.16±359.07	<0.001
	V_{5Gy} (%)	60.45±17.49	53.91±18.07	<0.001
	V_{1Gy} (%)	82.66±14.91	77.68±16.81	<0.001
Spinal cord	D_{max} (Gy)	12.12±3.77	12.05±3.71	0.494
Esophagus	D_{max} (Gy)	13.42±5.41	13.16±5.56	0.227
Stomach	D_{max} (Gy)	14.47±6.68	14.23±6.96	0.416
Bowel	D_{max} (Gy)	9.20±8.63	8.88±9.04	0.197
Heart	D_{max} (Gy)	17.92±14.48	16.40±14.17	0.029
Right kidney	D_{mean} (Gy)	1.81±2.38	1.36±1.88	<0.001
Left kidney	D_{mean} (Gy)	0.56±0.59	0.47±0.51	<0.001

Data were shown as mean ± standard deviation. D_{max}, maximal point dose; $D_{95\%}$, percentage of the planning target volume (PTV) receiving 95% of the prescription dose; D_{min}, minimum point dose; HI, homogeneity index, defined as $D_{2\%}$ of the PTV minus $D_{98\%}$ of the PTV divided by the prescription dose; CI, conformity index, defined as the prescription isodose volume to the PTV; HDS, high dose spillage (the percentage ratio of cumulative volume of all tissue outside PTV receiving a dose >105% of the prescription dose to the PTV; R50%, the ratio of the 50% prescription isodose volume to the PTV; D_{2cm}, the percent ratio of the maximum dose at 2 cm from the PTV to the prescription dose; D_{mean}, mean dose; V_{30Gy}, percentage of the total liver volume receiving ≥30 Gy; rV_{17Gy}, reverse V_{17Gy}, the normal liver volume receiving <17 Gy.

Table 5 Deviation according to RTOG 0915 protocol between Hi-ART and Radixact

Parameters	Deviation	Hi-ART	Radixact
CI	None	25 (89%)	25 (89%)
	Minor	3 (11%)	3 (11%)
	Major	0 (0%)	0 (0%)
R50%	None	1 (4%)	6 (21%)
	Minor	20 (71%)	19 (68%)
	Major	7 (25%)	3 (11%)

CI, conformity index, defined as the prescription isodose volume to the planning target volume; R50%, the ratio of the 50% prescription isodose volume to the planning target volume.

classic RILD has reported the rates of 5–38% (13,15-17). In this study, classic RILD occurred in 1 patient (4%) and non-classic RILD was occurred in 4 patients (14%). Among these, however, 2 patients might not be directly related to SBRT, considering the deterioration of underlying liver disease on the opposite segment to the SBRT site. One patient with underlying emphysema, who experienced spontaneous or procedure-related recurrent pneumonia, had grade 3 pneumonia after SBRT. Considering SBRT is commonly recommended as an alternative option for patients with HCC having comorbidities, we should pay attention to the probability of severe toxicity due to the unexpected interaction between the underlying disease and SBRT.

To the best of our knowledge, this is the first study to compare the dosimetric details between Hi-ART and Radixact, the 2 delivery modes of HT. HT utilizes the opening and closing of a 64-leaf, pneumatically powered, binary multileaf collimator with 51 equally spaced beam angles at 360° and the translational motion of the treatment couch at a constant speed (18). The initial system, Hi-ART, utilizes the fixed-jaw mode of the collimator for beam delivery. The collimator jaw of the machine is fully opened to the predetermined width as soon as one of the edges of the PTV in the longitudinal direction enters the beam and is only completely closed when the other edge of the PTV exits the beam. Therefore, the width of the penumbra of the PTV in the longitudinal direction completely depends on the selected field width (19). The next-generation system provides a dynamic jaw mode that can deliver a radiation beam dynamically to the superior and inferior borders of the target volume using narrower field widths (20). Several studies comparing fixed and dynamic jaws of HT have showed that dynamic jaw significantly improved target coverage and normal organ sparing regardless of the field width, and showed the best results with a field width of 2.5 cm (20-24). However, the beam-on time is increased in the case of a dynamic jaw with a field width of 2.5 cm, and is comparable in the case of dynamic jaw with a field width of 5 cm. A longer treatment time for HT compared with that of other RT machines is a drawback. Radixact, the newest system, significantly shorten the treatment time by using a higher dose rate. Previously, we reported that IMRT or SBRT using Hi-ART for HCC tends to increase IDS, although the clinical effect on hepatic toxicity might be minimal; minor and major deviations of R50% were noted in 41% and 50% of cases, respectively (7). Another study using Hi-ART for lung SBRT showed a similar result: minor deviation and major deviation of R50% were noted in 39% and 61% of cases, respectively (25). The current study showed similar deviation rates for Hi-ART (96%). On the other hand, Radixact significantly improved compliance of R50%: 21% followed the recommendation, and 68% and 11% had minor and major deviations, respectively. In addition, Radixact reduced the irradiated doses to normal organs. Therefore, our study showed a remarkable advantage of Radixact in improving target coverage and normal organ sparing with faster treatment delivery with a dynamic jaw and a field width of 2.5 cm ($P<0.001$).

The current study has limitations. First, this was a retrospective study. Therefore, selection and confounding biases may arise, and the rate of treatment-related toxicity may be underestimated. Second, the current study had a small sample size. Verification of our findings will be needed in future studies of more patients. Third, we applied a fixed-field width of 2.5 cm, fixed-modulation factor of 2.4, and same planning parameters, such as pitch, prescription point of PTV, and normal organ constraints, except change in the jaw mode for the same patient to simplify the effect on plan quality. However, these parameters may change in real clinical applications. Fourth, a unique rotational dose-delivery of HT could theoretically induce the cold spot at the peripheral region of the tumor within moving organ. Several studies, however, documented that a larger jaw size is less susceptible to the effect of tumor motion, larger penumbra by a larger jaw size ≥2.5cm could provide an additional dose to the tumor edge, regular respiratory motion would minimize dosimetric errors, and the fractionation ≥3 shows the constant dose-delivery (26,27). These support the safety of HT for SBRT to HCC. On the other hand, dynamic jaw of Radixact decrease the penumbra at the tumor edge. This might induce the cold spot at the tumor edge. Although the use of immobilization tool to control moving organ, the personalized PTV margins to compensate interfractional variation, the application of a larger jaw size ≥2.5 cm, and the fractionation ≥3 minimize peripheral dose uncertainty of the target for Radixact, further studies would be needed to validate the safety of dynamic jaw of Radixact. Lastly, we could not demonstrate the clinical benefit of Radixact, although dosimetric details were significantly improved compared with Hi-ART. Considering that previous studies using Hi-ART for HCC SBRT showed favorable outcomes compared with those of other RT machines, the physical advancement of Radixact might be minimal in the clinical setting (4). However, we

expect to maximize tumor control by improving the target coverage, minimize the potential risk of toxicity by reducing the irradiated doses to normal organs, and improve patient' convenience by reducing the treatment time.

In conclusion, this study using HT for HCC SBRT showed a LFFS rate of 76% and an OS rate of 53% at 3 years, respectively. Classic RILD and non-classic RILD occurred in 1 patient and 4 patients. These treatment outcomes were comparable with those of other SBRT studies for HCC. Radixact, the latest version, physically improves treatment efficiency by reducing treatment time and provides better organ sparing than Hi-ART. Further studies will be needed to evaluate the clinical significance of the dosimetric advances in Radixact.

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Footnote

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Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-1565/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-1565/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This retrospective study was approved by the Institutional Review Board of Soonchunhyang University College of Medicine, Bucheon (IRB No. 2021-04-004-001) and individual consent for this retrospective analysis was waived.

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