Radiofrequency ablation guided by cone beam computed tomography for hepatocellular carcinoma: a comparative study of clinical results with the conventional spiral computed tomography-guided procedure

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Abstract

Objective: To compare the outcomes of cone beam computed tomography (CBCT)-guided radiofrequency ablation (RFA) for hepatocellular carcinoma (HCC) with those of traditional spiral computed tomography (s-CT)-guided RFA.

Methods: This retrospective study analysed data from patients with HCC that underwent RFA guided by either CBCT or s-CT. A number of preoperative and postoperative characteristics, including operation time, ablation time, radiation dose and hospital stay were recorded for all patients. The incidence of intraoperative and postoperative complications was recorded. The therapeutic effect was evaluated at 1, 3 and 6 months after RFA.

Results: A total of 47 patients with HCC (12 females and 35 males) underwent successful RFA: 21 underwent CBCT-guided RFA and 26 underwent s-CT-guided RFA. Except for one case of pneumothorax in the s-CT group, no serious complications occurred. The objective response rate and disease control rate at 1, 3 and 6 months after RFA showed no significant differences between the two groups. Throughout the 6-month follow-up period, the complete ablation rate

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was 19 of 21 patients (90.5%) in the CBCT group and 19 of 26 patients (73.1%) in the s-CT group. **Conclusions:** CBCT was a safe and effective guiding modality for RFA in patients with HCC.

Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide and the second leading cause of cancer deaths in China.[1–3] At present, surgical resection and liver transplantation are the preferred treatments for early-stage HCC. However, more than 80% of patients are unable to undergo surgical resection at the time of diagnosis, and the recurrence rate is approximately 40–70% at 5 years after liver resection.[4–6] For those that are not candidates for surgery or those that experience postoperative recurrence of HCC, various interventional therapies, including transcatheter arterial chemoembolization (TACE) and thermal ablation, have been widely used and developed.[7] Many clinical studies and guidelines have found no significant difference in the overall survival rate and recurrence-free survival rate for radiofrequency ablation (RFA) and surgical resection in HCC patients with small tumours <3 cm in diameter.[8,9] For HCC with a diameter ≤2 cm, the 1-, 3-, and 5-year overall survival and recurrence-free survival rates of patients treated with RFA are better than those of patients that undergo surgical resection.[10–12] As the typical form of imaging-guided therapy, the most commonly used imaging guidance methods of RFA are spiral computed tomography (s-CT) and ultrasound (US). Cone beam computed tomography (CBCT) is a relatively novel imaging method, and by rotating the C-arm, stereographic and real-time tomographic images can be obtained. In recent years, RFA guided by CBCT has received increasing attention and application, showing unique technical advantages compared with s-CT guidance, but few published studies have reported on the difference between the two image-guiding modalities, especially in liver cancer.[13–15]

This study retrospectively analysed the clinical and follow-up data of patients that underwent CBCT-guided RFA in one clinical centre and compared the data with those from patients that underwent s-CT-guided procedures during the same time period. This study aimed to evaluate the safety and effectiveness of this novel guiding technology for the treatment of HCC.

Patients and methods

Patient population

This retrospective study enrolled consecutive patients diagnosed with HCC that were treated in the Department of Interventional and Vascular Surgery, Peking University First Hospital, Beijing, China between September 2016 and December 2017. The inclusion criteria were as follows: (i) patients in whom HCC was diagnosed by liver biopsy or in compliance with 2017 guidelines;[16] (ii) patients that underwent RFA guided by CBCT or s-CT as the sole imaging modality; (iii) conventional TACE was performed within 7 days before imaging-guided RFA;

(iv) patients that underwent preoperative contrasted s-CT or magnetic resonance imaging (MRI). The exclusion criteria were as follows: (i) multiple/diffuse lesions; (ii) chronic liver disease (hepatitis) or cirrhosis with a Child-Pugh score C; (iii) Barcelona Clinic Liver Cancer stage C or D. All patients underwent TACE before RFA to achieve a better visualization of the local lesion on the subsequent CT scan by deposition of lipiodol.

This study was approved by the Ethical Review Committee of Peking University First Hospital, Beijing, China (no. 2018研 254). All patients signed informed consent forms before their surgical procedures.

Radiofrequency ablation

All TACE and RFA procedures were performed by the same experienced team using the same angiography device (GoldSeal Innova[TM] 4100-IQ Plus; GE Healthcare, Piscataway, NJ, USA) and RFA equipment (model 1500X RF generator and StarBurst[®] SDE RFA electrode; AngioDynamics, Latham, NY, USA). The operation team was led by two of the authors (J.W. and T. L.), both of whom had >10 years of experience in interventional oncology.

The traditional s-CT-guided method was conducted as previously described.[17] CBCT-guided RFA was performed using the following steps. First, the position of the diaphragm in the breath-held state was marked under fluoroscopy on the body surface as the baseline. Then, a CBCT scan was performed to determine the puncture path using a radiopaque grid on the patient's body surface. The puncture was made when the patient's breath was synchronized with the diaphragm movement to obtain the baseline marker. The puncture path was adjusted in real time under fluoroscopy according to the patient's breathing rhythm. Intravenous anaesthesia was used for pain control throughout the procedure. The cumulative radiation doses of CBCT and dose-length product (DLP) of the s-CT group were recorded when the procedures were finished.

Follow-up and evaluation of therapeutic effect

All patients underwent routine enhanced CT or MRI at 1, 3 and 6 months after RFA. The therapeutic effect on the ablated lesions was evaluated according to the mRECIST criteria (2010 edition).[18] The following definitions were used: objective response rate (ORR) = complete remission (CR) + partial remission (PR); disease control rate (DCR) = CR + PR + stable disease (SD). The follow-up period of this study was 6 months. Complications such as pneumothorax, haemorrhage, hollow viscera injury or other RFA-related complications were recorded. The operation time, ablation time, radiation dose and postoperative hospital stay were also recorded for each patient.

Statistical analyses

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA). The mean $\pm$ SD or median values of continuous variables were compared between the two groups using an unpaired t-test or the Mann–Whitney U-test based on the normality of the data. Comparisons between the categorical data were evaluated using χ^2-test. A P-value <0.05 was considered statistically significant.

Results

This retrospective study enrolled 47 patients (12 females, 35 males) diagnosed with HCC. All 47 patients underwent TACE before RFA to achieve a better visualization of the local lesion on the subsequent

CT scan by deposition of lipiodol. Of the 47 patients, 21 showed better lipiodol retention so they received RFA under CBCT guidance, while the other 26 patients underwent s-CT-guided RFA. The demographic and clinical characteristics of the patients in the two groups are shown in Table 1. The only significant difference between the two groups was in age, with the patients in the s-CT group being significantly older than those in the CBCT group ($P = 0.006$).

The success rate for both techniques was 100%. In the CBCT group, the mean $\pm$ SD total operation time was 90.5 ± 33.8 min, the mean $\pm$ SD ablation time was 25.4 ± 9.1 min, and the mean $\pm$ SD radiation dose was 243.6 ± 192.6 mGy (Table 2). In the s-CT group, the mean $\pm$ SD total operation time was 65.8 ± 15.1 min, the mean $\pm$ SD ablation time was 19.4 ± 7.6 min, and the mean $\pm$ SD DLP was 2317 ± 1292 mGycm. Significant differences were observed in the total operation time and ablation time between the two groups ($P < 0.05$ for both comparisons). No serious complications were observed during

Table 1. Demographic and clinical characteristics of patients ($n = 47$) with hepatocellular carcinoma that underwent radiofrequency ablation guided by either cone beam computed tomography (CBCT) or spiral computed tomography (s-CT).

Characteristic	CBCT group $n = 21$	s-CT group $n = 26$	Statistical significance[a]
Age			
Range	29–76	41–86	
Mean $\pm$ SD	55.7 $\pm$ 11.8	65.2 $\pm$ 10.4	
Median (IR)	57 (11)	63 (14)	$P = 0.006$
Sex			
Female	6	6	
Male	15	20	NS
Tumour size, cm			
Range	1.2–9.1	1.0–5.5	
Mean $\pm$ SD	3.4 $\pm$ 1.9	2.7 $\pm$ 1.2	
Median (IR)	3.0 (2.0)	2.6 (1.8)	NS
Child-Pugh score			
A	20	24	
B	1	2	NS
BCLC stage			
A	9	11	
B	12	15	NS
ECOG performance status			
0	16	18	
1	5	8	NS
Vascular invasion			
Y	0	0	
N	21	26	NS
Metastases			
Y	4	1	
N	17	25	NS

Data presented as mean $\pm$ SD, range, median (IR) and n of patients.
[a]χ^2-test; NS, no significant between-group difference ($P \geq 0.05$).
IR, interquartile range; BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group.

Table 2. Perioperative characteristics of patients ($n = 47$) with hepatocellular carcinoma that underwent radiofrequency ablation guided by either cone beam computed tomography (CBCT) or spiral computed tomography (s-CT).

Characteristic	CBCT group $n = 21$	s-CT group $n = 26$	Statistical significance[a]
Total operation time, min	90.5 ± 33.8	65.8 ± 15.1	$P = 0.02$
Ablation time, min	25.4 ± 9.1	19.4 ± 7.6	$P = 0.02$
Intraoperative complications	0	1	NS
Postoperative complications	4	3	NS
Radiation dose[b]	243.6 ± 192.6	2317 ± 1292	NA
Postoperative hospital stay, days	4.0 ± 1.0	3.7 ± 0.9	NS

Data presented as mean $\pm$ SD and n of patients.
[a]Unpaired t-test; NS, no significant between-group difference ($P \geq 0.05$).
[b]The radiation dose of the CBCT group was the cumulative radiation dose (mGy) and the radiation dose of the s-CT group was dose-length product (mGycm).
NA, not applicable.

Table 3. Therapeutic effect in patients ($n = 47$) with hepatocellular carcinoma that underwent radiofrequency ablation guided by either cone beam computed tomography (CBCT) or spiral computed tomography (s-CT).

Therapeutic effect[a]	CBCT group $n = 21$			s-CT group $n = 26$		
	1 month	3 months	6 months	1 month	3 months	6 months
CR	19 (90.5)	19 (90.5)	19 (90.5)	25 (96.2)	22 (84.6)	19 (73.1)
PR	2 (9.5)	0 (0.0)	0 (0.0)	1 (3.8)	3 (11.5)	2 (7.7)
SD	0 (0.0)	2 (9.5)	0 (0.0)	0 (0.0)	1 (3.8)	2 (7.7)
PD	0 (0.0)	0 (0.0)	2 (9.5)	0 (0.0)	0 (0.0)	3 (11.5)
ORR	21 (100.0)	21 (100.0)	19 (90.5)	26 (100.0)	25 (96.2)	21 (80.8)
DCR	21 (100.0)	21 (100.0)	19 (90.5)	26 (100.0)	26 (100.0)	23 (88.5)
Complete ablation	19 (90.5)			19 (73.1)		
Recurrence during follow-up	2 (9.5)			7 (26.9)		

Data presented as n of patients (%).
[a]ORR = CR + PR; DCR = CR + PR + SD.
CR, complete remission; PR, partial remission; SD, stable disease; PD, progressive disease; ORR, objective response rate; DCR, disease control rate.

the 7-day observation period in either group, except one case of pneumothorax that occurred in the s-CT group during the ablation. There was no significant difference between the two groups in terms of mean $\pm$ SD postoperative hospital stay (4.0 ± 1.0 days in the CBCT group versus 3.7 ± 0.9 days in the s-CT group).

The ORRs at 1, 3 and 6 months in the CBCT group were 21 of 21 (100.0%), 21 of 21 (100.0%) and 19 of 21 (90.5%); and the DCRs were 21 of 21 (100.0%), 21 of 21 (100.0%) and 19 of 21 (90.5%), respectively (Table 3). The ORRs at 1, 3 and 6 months in the s-CT group were 26 of 26 (100.0%), 25 of 26 (96.2%) and 21 of 26 (80.8%); and

the DCRs were 26 of 26 (100.0%), 26 of 26 (100.0%) and 23 of 26 (88.5%), respectively. No significant differences were observed between the two groups. In the s-CT group, seven ablated lesions were found to be viable during the follow-up period compared with two that remained viable in CBCT group ($P = 0.026$).

Discussion

Computed tomography has been widely used in interventional procedures as a guidance modality, but the lack of real-time imaging has limited its use. In 1996, a report described a newly developed system that could provide the real-time reconstruction and display of CT images.[19] In that study, 57 patients underwent procedures using that system with a success rate of 100%.[19] However, according to the author, there was still some slight delay during real-time imaging processing and the operators were exposed to a high dose of radiation despite the proper protection being used.[19] In addition, the artifact generated by the needle tip could affect puncture accuracy.[19] Therefore, this system will not be suitable in some post-TACE patients that are scheduled to have RFA because of the obvious artifact generated by the retention of lipiodol.

Cone beam computed tomography is a revolutionary technology that integrates digital subtraction angiography and CT imaging technology to obtain three-dimensional and CT-analogous reconstructed images. As a novel imaging guiding modality, CBCT is thought to have important clinical value for percutaneous puncture procedures, especially RFA. Using multiplanar imaging reconstruction, the size, position and shape of target tumours can be fully and accurately evaluated, which is a distinct advantage for ablation of the lesions with iodized oil deposited after TACE. During RFA, the puncture process can be monitored in real time under fluoroscopy and needle deployment can be accurately adjusted according to the location of the lesion, which more effectively creates a sufficient ablation zone as a safety margin.[13,20] In order to further understand role of CBCT in image-guided RFA, this current study retrospectively reviewed and compared the clinical data from patients that had undergone CBCT-guided RFA with those that had undergone conventional s-CT-guided procedures.

In this current study, the technical success rate, incidence of postoperative complications and length of hospital stay showed no significant differences between the CBCT and s-CT groups. Because of the different mechanisms used in CBCT and s-CT, it was difficult to compare the effective radiation doses between the two groups. The cumulative radiation dose of CBCT was calculated. In contrast, the DLP of s-CT was recorded, which was considered to be the cumulative radiation dose of that group. A previous study reported that weight-based protocol modifications could significantly reduce the radiation dose during CT-guided percutaneous ablations without sacrificing image quality.[21] However, due to the different definitions and units used in the current study, it was not possible to directly compare the two groups in terms of radiation dose. Therefore, an accurate comparison of the effective radiation doses between the two image-guiding modalities requires further research. In this current study, the mean $\pm$ SD cumulative radiation dose of the CBCT group was 243.6 ± 192.6 mGy and the mean $\pm$ SD DLP of the s-CT group was 2317 ± 1292 mGycm. According to a previous study,[15] when using CBCT for image guidance, the cumulative radiation dose was 194.62 ± 105.51 mGy, which was similar to this current study. The total operation time of the CBCT group was significantly longer than that of the s-CT group.

The most likely reason for this is that the C-arm detector undergoes a time-consuming safety test before each scan, so the time of image acquisition is longer than that of conventional CT scans. In addition, the results of this current study demonstrated that the complete ablation rate was lower in the s-CT group (19 of 26 patients; 73.1%) than in the CBCT group (19 of 21 patients; 90.5%). CBCT involves real-time guidance under fluoroscopy and can perform multiplanar reconstruction, therefore it is more conducive to observing the details of lesions and is convenient for achieving complete ablation in all dimensions.[14] In addition, because of the combination of fluoroscopy and a CT scan, adjustment of the needle angle, depth and monitoring of the needle deployment can be simplified and made more efficient with CBCT, so the radiation dose in the CBCT group was lower than that in the s-CT group (Figure 1).

Spiral computed tomography has a superior advantage over cone beam CT in terms of density resolution, thus, it has been recommended for ablating lesions near abdominal organs such as the gallbladder, colon and stomach, which lack natural dense contrast.[22,23] Nevertheless, s-CT-guided puncture is always a blind process, so it is important for the patients to have good breath control. In this current study, there was one case of pneumothorax in the s-CT group that was due to the poor breath control of the patient during the procedure. Thus, for patients who cannot maintain steady breathing rhythms, CBCT is a better choice due to its unique real-time guiding characteristics. For lesions adjacent to the diaphragm and heart, which have natural density contrast for visual recognition, CBCT has the distinct advantage of guiding the puncture procedure and avoiding the occurrence of puncture-related complications (Figure 2). Even with poor breath control, the surgeon can adjust the direction and distribution of the needle tip under fluoroscopy without any damage to the diaphragm or the heart. This is not possible with s-CT guiding procedures.
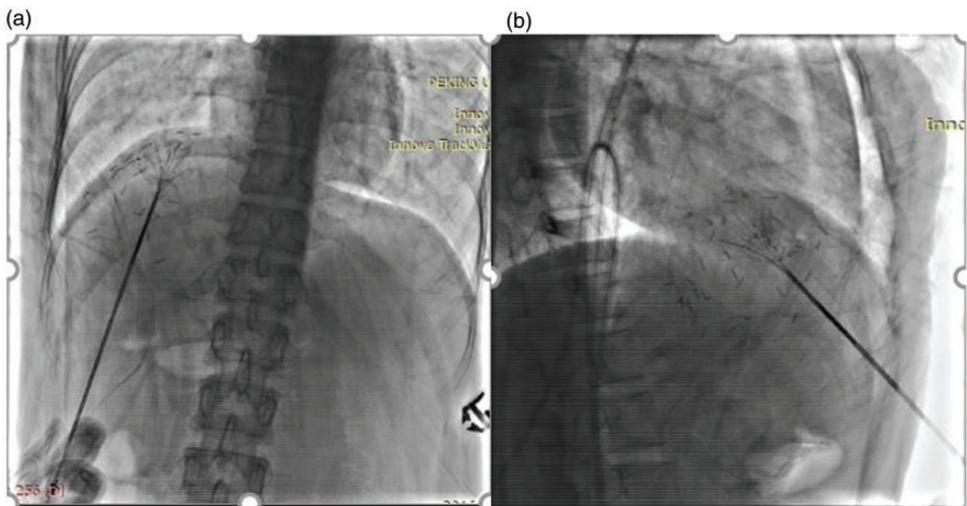
Figure 1. Adjusting the angle, depth and monitoring the electrode deployment can be simplified and more intuitive under fluoroscopy during cone beam computer tomography: (a) posterior-anterior position; (b) lateral position.
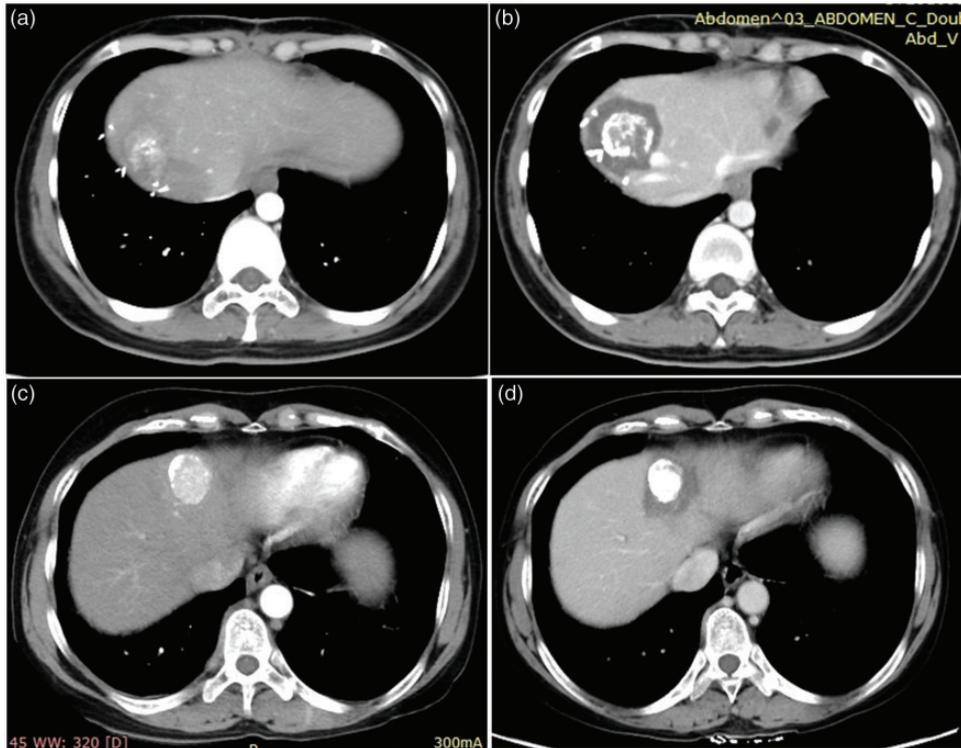
Figure 2. For some lesions near the top of the diaphragm, pericardium or other high-risk areas, the puncture and deployment under the guidance of cone beam computed tomography was more accurate and complete ablation was more likely to be achieved. (a) A 29-year-old female with hepatocellular carcinoma (HCC) recurrence after surgery. The lesion was near the top of diaphragm; and (b) the same patient after transcatheter arterial chemoembolization (TACE) and cone beam computed tomography (CBCT)-guided radiofrequency ablation (RFA). The lesion was eliminated completely. (c) A 63-year-old female patient with HCC detected adjacent to the pericardium; and (d) the same patient after TACE and CBCT-guided RFA. The lesion was eliminated completely.

During the 6-month follow-up period in this current study, no significant differences were observed in the ORR and DCR of the ablated lesions in the two groups. Throughout the follow-up period, seven lesions (26.9%) in the s-CT group and two lesions (9.5%) in the CBCT group were found to be residual or exhibit recurrence. However, due to the small sample size of this current study, it remains unclear whether the local lesion control rate of CBCT-guided RFA was better than that of s-CT. Further prospective studies with larger sample sizes are required.

The main limitation of this current study was that because CBCT is a relatively new method of image guidance, it has been used in Peking University First Hospital for less than 2 years. Therefore, the sample size of this study was relatively small. At present, patient data are still being collected and retrospective results with a larger sample size or prospective studies will be published in the future.

In conclusion, CBCT is a novel, image-guided technique that can play an important role in both transluminal and percutaneous procedures. This current

study has provided preliminary data that have shown that compared with traditional s-CT guidance, CBCT-guided RFA was associated with similar safety and efficacy for the treatment of HCC. Moreover, CBCT guidance was superior to traditional s-CT regarding the complete ablation rate and radiation doses. CBCT-guided RFA appears to be a safe and effective treatment for HCC.

Authors' contributions

TS Lyu and J Wang made substantial contributions to the conception and design of the study and drafting the manuscript. SJ Cao made substantial contributions to the analysis and interpretation of the data. L Song substantially contributed to the data acquisition and analysis. XQ Tong revised the manuscript critically for important intellectual content and was involved in data acquisition and analysis. YH Zou was involved in the conception and design of the study, data interpretation and analysis and revising the manuscript for intellectual content. All authors gave final approval of the version to be published. All authors agreed to be 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. All authors read and approved the final manuscript.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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