No-Touch vs. Conventional Radiofrequency Ablation Using Twin Internally Cooled Wet Electrodes for Small Hepatocellular Carcinomas: A Randomized Prospective Comparative Study

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Objective: This study aimed to compare the efficacy between no-touch (NT) radiofrequency ablation (RFA) and conventional RFA using twin internally cooled wet (TICW) electrodes in the bipolar mode for the treatment of small hepatocellular carcinomas (HCC).

Materials and Methods: In this single-center, two-arm, parallel-group, prospective randomized controlled study, we performed a 1:1 random allocation of eligible patients with HCCs to receive NT-RFA or conventional RFA between October 2016 and September 2018. The primary endpoint was the cumulative local tumor progression (LTP) rate after RFA. Secondary endpoints included technical conversion rates of NT-RFA, intrahepatic distance recurrence, extrahepatic metastasis, technical parameters, technical efficacy, and rates of complications. Cumulative LTP rates were analyzed using Kaplan-Meier analysis and the Cox proportional hazard regression model. Considering conversion cases from NT-RFA to conventional RFA, intention-to-treat and as-treated analyses were performed.

Results: Enrolled patients were randomly assigned to the NT-RFA group (37 patients with 38 HCCs) or the conventional RFA group (36 patients with 38 HCCs). Among the NT-RFA group patients, conversion to conventional RFA occurred in four patients (10.8%, 4/37). According to intention-to-treat analysis, both 1- and 3-year cumulative LTP rates were 5.6%, in the NT-RFA group, and they were 11.8% and 21.3%, respectively, in the conventional RFA group (p = 0.073, log-rank). In the as-treated analysis, LTP rates at 1 year and 3 years were 0% and 0%, respectively, in the NT-RFA group and 15.6% and 24.5%, respectively, in the conventional RFA group (p = 0.004, log-rank). In as-treated analysis using multivariable Cox regression analysis, RFA type was the only significant predictive factor for LTP (hazard ratio = 0.061 with conventional RFA as the reference, 95% confidence interval = 0.000–0.497; p = 0.004). There were no significant differences in the procedure characteristics between the two groups. No procedure-related deaths or major complications were observed.

Conclusion: NT-RFA using TICW electrodes in bipolar mode demonstrated significantly lower cumulative LTP rates than conventional RFA for small HCCs, which warrants a larger study for further confirmation.

Keywords: Hepatocellular carcinoma; Radiofrequency ablation; No-touch technique; Randomized controlled trial
INTRODUCTION

Radiofrequency ablation (RFA) is currently recommended as an intended curative treatment for very early or early stage hepatocellular carcinoma (HCC) according to several of the most prominent guidelines for the management of HCC [1-3]. However, although RFA is widely accepted as an effective treatment option for small HCCs in nonsurgical candidates, it has a significantly higher rate of local tumor progression (LTP) compared to surgical resection, limiting its use in patients with resectable HCCs [4-7]. Several studies have demonstrated that there are no significant differences in long-term therapeutic outcomes between RFA and surgery, albeit with high LTP in RFA [6,8,9]. However, in patients with LTP, the required number of interventional procedures for controlling recurrent tumors was significantly higher than that in patients without LTP to obtain a similar overall survival outcome [10]. Thus, it is clinically valuable to lower LTP rates with RFA, and for this purpose, the creation of a 5–10 mm ablative margin around the target tumor is necessary, which may not always be possible with RFA [11].

In 2016, Seror et al. [12] reported that no-touch RFA (NT-RFA) using multi-bipolar electrodes resulted in 94% 5-year LTP-free survival, an excellent therapeutic outcome for HCCs within the Milan criteria. Thereafter, several retrospective studies have also reported significantly better LTP rates of NT-RFA using multi-bipolar RF technology than conventional RFA using monopolar RF technology [13-16]. However, a prospective cohort study by Hirooka et al. [17] reported that NT-RFA using multi-bipolar electrodes showed no differences in LTP rates, compared with conventional RFA using monopolar electrodes, despite having significantly better intrasubsegmental tumor recurrence-free survival [17]. Furthermore, in previous studies [12-17], there were differences not only in RFA techniques but also in the number and types of RF electrodes and RF energy delivery modes (multipolar vs. monopolar). Thus, at present, it is not yet certain whether the better LTP rates of NT-RFA were due to the oncologically favorable features of NT-RFA, different efficacy of RF equipment, or differing background clinical characteristics [13-15,17]. Therefore, to answer the question of whether NT-RFA can indeed provide better therapeutic efficacy, we conducted a randomized prospective study comparing NT-RFA with conventional RFA using the same RF ablation system and electrodes for the treatment of small HCCs.

MATERIALS AND METHODS

This single-center, two-arm, parallel-group, prospective randomized controlled study was approved by the Institutional Review Board of Seoul National University Hospital (IRB No.1604-136-758, NCT 02806076). All participants provided written informed consent for enrollment in the study. This study was financially supported by the RF Medical Co., Ltd. However, the authors had complete control of patient enrollment, data collection, and analysis at all times, without any input from the funding source.

Study Participants

From October 2016 to September 2018, we recruited participants who met the following eligibility criteria: 1) age 20 to 85 years, 2) Child-Pugh class A, 3) treatment-naive HCC or new HCC that developed more than 2 years after initial curative treatment for HCC, and 4) tumor size ≤ 2.5 cm. The 2.5 cm size limit was selected based on the results of a previous study, which showed that the ideal inter-electrode distance for the creation of a spherical ablation zone with bipolar electrodes was 3 cm [18]. The exclusion criteria were as follows: 1) > 2 HCCs or diffuse type, 2) tumors adjacent to the portal or hepatic veins with < 5 mm proximity, 3) invisible tumor on ultrasonography (US)-MR/CT fusion technique, 4) presence of macrovascular invasion or extrahepatic metastasis (EM), or 5) severe coagulopathy or bleeding tendency (platelet count ≤ 50000/mm³ or international normalized ratio (INR) prolongation ≥ 50%). HCC was diagnosed based on its typical hallmarks on CT or the Korean guidelines for HCC management [19].

Group Assignment

Participants underwent a 1:1 random assignment to the NT-RFA or conventional-RFA group by stratified randomization and block randomization (Fig. 1). Randomization was stratified by the size of the tumor (< 2 cm or 2–2.5 cm), number of tumors (single or two), and type of HCC (treatment-naive or recurrent). The randomization process was performed using a web-based randomization service managed by our institution’s medical research collaboration center. Study participants and those assessing outcomes were blinded to group assignments.

RFA Procedure

One radiologist with 20 years of experience in
percutaneous RFA performed all RFA procedures with assistance from one radiology fellow or resident, on an inpatient basis, under conscious sedation. For RFA procedure planning, pre-procedural CT or MRI studies were reviewed, followed by real-time US-CT/MR fusion imaging (Easy fusion, Samsung Medison) for localization of the target lesion and evaluation of technical feasibility [20]. The detailed RFA procedure of conventional RFA with tumor puncture using twin internally cooled wet (TICW) electrodes (CWTN-T, RF Medical) is described in Supplement.

NT-RFA : bipolar RFA was performed using TICW electrodes and the same generator unit used in the conventional RFA group. For the NT-RFA technique, the two tines of TICW electrodes were inserted into the perimeter of the index tumor (generally 3–5 mm from the margin of the target tumor) at an inter-electrode distance of 2–3 cm, depending on tumor size, under the guidance of real-time US-CT/MR fusion imaging [14,15,17,21]. An example case is shown in Figure 2. However, if there was no safe route for insertion of electrodes into the target tumor using the NT technique under multimodality fusion imaging, we converted patients from the NT-RFA group to the conventional RFA group. Furthermore, if the electrode incidentally passed through the tumor, it was recorded and regarded as an unintentional protocol change into conventional RFA, and the conversion rates of NT-RFA to conventional RFA were calculated. An example of a converted case is shown in Figure 3.

Evaluation of Procedure and Follow-Up
After the completion of RFA procedures, multiphasic contrast-enhanced CT studies were immediately conducted to assess ablation size, post-procedural complications, and technical success based on the reporting criteria suggested by the International Working Group on Image-guided Tumor Ablation [22]. Technical success of RFA was defined as complete coverage of the target tumor by the ablation zone on immediate follow-up CT or MRI [22] (Fig. 2). Post-procedural complications were also evaluated according to the guidelines of the Society of Interventional Radiology [23]. A detailed evaluation of the ablation zone and sufficiency of the margin (> 5 mm) is described in Supplement. Any residual enhancement at the ablation margin was considered to be an unablated residual tumor [24], and patients underwent additional ablation on the same day.

After RFA, contrast-enhanced CT or MRI was performed one month after RFA, and every 3 months to detect LTP, intrahepatic distant recurrence (IDR), and EM during the initial 2 years, after which the interval for CT or MRI was adjusted according to the clinician’s decision in the range of 3–6 months [22]. Technical efficacy was defined as
complete coverage of the target tumor by the ablation zone, assessed by imaging at one-month follow up. LTP was defined as newly appearing tumor foci at the margin of the ablation zone after achieving treatment success in a follow-up study with contrast-enhanced CT or MRI [22].

Outcomes

The primary endpoint was to compare the cumulative incidence of LTP between the NT-RFA and conventional RFA groups. In addition, we determined the NT-RFA to conventional RFA conversion rates and evaluated the cumulative incidence of LTP in study patients according
to the received RFA techniques (as-treated analysis). As secondary endpoints, we also compared IDR, EM, and the following procedural characteristics between the two groups: technical parameters, technical success, technical efficacy, and rates of complications.

### Statistical Analysis

The sample size was approximated to be 55 patients in each group, but based on interim analysis, the study was terminated early in 78 patients (details in Supplement). Statistical evaluation was performed for the intention-to-treat analysis according to the initially assigned group and the as-treated analysis according to the actual treatment method [25]. Demographic factors and technical parameters were analyzed using the chi-squared test or Fisher’s exact test for categorical variables and the independent t test for continuous variables. Technical success, technique efficacy, and LTP rates were analyzed using per-nodule data, based on the as-treated analysis. The Kaplan-Meier method and log-rank test were used for survival analysis between the two groups. Cox proportional hazards regression analysis was performed to evaluate predictors of LTP (details in Supplement). Variables with a p value < 0.2, on univariable analysis, were included in the multivariable analysis. Statistical significance was set at p < 0.05. All statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp.) and R Statistical Software (version 4.0.3, R Foundation for Statistical Computing). Our institutional Medical Research Collaborating Center supported us in carrying out the statistical methodology.

### RESULTS

#### Participant Enrollment

Between July 2016 and September 2018, we screened 78 potentially eligible patients who were referred for RFA for study enrollment. Five patients were excluded for the following reasons: poor visibility despite fusion imaging (n = 1), refusal to submit informed consent (n = 2), and poor liver function (n = 2). Seventy-three participants with 76 HCCs were enrolled and randomly assigned to the

| Table 1. Characteristics of Patient Groups for Intention-to-Treat Analysis |
|---------------------------------|---------------------------------|-----------------|---|
| **Category** | **Conventional RFA (36 Patients with 38 HCCs)** | **NT-RFA (37 Patients with 38 HCCs)** | **P** |
| Sex, M:F | 27:11 | 27:11 | > 0.999 |
| Age, year | 62.5 ± 7.7 | 66.1 ± 11.8 | 0.118 |
| Origin of liver cirrhosis | | | |
| Hepatitis B virus-related | 24 | 27 | 0.464 |
| Hepatitis C virus-related | 8 | 7 | 0.773 |
| Alcoholism | 4 | 7 | 0.328 |
| Tumor number | | | 0.692 |
| One | 34 | 35 | |
| Two | 2* | | |
| Tumor location | | | 0.761 |
| Subcapsular | 6 | 7 | |
| Central | 32 | 31 | |
| Type of tumor | | | 0.312 |
| Naïve HCC | 23 | 28 | |
| Recurrent HCC | 13 | 9 | |
| Tumor size, cm | 1.63 ± 0.48 | 1.74 ± 0.45 | 0.230 |
| Lab | | | |
| Total bilirubin, mg/dL | 0.80 ± 0.58 | 0.81 ± 0.36 | 0.944 |
| Prothrombin time, INR | 1.07 ± 0.12 | 1.06 ± 0.09 | 0.751 |
| Albumin, g/dL | 3.97 ± 0.48 | 3.96 ± 0.42 | 0.920 |
| Platelet, 10^3/µL | 123.8 ± 54.2 | 134.4 ± 55.9 | 0.406 |
| Alpha fetoprotein, ng/mL | 236.0 ± 1269.3 | 48.8 ± 131.8 | 0.382 |
| Follow-up period, months | 30.6 ± 13.3 | 31.3 ± 11.4 | 0.664 |

Data are patient number or average ± standard deviation. *In one patient, only one of the two tumors was treated because of a poor sonic window. HCC = hepatocellular carcinoma, INR = international normalized ratio, NT = no-touch, RFA = radiofrequency ablation.
two groups. Four participants in the NT-RFA group were converted to conventional RFA. Therefore, the intention-to-treat analysis involved 36 conventional RFA participants with 38 HCCs vs. 37 NT-RFA participants with 38 HCCs, and the as-treated analysis comprised 40 conventional RFA participants with 42 HCCs vs. 33 NT-RFA participants with 34 HCCs (Fig. 1). There were no statistically significant differences in demographic factors and tumor characteristics between the groups (Tables 1, 2).

**Procedure Characteristics**

Procedure-related technical parameters according to intention-to-treat analysis are presented in Table 3. There were no significant differences in ablation size (Dmax, Dmin, Dv), ablation volume, effective ablation volume, and technical parameters, including procedure time, ablation time, and total energy in both groups (Table 3).

Among the NT-RFA group, conversion to conventional RFA was performed in four patients (10.8%, 4/37). The main reasons for conversion in these four patients were the lack of a safe access route and subcapsular location with insufficient peritumoral parenchyma (< 5 mm) (Fig. 3). According to the as-treated analysis, 76.1% (32/42) of patients achieved sufficient ablation margin (> 5 mm) in the conventional RFA group, while NT-RFA group patients achieved a higher rate of sufficient ablation margin (88.2%, 30/34), albeit without statistical significance (p = 0.178). Technical success was achieved in all cases. The technique efficacy rates of the conventional and NT-RFA groups at the 1-month follow-up were 100% (42/42) and 94.1% (32/34), respectively (p = 0.111). The mean follow-up period was 30.9 ± 12.3 months (median: 33.2 months).

**Procedure-Related Complications**

In the NT-RFA group, there were no procedure-related deaths or major complications. There was only one major complication of bleeding during the immediate follow-up CT in the conventional RFA group, which had spontaneously stopped on follow-up hepatic angiogram. There were also no significant differences between the two groups in minor

| Category                  | Conventional RFA (40 Patients with 42 HCCs) | NT-RFA (33 Patients with 34 HCCs) | P  |
|---------------------------|--------------------------------------------|----------------------------------|----|
| Sex, M:F                  | 29:12                                      | 25:9                             | 0.668 |
| Age, year                 | 63.4 ± 7.9                                 | 65.5 ± 12.2                      | 0.392 |
| Causes of liver cirrhosis |                                            |                                  |     |
| Hepatitis B virus-related  | 27                                          | 24                               | 0.561 |
| Hepatitis C virus-related  | 8                                           | 7                                | 0.867 |
| Alcoholism                | 4                                           | 7                                | 0.173 |
| Tumor number              |                                            |                                  | 0.916 |
| One                       | 38                                          | 31                               |     |
| Two                       | 2                                            | 2*                               |     |
| Tumor location†           |                                            |                                  | 0.468 |
| Subcapsular               | 6                                           | 7                                |     |
| Central                   | 36                                          | 27                               |     |
| Type of tumor             |                                            |                                  | 0.668 |
| Naïve HCC                 | 27                                          | 24                               |     |
| Recurrent HCC             | 13                                          | 9                                |     |
| Tumor size, cm            | 1.65 ± 0.49                                 | 1.71 ± 0.44                      | 0.606 |
| Lab                       |                                            |                                  |     |
| Total bilirubin, mg/dL    | 0.80 ± 0.56                                 | 0.81 ± 0.37                      | 0.897 |
| Prothrombin time, INR     | 1.07 ± 0.12                                 | 1.06 ± 0.09                      | 0.601 |
| Albumin, g/dL             | 3.94 ± 0.48                                 | 3.97 ± 0.47                      | 0.881 |
| Platelet, 10^9/µL         | 122.5 ± 52.0                                | 137.3 ± 58.0                     | 0.246 |
| Alpha fetoprotein, ng/mL  | 215.2 ± 1207.5                              | 52.7 ± 139.4                     | 0.452 |
| Follow-up period, months  | 30.7 ± 13.3                                 | 31.3 ± 11.4                      | 0.850 |

Data are patient number or average ± standard deviation. *In one patient, only one of the two tumors was treated because of a poor sonic window, †Tumor location was classified as a subcapsular or central tumor, based on whether it was within 1 mm from the liver capsule [34]. HCC = hepatocellular carcinoma, INR = international normalized ratio, NT = no-touch, RFA = radiofrequency ablation
complications, based on the as-treated analysis (n = 1, NT-RFA group; n = 2, conventional RFA group; \( p = 0.673 \)). Minor thermal injuries were reported in three of the cases in post-procedure CT: two cases in the gallbladder (one in each group) and one case in the stomach (conventional RFA group). None of the patients required additional medical treatment.

### Outcome-LTP, IDR, and EM

In the intention-to-treat analysis, the estimated 1-year and 3-year cumulative incidences of LTP were both 5.6% in the NT-RFA group, and 11.8% and 21.3%, respectively, in the conventional RFA group. The two groups did not differ significantly in LTP rates (log-rank test, \( p = 0.073 \)) (Fig. 4A). In the as-treated analysis, the estimated 1-year and 3-year cumulative incidences of LTP were both 0% in

### Table 3. Comparison of Technical Parameters between the Two Groups according to Intention-to-Treat Analysis

| Category          | Conventional RFA (36 Patients with 38 HCCs) | NT-RFA (37 Patients with 38 HCCs) | \( p \)  |
|-------------------|---------------------------------------------|-----------------------------------|--------|
| Power, W          | 29.4 ± 6.6                                  | 26.9 ± 4.9                        | 0.071  |
| Current, A        | 0.32 ± 0.05                                 | 0.30 ± 0.05                       | 0.190  |
| Impedance, Ω      | 100.9 ± 46.8                                | 93.34 ± 23.19                     | 0.374  |
| Energy, kcal      | 13.5 ± 8.0                                  | 13.1 ± 6.9                        | 0.856  |
| Ablation time, min| 12.08 ± 5.06                                | 12.12 ± 5.10                      | 0.973  |
| Dmax, cm          | 48.7 ± 8.0                                  | 50.6 ± 12.2                       | 0.420  |
| Dmin, cm          | 33.9 ± 5.7                                  | 35.6 ± 6.6                        | 0.218  |
| Dv, cm            | 54.0 ± 13.4                                 | 54.0 ± 13.7                       | 0.983  |
| Vab, mL*          | 48.7 ± 20.9                                 | 55.0 ± 31.3                       | 0.306  |
| Veff, mL†         | 22.1 ± 11.4                                 | 26.1 ± 14.4                       | 0.180  |
| Dmin/Dmax         | 0.70 ± 0.10                                 | 0.72 ± 0.14                       | 0.425  |
| Procedure time, min| 46.4 ± 12.8                                 | 48.8 ± 12.7                       | 0.431  |

Data are average ± standard deviation. *Vab - ablation volume \( (V = \pi/6 \times D_{\text{max}} \times D_{\text{min}} \times D_v) \), †Veff - effective ablation volume \( (V = \pi/6 \times D_{\text{min}}^3) \). HCC = hepatocellular carcinoma, NT = no-touch, RFA = radiofrequency ablation

Fig. 4. Comparison of cumulative incidences of local recurrence between the two groups (A) at intention-to-treat analysis and (B) as-treated analysis. *Graphs were obtained using Kaplan-Meier survival curves, and \( p \) values were calculated using the log-rank test. LTP = local tumor progression, RFA = radiofrequency ablation
In this prospective randomized controlled trial, NT-RFA using TICW electrodes demonstrated better LTP than conventional RFA using tumor puncture. According to the as-treated analysis, the estimated 1- and 3-year cumulative incidences of LTP were 0% in the NT-RFA group, which was significantly lower than the 15.6% and 24.5% in the conventional RFA group. In addition, the complication rate of NT-RFA (3.3%, 1/33) was shown to be similar to that of conventional tumor puncture RFA (7.5%, 3/40). Indeed, our study results are in good agreement with several previous retrospective studies [13,14,16,26] and a prospective cohort study [17] reporting lower LTP rates of NT-RFA with bipolar electrodes compared to conventional RFA with a monopolar electrode. However, while previous studies utilized different numbers and types of RF electrodes, as well as different RF energy delivery modes on both NT-RFA and conventional RFA groups, our study used the same RF equipment and RF delivery mode for both groups, suggesting that the better LTP rates of NT-RFA are due to the absence of tumor puncture.

**DISCUSSION**

The cumulative incidences of these analyses are summarized in Table 5.

**Table 4. Univariable and Multivariable Cox Regression Analyses in as-Treated Analysis of Risk Factors for Local Tumor Progression**

| Characteristics          | Univariable |          | Multivariable |          |
|--------------------------|-------------|----------|---------------|----------|
|                          |   P         | Hazard Ratio | 95% CI       |   P      |
| Sex                      | 0.762       |           |               |          |
| Age, year                | 0.844       |           |               |          |
| Tumor size, cm           | 0.328       |           |               |          |
| Tumor number             | 0.541       |           |               |          |
| Treatment history        | 0.337       |           |               |          |
| Tumor location           | 0.194       | 0.65     | 0.12–6.08     | 0.668    |
| Total bilirubin, mg/dL   | 0.423       |           |               |          |
| Prothrombin time, INR    | < 0.001     | 268.0    | 0.44–2.7 x 10^3 | 0.086   |
| Albumin, g/dL            | 0.016       | 0.82     | 0.16–3.80     | 0.795    |
| Platelet, 10^9/µL        | 0.204       |           |               |          |
| Alpha fetoprotein, ng/mL | 0.224       |           |               |          |
| Ablation volume, mL      | 0.440       |           |               |          |
| RFA type                 |             |           |               |          |
| NT-RFA vs. conventional RFA as reference | 0.002 | 0.061 | 0–0.497 | 0.004 |

Penalized maximum likelihood estimation was used in predictable factors with separation. CI = confidence interval, INR = international normalized ratio, NT = no-touch, RFA = radiofrequency ablation

**Table 5. Cumulative Incidences of Recurrence according to Intention-to-Treat and as-Treated Analysis**

| Outcome Parameter | Conventional RFA (%) | NT-RFA (%) |
|-------------------|----------------------|------------|
|                   | 1 Year | 2 Year | 3 Year | 1 Year | 2 Year | 3 Year | 1 Year | 2 Year | 3 Year |  P  |
| LTP                |        |        |        |        |        |        | 15.6   | 24.5   | 24.5   | 0.004 |
| IDR                |        |        |        |        |        |        | 33.1   | 44.3   | 47.2   | 0.746 |
| EM                 |        |        |        |        |        |        | 2.6    | 11.2   | 17.1   | 0.380 |

Among the NT-RFA group patients (n = 37), conversion to conventional RFA was performed in 4 patients (10.8%, 4/37) due to a lack of a safe access route and subcapsular location with insufficient peritumoral parenchyma (< 5 mm). EM = extrahepatic metastases, IDR = intrahepatic distant recurrence, LTP = local tumor progression, NT = no-touch, RFA = radiofrequency ablation
were due to the oncologically favorable features of the NT-RFA technique. Based on our study results, NT-RFA may be preferentially used for the treatment of small HCCs ≤ 2.5 cm compared to conventional RFA with tumor puncture.

Of note, although NT-RFA showed better LTP rates than conventional RFA, there was no significant difference in ablation size between the two groups. These results regarding ablation size could be attributed to the fact that if necessary to acquire optimal ablation margin, additional cycles of RFA were performed after repositioning of the electrode(s) in both groups. Therefore, the better LTP results of NT-RFA could be explained by several factors. First, the higher energy deposition in the peritumoral ablative margin, related to the geometry between the tumor and electrodes, in the NT-RFA group, might be an important contributing factor. According to a previous multicenter study [27], NT-RFA showed better LTP than standard monopolar RFA for HCCs located near large vessels, because more homogenous and extensive tissue necrosis and ablation zones were achieved beyond the macroscopic tumor boundary by placing the needles away from the tumor periphery. Second, blockage of drainage vessels from the target tumor may have been achieved in the study groups after RFA. Finally, our study results were achieved after ethanol injection, resulting in a lower risk of track seeding along the electrode [30].

In our study, four patients (10.8%, 4/37) were converted from the NT-RFA technique to the conventional RFA technique. This represents the technical difficulty of NT-RFA compared to conventional tumor puncture RFA, as NT-RFA necessitates the insertion of multiple electrodes outside the target tumor with ideal geometry to create an ablative margin around the tumor [13,31]. The insertion of two electrodes around the tumor, at equidistance, while avoiding vital structures, can be technically challenging under the guidance of the US. In that regard, real-time fusion guidance or CT guidance might be more advantageous than US guidance. We found that real-time US-CT/MR fusion guidance was very useful for placing electrodes in an ideal peritumoral position as it can provide better conspicuity of the target tumor as well as adjacent vascular structures or organs compared with B-mode US guidance [20,32,33]. Thus, to lower the technical difficulty of NT-RFA, additional modifications of RF energy delivery modes, such as combined bipolar and monopolar modes, could be used for NT-RFA. In this regard, further studies on the ideal RF delivery mode for NT-RFA, especially for larger tumors (≥ 3 cm), are warranted. Moreover, NT-RFA had great difficulty in placing the electrodes in the surrounding peritumoral liver parenchyma for subcapsular located tumors, especially near the hepatic angle or hepatic dome portion, and this was the main cause of conversion of NT-RFA to conventional RFA.

In conclusion, NT-RFA using TIWC electrodes in bipolar mode demonstrated significantly lower cumulative LTP rates
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than conventional RFA for small HCCs, which warrants a larger study for further confirmation.

**Supplement**

The Supplement is available with this article at https://doi.org/10.3348/kjr.2021.0319.

**Conflicts of Interest**

Jeong Min Lee received a research grant from RF Medical Co., Ltd. Other authors have no potential conflicts of interest to disclose.

**Acknowledgments**

We thank Chris Woo, BA for his English editing.

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