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의학 석사 학위 논문

Fluoroscopy-guided Radiofrequency
Ablation for Hepatocellular Carcinoma
Invisible on Ultrasonography:
A Retrospective Comparison with
Ultrasound-guided Ablation

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Fluoroscopy-Guided Radiofrequency Ablation for Hepatocellular Carcinoma Invisible on Ultrasonography: A Retrospective Comparison with Ultrasound-Guided Ablation

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Fluoroscopy-Guided Radiofrequency Ablation for Hepatocellular Carcinoma Invisible on Ultrasonography: A Retrospective Comparison with Ultrasound-Guided Ablation

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ABSTRACT

Introduction: Fluoroscopy-guided radiofrequency (RF) ablation is an emerging targeting strategy for hepatocellular carcinoma (HCC) invisible on ultrasonography (US). The purposes of this study were to evaluate the technical feasibility of this technique and to compare its therapeutic efficacy with that of US-guided RF ablation.

Methods: Between January 2006 and January 2012, 93 patients with 104 small HCCs (mean diameter 1.8 ± 0.5 cm) underwent percutaneous RF ablation. In 42 patients with 46 HCCs invisible on US, fluoroscopy-guided RF ablation was performed following chemoembolization (group A). The remaining 51 patients with 58 HCCs received US-guided RF ablation (group B). Technical success, technical effectiveness, complications, local tumor progression, and patients' survival were retrospectively compared between the two groups.

Results: Forty-five HCCs of group A became visible on fluoroscopy after chemoembolization, and RF ablation was technically successful (97.8%). Technical effectiveness was achieved in 45 HCCs of group A (97.8%) and 64 HCCs of group B (96.6%) ($p = 0.65$). There was no major complication in either group. The 1-, 3-, 5-year local tumor progression rates were lower in group A than those of group B

with marginal significance (0%, 3.7%, and 3.7% in group A vs. 13.0%, 13.0%, and 13.0% in group B) ($p = 0.05$). The 1-, 3-, 5-year overall patients' survival rates were 100%, 58.3%, and 51.2% (group A) and 82.4%, 54.9%, and 46.1% (group B) ($p = 0.26$). The 1-, 3-, 5-year recurrence-free survival rates were 68.8%, 37.5% and 25.3% (group A) and 48.7%, 27.8%, and 21.6% (group B) ($p = 0.38$).

Conclusions: Fluoroscopy-guided RF ablation following chemoembolization is a feasible and safe therapeutic option for small HCC invisible on US. Its therapeutic effect was comparable with that of US-guided RF ablation.

Keywords: Hepatocellular carcinoma, Radiofrequency ablation, Fluoroscopy

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INTRODUCTION

Percutaneous radiofrequency (RF) ablation is now accepted as one of the curative treatments for small hepatocellular carcinomas (HCCs) (1). Ultrasonography (US) is most commonly used imaging modality for targeting tumors during the procedure (2). However, tumor localization can be problematic in some cases, because many HCCs are not visualized on US due to their unfavorable location or isoechogenicity with the surrounding cirrhotic liver parenchyma (3). CT is another imaging modality that is commonly used for ablation therapy, but tumors invisible on US are frequently invisible on non-contrast CT as well (4).

To address this limitation, many strategies have been developed including contrast-enhanced US (5), CT/MR-US fusion imaging (6), and percutaneous coil placement (7). Fluoroscopy-guided RF ablation shortly following chemoembolization is one of these alternative targeting strategies (8). Intra-tumoral retention of iodized oil induced by chemoembolization provides radiographic contrast to the index lesion, and thus, it can serve as a landmark to facilitate targeting an index tumor under fluoroscopic guidance. Recently, several studies suggested excellent technical feasibility of fluoroscopy-guided RF ablation in treating US-invisible HCC (6, 9, 10). However, there have been only limited data including case reports or small case series. Moreover, to confirm its clinical usefulness, not only technical feasibility but also therapeutic efficacy should be verified. However, to our knowledge, there has been no study comparing the therapeutic efficacy

between this technique and conventional targeting methods. Therefore, the purposes of this study were to retrospectively assess the technical feasibility of fluoroscopy-guided RF ablation for small HCCs invisible on US and to compare its therapeutic efficacy with that of US-guided RF ablation.

MATERIALS AND METHODS

Patients

This retrospective study was approved by our hospital institutional review board. The requirement to obtain informed consent was waived. A search of our department database identified 191 patients who had undergone percutaneous RF ablation for HCC between January 2006 and January 2012. Ninety-eight patients were excluded because of i) HCC larger than 3 cm (n = 26) or ii) previous treatment for index tumor (n = 72). Therefore a total 93 patients with 104 small HCCs were enrolled in this study. In 42 patients with 46 HCCs, fluoroscopy-guided RF ablation was performed following chemoembolization (group A). Fluoroscopy-guided RF ablation was attempted only when the tumors were invisible on US because their isoechogenicity to the liver parenchyma (12 tumors, 26%) or unfavorable location (subphrenic [30 tumors] or subcapsular [4 tumors]). The remaining 51 patients with 58 HCCs received US-guided RF ablation (group B) (Figure 1).

All patients received a routine physical examination, laboratory tests, and imaging studies within 1 week before treatment. Imaging studies including US and contrast enhanced liver CT and/or MR were performed within 2 weeks before RF ablation. The diagnosis of HCC was based on American Association for the Study of Liver Diseases (AASLD) guidelines (11) as follows: typical vascular pattern (hypervascular in the arterial phase, and wash-out in the portal/delayed phase) of liver nodule in at least one of the contrast enhanced CT or MR, or a serum α -fetoprotein value exceeding 200 ng/mL. Histopathologic confirmation was obtained

in 29 patients. Tumor size was defined as the maximum diameter measured on CT or MR, and the segmental location of the tumor was determined based on Couinaud nomenclature. The patients' backgrounds and tumor characteristics are presented in table 1.

Procedures

Written informed consent was obtained from each patient before the procedures. All procedures were performed on an inpatient basis by three interventional radiologists (S.K., C.Y., and N.S.) with 15, 10, and 7 years of experience of chemoembolization and RF ablation at the beginning of this study. The patients received 0.05–0.1 mg of fentanyl citrate and 1.0–5.0 mg of midazolam for pain control; 5–15 mL of 1% lidocain was used for local anesthesia. Prophylactic antibiotics were not used before or after the procedure.

In group A, chemoembolization was performed before RF ablation according to previously published protocol (12). After celiac and superior mesenteric arteriography using a 5-F angiographic catheter (Cook, Bloomington, IN), the hepatic artery was catheterized. Then, a 3-F microcatheter (MicroPheret, Cook; Renegade, Boston Scientific, Natick, USA) was used to select the feeding arteries of the tumor. An emulsion of 1–3 mL of iodized oil (Lipiodol Ultra Fluid; Andre Guerbet, Aulnay-sous-Bois, France) and 10–20 mg of doxorubicin hydrochloride (Adriamycin RDF; Ildong Pharmaceutical, Seoul, Korea) was injected into the feeding arteries. The endpoint of chemoembolization was

identification of iodized oil retention in the index tumor on fluoroscopy and/or stasis of feeding arterial flow. The 5-F angiographic catheter was left in place for a post-RF ablation arteriography. Immediately after chemoembolization, fluoroscopy-guided RF ablation was performed. We used two commercially available RF systems: An internally cooled electrode with a 3 cm exposed tip (Cool-tip RF Ablation System; Valleylab, Boulder, Colorado) was used in 22 patients, and a multitined expandable electrode (Radiotherapeutic RF Ablation System; Boston Scientific, Natick, Massachusetts) was used in 20 patients. One RF electrode was used for each patient. After an appropriate RF electrode entry site was marked on the patient's skin with US, the RF electrode was advanced into the liver parenchyma aiming at the iodized oil accumulated in the index tumor(s) under fluoroscopy guidance. For subphrenic tumors, an oblique approach from the lower intercostal space was used rather than a transthoracic approach. US was concurrently used to avoid the traversal of critical structures such as large vessels and the gallbladder. Adequate position of the electrode into the index tumor was confirmed on multiple projections of fluoroscopy. When treating subphrenic tumor close to diaphragm, the distal end of the electrode was positioned not to pass through the diaphragm on lateral projection of fluoroscopy. RF energy was applied for 8–12 min for each tumor. When the tumor diameter was greater than 2 cm, multiple overlapping ablations were applied as needed, depending on tumor size, shape and location. At the end of the procedure, the electrode tract was ablated to prevent bleeding or tumor seeding. Immediately after RF ablation, a hepatic arteriogram was obtained to exclude arterial bleeding. Each patient was treated in

one treatment session (93 sessions for 104 tumors).

In group B, RF ablation was performed under US guidance. All RF devices and techniques were same with those in group A except guidance methods (fluoroscopy vs. US).

Follow-up Assessment

Follow-up contrast-enhanced CT or MR was obtained at 1 month after the procedures. Thereafter, the patients were followed up every 3-4 months using liver function tests, serum a-fetoprotein and liver CT/MR.

The standardized definitions were used to assess technical and clinical effectiveness of the procedures as follows (13); Technical success was defined as RF electrode was placed into the planned site and ablation was completed with a planned protocol. Technical effectiveness was defined as eradication of tumor enhancement with surrounding hypoattenuating non-enhancing area on 1-month follow up CT/MR. Local tumor progression was defined as the development of a new enhancing lesion within or adjacent to the ablation site on follow-up CT/MR. Distant metastasis was defined as a new HCC in the liver distant from the index tumor or in the extrahepatic regions. Two radiologists who had specialized in abdominal imaging for 10 and 12 years at the beginning of our study evaluated the CT/MR images.

Complications were assessed according to previously described guidelines on the basis of the number of ablation sessions (13, 14). Major complication was

defined as an event that led to substantial morbidity and disability, increasing the level of care, or resulted in hospital admission or substantially lengthened hospital stay. All other complications were considered minor. Patients were followed up until loss of follow-up or death on January 30, 2013. All patients were followed up for more than a year after the procedures.

Statistical Analysis

Comparison of baseline data between the two groups was conducted using the Student t test for the continuous variables and Fisher's exact test for categorical variables. The local tumor progression rate and survival rates (overall survival and recurrence-free survival) were estimated with the Kaplan–Meier method. The local tumor progression rate was calculated on a tumor basis; the overall survival rate was calculated on a patient basis. The differences in the survival rates between the two groups were compared using the log-rank test. Child–Pugh scores before and 4 weeks after treatment were compared using Wilcoxon's rank sum test. A *p* value of < 0.05 was assumed to be statistically significant. Statistical analyses were carried out with commercially available software (SPSS, Chicago, Illinois).

RESULTS

Technical Success and Technical Effectiveness

In group A, 45 out of 46 HCCs became visible on fluoroscopy after chemoembolization. In the 45 tumors, the RF electrodes were correctly positioned at the planned site of each tumor and RF ablation was completed with a planned protocol (Figure 1). The mean number of overlapping ablations was 2.2 per tumors (range 1–3). The overall ablation time was 18 min (range 8–40 min). Technical failure occurred in one patient with 1.6 cm subphrenic tumor. The tumor was not detected on hepatic angiogram and segmental chemoembolization was performed based on CT-documented tumor location. However, the tumor was not visualized on fluoroscopy after chemoembolization, which precluded subsequent RF ablation. Thus, based on intention-to treat analysis, technical success of group A was achieved in 97.8% (45/46). In group B, technical success was achieved in all patients (100%). The mean number of overlapping ablations was 2.2 per tumors (range 1–3). The overall ablation time was 20 min (range 8–40 min). All patients of the two groups tolerated the procedure well, with no complication during the procedures.

Technical effectiveness based on 1 month follow-up CT/MR was achieved in 45 tumors of group A (Figure 2) and 56 tumors in group B. Tumor enhancement disappeared and a sufficient ablative margin was apparent after one session of treatment. Therefore, technical effectiveness rates were 97.8% in group A and 96.6% in group B. There was no significant difference of technical effectiveness between

the two groups ($p = 0.65$).

Local tumor progression and distant metastases

In group A, the median follow-up period was 40.4 months (range, 13.3–82.3 months). During the follow-up period, one local tumor progression (2.1%, 1 out of 46) was found in one patient at 25 months after the treatment (Figure 3). Therefore, the 1-, 3-, and 5-year local tumor progression rates of group A were 0%, 3.7%, and 3.7% on a tumor basis, respectively. In group B, during the median of 42.9 months of follow-up period (range, 12.3–76.3 months), local tumor progressions occurred in 7 tumors (12.1%, 7 out of 58) of 7 patients at 3, 6, 7, 9, and 12 months after the treatment. The 1-, 3-, and 5-year local tumor progression rates were 13.0%, 13.0%, and 13.0%, respectively. The local tumor progression rates of group A were lower than those of group B with marginal significance ($p = 0.05$) (Figure 4).

In group A, 25 patients (59.5%) experienced intrahepatic ($n = 24$) and/or extrahepatic metastases ($n = 4$). The recurrent tumors were treated with RF ablation ($n = 10$), chemoembolization ($n = 22$), percutaneous ethanol injection ($n = 2$), surgical resection ($n = 2$), or transplantation ($n = 1$). In group B, 40 patients experienced intrahepatic ($n=36$) and/or extrahepatic ($n = 5$) recurrence (78.4%). The recurrent tumors were treated with RF ablation ($n = 13$), chemoembolization ($n = 28$), percutaneous ethanol injection ($n = 1$), surgical resection ($n = 4$), or transplantation ($n = 1$). The other 2 patients received no further treatments because

of poor liver profiles.

Patients' Survival

In group A, the cumulative overall survival rates at 1, 3, and 5 years were 100%, 68.3%, and 51.2%, respectively. The median survival time was 41.1 months. The overall survival rates of group B were 82.4%, 54.9%, and 46.1%, respectively (median 39.4 months). The overall survival rates were not significantly different between the two groups ($p = 0.26$) (Figure 5). The 1-, 3-, and 5-year recurrence-free survival rates were 68.8%, 37.5% and 25.3% in group A and 48.7%, 27.8%, and 21.6% in group B, respectively ($p = 0.38$) (Figure 6). At the end of the study period, 12 patients of group A had died 8.4–74.6 months (mean 31.8 ± 18.2 months) after the treatment. In group B, 10 patients had died 14.2–59.1 months (mean 35.1 ± 17.0 months) after the treatment. The causes of death included progression of HCC ($n = 10$), hepatic failure ($n = 5$), variceal bleeding ($n = 3$), postoperative complication ($n = 2$), and pneumonia ($n = 2$).

Complications

There was no major complication in both groups. Minor complications included fever, abdominal pain, and nausea/vomiting, which were resolved with medical management. No procedure related death was observed in either group. The mean baseline Child–Pugh score was 5.4 ± 0.6 in group A and 5.6 ± 1.0 in group B. The mean Child–Pugh scores 4 weeks after the procedures were 5.2 ± 0.6 in group

A and 5.5 ± 1.1 in group B. The baseline and 4 weeks Child-Pugh score were comparable between the two groups ($p = 0.26$ and $p = 0.44$, respectively).

Table 1. Patients' Backgrounds and Tumor Characteristics

Characteristics	Group A	Group B	P value
Number of patients	42	51	
Age, mean \pm SD	64 \pm 10.0	61 \pm 9.9	0.224
Gender			
Male	30 (71)	39 (76)	0.753
Female	12 (29)	12 (24)	0.753
Cause of cirrhosis			
HBV	31 (73)	36 (71)	0.911
HCV	6 (14)	7 (14)	1
other	5 (12)	8 (16)	0.824
Child-Pugh class			
A	39 (93)	44 (86)	0.494
B	3 (7)	6 (12)	0.691
C	0	1 (2)	1.000
Child-Pugh score	5.38 \pm 0.6	5.57 \pm 1.0	0.280
Number of tumors			
Single	38 (92)	44 (89)	0.763
2 or 3	4 (8)	7 (11)	0.763
Maximum tumor diameter			
\leq 2 cm	35 (83)	45 (88)	1
$>$ 2 cm	11 (17)	13 (12)	1
Alphafetoprotein			
\leq 100 ng/mL	36 (86)	38 (75)	0.365
$>$ 100 ng/mL	6 (14)	12 (24)	0.365
Previous treatment for HCC			
Yes	21 (50)	24 (47)	0.941
No	21 (50)	27 (53)	0.941

Note.—Numbers in parentheses are percentages

HBV hepatitis B virus, HCV hepatitis C virus, BCLC Barcelona Clinic Liver Cancer, NA not

Figure 1. Patients selection and study groups.

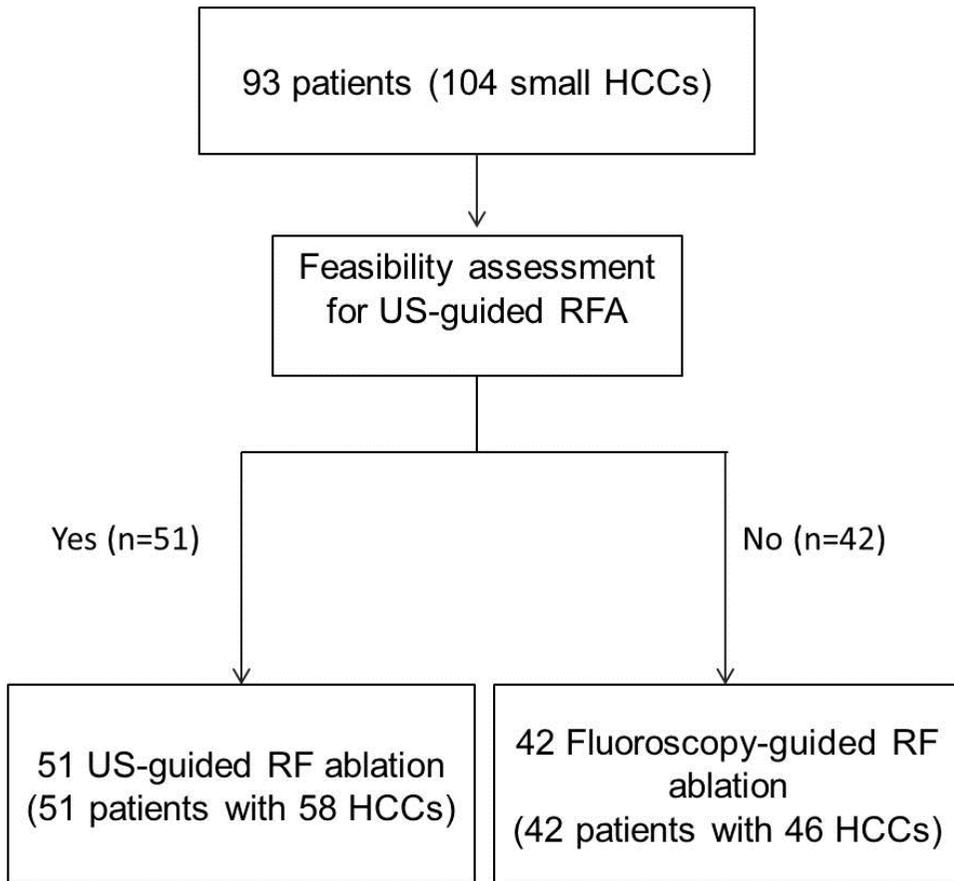
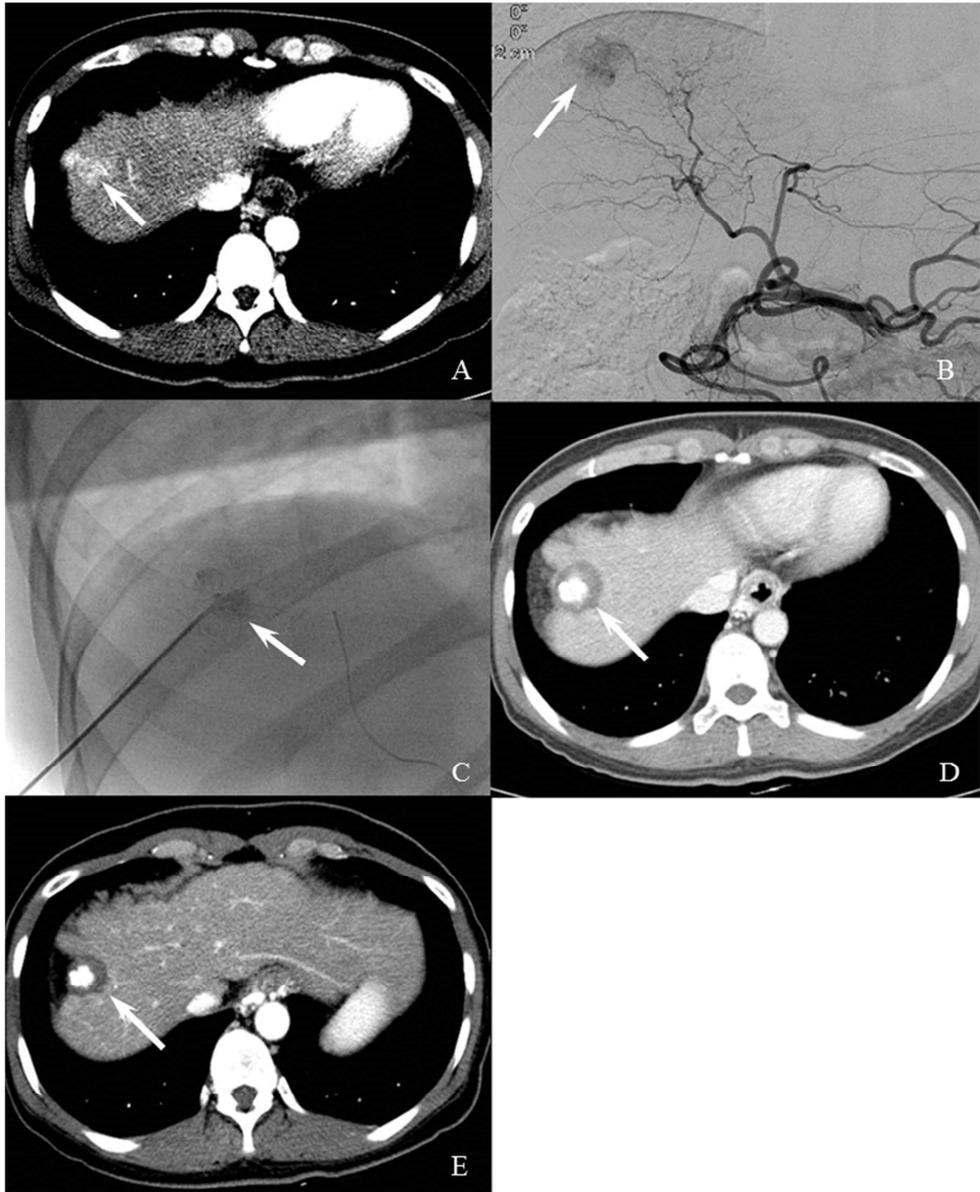
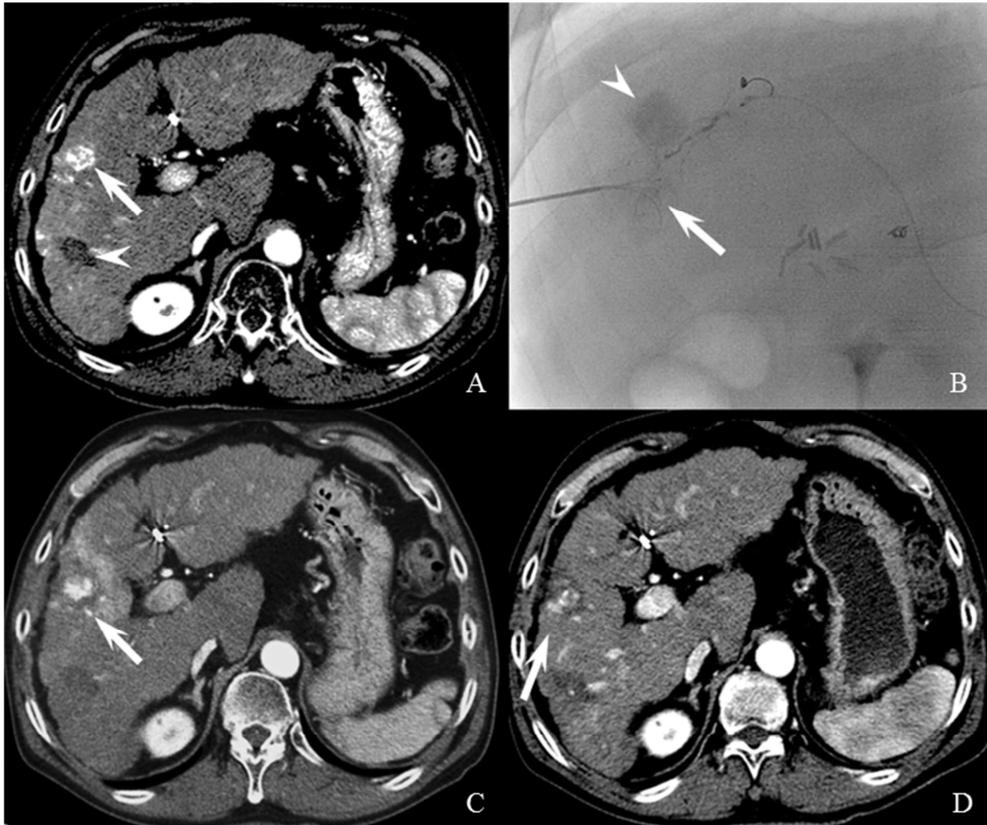


Figure 2. Images of a 46-year-old patient with a subphrenic HCC.



- A. An arterial phase liver CT showed a 2.3 cm contrast-enhancing tumor in right liver dome (arrow). The tumor was invisible on US because of its unfavorable location.
- B. A hepatic angiogram revealed a hypervascular tumor supplied by segment 8 hepatic artery (arrow).
- C. After chemoembolization, the tumor became visible on fluoroscopy, which facilitated RF ablation. Anteroposterior fluoroscopic image shows an expandable RF electrode accurately positioned into the index tumor with iodized oil retention (arrow).
- D. On 1-month follow-up CT, the ablation area completely surrounds the iodized oil retention in the index tumor (arrow).
- E. A follow-up CT obtained 14 months after treatment demonstrates shrink of the index tumor (arrows). There is no local or distant tumor recurrence.

Figure 3. Images of a 63-year-old patient with recurrent HCC.



- A. A contrast-enhanced CT shows a small HCC in hepatic segment 6 (arrow).
The tumor was not visualized on US due to its subcapsular location.
Arrowhead indicates previous RF ablation for HCC.
- B. Subsegmental chemoembolization was performed for opacification of the tumor (arrow). Immediately after chemoembolization, RF ablation was performed using a expandable electrode (arrowhead).
- C. On 1-month follow-up CT, the RF ablation area sufficiently surrounds the tumor with iodized oil retention (arrow).
- D. A local tumor progression was identified at the margin of ablation area (arrow) on 25-month follow-up CT.

Figure 4. Local tumor progression rates on a tumor basis after fluoroscopy- and US-guided RF ablation. The 1-, 3-, and 5-year local tumor progression rates were 0%, 3.7%, and 3.7% (group A) and 13.0%, 13.0%, and 13.0% (group B). The local tumor progression rates of group A were lower than those of group B with marginal significance ($p = 0.05$)

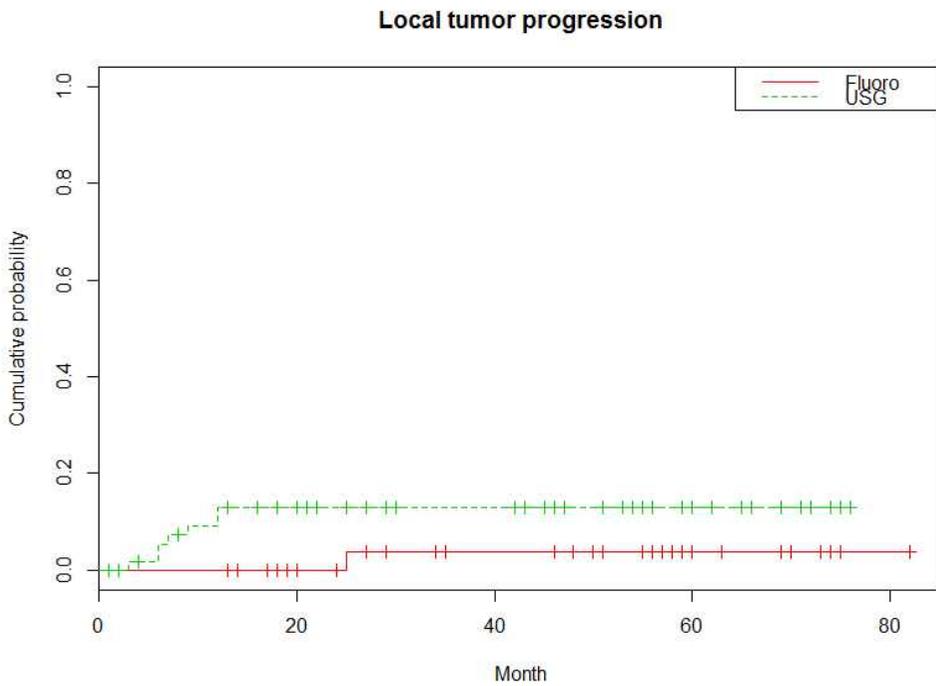


Figure 5. Overall patients' survival after fluoroscopy- and US-guided RF ablation.

In group A, the cumulative overall survival rates at 1, 3, and 5 years were 100%, 68.3%, and 51.2% (group A) and 82.4%, 54.9%, and 46.1% (group B). The overall survival rates were not significantly different between the two groups ($p = 0.26$).

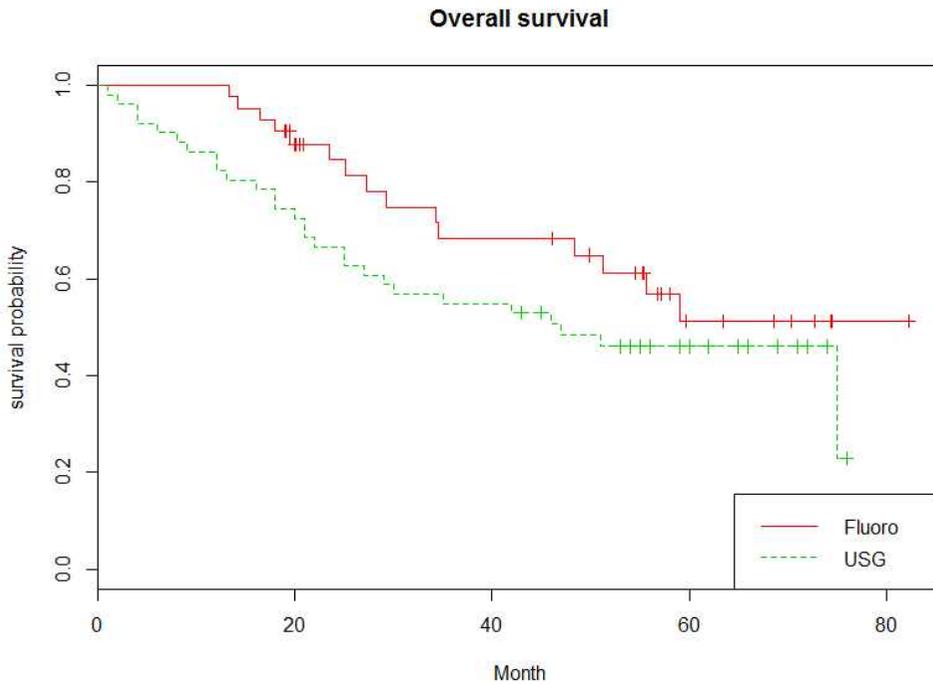
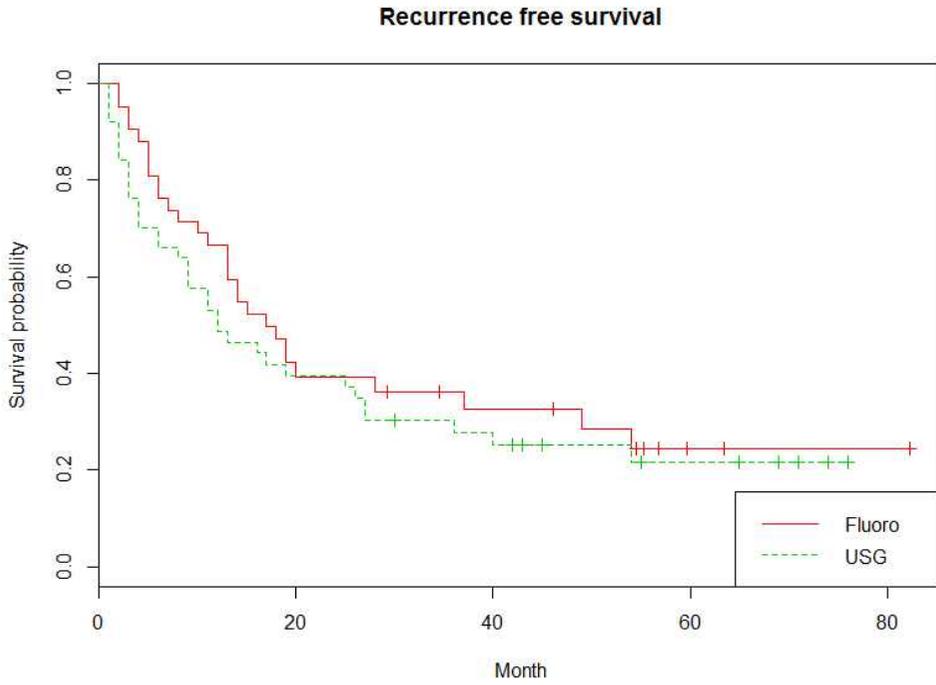


Figure 6. Recurrence-free survival after fluoroscopy- and US-guided RF ablation. The 1-, 3-, and 5-year recurrence-free survival rates were 68.8%, 37.5% and 25.3% in group A and 48.7%, 27.8%, and 21.6% in group B, respectively ($p = 0.38$)



DISCUSSION

Ultrasonography has been most widely used as a guiding modality for RF ablation. The virtues of US include easy availability, lower cost and real-time multiplanar imaging capability. However, HCCs are frequently not visualized on US due to their unfavorable location or isoechogenicity to the surrounding cirrhotic liver parenchyma (3). This limitation of US is getting more problematic as small HCCs are being detected more frequently than before with increasing use of CT or MR as a screening tool for HCC. Recently, Kim et al. (15) evaluated the technical feasibility of US-guided RF ablation for HCC. US-guided RF ablation was not feasible in about one-thirds of the candidates, mostly due to inability to visualize the tumors, especially for patients with smaller tumor and macronodular cirrhosis (15). Because of the limitation of US, CT has been implemented widely as an alternative guiding modality for RF ablation. However, US-invisible tumors are frequently invisible on non-contrast CT as well (4). Moreover, when performing CT-guided RF ablation for small tumors located in the liver dome, a steeply oblique approach or transthoracic access is required. The oblique approach may be technically cumbersome and time-consuming owing to limited range of CT gantry tilting. Transthoracic approach may be complicated with pneumothorax in up to 70% of cases (16). Another approach is to use MR guidance, which is time-consuming and applicable only to institutions equipped with a dedicated open MRI system and MR compatible RF ablation system (17). To resolve this dilemma, the use of fluoroscopic guidance has been attempted and reported in the literature, in which

radiopaque material is localized within or closely adjacent to the index tumor so that the exact or relative location of the tumor can be recognized by fluoroscopy. In previous studies, intra-tumoral retention of iodized oil or percutaneously placed metallic coils into the tumor could serve as a successful target point for RF ablation with fluoroscopic guidance (7, 8).

In our study, fluoroscopy-guided RF ablation following chemoembolization was technically successful for most HCC nodules (45/46, 97.8%). In 45 HCCs treated with this technique, technical effectiveness was obtained in all cases after single session of RF ablation, which was comparable with US-guided ablation (97.8% vs. 96.6%). This result supports the previous studies reporting excellent technical feasibility of this technique (95-100%) (18, 19), and suggests that fluoroscopy may be considered as a guiding method of choice when US-guided RF ablation is not feasible. The most important advantage of the fluoroscopy-guided procedure is that the index tumor can be accurately targeted regardless of their location. This is especially useful when treating liver dome lesions which are particularly challenging for RF ablation with other guiding modalities. In our series, 65% (30/46) of the tumors were located in the liver dome close to the diaphragm. Multiple projections of fluoroscopy provide real-time monitoring of diaphragmatic movement and simultaneous delineation of the RF electrode. Therefore, as long as the tumor became visible after chemoembolization, all subphrenic tumors could be confidently targeted and successfully ablated with a single session procedure. We used oblique approach of the electrode to avoid violation of the thorax or the pleura, and did not experience pneumothorax or

hemothorax.

Fluoroscopy-guided RF ablation also has some drawbacks. Because fluoroscopy does not provide clear soft tissue contrast, the RF electrode can pass through critical intrahepatic or extrahepatic structures. Therefore, complementary use of US is needed in some cases during the placement of the electrode. The iodized oil retention in index tumor can be variable according to tumoral vascularity. Therefore, as we experienced technical failure in one tumor (2.2%, 1/46), hypovascular HCC may not be visualized enough for accurate targeting on fluoroscopy. Takaki et al. (19) employed CT-fluoroscopy as a guiding modality for US-invisible small HCC and reported good clinical results. However, CT-fluoroscopy is associated with much higher radiation exposure than conventional fluoroscopy and more pneumothorax caused by transthoracic approach, just like CT-guided procedures (18).

In this study, we compared therapeutic efficacy between fluoroscopy- and US-guided RF ablation. Although the statistical significance was marginal ($p = 0.05$), it should be noted that local tumor progression rate of fluoroscopy group was lower than US group, with the tendency favorable to the fluoroscopy group (3.7% vs. 13.0%). We surmise that this result was caused by more accurate positioning of RF electrode in fluoroscopy group, especially when performing multiple overlapping ablations. During US-guided ablation, the hyperechoic area from microbubbles generated by previous ablation cycles often obscures the index tumor and position of electrode, which may preclude accurate repositioning of the electrode for subsequent ablation cycles, whereas the radio-opacity of index tumor

on fluoroscopy is not influenced by ablation cycles, therefore, the RF electrode can be moved more precisely. There was no significant difference in overall and recurrence-free survival rates between the two groups. Therefore, we believe that the therapeutic efficacy of fluoroscopy-guided RF ablation is at least equal to that of US-guided procedure despite unfavorable location of the tumors.

This study has several major limitations. First, it is a retrospective study, with all its inherent limitations. Especially, RF ablation for treatment of the index tumor was determined by attending physicians' discretion. Therefore, the indication of RF ablation could not be well-defined, and this may have caused bias on our results. Second, the diagnosis of HCC was based on imaging characteristics without pathological proof in many patients. This might have led to include only hypervascular tumors, which easily became visualized on fluoroscopy by chemoembolization. This may cause a positive bias on technical feasibility of the procedures. Third, we used doxorubicin-iodized oil emulsion rather than iodized oil alone for visualization of the index tumor and thus, the therapeutic efficacy of fluoroscopy group might have been improved compared with that of RF ablation alone. In addition, about half of patients had undergone previous treatments for HCCs. Although the treatments were for HCC other than the index tumor, the presence of previous tumor can have influences on tumor progression and/or patients' survival.

In conclusion, this study indicates that fluoroscopy-guided RF ablation following chemoembolization is a feasible and safe therapeutic option for small HCC. Most US-invisible HCCs including tumors with unfavorable location could

be successfully treated using this technique. Its therapeutic efficacy was comparable with that of US-guided RF ablation.

REFERENCES

1. Llovet JM, Bruix J. Novel advancements in the management of hepatocellular carcinoma in 2008. *Journal of hepatology*. 2008;48 Suppl 1:S20-37.
2. Shiina S. Image-guided percutaneous ablation therapies for hepatocellular carcinoma. *Journal of gastroenterology*. 2009;44 Suppl 19:122-31.
3. Rhim H, Lee MH, Kim YS, Choi D, Lee WJ, Lim HK. Planning sonography to assess the feasibility of percutaneous radiofrequency ablation of hepatocellular carcinomas. *AJR American journal of roentgenology*. 2008;190(5):1324-30.
4. Park BJ, Byun JH, Jin YH, et al. CT-guided radiofrequency ablation for hepatocellular carcinomas that were undetectable at US: therapeutic effectiveness and safety. *Journal of vascular and interventional radiology : JVIR*. 2009;20(4):490-9.
5. Masuzaki R, Shiina S, Tateishi R, et al. Utility of contrast-enhanced ultrasonography with Sonazoid in radiofrequency ablation for hepatocellular carcinoma. *Journal of gastroenterology and hepatology*. 2011;26(4):759-64.
6. Lee MW, Rhim H, Cha DI, et al. Percutaneous radiofrequency ablation of hepatocellular carcinoma: fusion imaging guidance for management of lesions with poor conspicuity at conventional sonography. *AJR American journal of roentgenology*. 2012;198(6):1438-44.
7. Adam A, Hatzidakis A, Hamady M, Sabharwal T, Gangi A. Percutaneous coil placement prior to radiofrequency ablation of poorly visible hepatic tumors. *European radiology*. 2004;14(9):1688-91.

8. Gandhi S, Iannitti DA, Mayo-Smith WW, Dupuy DE. Technical report: Lipiodol-guided computed tomography for radiofrequency ablation of hepatocellular carcinoma. *Clinical radiology*. 2006;61(10):888-91.
9. Lee MW, Kim YJ, Park SW, et al. Percutaneous radiofrequency ablation of liver dome hepatocellular carcinoma invisible on ultrasonography: a new targeting strategy. *The British journal of radiology*. 2008;81(965):e130-4.
10. Lee MW, Kim YJ, Park SW, et al. Percutaneous radiofrequency ablation of small hepatocellular carcinoma invisible on both ultrasonography and unenhanced CT: a preliminary study of combined treatment with transarterial chemoembolisation. *The British journal of radiology*. 2009;82(983):908-15.
11. Bruix J, Sherman M, Practice Guidelines Committee AAftSoLD. Management of hepatocellular carcinoma. *Hepatology*. 2005;42(5):1208-36.
12. Kang SG, Yoon CJ, Jeong SH, et al. Single-session combined therapy with chemoembolization and radiofrequency ablation in hepatocellular carcinoma less than or equal to 5 cm: a preliminary study. *Journal of vascular and interventional radiology : JVIR*. 2009;20(12):1570-7.
13. Goldberg SN, Grassi CJ, Cardella JF, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria. *Journal of vascular and interventional radiology : JVIR*. 2009;20(7 Suppl):S377-90.
14. Sacks D, McClenny TE, Cardella JF, Lewis CA. Society of Interventional Radiology clinical practice guidelines. *Journal of vascular and interventional radiology : JVIR*. 2003;14(9 Pt 2):S199-202.
15. Kim JE, Kim YS, Rhim H, et al. Outcomes of patients with hepatocellular

- carcinoma referred for percutaneous radiofrequency ablation at a tertiary center: analysis focused on the feasibility with the use of ultrasonography guidance. *European journal of radiology*. 2011;79(2):e80-4.
16. Shibata T, Shibata T, Maetani Y, et al. Transthoracic percutaneous radiofrequency ablation for liver tumors in the hepatic dome. *Journal of vascular and interventional radiology : JVIR*. 2004;15(11):1323-7.
 17. Mahnken AH, Buecker A, Spuentrup E, et al. MR-guided radiofrequency ablation of hepatic malignancies at 1.5 T: initial results. *Journal of magnetic resonance imaging : JMRI*. 2004;19(3):342-8.
 18. Lee MW, Kim YJ, Park SW, et al. Biplane fluoroscopy-guided radiofrequency ablation combined with chemoembolisation for hepatocellular carcinoma: initial experience. *The British journal of radiology*. 2011;84(1004):691-7.
 19. Takaki H, Yamakado K, Nakatsuka A, et al. Computed tomography fluoroscopy-guided radiofrequency ablation following intra-arterial iodized-oil injection for hepatocellular carcinomas invisible on ultrasonographic images. *International journal of clinical oncology / Japan Society of Clinical Oncology*. 2011.

초 록 (국문)

서론: 투시 유도 고주파절제술은 초음파상 보이지 않는 간세포암에 대해 주목 받고 있는 치료 방법이다. 본 연구는 이러한 치료 방법의 기술적 유용성을 평가하고 그 치료 효과를 초음파 유도 고주파절제술과 비교한다.

방법: 2006년 1월부터 2012년 1월까지 93명의 환자에서 104개의 간세포암(평균 1.8 cm, 표준편차 0.5 cm)에 대해 경피적 고주파절제술이 시행되었다. 이 중 42명의 환자에서 46개의 간세포암이 초음파상으로 보이지 않았고, 화학색전술에 이은 투시 유도 고주파절제술을 시행하였다 (A군). 나머지 51명의 환자에서 58개의 간세포암에 대해 초음파 유도 고주파절제술을 시행하였다 (B군). 이 두 군에서 기술적 성공률, 기술적 유효성, 합병증, 국소종양악화, 생존율 등을 후향적으로 비교하였다.

결과: 군에서 45개의 간세포암이 화학색전술 이후 투시상 확인되었고, 고주파절제술을 성공적으로 시행하였다 (97.8%). 기술적 유효성은 A군에서 97.8% 였고 B군에서는 96.6% 였다 ($p=0.65$). 양 군에서 주요 합병증은 발생하지 않았다. 1년, 3년, 5년의 기간 동안 국소종양악화는 B군보다 A군에서 다소 낮았다 (A군에서 각각 0%, 3.7%, 3.7%, B군에서 각각 13.0%, 13.0%, 13.0%, $p=0.05$). 1년, 3년, 5년 생존률은 A군에서 각각 100%, 58.3%, 51.2% 였고, B군에서 각각 82.4%, 54.9%, 46.1% 였다 ($p=0.26$). 1년, 3년, 5년 동안 재발 없는 생존률은 A군에서 각각 68.8%, 37.5%, 25.3% 였고, B군에서 각각

48.7%, 27.8%, 21.6% 였다 ($p=0.38$).

결론: 초음파상 보이지 않는 간세포암에 대한 화학색전술 후 투시 유도 고주파절제술은 시행하기 용이하며 안전한 치료 방법이며, 그 치료적 효과는 초음파 유도 고주파절제술과 비등하다.

주요어: 간세포암, 투시 유도, 고주파절제술

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