

# Safety Technique for Radiofrequency Ablation of Hepatocellular Carcinoma in High-Risk Locations

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## Keywords:

Hepatocellular carcinoma; Radiofrequency ablation; Complication

## 1. Abstract

**1.1 Aims:** Although radiofrequency ablation (RFA) is considered a safe and minimally invasive procedure for hepatocellular carcinoma (HCC), it is sometimes associated with serious complications. In this report, we describe methods that can be used to prevent these complications.

**1.2. Methods and Results:** HCC is the sixth most common malignancy and the fourth leading cause of cancer-related death worldwide. Compared to surgery, RFA is less invasive, however, this depends on the tumor stage. RFA is a curative treatment option, but occasionally RFA may cause serious adverse events depending on the HCC location.

So we describe here, how RFA can be used to avoid damage to the bile duct and gallbladder, and to accurately treat lesions around the heart. All cases were single tumor and the size were less than 3cm. Tumors that exist in these three difficult areas, complications could be avoided by devising treatment.

**1.3. Conclusion:** Caution should be exercised regarding serious adverse events that may occur with RFA due to the HCC location.

## 2. Introduction

Hepatocellular Carcinoma (HCC) is the sixth most common malignancy and the fourth leading cause of cancer-related death worldwide

[1]. Extensive research on systemic treatment has been conducted, and recently, novel drugs, including sorafenib, lenvatinib, regorafenib, and ramucirumab, have been proven effective in clinical trials [2-4]. Sorafenib, a multikinase inhibitor, is the first targeted agent that has been approved as first-line therapy for advanced HCC.<sup>5</sup> In Japan, more than 60% of HCC cases are diagnosed at an early stage (Barcelona Clinic Liver Cancer stage 0 or A), which can be treated with curative therapies, such as surgical resection, local ablation, and liver transplantation.<sup>6</sup> Radiofrequency ablation (RFA) is a safe and minimally invasive procedure in HCC. RFA was first used in Japan in 1999. Although RFA is considered a safe and minimally invasive procedure, several complications have been reported [7-17] Ding J et al. reported mortality and complication rates of 0.038 and 3.54%, respectively, across 20 centers in Japan between January 1999 and October 2010.<sup>15</sup> Major post-RFA complications, such as hepatic failure, intraperitoneal bleeding, hepatic abscess, bile duct injury, tumor seeding, and gastrointestinal perforation, have been reported [18-20]. The estimated mortality rate ranges between 0.1%-0.5%, while the major complication rate is 2.2%-3.1% [21]. Based on these data, we confirmed that RFA may be a safe and well-tolerated treatment for HCC. However, it may cause serious adverse events depending on the HCC location. Therefore, we described how RFA can be used to avoid damage to the bile duct and gallbladder, and to accurately treat lesions around the heart.

### 3. RFA Methods

#### 3.1. Lesion Near the Main Bile Duct

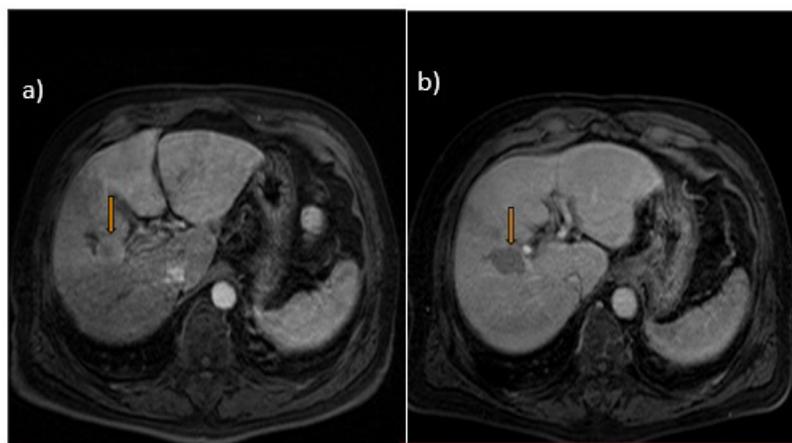
The Glisson's capsule extends into the liver as sheaths around the hepatic bile ducts, hepatic arteries, and portal veins. When RFA is used for HCC lesions that are adjacent to the Glisson's capsule, surrounding organs may be affected, and thereby increasing the risk of complications such as intrahepatic bile duct dilatation, hepatic arterioportal (AP) fistula, and hepatic infarction. Most of these complications are irreversible and may negatively affect liver function and prognosis.

Wakamatsu et al. reported that complications due to RFA, such as AP fistula, intrahepatic bile duct dilatation, and hepatic infarction developed in 10.0% of patients, 8.2%, and 1.2%, respectively [22]. RFA is contraindicated for the treatment of liver tumors located <1 cm from the main biliary duct and a bilioenteric anastomosis [23]. RFA of central liver tumors is a relative contraindication because of the risk of injury to the major bile ducts; [24-26] thermal damage may occur. This is because bile juice movement in the bile duct is very slow; therefore, intrahepatic bile ducts near the tumor are prone to thermal injury. The endoscopic nasobiliary drainage (ENBD) tube is used in clinical settings to avoid bile duct damage by cooling with

a chilled saline solution infusion; however, acute pancreatitis occurs sometimes, and it may be severe [27, 28]. In 2017, Xin et al. reported that transhepatic cholangial drainage with intraductal chilled saline perfusion (PTCD-ICSP) appears to be a safe and effective technique for the management of larger HCCs (>3 cm) [29].

(Figure 1(a, b)) shows HCC located near the main hepatic bile duct. The tumor was single and 2.8 cm in size, but this patient had a very high risk of thermal bile duct damage. Therefore, we placed an ENBD tube for bile duct cooling during RFA (Figure 1c). Since acute pancreatitis occurred after endoscopic retrograde cholangiopancreatography, we removed the tube. We then chose a method that could do the ablation adequately and not damage the bile ducts. We punctured the intrahepatic secondary bile duct branch with a 21G elastor needle, and the mantle was inserted into the common hepatic duct using a micro guide wire. When we performed the RFA, the outer jacket of the elastor needle was fixed and cooled by splashing chilled saline (Figure 1d).

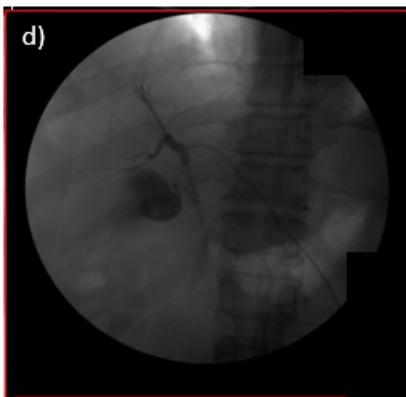
We described this RFA method in our previous report.<sup>30</sup> This method is safer, simpler, and associated with shorter hospital stays and lower medical costs than PTCD-ICSP and ENBD; therefore, it may be very beneficial to patients.



**Figure 1 (a, b):** In the arterial phase, the hepatocellular carcinoma was enhanced in the hilar area.



**Figure 1(c):** We inserted the endoscopic nasobiliary drainage tube for bile duct cooling using endoscopy.



**Figure 1(d):** We inserted the transhepatic cholangial drainage tube for bile duct cooling under ultrasonography guidance.

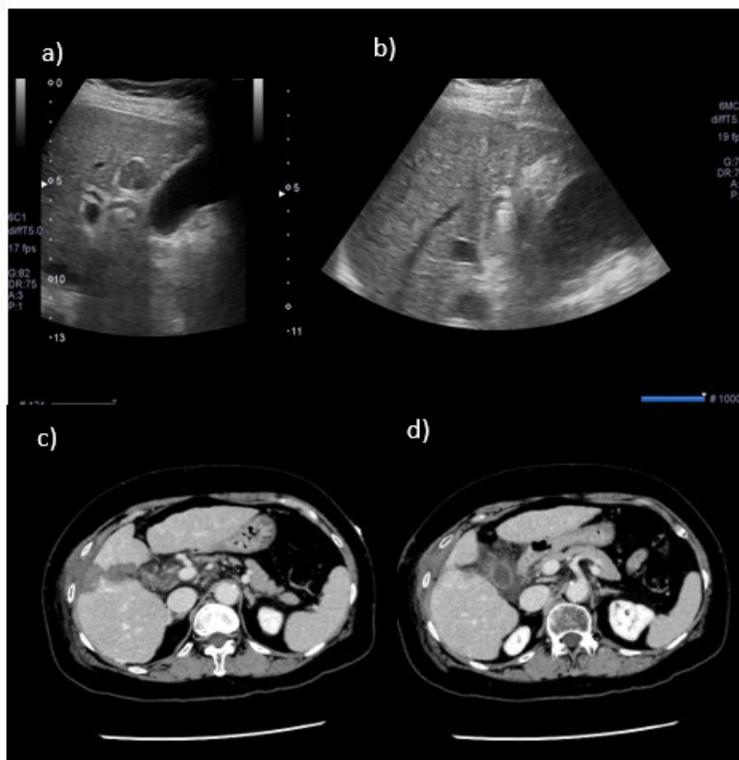
### 3.2. Lesion Near the Gall Bladder

RFA for HCC is performed at a distance less than 1 cm to the gallbladder due to the risk of hematoma formation in the gallbladder, intralesional hemorrhage, and gallbladder perforation. Several authors suggested that percutaneous treatment can be safely used to ablate tumors close to the gallbladder, using bile aspiration and injection of sterilized solution into the gallbladder fossa to space out the tumor from the gallbladder [31], or assisted by a laparoscopic approach [32]. (Figure 2) shows a HCC in contact with the gallbladder. The tumor was single and 2cm in size. The HCC was located at a site with a great risk of RFA-related complications.

Therefore, we performed percutaneous transhepatic gallbladder aspi-

ration with a 21G elastor needle to cool the gallbladder with a chilled saline solution infusion after aspiration bile juice. The outer jacket of the needle was fixed and flash-cooled with saline. The tumor was ablated while refluxing cold saline into the gallbladder.

After the ablation was completed, the fluid in the gallbladder was sucked as far as possible. The next day, the thickening of the gallbladder wall was observed on Computed Tomography (CT) (Figure 2 c, d); however, a successful ablation was performed, without infection, hemorrhage, and perforation. Three months later, the thickening of the gallbladder wall had disappeared on CT. There has been no recurrence for more than 3 years. Our method using the 21G elastor needle has the potential to be safer and simpler, with shorter hospital stays and lower medical costs.

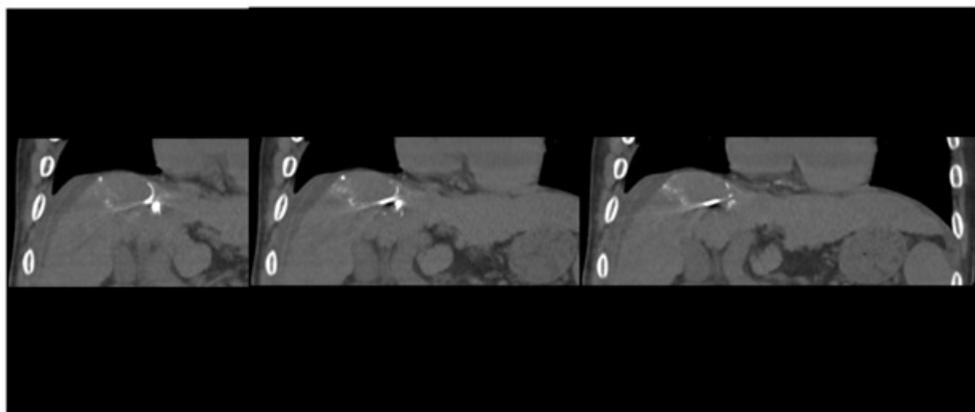


**Figure 2:** For the lesion near the gallbladder, we ablated the hepatocellular carcinoma under cooling conditions with a 21G elastor needle. The next day, gallbladder wall edema was observed, without any serious complications.

### 3.3. Lesions Near the Heart

When puncturing lesions near the heart, the deployment needle is considered safe because the needle is fixed during ablation. However, it is difficult to confirm the location of all the needle tips after deployment using ultrasonography. To resolve this problem, using the interventional radiology-computed tomography (IVR-CT) room is safe and contribute to treatment to obtain an appropriate ablated range. This is because after puncturing under ultrasound guidance, it can be fixed by deploying the RFA needle and confirming the dis-

tance to the heart by CT. Furthermore, we can determine whether it is hitting the target lesion and if it is determined that the ablation range near the heart is insufficient, we can advance the needle under combination with CT guide (Figure 3). For lesions larger than 2 cm located around the heart, we perform RFA in an IVR-CT room to detect the location of the needle tip after deployment before the start of ablation. This procedure has no associated complications, and a sufficient safety margin has been obtained in all patients who underwent this procedure.



**Figure 3:** Under computed tomography (CT) assistance, we punctured the hepatocellular carcinoma under ultrasonography guidance. The target tumor near the heart was punctured. A needle was deployed; therefore, the needle was fixed in the liver, and the ablation range and safety were confirmed by CT imaging.

### 4. Discussion

RFA is the standard local treatment for HCC worldwide in patients with <3 tumors that are <3 cm in diameter [33, 34]. In the last 20 years, novel treatment methods have been established in Japan, and the disease control rate is comparable to that surgical resection <2 cm in diameter. However, some tumor locations are considered high-risk; therefore, it is important to devise means of preventing complications.

### 5. Conclusion

Serious adverse events may occur with RFA due to the HCC location. We must be careful to avoid complications.

### References

1. Llovet JM, Zucman-Rossi J, Pikarsky E, Sangro B, Schwartz M, Sherman M et al. Hepatocellular carcinoma. *Nat Rev Dis Prim.* 2016; 2: 16019.
2. Kudo M, Finn RS, Qin S, Han KH, Ikeda K, Piscaglia F et al. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: A randomised phase 3 non-inferiority trial. *Lancet.* 2018; 391: 1163-73.
3. Bruix J, Qin S, Merle P, Granito A, Huang YH, Bodoky G et al. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): A randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet.* 2017; 389: 56-66.
4. Zhu AX, Kang YK, Yen CJ, Finn RS, Galle PR, Llovet JM et al. Ramucirumab after sorafenib in patients with advanced hepatocellular carcinoma and increased  $\alpha$ -fetoprotein concentrations (REACH-2): A randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol.* 2019; 20: 282-296.
5. Llovet JM, Ricci S, Mazzaferro V, Hilgard P, Gane E, Blanc JF et al. Sorafenib in Advanced Hepatocellular Carcinoma. *N Engl J Med.* 2008; 359: 378-390.
6. Kudo M. Surveillance, diagnosis, treatment, and outcome of liver cancer in Japan. *Liver Cancer.* 2015; 4: 39-50.
7. Livraghi T, Solbiati L, Meloni MF, Gazelle GS, Halpern EF, Goldberg SN et al. Treatment of focal liver tumors with percutaneous radio-frequency ablation: complications encountered in a multicenter study. *Radiology.* 2003; 226: 441-451.
8. de Baère T, Risse O, Kuoch V, Dromain C, Sengel C, Smayra T et al. Adverse events during radiofrequency treatment of 582 hepatic tumors. *AJR Am J Roentgenol.* 2003; 181: 695-700.
9. Rhim H, Yoon KH, Lee JM, Cho Y, Cho JS, Kim SH et al. Major complications after radio-frequency thermal ablation of hepatic tumors: spectrum of imaging findings. *Radiographics.* 2003; 23: 123-134.
10. Buscarini E, Buscarini L. Radiofrequency thermal ablation with expandable needle of focal liver malignancies: complication report. *Eur Radiol.* 2004; 14: 31-37.
11. Kasugai H, Osaki Y, Oka H, Kudo M, Seki T, Osaka Liver. Cancer Study Group Severe complications of radiofrequency ablation therapy

- for hepatocellular carcinoma: an analysis of 3,891 ablations in 2,614 patients. *Oncology*. 2007; 72: 72-75.
12. Chen TM, Huang PT, Lin LF, Tung JN. Major complications of ultrasound-guided percutaneous radiofrequency ablations for liver malignancies: single center experience. *J Gastroenterol Hepatol*. 2008; 23: e445-e450.
  13. Kong WT, Zhang WW, Qiu YD, Zhou T, Qiu JL, Zhang W et al. Major complications after radiofrequency ablation for liver tumors: analysis of 255 patients. *World J Gastroenterol*. 2009; 15: 2651-6.
  14. Shiina S, Tateishi R, Arano T, Uchino K, Enooku K, Nakagawa H et al. Radiofrequency ablation for hepatocellular carcinoma: 10-year outcome and prognostic factors. *Am J Gastroenterol*. 2012; 107: 569-577.
  15. Ding J, Jing X, Liu J, Wang Y, Wang F, Wang Y et al. Complications of thermal ablation of hepatic tumours: comparison of radiofrequency and microwave ablative techniques. *Clin Radiol*. 2013; 68: 608-615.
  16. Mulier S, Mulier P, Ni Y, Miao Y, Dupas B, Marchal G et al. Complications of radiofrequency coagulation of liver tumours. *Br J Surg*. 2002; 89: 1206-22.
  17. Bertot LC, Sato M, Tateishi R, Yoshida H, Koike K. Mortality and complication rates of percutaneous ablative techniques for the treatment of liver tumors: a systematic review. *Eur Radiol*. 2011; 21: 2584-96.
  18. Perkins JD. Seeding risk following percutaneous approach to hepatocellular carcinoma. *Liver Transpl* 2007; 13:1603.
  19. Chen TM, Huang PT, Lin LF, Tung JN. Major complications of ultrasound-guided percutaneous radiofrequency ablations for liver malignancies: single center experience. *J Gastroenterol Hepatol*. 2008; 23: e445-e450.
  20. Zavaglia C, Corso R, Rampoldi A, Vinci M, Belli LS, Vangeli M et al. Is percutaneous radiofrequency thermal ablation of hepatocellular carcinoma a safe procedure? *Eur J Gastroenterol Hepatol*. 2008; 20: 196-201.
  21. Complications of radiofrequency ablation in hepatocellular carcinoma. *Abdom Imaging*. 2005; 30: 409-418.
  22. Wakamatsu T, Ogasawara S, Chiba T, Yokoyama M, Inoue M, Kanogawa N et al. Impact of Radiofrequency Ablation-Induced Glisson's Capsule-Associated Complications in Patients with Hepatocellular Carcinoma. *PLoS One*. 2017; 12: e0170153.
  23. Crocetti L, de Baere T, Lencioni R. Quality improvement guidelines for radiofrequency ablation of liver tumours. *Cardiovasc Intervent Radiol*. 2010; 33: 11-17.
  24. Elias D, Sideris L, Pocard M, Dromain C, De Baere T. Intraductal cooling of the main bile ducts during radiofrequency ablation prevents biliary stenosis. *J Am Coll Surg*. 2004; 198: 717-721.
  25. Livraghi T, Solbiati L, Meloni MF, Gazelle GS, Halpern EF, Goldberg SN et al. Treatment of focal liver tumors with percutaneous radiofrequency ablation: complications encountered in a multicenter study. *Radiology*. 2003; 226: 441-451.
  26. Crocetti L, de Baere T, Lencioni R. Quality improvement guidelines for radiofrequency ablation of liver tumours. *Cardiovasc Intervent Radiol*. 2010; 33: 11-17.
  27. Ohnishi T, Yasuda I, Nishigaki Y, Hayashi H, Otsuji K, Mukai T et al. Intraductal chilled saline perfusion to prevent bile duct injury during percutaneous radiofrequency ablation for hepatocellular carcinoma. *J Gastroenterol Hepatol*. 2008; 23: e410-e415.
  28. Ogawa T, Kawamoto H, Kobayashi Y et al. Prevention of biliary complication in radiofrequency ablation for hepatocellular Carcinoma-Cooling effect by endoscopic nasobiliary drainage tube. *Eur J Radiol*. 2010; 73: 385-390.
  29. Li X, Yu J, Liang P, Zhiyu H, Fangyi L, Xin L et al. Ultrasound-guided percutaneous microwave ablation assisted by three-dimensional visualization operative treatment planning system and percutaneous transhepatic cholangial drainage with intraductal chilled saline perfusion for larger hepatic hilum hepatocellular (D ≥ 3 cm): preliminary results. *Oncotarget*. 2017; 8: 79742-9.
  30. Takashima H, Moriguchi M, Hayashi N et al. A simple method to avoid bile duct injury during percutaneous radiofrequency ablation therapy for hepatocellular carcinoma. *Case Rep Oncol*. 2020; 13: 1337-42.
  31. Levit E, Bruners P, Gunther RW, Mahnken AH. Bile aspiration and hydrodissection to prevent complications in hepatic RFA close to the gallbladder. *Acta Radiol*. 2012; 53: 1045-8.
  32. Jiang K, Su M, Zhao X, Chen Y, Zhang W et al. "One-off" complete radiofrequency ablation of hepatocellular carcinoma adjacent to the gallbladder by a novel laparoscopic technique without gallbladder isolation. 2014; 68: 547-54.
  33. JSH Consensus-Based Clinical Practice Guidelines for the Management of Hepatocellular Carcinoma: 2014 Update by the Liver Cancer Study Group of Japan on behalf of the Liver Cancer Study Group of Japan. *Liver Cancer*. 2014; 3: 458-68.
  34. Omata M, Cheng AL, Kokudo N et al. Asia-Pacific clinical practice guidelines on the management of hepatocellular carcinoma: a 2017 update. *Hepatol Int*. 2017; 11: 317-370.